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INFORMATION FOR AUTHORS

About the Journal

The Thai Journal of Surgery is the official publication of The Royal College of Surgeons of Thailand issued quarterly.

The Thai Journal of Surgery invites concise original articles in clinical and experimental surgery, surgical education, surgical history, surgical techniques and devices, as well as review articles in surgery and related fields. Papers in basic science and translational medicine related to surgery are also welcome. The Thai Journal of Surgery is dedicated to serving the needs of the Members of The Royal College of Surgeons of Thailand, specifically the younger researchers and surgeons in training who wish to have an outlet for their research endeavors. The Royal College strives to encourage and help develop Thai Surgeons to become competent researchers in all their chosen fields. With an international outlook, the Thai Journal of Surgery welcomes submissions from outside of Thailand as well.

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Manuscripts

Manuscripts should be typed on size A4 page in Microsoft Word using pt. 11 Times New Roman font, with double spacing and at least 2.5 cm margins. Separate pages: title page, text, acknowledgments, references, individual tables, abstract in Thai, and legends (as the format in this journal). Number pages consecutively, beginning with the title page. Type the page number in the upper right-hand corner of each page. Metric measurements should be used. Generic names for drugs should be used and if trade name is mentioned, it should be put in parenthesis.

The title page of the manuscript should be typed on a separate sheet and contain the following information:

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References must be listed on a separate sheet in numeric order as referred to in the article, not alphabetically. Only references mentioned in the text should be listed and should be selective with not more than 30 references except under unusual circumstances. Number references consecutively in the order in which they are first mentioned in the text. Identify references in text, tables, and legends by Arabic numerals (in superscript). The references must be verified by the author(s) against the original documents. Example forms of references are given below.

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1. Standard Journal Article:

List all authors when four or less; when five or more, list only first three and add et al.

Soter NA, Wasserman SI, Austen KF. Cold urticaria: release into the circulation of histamine and eosinophil chemotatic factor of anaphylaxis during cold challenge. N Engl J Med 1976; 294:687-90.

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Books and Other Monographs

3. Personal Author(s):

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6. Chapter in Book:

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7. Agency Publication:

National Center for Health Statistics. Acute conditions: incidence and associated disability, United States, July1968-June1969. Rockville. Md.: National Center for Health statistics, 1972. Vital and health statistics. Series 10: Data from the National health Survey, No. 69: (DHEW publication no. (HSM) 72-1036).

Other Articles

8. Newspaper Article:

Shaffer RA. Advances in chemistry are starting to unlock mysteries of the brain: discoveries could help cure alcoholism and insomnia, explain mental illness. How the messengers work. Wall street Journal 1977 Aug 12(col. 1), 10(col. 1).

9. Magazine Article:

Roueche B. Annals of medicine: the Santa Claus culture. The New Yorker 1971 Sep 4:66-81.

Abbreviations

Use only standard abbreviations of commonly used approved abbreviations. Avoid abbreviations in the title. The full term for which an abbreviation stands should precede its first use in the text unless it is a standard unit of measurement.

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Editorial

Panuwat Lertsithichai, MD
Editor-in-Chief of the Thai Journal of Surgery
On Behalf of the Editorial Team

We end the 40th anniversary volume of the Thai Journal of Surgery with three special articles. The first is part of a historical overview of research in vascular surgery in Thailand within the past 40 years from the vantagepoint of Professor Pramook Mutirangura, the current President of The Royal College of Surgeons of Thailand who is also a renowned vascular surgeon. The second is a brief tribute to the friendship, or rather the fruitful collaboration, between the field of cardiothoracic surgery in Thailand and the Thai Journal of Surgery. The last special article is a rather long review of breast cancer surgery and research in Thailand seen through the lens of the Thai Journal of Surgery, albeit a very wide-angle lens. What these three articles have in common is the sense of celebration in the innovative and wide-ranging way surgical research was and is being done in Thailand. Of course, these are well exemplified in the pages of the Thai Journal of Surgery.

In addition, we have 2 case reports and 3 original articles. There are three cases of hepatic cysts managed by laparoscopic unroofing, from Sawanpracharak Hospital, and a case of tuberculous infection of the adrenal gland from Phayao University Hospital. The presentation of these interesting cases is an indication of the excellent clinical work our surgical colleagues are doing all over the country. We have Professor Surasak Sangkhathat's team at Prince of Songkhla University also hard at work to bring us a Python-based statistical software designed for surgical trainees, built almost from scratch. The use of powerful software for data management is certainly the future of surgical care. The cardiothoracic surgical team from Maharat Nakorn Ratchasima Hospital is again building on their continuing work with EuroScore II in patients with the difficult and often challenging infective endocarditis. A young general surgeon from Trang Hospital is showing us excellent results with laparoscopic surgery for colorectal cancer despite many limitations. We encourage all our colleagues to join the endeavor towards surgical excellence and reporting their efforts in the Thai Journal of Surgery.

Last, but not least, we have the second part of abstracts of presentations made at the 46th Annual Scientific Congress of The Royal College of Surgeons of Thailand. These abstracts are often a first glimpse of Thai surgeons' scientific interests and activities. They are important records of many events which might otherwise be lost to history. The next 10 years of Thai surgery will be no less interesting than the previous 40 years – and we, the Thai Journal of Surgery, will be present to record the most important of these activities.

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Special Article

Research Development of Vascular Surgery in Thailand

Pramook Mutirangura, MD, FRCST, FRCS (Edinburgh)

President of The Royal College of Surgeons of Thailand
Past President of Thai Vascular Association

Abstract Vascular surgery in Thailand has been developing the research in 5 clinical aspects: peripheral arterial occlusive diseases (PAOD), aneurysm, venous thromboembolism, varicose vein and vascular access for hemodialysis to improve surgical care of vascular diseases toward international standard. The present article summarizes the development of research on PAOD in the past 40 years.

Vascular surgery in Thailand in the past 40 years has been developing the research in 5 clinical aspects, peripheral arterial occlusive diseases (PAOD), aneurysm, venous thromboembolism, varicose vein and vascular access for hemodialysis to improve surgical care of vascular diseases toward international standard. The present article reviews the development of research on PAOD. Epidemiologic study of atherosclerosis obliterans in lower extremities in Thai patients was the original clinical research of PAOD in Thailand. Diabetes mellitus and cigarette smoking were announced as the major risk factors in this clinical problem, causing major limb loss and high mortality in our population. The most effective treatment during that time was arterial bypass surgery. Major limb amputation with poor quality of life at postoperative period induced a higher mortality rate than revascularization procedure. The research has encouraged surgeons to attempt surgical revascularization for limb salvage rather than major amputation.[1]

Regarding diabetic mellitus being the major risk factor of PAOD, the comparative study in clinical aspects of PAOD in diabetic patients and non-diabetic patients were carried out. The arterial occlusions have been involved more distally and more multiple levels in diabetic patients. Limb infection were also found more frequently in diabetic patients causing major limb loss. This research provided the information for the strategy of arterial bypass surgery more extensively in the distal

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area of arterial occlusion particularly in diabetic patients. The composite vascular conduit has been created for the numerous extensive and innovative surgical procedures to achieve limb salvage. However, the clearance of foot infection was the priority to surgical revascularization in diabetic patients.[2]

Arterial embolism was the major cause of acute limb ischemia requiring emergency revascularization with substantial varieties of treatment outcome. The most important prognostic factor was the duration between the onset of disease and the timing of revascularization. The research clarified that the surgical treatment within 24 hours achieved more than 90% successful limb salvage whereas the revascularization procedure after 24 hours had only 40% success rate requiring more adjunct procedures for the better outcome. This research has created a strong policy to educate the surgical trainees and general practitioners for the early diagnosis of this disease from clinical criteria.[3]

The common causes of acute limb ischemia were acute arterial embolism and acute arterial thrombosis carrying the different types of revascularization procedure. Acute arterial embolism could be simply treated by surgical embolectomy whereas acute arterial thrombosis required the more complicated procedures for limb salvage such as arterial endarterectomy, arterial bypass surgery or endovascular therapy which were not available through the whole country. For general surgeons working in countryside without the facilities of angiography, surgical equipment for complex vascular procedure and endovascular devices, the differentiation of these diseases by clinical manifestations was essential for the decision making of treatment in their hospitals with limitation of facilities or referral to the medical center. The research of clinical differentiations of these diseases was conducted for this purpose and the results were in the followings. The progression of severity of acute limb ischemia due to arterial embolism was more rapidly worse than arterial thrombosis. History of intermittent claudication was found more commonly in arterial thrombosis. Normal peripheral ankle pulses in contralateral limbs were more detected in arterial embolism. The clinical risk factors such as atrial fibrillation was more associated in arterial embolism whereas diabetes mellitus and smoking were more commonly found in arterial thrombosis. This research provided clinical information useful for general surgeons in taking care of patients with acute limb ischemia.[4]

The clinical trial of stem cell therapy was originally conducted to avoid major amputation in patients with chronic limb threatened ischemia (CLTI) and poor distal arteries prohibiting revascularization procedure for limb salvage. With the cooperation of Ben-Gurion University in Israel, stem cells (angiogenic cell precursors) being cultivated and proliferated from peripheral blood were subsequently injected into calf muscles of patients with critically ischemic limbs and ischemic ulcer. The success rate of healing of ischemic ulcers was 80%. This was the first clinical trial of stem cell therapy for CLTI in Thailand.[5] Subsequently, the new generation of stem cells has been developed and cultivated in the same institute to clarify the possibility of their efficiency in vitro.[6] Then, a clinical pilot study of the effectiveness of this generation of stem cells has been conducted in CLTI patients with 87% successful outcome of limb salvage.[7]

In patients with foot ulcer particularly in diabetic patients, the possibility of complete healing could be determined by transcutaneous oxygen pressure measurement. This prediction was extremely important in clinical practice whether the revascularization was required. This research was originally conducted to determine the level of skin oxygen pressure required for successful healing of foot ulcer. The results of this study could clarify the clinical application of this laboratory test for the effective evaluation of this common problem in general practice.[8] The innovation of original treatment modality for the reperfusion injury of severely acute limb ischemia of bilateral lower extremities was to divert venous blood from leg veins through hemodialysis machine and subsequently to reinfuse into systemic circulation through neck vein during revascularization procedure. The venous blood containing high potassium and anaerobic metabolic acids were equilibrate in the hemodialysis process instead of entering into systemic circulation. This innovative model could save life and limb of patients suffering from the reperfusion injury in acute limb ischemia, a high mortality and morbidity condition.[9]

Poor distal artery run off prohibits successful revascularization procedures for chronic limb threatened ischemia (CLTI) either arterial bypass surgery or endovascular therapy. Major limb amputation is inevitable in this situation. A case series with innovative surgical procedure to revascularize ischemic foot through the deep vein at the ankle with the disruption of distal vein valve for limb salvage in CLTI with non-reconstructable distal arteries was announced in the publication.[10]

The surgical technique has been worldwide accepted for the achievement of limb salvage in the desperate situation and presented in the international vascular meeting for more than 10 years. Furthermore, endovascular procedure has currently created by using the same principle of this surgical technique.[11]

After developing the composite graft to be vascular conduit in arterial bypass surgery, multiple extensive surgical procedures have been created for successful revascularization in the highly complicated PAOD. A case of the most extensive arterial bypass from ascending thoracic aorta to bilateral popliteal arteries for the advanced arterial occlusive disease from aorto-iliac, ilio-femoral, and femoro-popliteal arteries and failure of multiple attempts of axillo-bifemoral bypasses has been reported. The long-term patency of this procedure was 9 years without reintervention procedure.[12]

Two epidemiologic studies of Buerger's disease were carried out in Thai patients. This disease was found mostly in young men with heavy smokers causing inflammatory occlusive disease of upper and lower extremity arteries. There was a seasonal variation of this disease in the Northern part of Thailand.[13] The highest prevalence of this disease was in winter followed by rainy and summer season. However, the incidence and recurrence of this disease were decreased in the Northern part of Thailand. This information may be due to the successful campaign of cigarette cessation in the community.[14]

A case series of necrotizing arteritis from Pythium insidiosum (vascular pythiosis) were reported.[15,16] This disease was found in Thalassemic patients working in the swamps with accidental minor injuries of their feet. This fungus mainly found in standing water and occasionally soil in the tropical countries could penetrate through small wounds and cause necrotizing inflammation in the surrounding arteries with rapid progression towards proximal arteries of lower extremities. The diagnostic modalities of this disease were identification of microorganism, immunological studies, computed tomographic angiography (CTA). Adequate surgical removal of microorganisms was only treatment option. Major limb amputation was most commonly carried out among these patients. The residual microorganisms would definitely cause recurrent disease and mortality. Therefore, when the disease has been involved the arteries above the groins, the mortality of these patients was 100%. A challenging case of supra-inguinal vascular pythiosis successfully treated by aggressive surgical eradication has been reported.[17] A patient with infected aneurysm of external iliac artery and thrombosis of the whole lower extremity arteries was treated by above knee amputation and extensive surgical removals of all iliac arteries with surrounding tissues. This patient has survived after 3-year follow up with good condition. Furthermore, the factors influencing the outcomes of treatment of this disease were identified through a retrospective case record review of these patients.[18] Early detection of this disease combined with multidisciplinary approach to treatment including aggressive surgical removal, antifungal agents, and immunotherapy offered the best outcome of management.

Arterial embolism is the well known as the cause of acute limb ischemia whereas chronic arterial embolism has never been recognized in the arterial occlusive disease of lower extremities. The epidemiologic study of chronic arterial embolism was carried out to demonstrate that this disease could be one of the causes of chronic limb threated ischemia carrying different types of treatment from atherosclerosis obliterans (peripheral atherosclerotic occlusive disease) and worst prognosis requiring major limb amputation in late stage of disease with fibrotic arteries.[19] The information of this study has encouraged the awareness of this disease in order to provide the treatment at early stage to improve limb salvage rate in surgical practice.

Arterial embolism could originally be treated by surgical embolectomy with balloon Fogarty catheter in immediately threatened acute limb ischemia. Later, chemical thrombolytic therapy was introduced to dissolve thrombus in the artery as another therapeutic option of this disease. With the delayed effect of successful treatment, the latter treatment modality has been applied in the lesser degree of acute limb ischemia. Subsequently, the clinical study of the effectiveness of catheter-directed thrombolytic therapy was carried out for the treatment of marginally threatened acute limb ischemia in Thailand.[20] Despite the successful outcomes, the awareness of this treatment modality was major bleeding requiring the intensive monitoring of coagulation study. Moreover, when arterial embolism occurred more than 24 hours, the thrombus induced an inflammatory reaction and adhesiveness at inner layer of arterial wall. At this stage, balloon Fogarty catheter could not completely remove thrombus from arterial lumen. The clinical study of the effectiveness of intraoperative thrombolytic therapy in

conjunction with surgical embolectomy of immediately threatened limb ischemia of lower extremities was carried out in Thailand.[21] The technique could improve the successful thrombus removal in the delayed treatment of acute arterial embolism.

The limited awareness of carotid artery stenosis, one of the common causes of ischemic stroke in general practice resulted in minimal prevalence of surgical correction for this disease in Thailand. With the improvement of duplex ultrasonography to demonstrate the pathology of carotid artery, the number of carotid endarterectomies has been substantially increased among several vascular surgery training centers. A case series of 100 patients undergoing carotid endarterectomy for symptomatic extracranial carotid artery stenosis with 10-year follow up has been reported from a university hospital with successful outcomes.[22]

With the improvement of vascular service in Thailand toward international standard, the invitations to participate in global clinical trials were sent to Thai Vascular Association and distributed to all vascular surgery training centers in Thailand with achievement of the awards of the clinical trials.[23-25]

Conclusion

In conclusion, this summary of research development of peripheral arterial occlusive disease should provide the information as a history and basic knowledge of this clinical aspect in Thai population for the future research project to improve the management of this major problem of vascular surgery in Thailand.

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Special Article

Thoracic Surgery and The Thai Journal of Surgery: 40-year-old Friendship

Punnarerk Thongcharoen, MD, FRCST

Representative of Thoracic Surgeons in RCST Executive Committee 2021-2023
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The thoracic surgery started its journey in Thailand more than 70 years ago. Initially, most of the cases are pulmonary, pleural, mediastinal, and esophageal diseases. With supports from international organizations such as the World Health Organization (WHO), several thoracic surgeons and anesthetists came from the United States of America (US) to team up with Thai thoracic surgeons and anesthetists started the thoracic surgical serviced in several hospital such as Siriraj Hospital, Chulalongkorn Hospital and Nonthaburi Chest Hospital (currently, Central Chest Institute of Thailand, CCIT)[1,2]. Before 2500 B.E. the cardiac operation was firstly performed.

After year 2500 B.E., more Thai doctors and surgeons went for further training in thoracic surgery abroad, mostly US and the United Kingdom (UK). They came back and introduced modern thoracic surgery to Thailand. The cardiac operations using cardiopulmonary bypass (using the heart-lung machine) have been performed since 2503 B.E. starting with simple cardiac operations, closure of atrial septal defect for example. At that time, Thailand was one of the leaders in thoracic surgery in Asia.

With more thoracic surgeons trained from western countries coming back, the thoracic surgery expanded from the medical service activity to other areas especially education/ training and research. To mark the launch of the Thai Journal of Surgery (TJS), the thoracic surgeons (Sakiyalak P, Gherunpongs C, Sriyoschart S, Prachuabmoh K) published their experience in this field with a case series report of coronary artery-cardiac chamber fistula[3]. After this landmark published article, there were articles from thoracic surgeons around the country published in this journal almost every volume for many years. However, most of the published works were case series reports.

Along with the progression of the research and scientific works, there was a huge step of the thoracic surgery development when the thoracic surgery training curriculum was established. The first thoracic surgical training began in the year 2526 B.E. at Faculty of Medicine Siriraj Hospital[4].

With more thoracic surgeons went for further training abroad, the thoracic surgery in Thailand has been improving in every area mainly adult cardiac, congenital cardiac, aortic, and thoracic fields. Soon after minimally invasive surgery had been introduced in Thailand around thirty years ago, minimally invasive coronary and valve surgery, endovascular repair and video-assisted thoracic procedures were started. Once again, we are now one of the leaders in minimally invasive surgery in Asia. So, the submitted articles have been accepted and published in

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several key international journals. While, recently, there has been increasing number of general surgery articles submitted and published. These explain why there has been no thoracic article in the Thai Journal of Surgery for more than twenty years.

Interestingly, not only Thai doctors submitted their works to TJS, but there were also many foreign surgeons did so. And among these surgeons, there were some of the world-famous thoracic surgeons as well. Donald B Effler[5] who was one of the pioneers in open heart surgery presented his experience in mechanical valve complications in 2540 B.E. Naruke T[6] who was the world authority in lung cancer, raised the attention for early detection of lung cancer in the same year.

Thoracic surgery in Thailand has grown up alongside with the Thai Journal of Surgery for 40 years. With widespread of innovative surgical techniques, novel surgical managements, and knowledge sharing strategies, we, the thoracic surgeons, are looking forwards to seeing the continuing and sustainable development of TJS, for the benefits of thoracic surgery as well as other surgical specialty.

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Special Article

Breast Cancer and Breast Cancer Surgery in Thailand: A View from The Thai Journal of Surgery

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Abstract In the present article we review the recent history of breast surgery in Thailand, as exemplified by the articles published in the Thai Journal of Surgery within the past 40 years. We will focus exclusively on breast cancer, as most of the articles as well as abstracts published in the Journal were concerned with this topic. We will, more or less, be looking at these articles and papers chronologically rather than thematically, to show how ideas and practices change with time relative to one another. Contributions from outside of Thailand are included to help set the world stage at any particular period. Short summaries of certain key developments in the same period from the author's perspective are provided as an introduction to some articles. The overall presentation is unabashedly that of "whiggish" historiography, viewing everything from the high point of current knowledge. This approach is perhaps easier for clinicians to understand and tells a valid story of how we arrive at the present state of affairs, regardless of what the future may bring. We divide the review into sections named after the decade of publication and some dominant themes within that decade. At the end, we briefly list contributions on breast cancer in published abstracts of presentations given at the Annual Congress of the Royal College of Surgeons of Thailand within the past 40 years.

Keywords: Breast cancer, Breast cancer surgery, Thailand

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1970 - 1980: Setting the stage

First, let us quickly review the state of breast cancer surgery at the end of the 1970's. Breast cancer treatment for most of the 1970's was still dominated by radical surgery. After the establishment of basic surgical principles of breast cancer surgery in the early part of the 20th century (the "Halstedian paradigm"), surgical treatment remained, for the most part, essentially unchanged for 50 years. Although radiotherapy and various drugs for breast cancer were commonly used for more advanced stages, their use was limited in the earlier stages, as the evidence supporting their effectiveness was unclear, and their complications were considerable. Other surgical alternatives to mastectomy were not widely accepted, in particular breast conserving surgery was viewed as an inferior modality or valid only for very early stage breast cancers. However, breast reconstruction after mastectomy was becoming more popular and increasingly used. Axillary surgery as a separate consideration in breast cancer surgery for practical purposes did not exist. Less radical surgery, in the form of various modified radical mastectomies, won out at the end of the decade.

The very first issue of the Thai Journal of Surgery ("TJS") in 1980 contained an article by Professor Sompong Raksasook, from Ramathibodi Hospital Medical School, dealing with the then still controversial point of the relationship between fibrocystic condition (FCC) and breast cancer.[1] In a series of 256 patients diagnosed with FCC, of whom 103 were followed from 1 to 8 years, no breast cancer was detected. The study concluded that the evidence for an association between FCC and breast cancer was unclear. In the same volume, an observational study comparing Halsted radical mastectomy with or without radiation, simple mastectomy with or without radiation, and wide excision alone, in a randomly chosen group of 100 patients, the majority of whom had early stage cancers, was also reported by Professor Sompong.[2] This article clearly shows the ambivalence at that time towards the trend to less radical surgery, at least in Thailand. While not condemning simple mastectomy or wide excision, the author clearly favored radical mastectomy. It is notable also for an emphasis on arm lymphedema, of any degree, reporting an incidence of 35% for radical mastectomy. Irradiation was an important risk factor for lymphedema. As was common at the time, chemotherapy use was limited, and the analysis of cancer survival did not adjust for confounding factors (it was obvious that radical mastectomy was used for earlier stage cancers, and simple mastectomy mainly for more advanced cancers). With an average follow-up time of 39 to 46 months, the reported "within 5-year survival" was 69% and 82% for simple and radical mastectomy, respectively, an excellent result for the time.

1980 – 1990: Poor outcomes and systemic therapy

In volume 4 of the TJS in 1983, Professor Michael Baum, at that time of King's College Hospital Medical School, London, UK, in a review article attacked the Halstedian paradigm of breast cancer and presented the view favoring early breast cancer dissemination, by then the new predominant paradigm.[3] In operable breast cancer, prognosis was determined more by micrometastatic disease at the time of presentation than by local disease; micrometastasis can occur quite early on; axillary lymph node status reflected preexisting micrometastasis; and removing axillary nodes did not improve survival. Professor Baum discussed limited axillary dissection and suggestions for lymph node sampling, but then emphasized the need to await long-term results of large clinical trials comparing mastectomy to breast conserving surgery, still on going at that time, before embarking on conservative surgery in routine clinical practice.

An interesting review paper on the epidemiology and risk factors of breast cancer was published also in 1983, from the Edinburgh Breast Screening Clinic at the University of Edinburgh, UK.[4] It is remarkable that new knowledge on risk factors gained since then is more of a refinement rather than anything groundbreaking. There was a discussion of possible environmental and endocrine factors in explaining age-related breast cancer incidence differences between Western and Eastern women. The then recently launched (1979) mammographic screening trial in the UK was described, with the hope of bringing down the 30% prevalence of stage III breast cancers in the UK at that time. A laboratory study funded by the Tenovus Institute for Cancer Research, Cardiff, UK, investigated the uses of salivary steroid hormone assays,[5] which in retrospect proved to be less useful than expected in breast cancer. Another laboratory study from Siriraj Hospital described dextran-coated charcoal versus polyethylene glycol methods of detecting estrogen receptor (ER) and progesterone receptor (PgR) in 381 breast cancer specimens, with clinical correlates.[6] We now, of course, routinely use immunohistochemical methods. A multicenter study of hormonal receptor expression as-

says as well as tamoxifen binding to cytosolic ER in 120 breast specimens, led by Chulalongkorn Hospital and the Thai National Cancer Institute, was also reported.[7] The latter 2 studies revealed interesting patterns of ER and PgR expressions in Thai breast cancer patients. These papers on epidemiology, risk factors, diagnosis and prognosis of breast cancer were of exceptional quality.

Possible mechanisms of action of tamoxifen on breast cancer were discussed in an article from the Tenovus Institute.[8] Tamoxifen had been under investigation, partly funded by the Tenovus Institute itself, and used for treating breast cancer for some time although its mechanism of action was not completely clear. The term Selective Estrogen Receptor Modulator (SERM) did not yet exist. Tamoxifen was on the market but expensive at the time (branded as Nolvadex, ICI, later AstraZeneca), and was not yet widely used in Thailand. Immediately following the tamoxifen article was an article on the prognosis of breast cancer by the Tenovus group in collaboration with the group from City Hospital, Nottingham, with special reference to the presence of ER and PgR in the tumor as prognosticators.[9] The latter group, of course, later developed the well-known Nottingham Prognostic Index for breast cancer.

There were a few papers on the hormonal treatment of breast cancer published in 1983. One excellent review article on tamoxifen, with an early form of meta-analysis, was from the Pharmaceuticals Division in the Medical Department of the Imperial Chemical Industries (ICI) UK,[10] prior to the Pharmaceutical Division's demerger to form the Zeneca Group in 1993. ICI, of course, developed tamoxifen. From its origins in the 1950's as a possible morning-after contraceptive pill to a treatment for infertility, then to an antitumoral agent in the 1970's, tamoxifen is one of the most important therapeutic agents developed for breast cancer in the past 50 years. In the early 1980's the use of tamoxifen in the adjuvant setting was just beginning, in contrast to its use in the metastatic setting, which was established. There were 6 recently conducted randomized controlled trials (RCT) collected in the review, with average follow-up duration ranging from 15 to 48 months. Stages I to III breast cancer patients either received tamoxifen, 20 to 40 mg per day in divided doses for 1 to 2 years, or none, but conventional radiotherapy and chemotherapy were given to some patients in both groups. The pooled analysis showed that there was an average reduction of 23.5% in breast cancer "failures" (mainly recurrences) in the tamoxifen group, which was a highly significant result.

Surgical manipulation of hormonal influences on breast cancer has always been a treatment of last resort, even today, sometimes used for metastatic or aggressive and hormonal responsive cancers in premenopausal women. These operations were of considerable morbidity, and in the past included oophorectomy, adrenalectomy and hypophysectomy. The hope of reducing the need for these operations came with the discovery that Gonadotropin-Releasing Hormone (GnRH) agonists at high dose could produce a "medical oophorectomy" (medical castration) as described in an article by researchers from the Tenovus Institute and the ICI.[11] ICI, of course, was developing a version of a GnRH agonist at the time. The article reported promising animal studies and a few cases of successful use in breast cancer patients. These drugs are now used in routine practice but are still expensive. It is noteworthy that drug companies and research institutes were collaborating very closely at that time, publishing articles together widely in all types of medical publications.

An epidemiological and demographical study of breast cancer in Thailand from the Thai National Cancer Institute (NCI) was published in 1984.[12] There were data on 331 patients seen during 1975 – 80, sent from 123 hospitals all over Thailand. Although the list of participating hospitals did not include those of some major medical schools, Siriraj Hospital was included. The very small number of breast cancer patients in the study raises the issue of completeness of data collection. Nonetheless, breast cancer was consistently the 2nd most common malignancy in Thai women at that time, with a peak frequency between 40 to 50 years of age, and 40% were seen in farmers and laborers. Metastatic disease was seen in 36% of patients. The annual incidence reported for the years between 1970 – 1980 showed an increasing trend, ranging from 1.5 to 2.6 per 100,000, but this was more than 10 time lower than those of Western countries at the time.[4]

A review of breast cancer cases and treatment at Chulalongkorn Hospital is an interesting snapshot of patient characteristics and clinical practice in Thailand in the late 1970's.[13] In a series of 322 female patients, treated during a 5 year period (1975 – 80), the peak frequency was between ages 41 to 50 years, and most were found to have advanced stage cancer (stages III and IV, 57%). Half of patients never returned for their follow-up after surgery, with only 25% remaining in follow-up after

3 years. Modified radical mastectomy was the main treatment modality for stages I and II breast cancers, while simple mastectomy was used for stage III cancers with clinically negative axillary nodes. (Note that staging systems used then were somewhat different from those of the present time, but most followed the AJCC TNM system). Radiation was mainly used for patients with recurrent disease, or those refusing surgery. Relatively few patients received radiation therapy in combination with surgery, and most of these patients had extensive regional nodal involvement. Similarly, chemotherapy and hormonal therapy were reserved for advanced cancers, mainly metastatic and recurrent disease. There were no data on cancer survival. Most of the discussion section was focused on socioeconomic limitations in Thailand at the time, explaining why radiotherapy and chemotherapy were used only sparingly and why radical surgery was still the best option.

A small clinical trial from Ramathibodi Hospital in 1980 led by Professor Sompong attempted to clarify the benefit of adding chemotherapy to locoregional treatment of early stage breast cancer.[14] While clinical trials conducted in other countries showing some benefit of adjuvant chemotherapy for early stage breast cancer existed at this time, in Thailand the use of adjuvant chemotherapy was limited, as mentioned before. Professor Sompong wanted to show similar benefits in Thai patients to encourage the use of adjuvant chemotherapy. But with a sample of 46 pseudo-randomized patients and a drop out of 12 leaving 34 in the analysis, no statistically significant differences between chemotherapy and no chemotherapy could be demonstrated after an average follow-up of only 22 months. Also, chemotherapeutic agents used in the study are no longer commonly in use for breast cancer today (thiotepa and nandrolone decanoate, the latter an androgenic steroid) and only 2 to 3 courses were given, each course lasting about 2 months.

Chemotherapy for operable breast cancer, often called adjuvant chemotherapy because it was seen as an "add-on" to surgical treatment when it was first introduced, was the subject of a 1983 review article by investigators from Manchester and Birmingham, UK.[15] The article is a masterpiece of clear and concise writing, worth reading as an introduction to the basic ideas of chemotherapy even today. After discussing the evidence behind the early dissemination theory of breast cancer, a brief overview of the rationale of adjuvant chemotherapy, as well as timing and duration of therapy, and evidence supporting early deposition theory of micrometastasis was given. Summaries of mostly small clinical trials of single chemotherapeutic agents were provided and contrasted with studies of combination chemotherapy. Even at this early date, the CMF (Cyclophosphamide, Methotrexate, 5-fluorouracil) RCT from Milan, Italy, which was the largest and had the longest follow-up up to that time, stood out as showing relatively clear evidence of efficacy of adjuvant chemotherapy and a significant overall survival benefit, but only for premenopausal patients. Other early and promising trials ongoing at that time, controlled or otherwise, with smaller number of patients, included those of chemotherapy in combination with tamoxifen, and chemotherapy regimens based on doxorubicin. Interestingly the usefulness of the concept of immunomodulators was tested using non-specific agents such as the BCG vaccine and levamisole but without success. Lingering questions remained at the end of the review, including the dosing of chemotherapeutic agents, timing of initiation, duration of treatment, effects with and of radiotherapy, effects on and of ovarian suppression, and selection of patients for chemotherapy and long-term toxicity and adverse events including secondary malignancies.

A study of the results of chemotherapy used in breast cancer from Siriraj Hospital by Professor Thira Limsila, published in 1984, was an interesting window into local practice and treatment results at another major medical institution.[16] For example, in the 1970's, among 152 stage II breast cancers who underwent surgery and radiotherapy, those who completed treatment (only 64% did so) had a recurrence rate of 63%, although the time frame was not reported. However, the study's main focus was on the 50 breast cancer patients who were treated with chemotherapy after failure of these "conventional" treatments in the period between 1969 – 1981 and all of whom died by the last follow-up in 1983. We assume, as was the case with Chulalongkorn Hospital, that chemotherapy was provided only for advanced, metastatic or recurrent disease, and thus these 50 patients represented almost all the experience with chemotherapy for breast cancer at Siriraj Hospital up to that time. There were multiple regimens of single or combination chemotherapy, in addition to radiotherapy and hormonal therapy, the latter including surgical and radiological castration. Of the 50 patients, 44 had prior surgery, and radical mastectomy was the most frequently used procedure.

Almost all patients had multiple organ metastasis, the most common site being the lungs. These drugs were given with doses dependent upon patient condition and tumor response, as well as the presence of bone marrow toxicity and drug resistance. Results included the finding that CMF regimen had the best tumor response and best patient survival, and could be improved if doxorubicin was added. With such a poor-risk sample, however, it was not surprising that 62% would die within the 1st year and only 4% survived past the 4th year. The article ended with an emphasis on a multidisciplinary approach to breast cancer management.

Reconstruction after mastectomy was the subject of an article, in 1985, from a private plastic surgery clinic in Belleville, Illinois, USA.[17] It is interesting to see the latissimus dorsi myocutaneous flap combined with silicone prothesis being used to reconstruct the breast at this time. This is at present at least as common as pure autologous reconstruction. CO2 laser was used for dissection and hemostasis at the clinic, and this in fact was the main selling point of the paper. The attitude towards reconstruction at this date can be seen by the authors' reassurances that plastic surgeons will not interfere with cancer surgery, that "early" reconstruction at 6 months after cancer surgery was safe, and the silicone prosthesis itself was safe. The result of reconstruction was not particularly nice, as the authors mentioned tempering patient expectations with "the result is no cosmetic triumph", "her breasts will not be equal", and "the aim is to look well in clothes … and not in the nude".

1990 - 2000: Conservative surgery and achieving world-class standards

We now jump to 1990 with an article on breast lumps from Siriraj Hospital.[18] The study comprised of 1,060 cases operated on during 1973 – 1984. There was mention of the increasing use of radiologic methods of diagnosis, but more emphasis was on clinical methods. If the lump was of high suspicion for cancer on clinical and radiologic grounds, an excisional or incisional biopsy would be performed under general anesthesia, so that breast cancer surgery could be done in a single setting if the result of the frozen section examination was positive for cancer. This was called the "double set-up" procedure, and is rarely performed today (see below). Although the highest frequency of breast cancer was still in the age group 41 to 50 years, as a proportion of all breast lesions the percentage of breast cancer was highest (81%) in patients older than 60 years. The overall proportion of breast cancer was 19% (199/1,060). In an earlier study from Chulalongkorn Hospital examining breast specimens obtained between 1977 – 1981,[19] the annual proportion of cancer varied from 13% to 16%, which was somewhat lower. Interestingly, both the latter and current study found that 7% of breast cancers occurred in patients younger than 30 years. This was 2 to 3 time higher than those seen in Western countries, and was confirmed in later studies from other institutions in Thailand and East Asia. A recommendation for surgical treatment of breast cancer in the Siriraj article now included breast conserving surgery ("segmental mastectomy") with breast irradiation, and axillary lymph node dissection for stages I and II disease, as well as adjuvant chemotherapy for stage II disease. It seems that by the late 1980's mature results from clinical trials comparing breast conserving therapy and mastectomy as well as adjuvant chemotherapy trials were making an impact on clinical practice in Thailand. But by no means was breast conserving surgery widely practiced in the country at this time.

The impact of mammography on the diagnosis and management of breast cancer was the subject of a retrospective study from Samitivej Hospital published in 1991.[20] Mammography was increasing used in Thailand since the mid 1980's, as exemplified by Samitivej Hospital's program beginning in 1988. Included in the study were 838 mammograms performed during the period 1988 – 1990, with 47% for screening and 53% for diagnostic purposes. Biopsies were done in 134 patients, of whom 38 (28%) had cancer. Overall sensitivity and specificity of the mammogram for detecting cancer were 42% and 85%, respectively. This value for sensitivity would be considered rather low by current standards. Other uses of mammography, specifically for localization of non-palpable lesions and confirmation of complete removal during surgery, were described. Early diagnosis of non-palpable cancers was enthusiastically emphasized. In view of later screening mammography controversy, it was remarkable that cost-effectiveness, radiation safety, accuracy, and proper selection of patients were also mentioned in the article.

By the year 1998 we enter a more familiar territory. Within a period of less than 20 years adjuvant and neoadjuvant chemotherapy was clearly established for breast cancer in Thailand. Standard chemotherapy regimens were being used all over the country and CMF

and anthracycline-based chemotherapy were the norm. Tamoxifen was also widely used. Indications for radiotherapy became clearer. A major reason for this change was the accumulating high-quality research work and a framework for thinking about and synthesizing evidence. Statisticians and clinical epidemiologists began systematically collecting such evidence for synthesis, forming various research groups with specific clinical disciplines. The most prominent, in breast cancer, was perhaps the Early Breast Cancer Trialists' Collaborative Group (EBCTCG), a global research collaboration based in Oxford, UK, established in 1985. Their earliest publication was a systematic review of tamoxifen and chemotherapy for early breast cancer, in 1988.

As breast cancer survival improved dramatically, women became more aware of the disease and its consequences. Breast cancer screening became more common, and breast cancer incidence began to rise, slowly edging out cancer of the uterine cervix to become the number one cancer in Thai women by the beginning of the new millennium. Refinement of indications and new predictors for various surgical and adjuvant therapy for breast cancer emerged. Dramatic innovations in the surgery for breast cancer were just behind the corner and the era of targeted therapy for cancer was dawning.

A review of breast cancer survival and prognosis from the Thai NCI was published in 1998.[21] There were 873 patients in the study treated between 1992 – 1996. The average age was 48 years, with a standard deviation (SD) of 12 years. By this time, using the TNM staging system, almost 60% had early stage breast cancer, and 12% had metastatic disease. Invasive ductal carcinoma constituted 81% of all cancers. Chemotherapy was now used in stages I to III breast cancer in over 70% of patients. Hormonal therapy was used in 30% of patients. Stage I breast cancer had an expected survival of over 80% at 5 years, but stages II and III had significantly lower survival, at slightly over 60% and 30% respectively. Stage IV cancer had slightly above 10% 5-year survival. Prognostic factors considered included TNM stage, histology, tumor grade, ER and PgR status, which could now be obtained almost routinely, menopausal status, socioeconomic status and various types of cancer treatment. HER2/neu (currently, ERBB2) expression was being increasingly used as another important prognosticator.

Breast conserving therapy (BCT) was, by the end of 1990's, an established alternative to mastectomy, widely believed to have equivalent survival whenever BCT was feasible. Long-term evidence from well-conducted, large clinical trials was available. In fact, a high rate of BCT became, for a time, a measure of quality of a specialist Breast Cancer Center. But a key requirement was radiation therapy to the remaining breast tissue. Recurrence after BCT was still somewhat unpredictable, but might there be markers or predictors of recurrence after breast irradiation? A study published in 1999, from the University of Florida Health Science Center, Jacksonville, USA, attempted to find such markers.[22] There were 112 breast cancer patients in the study who were treated with BCT between 1983 – 1994 at the Center. First of all, these were rather good risk patients with a median age of 59 years, with 91% of patients having tumors less than 2 cm in size and 65% were node negative, and adjuvant chemotherapy (all either CMF or doxorubicin + cyclophosphamide) and hormonal therapy were given as indicated. Whole breast irradiation with total doses of 5000 to 5040 cGy was given in 25 to 28 fractions in addition to 5 fractions of 1000 cGy boost to the tumor bed, as well as supplemental supraclavicular and axillary irradiation for patients with large tumors or axillary lymph node involvement. After a median follow up of approximately 7 years, 5-year disease-free survival probabilities were 92%, 85% and 83% for stages I, II and III cancer, respectively. This was an outstanding result, even for today, though limited by the sample size. The survival gaps of different-stage cancers were closing partly because of more effective and tailored treatment.

Second, the paper focused on immunohistochemical markers, recently introduced into routine practice, so methods used could differ between institutions and standardization was an issue. These markers included ER, PgR, HER2/neu (oncogene), p53 (tumor suppressor gene) and MDR1, the latter being a marker for multidrug resistance. The principal finding was that both p53 and MDR1 were frequently (50% to 80%) positive in local or distant recurrences (these were few, however). These latter markers may, as the authors hypothesized, represent predictors of resistance to radiation or chemotherapy. We have now entered the molecular / genetic era of cancer therapy, and as the human genome project was in its final phase the dream and realization of personalized medicine based on knowledge of the genome seemed almost inevitable.

With increasing use of BCT in Thailand, it was natural to ask the patient what her preference would be if given a choice between BCT and mastectomy, and why.

A study from Ramathibodi Hospital was published in 1999, in which patients were asked precisely these questions.[23] A questionnaire was administered to 263 patients seen at the breast clinic of the hospital. Of these, 60 had already been treated for breast cancer by mastectomy, and 203, some of whom did not have cancer, had yet to be surgically treated. Of those who were treated and followed for less than 3 months, 68% preferred mastectomy and 32% preferred BCT. Of those treated and followed for more than 1 year, 75% preferred mastectomy and 25% preferred BCT. However, when asked whether breast reconstruction or the use of breast prosthesis was desirable, 32% to 56% of the treated patients (by mastectomy) answered in the affirmative. In the untreated group, 46% of those who had cancer preferred mastectomy and 54% preferred BCT, while those who did not have cancer preferred mastectomy in only 28% and BCT in 72%. When the two groups were combined, factors significantly related to the preference for BCT included: younger age (less than 40 years); being single; fear of, or perceived, image problems; being a student or an office worker or working for the government; and not yet surgically treated for cancer. It seems, for Thai patients at that time, that once mastectomy had been performed or decided on, there was not much regret, but prior to surgery there was slight preference for mastectomy over BCT. Times have changed, however, and as the younger generation ages and a few have become breast cancer patients themselves, BCT is now a dominant preference, at least in certain regions of the country.

The early dissemination theory of breast cancer posited that axillary surgery did not improve survival, but information on regional disease in the axilla was important for prognosis and prediction of appropriate treatment. It seems logical that if minimal axillary surgery can be performed to obtain sufficient information on nodal metastasis, the morbidity associated with axillary dissection might be reduced. At the very least, if nodal metastasis cannot be detected or predicted to be minimal, then full axillary dissection can be omitted. This would be feasible if there were an identifiable small group of regional nodes that first drains cancerous cells, and these nodes could be removed for preliminary examination. Such elegant ideas began to take shape in the early 1990's alongside the successful implementation of a similar idea in the treatment of cutaneous melanoma and squamous cell carcinoma. This was the beginning of sentinel lymph node biopsy in breast cancer, now a standard practice globally. The rapidity of its acceptance is in contrast to the much more gradual acceptance of BCT.

Two studies on sentinel lymph node biopsy (SLNB) was published back to back in 1999. One study was from the Orebro Medical Center in Sweden.[24] This was a pilot study to evaluate the accuracy of SLNB in 61 clinical node-negative stages I to III breast cancer patients, treated between March 1998 – April 1999, using a combination of radiotracer (Tc99 nanocolloid) and a blue dye (Patent Blue V) to identify SLNs. Preoperative scintigraphy as well as intraoperative gamma radiation probe were used to localize the radiotracer. All patients underwent standard axillary lymph node dissection after SLNB. The axillae contained metastasis in 34% of patients. An average of 2 SLN's were removed. The combined identification rate was 92% and the false negative rate was 14%, slightly higher than that acceptable today. The study concluded, "before being use [sic] in routine clinical practice, results from randomized clinical trials are needed".

Another SLNB study was from Siriraj Hospital,[25] led by Professor Adune Ratanawichitrasin, probably the first such study in Thailand, conducted between December 1998 – May 1999. This was also a pilot study, but using only isosulfan blue dye (ISB) to identify the SLNs. There were 15 early stage breast cancer patients. ISB dye, made in-hospital as a 1% solution, was injected at multiple sites around the tumor or tumor cavity, totaling 3 to 5 mL. After SLNB, axillary dissection was done on all patients. On average 2.5 nodes were removed. The identification rate was 87% (13/15). The false negative rate was 17% (1/6). The authors concluded that "further studies should be carried out…".

A brief review article on SLNB was published in 2000, from Samitivej Hospital.[26] It concisely summarized the importance of axillary staging in breast cancer, and the origins and rationale of SLNB. Several agents for lymphatic mapping or tracers were discussed along with their benefits and drawbacks. The article mentioned the controversy surrounding the routine use of SLNB at the time, and the remaining technical issues needing clarification or further study before such routine use. Some of these included the choice and timing of tracer injection, the appropriate selection of patients, methods of staining sections, the role of internal mammary nodes, and the accuracy of SLNB itself. Most of these issues have now been resolved, but the tone of the article was

cautiously optimistic, a very reasonable stance when new medical innovations are evaluated.

2000 – 2010: SLNB, HER2 and breast reconstruction

Accurate prediction of axillary lymph node metastasis in all cases of breast cancer prior to surgery is almost like the Holy Grail in the sense that it has never been found, and may perhaps never be found. Nevertheless, in extreme cases the prediction of no metastasis or definite metastasis might be accurately and reliably made. Those in between can undergo SLNB. With such predictions, unnecessary axillary surgery could be reduced even further. Some predictive or scoring systems are in current use for these purposes, such as the Memorial Sloan Kettering Cancer Center (MSKCC) Nomograms (e.g., for SLNs), an online tool, but their accuracy and reliability might not be as good as we would like. This is in the nature of the methodology used for their development and implementation. The use of Artificial Intelligence in this area could perhaps improve the usefulness of predictive systems.

A study from Vajira Hospital in 2002 was similar in spirit,[27] attempting to determine predictors of metastasis to axillary lymph nodes prior to surgery. This was a retrospective study of 203 stages I to III breast cancer patients, treated between 1994 - 2001. Of these 42% (85/203) had axillary node metastasis. Factors predictive of axillary lymph node metastasis on multivariable analysis included presence of palpable mass, tumor size greater than 1.5 cm, and presence of lymphovascular invasion (LVI). The absence of all 3 risks was associated with only 3.7% axillary node metastasis. Note, however, that LVI might be difficult to determine preoperatively if inadequate biopsy methods were used.

Breast reconstruction and breast conserving surgery (BCS) were now being used extensively for breast cancer. In Thailand, the trend was similar. In particular, breast reconstruction immediately after mastectomy was now on the rise, mainly using autologous tissue such as the Transverse Abdominis Myocutaneous (TRAM) flap. Breast reconstruction overshadowed BCS in many institutions possibly due to patient preference, since there is no remaining breast to worry about, and surgeon preference, perhaps because of the enticing technical challenge and perceived cosmetic advantages. The dominant technique was the pedicled TRAM flap, with the occasional "free" flap (myocutaneous flaps, mainly from the abdominal area, with attached vascular supply to be anastomosed to local recipient vasculature) being employed.

A study published in 2004 from Siriraj Hospital addressed a problem with breast reconstruction and BCS when the nipple is left in situ or used as a graft.[28] This was the nipple areolar complex (NAC) involvement in breast cancer. The study was performed on 46 mastectomy specimens obtained from stages I to III breast cancer patients treated during the period July 2003 – May 2004, who had no clinical NAC lesions. The aim was to test the accuracy of frozen section examination of the subnipple area compared to permanent section, and to identify risk factors for positive NAC involvement. The proportion of NAC involvement was 37% (17/46). The sensitivity of the frozen section examination was 88% and the specificity was 97% compared to permanent section. Only two factors were related positive NAC involvement: larger tumors and larger tumor size to tumor-to-NAC distance ratio (as measured on mammography). Thus, after selecting appropriate patients based on these risk factors, intraoperative frozen section examination may help further decide whether to preserve the NAC or not.

By this time the first successful targeted therapy for breast cancer had been developed and was on the market, but was still very expensive and not in wide spread use in Thailand. This was trastuzumab, an "anti-HER2" monoclonal antibody, US FDA approved in 1998 via expedited process. It is difficult to overstate its importance. Targeted therapy refers to treatment focused on the tumor and sparing normal cells, via some molecular mechanism specific to a tumor's growth and viability, such as the HER2 receptor proteins over-expressed under genetic mutations specific to the tumor. In contrast, chemotherapy is non-specific and will affect any fast-dividing cell. This was an almost revolutionary approach to treating cancer, brought about by the exponential growth in the knowledge of tumor molecular biology. The rapid development in the biotechnology industry, including gene and protein sequencing technology, of the 1970's through to the 1990's laid the groundwork. We are still in the midst of this development.

Testing for HER2 protein overexpression via immunohistochemical (IHC) staining methods in the early days were riddled with inaccuracy, poor reproducibility and lack of standardization. It was only after the year 2006 that guidelines and recommendations for standardization of laboratory practices became widely accepted, which helped reduce variation in test results. Similar

standardization occurred in Thailand some time later. This was extremely important for the effective use of trastuzumab, and a big step towards the drug becoming more widely available.

A study from Rajavithi Hospital in 2005 attempted to determine the relationship between HER2 overexpression and other predictive and prognostic IHC markers in breast cancer.[29] There were concerns with the accuracy of the IHC test for HER2 in the study, as an unapproved antibody staining technique was used, but the test was validated by the fluorescence in-situ hybridization (FISH) technique. FISH is a test for gene amplification and may complement IHC methods especially if the IHC staining test result is equivocal. The study was performed on 251 specimens from 251 breast cancer patients treated between January 2003 – February 2005. Axillary lymph nodes were positive for cancer in 41% of patients, ER was positive in 39%, PR was positive in 28% and HER2 was positive in 25%. The proportion of positive HER2 was in accord with results from other and later studies, both in and outside of Thailand. There was a negative correlation between ER, PR positivity and HER2 positivity and a positive correlation between axillary lymph node positivity and HER2 positivity. These findings are commonly accepted today.

Refinements in the use and technique of SLNB continued throughout the decade. An important clinical trial on the use of SLNB as the sole staging procedure in certain patients with minimal positive SLNs was published at the end of the decade (the ACOSOG Z0011 trial from the American College of Surgeons Oncology Group), which also established its safety as the sole therapeutic axillary procedure for those patients. Micrometastasis seen on SLNB was no longer an indication for further axillary clearance, according to another trial published in the early 2010's (IBCSG 23-01). Detected macrometastasis in the axilla, however, continued to be treated mainly by surgery.

A study from Phramongkutklao Hospital and College of Medicine in 2005 examined the accuracy of bisectioning versus serial sectioning of the SLNs in detecting macrometastasis.[30] At the institute, SLNs were often bisected for pathological examination, and this had led to the concern that the bivalve method might not be sufficiently accurate, hence the present study was conceived. There were 45 early stage breast cancer patients in the study, who were treated between January 2000 – June 2004. The blue dye method was used for detecting SLN's, with an identification rate of 93% (42/45). The average number of nodes removed was 1.8 nodes, and 76 nodes were available for study. The bivalve method was compared to the conventional serial sectioning at 2 mm intervals, using routine hematoxylin and eosin (H&E) staining as well as cytokeratin IHC. There were 28 positive nodes and 48 negative nodes on bisection examination. Since the only possible difference in the detection of macrometastasis would be for nodes found negative on bisection, the focus was on the serial sectioning for the 48 negative nodes. Due to certain management and other errors, only 42 negative nodes were available. All 42 nodes were also negative on serial sectioning. Thus, bisectioning seemed to be similar to serial sectioning in the detection of macrometastasis. If true, this might help expedite the pathological analysis of SLNs. Of course, with only 76 nodes and incomplete information, further study is necessary.

Another study of SLNs compared scrape imprint cytology to serial sectioning.[31] This study was from Prince of Songkhla University, and included 72 lymph nodes harvested from 33 breast cancer patients treated between April 2005 – March 2006. Combined ISB dye and isotope tracer were used to identify SLNs, with an identification rate of 97%. Scrape imprint of the SLNs was stained with cytokeratin ICC (immunocytochemical) methods which yielded results in 30 minutes. Thus, imprint cytology might be useful for intraoperative detection of cancer in the SLNs. If this was negative, the nodes would then be sent for routine serial sectioning with H&E, and if H&E was negative, further 20-micron section of the nodes with cytokeratin IHC staining was done. The sensitivity of scrape imprint ICC was 33% (5/15), the sensitivity was 94% (17/18) compared to serial sectioning and H&E + IHC. It was concluded that imprint ICC was not sufficiently accurate but further study might be needed. Note that the use of cytokeratin IHC in permanent sections is generally not recommended today by many international cancer societies following several recent studies, since further detection of micrometastasis might not be clinically meaningful.

Methods of tissue biopsy have made a huge impact on clinical practice. We will discuss this topic after the presentation of a study from Suratthani Hospital.[32] This was published in 2008, but was a prospective study of 92 patients with breast tumors treated between October 2004 – September 2005. The average tumor size was 3.1 cm with a range between 1.8 cm to 8.2 cm. Core needle

biopsy (CNB) was performed using a manual small-bore biopsy needle (probably 14-gauge) under local anesthesia, with palpation as the localization method, obtaining 3 to 5 core specimens for examination. All lesions were subsequently excised or incised for definite diagnosis. There were 86 cancers. The sensitivity of the CNB was 92% (79/86) and the sensitivity was 100% (6/6). The false negative rate was 8%. These measures of accuracy were comparable to those published elsewhere for small-bore CNB. Complications were minor, consisting of pain and bruising at the biopsy site.

Core needle biopsy is now standard for breast cancer. With over 90% sensitivity (close to 100% with large-bore, 11-gauge, CNB) and almost 100% specificity for the diagnosis of cancer, and the possibility of obtaining prognostic and predictive markers at the same time, it is the initial biopsy method of choice. If the breast lesion is suspected of being cancerous, CNB is performed first, by an experienced radiologist or surgeon under imaging guidance, and the results are discussed with the patient. Locally advanced lesions or subcutaneous nodules can be biopsied using core needles as well. Subsequent surgical treatment planning is minimally affected by CNB, unlike excisional or incisional biopsy. Excision may still be required if the result of CNB is equivocal or in conflict with other evidence, or if CNB is not feasible. "Double set-up" procedures for simultaneous diagnosis and treatment of breast cancer are no longer routine. With CNB, the patient has more control over her treatment decisions.

We end this decade with a small study on the impact of waiting times on cancer survival, from Ramathibodi Hospital, published in 2009.[33] The study is used as a summary of the practice and what was achieved in Thailand by the year 2000. The study was based on 359 breast cancer patients treated between January 2000 to December 2001 with available information. Of note, at this date only 1% of patients had BCT, the rest had modified radical mastectomy. All had axillary node dissection. Open biopsy was done in 77% of patients (278/359), including double set up in 35% (125/359). CNB was done, mainly by surgeons, in only 16% (56/359). Fine needle aspiration cytology (FNAC) was used for diagnosis in the remaining. The only IHC marker available was the ER, obtained in 80% of patients. Despite an average tumor size of 3.2 cm (SD, 1.6 cm), most patients had TNM stages I and II (80%) disease. The median follow-up time was 66 months and the 5-year overall survival of the whole cohort was 90% (95% confidence interval [CI]: 86% - 93%) and the 5-year disease free survival was 79% (95% CI: 74% - 83%). The overall survival was certainly world-class, even for today. The lower disease-free survival probably reflected considerable recurrence, but with longer survival, possible with powerful therapeutic agents and treatment guidelines available before the new millennium. Adjuvant chemotherapy and hormonal therapy were used in 74% and 52% of patients, respectively, with chest wall irradiation used in 30%. These percentages are similar to what are seen today, except for the current increased use of radiation therapy.

Waiting time, here defined as the time from diagnosis to surgery (patients who had neoadjuvant chemotherapy were excluded), did not have a significant effect on breast cancer survival. Perhaps this was because the median waiting time was only 1.9 weeks (range, 1 day to 32 weeks). At present, the waiting time in many major breast cancer centers could be much longer. One interesting finding was that open biopsy was associated with poorer survival, as compared to needle biopsy, despite adjusting for many confounding factors in the analysis. The most rational explanation for this, however, was residual confounding from other unknown poor prognostic features associated with open biopsy, rather than open biopsy itself.

2010-2019: Minimal disease and oncoplastic surgery

As screening mammography became increasing popular in Thailand, the proportion of ductal carcinoma in situ (DCIS) began to rise. CNB findings of DCIS were of some concern as some of these patients actually had invasive cancer. A study from Ramathibodi published in 2012 addressed the upgrading or upstaging rate of CNB-diagnosed DCIS.[34] There were 88 patients diagnosed as having DCIS with or without microinvasion on CNB seen between 2008 – 2010. There were 59 patients having CNB-diagnosed pure DCIS and 19 having DCIS with microinvasion. For those with pure DCIS on CNB, the upstaging rate to macroinvasive cancer (after removal of the whole lesion) was 19% (11/59), and to DCIS with microinvasion, 24% (14/59). The upstaging rate for DCIS with microinvasion to macroinvasive cancer was 34% (10/29). No clinical nor IHC factors were related the upstaging, probably because of the small sample size. Interestingly, if the final diagnosis was pure DCIS, no axillary lymph node metastasis was found, but with microinvasion, lymph node metastasis was detected in

5%. Invasive cancer had 24% axillary node involvement. Thus, SLNB might be omitted for microinvasive cancer if more supporting evidence exists, such as that from the 2005 study from Chiangmai University (see below in the abstracts section).

Non-palpable breast lesions were becoming more common with screening mammography as well. In a study from Chiangmai University Hospital, in 2015, 168 patients with non-palpable BI-RADS (Breast Imaging-Reporting and Data System) category 4 to 5 mammograms underwent image-guided excisions during January 2009 – December 2014.[35] The risks of malignancy in these patients were 20% for those with BI-RADS category 4 (29/145) and 77% for those with BI-RADS category 5 (10/13). Overall 254 lesions were biopsied. Of these, 48 were malignant. DCIS was seen in 58% of all malignant lesions (28/48). DCIS was fast becoming a common breast "cancer" in Thailand, approaching proportions seen in Western countries (a quarter of all breast cancers) at some institutions.

With smaller cancers and low-risk lesions, some of which were detected via screening mammography only, BCT was gaining ground in Thailand once again. In the previous decade, breast reconstruction was probably more common than BCT in Thailand. Now the numbers are reversed in some institutions, and at certain periods BCT constituted 50% of all breast cancer surgery. Oncoplastic surgery, a termed coined in Europe in the 1990's, was the name of an approach to BCS whereby oncologic principles are combined with plastic surgical techniques to aid wide excisions of cancer while maintaining or recreating acceptable cosmesis. After BCS, the ipsilateral breast may be smaller but minimally deformed using some tissue displacement method, or larger or of similar size using volume replacement, or the contralateral breast can be made smaller in a mammoreduction strategy. Once again, surgery for breast cancer was transformed, and the quality of life of the patient who may achieve long term survival became paramount.

A study from Udonthani Cancer Center reported a series of early stage breast cancer patients undergoing BCS with volume replacement using pedicled latissimus dorsi (LD) flap.[36] There were 28 patients who underwent BCS with LD flap volume replacement between 2008 – 2010. A similar group of 22 patients underwent BCS alone in the same period. The most common complication was seroma formation at the donor site area, but there was no flap necrosis or flap loss. After a median follow-up time of 28 and 30 months, there were 1 local recurrence in each group, and 2 distant recurrences in each as well. Thus, with a limited follow-up the oncologic safety was comparable between BCS with and without LD flap reconstruction. The cosmetic outcome was rated excellent by 79% of patients (22/28).

Another type of volume replacement is autologous fat grafting, the subject of a study from Siriraj Hospital published in 2014.[37] In 96 early-stage breast cancer patients who underwent BCS between January 2007 – December 2010, autologous free dermal fat graft (FDFG) was obtained from the patients' lower abdominal wall, and placed into the tumor cavity of the breast after wide excision. This was truly an innovative and elegant idea. The graft was cut from the lower abdomen, including the skin, and de-epithelialized, then shaped to fit the cavity and to maintain normal breast contour. The dermal side was placed on the bared pectoral muscles, so a vascular supply to the graft could be established. Most patients (93%) did not experience graft-related complications. All such complications were graft-related mastitis, requiring graft removal or re-excision in 4 patients (4%). Donor site complications occurred in 10 patients (10%) most of which were seroma formation. The presence of the graft did not delay adjuvant treatment and did not interfere with the detection of recurrent disease. In fact, ipsilateral breast cancer recurrence was found in 5 patients and distant recurrence in 3 after a median follow-up of 45 months. The disease-free survival was 84% at 33 months. Although there were major drawbacks such as the need for two surgical procedures (done simultaneously) at two sites, some significant inflammatory reaction, and graft viability issues, this ingenious method certainly merit more careful study or modifications of technique.

Another, similar idea is to use synthetic or biocompatible material to at least partially fill the tumor cavity, which would elicit less inflammatory response and is surgically less invasive. At present, no ideal material is available, but existing materials such as acellular dermal matrix grafts or polypropylene mesh can be used. Prior studies of such materials usually describe attempts to fill the whole cavity, which often induce inflammatory and infectious complications. The more recent idea is to use these materials as a temporary scaffold, to keep the cavity from collapsing and allow surrounding cells to migrate into the cavity and build new tissues. Thus, there is no need to use large quantities of foreign mate-

rial. However, the scaffold hypothesis is without solid supporting evidence (no pun intended), so more study is also needed.

The last refinement of the SLNB technique in the present review is the use of one step nucleic acid amplification (OSNA) assay. An excellent, detailed, and well-written article, from Siriraj Hospital and published in 2014, described a study combining molecular genetic techniques with minimally invasive axillary surgery, two great innovations from the final decades of the 20th century.[38] A sample of 111 SLN's detected using blue dye alone was taken from 62 early-stage breast cancer patients treated between July 2011 – January 2012. The idea behind the use of OSNA was to rapidly detect the presence of metastatic cells in SLN's by using real-time polymerase chain reaction (RT-PCR) techniques to identify tumor-specific genes or gene-related elements in the nodal tissue. In the present study that gene-related element was CK19 mRNA, which could be reverse-transcripted and amplified for detection. The Siriraj study compared OSNA to frozen section examination (and also imprint cytology), using permanent section as gold standard, to determine the relative accuracy of OSNA as an alternative method for intraoperative detection of cancer cells in SLNB specimens.

The SLN's were sectioned at 2 mm intervals, and alternate sections were sent for OSNA and the rest for histopathology. Positive results based on OSNA were defined essentially in terms of CK19 mRNA copy number with a cut-off value. After "discordant analysis" by the authors, the final accuracy measures of OSNA and frozen section examination, relative to permanent section, were: 86% and 93% sensitivity, respectively for OSNA and frozen section, and 93% and 100% specificity, respectively for OSNA and frozen section. It is debatable whether permanent section can be considered a true gold standard in the setting where, in theory, molecular techniques may be more sensitive. Nonetheless, for practical purposes such results are promising for OSNA. With an average reporting time of 47 minutes, OSNA is a viable alternative to intraoperative frozen section examination when the latter is not available. The cost, the need for laboratory space and equipment, and the skills needed to process the tissue and interpret the results will have to be considered. However, OSNA may be used to detect other cancer-related genes of interest, and the consequent research possibilities may make OSNA worth the cost.

As older ideas, techniques and practices are questioned and probed, improvements seem possible. Sometimes that might be the case and sometimes not. But this uncertainty should not detract the clinician-investigator from testing out some of the more interesting, low-risk ideas. An RCT from Surin Hospital was performed to compare the effects of lymphatic ligation versus no ligation in axillary lymph node dissection (ALND), on the occurrence of postoperative seroma.[39] This is an interesting and simple-to-conceive-but-not-to-implement idea. There were 68 breast cancer patients with positive SLNB treated between January 2014 – November 2017 who consented to participate in the study and were randomized to either the lymphatic ligation group or no ligation group (conventional surgery) during ALND. A total of 69 axillae were studied, 34 in the lymphatic ligation group, and 35 in the conventional group. Lymphatic ligation was described in the article but it was difficult to understand how it was actually done or how complete the ligation might be. Two vacuum drains were placed and the drainage was monitored till drain removal, about 2 weeks later (median duration of drainage were 11 days and 15 days for the ligation group and no ligation group, respectively). Total drain volumes were not statistically different between the two groups, though the median value was larger for the no ligation group (785 mL vs. 1,020 mL). Incidences of seroma formation after drain removal were 24% (8/34) and 29% (10/35) for the ligation and no ligation groups, respectively, which were also not statistically different.

This was the first properly conducted RCT on the subject of breast cancer to be published in the TJS, and the results should be valid, in principle. Thus, lymphatic ligation, if done correctly, likely has a small effect on the occurrence of seroma. But the current understanding is that serous fluid formation in ALND is mostly from an inflammatory reaction to surgery and not mainly from lymphatic leakage. This trial indirectly supports the latter hypothesis.

There are favorable histological subtypes of breast cancer with good prognosis, and treatment for these cancers should therefore be less aggressive. Recognized favorable subtypes include pure tubular, cribriform and mucinous carcinoma, among others. Papillary cancers, not to be confused with micropapillary cancer, can include tumors with invasive and non-invasive behavior. Encapsulated and solid papillary carcinoma have behaviors similar to that of non-invasive cancer and are recognized as favorable subtypes in all guidelines. But

papillary cancers with invasive features are not generally so recognized. A retrospective study from Ramathibodi Hospital, published in 2019, attempted to define the behavior of papillary cancers, and more specifically invasive papillary cancer.[40] There were 86 patients, with 64 (74%) having invasive papillary cancer. There were no recurrences nor deaths due to cancer after a median follow up of only 22 months. The study concluded that papillary breast cancers, including invasive types as well, might all have favorable prognosis. But this could be so at most only in the short term. Unfortunately, the study was also limited by diagnostic accuracy issues, with questionable diagnosis of invasive papillary cancer in some cases.

Radiotherapy for pN1 (number of positive axillary nodes between 1 to 3 on pathological examination) breast cancers has been on the rise in the past 5 to 6 years. A part of the reason for this trend must be the EBCTCG individual-patient data meta-analysis, published in 2014, supporting favorable long-term (up to 20 years) effects (e.g. increased patient survival) of radiation therapy on mastectomy patients with 1 to 3 positive axillary nodes. This trend is disturbing for several reasons, which we will not dwell on. But a study from Siriraj Hospital published in 2018 was a welcome rebuttal to this trend.[41] The study was a retrospective review of 158 breast cancer patients with tumor size less than 5 cm who had 1 to 3 positive axillary nodes. All were treated between 2000 – 2001, and followed for over 10 years (no exact duration was given). Overall survival and disease-free survival at 15 years were not significantly different between patients receiving or not receiving radiotherapy. However, there was a larger difference in disease-free survival between the two groups for patients with negative hormonal receptor status. Limitations of the study, of course, included the small sample size and the inevitable selection bias. But this result was in keeping with the common sense thinking that low-risk, hormonal positive patients can probably do without radiation therapy. Some of the recent perceived increase in ipsilateral arm lymphedema must at least be attributed to the increased use of radiation therapy, but are these increases justifiable in all cases?

The finding that locoregional therapy can affect long-term survival is in contrast to the predictions of the early dissemination theory of breast cancer. This is not to say that the theory is wrong, but that a more nuanced theory is needed to explain long-term observations. For example, instead of stating that the survival of the breast cancer patient is determined prior to surgery because of the presence of micrometastasis from the very beginning (if systemic treatment were not subsequently given), it is probably more accurate to propose that there might be multiple episodes of microdissemination. One such episode can occur during locoregional treatment failure, with more insidious or longer-term consequences.

The final set of 3 articles deal with reconstructive and oncoplastic surgery, all published in the 40th issue of the TJS (2019). These were all from Ramathibodi Hospital.[42-44] The practice reflected in these articles should represent similar practices elsewhere in Thailand. The first article was about an "in vivo" anatomical study of the deep superior epigastric artery (DSEA), one vital vascular structure to be aware of and preserved when a pedicled TRAM flap is harvested.[42] During hepatobiliary procedures on 7 patients, where upper abdominal incisions needed to be made, an anatomical dissection was carried out during the surgery. Prior informed consent was obtained from all patients. Various danger and safety zones were mapped and correlated with surface markings. It was hoped that this information would be useful in TRAM procedures on future patients. However, pedicled and free TRAM flaps are less frequently used today because of significant complications and morbidity, and difficulties of technique, requiring a steep learning curve. Breast reconstruction after mastectomy is currently dominated by implant-based procedures.

The second article was about a surgical technique, illustrated with actual cases.[43] The article detailed yet another volume replacement procedure in BCS, this time using local cutaneous rotation flaps. The description was very concise but the highlight was a set of clear, self-explanatory step-by-step photographs in color. The last article was also on a type of BCS oncoplastic procedure, a mammoreduction-based strategy.[44] It reviewed and described in some detail the principles of vertical scar mammoplasty, in the spirit of Lassus and Lejour. Information on the assessment and preparation of the patient, a brief set of operative instructions and the description of the more common operative and postoperative complications were all provided. Also, excellent step-by-step color photographs of actual cases were again included. The appearance of these articles was a sign of the increased popularity of BCT among breast cancer patients, as well as their desire for good cosmetic outcomes.

1980 – 2019: Abstracts from the annual congress of the RCST

In this section we review all the developments thematically, almost as a recapitulation of what was essentially provided in the published articles, but now culled from published abstracts of presentations made during the Annual Congress of the Royal College of Surgeons of Thailand (RCST) within the past 40 years. This is to do justice to the many surgeons and their great institutions whose work also contributed to the development of breast cancer surgery and treatment in Thailand. There were so many interesting accounts that we will confine ourselves to just briefly list some of them. We apologize if some contributions have been left out, not because of lack of importance but because of overlap or lack of information or simply because of inadvertent omission. The main problem with some abstracts is that very little detail is provided, and we did not attempt to determine whether any of these studies was eventually written up and published as a full paper. Some, however, were written up and published in the TJS, and thus are not listed in this section. Here, we use the words "published" and "reported" synonymously, referring to the publication of the abstract in the TJS. The actual public presentation of the corresponding study was usually given a year earlier.

Basic science and tumor markers in breast cancer

A study of the role of dendritic cells in the development of breast cancer published in 2001, from Phramongkutklao Hospital, seemed to show reduced ability of these cells to stimulate T cell proliferation and mixed lymphocyte reaction in breast cancer patients as compared to non-cancer controls. A study from Chulalongkorn Hospital examined the tumor markers CA 15-3 and CEA as predictors of recurrence after breast cancer treatment, published in 2013. Increases in the value of both tumor markers (above a certain cut-off value) were associated with larger tumor size, nodal involvement, and higher cancer stage prior to treatment, but also with recurrence and metastasis after treatment. It was concluded that tumor markers should be used for post-treatment monitoring. In 2013 an abstract was published of a study from Siriraj Hospital determining the relation between vascular endothelial growth factor (VEGF) polymorphism and breast cancer susceptibility and aggressiveness. Genotyping of the VEGF gene was done on 483 breast cancer patients and 524 controls. Two VEGF genotypes were associated with more aggressive cancers as well as higher risk of having breast cancer, and one had higher VEGF mRNA expression, which in turn was also associated with more aggressive cancer. A study from the Thai NCI published in 2014 examined the stem cell markers CD44+/CD24-/ALDH1 in 140 triple negative breast cancers. There were no clear relationships between the presence of these markers and other poor prognostic features. A study from Siriraj Hospital published in 2019 found high expression of prolactin receptor (PRLR) via IHC in breast cancer tissue to be associated with lower overall survival. This study was performed on 237 breast cancer patients and 119 controls, and also found certain PRLR genotype to be associated with poorer survival as well.

Adjuvant systemic therapy in breast cancer

Adjuvant chemotherapy was used in a series of 47 breast cancer patients from the Thai NCI (but the surgery-only group had slightly better 5-yr survival) and a successful use of neoadjuvant chemotherapy was reported from Siriraj Hospital; these were both published in 1985. By 2001, a review of systemic treatment for breast cancer from the UK published as an abstract in the TJS, mentioned the use of vinorelbine, taxanes, and trastuzumab in the treatment of metastatic breast cancer, and even high-dose chemotherapy with bone marrow transplantation (which was deemed of limited use by then). Neoadjuvant chemotherapy was also mentioned as a means to BCT. A case series from Prince of Songkhla University, published in 2004, used letrozole as a second line endocrine therapy for metastatic breast cancer after failure of tamoxifen in 7 patients.

Breast cancer survival, incidence and risk factors

In 1989 the Thai NCI reported, in 107 breast cancer patients, 5-year survival rates of 91%, 83%, 38% and 0% for stages I, II, III and IV disease, respectively, and concluded that MRM was the method of choice for the treatment of operable breast cancer. Siriraj Hospital published in 1993 a study of characteristics of 890 breast cancer patients and their treatment. Symptoms were present (palpable mass) in 77% of patients, with half having palpable axillary node metastasis. Stage II disease was present in 55% of patients, MRM was performed in 88%, and chemotherapy was given in 26%. A case-control study of the effect of hormonal replacement therapy (HRT) on breast cancer risk (623 cases and 679 controls),

from Siriraj Hospital, was published in 2002, and did not show a significant association on a multivariable analysis. From the Prince of Songkhla University, a study was published in 2005 examining the relationship between body mass index and breast cancer survival, but found no such relationship in 1,153 breast cancer patients. Another study from Prince of Songkhla University reported in 2007 found the adjusted breast cancer incidence for Songkhla Province in 2005 to be 24.3 per 100,000, which was the highest of all cancers in women, followed by that of uterine cervical cancer, at 16 per 100,000. The incidence of breast cancer in Thailand has been the highest of all cancers in women since 2001. Younger (<40 years) breast cancer patients (n=298) were compared with older (> 40 years) breast cancer patients (n = 1,062) in terms of 5-year disease-free and overall survival, in yet another study from Prince of Songkhla Hospital, published in 2013. Despite higher proportions of lymphovascular invasion and negative ER status in the tumors of younger patients, all outcomes were similar between the two age groups, with similar types of surgical procedures, types and frequency of adjuvant chemotherapy and hormonal therapy, and similar frequency of radiotherapy being provided to both. Finally, also from Prince of Songkhla University, and published in 2013, 152 node-negative breast cancer patients followed for a median of 52 months tended to have higher recurrence if younger than 50 years with HER2 overexpressed tumors (these results were not statistically significant).

Immunohistochemistry and diagnosis of breast cancer

A study from Chulalongkorn Hospital, published in 1991, compared ER assay results between biopsy and mastectomy specimens from 20 patients and concluded that ER assay from mastectomy specimens was more reliable. Another study from Chulalongkorn Hospital in 1993 evaluated the accuracy of FNAC in the diagnosis of breast cancer in 414 patients with available histological data. The sensitivity was 92% and specificity was 96%. A similar study on the accuracy of FNAC in 78 palpable breast lesions was published in 1999 from Ramathibodi Hospital, with similar conclusions. The usefulness of mammography in breast cancer patients was underscored by the detection of bilateral breast cancer in 6 of 161 patients, all without contralateral breast symptoms, in a study published in 1994 from Samitivej Hospital. A study from Maharaj Nakorn Chiangmai Hospital published in 2000 could not establish any relationship between clinical information, including TNM cancer staging, and hormonal receptor status in 355 breast cancer patients. A similar study from Prince of Songkhla University published in 2003, with a sample of 374 patients, found a positive correlation between hormonal receptor positivity and age, but no association between hormonal receptor status and TNM staging or axillary lymph node status. In 2003 as well, a study of 109 breast cancer patients with known HER2 expression status, examined the latter's association with certain risk factors. This study was from Phramongkutklao Hospital, and the prevalence of HER2 overexpression in the study was found to be 39%, but without any apparent association between HER2 status and any clinical, anatomical, pathological and treatment factors. Another study published in 2008, also from Phramongkutklao Hospital, demonstrated concordance of IHC markers between the primary tumor and metastatic tumor in the axillary nodes in 28 breast cancer patients. In another series of 442 breast cancer cases from the same institution and published in the same issue, HER2 overexpression was now seen in 18% of cases, with the same proportion (18%) of triple negative cancers. Some poor-risk clinical and IHC characteristics were related to these subtypes. A study from Thammasat University published in 2019 estimated the positive predictive values (for breast cancer) of certain patterns of calcifications seen on mammograms in a sample of 62 patients (with 72 lesions) who underwent needle localized excision. It was found that amorphous, fine pleomorphic and fine linear branching calcifications were associated with positive predictive values for breast cancer of 38%, 42% and 33%, respectively.

Interesting clinical studies and quality of life

An interesting study using a small 3-mm endoscope (ductoscope) to explore the inside of cystic breast lesions, from Vajira Hospital, was published in 2000. There were 4 patients in the study, all of whom underwent the procedure under local anesthesia, and biopsy under direct vision through the scope was done in one patient. An RCT comparing one (axillary drain only) and two drains after MRM in 60 breast cancer patients from Prince of Songkhla University and published in 2001 seemed to show no significant differences between the two groups in terms of drainage volume and occurrence of seroma or hematoma. Another RCT comparing compressive brassiere to conventional (plaster-based) compression

dressing after MRM in 56 patients, form Vajira Hospital and published in 2005, also showed no significant difference in the occurrence of seroma. Quality of life of breast cancer patients who underwent various surgical procedures was measured using validated questionnaires including WHO QOL-BREF and Functional Assessment for Cancer Therapy G and B Questionnaires, which were reported from Vajira Hospital and Siriraj Hospital in 2009. A study using talcum powder (applied to the mastectomy cavity) to reduce drainage after mastectomy was reported in 2014, from Ramathibodi Hospital. In an unreported number of patients randomized to talc or no talc group, it was found that talcum powder did not significantly reduce overall drainage at 2 weeks. A study comparing traditional electrosurgery with a low thermal system (PEAK Plasmablade, Metronic Co.) for dissection during mastectomy was reported in 2018 from Siriraj Hospital. This was an RCT with 50 patients, and no significant differences were found in terms of blood loss, postoperative pain, drainage volume, seroma formation and other complications, between the two groups.

Axillary surgery and SLNB

SLN imprint cytology for intraoperative detection of metastatic cells was reported in 1999 from Siriraj Hospital, in 55 patients. The sensitivity was 82% and specificity was 100% compared to routine H&E. Factors related to SLN identified with isosulfan blue dye alone was also examined. It was found that surgeon experience was the most important factor. A study from Ratchaburi Hospital reported in 2005 showed, in a sample of 16 clinically node-negative breast cancer patients, that SLNB under blue dye alone had a 100% identification rate, and a false negative rate of 6.25% (1/16). A study of 60 breast cancer patients, published in 2005, from Chiangmai University, found T1a tumors (size less than 5 mm) to have no axillary lymph node metastasis (0/2), and hence suggested that axillary surgery for these lesions might be omitted. A comparative study of 112 pathological node negative breast cancer patients who underwent ALND and 85 similar patients who underwent SLNB alone was conducted at Siriraj Hospital and published in 2007. After at least a year of follow up there was 9.8% increase in ipsilateral arm circumference in the ALND group, as compared with 1.2% in the SLNB group. The feasibility of local anesthesia (LA) for SLNB was studied at Ramathibodi Hospital, on 39 breast cancer patients who underwent SLNB under LA, compared with 107 similar patients who underwent SLNB under general anesthesia (GA). The study was published in 2007, and showed similar identification rates and numbers of SLNs removed between the two groups, with similar ratios of positive nodes. No patient in the LA group required GA to complete the procedure. From Phramongkutklao Hospital, in a study reported in 2009, there was comparable accuracy between frozen section and cytological methods of intraoperative detection of SLN metastasis in 166 nodes examined. Statistical predictive models for the presence of metastasis in non-SLNs were developed and published in 2016, from Siriraj Hospital. The area under the ROC curve (AUC) was reported to be between 0.801 to 0.831 in the validation data set. From the same institution, reported in 2018, the addition of tumor load as determined by OSNA was used to create yet another predictive system with a similar AUC. A study from Chulalongkorn Hospital reported in 2018 used a multigene test risk score for disease recurrence (PAM50 ROR) to predict axillary lymph node status in hormone positive, T1 breast cancer patients. There were 34 patients and the AUC was 0.75, and a cut-off value for the score was determined. Finally, in 2018, Prince of Songkhla University reported the use of indocyanine green fluorescent imaging for the detection of SLNs.

Breast conserving surgery and oncoplastic surgery

BCT with ALND was reported in 24 patients from the Thai NCI in 1987 without long-term follow-up; and again in 1989 with 33 stages I to II patients. In a study from Siriraj Hospital, published in 2012, risk factors for recurrence after BCT ("lumpectomy") for DCIS was examined in 135 patients treated between 1999 – 2010. Positive or close surgical margin was the most important risk factor for recurrence. A study from Chulalongkorn Hospital reported in 2017 looked at complications associated with using intraoperative radiation therapy (IORT) to boost the tumor bed in 109 patients undergoing BCS with IORT (Intrabeam System). Complications specific to IORT were not clearly reported. In a study examining residual cancer after BCS, reported in 2017 from Ramathibodi Hospital, in patients with 143 primary breast cancer resections who had secondary surgery as well, residual cancer was found even after free margin excision in as many as 12% (2/25). But conversely, with involved margins, as many as 44% (28/64) did not have any residual cancer. A portable machine with software

for 3-dimensional scanning of intraoperative breast specimens using x-rays was developed by researchers from Prince of Songkhla University in collaboration with the NSDTA, Thailand, reported in 2018. The machine, a prototype ("MiniiScan"), was able to detect lesions and determine resection margins as well as conventional mammography but took a much shorter time.

Breast reconstruction

A report of a transverse rectus abdominis "island flap" for reconstruction after MRM was published in 1987; this was probably a variation of the pedicled TRAM flap. In 1990, two reports from Siriraj Hospital described the first use of pedicled TRAM flap (in 1987), which was done for reconstruction after chest wall resection in 2 cases; thereafter the TRAM flap was used for immediate reconstruction in 5 patients with stages I to II breast cancer. Also described were 2 patients who underwent delayed reconstruction using the TRAM flap, and a prothesis-based procedure ("tissue expander") was used for immediate reconstruction after mastectomy in 2 further patients. Free TRAM was described for 2 breast cancer patients after mastectomy from Ramathibodi Hospital and was published in 1991. Mammoreduction, based on the inferior dermoglandular pedicle, was used for the contralateral breast in a case of immediate reconstruction for ipsilateral breast cancer, as reported from Siriraj Hospital in 1991. A review of postmastectomy breast reconstruction from Ninewells Hospital in Dundee, Scotland, was published in 2001, in which the dominant reconstruction method was the TRAM flap. A case of Deep Inferior Epigastric Perforator (DIEP) free flap used in a breast cancer patient was reported from Siriraj Hospital in 2001. Extended LD flap as the sole reconstructive modality was reported for 46 lesions in 41 patients in 2007, from Ramathibodi Hospital. Good results with minimal morbidity was observed in the short-term (median follow-up of 8 months). Good short-term results (14 months) for immediate pedicled TRAM flap reconstruction was reported for 14 patients from Ratchaburi Hospital in 2008. A study from Chulalongkorn Hospital reported in 2016 looked at the discrepancy between clinical TNM staging and pathological TNM staging in 87 breast cancer patients who underwent mastectomy with immediate reconstruction. The most marked discrepancy was for N staging, and it was suggested that further preoperative imaging study or cytological diagnosis might be used to reduce the discrepancy to better plan reconstructive procedures. A comparison of complications and recovery after surgery between extended LD and LD with prosthesis for breast reconstruction in 31 breast cancer patients was reported from Ramathibodi Hospital in 2019. Both procedures had similar complication rates but LD with prothesis had slightly faster recovery. Also from the same institution in the same year, 63 breast cancer or high-risk patients who underwent 65 nipple sparing mastectomies with reconstruction were followed for evidence of local regional recurrence. After a mean follow-up of 40 months, 3 patients who had cancer experienced locoregional recurrence, 2 in the regional nodes and one had Paget's disease of the nipple.

2021: Conclusion

We have traveled quite far in the past 40 years. The TJS perspective of breast cancer is unavoidably biased but the view has been incredibly wide. We have seen changes in the theory and practice of breast cancer surgery, the rise of adjuvant therapy including chemotherapy, hormonal therapy, targeted therapy and increased use of radiotherapy. Molecular pathology and diagnostic radiology were also included. We also saw dramatic changes in diagnostic strategies and the approach to prognosis, with more empowerment to patients. There were unfortunately too few contributions from other disciplines, but that is in the nature of the specialty journal. While there were real improvements in all aspects of breast cancer, whether it be more accurate diagnosis, the identification of important prognosticators, the introduction of less invasive and less disfiguring surgery, and the dramatic increase in breast cancer survival as well as the inclusion of patients and their families in the therapeutic process, there are still so many remaining issues that require more thought and creativity for their resolution. The current "theory of breast cancer" is inadequate. Why is breast cancer on the rise? We need better diagnostic technology (better accuracy), more precise surgery and systemic therapy suited for the individual patient and her disease ("precision medicine"). Are we doing too little in certain areas (primary and secondary cancer prevention) or too much in others (overdiagnosis and overtreatment)? Are we overemphasizing the seriousness of some conditions (certain types of DCIS), alarming the public with an iatrogenic rise in cancer incidence and then inadvertently creating a sense of achievement by overtreatment? How will we use proven innovations in

a cost-effective manner in an efficient breast cancer care system? With so many questions to ask and countless ways to answer them, there is always a place to publicize your ideas and we, at the TJS, will be ready and more than happy to consider your contributions. Welcome to the next 40 years of the TJS, at least!

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Original Article

Clinical and Oncological Outcomes of Laparoscopic Colorectal Surgery for Colorectal Cancer at Trang Hospital

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Abstract

Background & Objective: Colorectal cancer is the third most common cancer in both men and women in Thailand and around the world. Laparoscopic colectomy (LC) has gained wide acceptance as a curative procedure for colorectal cancer treatment. However, in Thailand, LC is practiced in high-volume hospitals. A predisposing factor for a higher morbidity rate of LC was male gender. The primary aim of this retrospective study was to review the clinical and short-term oncological outcomes of laparoscopic colectomy for colorectal cancer from the preliminary first-hand experience of a general surgeon performing LC at Trang Hospital. The secondary aim was to test the hypothesis that male gender has no impact on the clinical and short-term oncological outcomes.

Patients and Methods: A retrospective study was conducted at Trang hospital in all colorectal cancer patients who underwent laparoscopic colorectal surgery between August 2017 and December 2019. Patient characteristics, perioperative, pathologic and short-term oncological outcomes were reported and compared between the genders.

Results: In 19 colorectal cancer patients who underwent laparoscopic colorectal resection, there was a significant difference in tumor size between the men and women ($p = 0.049$) but no differences in perioperative outcomes between the two genders ($p > 0.05$). The overall conversion rate was 26%, the intraoperative complication rate was 5% and the postoperative complication rate was 16%. The mean follow-up period was 29 ± 11 months. There were no differences in the disease-free survival (DFS) (67% vs. 90%; $p = 0.224$) and overall survival (OS) (78% vs. 100%; $p = 0.125$) between men and women. The 2-year DFS and OS of all patients were 83% and 89%, respectively.

Conclusion: General surgeons can perform laparoscopic colorectal resection effectively and safely with acceptable outcomes. Male gender has no impact on the outcomes of laparoscopic colorectal resection in patients with colorectal cancer.

Keywords: Laparoscopic colorectal surgery, Colorectal cancer, Short-term outcomes

Introduction

Colorectal cancer (CRC) is the third most common cause of death from cancer among both men and women in Thailand and around the world.[1,2] Laparoscopic colectomy (LC) has gained wide acceptance as a curative surgical procedure for colorectal cancer since it was first introduced in 1991. Many randomized controlled trials have showed that LC has better short-term surgical outcomes while providing equally effective oncological outcomes compared to open colectomy (OC).[3-8]

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Between 2004 to 2014, the rate of LC has increased to more than 50% in high-income countries, including South Korea, the Netherlands and the United States.[9]

In Thailand, there appears to be a slow adoption rate of LC. The majority of LC for CRC is still being practiced only in high-volume hospitals by board-certified colorectal surgeons or well-trained laparoscopic surgeons. Some limitations could be due to surgeon-related factors (e.g. a steep learning curve for LC, and lack of adequate training or mentorship system) and specific regional health system factors (e.g. financial constraints, operating room time and resource limitations, unfavorable hospital reimbursement models and lack of access to relevant technology).[2] With the increasing need and desire to provide the benefits of LC to all colorectal patients, from the point of view of Thai general surgeons, it is important to increase the use of LC in low volume hospitals as well.

LC for CRC performed by general surgeons at Trang hospital was begun in August 2017. In the initial phase of LC, understanding the technical aspects of the procedure and being aware of risk factors related to operative complications are essential to minimizing operative morbidity and mortality. Previous studies have shown that male sex, lower location of rectal cancer, larger tumor size, preoperative chemoradiation (CCRT), and longer operative time were associated with a higher risk of postoperative morbidity.[10] Anastomotic leakage was reported to be more common among men, which may be related to their narrow pelvises.[10-13] A study by Kit et al[14] found that the conversion rate among patients was 2.7 times higher in men than in women. Male gender was a significant risk factor for conversion to open surgery in other studies as well.[15-18] In practice, however, some surgeons have observed a higher conversion and complication rates in female than in male patients.

The primary aim of this retrospective study was to review the clinical and short-term oncological outcomes of laparoscopic colectomy for colorectal cancer from the preliminary first-hand experience of a general surgeon at Trang Hospital. The secondary aim was to test the hypothesis that male gender has no impact on the clinical and short-term oncological outcomes.

Patients and Methods

Medical records of 21 patients who underwent laparoscopic colectomy between August 2017 and December 2019 at Trang Hospital were reviewed. Two patients with pathologic reports of adenoma were excluded. The data of 19 patients who had adenocarcinoma and were followed up until December 2020 were collected for analysis; these included baseline characteristics, perioperative outcomes, pathologic outcomes and short-term oncological outcomes. The outcomes of all patients were compared between genders.

All statistical analyses were performed using the statistical package SPSS v.26.0 (IBM, New York, USA). The outcomes of both genders were compared using the chi-square and Fisher's exact test for categorical variables and t test for continuous variables. Disease free survival (DFS) and overall survival (OS) were estimated using the Kaplan-Meier method and compared using the log-rank test. A p value of 0.05 or less was considered statistically significant. Institutional Review Board approval was obtained for this study.

Results

Data of all 19 patients who had the pathologic diagnosis of adenocarcinoma in between August 2017 and December 2019, and were followed up until December 2020 were collected retrospectively for analysis. There were 9 men (47%) and 10 women (53%). The mean age ± SD of all patients was 59.6 ± 16.6 years (range, 27 to 84 years). Most patients had rectal cancer (63%). Most did not receive preoperative chemoradiation (84.2%). The mean maximal tumor diameter ± SD was 50 ± 21.3 mm (range, 20 to 100 mm.). One female and two male rectal cancer patients received neoadjuvant chemoradiation therapy (CCRT) because of stage IV disease or large tumor size, although there was no obstruction. Most patients underwent laparoscopic colectomy within 4 weeks after completion of clinical or radiological staging. A comparison of preoperative data between male and female patients is shown in Table 1. There was a significant difference in tumor size between the two genders ($p = 0.049$).

The mean operative time ± SD of all patients was 301 ± 97 mins (range, 180 to 538 mins). The mean number of retrieved lymph nodes ± SD was 13 ± 7. The conversion rate was 26% (5/19). Three cases (one male and two female patients) required conversion to open surgery due to large tumor size making laparoscopic manipulation difficult.

Table 1 Patient characteristics

Characteristic	Men (N=9)	Women (N=10)	*p*-value
Age (years): mean ± SD	55.3 ± 17.9	63.5 ± 15.3	0.299
Tumor location: number (%)			0.078
Right side	0	2 (20)	
Left side exclude rectum	1 (11)	4 (40)	
Rectum	8 (89)	4 (40)	
Diameter of tumor (mm): mean ± SD	60.0 ± 18.9	41.0 ± 19.9	0.049
Preoperative therapy: number (%)			0.201
Chemotherapy	2 (22)	0	
Chemoradiotherapy	0	1 (10)	

Table 2 Perioperative outcomes

Outcome	Men (N=9)	Women (N=10)	*p*-value
Operating time (minutes): mean ± SD	290.3 ± 77.6	310.1 ± 115.4	0.671
Lymph nodes harvested (number): mean ± SD	13 ± 6	12 ± 8	0.935
Conversion to open surgery: number (%)	2 (22)	3 (30)	0.999
Intraoperative complications: number (%)			0.999
Bladder injury	0	1 (10)	
Colostomy	1 (11)	2 (20)	0.999
Postoperative complications: number (%)			0.399
Urinary tract infection	0	1 (10)	
Anastomotic leakage	0	0	
Wound infection	0	1 (10)	
Bowel obstruction	1 (11.1)	0	
Deaths: number (%)	0	0	
Length of hospital stay (days): mean ± SD	9 ± 4	9 ± 2	0.725

One male patient with stage IV rectal cancer needed conversion to open surgery because of failure to insert the linear stapler passed his 10 cm size tumor in a narrow pelvic space for distal rectal transection. The last case that required conversion was a female patient who had received preoperative CCRT.

The overall complication rate was 21% (4/19). There was one intraoperative complication, which was a bladder injury occurring while dissecting a T4 rectal tumor from the bladder. This was detected intraoperatively and was successfully treated by conversion to open surgery to determine whether simple suture repair or partial cystectomy should be performed. There were 3 postoperative complications, including one urinary tract infection, one wound infection, and one with an episode of bowel obstruction.

The mean length of hospital stay was 9 ± 3 days. There was no difference in perioperative outcomes between genders (Table 2). Male and female patients were similar each other, in terms of operating time, number of harvested lymph nodes, conversion to open surgery, intraoperative complications, postoperative complications and length of hospital stay. There was no death within 30 days of surgery in either group. The most common tumor histology was well differentiated adenocarcinoma, seen in 84% of all patients (16/19). There was no significant difference in pathologic findings between genders (Table 3). Tumor margins were free from cancer in all resections.

The mean follow-up period ± SD was 29 ± 11 months, with a median follow-up of 32 months (range, 5 to 41 months).

Table 3 Pathologic outcome

Outcome	Men (N=9)	Women (N=10)	*p*-value
Tumor differentiation: number (%)			1.000
Well differentiated	8 (89)	8 (80)	
Moderately differentiated	1 (11)	2 (20)	
Poorly differentiated	0	0	
T category: number (%)			0.466
T1	1 (11)	1 (10)	
T2	0	2 (20)	
T3	6 (67)	4 (40)	
T4	2 (22)	3 (30)	
N category: number (%)			0.08
N0	6 (67)	5 (50)	
N1	3 (33)	1 (10)	
N2	0	4 (40)	
M category: number (%)			0.582
M0	7 (78)	9 (90)	
M1	2 (22)	1 (10)	
pTNM stage: number (%)			0.699
I	1 (11)	2 (20)	
II	4 (45)	3 (30)	
III	2 (22)	4 (40)	
IV	2 (22)	1 (10)	
Lymphovascular invasion: number (%)			0.252
Yes	4 (44)	2 (20)	
No	5 (56)	8 (80)	
Resection margin positive: number (%)	0	0	

Table 4 Oncological outcomes

Outcome	Men (N=9)	Women (N=10)	*p*-value
Postoperative chemotherapy: number (%)	6 (67)	6 (60)	0.999
Recurrence: number (%)			0.400
Liver	1 (11.1)	0	
Lung	0	0	
Distant lymph node	0	0	
Other local recurrence	0	0	
Follow-up time (months): mean ± SD	26.9 ± 12.5	31.5 ± 8.7	0.360

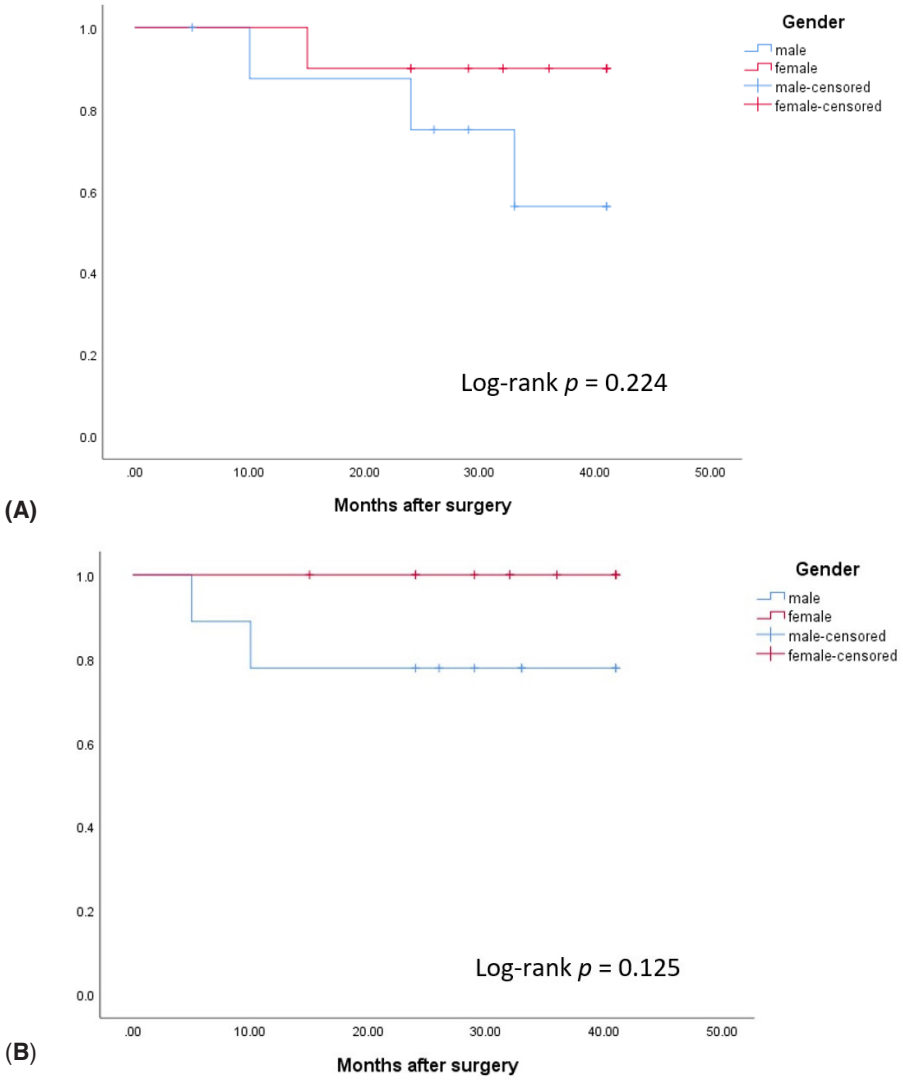

Figure 1 Kaplan-Meier curves of disease-free survival (A), and over-all survival (B) overall survival, after laparoscopic colectomy; log-rank test p-values are also provided.

Postoperative adjuvant chemotherapy was given to 63% of patients (12/19), with a similar proportion for each of the two genders. There was no local recurrence. Unfortunately, one male patient had liver metastasis. There was no difference in the recurrence rates between genders, as shown in Table 4. There was no difference in disease free survival (DFS) (67% vs. 90%; $p = 0.224$) and overall survival (OS) (78% vs. 100%; $p = 0.125$) between male and female patients (Figure 1). The 2-year DFS and OS rates of all patients were 83% and 89%, respectively.

Discussion

Previous studies have shown that laparoscopic colectomy in men is associated with a higher postoperative morbidity than in women. Multiple studies have found that male gender is one of the risk factors for anastomotic leakage.[10-13] Kit et al[14] found that the conversion rate was 2.7 times higher in men than women. Other studies also found that male gender is a risk factor for conversion to open surgery.[15-18] In the present study, there was no anastomotic leakage. The conversion rate was similar between men and women. Complications were even slightly more frequent in women than in men, but without statistical significance.

The overall conversion rate in this study was 26%, higher than the 0 to 25% seen in others studies.[3,6,10-11,14-15,17-22] This higher rate can be explained by the learning curve period.

A study found that the conversion rate was 38% during the first year of implementing LC, which gradually decreased to 16% in the 6th year.[24] The effect of conversion on patient morbidity and mortality is unclear. Recent studies describe similar outcomes after conversion to open surgery compared to the open surgery without LC.[25]

The reported incidence of intraoperative adverse events ranges from 0 to 8%.[23,26] The intraoperative complication rate in the present study was 5%, which was within the reported range. Previous studies reported postoperative complication rates to be between 4% to 17% for colorectal cancer surgery[8,20,22-23] and 21% to 32% in rectal cancer surgery.[6,10,22] The postoperative complication rate of 16% in the present study was also within the published range. The 30 day postoperative mortality was reportedly between 0.7% to 2.9%[6,10,21-23,26] but there was no 30 day postoperative mortality in the present study.

The two-year recurrence rate in the present study was 7%, and was due to distant recurrence. There was no local recurrence, which suggested that oncological clearance was acceptable. This recurrence rate compared favorably to those of the published literature (9% to 25%).[5-6,8,20] The one distant recurrence in the present study was liver metastasis in a male patient, and the liver was the most common recurrence site as described by Fleshman[7] and Miyo.[20] Male gender was also found to be a predictive factor of colorectal cancer recurrence in a previous study.[22]

In the present study the two-year disease-free survival (DFS) of all patients was 83% and the two-year overall survival (OS) of all patients was 89%. These survival probabilities were similar to those previous reported, which found the two-year DFS to be between 74% to 99%,[8,19-20,23] and the two-year OS to be 75% to 92%.[4,6,18,20,23-24] No significant differences in these survivals between the two genders were found in the present study. The study by Carter, et al.[27] found that women had significant longer survival than men. The present study found a similar, but non-significant, trend. The low recurrence rate and high OS in the present study maybe due to the short follow-up and favorable tumor histology.

There were several limitations in the present study. Firstly, the number of patients included in this study was much too small. Larger sample sizes will enable a more reliable and powerful comparison. Secondly, colorectal cancers at different sites were pooled together in the analysis of the outcomes. This is debatable because the lymphatic drainage route, extent of dissection, operative techniques, and even biologic behavior are different for tumors at different locations. In future studies, with an increase in the number of patients, an analysis based on tumor location may be possible. Lastly, only short-term results were reported, and longer follow-up should also be done.

Conclusion

General surgeons can perform laparoscopic colorectal resection effectively and safely with acceptable outcomes. Male gender has no impact on the outcomes of laparoscopic colorectal resection in patients with colorectal cancer in the present study.

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บทคัดย่อ **ผลการรักษาทางคลินิก และมะเร็งวิทยาของการผ่าตัด Laparoscopic colorectal surgery ในผู้ป่วยมะเร็งลำไส้ใหญ่และไส้ตรงโดยศัลยแพทย์ทั่วไปในโรงพยาบาลตรัง**

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กลุ่มงานศัลยกรรม โรงพยาบาลตรัง

ความเป็นมาและวัตถุประสงค์: มะเร็งลำไส้ใหญ่และไส้ตรง เป็นมะเร็งที่เป็นสาเหตุของการเสียชีวิต 3 อันดับแรกของทั้งเพศชายและเพศหญิงในโลกและในประเทศไทย การผ่าตัดส่องกล้องรักษามะเร็งลำไส้ใหญ่และไส้ตรงเป็นที่ยอมรับอย่างกว้างขวาง ในประเทศไทยการผ่าตัดแบบนี้ยังจำกัดในโรงพยาบาลมหาวิทยาลัยขนาดใหญ่ และการผ่าตัดนี้ในเพศชายเป็นปัจจัยที่ทำให้เกิดทุพพลภาพหลังการผ่าตัดมากขึ้น วัตถุประสงค์หลักของการศึกษานี้ คือ รายงานผลการรักษาทางคลินิกและมะเร็งวิทยาในระยะสั้นของผู้ป่วยที่ได้รับการวินิจฉัยว่าเป็นมะเร็งลำไส้ใหญ่และไส้ตรง ที่ได้รับการรักษาโดยการผ่าตัดส่องกล้องตัดต่อลำไส้ใหญ่ในโรงพยาบาลตรัง และวัตถุประสงค์รอง คือ การทดสอบสมมติฐานว่าเพศชายไม่ได้มีผลต่อผลการรักษาทางคลินิกและมะเร็งวิทยาในระยะสั้นของผู้ป่วย

วิธีการศึกษา: รวบรวมข้อมูลผู้ป่วยทั้งหมด 19 รายที่มีผลพยาธิวิทยาวินิจฉัยว่าเป็นมะเร็งลำไส้ใหญ่และไส้ตรงที่ได้รับการผ่าตัดโดยการผ่าตัดส่องกล้องตัดต่อลำไส้ใหญ่ ในโรงพยาบาลตรังตั้งแต่เดือนสิงหาคม 2560 ถึงเดือนธันวาคม 2562 โดยเก็บข้อมูลและรายงานผลการผ่าตัดในระยะสั้น ผลทางพยาธิมะเร็งวิทยา และผลการรักษา อัตราชีพรอดอย่างปราศจากโรค อัตราการรอดชีพโดยรวมจนถึงเดือนธันวาคม 2563 ในผู้ป่วยทั้งหมดและศึกษาเปรียบเทียบผลดังกล่าวระหว่างกลุ่มผู้ป่วยเพศชายและเพศหญิงร่วมด้วย

ผลการศึกษา: ผู้ป่วยมะเร็งลำไส้ใหญ่และไส้ตรงที่ได้รับการผ่าตัดส่องกล้องตัดต่อลำไส้ใหญ่ทั้งหมด19 ราย ผู้ป่วยเพศชายมีค่าเฉลี่ยขนาดเนื้องอกใหญ่กว่าเพศหญิงอย่างมีนัยสำคัญ ($p = 0.049$) แต่ไม่พบความแตกต่างของผลการผ่าตัดในระหว่างเพศ อัตราการเปลี่ยนผ่าตัดจากการส่องกล้องเป็นเปิดหน้าท้องทั้งหมดร้อยละ 26 มีภาวะแทรกซ้อนทั้งหมดร้อยละ 21 แบ่งเป็นภาวะแทรกซ้อนระหว่างผ่าตัดร้อยละ 5 และ ภาวะแทรกซ้อนหลังการผ่าตัดร้อยละ 16 ซึ่งไม่แตกต่างกันในทั้งสองเพศ ไม่มีผู้ป่วยเสียชีวิตจากการผ่าตัด ระยะเวลาการนอนโรงพยาบาลเฉลี่ยทั้งหมด คือ 9 ± 3 วัน ไม่ความแตกต่างของอัตราการเปลี่ยนเป็นผ่าตัดเปิดหน้าท้อง ภาวะแทรกซ้อน และระยะเวลาการนอนโรงพยาบาลในเพศชายและหญิง การติดตามผู้ป่วยทั้งหมดเป็นระยะเวลาเฉลี่ย 29 ± 11 เดือน (พิสัย 5 ถึง 41 เดือน) อัตราชีพรอดอย่างปราศจากโรค (disease free survival) และอัตราการชีพรอดโดยรวม (overall survival) ระยะ 2 ปี คิดเป็นร้อยละ 83 และ 89 ตามลำดับและไม่พบว่าแตกต่างกันทางสถิติในระหว่างเพศ

สรุปผลการศึกษา: การผ่าตัดส่องกล้องตัดต่อลำไส้ใหญ่ในผู้ป่วยมะเร็งลำไส้ใหญ่และไส้ตรงโดยศัลยแพทย์ทั่วไปพบว่ามีความปลอดภัยและมีประสิทธิภาพที่ยอมรับได้ และเพศไม่ได้ส่งผลต่อผลลัพธ์ของการรักษา ควรส่งเสริมการผ่าตัดส่องกล้องให้มากขึ้นในกลุ่มศัลยแพทย์ทั่วไป

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Original Article

SURPY Python Toolkit for Data Analysis

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Abstract ***Objective:*** SURPY is a Python-based package for statistical analysis available on PyPi repository. The present study aims to evaluate performance of the SURPY package in providing basic data analysis compared to a standard statistical package, Stata v.14 (StataCorp, College Station, TX, USA).

Methods: Datasets from previously published studies were retrieved for analysis. The data was transferred to the .DTA format for analysis using the Stata v.14 program and was imported as a dataframe into the Python 3.0 environment, to be analysed by the 'soap' (surgical outcome analysis program) package of SURPY 1.1.7. Results of the analysis from the 2 programs were compared.

Results: The soap package from the SURPY program was able to import data stored in the Microsoft Excel format and calculate basic descriptive statistics. The program correctly performed *t*-tests and Mann-Whitney U tests. Also, the program was able to produce Kaplan-Meier survival curves and perform log-rank tests, which gave similar outputs compared to those from the Stata program.

Conclusion: The SURPY program can be used for simple data analysis, which could be useful for surgeons who are not familiar with typing commands in commonly used statistical programs. The SURPY program can be further developed to incorporate graphic user interface.

Keywords: Data analysis, Python program

Introduction

Various computer packages are available for surgical data analysis, such as Stata, the R program, and Microsoft Excel. However, most of these programs require a certain level of computing skills and might not be friendly enough for the average surgeon to use. Also, some statistical packages are not suitable for datasets with large dimensions.[1]

Python is a high-level programming language created in the late 1980s by Guido van Rossum and his colleagues in the Netherlands.[2] As the program is developed under an open-source license, and is currently administered by the Python Software Foundation, it is free to use, modify and distribute. The python interpreter, now version 3.9.0 (October 2020), is free to download into most operating systems, including

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Windows, Linux and Mac OS.2 The repository hub for Python open-source packages is PyPI (https://pypi.org). Python has become more popular in recent years among data scientists, especially for statistical analysis, natural language processing and machine learning.[3,4] In the health care services, Python packages have been built for various purposes, such as medical image analysis, machine learning for risk prediction, clinical trial data management and bioinformatics.[5-8]

SURPY is a Python-based program, developed by the authors, designed for surgical data analysis and ease of use. The program includes packages for data description, statistical testing, tests for association, and simple survival analysis. Surgical data analysis usually includes data summary, analysis for association between variables and data displays with graphs and tables. The present study aims to compare the results of simple data analysis between SURPY and Stata programs.

Materials and Methods

SURPY began as a Python project to provide a simple tool for basic statistical analysis in surgery. The first version was launched in PyPI on January 25, 2021. The latest version, SURPY 1.1.7 released on April 8, 2021, was used in the present study. The 'soap' package in the SURPY at that time included sub-programs for data description (soaplore(data, outcome), parametric and non-parametric tests between 2 groups (soap_TU(data,outcome,variable)), soap_multi_T(data, outcome) [tests of multiple quantitative variables between groups defined by a fixed binary variable] and soap_T_for_multibinary(data, variable) [tests of a fixed quantitative variable between groups defined by multiple binary variables], chi-square tests of association between 2 categorical variables (soap.soap_x_tab(data, variable_a, variable_b)) and (soap_x_across(data,outcome)), and Kaplan-Meier survival curve estimation (single_kmc(data, status, interval)) as well as comparisons between survival curves (compare_kmc(data, factor, status, interval)) (Figure 1).

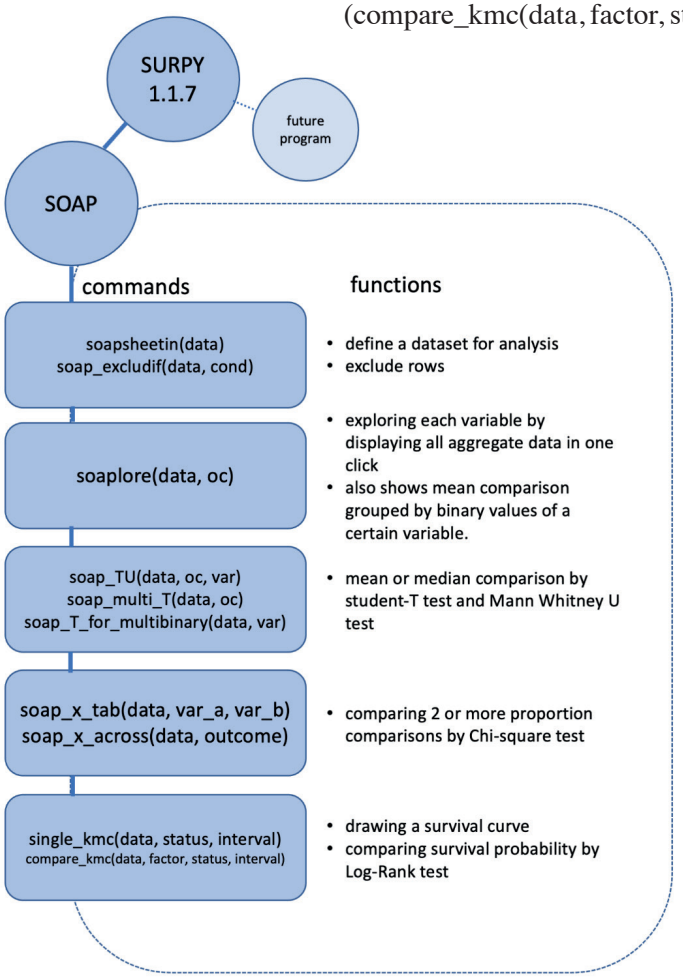


Figure 1 Components of the soap program in SURPY package version 1.1.7 released April 8, 2021

Datasets derived from previously published studies by the authors were used in the present study for re-analysis using both the SURPY program version 1.1.6 and a reference statistical program, Stata version 14 (StataCorp, College Station, TX, USA). The results of this analysis were compared in terms descriptive or summary statistics, p-values from t-test and chi square tests, and Kaplan-Meier plots.

Results

As all datasets were originally stored in the Microsoft Excel format, they were converted to the DTA file format (filename.dta) by using the StatTransfer version 12 program. Accessing the SURPY package can be done through downloading from PyPi (https://pypi.org/project/SURPY/) (Figure 2) and the manual can be found on https://github.com/sasurasa/Surgical-Outcome-Analysis-on-Python/blob/SURPY/SURPY%20manual%20190321SS.pdf. SURPY correctly displays summary statistics for each variable in the dataset. The program can also compare mean values of quantitative variables between categories of binary variables (Figure 3).

In significance testing of quantitative variables between 2 groups, either Student's t test or Mann-Whitney U test are commonly used. The soap package on SURPY can perform these tests well. All p-values obtained using the package were similar to those calculated by the reference program. In addition, the package can display Box-and-Whisker plots for visual comparison between groups (Figure 4).

When a researcher needs to perform multiple comparisons of quantitative data between categories of a fixed binary variable, the code 'sp.soap_multi_T(data, oc)' returns the same results as when using the Stata program. Similarly, performing comparisons of a single quantitative variable between categories of multiple binary variables could be done with one click using the command 'sp.soap_T_for_multibinary'.

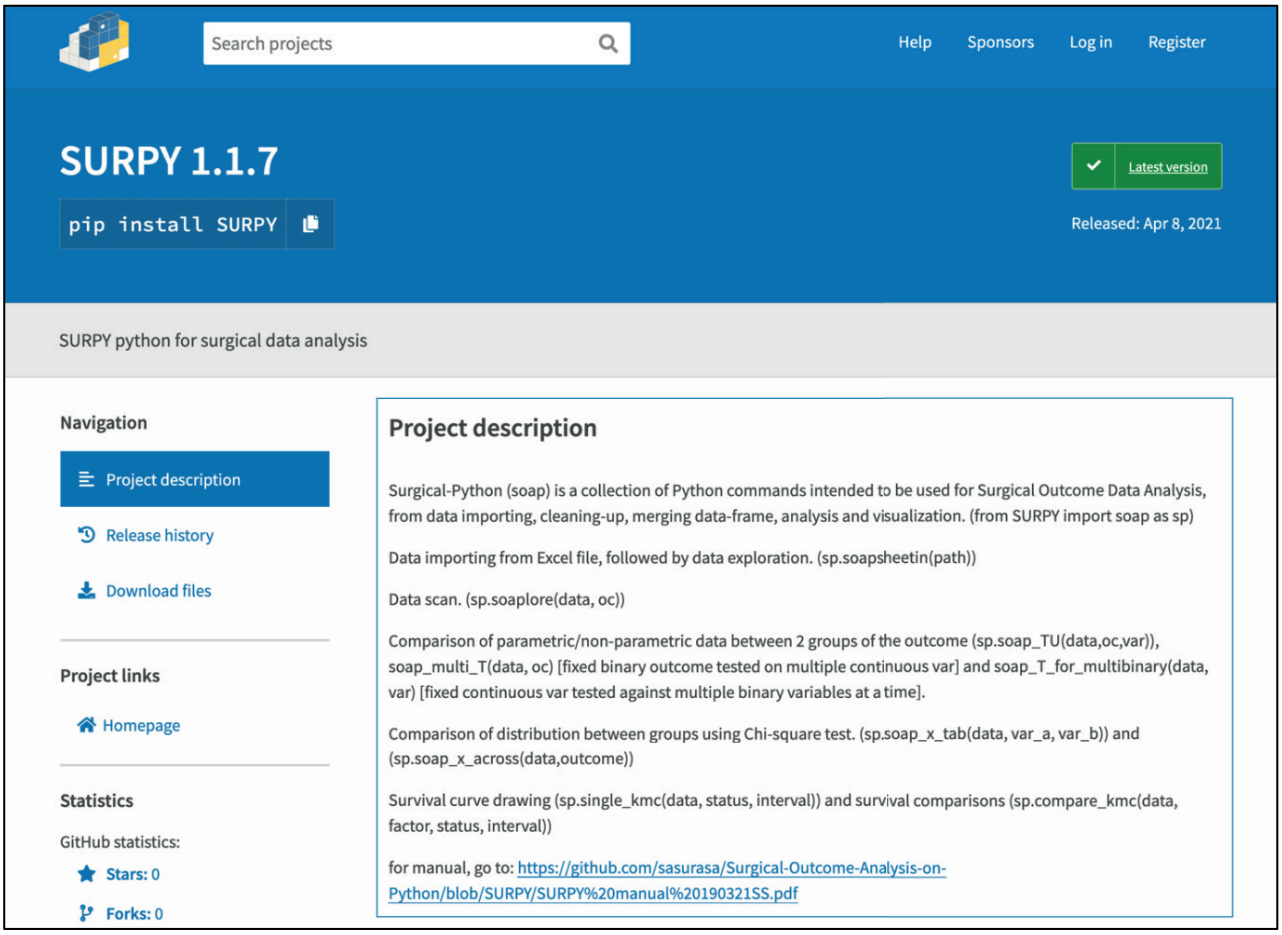


Figure 2 The repository page of the SURPY program which can be accessed at https://pypi.org/project/SURPY/

A

	bh	cea	modesx	operation	treatyear
count	716.000000	1112.000000	1159.000000	1162.000000	1164.000000
mean	196.500000	163.750899	0.073339	5.067126	2008.759450
std	373.926905	728.424751	0.279968	3.946320	2.585535
min	113.000000	0.000000	0.000000	0.000000	2004.000000
25%	155.000000	4.000000	0.000000	3.000000	2007.000000
50%	161.000000	17.000000	0.000000	4.000000	2009.000000
75%	168.000000	88.000000	0.000000	7.000000	2011.000000
max	7174.000000	10500.000000	4.000000	15.000000	2014.000000

	surgeon	ajcc	lhs	fstchm	totcyc
count	1160.000000	1158.000000	1149.000000	1135.000000	797.000000
mean	17.174138	2.702936	14.280244	4.103084	5.336261
std	26.437626	0.884814	8.777732	2.647574	4.627029
min	0.000000	1.000000	2.000000	0.000000	0.000000
25%	8.000000	2.000000	10.000000	1.000000	2.000000
50%	8.000000	3.000000	12.000000	4.000000	6.000000
75%	12.000000	3.000000	16.000000	7.000000	8.000000
max	99.000000	4.000000	88.000000	8.000000	36.000000

B

sex	cea	modesx	operation	treatyear	surgeon	ajcc
0	185.031509	0.070288	5.022364	2008.771930	16.982400	2.664526
1	138.540275	0.076923	5.119403	2008.744879	17.398131	2.747664

sex	lhs	fstchm	totcyc	targetx	ocmtcour	opyear
0	14.672609	4.117550	5.108747	25076.190231	7.543750	2008.771930
1	13.825188	4.086629	5.593583	20683.046703	7.491018	2008.744879

Figure 3 Output of the command sp.soaplore(data, 'sex') displaying descriptive statistics; (A) summary of each variable displaying the mean, median, minimum, maximum, standard deviation and interquartile range; (B) displaying mean values of quantitative variables according to categories of a binary variable (sex in this case) for comparative purposes.

A

```
>>> sp.soap_TU(data, 'ev', 'lsm')
lsm
     count       mean        std   min    25%   50%   75%   max
ev
0    15.0  17.366667  20.646053   3.0   5.55   8.2  14.5  75.0
1     5.0  33.700000  25.119415  11.3  16.80  28.9  36.5  75.0
------------------------------------------------------------

Ttest_indResult(statistic=-1.4562389048044695, pvalue=0.16254863419294766)
MannwhitneyuResult(statistic=14.5, pvalue=0.024724498879759953)
```

B

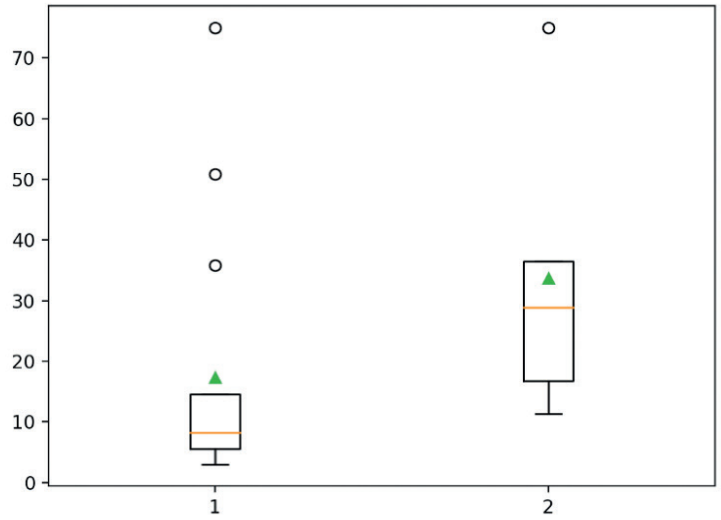


Figure 4 Demonstrating (A) the comparison of the means and medians between 2 groups, as well as performing the *t*-test and Mann Whitney U test; (B) Box-and-Whisker plot of a comparison of a quantitative variable between 2 categories, which shows values of the median (orange lines), the mean (green triangles), interquartile range (box), whiskers, and outliers (circles)

```
>>> sp.soap_x_tab(data, 'ev', 'portalht')
================================================================================

Data dimension:  (2, 2)
Chi-square value =  0.0
Chisquare p-value = 1.0
================================================================================



         ev  portalht0  portalht1  horizonsum  %portalht0  %portalht1
0         0         14          1          15   93.333333    6.666667
1         1          4          1           5   80.000000   20.000000
2  vertisum         18          2          20   90.000000   10.000000
```

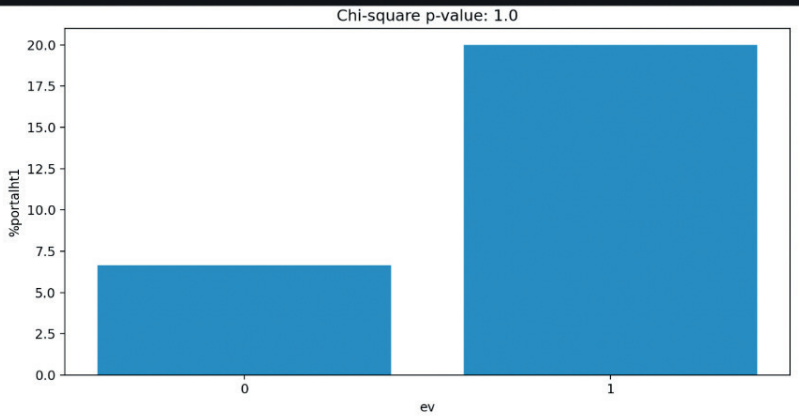
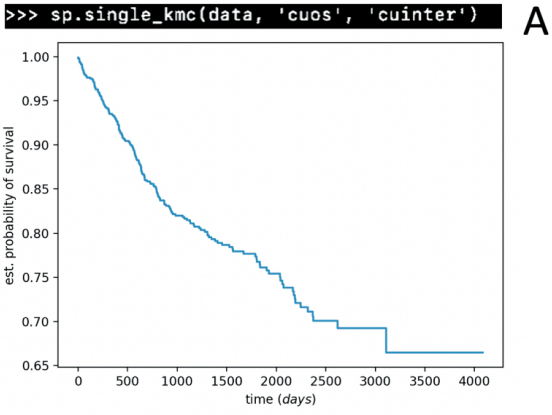
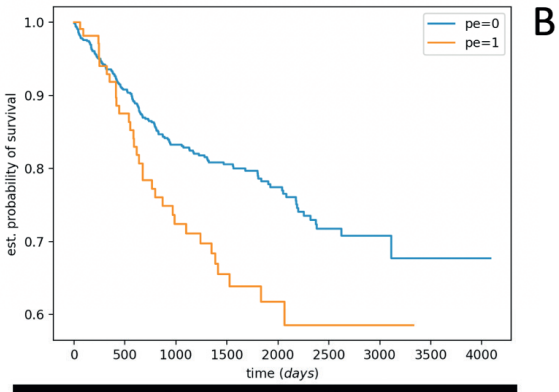


Figure 5 Demonstrating a 2 x 2 table, results of chi-square testing and p-values, and a bar-chart showing percentages






```
test_statistic    p  -log2(p)
          7.70 0.01      7.50
```

Figure 6 Showing Kaplan Meier survival curves produced by the soap program on SURPY 1.1.7 for: (A) a single group; (B) for 2 groups with a log-rank test statistic.

Performing cross tabulation of any 2 binary categorical variables or chi-square tests for 2 binary variables using the code 'sp.soap_x_tab(data, var_a, var_b) gave the same p-values as those derived from Stata (Figure 5). In addition, the soap program correctly calculated chi-square tests for all pairs of categorical variables in the dataset.

Similar to Stata's sts command, the SURPY program can display simple Kaplan-Meier survival curves (Figure 6). In addition, the program also correctly returns p-values of the log-rank test. However, SURPY has not been scripted for comparing differences in survival probabilities for 3 or more categories. In addition, it has not been scripted for customization of the graphs.

Discussion

The SURPY program is an initiative by the authors to develop a clinician-friendly platform for statistical analysis of large datasets. These first versions of the package were to help clinicians calculate basic summary statistics, perform simple statistical or significance tests, and to do basic survival analysis with Kaplan-Meier estimates and log-rank tests These requirements were derived from our experience in teaching data analysis for surgical trainees.

Python is an open-source interpretation language that has gained increasing popularity for use in writing programs for analyzing large, complex data sets.9 In the health sciences, python is employed as a programming language for various data-driven uses including large longitudinal data mining, deep learning, predictive modelling and high-throughput genomic data analysis.[10-12]

The SURPY package is aimed towards basic statistical analysis. Although typical clinical or surgical datasets can be managed effectively with various available statistical packages, we found that many surgeons avoided performing data analysis themselves because of the perceived difficulty in using these available packages. The goal of SURPY is to facilitate basic data analysis once a dataset is uploaded and types of variables in the data are defined. With a couple of clicks, all statistical associations of interest within the datasheet will be displayed in forms of networking diagrams and graphs.

The 'soap' is our pilot release of a more comprehensive toolkit, to demonstrate proof of concept. The program returns basic summary statistics across the sheet, as well as all statistical associations when categorical outcomes of interest are defined. One limitation of the current program is that the script does not automatically discriminate between quantitative or categorical numerical values. For tests of association, the program is scripted to identify a numerical variable with 5 or less unique values as a categorical variable.

To provide a comprehensive solution for all surgical data analysis, the program requires continuing development. Notably, functions for multivariate analysis, customized tests of association and a graphic user interface need to be provided to enhance the usefulness of the program.

Conclusion

In summary, the soap package of the SURPY program was developed for surgical data analysis. The release of the program and benchmarking against a standard statistics program have proven its original concept that automation of data processing is feasible.

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Original Article

Validation of Euroscore II Cut-off at 12% for Active Infective Endocarditis

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Abstract

Objective: Patients with infective endocarditis (IE) have a high risk of perioperative death. An accurate and reliable predictive score is crucial for decision making. The aim of this study is to externally validate Euroscore II, at a cut-off of 12%, in the prediction of hospital mortality.

Patients and Methods: Data were collected from medical records of patients who were diagnosed with active IE between June 1st 2017 and June 1st 2020. Preoperative Euroscore II was calculated. Patients were categorized into 2 groups according to Euroscore II: those with scores < 12 and ≥ 12. The discriminatory ability using the cut-off value was determined from observed perioperative mortality.

Results: There were 43 patients diagnosed with active IE. None had prosthetic IE. Most were male (56%). The mean age was 47.7 years. Large vegetation was found in 89%. Only one patient had ejection fraction < 40%. The most common clinical manifestation was heart failure (81%). Around four-fifths had single valvular involvement (82%). The most affected site was the aortic valve (44%). Median time from diagnosis to surgery was 7.5 days. Median duration of aortic cross-clamp time and cardiopulmonary bypass time were 83 mins and 99 mins respectively. The mean Euroscore II was 8.6%. There was 7% mortality (3/43). All deaths occurred in patients with Euroscore II ≥ 12 (30% actual mortality in this group). By using cut-off value of Euroscore II at 12%, the area under the receiver operating characteristic curve was 91.3% (95% CI 85.3 – 97.2%).

Conclusion: This study confirmed the validity of using Euroscore II ≥ 12% to help discriminate high-risk active IE patients. It might be accurate enough external to help decision making for surgery in high-risk active IE patients in centers with similar circumstances.

Keywords: Active infective endocarditis, Euroscore II, External validity

Introduction

From our previous study, active infective endocarditis (IE) patients with values of Euroscore II at least 12% had significantly higher mortality when compared to patients with Euroscore II less than 12%.[1] In the present study, we aimed to externally validate this cut-off value in an independent group of patients with active IE. The management of IE is focused on early surgery, but patients who undergo early surgery have a 50% chance of active IE. Active IE might increase hospital mortality by up to 20 %.[2,3] The ability to accurately predict hospital mortality is therefore of paramount importance in surgical decision making.

The original Euroscore is one of the most useful

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scores for predicting in-hospital mortality and long-term survival in patients undergoing coronary artery bypass grafting (CABG)[4,5] as well as valvular surgery[6]. A limitation of this score is that it overestimates mortality in patients with Euroscore ≤ 6 undergoing valvular surgery, and underestimates mortality in patients with Euroscore > 13.[7,8] Although Euroscore II has better predictive ability than the original Euroscore especially for isolated CABG, CABG with aortic valve replacement (AVR), and isolated valve surgery,[9-11] it still underestimates actual mortality in high-risk patients.[12,13]

Based on these studies, to increase the usefulness and reliability of the Euroscore II, we focused only a subset of diseases in a specific population. We chose patients with active IE, as these patients have relatively poor outcomes after cardiac surgery. The scoring system used for counselling patients and their family must be very accurate in this situation.

Patients and Methods

The present study was approved by the Maharat Nakhon Ratchasima Hospital institutional review board (IRB) on June 18th, 2020. Data were retrospectively collected from patients 18 years or older who were diagnosed as having infective endocarditis according to modified Duke's criteria, between June 1st, 2017 to June 1st, 2020. Patients with intraoperative findings of obvious active endocarditis, and those who had antibiotics treatment less than 4 to 6 weeks were considered to have active IE.[14] Data collected included demographic data; echocardiographic data; type of endocarditis categorized as definite, possible, native, and prosthetic valve endocarditis; and lastly in-hospital mortality. The Euroscore II was calculated using an online application.

All patients were managed by an IE multidisciplinary team. Preoperative evaluation included transthoracic echocardiography (TTE) and coronary angiography (CAG) in patients who were 40 years or older. Surgery was performed via full sternotomy with standard cardiopulmonary bypass under mild to moderate hypothermia (body temperature of 32 to 34 ˚C). Cold-blood cardioplegia was used for myocardial protection. The aortic valve was exposed via oblique aortotomy and the mitral valve was exposed via Waterston groove or biatrial-transseptal approach. Infected valves would be radically excised. Prosthetic valves were selected according to patients' preferences or the surgeon's decision. Valve repair was performed if there was a high likelihood of a successful and durable repair of remaining normal valvular leaflet, as determined by direct visualization and intraoperative transesophageal echocardiography (TEE). All patients were transferred to the ICU for postoperative care, then to a step-down unit. Antibiotics was continued until completion of the planned course.

Numerical data were analyzed and presented in frequencies, percentages, means and standard deviations. P-values less than 0.05 were considered statistically significant. The discriminatory ability of the Euroscore II cut-off at 12% was assessed using estimated area under the receiver operating characteristic curve (AUROC), and its 95% confidence interval (95% CI).

Results

There were 43 patients who had native-valve active endocarditis. There was no patient with prosthetic-valve endocarditis during the study period. Most patients were men (56%). The mean age was 47.7 ± 14.7 years. Comorbidities included renal insufficiency (serum creatinine of at least 2 mg/dL), coronary artery disease, diabetes mellitus, rheumatic heart disease, congenital heart disease, hypertension and stroke (see Table 1). Hypoalbuminemia was seen in 32 patients (74%). Around one-third of patients (37%) had anemia. The presence of vegetation that was larger than 10 mm was found in 32 cases (89%). Only 1 patient (2%) had an ejection fraction (EF) less than 40%. Clinical manifestations included congestive heart failure (81%), new murmur (70%), embolic events (28%) and sepsis (19%).

Around four-fifths of cases had single valvular involvement (82%). There were 8 patients (19%) who had combined aortic and mitral endocarditis. The most affected site was the aortic valve (19 patients, 44%). The second most common site was the mitral valve (15 patients, 35%). Isolated tricuspid endocarditis was found in only 1 patient (2%).

All patients underwent urgent surgery. Median interval from the day of diagnosis to surgery was 7.5 days with an interquartile range (IQR) of 5 to 15 days. The median aortic cross-clamp time was 83 minutes (IQR, 66 to 108 mins) and the median cardiopulmonary-bypass (CPB) time was 99 minutes (IQR, 79 to 134 mins). The median length of stay in cardiac-care unit (CCU) was 5 days (IQR, 3 to 10 days). The median length of postoperative stay was 15 days (IQR, 10 to 23 days). The median length of overall-hospital stay was 30 days (IQR, 20 to 43 days) (see Table 1).

Table 1 Baseline, disease and operative characteristics of patients

		Euroscore		
Characteristics	**All patients (n=43)**	**< 12 (n = 33)**	**≥ 12 (n = 10)**	***p*-value**
Age(years): mean (SD)	47.7 (14.7)	57.7 (10.2)	44.6 (14.7)	**0.012**
Male gender: num (%)	24 (56)	18 (55)	6 (60)	0.999
Comorbid disease: num (%)				
DM	3 (7)	1 (3)	2 (20)	0.130
HT	8 (19)	5 (15)	3 (30)	0.362
Renal insufficiency (Creatinine > 2.0)	1 (2)	1 (3)	0	0.999
Coronary artery disease	2 (5)	1 (3)	1 (10)	0.415
Stroke	2 (5)	2 (6)	0	0.999
Rheumatic	4 (9)	4 (12)	0	0.558
Congenital heart disease	4 (9)	2 (6)	2 (20)	0.226
Laboratory finding: num (%)				
Albumin < 3 gm/dL	32 (74.4)	23 (69.7)	9 (90)	0.409
Hct < 30%	16 (37.2)	13 (39.4)	3 (30)	0.719
EF < 40%: num (%)	1 (2)	1 (3)	0	0.999
Vegetation size: num (%)				0.591
< 10 mm.	4 (11)	4 (14)	0	
10 to 15 mm.	18 (50)	15 (52)	3 (30)	
> 15 mm.	14 (39)	10 (34)	4 (40)	
Clinical presentation: num (%)				
New heart murmur	30 (70)	23 (70)	7 (70)	0.999
Embolic events	12 (28)	10 (30)	2 (20)	0.698
Sepsis	8 (19)	6 (18)	2 (20)	0.999
Congestive heart failure	35 (81)	27 (82)	8 (80)	0.999
Involved structures: num (%)				**< 0.001**
AV	19 (44)	16 (49)	3 (30)	
MV	15 (35)	15 (45)	0	
TV	1 (2)	0	1 (10)	
AV+MV	8 (19)	2 (6)	6 (60)	
Time to surgery (day): (median IQR)	7.5 (5, 15)	7.5 (4, 15)	7.5 (6, 15)	0.744
Clamp time (minutes): (median IQR)	83 (66, 108)	78 (62, 92)	114 (83, 156)	**0.033**
Bypass time(minutes): (median IQR)	99 (79, 134)	94 (77, 106)	143 (102, 183)	**0.030**
CCU stay (day): (median IQR)	5 (3, 10)	5 (3, 7)	7 (2, 13)	0.688
Post op. stay (day): (median IQR)	15 (10, 23)	15 (9, 21)	15.5 (13, 34)	0.335
Hospital stay (day): (median IQR)	30 (20, 43)	25 (18.5, 43.5)	35 (30, 42)	0.165

SD: standard deviation; DM: diabetes mellitus; HT: hypertension; wbc: white blood cell count; HCT: hematocrit; AV: aortic valve; MV: mitral valve; TV: tricuspid valve; CCU: critical care unit; IQR: interquartile range

Using the Euroscore II cut-off value of 12%, we compare patients with Euroscore II < 12% to those with Euroscore II ≥ 12 %. In the group with Euroscore II < 12%, with 33 patients, the mean age was significantly higher (*p*-value = 0.012). The group with Euroscore II ≥ 12%, with 10 patients, had tricuspid valve involvement in only 1 patient (10%), and combined aortic and mitral endocarditis in 6 patients (60%). The median operative times were significantly longer in the group with Euroscore II ≥ 12% (see Table 1).

The mean Euroscore II of all patients was 8.6% (range, 0.8% to 33.9%). There were 3 in-hospital deaths (7%). The mean Euroscore II in the group with Euroscore II < 12% and ≥ 12%, was 4.8% (range, 0.8% to 11%) and 21.4% (range, 13.5% to 33.9%) respectively. All patients who died postoperatively had Euroscore II ≥ 12 %. By using cut-off value of Euroscore II at 12%, the discriminatory ability of the Euroscore II to predict operative deaths as measured using the AUROC was 91.3% (95% CI 85.3- 97.2%) (see Figure 1).

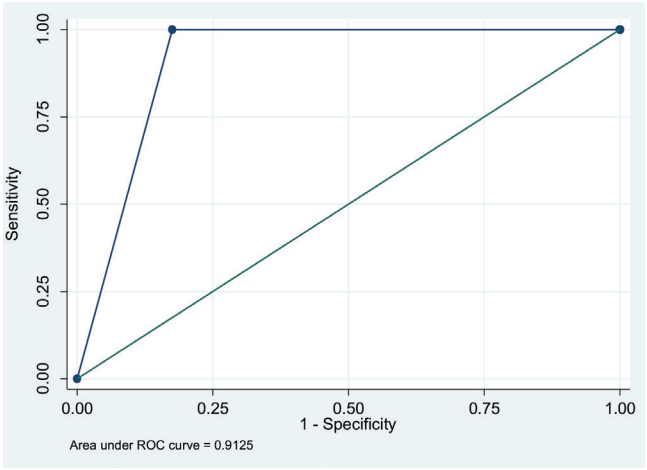

Figure 1 ROC curve for the Euroscore II cut-off at 12%

The majority of the patients had creatinine clearance of at least 50 mL/min (79%), good LV function (86%), no pulmonary hypertension (88%), and isolated single-valve endocarditis (72%). Almost half of the patients had functional class (NYHA) IV and were presented in a critical state (47%). In patients with Euroscore II ≥ 12%, 80% of patients had creatinine clearance < 50 mL/min, 90% had NYHA class IV and almost all were in a critical state. These risk factors were all significantly more frequent in patients with Euroscore II ≥ 12% than in those with Euroscore II < 12%. At least two interventions were needed in 70% of these patients (see Table 2).

Table 2 Euroscore factors

		Euroscore		
Factors	**All patients (n = 43)**	**< 12 (n = 33)**	**≥ 12 (n = 10)**	***p*-value**
Age: mean (SD)	47.7 (14.7)	57.7 (10.2)	44.6 (14.7)	0.012
Female gender: num (%)	19 (44)	15 (46)	4 (40)	0.999
Renal impairment: num (%)				< 0.001
Creatinine clearance > 85 ml/min	19 (44)	19 (58)	0	
Creatinine clearance 50 - 85 ml/min	15 (35)	13 (39)	2 (20)	
Creatinine clearance < 50 ml/min	9 (21)	1 (3)	8 (80)	
Extracardiac arteriopathy: num (%)	2 (5)	1 (3)	1 (10)	0.415
Poor mobility: num (%)	3 (7)	3 (9)	0	0.999
Previous cardiac surgery: num (%)	1 (2)	1 (3)	0	0.999
Chronic lung disease: num (%)	0	0	0	NA
Critical preoperative state: num (%)	20 (47)	11 (33)	9 (90)	0.003
Diabetes on insulin: num (%)	0	0	0	NA
NYHA: num (%)				0.004
II	10 (23)	9 (27)	1 (10)	
III	13 (30)	13 (40)	0	
IV	20 (47)	11 (33)	9 (90)	
LV function: num (%)				0.999
Good (> 50%)	37 (86)	28 (85)	9 (90)	
Moderate (31-50%)	6 (14)	5 (15)	1 (10)	
Poor (21-30%)	0	0	0	
Pulmonary hypertension: num (%)				0.059
no	38 (88)	30 (91)	8 (80)	
31 - 55 mmHg	3 (7)	3 (9)	0	
> 55 mmHg	2 (5)	0	2 (20)	
Urgency: num (%)				
Urgency	43 (100)	33 (100)	10 (100)	NA
Emergency	0	0	0	
Weight of the intervention				0.001
non - CABG	31 (72)	28 (85)	3 (30)	
2 procedures	10 (23)	5 (15)	5 (50)	
3 procedures	2 (5)	0	2 (20)	

Discussion

The results of the present study seemed to confirm that a Euroscore II ≥ 12% was correlated with significantly increased in-hospital mortality in patients with active IE. The cut-off value of 12% was obtained from a previous study which enrolled 121 patients who had active IE. This cut-off value provided a sensitivity of 40.9%, specificity of 92.2%, positive predictive value (PPV) of 75% and negative predictive value (NPV) of 73.2%.[1] In the present validation study, this cut-off value was used to predict in-hospital mortality in patients with active IE at the same Medical Center as that of the previous study. Patients thus had similar demographics, were looked after by the same care team, and treated under the same management protocols. The time frame of the present study was a continuation of the previous study. The present in-hospital mortality was 7% which was lower than that of the previous study. However, all deaths occurred in the group with Euroscore II ≥ 12%. The mean Euroscore II in this group was similar to the mean Euroscore II from the previous study in patients who died.[1] The AUROC in the present study was 91.3% (95% CI: 85.3% to 97.2%).

Koshy et al. studied the validity of Euroscore II in patients with active IE. They found that Euroscore II > 12% accurately predicted early and mid-term mor-tality with a sensitivity of 73%, specificity of 88%, PPV of 44% and AUROC of 80%.[15] These results seem to suggest that the cut-off value of 12% can be applied to other centers with similar settings. The patients' characteristics were similar to those of our study, although there might be some differences in the comorbidities which we found underlying rheumatic valvular heart disease in 9% whereas in their study they found 84%.

IE is considered one of the most severe valvular heart diseases. In-hospital mortality is approximately 9.6% to 45%.[16-18] This can increase to 25% to 36% if urgent surgery is needed.[19] Currently the treatment for IE is focused on early surgery, which may increase the chances of encountering active IE, so the in-hospital mortality is around 5% to 26%, which is relatively high.[20-26] Therefore, it is useful to have an accurate scoring system such as Euroscore II in the counseling and decision making in surgery.

Siregar et al. studied the performance of the original Euroscore. They found that this score was not sufficiently accurate in predicting operative mortality due to overestimation.[27] Although Euroscore II was developed for improved accuracy, to substitute for the original Euroscore, by increasing the number of patients in the development set from 19,000 to 22,381 from 154 centers in 43 countries, these patients were of diverse demographic, geographic, socioeconomic, and cultural background. Stavridis et al. found that the Euroscore II in patients who underwent cardiac surgery had an AUROC of 85% (95% CI: 75% to 94%).[28] Kartal et al. studied a subgroup of patient undergoing isolated coronary artery bypass and isolated mitral valve replacement surgery. They found that Euroscore II had good accuracy in predicting postoperative mortality.[29]

There are many reports confirming good accuracy of Euroscore II. When the details of the development of both versions of the Euroscore were examined, active IE was considered an important factor in the prediction of mortality. However, the number of patients with active IE was only 202 (1.1%) and 497 (2.2%) in the original Euroscore and Euroscore II development sets, respectively.[30] There were a few studies on Euroscore II in active IE, which underestimated the actual mortality but showed better accuracy than the original Euroscore, which overestimated actual mortality.[31-32] It is difficult to define the appropriate cut-off value of Euroscore II that is accurate and reliable enough for use in difficult treatment decisions.

There are several limitations in the present study. The present study is a retrospective observational study. It cannot adjust or control for all confounding factors. Conclusions from a study of patients at one Medical Center may not be applicable to other patients in other institutions. IE is not a common disease. There were too few patients in the present study (43) and too few outcomes (3) for the conclusions to be reliable. Further collection of data will require a prolonged period of study, during which time patient characteristics and treatment practices may change. Therefore, the cut-off value may change with time as well. The first important thing in applying the cut-off value of 12% is that the clinical circumstances must be similar.

Conclusion

The present study seemed to confirm the external validity of the cut-off value of Euroscore II at 12% in patients with active IE. Scores higher than the cut-off

were associated with significantly higher mortality. It might be useful for surgical decision making in high-risk active IE patients at medical institutions with similar circumstances.

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บทคัดย่อ **ความเที่ยงตรงของ Euroscore II ในการพยากรณ์โอกาสการเสียชีวิตของผู้ป่วยลิ้นหัวใจติดเชื้อในระยะรุนแรง**

คมกฤษณ์ โกมุทรินทร์, พบ.

นิสิต พูลธนะนันท์, พบ.

กลุ่มงานศัลยกรรม โรงพยาบาลมหาราชนครราชสีมา จังหวัดนครราชสีมา

ความเป็นมา: ผู้ป่วยที่มีภาวะลิ้นหัวใจอักเสบติดเชื้อในระยะเฉียบพลันมีความเสี่ยงสูงต่อการเสียชีวิตภายหลังการผ่าตัด ตัวเลขพยากรณ์ความเสี่ยงก่อนการผ่าตัดที่เชื่อถือได้เป็นข้อมูลที่มีความสำคัญอย่างยิ่งในการตัดสินใจรักษา การศึกษานี้จึงมีขึ้นเพื่อจุดประสงค์ในการพิสูจน์ความตรงภายนอกของค่า Euroscore II ที่ ≥ 12 ในการทำนายโอกาสในการเสียชีวิตจริง

วิธีการศึกษา: การวิจัยนี้เป็นการศึกษาย้อนหลังซึ่งรวบรวมข้อมูลของผู้ป่วยที่ได้รับการวินิจฉัยมีการติดเชื้อในระยะเฉียบพลันของลิ้นหัวใจตั้งแต่ 1 มิ.ย. 2560 ถึง 1 มิ.ย. 2563 ผู้ป่วยถูกแบ่งเป็น 2 กลุ่มตามค่า Euroscore II (< 12 และ ≥ 12) ค่าพยากรณ์โอกาสเสียชีวิตจะถูกนำมาเปรียบเทียบกับอัตราการเสียชีวิตที่เกิดขึ้นจริง

ผลการศึกษา: มีผู้ป่วยทั้งหมด 43 รายที่ได้รับการวินิจฉัยการติดเชื้อในระยะเฉียบพลันของลิ้นหัวใจ ไม่มีผู้ป่วยรายใดที่มีการติดเชื้อของลิ้นหัวใจเทียม ส่วนมากเป็นผู้ป่วยชาย (56%) อายุเฉลี่ย 47.7 ปี พบว่ามีก้อนเชื้อโรคขนาดใหญ่ (Large vegetation) 89% มีผู้ป่วยเพียง 1 รายเท่านั้นที่มีการบีบตัวของหัวใจน้อยกว่า (Ejection fraction) 40% ส่วนมากผู้ป่วยมาด้วยภาวะหัวใจล้มเหลว (81%) ผู้ป่วยมักมีลิ้นหัวใจอักเสบติดเชื้อเพียงลิ้นเดียว (82%) ส่วนมากมักเป็นที่ลิ้นหัวใจเอออร์ติก (44%) ระยะเวลาเฉลี่ยหลังจากได้รับการวินิจฉัยจนถึงการผ่าตัดคือ 7.5 วัน ระยะเวลาเฉลี่ยของการหยุดหัวใจ และการใช้หัวใจและปอดเทียมอยู่ที่ 83 และ 99 นาที ตามลำดับ ค่าเฉลี่ย Euroscore II อยู่ที่ 9% ผู้ป่วยเสียชีวิตทั้งหมดอยู่ในกลุ่ม Euroscore II ≥ 12 (อัตราการเสียชีวิตที่เกิดขึ้นจริงในกลุ่มนี้คือ 30%) เมื่อใช้ค่า Euroscore II ที่ 12% เป็นเกณฑ์พิจารณาในการหาค่าความแม่นยำต่อการทำนายการเสียชีวิต พบว่าค่าพื้นที่ใต้กราฟ (Area under receiver operating characteristic curve) คือ 91.3% ค่าความเชื่อมั่น 95% (95% confidence interval) 85.3-97.2

สรุปผลการศึกษา: การศึกษานี้ยืนยันถึงความเที่ยงตรงของค่า Euroscore II ≥ 12% ซึ่งมีความสัมพันธ์กับอัตราการเสียชีวิตที่เกิดขึ้นจริงสูงขึ้นกว่าที่คำนวณได้ในผู้ป่วยที่ได้รับการวินิจฉัยมีการติดเชื้อในระยะเฉียบพลันของลิ้นหัวใจ มีความน่าเชื่อถือเพียงพอในการนำไปใช้เพื่อช่วยตัดสินใจก่อนผ่าตัดในผู้ป่วยความเสี่ยงสูงที่ได้รับการวินิจฉัยมีการติดเชื้อในระยะเฉียบพลันของลิ้นหัวใจในสถานพยาบาลที่มีสภาพแวดล้อมคล้ายคลึงกัน

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Case Report

Primary Adrenal Tuberculosis: A Case Report

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Abstract Tuberculosis (TB) is a world-wide epidemic. The World Health Organization estimated a global incidence of around 10 million new cases in 2019, and it is one of the top 10 causes of death in the world with 1.2 million deaths annually. Tuberculosis is mainly a pulmonary disease, and extra-pulmonary tuberculosis accounts for 5% to 15% of all cases. Primary adrenal tuberculosis is rare, constituting 6% of all TB cases. We report a case of primary adrenal tuberculosis, with a discussion of the clinical features, radiologic and pathological findings and treatment outcomes. A review of the current knowledge of this disease is also provided.

Keyword: Primary adrenal tuberculosis

Case Report

A 70-year-old man presented with remittent fever for 2 weeks, there was severe generalized abdominal pain with no radiation, anorexia, or weight loss. No other gastrointestinal symptoms or urinary symptoms were reported. He had been diagnosed with type 2 diabetes mellitus for 30 years, which was poorly controlled, and rheumatoid arthritis for 20 years.

He denied having a previous history of tuberculosis infection but did have a history of contact with pulmonary tuberculosis patients 10 years previously. There was no family history of endocrine neoplasms or early cerebral or cardiovascular disease. He underwent a tuberculin skin test in 2007 which showed induration (unknown diameter) that may be attributed to a prior BCG vaccination.

The general appearance was not pale, there was no facial plethora, and the skin did not easily bruise. Physical examination revealed mild abdominal distension, but no superficial vein dilatation, no purplish striae, no palpable mass, the liver and spleen were not palpable, and there was no lymphadenopathy. Cardiac, respiratory, and neurological examinations showed no abnormalities. There were no signs and symptoms characteristic of adrenal insufficiency. Laboratory analysis was performed, which showed normal findings. There was no evidence of pulmonary tuberculosis via chest radiography. The patient underwent axial helical computerized tomography (CT) of the whole abdomen. This revealed an irregular enhancing hypodensity of the bilaterally enlarged adrenal glands (7.3 cm × 2.9 cm × 6.6 cm on the right, 5.9 cm × 2.6 cm × 6.6 cm on the left) but no intra-abdominal lymphadenopathy (Figure 1). On review of his prior CT scan of the abdomen, the patient had bilaterally enlarged adrenal glands at the time of his initial presentation as well.

A dedicated adrenal washout CT protocol consists of a non-contrast and a contrast-enhanced scan with a delay of 60 to 90 seconds, and a delayed scan at 15 minutes. Absolute enhancement wash out > 60% is proof of an adenoma. The absolute wash out was 63.6% in the present case.

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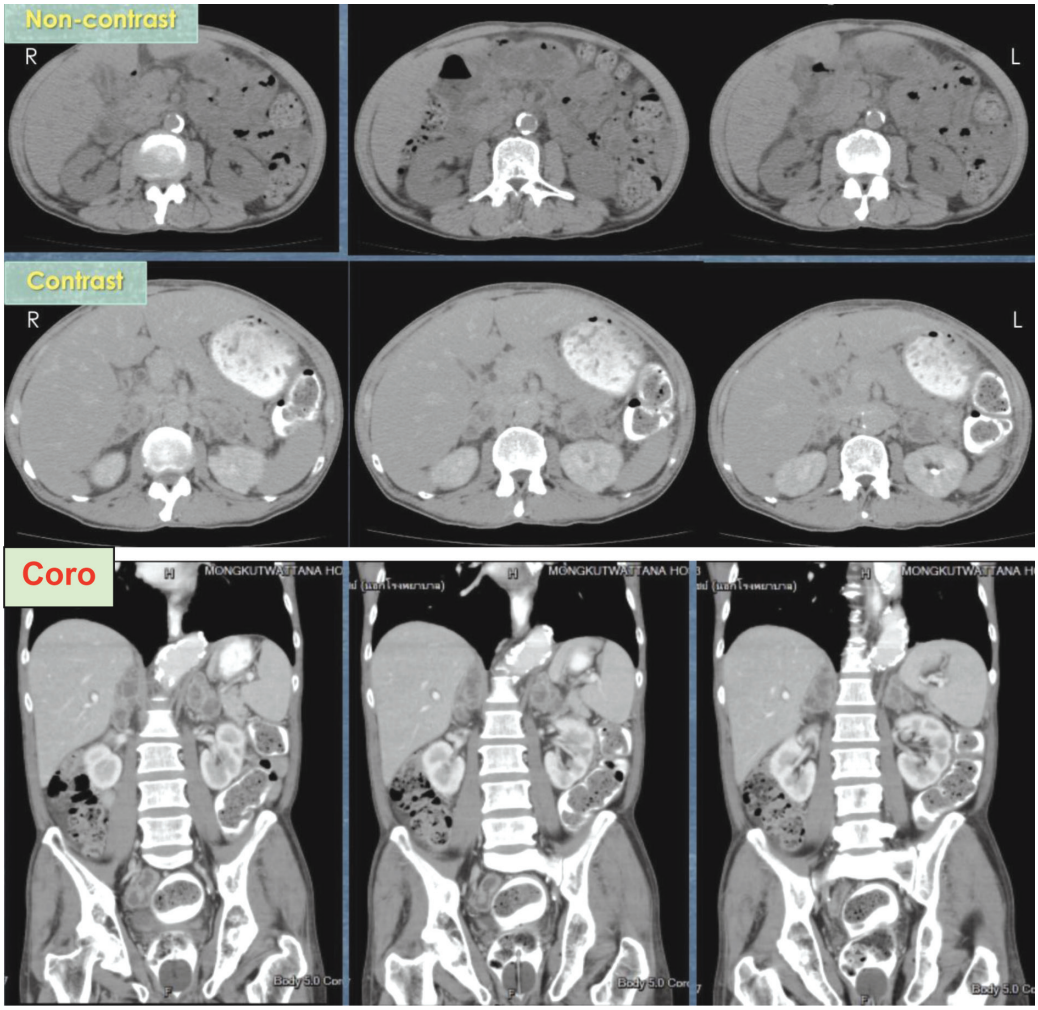

Figure 1 CT scan of the abdomen and pelvis with oral and intravenous contrast. Upper row: the unenhanced image; the middle and lower rows: contrast-enhanced CT scans show enlargement of bilateral adrenal glands with peripheral rim enhancement on the axial (middle) and coronal (lower) views

The biochemical and hormonal data in patients with bilateral adrenal mass are evaluated to compare the differences between adrenal adenomas and other benign lesions and to find the relationship between metabolic parameters and adrenal hormones. We performed an assessment of the production of cortisol in both adrenal glands and autonomous cortisol secretion and found the morning cortisol to be 16.72 ug/dL (normal range, 7 to 28 ug/dL); the one mg overnight dexamethasone suppression test showed cortisol levels of 13.6 ug/dL and 10.70 ug/dL (over 2 times the normal value < 1.8 ug/dL); the midnight serum cortisol level of 1.09 ug/dL; and the 24-hour urine free cortisol for two consecutive days were as shown in Table 1.

Table 1 The results of 24-hour urine free cortisol and urine creatinine tests

	Day 1	Day 2	Normal range
24-hour urine free cortisol (ug/day)	292	230	50-190
24-hour urine creatinine (gm)	0.795	0.593	0.86
24-hour urine vol (mL)	2,700	2,800	

Table 2 The results of 24-hour urine metanephrine, normetanephrine and creatinine tests

	Day 1	Day 2	Normal range
24-hour urine Metanephrine (nmol/day)	571	579	< 1,777
24-hour urine Normetanephrine (nmol/day)	3,962	2,492	< 3,279
24-hour urine creatinine (gm)	0.854	0.802	0.86
24-hour urine vol (mL)	2,500	2,850	

From the above results, it might be concluded that the patient had hypercortisolism and no adrenal insufficiency, but these values still lie within the range of false positives. Because there were no characteristics of Cushing's syndrome, the abnormal examination might be caused by stress from the infection, or there may be other causes instead of Cushing's syndrome, as will be discussed later.

An assessment of the production of catecholamine via the 24-hour urine tests for metanephrine, normetanephrine and urine creatinine is shown in Table 2.

The results in Table 2 show that the 24-hour urine normetanephrine is higher on the first day, but does not exceed two times greater than normal, so it was possible that stress and infection might be the cause of the elevation. Likewise, the signs, symptoms, and radiological examination results did not indicate pheochromocytoma. The patient did not undergo biochemical testing for hyperaldosteronism because of the normal blood pressure.

With these biochemical test results, the prolonged fever and subacute abdominal pain of the patient most likely resulted from infectious diseases. The radiological features with bilateral adrenal enlargement were compatible with tuberculosis and histoplasmosis. However, because the size of the adrenal glands exceeded 6 cm, it was not possible to rule out malignant tumors. The patient therefore underwent laparoscopic left adrenalectomy for diagnostic purposes.

The right lateral decubitus position was used, along with a 10 mm port for the laparoscope, and two 5 mm ports for working instruments. The pathological specimen is shown in Figure 2, showing grossly extensive caseous necrosis, and extensive caseating granulomatous inflammation. On microscopical examination, epithelioid cells were found, including Langerhans giant cells surrounding the necrotic area, with adrenocortical remnants (see Figure 3). A tissue sample was sent for RT-PCR testing for mycobacterium tuberculosis which confirmed the diagnosis.

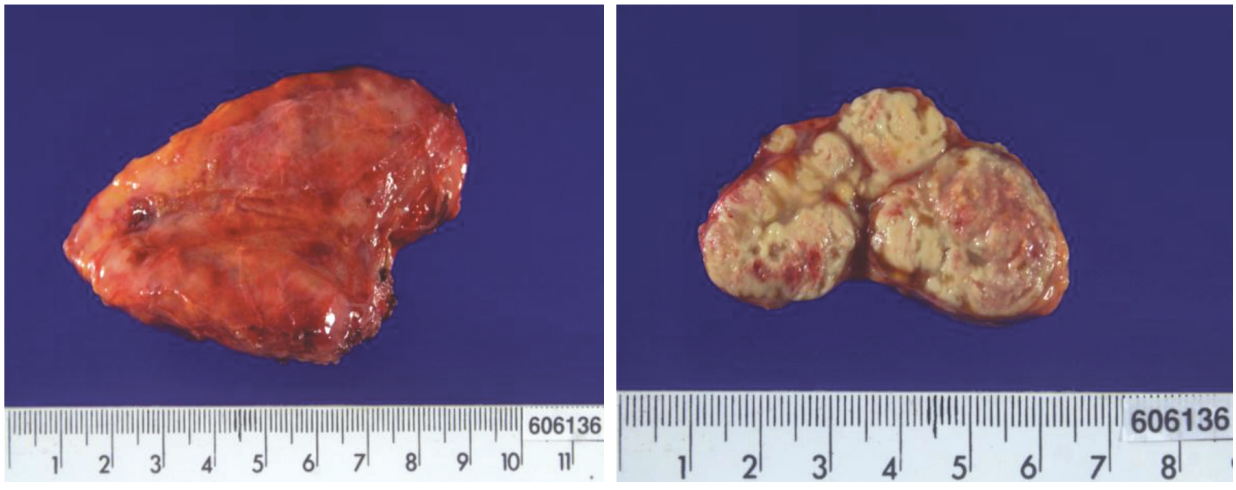

Figure 2 Gross specimen of the left adrenal gland: above, intact surface pathology showing a bulging glandular surface with some adhesion to surrounding soft tissue; below, the cut surface shows extensive caseous necrosis in the central part of the gland

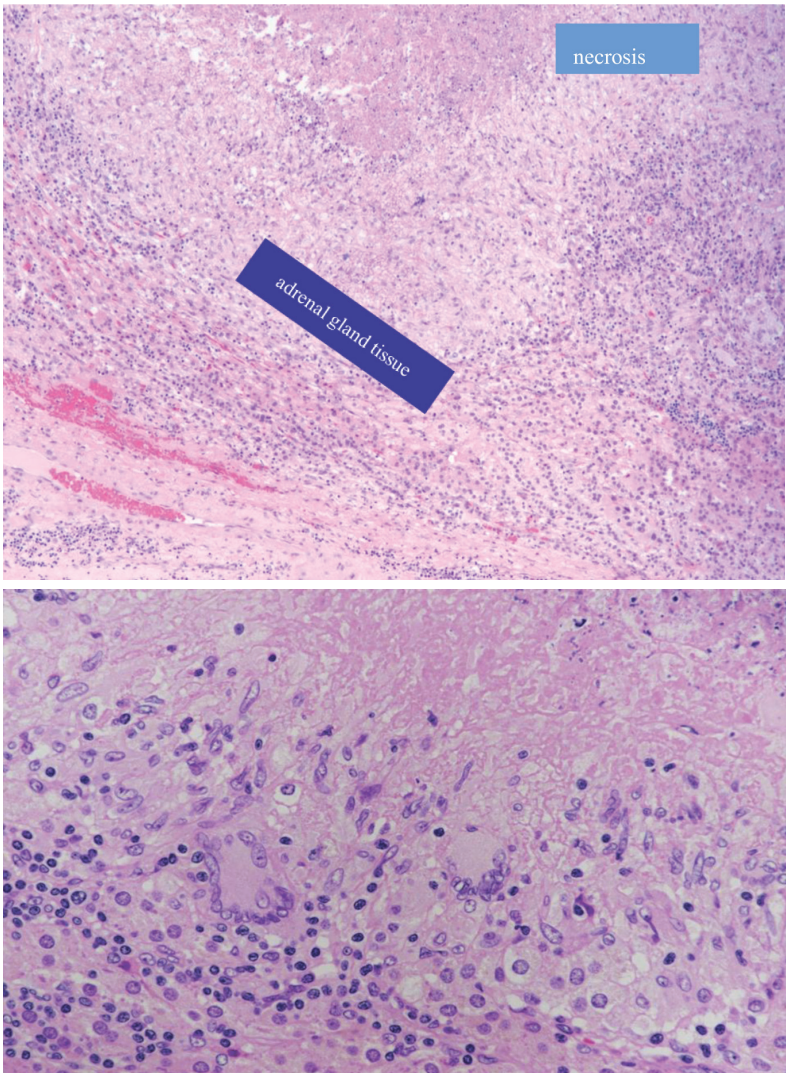

Figure 3 Microscopic examination (Hematoxylin & Eosin): above (10X), extensive necrosis leaving only a thin layer or scattered area of adrenocortical tissue remnants; below (20X), cellular reaction in the lesion including lymphocytes, epithelioid cells and Langhans-type multinucleated giant cells

Based on the pathological and PCR results, it can be concluded that the patient had tuberculosis of the adrenal glands. Treatment consisted of anti-tuberculosis drugs similar to those for pulmonary tuberculosis: Isoniazid, Rifampicin, Pyrazinamide, and Ethambutol for 2 months, followed by Isoniazid and Rifampicin for 4 months, for a total treatment period of 6 months. Follow-up after anti-tuberculosis treatment showed that the patient had improved symptoms without adrenal insufficiency.

Discussion

Primary adrenal tuberculosis accounts for approximately 6 percent of all tuberculosis infections. The mean age of at diagnosis is 61 years1-3 The ratio of male to female patients varies among studies.1,4 Risk factors for tuberculosis include diabetes, steroid medication, cancer, and chemotherapy.[1] Our patient was older than the reported average, but had risk factors including poorly controlled diabetes and the long term use of immunosuppressive drugs. Primary adrenal tuberculosis often presents with symptoms of primary adrenal insufficiency. Symptoms of primary adrenal insufficiency appear when more than 90% of the adrenal glands have been destroyed. Common features of adrenal insufficiency include weight loss, anorexia, nausea, vomiting, lethargy, fatigue, and high grade fever.[2,4,5] One case with abdominal pain was reported from India.[5]

The median duration of symptoms before medical consultation for adrenal tuberculosis is 6 months (range, 0.25 to 92 months).[2-7] However, our patient came for consultation with fever and abdominal pain after only 2 weeks, similar to a case of primary adrenal tuberculosis from Italy.[4] If patients are seen early on in the course of illness, it is possible to provide early diagnosis and care such that adrenal function can be preserved.

Major CT findings in adrenal tuberculosis include bilateral enlargement of the adrenal glands with calcification. When adrenal tuberculosis is active, enhanced CT shows increased enhancement of the periphery of the gland, with the central area showing a lower degree of attenuation. Idiopathic adrenal insufficiency is not characterized by either adrenal enlargement or calcification on CT. According to Guo et al,[5] adrenal gland enlargement on CT is frequently recognized within a year of the disease onset. However, the enlarged adrenals gradually shrink because of fibrosis and calcification.[5] Sun et al[6] identified adrenal gland enlargement on CT images within the first four years after the onset of adrenal gland tuberculosis. In our patient, bilateral adrenal enlargement without calcification was observed. Malignancy cannot be completely excluded by either CT, magnetic resonance imaging (MRI), or positron emission tomography (PET) as bilateral enlargement is also a common finding in malignant lesions.[7,8]

Radiographic features from CT scan depend of the stage of disease. There are two stages. In the acute or recent infection (< 2 years) stage, findings include irregular, central hypodensity, bilateral adrenal enlargement, and peripheral rim enhancement.[3] In the chronic infection stage, findings include adrenal gland atrophy and calcification. The CT findings for our patient showed bilateral adrenal gland enlargement and peripheral rim enhancement, which were compatible with active tuberculosis infection of less than 2 years.

CT findings of bilateral adrenal enlargement could be due to other conditions. In a study of 70 patients with bilateral adrenal gland enlargement, 40% was due to pheochromocytoma, 27% was from adrenal tuberculosis, 10% had primary adrenal lymphoma, 6% was from metastases, 4% had non-functioning adenomas, 4% had primary bilateral macronodular adrenal hyperplasia, and 9% had other conditions such as histoplasmosis.[4] Other radiological characteristics that can help distinguish adrenal tuberculosis from adrenal cancer such as atrophic glands, calcification, and peripheral rim enhancement are often absent.[8]

Every patient with an adrenal incidentaloma should undergo careful assessment for symptoms and signs of adrenal hormone excess.[9] These adrenal tumors may be hormonally active or non-functional, malignant or benign. All patients should undergo biochemical testing for pheochromocytoma, either with plasma or urinary catecholamine measurements. This is particularly important before surgery, which is routinely recommended for tumors larger than 4 cm in diameter, for cases without a clear-cut diagnosis, and for those with increased hormonal secretion or imaging characteristics of malignancy. Hypertensive patients should undergo biochemical testing for hyperaldosteronism. Patients with features consistent with Cushing's syndrome, such as glucose intolerance, weight gain, and unexplained osteopenia should be evaluated for excess cortisol. For the latter, the dexamethasone suppression test and late-night salivary cortisol may be preferred over measurements of urine cortisol.

Adrenal tuberculosis may result in hypercortisolism due functional changes in the hypothalamus-pituitary-adrenal (HPA) axis caused by the cell walls of the mycobacterium, which is a component of lipoarabinomannan (LAM). LAM can stimulate post-inflammatory cytokines such as IL-1β, IL-6 and TNFα, which increase CRH and ACTH secretion from the pituitary gland.[6,10] In addition, stress and poorly controlled diabetes can also contribute to the stimulation of the HPA axis, as was seen in our patient.[6,11-13]

In the present case we chose laparoscopic adrenalectomy for definitive diagnosis. Typically, fine needle biopsy is often performed for the diagnosis of adrenal tumors larger than 4 cm in size, but in our case it was avoided for several reasons. Firstly, the patient's adrenal anatomy was not amenable for accurate image-guided biopsy. Secondly, as the adrenal size was greater than 6 cm, there was a considerable risk of internal organ damage and hemorrhage. Thirdly, CT results showed that the patient's adrenal glands were likely surrounded by necrotic tissue, which could decrease the accuracy of fine needle biopsy. Nirag et al[9] also noted that percutaneous image-based fine needle aspiration of adrenal tumors has incorrect diagnosis rates ranging from 0% to 37%. Mazzaglia et al[10] stated that needle biopsy could be valuable for the diagnosis of metastatic tumors, but is not suitable for differentiating between benign and malignant tumors. A more accurate and safer route for

needle biopsy would be endoscopic ultrasound-guided fine-needle aspiration,[9] but this was not available at our institution. Hence, in our case, laparoscopic adrenalectomy was used to establish a definitive diagnosis.

Treatment for adrenal tuberculosis is based on standard anti-tuberculosis drugs, consisting of isoniazid, rifampicin, pyrazinamide, and ethambutol for 2 months, followed by isoniazid and rifampicin for 4 months, for a total duration of 6 months.[18] If the patient is diagnosed with primary adrenal insufficiency, or is at risk of developing adrenal crisis due to rifampicin increasing cortisol metabolism through cytochrome P450 3A4, it is important to monitor symptoms of adrenal insufficiency, and to adjust steroid dosages accordingly.7,19 The prognosis of adrenal tuberculosis depends on the timing of the diagnosis and treatment. If adrenal insufficiency develops after the treatment, due to atrophy of the glands, it will persist life-long.[19]

Conclusion

Primary adrenal tuberculosis is rare, accounting for approximately 6 percent of all tuberculosis infections. We should be aware of this disease in patients with bilateral adrenal tumors. The disease may cause primary adrenal insufficiency, so early diagnosis and evaluation of hormone function is important. Treatment include anti-tuberculous drugs and surgical intervention when indicated, which can lead to good prognosis and desirable outcomes.

Conflict of Interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

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Case Report

Three Simple Hepatic Cysts Successfully Managed Using a Laparoscopic Approach

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Abstract Hepatic cysts are not an uncommon condition, and most are simple cysts, which cause no symptoms and are usually diagnosed incidentally during imaging for other diseases. However, problems may occur if they grow above a certain size. Complications, such as hemorrhage, infection or rupture are rare, but can be life-threatening or emergency conditions. The author reported three cases of simple hepatic cysts, each with a different clinical presentation. The first patient presented as an emergency condition due to ruptured hepatic cyst. The second patient was asymptomatic and was incidentally diagnosed while imaging for gallstones. The last patient had symptoms of pressure effect from a large cyst. All patients could be managed by a laparoscopic approach without conversion to open surgery.

Keywords: Simple hepatic cyst, Laparoscopic fenestration

Introduction

Hepatic cyst is not a rare condition. The prevalence of the cyst could be as high as 4.7% in the general population.[1-2] However, most are asymptomatic, with only 5% having clinical symptoms.[3] Intervention for the cyst is indicated when it is large enough to create a pressure effect on adjacent organs. Complications such as hemorrhage, rupture or infection, may occur and may require emergency interventions. There are many treatment options for hepatic cysts but laparoscopic surgery is probably the most effective.[4-6] The present article reports three patients with hepatics cysts.

Case Report

During April 2010 - July 2019, three cases of simple hepatic cysts which were treated using laparoscopic surgery at Sawanpracharak Hospital were reviewed. Medical records, medical imaging, operative and histopathology reports associated with all three cases were reviewed.

Case 1

A 72 year-old woman with hypertension, Alzheimer's disease, simple goiter, with stable cerebrovascular disease was diagnosed with simple hepatic cysts three years earlier but was lost to follow up. She was referred from a rural hospital with acute abdomen. She experienced abdominal distention with constipation for 5 days before a sudden epigastric pain, which progressed to generalized abdominal pain. On arrival, her blood pressure was 120/68 mmHg, pulse, 74 beats per minute, respiratory rate, 20 per minute with a temperature of 38.4 degree Celsius. She was confused and looked pale. Her blood test showed mild anemia and leukocytosis (hematocrit, 33%, hemoglobin, 11.2 mg/dL, white blood count, 12,000/mm^3 with 78% neutrophils and a platelet count of 123,000/mm^3).

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Examination of the abdomen showed generalized tenderness with guarding. She was diagnosed with peritonitis of unknown cause. Differential diagnosis included peptic ulcer perforation, complicated cholecystitis and complicated liver cyst. After resuscitation, laparoscopic diagnosis was performed. A 10 mm camera port was placed at sub-umbilicus. There was 1,500 mL of chocolate-colored fluid in the abdomen, and a ruptured large hepatic cyst at right lobe of liver was found (Figure 1). Two more instrument ports were placed at the epigastrium (10 mm) and at the right subcostal area (5 mm). The inner surface of cyst wall was smooth, with no abnormal lesions or active bleeding. The cyst was unroofed, beginning at the rupture site to the junction of the cyst wall and normal liver parenchyma. The cyst wall was removed as much as possible. The operation took 80 minutes. She had an uneventful recovery and was discharged on the 4th post-op day. Pathological diagnosis was simple cyst with no malignancy.

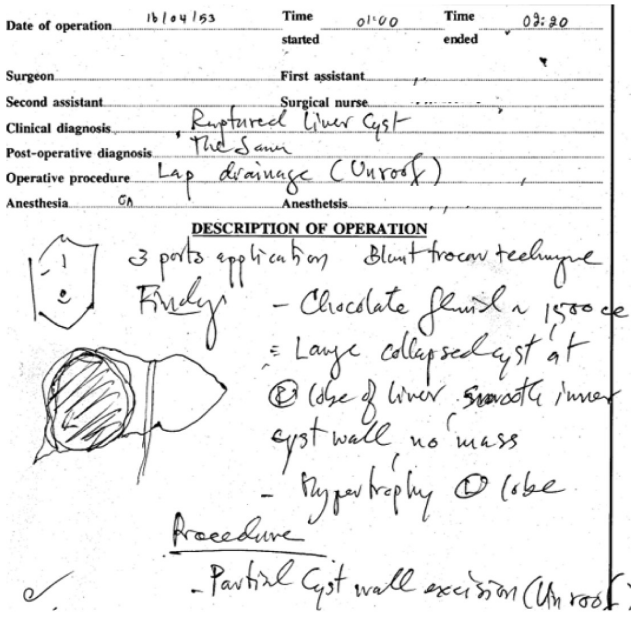
Date of operation 16/04/53 Time started 01:00 Time ended 07:30
Surgeon First assistant
Second assistant Surgical nurse
Clinical diagnosis Ruptured liver cyst
Post-operative diagnosis The Same
Operative procedure Lap drainage (Unroof)
Anesthesia GA Anesthetists
DESCRIPTION OF OPERATION
3 ports application Blunt trocar technique
Findings - Chocolate fluid ~ 1500 cc
= Large collapsed cyst at
Rt lobe of liver Smooth inner
cyst wall no mass
- Hypertrophy Rt lobe
Procedure
- Partial Cyst wall excision (Unroof)

Figure 1 Operative notes for case 1

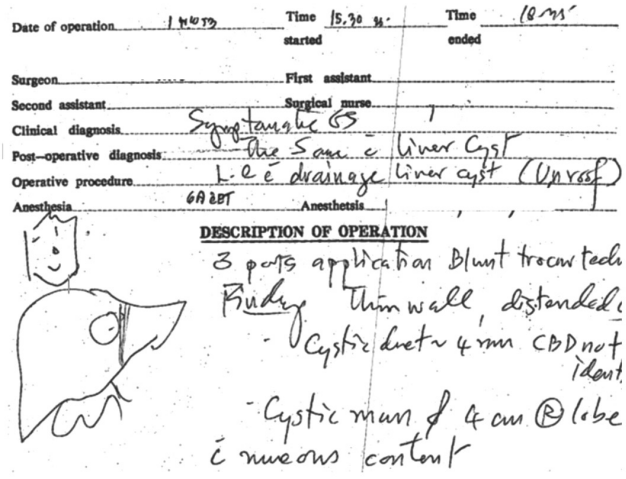
Date of operation 1/4/53 Time started 15.30 hrs Time ended 18 hrs
Surgeon First assistant
Second assistant Surgical nurse
Clinical diagnosis Symptomatic GS
Post-operative diagnosis The Same + Liver Cyst
Operative procedure L-C + drainage liver cyst (Unroof)
Anesthesia GA + BPT Anesthetists
DESCRIPTION OF OPERATION
3 ports application Blunt trocar tech
Findings Thin wall, distended
- Cystic duct ~ 4 mm CBD not
identified
- Cystic mass @ 4 cm Rt lobe
+ mucous content

Figure 2 Operative notes for case 2

Case 2

A 42 year-old woman presented with epigastric pain for 1 month. Ultrasonography revealed a 2 cm gallstone and one 4 cm liver cyst at right lobe of liver. She was diagnosed with symptomatic gallstone and incidental liver cyst. She was scheduled for elective laparoscopic cholecystectomy and concomitant laparoscopic unroofing of liver cyst. Three ports were placed at the sub-umbilicus (10 mm), epigastrium (10 mm) and right subcostal area, mid-clavicular line (5 mm). Operative findings revealed a thin walled gallbladder and a 4 cm hepatic cyst at right lobe of liver (Figure 2). The gallbladder was removed followed by cyst wall unroofing. The operative time was 65 minutes. She had a good recovery and was discharged on the 3rd post-op day. The pathological report was chronic cholecystitis with simple liver cyst.

Case 3

A 65 year-old woman presented with tightness at the right upper quadrant for 6 months. She had no other GI symptoms. Physical examination revealed a huge mass at the right upper abdomen, without local tenderness or peritoneal signs (Figure 3).

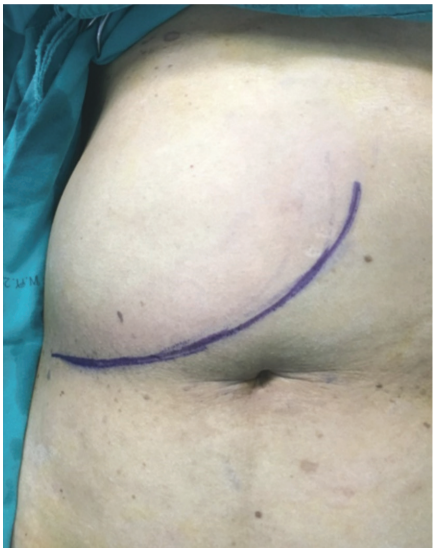

Figure 3 Skin outline of the cyst in case 3

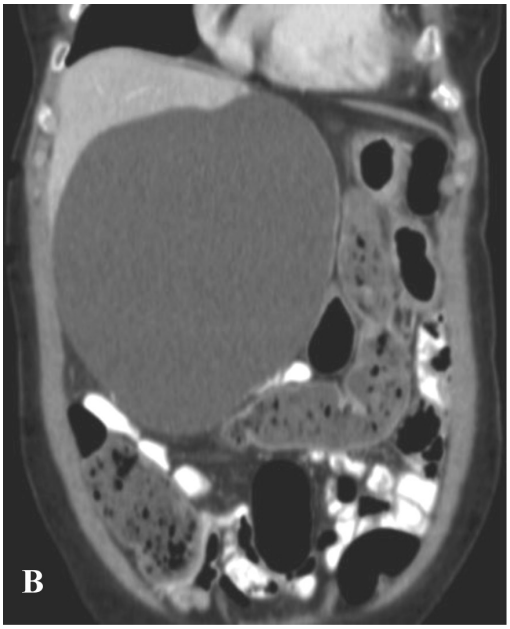

Figure 4 Cystic mass from CT scan of case 3

CT scan showed a large cystic mass 19 cm × 11 cm × 12 cm at the right upper quadrant (Figure 4). The nature of the cyst could not be determined. Differential diagnosis included liver cyst, pancreatic pseudocyst and mesenteric cyst. Laparoscopic diagnosis was planned. Because of the size of the lesion, ports were placed at the sub-umbilicus (10 mm), mid suprapubic (10 mm) and left subcostal (5 mm). Operative findings revealed a huge cystic mass at the right lobe of liver, abutting the gallbladder and extended to left lobe. The content inside the cyst was serous fluid. To facilitate the approach to the lesion, the cyst wall was punctured and decompressed with suction. Once the cyst collapsed, the dissection started at left lobe, by trimmed along the junction until the gallbladder was reached. The gallbladder was dissected and removed en bloc with the cyst (Figure 5). However, it is impossible to remove both specimens via the 10 mm port. They were therefore separated and removed individually (Figures 6 and 7).

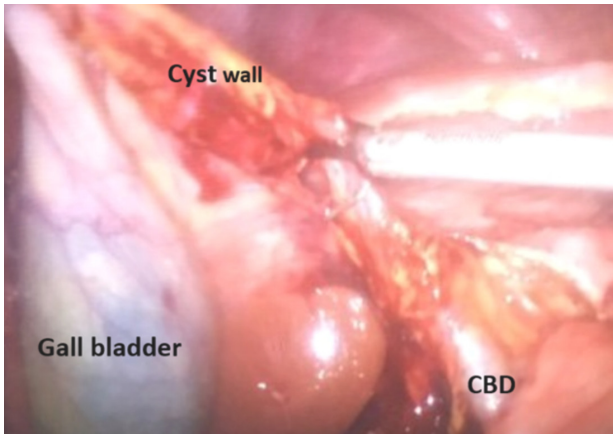

Figure 5 En bloc resection of the cyst and gall bladder

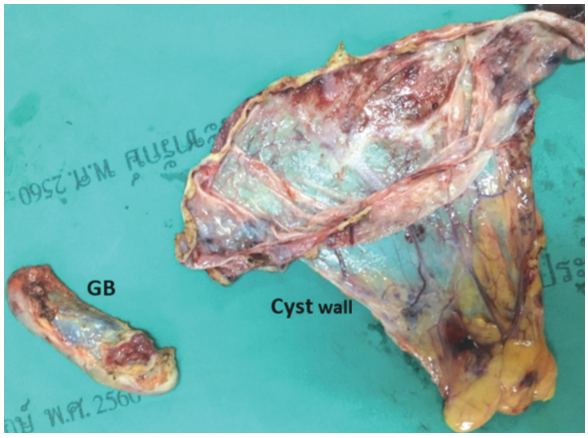

Figure 7 Gallbladder and cyst wall

Figure 6 Individual removal of specimens

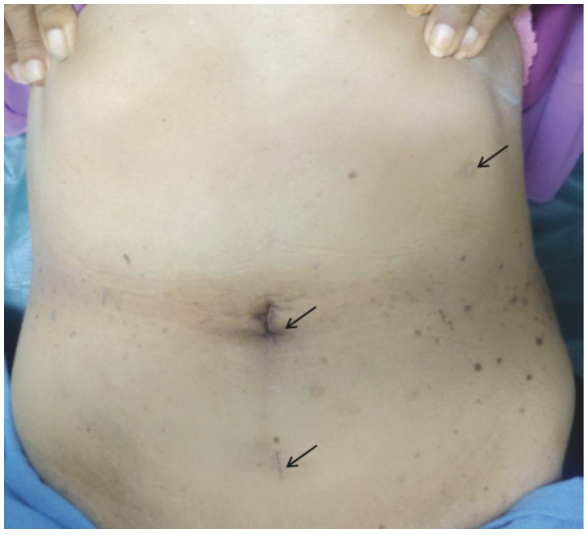

Figure 8 Complete recovery with near-invisible scar

One Jackson-Pratt drain was placed at the surgical site. The operation took 80 minutes. The patient recovered very well and could be discharged home with drain on the 2nd post-operative day. The patient gained a full recovery (Figure 8). The pathological diagnosis were mild chronic inflammation of gallbladder and simple cyst.

Discussion

Simple hepatic cysts are congenital malformations of biliary ducts and the contents within the cyst are usually clear serous fluid[7]. With routine use of ultrasound for abdominal symptoms or for screening, the diagnosis of liver cyst has inevitably increased[8]. Patients with liver cysts are usually asymptomatic, especially those whose liver cysts are of less than 4 cm in size. The management of these patients is wit and see. If complications of the cyst such as intracystic hemorrhage, cyst rupture, infection or compression of adjacent organs occur[9-11] then some form of intervention is indicated. Therapeutic procedures include needle aspiration or percutaneous drainage with or without injection of sclerosing agents[12], unroofing [fenestration], cystojejunostomy[13] and varying degree of liver resection[14]. Needle aspiration is safe, least invasive, and provides rapid relief of symptoms and tissue samples for pathology. However, it is associated with a high failure rate and rapid recurrence[15-19]. Needle aspiration is usually reserved for patients who are not candidates for surgery and general anesthesia[5].

Laparoscopic fenestration was first described in 1991 by Paterson-Brown and Garden using a ND-YAG laser[20] and has been proven to be safe and shown to have a lower recurrence rate, ranging from 0 to 14.3%[21-22]. Laparoscopy can be used to directly examine the interior surface of the cyst, thus ruling out other lesions.[23-24] Treatment of the cyst is based on the destruction of the secreting epithelial layer of cyst wall. The surgical principle is to remove the cyst wall completely or detach it as much as possible, to prevent recurrence. However complete resection of the cyst is not recommended because of the high risk of complications. [25] Complications associated with the operation include hemorrhage and bile leakage.

In this report, the first case was operated under emergency condition. Diagnostic laparoscopy was performed to determine the cause of peritonitis prior to definitive surgery. Furthermore, if the causes were peptic ulcer perforation, complicated cholecystitis or complicated liver cyst, these conditions could be treated laparoscopically (laparoscopic simple closure, laparoscopic cholecystectomy and laparoscopic unroofing). These operations could be carried out without difficulty.

In the second case, the small hepatic cyst (4 cm) was an incidental finding and did not cause symptoms. Although there was no indication for surgical treatment of a small and asymptomatic liver cyst, incidental laparoscopic unroofing could be justified for the following reasons. First, the lesion was small and superficial, and unroofing could be done quickly after cholecystectomy. Second, once the lesion has been removed, there would be no need for long term follow-up with imaging studies. She would be anxiety-free about her cyst. If the lesion progressed, or if complications occur, she would need another operation.

In the third case, imaging studies could not identify the diseased organ. Diagnostic laparoscopy could provide more information or yield a diagnosis and help plan further treatment. The huge cystic lesion in the liver seen on laparoscopy confirmed a liver cyst, and the serous content within the cyst suggested a benign condition. Draining the content at an early stage was crucial. It offered a clear outline of the lesion and suggested that laparoscopic unroofing was feasible. A vessel sealing device (Harmonic, Ethicon, and Johnson & Johnson) was used at certain areas of hyper-vascularization. The combined operation of unroofing and cholecystectomy was performed without much difficulty.

In all three cases, the epithelial lining of the intrahepatic part of the cyst was left alone while the free part of the cyst wall was removed as much as possible, which should prevent recurrence. There was no conversion to open surgery. No post-operative complications occurred. With the benefit of minimally invasive surgery, patients had a rapid recovery and a short hospital stay. These procedures did not require suturing or anastomosing or the use of advanced laparoscopic instruments. Surgeons should be encouraged to perform this operation.

Conclusion

Three cases of simple hepatic cysts were reported. Each had different clinical presentations. One presented with an emergency condition, one was asymptomatic and one had pressure-effect symptoms. All patients could be managed successfully using basic laparoscopic surgical techniques.

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บทคัดย่อ **รายงานการรักษาผู้ป่วยถุงน้ำในตับชนิดธรรมดาที่มาด้วยอาการแตกต่างกัน จำนวนสามรายและสามารถให้การรักษาด้วยวิธีการผ่าตัดผ่านกล้อง**

วันชัย มานะกิจศิริสุทธิ, พบ.

กลุ่มงานศัลยกรรม โรงพยาบาลสวรรค์ประชารักษ์ จังหวัดนครสวรรค์

โรคถุงน้ำในตับชนิดธรรมดาเป็นภาวะที่อาจพบได้ ผู้ป่วยส่วนใหญ่ไม่มีอาการและมักจะตรวจพบโดยบังเอิญในขณะทำการตรวจวินิจฉัยโรคอื่น อย่างไรก็ตามโรคนี้อาจทำให้เกิดอาการได้ถ้าถุงน้ำมีขนาดใหญ่ขึ้นหรือเกิดภาวะแทรกซ้อน เช่น ถุงน้ำแตกหรือมีเลือดออกในถุงน้ำ ผู้นิพนธ์ได้รายงานผู้ป่วยโรคถุงน้ำในตับชนิดธรรมดาจำนวน 3 รายที่มาด้วยอาการแตกต่างกัน รายแรกมาด้วยภาวะฉุกเฉินคือถุงน้ำในตับแตก รายที่สองมาด้วยอาการนิ่วในถุงน้ำดี ตรวจพบถุงน้ำโดยบังเอิญ รายสุดท้ายมาด้วยอาการแน่นท้องจากถุงน้ำที่มีขนาดใหญ่ ผู้ป่วยทุกรายได้รับการรักษาด้วยวิธีการผ่าตัดผ่านกล้องเป็นผลสำเร็จโดยไม่ต้องเปลี่ยนการผ่าตัดเป็นแบบแผลเปิดและไม่พบภาวะแทรกซ้อน

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Poster Award

A CASE REPORT: A HUGE ATRIAL MYXOMA LOCATED IN RIGHT ATRIAL CHAMBER WITH CAUSED SEVERE TRICUSPID VALVE REGURGITATION

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Background: Myxomas are the most common primary cardiac tumors. Myxomas most commonly occur in the atria. Approximately 75% arise in the left atrium (LA), and 15% to 20% arise in the right atrium (RA). We report a case of a large myxoma in RA, which is a huge obstructive and uncommon location for this type of tumor.

Objective: The purpose of this paper is to report a case of a large myxoma in RA, which is a huge obstructive and uncommon location, and treatment recommendation.

Methods: Case presentation; a 32-year-old Thai woman, with no underlying disease, who complained of progressive chest pain and dyspnea on exertion in the last three months prior to admission. A cardiovascular examination revealed that her heart rhythm was regular with pansystolic murmurs at the left parasternal border. Chest X-ray (CXR) showed clear lung fields, cardiomegaly with globular heart shape and biatrial enlargement. An electrocardiogram showed sinus rhythm with 1st degree AV block and right axis deviation with the right bundle branch block. A transthoracic echocardiogram (TTE) showed a moving huge heterogenous mass in the RA with stalk attached to lateral RA wall that protrudes to the Right Ventricle (RV); good ejection fraction (EF) = 71%.

Results: Our patient underwent surgical treatment with conventional cardiopulmonary bypass technique. We performed an excision of a $7 \times 5 \times 9$ cm. mass which was implanted at the junction between the openings of inferior vena cava, coronary sinus and protrude tricuspid valve (TV) which caused severe TV regurgitation and severe anulus dilation that is difficult to repair. Finally, we proceeded to tricuspid valve replacement (TVR) with tissue valve. With regard to the post operative follow-up, in 6 months the EKG showed sinus rhythm with 1st degree AV block. The chest X-ray showed clear lung fields with normal heart size. A TTE showed good EF and good TV function with no chamber enlargement.

Conclusion: In this case report, the emphasis is on the rarity of the huge myxomas in the RA and protruding TV which caused severe TV anulus dilatation and has difficulty to repair; a TVR with tissue valve was finally carried out.

Keywords: Huge myxomas, Right atrium myxomas, Tricuspid valve replacement

INCIDENCE OF COMPLICATED APPENDICITIS DURING THE COVID-19 PANDEMIC: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Measures taken to prevent the spread of coronavirus disease 2019 (COVID-19) slow surgical processes, and patients are avoiding presenting at emergency departments during the outbreak because of fears of contracting the contagious disease.

Objectives: This meta-analysis aimed to analyze the rate of complicated appendicitis before and during the COVID-19 pandemic.

Methods: We systematically reviewed the PubMed and SCOPUS databases for articles published from 2000 to 2021. The primary outcome of complicated appendicitis incidence was compared between before and during the COVID-19 pandemic period. We performed a meta-analysis using a random-effects model analysis.

Results: A total of 3,559 patients with acute appendicitis were included. The overall rate of complicated appendicitis was significantly higher during the pandemic (relative risk, 1.55; 95% confidence interval [CI], 1.26 -1.89). The time from onset of symptoms to hospitalization was 0.41 hours longer during the pandemic, which was not significantly different (standardized mean difference, 0.41, 95% CI, –0.03 to 1.11). The operating time during the pandemic was significantly shorter than that before the pandemic (83.45 mins and 71.65 mins, p = 0.01).

Conclusions: Our study found a correlation between the pandemic and severity of acute appendicitis. The higher rate of complicated appendicitis in the pandemic period indicates that patients require timely medical attention and treatment despite fears of contracting disease.

Keywords: Acute appendicitis, Complicated appendicitis, COVID-19, SAR-CoV-2

LAPAROSCOPIC-ASSISTED IVOR-LEWIS ESOPHAGECTOMY WITH DOUBLE TRACT RECONSTRUCTION, FIRST CASE IN SONGKHLA PROVINCE

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Background: Esophagogastric junction (EGJ) cancer is a low prevalent cancer therefore it does not have the standard of treatment. Various type of resection and reconstruction have been done. In part of resection, proximal gastrectomy with distal esophagectomy is the optimal operation because of concerning about the margin of resection and regional lymph node clearance. For reconstruction, esophagogastrostomy anastomosis was performed for a long time but recent research reveal reflux esophagitis and anastomotic stricture as a long term sequelae of this type of anastomosis. Recently, it is report of new reconstructive type for proximal gastrectomy. Double tract reconstruction is a type of reconstruction that was developed to overcome this problem and many literatures show a benefit in lowering chance of reflux esophagitis and anastomotic stricture.

Objective: To present case of EGJ cancer that was treat with Ivor-Lewis esophagectomy with double tract reconstruction.

Methods: 78 year old man, He present with dysphagia and body wight loss. Esophagogastroscope was reviewed circumferential mucosal mass at EGJ (35 cm from incisor). This tumor does not invade to fundus and lesser curvature. Pathologic report from biopsy is moderate differentiated adenocarcinoma.

1 month before esophagogastrectomy, we created feeding jejunostomy to improve nutrition. For adequate margin and lymph node harvesting, we decided to do laparoscopic-assisted proximal gastrectomy plus Ivor-Lewis esophagectomy.

Results: Upper gastrointestinal contrast study was done at postoperative day 10. The contrast could pass through both remnant stomach and small bowel without leakage. Final pathologic staging was T3N0M0 and free resection margin. The patient can be discharged from hospital at postoperative day 12 without any complication. At follow up on 2 weeks after discharge, the patient can eat regular diet without obstruction and do not developed reflux symptom. He was sent to medical oncologist to request for chemotherapy.

Conclusions: Laparoscopic-assisted Ivor-Lewis esophagectomy with double tract reconstruction is feasible and the best choice to prevent risk of postoperative reflux esophagitis and anastomotic stricture.

Keywords: Esophagogastric junction cancer, Esophagectomy, Double tract reconstruction

THE SUCCESS OF SECONDARY WOUND HEALING IN HUGE CHRONIC UNHEALED ACETABULAR WOUND USING HEMOGLOBIN SPRAY

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Objective: A wound resulting from hip disarticulation required a flap to close the large dead space in the acetabulum. The possibility of using a flap from the abdomen and gluteus was limited due to a suprapubic cystostomy and a grade IV pressure ulcer at the sacrum and ischium. Negative pressure wound therapy (NPWT) could have been beneficial for promoting granulation tissue, but this patient could not tolerate pain. To manage this complex case, a decision was made to use topical haemoglobin spray* (comprising purified haemoglobin which can bind oxygen from the atmosphere and diffuse it into the wound bed to increase oxygen availability to the wound tissue) to accelerate healing.

Methods: Case report: Thai male 55-year-old patient was diagnosed with bilateral aortoiliac artery occlusion and treated with a bypass graft from the right axillary artery to the right common femoral artery. Subsequently, an above-knee amputation of the right leg was required. The patient developed a large wound at the acetabulum, resulting from left hip disarticulation. He also had a grade IV pressure ulcer at the left ischium and sacrum. The patient also had a suprapubic cystostomy performed due to an infected wound at the perineum.

Result: During his hospital stay, the patient received debridement and NPWT for two sessions for the left acetabulum wound. However, he could not tolerate the pain. Therefore, to promote healing, topical haemoglobin spray was applied once daily. The wound completely healed within 12 weeks.

Conclusion: Topical haemoglobin spray dressing may be beneficial for the management of complex wounds. When treatment options were limited for this patient, topical haemoglobin spray was associated with successful healing by secondary intention.

USEFULNESS AND OUTCOME OF WHOLE-BODY COMPUTED TOMOGRAPHY (PAN-SCAN) IN TRAUMA PATIENTS: A PROSPECTIVE STUDY

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Background: Severe trauma mechanism can cause multi-organ injury which physicians can missed a significant organ injury lead to increase morbidity and mortality rate.

Objectives: Pan-scan detected of significant injury and lead to proper management including of prioritization for the patients without delay.

Methods: A prospective study from January 2019 to March 2021 trauma patients whom were triage in trauma level I and II, and dangerous mechanism. A retrospective of trauma patients who underwent selective scan before implementation of pan-scan protocol were collected for clinically benefit compared.

Results: A total of 22 patients were enrolled in prospective study. The pan-scan detected significant organ injury 86%. Prioritization of organ management has change after underwent pan-scan in 64% (major change 64.29% and minor change 35.71%). Base of skull fracture, small bowel injury, retroperitoneal injury, kidney and bladder injury, and occult pneumothorax were statistically significant found by pan scan ($p < 0.05$). There was no agreement between occult pneumothorax and base of skull fracture after underwent pan-scan with kappa scale -0.084 and -0.073 retrospectively. Door to CT time trend to faster in pan-scan without statistically significant compared to selective scan, 59.5 (34) mins and 72 (86) mins (p-value = 0.13).

Conclusions: Pan-scan help detected significant injury in hidden area such as base of skull, small bowel, and retroperitoneum lead to proper management and prioritization of management.

Keywords: Pan-CT scan, Whole body CT scan, Trauma, Pan-scan, Multiple trauma

Free Paper Cardiovascular Thoracic Surgery

RELATIONSHIP BETWEEN RV-TO-LV RATIO AND IN-HOSPITAL MORTALITY IN PATIENT WITH ACUTE MASSIVE PULMONARY EMBOLISM; PRELIMINARY STUDY IN SONGKLANAGARIND HOSPITAL

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Background: Acute pulmonary embolism (PE) is a rare condition that has high morbidity and mortality. With good resolution of CT angiographic study, severe of PE can be evaluated in more details.

Objective: This study aims to look for core-relation between parameters derived from preoperative CT and in-hospital mortality in patient with acute massive PE.

Methods: A retrospective review of patient with acute massive PE in our institute was conducted from the year 2009 to 2019. Data were retrieved from electronic medical records and radiological archives. Thrombus size was calculated by measuring three-dimension of intrapulmonary arterial thrombus, RV/LV means ratio of the greatest diameter of mid-chamber of right ventricle and left ventricle respectively.

Results: A total of 43 patients were included in this analysis (28 Female and 15 Male). Average age was 55.4 years (range 15-79 years). The most underlying conditions were malignancies, renal insufficiency and venous thromboembolism. In-hospital mortality 10 in 43 cases (23.2%). Median clot size was 20.9 milliliters (IQR 11.9-27.6), Median RV to LV ratio was 1.58 (IQR 1.22-1.85). Factor associated with in-hospital mortality included pre-operative blood pH (p-value 0.02) and post-operative blood pH (p-value < 0.01). RV to LV ratio in mortality case was 1.8 while in survival case was 1.6 (p-value = 0.12). However, when removed 3 outliers from analysis, RV to LV ratio in mortality case was significantly higher than that of the survival cases (p-value = 0.03)

Conclusion: RV to LV ratio maybe a predictor of mortality in a patient with acute massive PE. The study should be continued to include more data.

Keywords: Pulmonary embolism, Computerized tomographic pulmonary angiography, RV to LV ratio, Mortality

Free Paper General Surgery

A COMPARISON OF OUTCOMES BETWEEN MULTICENTRIC AND MULTIFOCAL BREAST CANCER VERSUS UNIFOCAL BREAST CANCER IN RAJAVITHI HOSPITAL

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Background: The current 8th edition of the AJCC staging system of breast cancer defines tumor stage using only the largest tumor focus. This method may underestimate the total tumor burden in multifocal and multicentric breast cancer (MMBC). The optimal surgical treatment for multiple ipsilateral breast cancer remains a long-debated subject. The prognostic significance of multifocal and multicentric breast cancers are not well established.

Objectives: we evaluated whether patients with multifocal and multicentric breast cancer have different outcomes compared to unifocal disease in term of survival.

Methods: The subjects of this retrospective study were patients who underwent definitive surgery for invasive breast carcinoma at our hospital between October 2013 and January 2016. Prognostic factors and outcomes were collected from hospital database. The patient who received neoadjuvant therapy, or in metastatic stage was excluded. We evaluated overall survival using the Kaplan–Meier method.

Results: Of the 223 patients, 18 (8.1%) had multifocal-multicentric breast cancer (MMBC). The MMBC group was worse in histologic grade ($p = 0.015$), N-stage ($p = 0.006$), pathologic stage ($p = 0.034$) and more positive HER-2 ($p = 0.001$). The Overall survival were 101.2 months in patients with UBC, and 64.6 months in patients with MMBC ($p = 0.142$). All of the patient in MMBC group underwent total mastectomy.

Conclusions: Multifocal-Multicentric breast cancer are more likely to have poorer prognostic factors, they have higher histologic grade, higher in N-stage and pathologic stage. However, MMBC itself may not be predictive of a worse outcome. Our findings support the current TNM staging system of using the diameter of the largest lesion to assign T stage.

Keywords: Breast cancer, Multicentric, Multifocal, Tumor size, Survival

A SURVIVAL OUTCOMES OF POST D2GASTRECTOMY FOR ADVANCED GASTRIC CANCER TREATMENT, A DECADE EXPERIENCE IN VAJIRA HOSPITAL

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Background: Gastric cancer is one of the leading causes of cancer death worldwide. Gastrectomy with D2 lymph node dissection (D2 gastrectomy) is the standard treatment for resectable disease. The role of multimodality treatment and minimally invasive surgery have been proposed but the results of real-world practice are limited.

Objective: To evaluate overall survival (OS) and disease free survival (DFS) of gastric cancer patients who underwent D2 gastrectomy in Vajira Hospital. The factors that related to survival outcomes were evaluated.

Methods: The retrospective data of 71 gastric adenocarcinoma patients who underwent surgery at Vajira Hospital between 1 January 2012 – 30 April 2020 was reviewed. The patient characteristics, OS, DFS and prognostic factors were evaluated.

Results: The median age of patient was 67 years (range 27 to 94). Majority of patients was advanced cancer, 45.1% in stage III and 14.1% in stage IV, respectively. Most of patients (47 patients, 66.2%) underwent laparoscopic surgery. The lower 1/3 of stomach was the most common location of cancer (35 patients, 49.3%). The median number of dissected and metastatic lymph node were 30 nodes (range, 6-94) and 3 nodes (range, 0-28), respectively. A 71.8% of patients were received chemotherapy either as neoadjuvant treatment (4.2%) or as adjuvant therapy (67.6%). With the median follow up time at 22 months (range, 0-128), the 5 years OS was 69.2% and 5 years DFS was 44.6%. The multivariate showed the presence of positive peritoneal cytology was

the poor prognostic index for DFS (HR, 147.9, 95% CI, 8.6-2553.9).

Conclusion: The outcomes of the patients with advanced gastric cancer that undergone D2 --gastrectomy operation in Vajira Hospital were analyses in 5-years overall survival was 69.2% and 5-years disease free survival was 44.6%. The positive peritoneal cytology associated with poor DFS.

ACCURACY OF DIETARY EVALUATION PROGRAM FOR PATIENTS IN RAJAVITHI HOSPITAL

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Background: Nutritional assessment, by evaluating food consumption is important and necessary in surgical patients because in pre-operation and post-period then increase energy consumption, then the surgical patients are at the risk of malnutrition.

Objective: The aim of this study was to evaluate the accuracy test of dietary evaluation program by comparing the total energy and protein intake to the dietary evaluation program and weighted caloric count.

Methods: A prospective study from 30 surgical patients who eat soft or regular diet in Rajavithi Hospital from October 2020 to May 2021. The recorders of this research will fill out the administered dietary evaluation program, then they will calculate to total energy (kcal) and protein intake (gm) that will be compared to the standard method from weighted food caloric count.

Results: The mean of total energy from the dietary evaluation program and the caloric count were 1786.50 ± 629.51and 298.642 ± 103.018 kcal (p-value = 0.218). The mean of total protein intake was 75.39 ± 30.25 and 77.87 ± 32.31 gm (p-value = 0.037), and Pearson's product moment correlation coefficient of total calories and total protein between the dietary evaluation program and the caloric count were 0.940 (p-value < 0.001) and 0.959 (p-value < 0.001). The comparison of total energy and total protein between the dietary evaluation program and the caloric count, was different < 15%, accuracy rate was 86.66% (SE = 0.021) and 66.66% (SE = 0.04). And there is no difference of total energy and protein intake in lunch (p-value = 0.107).

Conclusions: The dietary evaluation program can be used to assess total energy and protein intake in the surgical patients because the mean of total energy and protein between the dietary evaluation program and the caloric count was not significantly different , and Pearson's product moment correlation coefficient of total calories and protein between the dietary evaluation program and the caloric count was related which was compared

AVERAGE DIAMETER OF ABDOMINAL AORTA IN THAI PATIENTS BY MULTIDETECTOR COMPUTED TOMOGRAPHY, A SINGLE-CENTER STUDY

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Background: One of the indications for elective surgery in AAA concerns with the diameter of the aneurysm (≥ 5.5 cm in man and 5.0 cm in woman). Normally, an average diameter of aorta is affected by sex, race and age. A pilot study shows the normal average diameter of the abdominal aorta of Thai people is smaller than to Caucasian. There are few literatures about average diameter of abdominal aorta in Thai people. This data can be used as reference and would affect future studies.

Objective: To measure diameter of abdominal aorta in multi-segments in both coronal section and transverse section for a reference of a normal average diameter in Thai adults, both male and female.

Methods: In 2018, all patients age more than 50-year-old who underwent CT abdomen with contrast media were randomized for 400 peoples in each age groups (50s,60s,70s and 80s or older) by computer. After exclusion criteria, 280 subjects were recruited. Abdominal aorta was measured for its diameter in 4 segments; supra-renal, infra-renal, aortic bifurcation, and common iliac artery (CIA) both right and left. Each segment was measured in two-dimension, coronal and transverse view.

Results: The difference of average diameter by sex in all level were statistically significant; suprarenal (male 23.0 ± 2.4 mm, female 20.8 ± 2.2 mm, p < 0.01), Infrarenal (male 18.1 ± 1.9 mm, female 15.9 ± 2.0 mm,

$p < 0.01$), Aortic bifurcation (male 17.6 ± 2.1 mm, female 16.0 ± 2.4 mm, $p < 0.01$), Right CIA (male 11.3 ± 1.9 mm, female 10.3 ± 2.0 mm, $p < 0.01$), Left CIA (male 11.0 ± 2.0 mm, female 10.1 ± 1.9 mm, $p < 0.01$). and the average diameter of aorta was also statistically significant by age group such as Suprarenal level (50s 19.9 ± 1.9 mm, 60s 20 ± 1.7 mm, 70s 21.4 ± 2.6 mm, 80s and older 21.8 ± 2.1 mm, $p < 0.001$).

Conclusion: Age, Sex, and Race have correlation to diameter of abdominal aorta. It is useful for further study about the risk of rupture of AAA in Thai patients which can may change the indication of elective surgery.

Keywords: Average diameter abdominal aorta, Factors affect diameter aorta, Normal aorta

CHARACTERISTICS OF TRAUMATIC PNEUMOTHORAX IN SEVERE TRAUMATIC BRAIN PATIENTS FROM ROAD TRAFFIC ACCIDENT

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Background: Pneumothorax is a common condition in blunt chest injury. This condition maybe missed diagnosis during clinical assessment in unconscious patients with the emergency condition. The delay diagnosis increases morbidity and mortality rate.

Objectives: Primary objective of the study was to determine characteristics for screening and diagnosis of traumatic pneumothorax condition in severe traumatic brain patients from road traffic accident. Secondary objective was to determine prevalence of traumatic pneumothorax condition in severe traumatic brain patients from road traffic accident.

Methods: The retrospective study reviewed in medical records of the 15-year-old and above patients with severe traumatic brain injury by traffic accident from 1 January 2009 to 31 December 2018. The patients were divided into two groups; the pneumothorax and without pneumothorax. Pneumothorax was diagnosed by surgeons at the emergency department with clinical manifestations from ATLS such as dyspnea, decrease breath sound, trachea shift, subcutaneous emphysema and others. Signs of pneumothorax on chest radiographs or CT and presenting of air leakage after intercostal drainage. The data were analyzed using with R program.

Results: Six hundred and eighty-six patients were identified. Five hundred and nighty-seven patients were males (87%) with median age 33 years. The cause of traffic accident was from motorcycle 571 (83.3%), motor vehicle 76 (11%) and pedestrian injuries 39 (5.7%). One hundred and twenty-two patients (18%) were diagnosed pneumothorax. A comparison between patients in pneumothorax and without pneumothorax from univariate revealed ISS score = 29 ($p < 0.001$), systolic blood pressure 128 mmHg ($p < 0.045$), pulse rate 106/min ($p = 0.005$), $SpO_2 = 94$ ($p < 0.001$), high number of rib fracture ($p < 0.001$) were significant factor in pneumothorax group. On multivariate analysis revealed only $SpO_2 \leq 95$ (odds ratio, 5.12; $p = 0.002$) were significant factor in pneumothorax group. There was no difference between the two groups in diastolic blood pressure, respiratory rate, trachea shift, wound at chest wall, lung contusion. In pneumothorax group about 50% had normal breath sound, and just only 25% had subcutaneous emphysema.

Conclusions: Hypoxemia, $SpO_2 \leq 95\%$ significantly to be parameter for diagnosis of traumatic pneumothorax condition in severe traumatic brain patients. Subcutaneous emphysema was found only 25% and normal breath sound cannot be excluded for traumatic pneumothorax condition.

Keywords: Pneumothorax, Traffic injury, Pneumohemothorax, Blunt chest injury

COMPARATIVE OUTCOMES OF GI STIMULANT DRUGS; DOMPERIDONE (MOTILIUM®) VERSUS MOSAPRIDE CITRATE (GASMOTIN®) IN POSTOPERATIVE PEPTIC ULCER PERFORATION PATIENT, RANDOMIZED CONTROL TRIAL

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Background: Enhanced recovery after surgery (ERAS) protocols was achieved to used in elective surgery. Early oral feeding in post-operative patients can shorten time of hospital stay and decrease costs and risk of infection.

Objective: The study was carried out to compare two oral prokinetic drugs in Hatyai Hospital for promote the oral feeding in post-operative peptic ulcer perforation repair patient.

Methods: This trial was conducted with the 50 participants who diagnosed with peptic ulcer perforation who were operated by suture repair with omental patch

in Hatyai Hospital. Post-operative patients randomly allocated to two group. Both groups received oral diet in 24 hours postoperative. First group received Domperidone and another group received Mosapride citrate, time of hospital stay and complication were recorded.

Result: Fifty patients were included. Each group were 25 patients. There are not significant differences time of hospital stay between Domperidone group and Mosapride citrate group (66.92 and 73.52 hours, P = 0.915). Complication rate is not significant different.

Conclusion: Early oral feeding in patients who underwent perforated peptic ulcer repair appeared to be as safe. No prokinetic drugs has superior effect than each other.

Keywords: GI stimulant drugs, Enhanced recovery after surgery, Peptic ulcer perforation

COMPARISON OF CLINICAL OUTCOMES BETWEEN PLASTIC AND LUMEN-APPOSING METAL STENT FOR ENDOSCOPIC ULTRASOUND-GUIDED PANCREATIC FLUID COLLECTIONS DRAINAGE IN RAJAVITHI HOSPITAL

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Background: EUS-guided drainage is the procedure of choice to treat pancreatic fluid collection (PFC) and traditionally using plastic stent placing through the created fistula tract between transmural and the pancreatic pseudocyst or wall-off pancreatic necrosis (WON) for drainage. Rajavithi Hospital has first imported lumen apposing metal stent (LAMS) since November 2016 for drainage of WON according to the necrotic tissue made more thickness of the content causing difficult to drain and for further performing necrosectomy if needed. No available clinical results have been studied to compare with plastic stents.

Objectives: The primary outcome was to compare the duration of stent stay of EUS-guided PFC drainage between plastic stent and LAMS. The secondary outcomes were to compare the technical success, adverse event, procedure time, and cost of procedure.

Methods: This was a retrospective study that had been using the database of patients with PCF who underwent EUS-guided drainage from the Department of General Surgery, Rajavithi Hospital, Thailand since November 2016 to October 2020.

Results: A total of 31 patients with PFCs who were underwent EUS-guide transmural drainage**.** Plastic stents were used in 10 patients, and 21 patients used LAMSs**.** The mean duration of stent stay was 74.20 days in plastic stent group and 63.95 days in LAMS group (p = 0.512). The overall technical success rate was 96.8%. The time procedure of LAMS group was significantly longer (p = 0.032). Overall procedure-related adverse events occurred in 2 of 31 patients (10.0% in plastic stent groups VS 4.8% in LAMS group, p = 1.000). The total procedure-related costs were 38,056.1 THB in plastic stent groups and 93,498.7 THB in LAMS groups (p < 0.001).

Conclusion: EUS-guided drainage of PFCs by using LAMS had safe and effective for drainage of PFCs. LAMS is suggested to treat the PFCs especially in WON.

Keywords: Pancreatic fluid collection, Endoscopic ultrasound-guided drainage, LAMS

COMPARISON OF OUTCOMES OF STANDARD TOTALLY EXTRAPERITONEAL (TEP) AND ENHANCED VIEW TOTALLY EXTRAPERITONEAL (eTEP) TECHNIQUE IN INGUINAL HERNIA REPAIR; A PILOT RANDOMIZED CONTROLLED TRIAL STUDY

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Background: Nowadays, laparoscopic inguinal hernia repair has become the standard treatment of inguinal hernia repair. Two standard techniques are totally extraperitoneal approach (TEP) and trans-abdominal preperitoneal approach (TAPP). TEP technique have more strength than TAPP in that it is not injure peritoneum and has lower risk of intra-abdominal organ injury. However, TEP also have its weakness in limited space of dissection. Many modification techniques of TEP have been proposed. Enhanced view TEP (eTEP) is one of the popular techniques which to overcome aforementioned limitation. There has been no study comparing the result of TEP and eTEP until now.

Objective: This study compared intraoperative and postoperative outcome of patient received TEP and eTEP technique repair.

Methods: Forty-one patients with inguinal hernia were enrolled in this pilot study. Twenty-seven patients received TEP repair and twelve patients received eTEP repair. The demographic data, intra-operative variable (including operative time, estimated blood loss, intra-operative findings, mean arterial pressure, $EtCO_2$, and intra-op complication) and post-operative variables (post-operative pain, patient satisfaction, post-operative complication) were recorded.

Results: The Demographic data of patients, operative time and estimated blood loss were similar in both groups. There were 2 conversions from TEP to TAPP. There was 1 recurrence in TEP group during follow up. The post-operative pain in both groups has no differences and not exceeds 6 (from VAS 1-10). All patients have satisfied for operation and for wound in both group but have more satisfaction more for wound in TEP group. (p-value 0.024).

Conclusion: eTEP is the modification technique of TEP which provide same perioperative outcome and lower conversion rate (to TAPP approach) comparing with standard TEP. The drawback of eTEP is less cosmesis result of surgical scar.

DO WE NEED FASCIAL CLOSURE FOR 12 MM TROCAR? A COMPARATIVE STUDY OF TROCAR SITE HERNIA WITH LONG-TERM FOLLOW-UP

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Background: Fascial wound closure was recommended for the prevention of trocar site hernia (TSH) when using ≥ 10 mm size trocar. Although, the incidence of TSH was rare. Therefore, we would like to identify the necessity of fascial closure in a 12-mm non-bladed trocar with long-term cross-sectional imaging follow-up.

Methods: 254 patients undergone laparoscopic surgery with 12 mm non-bladed trocar at Minimally Invasive Unit, Siriraj Hospital between July 2010 and December 2018 were retrospectively analyzed. All of the patients have cross-sectional imaging for evaluation of TSH. 70 patients (111 ports) were categorized into "fascial closure" group and 184 patients (279 ports) were categorized into "non-fascial closure" group.

Results: Median interval of follow-up time was 43 months. We identified TSH 3 patients in non-fascial closure group whereas no TSH in fascial closure group [3/279 (1.1%) vs 0/111 (0%), $p = 0.561$]. Two TSH cases were asymptomatic and one of two cases was received elective repair surgery.

Conclusion: There is no significant difference of TSH between the fascial closure and non-fascial closure group in this recent study. However, the number of patients in the fascial closure group is limited.

Keywords: Laparoscopy, Trocar site hernia, Port site hernia

EFFICACY OF 2% XYLOCAINE VISCUS IN PAIN CONTROL AFTER POST HEMORRHOIDECTOMY: A RANDOMIZED CONTROLLED TRIAL

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Background and Objective: In a general population about 5% is affected by symptoms related to hemorrhoid which is usually conservatively treated. Patient who fails medical treated are candidate for surgical treatment however, post-operative pain is main challenges and frequent complaints. Therefore, to determine efficacy of 2% xylocaine viscus in pain control after post hemorrhoidectomy, a randomized controlled trial was done.

Methods: A total of 40 elective hemorrhoidectomy patient was recruited and double-blind randomized patient into two group. After surgery, one group received 2% xylocaine viscus and other group received placebo KY-jelly. Pain measurement was done using visual analog scale (VAS) 2 hours, 6 hours, 12 hours and 24 hours after surgery which is the primary outcome. Secondary outcome is the requested frequency and dosage of morphine, first spontaneous voiding time, frequency of single urinary catheterization was obtained.

Results: A total of 40 patients were included in Randomized control trial (20 in each group). The result revealed that 2% xylocaine viscous group has significantly lower pain score compare to placebo group

($P < 0.05$, 95% CI 0.84 to 3.46) especially 6 hours after post-operation. The frequency and dosage of morphine injections, frequency of catheterization was significantly lower in 2% xylocaine viscous group. There was no statistically significant difference between the intervention and control group of sex, ages, BMI, operative time and number of hemorrhoids excised. ($p > 0.05$ for all). No post operation or systemic complications were observed in both groups.

Conclusion: 2% xylocaine viscous decreased pain intensity and morphine requests, reduced the frequency of single catheterizations after hemorrhoidectomy.

Conflict of interest: There are no actual or potential conflicts of interest to declare.

Keywords: Hemorrhoidectomy, Pain post hemorrhoidectomy, Xylocaine viscous

ENDOVASCULAR STRATEGIES AND 10-YEAR-OUTCOMES FOR TREATMENT OF ASYMPTOMATIC ABDOMINAL AORTOILIAC ANEURYSM

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Background: Abdominal aortoiliac aneurysm (AAIA) has been reported involvement about 10% of abdominal aortic aneurysm. Endovascular treatment of AAIA is challenging due to the internal iliac artery (IIA) involvement. IIA embolization and limb extension to external iliac artery (IIAE + EE) to avoid type 1B endoleak may result in ischemic complications. IIA preservation strategy, which are bell-bottom technique (BBT; iliac limb ≥ 24 mm) and iliac branched device (IBD) is proposed to avoid these complications.

Objective: To compare early and late outcomes among three endovascular approaches for AAIA.

Methods: From January 2010 to December 2019, 174 patients with asymptomatic AAIA divided into 147 of non-IBD (IIAE + EE and BBT) and 27 of IBD were enrolled (82.8% male; median age 76 years; range 56-90 years). Three endovascular strategies consisted of 106 of BBT, 113 of IIAE+EE, and 32 of IBD. Primary outcomes were intra-operative limb complications and 30-day mortality. Secondary outcomes were postoperative buttock/pelvic ischemia, freedom of re-intervention among three strategic treatments, and overall survival at 10 years follow-up.

Results: Intra-operative limb complications were not statistically significant among BBT (7.5%), IIAE+EE (3.5%), and IBD (3.1%), *P*-value = 0.349. There was no statistical significance in perioperative mortality between non-IBD group (1.4%) and IBD group (0%), *P*-value = 1). During 10 years follow-up, the rate of iliac limb reintervention was significantly higher in BBT compared with IIAE+EE and IBD (12.3%, 1.8%, and 6.2%, *P*-value = 0.004). The incidence of buttock claudication was significantly greater in bilateral IIAE+EE group compared with unilateral IIAE+EE and no IIAE group (25%, 11%, and 2.5%, *P*-value < 0.004), similarly with the incidence of pelvic organ ischemia (15%, 1.2%, and 0%, *P*-value < 0.001) There was no statistical significance in overall 10-year survival rates between non-IBD and IBD groups (44.4% vs 46.3%, *P*-value = 1).

Conclusions: The early and late mortality were comparable between non-IBD and IBD groups. To avoid pelvic and buttock ischemic complications, IIA preservation strategy should be recommended. It is due to the higher rate of reintervention in BBT group, the IBD strategy might be preferred for AAIA.

Keywords: Abdominal Aortoiliac Aneurysm, EVAR, Iliac Branched Device, Bell-Bottom Technique, Internal Iliac Artery Embolization

EX-SMOKER WAS THE PROGNOSTIC FACTOR FOR AMPUTATION IN PAD IN SRINAGARIND HOSPITAL

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Background: Peripheral arterial disease (PAD) refers to partial or complete occlusion of the peripheral vessels of the upper and lower limbs. The prevalence of PAD is increasing in the future due to the rise in its major risk factors. This disease has high morbidity and mortality. Several factors have been reported (mostly from studies conducted in Western countries) to be associated with major amputation in PAD cases such as DM, HT, Renal disease and drugs.

We conducted a pragmatic study, looking at a 10-year period, aimed at understanding the prognostic factors related to amputation in PAD in a university hospital.

Objective: The outcome of this study was the prevalence of amputation in PAD patient, and it factor.

Methods: This was a retrospective study conducted at faculty of medicine in the Khon Kaen University (Thailand). All patients diagnosed with PAD that were treated between 2008 and 2018 were consecutively enrolled. The diagnosis of PAD was made by clinical presentations or ABI < 0.9. The outcome of this study was the prevalence of amputation in PAD patient, and it factor. Prognostic factors were determined using Logistic regression analysis.

Result: There were 223 PAD patients treated at the university hospital during the 10-year period of the study. The median age of all patients was 65 years (range 59-76 years). Of those, 221 (99.1%) were symptomatic with major tissue loss 81 (36.32%), minor tissue loss 56 (25.11%), ischemic rest pain 54 (24.22%) and claudication 30 (13.4%). A total of 68 patients (30.49%) was amputated. Ex-smoker was the only one significant factor associated with amputation.

Conclusion: Ex-smoker was the prognostic factor for amputation in PAD patient.

Keywords: Peripheral arterial disease, Lower limb amputation

FACTOR RELATED EARLY AND UNPLANNED PERCUTANEOUS TRANSHEPATIC BILIARY DRAINAGE EXCHANGE A RETROSPECTIVE STUDY

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Background: Patients often require more than one time procedure to these disorders and often need to repeat PTBD before the appointment. Many problems are followed after unplanned PTBD such as not enough hospital bed for admission, worsen of patients' symptom. In Rajavithi Hospital, there is not enough data to evaluate the cause of unplanned PTBD, this study's aim to find factors that may increase the risk of early and unplanned PTBD exchange.

Objectives: Percutaneous transhepatic biliary drainage (PTBD) is the common therapeutic procedure for biliary obstruction in both benign and malignancy conditions.

Methods: A total of 544 PTBD procedures performed in 135 patients at the Interventional radiology department of our hospital between January 2019 to December 2020, were retrospectively evaluated. Baseline characteristic of patients and procedure were assessed. Univariate logistic regression was used to analyzed risk factors for requiring unplanned repeat PTBD. Chi-square test or Fisher exact test was used to statistically analyze the results. The level of significance was set at $p < 0.05$.

Results: 101 patients underwent PTBD for malignancy condition (74.8%) and the rest received PTBD for benign condition (25.2%). 71 patients had an unplanned repeated PTBD before there appointment, 56 from 71 patients (55.4%) were diagnosed with malignancy condition. Most common indication was dislodgement (66/71 98.5%). Perihilar Cholangiocarcinoma is the main diagnosed in unplanned group (34/71 47.9%). All these factors included: patient's disease, stage of cancer, size, position, type, fixation of stent was not associated with significant risk of early PTBD exchange.

Conclusion: Although our study shows that no factor was statistically significant relate with risk of early PTBD exchange, patients present with perihilar cholangiocarcinoma trend to had much greater number of unplanned PTBD exchange.

FACTORS AFFECTING THE FREE PERITONEAL CANCER CELLS IN ADENOCARCINOMA OF STOMACH AND ESOPHAGOGASTRIC JUNCTION

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Background: Advance gastric cancer with positive peritoneal cytology M1(cy+) is the marker of metastatic disease with poor prognosis. However, there is no standardized preoperative investigation for prediction.

Objectives: This study was to identified risk factor for M1(cy+) in adenocarcinoma of stomach and esophagogastric junction (GC and AEG) as a primary outcome. The secondary outcome was overall survival and disease-free survival.

Methods: The study included 349 patients who was diagnosed with GC and AEG underwent curative surgery and had peritoneal fluid cytology report in Siriraj hospital. Univariate and multivariate analyses were done for factors associated with positive cytology. Kaplan-Meier analyses was performed for overall survival and disease-free survival.

Results: From January 2005 to December 2020, 349 patients were reviewed who underwent curative surgery and peritoneal washings ; 32 (9.2%) had positive cytology; 188 (53.8%) had negative cytology and 129 (36.9%) had atypical cell cytology. Poorly differentiation, T4 staging, N3 staging and LN ratio > 0.4 were significantly associated with positive cytology. Multivariate analysis revealed that N3 stage and LN ratio > 0.4 were significant risk factor affected cytology. In subgroup analysis in patients age under 70 years found that AEG type II and III (OR 7.06, $p = 0.009$) and LN ratio > 0.4 (OR 14.68, $p = 0.024$) were associated with M1(cy+). 5-year overall survival of positive, atypical and negative cytology were 8.3%, 27.2% and 25.3% ($p < 0.001$). 3-year disease free survival were 0%, 17.8% and 17.4% ($p < 0.001$) respectively.

Conclusion: Advanced nodal metastasis and poorly differentiated histopathology were associated with positive cytology. Presence of peritoneal cancer cell was associated poor prognosis. Therefore, this study may guide to select patient for preoperative treatment to improve oncological outcome of M1(Cy+) GC and AEG.

IMPACT OF PREOPERATIVE ESOPHAGOGASTRODUODENOSCOPY IN PATIENTS UNDERGOING BARIATRIC SURGERY

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Background: Preoperative esophagogastroduodenoscopy (EGD) in patients undergoing bariatric surgery can help surgeon detecting the abnormalities in the upper gastrointestinal (UGI) tract that may require a change in surgical plan. However, there is controversy on the need for EGD before bariatric surgery.

Objectives: We aimed to determine the prevalence of UGI abnormalities and to evaluate the predictive factors of abnormal findings that require a change in surgical plan or cause a delay in surgical treatment in patients undergoing bariatric surgery.

Methods: We retrospectively reviewed the medical records of patients undergoing EGD before bariatric surgery from January 2012 to July 2020. The EGD findings were classified into 4 groups based on their effects on management. Group 1 had normal finding. Group 2 had abnormal findings that did not require a change in surgical management. Group 3 had abnormal findings that required a change in the surgical plan or caused a delay in surgical treatment. Group 4 had contraindications to surgery. Predictive factors for the groups requiring a change in surgical plan or cause a delay in surgical treatment (Group 3&4) were analysed using univariate and multivariate analyses.

Results: A total of 461 patient records (63.8% females) were reviewed. Mean age was 35.1 ± 11.2 years and mean BMI was 47.7 ± 8.7 kg/m^2. The prevalence of endoscopic findings in Groups 1, 2, 3, and 4 were 42.5%, 35.6%, 21.9%, and 0%, respectively. The most common abnormal findings were non-erosive gastritis (31.2%) followed by *Helicobacter pylori* infection (18.7%), and hiatal hernia (10.2%). Male sex and NSAID use were significantly associated with the detection of Group 3&4 lesions either on univariate or multivariate analysis, while type 2 diabetes mellitus (T2DM) was a significant protective factor on multivariate analysis. Subgroup analysis in patient with age ≥ 40 years old, multivariate analysis revealed age, BMI and NSAID use were significantly associated with the detection of Group 3&4 lesions, while T2DM was still a significant protective factor.

Conclusions: There was a high prevalence of abnormal endoscopic findings in Thai patients undergoing bariatric surgery. Preoperative EGD is helpful to screen the UGI abnormalities, particularly in male and patients using NSAID.

Keywords: EGD, Bariatric surgery, Esophagogastroduodenoscopy, Preoperative EGD.

INCIDENCE AND PREDICTIVE FACTORS OF GALLSTONE DISEASES AFTER BARIATRIC SURGERY: A SINGLE-CENTER RETROSPECTIVE STUDY

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Background: Several reports showed high incidence of gallstone diseases after bariatric surgery. The amounts and rate of weight loss is known as the predictive factors for gallstone formation. However, the incidence and predictive factors in Asian populations have not been adequately studied.

Objective: We aimed to evaluate the incidence and predictive factors of gallstone diseases after bariatric surgery in the Thai population.

Methods: Patients who underwent laparoscopic sleeve gastrectomy (LSG) and laparoscopic Roux-en-Y gastric bypass (LRYGB); between 2012 and 2019, were retrospectively reviewed. All patients underwent routine preoperative imaging for gallstone diseases. Follow-up imaging for gallstone diseases was performed every year after surgery, or once the patients became symptomatic. Patients with preexisting gallstone, gallbladder polyp, the absence of postoperative imaging for gallstone diseases, previous cholecystectomy/ bariatric surgery, or taking gallstone-lowering prophylactic agent were excluded. Predictive factors for postoperative gallstone diseases were analyzed using univariate and multivariate analysis.

Results: A total of 243 patients (62.1 % females), who underwent LSG (70.8%) or LRYGB (29.2%), with a mean (SD) age of 36.4 (11.2) years were included for analysis. The incidence of postoperative gallstone diseases was 19.3 % (symptomatic 1.2% and asymptomatic 18.1%), with a median follow-up of 24.6 (range 6.1-98.4) months. Preoperative body mass index (Pre-BMI) was significantly associated with the development of postoperative gallstone diseases [OR (95% CI): 1.07 (1.02, 1.12), $p = 0.004$], while gender, age, comorbidities, type of procedure, percentage of total weight loss and rate of weight loss were not associated with postoperative gallstone disease developments. Furthermore, patients with a BMI ≥ 50 kg/m^2 were 3 times more likely to develop postoperative gallstone diseases after bariatric surgery compared to those with a BMI < 50 kg/m^2 [OR (95% CI): 3 (1.26, 7.13), $p = 0.013$].

Conclusion: The incidence of gallstone diseases after bariatric surgery was relatively high. Pre-BMI was being only predictive factor in this study. Regular screening of gallstone should be considered after bariatric surgery, particularly in patients with high BMI. However, only a few patients developed symptomatic gallstone. Further studies should be conducted to determine the benefit of gallstone-lowering prophylactic agents on the reduction of postoperative gallstone diseases.

Keywords: Incidence, Factor, Obesity, Bariatric, Gallstone

INCIDENCE OF COLORECTAL POLYP AT 4-YEARS IN COLORECTAL CANCER PATIENTS AFTER CURATIVE SURGERY

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Background: In Thailand, colorectal cancer is the third and fourth most common cancer. Surgery is the main strategy of treatment and surveillance program is recommended to monitor the recurrence of the disease. Adenoma-carcinoma sequence is one of the important mechanisms of colorectal cancer. Colonoscopy is essential methods to detect colorectal neoplasm and neoplastic polyp. However, no standard global consensus exists for the details of a follow-up interval for each tool in a surveillance program.

Objective: To determine the incidence and predicting factors of new colorectal polyps at 4-years following curative surgery in colorectal cancer patients who had normal or non-advanced adenomatous polyp at 1-year post- operative colonoscopy.

Methods: Colorectal cancer patients who underwent curative resection at Songklanagarind Hospital by one colorectal surgeon from July 1, 2003 to December 31, 2015 were. A total of 347 patients who had negative results or non-advanced adenomatous polyp at the first-year received colonoscopy 3 years later.

Once a lesion was detected, a biopsy sample was collected. The incidence of polyp was investigated and the predictors associated with the occurrence of polyp were calculated by multivariate logistic regression analysis.

Results: Among 347 patients, 193 (56%) were male and 154 (44%) were female. The adenomatous polyp at second colonoscopy at 4 years after surgery was found in 129 patients (69%) of 187 lesions, with 2 cancer lesions (1%). Patients who had adenomatous polyp at the first postoperative colonoscopy had statistically significant adenomatous polyp detection at 3 years later more than those who had no polyp detection (60% vs 18%, $p < 0.001$). The predicting factors significantly associated with colorectal adenomatous polyp detection at 4-year post operation were age > 70 years (adjusted OR 4.6: 95% CI 1.58-13.41, $p = 0.005$) and hypertension (adjusted OR 1.75: 95% CI 1.05-2.96, $p = 0.038$). On the other hand, primary rectal cancer and right-side colon cancer were significantly associated with a lower incidence of colorectal polyp; adjusted OR 0.41: 95% CI 0.23-0.72, $p = 0.002$ and adjusted OR 0.38: 95% CI 0.17-0.84, $p = 0.017$, respectively.

Conclusions: Incidence of adenomatous polyp detection at 4-year postoperative colonoscopy was one-fourth; therefore, surveillance colonoscopy at this period was essential especially for patients who had adenomatous polyp detection at 1-year postoperative colonoscopy, > 70 years old, hypertension and left side colon.

Keywords: Colorectal cancer, Surveillance colonoscopy, Polyp, Predicting factor

INCIDENCE OF WEIGHT REGAIN FOLLOWING LAPAROSCOPIC SLEEVE GASTRECTOMY (LSG)

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Background: Laparoscopic sleeve gastrectomy (LSG) is the most popular bariatric procedure in treating morbid obesity patients worldwide. LSG is providing the good long term results including weight loss, the resolution of comorbidities and the quality-of-life improvement. Nevertheless, weight regain after LSG is the concern issue and still underdetermine.

Objective: To determine the incidence of weight regain after LSG in Srinagarind Hospital.

Methods: Retrospective review of the patients who underwent LSG between July 2011 to January 2019. The patients were tracked two years after operation. Demographic data, lowest and highest weight were collected. The primary outcome was incidence of weight regain after LSG. The secondary outcome was to identify factors correlated to weight regain after LSG.

Results: A total of 112 patients underwent LSG during the study period which complete 2-year follow-up were 73 patients (65.18%). There were 48 female (66%) and 25 male (34%) patients, with median age of 37 years (range; 15-69). The median preoperative body weight and body mass index (BMI) were 109 kg (range; 70-233) and 41.79 kg/m2, respectively. The mean excess weight loss (EWL) in 2 years was 76.53% (range; 13.90-83.34). Our study defined weight regain as an increase of > 25%EWL from nadir. The incidence of weight regain at 2 years after LSG was 13.70% (n = 10). Weight regain was higher in larger bougie size more than 38Fr with OR of 1.61 (95%CI 1.002-2.58). The other factors including initial weight, initial BMI, comorbidities were not significantly correlated with weight.

Conclusion: The short-term outcome of LSG has been promising in term of weight loss. The incidence of weight regain after LSG in our study was acceptable. However, the adequate long-term follow-up was needed to evaluate the result of this operation.

Keywords: Weight regain, Laparoscopic sleeve gastrectomy, Morbid obesity, Bariatric surgery

LAPAROSCOPIC CHOLECYSTECTOMY IN THE CRITICAL VIEW OF SAFETY ERA: A SINGLE CENTER ANALYSIS

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Background: The incidence of bile duct injury (BDI) after laparoscopic cholecystectomy is 0.4-1.5%. The critical view of safety (CVS) identification technique is a means to identify cystic duct and cystic artery. This technique can reduce the incidence of biliary injuries.

The three elements of CVS identification are to clearing the hepatocystic triangle, take the lower part of the gallbladder off from cystic plate and identify only two structures that enter the gallbladder. There is reliable evidence that CVS identification is effective in preventing biliary injury.

Objective: To determine the important of critical view of safety timeout technique in laparoscopic cholecystectomy.

Methods: Since November 2015 to November 2019, the data of patients submitted to laparoscopic cholecystectomy in Hatyai Hospital, were included. A critical view of safety (CVS) identification was performed for some patients underwent laparoscopic cholecystectomy. After identified CVS, we also performed CVS-timeout, that announced to colleagues about CVS information. Demographic characteristic of the patients, as well as intraoperative and postoperative complication were recorded.

Results: Data of 1041 patients were analyzed. The study population was categorized into two groups according to the evidence of BDI, present (Group A; n = 14) and absence (Group B; n = 1027). The non-CVS timeout was found in 50% of procedure in the group A, and 61.5% in the group B and evaluating the operative time of procedure was associated with significantly lower incidence of BDI. Surgical site infection (SSI) is the most postoperative complication, that was about 36 patients (3.45%). The others complication including postoperative collection, cholangitis, incisional hernia was found in few patients.

Conclusions: The CVS timeout technique in laparoscopic cholecystectomy was not associated significantly lower incidence of BDI.

Keywords: Critical view of safety, Laparoscopic cholecystectomy

NEGATIVE APPENDECTOMY RATE IN PATIENT DIAGNOSED WITH ACUTE APPENDICITIS IN SONGKLANAGARIND HOSPITAL DURING 2015 – 2019

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Background: The diagnosis of acute appendicitis has still challenged and often turns out to be the negative appendectomy in the operation. The disadvantages of negative appendectomy do not only waste time and increase the hospital cost unnecessarily but also increase the risk of the patient getting from the operation, anesthesia and post-operative complications.

Objective: This study aims to find the negative appendectomy rate in patients diagnosed with acute appendicitis in Songklanagarind Hospital during 2015-2019.

Methods: This study was a retrospective cohort study in the patients preoperatively diagnosed with acute appendicitis and underwent the appendectomy at Songklanagarind Hospital from January 2015 to December 2019. The negative appendectomy was defined as the final pathologic results confirmed normal, congestion or peri-appendicitis. The categorical data was compared. The logistic regression measured the relationship between dependent and one or more independent variables.

Results: The study population was 892 patients which was 54.3% in female. The five-year negative appendectomy rate was 8.6% (n = 77) which was 70% in female (n = 54). The factors associated with increasing the negative appendectomy rate were female (OR 2.23, $P = 0.003$), age-40 years old (OR 2.35, $P = 0.003$), no history of diarrhea (OR 2.42, $P = 0.017$). Whereas the factors related to decline the negative appendectomy rate were white blood cell count (WBC) $\geq$ 10,000 (OR 0.39, $P = 0.016$), neutrophil (N) $\geq$ 75% (OR 0.28, $P < 0.001$), positive appendicitis from ultrasonography of abdomen (OR 0.04, $P < 0.001$), and from computed tomography of abdomen (OR 0.07, $P < 0.001$)

Conclusion: The negative appendectomy rate was less than 10% in this study. Female, age 40-years old and history of diarrhea were related to increase the negative appendectomy. The factors that related to decline the negative appendectomy were leukocytosis with cells shift to the left, positive acute appendicitis from abdominal ultrasonography and CT scan. However, to request the further imaging studies to diagnose patients who suspected acute appendicitis depends on the risk and benefit of each patient and investigation.

Keywords: Acute appendicitis, Negative appendectomy, Alvarado score, Factors

OUTCOMES OF EARLY LAPAROSCOPIC CHOLECYSTECTOMY VERSUS DELAYED LAPAROSCOPIC CHOLECYSTECTOMY IN ACUTE CHOLECYSTITIS IN SRINAGARIND HOSPITAL

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Background: Early laparoscopic cholecystectomy (LC) is a modern trend treatment of acute cholecystitis. In Srinagarind Hospital has just followed Tokyo guideline 2018 with concern about complication, conversion and cost effectiveness. The aim of this study was to evaluate the safety, length of stay and overall hospital cost of early LC comparing with delayed LC in acute cholecystitis patients.

Methods: Between January 2012 to March 2021, we carried out a retrospective cohort study in Srinagarind Hospital by finding the inpatient department data. We included an acute cholecystitis patient with early LC (LC within 72 hours after diagnosis) and delayed LC (LC more than 72 hours after diagnosis) with randomly collected data in 61 patients in each group.

Results: The patient characteristic in 2 groups was no different in gender (male (60.66% VS 52.46%); $P = 0.361$), weight (65.6 ± 12.74 VS 65.91 ± 16.88; $P = 0.699$) and BMI (24.39 ± 4.33 VS 25.65 ± 6.06; $P = 0.376$). The severity of acute cholecystitis was no different in 2 groups [(mild (47.54%: 63.93%), moderate (29.51%: 18.03%), severe (22.95%: 18.03%); $P = 0.172$].

We found statistically significant differentiation between early and delayed LC in mean. Overall hospital cost (76295.35 ± 79,041.85 VS 91,810.31 ± 104,845.3 (Thai Baht); $P = 0.007$) length of stayed (8.44 ± 6.66 VS 13.87 ± 5.25 day; $P < 0.001$) and number of ports [3 ports 40.98% (n = 25) VS 68.85% (n = 42 and 4 ports (59.02% (n = 36) VS 31.15% (n = 19) $P = 0.002$]. There was no statistically significant differentiation in complication rate (9.8% (n = 6) vs 4.9% (n = 3); $P = 0.491$), estimate blood loss (75.67 ± 108.73 VS 68.64 ± 176.43; $P = 0.095$), operative time (101.57 ± 36.86 VS 110.82 ± 49.20 minute; $P = 0.346$) and conversion rate (14.7% (n = 9) VS 18.0% (n = 11); $P = 0.807$).

Conclusions: Early LC was practicable and feasible for acute cholecystitis in Srinagarind Hospital. There are safe, shorter length of stay, and lower overall hospital cost with no statistically different of complication rate, operative time and conversion rate. However, the early LC group required a greater number of port than in delayed LC group.

Keywords: Acute cholecystitis, Early laparoscopic cholecystectomy

PATENCY OF BRACHIAL VEIN TRANSPOSITION ARTERIOVENOUS FISTULAS FOR HEMODIALYSIS ACCESS IN RAJAVITHI HOSPITAL

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Background: Nowadays, end stage renal disease (ESRD) is one of the most problem that effect world population. Most of ESRD patients (about 65%) need to hemodialysis. Due to KDOQI guideline "Fistula first", most of ESRD patient must have hemodialysis with arteriovenous fistulas (AVF). In Rajavithi Hospital, we have Brachial artery-Basilic vein transposition AVF operation in the patient that are hostile vascular so this is the point the we want to study the primary patency of BVTs-AVFs.

Objective: Aim of this study are "to study the patency and complication of Brachial vein transposition arteriovenous fistulas for hemodialysis access in Rajavithi Hospital".

Methods: Research design is Retro-Prospective study from the data in July 2017 - July 2021 by examing the primary patency of Brachial vein transposition arteriovenous fistulas for hemodialysis access in Rajavithi Hospital. The study data include general information of patients, primary patency and complication of Brachial vein transposition arteriovenous fistulas.

Results: 51 patients underwent Brachial vein transposition arteriovenous fistulas. The primary patency at 3 months, 6 months, 12 months, 18 months and 24 months was analysis by Kaplan-Meier curve the result is 100%, 95%, 60%, 54% and 42% respectively. 14 patients (27%) had post-operative complication. 7 patients (50%) were thrombosed AVF, 3 patients (21%) were AVF stenosis, 2 patients (14%) were central vein stenosis, 1 patient (7%) was infected AVF and 1 patient (7%) was hematoma.

Conclusions: Brachial vein transposition arteriovenous fistulas is one suitable procedure for hostile vascular patients.

Keywords: Brachial vein transposition arteriovenous fistulas, Hemodialysis access, Arteriovenous fistulas, Patency

POSTOPERATIVE SURGICAL COMPLICATIONS AFTER KIDNEY TRANSPLANTATION: A 10-YEAR REVIEW

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Background: Kidney transplantation has been the standard of care in end-stage renal disease. However, surgical complications are still a source of morbidity and mortality.

Objective: To explore the incidence of 90-day postoperative surgical complications following kidney transplantation and their relationship to graft survival in our institution.

Methods: A ten-year retrospective cohort study of consecutive kidney transplant patients from January 2008 to December 2017 ended the follow-up period in December 2019. The incidence and type of postoperative surgical complications within 90 days were determined. Overall graft survival was analyzed using the Kaplan-Meier method. Cox proportional hazard was employed to determine the relationship between surgical complications and graft survival.

Results: Among the total 462 patients, the incidence of 90-day postoperative surgical complications was 17.32% [95% CI: 13.98-21.08%] (n = 80). Surgical complications were bleeding (48.75%), vascular complications (40.00%), urological complications (11.25%), wound complications (6.25%), lymphocele (1.25%). No mortality related to surgical complications was found. The median follow-up was 70.9 months with 37 graft losses observed. The mean graft survival was 133.33 (95% CI: 129.80-136.87) months. Graft survival rates at 1, 3, 5, 7, 10 years were 98.04%, 96.21%, 93.90%, 91.33%, 87.73%, respectively. No significant difference in graft survival between patient with and without complications was observed (HR 1.24 [95% CI: 0.56-2.71], $p = 0.594$). The causes of graft loss were graft rejection (89.19%) and surgical causes (10.81%). Of those who underwent graft nephrectomy, 2 out of 3 cases resulted from surgical complications including renal venous thrombosis and ureteral necrosis.

Conclusions: Our postoperative surgical complications were comparable with the previously reported. Though not significantly associated with kidney graft survival, they were a major contributor to graft nephrectomy. Early diagnosis and management of surgical complications play an important role in post-kidney transplantation care.

Keywords: Kidney transplantation, Surgical complication, Graft survival

PREDICTION FOR BREAST CANCER IN BI-RADS CATEGORY 4 LESION CATEGORIZED BY AGE AND BREAST COMPOSITION OF WOMEN IN SONGKLANAGARIND HOSPITAL

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Background: Older age and dense breast are the important risk factors for breast cancer. The ACR BI-RADS lexicon 5th edition does not mention how patient age and breast density may affect the category assessment.

Objectives: To investigate whether patient age and breast density influence the positive predictive value (PPV) of mammographic and ultrasonographic findings categorized as BI-RADS category 4 and subcategories 4a, 4b, and 4c among female patients.

Methods: A retrospective study was conducted in Songklanagarind Hospital between January 1, 2016 and December 31, 2017 in female patients older than 18 years who had breast lesions categorized as BI-RADS category 4 and subcategories 4a, 4b, 4c. A total of 961 breast lesions consisted of 772 (80.33%) benign lesions and 189 (19.67%) malignant lesions. Categorization was done in each lesion based on age ranges of ≤ 35 years, > 35 to 60 years, and > 60 years, and breast density were categorized by mammographic breast composition into

"Dense breast" and "Non-dense breast". The PPV for each BI-RADS category was calculated based on the pathological diagnoses and were compared using the chi-square test.

Results: The overall PPV in each subcategory was in the reference range. The PPV increased with increasing age: 4% vs. 22.63% vs. 36.67% for category 4 (*p*-value = 0.01); 0% vs. 5.81% vs. 6.88% for subcategory 4a (*p*-value = 0.002); 6.67% vs. 26.62% vs. 51.35% for subcategory 4b (*p*-value = 0.001); and 33.33% vs. 76.92% vs. 81.82% for subcategory 4c (*p*-value = 0.02). The breast density-related PPV was significantly higher in non-dense breast compared to dense breast: 48.78% vs 26.67% for subcategory 4b (*p*-value = 0.012); and 95% vs 71.42% for subcategory 4c (*p*-value = 0.034).

Conclusion: A significantly positive association was found between PPV and age in patients in BI-RADS subcategories 4a, 4b, and 4c. The dense breast lowering the effectiveness of mammograms.

Keywords: Age, BI-RADS category 4, Breast cancer, Breast composition, Prediction

PREDICTOR OF ANASTOMOTIC LEAKAGE AFTER COLORECTAL CANCER SURGERY IN HATYAI HOSPITAL

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Background: Anastomotic leakage remains a severe complication after abdominal surgery with considerable morbidity and mortality. The rate of anastomotic leakage varies in studies, but almost always, the incidence is higher in the colorectal resections.

Objective: The aim of this study was to evaluate the predictor for anastomotic leakage after colorectal cancer surgery with anastomosis in Hatyai Hospital.

Methods: This was a retrospective study of 618 colorectal cancer patients who colorectal surgery underwent anastomosis between January 2012 and April 2020. Preoperative data and surgery related variables were examined by univariate and multivariate analyses. The outcome of interest was clinical anastomosis leakage.

Results: The overall anastomosis leakage rate was 10.2 % (58/566). In univariate analysis, rectum cancer (P = 0.001), operative time > 180 min (P = 0.042),intraoperative blood loss > 300 ml (P = 0.033), anastomosis with staple (P = 0.041), albumin < 3 (P = 0.024) were significantly associated with anastomosis leakage. Multivariate analysis identified rectum cancer (odds ratio [OR] 4.01; 95 % confidence interval [CI] 1.25–12.89; P = 0.02), anastomosis with staple (OR 4.58; CI 1.22–17.20; P = 0.024), albumin < 3 (OR 4.62 CI 1.18–15.50; P =0.033) as independent risk factors for anastomosis leakage

Conclusions: Anastomotic leakage remains a major issue in colorectal surgery. In this study, rectum cancer resection, anastomosis with stapler and hypoalbuminemia should be taken into account when analysing the association between leakage and predictive factors. This suggestion, full awareness of risk factors is essential for identifying high risk patients and properly select them for diverting stomas in order to mitigate the severe clinical consequences of anastomotic leakage.

Keywords: Anastomosis leakage, colonic surgery, rectal surgery

PRELIMINARY RESULTS OF A STUDY ON PREVALENCE OF BACTERIAL AND FUNGAL COLONIZATION ON GASTROSTOMY TUBE

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In the era of elderly society, the incidence of disease induces dysphagia such as neurogenic and GI malignant are increase. Percutaneous endoscopic gastrostomy (PEG) plays a major role for nutritional route access for these kinds of patients. The viability period of PEG still questionably, most of PEG were removed when its physically damages. The biologically index data still unknown. This prospective descriptive study is to compare organism colonization with time of two kind of PEG tube placement. The time that colonization reach virulence level will determine the appropriate PEG exchange time. This study of 59 cases divided in two kind of PEG tube such as retrievable 12 case (20.3%) and non-retrievable 47 cases (79.7%).

The PEG tube was removed when physically damaged or distort or dysfunctions in various period. Removed PEG tube were cultured separately between intragastric and extragastric part. The organism colony were identified and collected. Average time of PEG removal were 432 days (14-1056days) and 153.4 days (28-574 days), there are positive culture in 4 (33.3%) and 35 (74.5%) cases for retrievable and non-retrievable PEG respectively. Non-retrievable PEG found bacterial colonization up to 10^5 CFU/ml for 14 cases (29.8%) in average 140.5 days (84–174 days) while colonization in all retrievable type is not exceed the virulence level. The incidence rate of bacterial colonization is 0 per 100 day (95% CI 0-0.071) and 0.147 per 100 day (95% CI 0.081-0.247) for retrievable and non-retrievable PEG respectively ($p = 0.0057$). The outcome of this study shows possibility of bacterial colonization occur in all PEG type and increase to virulence level for non-retrievable significantly higher than retrievable type. This data analysis recommended time to exchange a new non-retrievable PEG should not exceed than 140 days and longer viability for retrievable type can be used until PEG tube damages or dysfunction.

Keywords: Bacterial colonization, PEG, Gastrostomy, Retrievable, Culture

PROGNOSTIC AND PREDICTIVE FACTORS TO DETERMINE 5-YEAR OVERALL SURVIVAL IN STAGE 2 AND 3 COLON CANCER AFTER CURATIVE SURGERY

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Background: The primary treatment of colon cancer stage 3 is surgical resection with adjuvant chemotherapy (CMT) routinely recommended to improve overall survival (OS) but the benefit of adjuvant CMT in stage 2 disease is controversial. Even though, adjuvant CMT is recommended in high-risk stage 2 patients, the 5-year OS not to change.

Objective: To evaluate the 5-year overall survival (OS) of stage 2 and 3 colon cancer patients who underwent curative surgery and to identify prognostic factors that affected the OS.

Methods: This retrospective-prospective study reviewed the medical records of 325 patients who were diagnosed with colon cancer and underwent curative surgery at Songklanagarind Hospital by one colorectal surgeon between July 2003 and March 2020. Personal factors, clinical factors, and pathological factors were collected. Survival analysis was done and prognostic factors were identified.

Results: The 5-year OS of stage 2 and 3 colon cancer patients who underwent curative surgery was 85% and 74%, respectively. A substage analysis demonstrated 5-year OS rates of 100%, 89%, 81%, 78%, and 70% in stages 3A, 2A, 2B, 3B, and 2C, respectively. Statistically significant factors related to poor OS were age ≥ 65 years (hazard ratio [HR] 4.11, $p < 0.001$), preoperative plasma neutrophil-lymphocyte ratio > 5 (HR 2.25, $p = 0.025$), preoperative plasma D-dimer ≥ 1.3 mcg EFU/ml (HR 1.73, $p = 0.04$), tumor size ≥ 10 cm (HR 2.82, $p = 0.004$), high pT stage (HR 6.68, $p = 0.03$), mesenteric resection margin < 8 cm (HR 15.9, $p = 0.007$), regional lymph node metastasis (HR 2.72, $p = 0.004$), and lymph node ratio ≥ 0.35 (HR 2.06, $p = 0.04$). Compared with early stage 3 patients, the statistically significant factors in late stage 2 patients were high preoperative neutrophil-lymphocyte ratio and D-dimer, large tumor size, high pT stage, and short mesenteric resection margin.

Conclusion: Five-year OS in stage 2 colon cancer patients was higher than those in stage 3. However, preoperative neutrophil-lymphocyte ratio, D-dimer, tumor size, pT stage, and mesenteric resection margin were the prognostic factors to statistically significant result in a poor 5-year OS after curative resection in late-stage 2 colon cancer patients compared with early-stage 3 colon cancer patients.

Keywords: Colon cancer, Prognostic factor, Overall survival

PROSPECTIVE STUDY OF PHYSICAL CHANGE AFTER GASTRECTOMY FOR ADENOCARCINOMA OF STOMACH AND ESOPHAGOGASTRIC JUNCTION

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Background: Most patients who underwent radical gastrectomy experienced high degree of weight loss, and declined physical status. This study based on hypothesis that the patients who receive intensive pre- and post-operative care may result in lower body weight loss.

Objectives: To evaluate physical changes including body weight (BW), body mass index (BMI), % body fat (% BF), basal metabolic rate (BMR), muscle mass (MM), gait speed (GS) and handgrip strength (HGS) after gastric surgery compared between conventional care and intensive care at Siriraj Hospital.

Methods: Patients who underwent gastrectomy for adenocarcinoma of stomach (GC) and esophagogastric junction (AEG) during October 2018 to March 2021 were included. The physical outcomes compared between intensive care (ERAS) and conventional care (CC) were analyzed in all group analysis (all extension of surgery) and subgroup analysis (subtotal gastrectomy includes proximal and distal gastrectomy; total gastrectomy group includes total and extended gastrectomy).

Results: Sixty (31 ERAS, 29 CC) patients were included. ERAS has shorter % weight loss (% BWL) at 1st month in all group analysis (6% vs 9%, $p = 0.036$) and subgroup analysis of total gastrectomy group, (5% vs 9%, $p = 0.034$). There was no different % MM loss between ERAS and CC group at 1st month (5.3% vs 2.9%, $p = 0.411$), 3rd month (4.5% vs 7.2%, $p = 0.618$) and 6th month (6.5% vs 11.7%, $p = 0.45$). There was no different in GS change between groups in all group analysis. But in subgroup analysis, GS in total gastrectomy group recovered within 1 month (-0.13 vs 0.23, $p = 0.018$). In subgroup analysis, there was no different HGS change at 1st month (-0.002 vs 0.02, $p = 0.521$), 3rd month (0.11 vs -0.68, $p = 0.056$) and 6th month (0.05 vs -0.07, $p = 0.252$), there was no different BMR change at 1st month (65 vs 62, $p = 0.923$), 3rd month (91 vs 112, $p = 0.719$) and 6th month (236 vs 167, $p = 0.244$). % BF loss showed no different between groups in all group analysis. In subgroup analysis, % BF loss increase in ERAS at 6th month in total gastrectomy group (68% vs 27%, $p = 0.029$).

Conclusion: ERAS show benefit in lower percentage body weight loss and recovery gait speed in gastric and AEG cancer patient who underwent radical gastrectomy.

Keywords: Adenocarcinoma of stomach and esophagogastric junction, Gastric surgery, Physical change, ERAS

REPORT OF INCIDENCE OF SEVERELY INJURED PATIENTS FROM TRAFFIC ACCIDENTS AT SRINAGARIND HOSPITAL

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Background: Road traffic injury in Thailand is rising every year and road traffic death is in the second place among all countries.

Objectives: To report the incidence of severe injury from road traffic injury in Srinagarind Hospital and identify factors in pre-hospital setting that may influent severe injury.

Methods: A retrospective study was carried out in Srinagarind Hospital over 1 June 2010 to 31 May 2016, included patients that have been at emergency room (ER) from road traffic accidents. Demographic information, time, type of accidents, type of vehicles, risky behavior such as alcohol drinking, mobile phone using or neglect to wear helmet nor seatbelt were recorded. Injury severity score (ISS) more than 15 was classified as severe injury (SI). Only outcome at ER were analyzed.

Results: Total 15,416 records were analyzed. There were 518 cases with SI, 9 were death at ER and 2,981 were admitted. Most patients were biker (13,432 (87.13%)), age below 25 years (8,443 (55.42%)) and male (8,120 (52.67%)). Major accidents occur during 4.00 PM to 11.59 PM (5,882 cases). SI was statistic significant associated with being male (OR = 3.66 [95% CI: 2.95-4.55]), increasing of age especially more than 65 years (OR = 3.93 [95% CI: 2.64-5.85]), accidents occurred during 00.00 to 7.59 AM (OR 1.99 [95% CI: 1.57-2.53]). Transfer time more than 180 minutes was also associated with SI (OR 2.32 [95% CI: 1.93-2.80]). Helmet and seatbelt using were protective factors from SI (OR 0.3, *P*- value < 0.001 and OR 0.49, *P*-value < 0.001 respectively).

Conclusion: Most severe cases were male and associated with increasing of age. Even though there was law of using protection during driving, only few would comply and affected with more SI. Nighttime and longer time before arrived hospital were also associated

with more SI which can be an emphasis on emergency trauma team at pre-hospital setting.

RISK FACTOR OF MORTALITY IN NECROTIZING FASCIITIS PATIENTS AT HATYAI HOSPITAL

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Background: Necrotizing fasciitis (NF) is aggressive skin and soft tissue infections characterized by necrosis of the fascia and subcutaneous tissue, accompanied by severe systemic toxicity, associated with higher mortality rate if delayed diagnosis and surgical intervention. Early diagnosis and treatment will decrease mortality rate.

Objective: Aim of this study to identify risk factor that increase mortality rate in patients with NF and developed clinical scoring for predicted mortality rate in NF patients.

Methods: Retrospective cohort study was performed in Hatyai Hospital from January 2015 to July 2019 medical records, microbiological tests and laboratory parameters of 296 NF patients were reviewed for the study. Multivariate with logistic regression analysis was used to explored for potential predictor, and internal validation was done with Cross-validation method.

Results: Total 296 patients were diagnosed with NF. The results showed that mortality rate and survive were 54(18.24%) and 242(81.76%) respectively. According to multivariable with logistic regression showed Chronic kidney disease (OR 6.68, 95% CI 1.90-23.55); pulse rate (OR 1.05, 95% CI 1.02-1.08); Fasting blood sugar (OR 1.01, 95% CI 1.00-1.01); treatment (OR 1.98, 95% CI 0.99-3.93) were risk factor of mortality in NF patient. The developed clinical score was comprised of Chronic kidney disease, pulse rate, Fasting blood sugar and treatment, the area under ROC curve was 0.824.

Conclusions: Prognosis factor of mortality in NF were Chronic kidney disease, pulse rate, Fasting blood sugar and treatment, patients who have these condition should perform closed monitoring and aggressive treatment to decrease mortality.

Keywords: Risk factor, Clinical predictor, NF, Mortality, Prognosis

SINGLE-INCISION LAPAROSCOPIC CHOLECYSTECTOMY VS THREE-PORT LAPAROSCOPIC CHOLECYSTECTOMY: A RETROSPECTIVE STUDY AT CHIANGRAI PRACHANUKROH HOSPITAL

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Background and Objectives: Laparoscopic cholecystectomy is the standard treatment for most gallbladder diseases. Single-incision laparoscopic surgery was introduced aiming to decrease the invasiveness of the procedures. The aim of this study was to compare the clinical outcomes of SILC with Three-port LC.

Methods: This was a retrospective chart review of 126 Thai patients with symptomatic cholecystolithiasis who were enrolled for laparoscopic cholecystectomy by a single surgeon at Chiang Rai Prachanukroh Hospital, Thailand from July 2016 to December 2019. 63 patients underwent single-incision laparoscopic cholecystectomy (SILC group); other 63 patients underwent three-port laparoscopic cholecystectomy group (LC). The primary endpoints were postoperative pain score (at 4 hours and 12 hours) and patient complications, while the secondary outcomes were operative time, estimated blood loss, opioid requirements, and duration of hospital stay.

Results: The result showed no differences between both groups regarding baseline characteristics. According to the visual analog pain scale, pain at 4 hours postoperatively was significantly lower in the SILC group (3.92 ± 1.68 vs 4.86 ±1.63, $p < 0.05$) but showed no difference at 12 hours postoperatively. The total morphine consumptions were not different between the two groups (median 3.0, IQR 6 in SILC vs median 3.0, IQR 4 in TILC, $P = 0.611$). Operative time was similar in both groups (45.9. ± 16.59 in SILC vs 51.48 ± 18.54 in TILC, $P = 0.077$). No statistically significant differences were found between both groups with regard to perioperative, postoperative complications, length of hospital stay, readmissions, and mortality.

Conclusion: Single-incision laparoscopic cholecystectomy (SILC) has shown to be a safe and feasible procedure with a low complications rate in selected patients with no difference in wound pain. It provides the patient an almost non-visible scar while preserving the optimal quality of surgery.

Keywords: Laparoscopic cholecystectomy, Single-port, Three-port, Post-operative pain, Safety

STRATEGIES AND OUTCOMES IN MANAGEMENT OF ABDOMINAL AORTO-ENTERIC FISTULA

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Background: Abdominal aortoenteric fistula (AEF) is a rare clinical entity. The goals of surgery are confirmed diagnosis, bleeding control, repair of bowel defect, eradication of infection, and revascularization. Many studies compared open aortic repair (OAR) with endovascular aortic repair (EVAR) in this condition. Aim of this study is to compare the early and late outcomes of AEF in EVAR and open enterorrhaphy (EVAR+OE), EVAR and, OAR.

Objective: To analyze the three strategic treatments for early and late outcomes in AEF.

Methods: Over 16-year period between 2006-2020, 22 patients (13 primary, 15 males, mean age 67.41 years) were included: 10 of EVAR+OE, 6 of EVAR, and 6 of OAR. Primary end point was 30-day mortality. Secondary end point included operative details and post-operative complications. Kaplan-Meier analysis was used to analyze 5-year overall survival and free time re-intervention.

Result: There were no significant differences among groups in baseline characteristics. The most common location of aneurysm was infrarenal (68.2%). Duodenum was the most common site for intestinal involvement (72.7%). OAR had the statistical significance in longer operative time ($p = 0.009$) and higher intraoperative blood loss compared with the other 2 groups ($p = 0.02$). The 30-day mortality was not statistically significant in all groups:10% (1/10) of EVAR+OE, 16.7% (1/6) of EVAR and, 16.7% (1/6) of OAR ($p = 0.902$). In addition, there were no significant differences in the postoperative complications, intensive care unit and hospital stay. At 5 years follow-up, the overall survival rates in the EVAR+OE, EVAR, and OAR groups were 68.6%, 16.7%%, and 83.3%, respectively ($P = 0.105$). Also, the free time re-intervention among three groups was not statistically significant (90% of EVAR+OE, 66.7% of OAR, and 66.7% of EVAR, $p = 0.396$).

Conclusion: OAR is still the gold standard for AEF with good long-term outcome. Definite treatment with only EVAR might lead to high 30-day mortality and low survival rate at 5 years. EVAR+OE was acceptable postoperative mortality. Furthermore, EVAR+OE could achieve satisfactory the rates of survival and free-time reintervention compared with OAR.

SURVIVAL OUTCOME AND PROGNOSTIC FACTORS OF DISTAL CHOLANGIOCARCINOMA AFTER CURATIVE RESECTION IN NORTHEAST OF THAILAND

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Background: Cholangiocarcinoma (CCA) had highest incidence in Northeast of Thailand. Perihilar and intrahepatic type CCA had poor prognosis even after curative resection. Survival of distal cholangiocarcinoma (dCCA) remain unclear. The aim of this study was to examine survival and prognostic factors of dCCA after curative surgery.

Methods: 57 patients who underwent pancreaticoduodenectomy between January 2009 and December 2020 for dCCA were included in this study. Survival was estimated using the Kaplan-Meier method. Demographic data, laboratory data, surgical procedure and histopathological data were recorded. Prognostic factors related to survival were analyses by bivariate and multivariable cox proportional hazard model.

Results: The mean age was 63 years and 30 (52.63%) of the patients were female. Jaundice was present at diagnosis in 68.42% of the patients. Post-operative morbidity was 40% including pancreatic fistula 11 (19.30%), wound infection 9 (14.04%) and bile leakage 3 (5.26%). Overall median survival time was 17 months and survival rate at 1, 3 and 5 years were 63.9%, 20.5%, and 17.9%, respectively. Independent prognostic factors were serum bilirubin > 5 mg/dl (HR 2.40, 95% CI 1.11-5.19, p-value = 0.03), pathological T3 (HR 3.32, 95% CI 1.23-8.93, p-value = 0.01), and lymph node metastasis (HR 3.21, 95% CI 1.16-8.86, p-value = 0.02).

Conclusion: Curative resection for dCCA was safe but survival outcome still poor. Adjuvant or neoadjuvant treatment in lymph node metastasis and T3 may improve patient's survival.

Keywords: Distal cholangiocarcinoma, Pancreaticoduodenectomy, Northeast of Thailand

THE EFFICACY OF ERAS IN EMERGENCY SURGERY FOR PERFORATED PEPTIC ULCER

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Objective: To determine the efficacy of Enhanced recovery after surgery (ERAS) toward a group of emergency patients with perforated peptic ulcers (PPU).

Methods: The retrospective observational study was examined between May 2017 and July 2020 at Surin hospital. The comparison between post-operative care of perforated peptic ulcers in high compliance ERAS group (ERAS adherences > 63.6% from selected 17 ERAS adherences) and low compliance ERAS group (ERAS adherences < 63.6%). The primary outcome was length of hospital stays and secondary outcomes were post-operative complications of perforated peptic ulcers.

Results: There were 292 patients assembled in this study that divided into two groups There were 121 patients in the high compliance ERAS group and 171 patients in the low compliance ERAS group. Mean of length of hospital stays (LOS) was significantly shorter in the high compliance ERAS group (6.42 days, range 2-9) compared with the low compliance ERAS group (7.88 days, range 2-58), $P = 0.000$. Incidence of superficial surgical site infection and pneumonia of the high compliance ERAS group lower than the low compliance ERAS group significantly ($P = 0.016$ and $P = 0.008$)

Conclusion: The ERAS program can adapt for perforated peptic ulcer and decrease length of hospital stays, superficial surgical site infection and pneumonia.

Keywords: ERAS, ERAS in emergency, Perforated peptic ulcer, Upper gastrointestinal surgery

THE EFFICACY OF TOPICAL TRANEXAMIC ACID ON SEROMA AFTER MASTECTOMY

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Background: Post mastectomy seroma is a complication that result in delayed surgical wound healing and the next step specific treatment. Tranexamic acid (TXA) is proven to reduce postoperative blood loss and transfusion.

Objective: To evaluate the efficacy of topical TXA during the wound closure in participants undergoing mastectomy in reducing seroma formation.

Methods: This prospective, double-blind, randomized controlled trial, enrolled women 18-year-old or older with breast cancer, who were underwent mastectomy with or without axillary lymph node dissection at Naresuan University Hospital and Kamphaengphet Hospital between January 15th, 2020 to February 28th, 2021. Participants were randomized to topical TXA or normal saline (placebo) group. The primary outcome was the volume of seroma as measure by drain production within 24 hours. Secondary outcomes were total seroma, duration of drainage and serious complications of the use of topical TXA.

Results: A total of 94 women were randomized and included in this study (47 in the TXA and 47 in placebo group). TXA group reduced mean drain production within 24 hours (114.40 vs 151.09 ml; mean difference 36.68 (95% CI 12.21 to 61.15) ml, $p = 0.004$), reduced mean total drain production (529.89 vs 686.91 ml; mean difference 157.02 (95% CI 4.39 to 309.67) ml, $p = 0.044$), and reduced mean duration of drainage (9.66 vs 11.30 days; mean difference 1.64 (95% CI 0.19 to 3.09) days, $p = 0.027$). There was no significant difference in postoperative complications between TXA and placebo ($p > 0.05$).

Conclusion: The topical TXA has shown benefit in reducing seroma formation and safe.

Keywords: Topical tranexamic acid, Seroma formation, Mastectomy

THE STUDY OF BILIARY CANNULATION TECHNIQUE IN ERCP THAT SUITABLE FOR AMPULLA OF VATER CONFIGURATIONS

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Background: Endoscopic retrograde cholangiopancreatography is a procedure used to diagnosis and treatment of biliary system that requires

selective cannulation of the relevant ductal system. Numerous clinical trials to improve the success rate of biliary access in difficult biliary cannulation during ERCP. However, there are limited data on the biliary cannulation technique in ERCP that suitable for Ampulla of vater configurations.

Objective: The aim of the study was biliary cannulation technique in ERCP that suitable for Ampulla of vater configurations.

Methods: Between November 2019 and June 2021, this cross-sectional descriptive study enrolled 215 patients with naïve papillae at Hatyai Hospital. Ampulla of vater configurations were divided into 8 types including Nipple, Behind fold, Turtle, Wavy, Intra-diverticular, Peri-vatarian, Bilateral diverticulum and Subpyloric. We collected data of successful biliary cannulation technique that endoscopist used. The primary outcome was biliary cannulation technique that suitable for Ampulla of vater configurations. The secondary outcomes were variation of Ampulla of vater configurations and complications.

Results: A total of 215 patients, 139 (64.6%) had Turtle type (Guidewire 74.8%, Pre-cut 17.3%), 21 (9.8%) had Behind fold type (Guidewire 71.5%, Pre-cut 19%), 17 (7.9%) had Peri-vatarian type (Guidewire 64.7%, Pre-cut 23.5%), 11 (5.1%) had Bilateral diverticulum type (Guidewire 45.5%, Double wire/Parallel pancreatic duct stent 36.4%), 10 (4.7%) had Wavy type (Guidewire 60%, Pre-cut 40%), 9 (4.2%) had Intra-diverticular type (Guidewire 44.4%, Ampulla reposition 33.3%), 6 (2.8%) had Nipple type (Guidewire 66.7%, Double wire/ Parallel pancreatic duct stent 16.7%, Ampulla reposition 16.7%) and 2 (0.9%) had Subpyloric type (Guidewire 100%). The overall complication rate was 6% (13/215) (9 mild pancreatitis, 1 duodenal perforation, 3 mild cholangitis) ($x^2 = 0.97$).

Conclusion: Guidewire was the most technique that was successfully cannulated all type of Ampulla of vater configurations. Turtle type was the most common Ampulla of vater configurations in the study group. ERCP-related complications were not associated with biliary cannulation technique.

Keywords: Ampulla of vater configurations, Biliary cannulation technique, Endoscopic retrograde cholangiopancreatography, ERCP-related complications.

TIME FROM ONSET TO OPERATION THAT ASSOCIATED WITH RUPTURED APPENDICITIS OR OTHER COMPLICATED APPENDICITIS AFTER CORRECTED WITH CONFOUNDING FACTORS

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Background: Appendicitis is one of the most frequently operative diseases that is found in the surgery department. Ruptured appendicitis is associated with higher morbidity compared with uncomplicated appendicitis such as surgical site infections or prolonged length of hospital stay and increased treatment costs. Delayed treatment might be associated with complicated appendicitis. Hence, selection and prioritization to put the patient on timely treatment is the key of best resource management for patient safety.

Objective: We hypothesized that timing of abdominal pain was associated with complicated appendicitis. The aim of this study was to investigate the predictors of complicated appendicitis. So, these factors can be used for patient selection and prioritization to treatment.

Methods: The studied sample was the patients who were diagnosed with acute appendicitis during March to August 2019 in Hatyai Hospital. The data were analyzed using descriptive statistics, survival analysis and logistic regression.

Results: Of 374 cases reviewed, 281 cases were eligible for analysis due to the completeness of data. Of these, 201 cases (71.53%) were non-complicated appendicitis, 80 cases (28.47%) were complicated appendicitis. The time from first pain to operation (mean ± SD) is lower in non-complicated appendicitis, compared with complicated appendicitis (25.72 ± 21.30 VS 68.90 ± 68.48 hours, respectively). The risk of complicated appendicitis was increased with increment of delayed treatment every 6, 12, 24 hours with the adjusted OR 1.20, 1.44, 2.07 respectively. Age was also an independent risk factor, with adjusted OR of 2.94 and 6.13 in a group of age 40-60 years and more than 60 years respectively. Additionally, body temperature was a strong predictor with adjusted OR of 3.19 and 12.82 in a group of 37.9-39.0°C and more than 39.0°C respectively.

Conclusion: Time, age and body temperature are the important risk factors of complicated appendicitis.

Keywords: Acute appendicitis, Complicated appendicitis, Time, Risk factors

USE LIVER FUNCTION TEST FOR PREDICTING COMMON BILE DUCT STONE IN ACUTE CHOLECYSTITIS

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Background: Liver functional tests due to cholecystitis might change by inflammatory process and changed in some value changed might help us to stone prediction in common bile ducts and decrease hazards of performing ERCP and other invasive procedures.

Objective: The study aimed to investigate the diagnostic value of liver function enzymes in patients with common bile duct stone that presented with acute cholecystitis in Kamphaeng Phet Hospital.

Methods: A retrospective study was performed on 230 patients with acute cholecystitis from October 2015 to June 2020 in Kamphaeng Phet. And then divided patients to 2 groups, 167 acute cholecystitis with common bile duct stone patients (experimental group), 63 acute cholecystitis without common bile duct stone patients (control group) Hospital. Blood sample was extracted from each participant, and biochemical tests were performed for ALT, AST, ALP, TB and DB. Receiver operating characteristic (ROC) analysis was performed to evaluate the diagnostic value of each biochemical parameter for common bile duct stone.

Results: The results experimental group had markedly increased serum levels of ALT, AST, ALP, TB and DB than the control group. ROC analysis revealed that of the 6 biochemical parameters, all parameter had area under the curve (AUC) > 0.8. ALT and AST had low sensitivity (75.50%; 79.8%) and low specificity (74.6%; 71.4%) at the optimal cutoff value (≥ 50 U/L; ≥ 55 U/L; 95%). ALP and TB had high sensitivity (84.4%; 80.2%; 82.0%) and low specificity (74.6%; 76.2%) at the optimal cutoff value (≥ 120 U/L; ≥ 1.8 U/L; 95%) stones. ALP, But DB had high sensitivity and high specificity (82.0%; 82.5%) at the optimal cutoff value ≥ 0.9 U/L; 95%.

Conclusion: Logistic regression analysis revealed that ALT and AST were independent predictors of common bile duct (CBD) TB and DB might be recommended as diagnostic biomarkers for CBD stone. The liver function test could be screening method for diagnosis for CBD stone.

Free Paper Oncology Surgery

THE DIAGNOSIS VALUE OF SERUM C-REACTIVE PROTEIN AND PLEURAL FLUID AMYLASE LEVEL FOR ANASTOMOTIC LEAKAGE AFTER ESOPHAGECTOMY

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Background: The anastomotic leakage after esophagectomy is significant cause of morbidity and mortality. Early detection and management are crucial to prevent death. Several screening modalities are available to detect anastomosis leakage but no standard of modalities.

Objective: This study evaluates the prognostic effectiveness of pleural fluid amylase levels in detecting early anastomosis leakage after esophagectomy compared with serum c-reactive protein (CRP).

Methods: Between January 2018 and May 2021 46 esophagectomies were performed in our department. Pleural fluid amylase levels and serum CRP levels were collected in 32 of these patients on 1-6 postoperative days. Early anastomotic leakage was defined as occurring with the chest tubes in place and cervical surgical wound. We performed to compare the ability of pleural fluid amylase levels and serum CRP to detect anastomotic leakage and to determine the accuracy of cutoff values.

Results: Overall anastomotic leakage rate was 31% (10/32). The multivariate test showed a significant association between pleural fluid amylase level and anastomotic leakage ($p < 0.001$).

A cutoff of pleural fluid amylase level 349 IU/L on POD 3 (AUC 0.87, sensitive 76.7%, specific 95.5%) for a clinically significant leakage and accurately 92.7% of patients and cutoff of pleural fluid amylase level 880 IU/L on POD 5 (AUC 0.78, sensitive 50 %, specific 87.7%) for a clinically significant leakage and accurately 88.2% of patients No significant associate serum CRP with anastomosis leakage.

Conclusion: Increased postoperative levels of pleural fluid amylase are associated with anastomotic leakage after minimally invasive esophagectomy. A pleural fluid amylase combined with reassuring clinical may be useful to exclude leakage. This may help to detect anastomotic leakage then effect to the surgeon's clinical decision-making and allow early feeding and hospital discharge.

Keywords: Anastomotic leakage, Esophagectomy, Amylase, C-reactive protein

Free Paper Pediatric Surgery

CLINICAL CHARACTERISTICS OF PEDIATRIC PATIENTS WITH CERVICAL LYMPHADENOPATHY WHO UNDERWENT SURGICAL BIOPSIES

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Background: Lymphadenopathy is common in children and is often a diagnostic challenge for clinicians. It may be one of the symptoms of many diseases including granulomatous diseases and malignancy**.** The cervical region is the most commonly involved area among peripheral lymphadenopathy. Surgical biopsy often provides a definitive diagnosis but may be unnecessary in some cases.

Objectives: The objective of this study was to retrospectively describe cases of pediatric patients with cervical lymphadenopathy who have undergone surgical biopsy and to determine clinical factors that can predict the likelihood of lymph node which need further management (LNFM) including granulomatous and malignant lymph node.

Methods: The data of 87 cases with unexplained cervical lymphadenopathy and underwent surgical biopsy was collected. Receiver operating characteristic analysis was performed to find out the parameter for size of the lymph node. Logistic regression was applied to determine independent predictors of LNFM, granulomatous lymph node, and malignant lymph node.

Results: On final diagnosis, 37 lesions (42.53%) were benign, 36 lesions (41.38%) were granulomatous, and 14 lesions (16.09%) were malignant. The ROC analysis shows that size of the lymph node threshold that maximized sensitivity and specificity was 2 cm in order to predict LNFM group. Multivariate logistic regression model indicated that submandibular location (OR, 11.86; 95% CI, 2.54-55.38; *p*-value = 0.002), and abnormal CXR (OR, 20.72; 95% CI, 2.13-201.49; *p*-value = 0.009) were significant independent predictors of LNFM. Further subgroup analysis demonstrated that abnormal CXR (OR, 10.16; 95% CI, 1.48-69.92; *p*-value = 0.018) was significant independent predictor of malignant lymph node. In addition, redness (OR, 10.16; 95% CI, 1.48-69.92; *p*-value = 0.018), and submandibular location (OR, 14.64; 95% CI, 2.00-106.98; *p*-value = 0.008) were significant independent predictors of granulomatous lymph node.

Conclusions: Submandibular location and abnormal CXR are associated with LNFM. Abnormal CXR is associated with malignant lymph node. Overlying skin redness and submandibular location are associated with granulomatous lymph node. These data should be helpful to supplement clinical judgment in determining which enlarged cervical node is an LNFM.

Keywords: Cervical lymphadenopathy, Reactive lymphoid hyperplasia, Granulomatous, Lymphoma, Children

EARLY SURGICAL COMPLICATIONS FOLLOWING TRANSANAL ENDORECTAL PULLTHROUGH FOR HIRSCHSPRUNG'S DISEASE

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Background: Transanal endorectal pullthrough (TERPT) is a standard procedure for Hirschsprung disease (HD) in the pediatric surgery center. Many studies had reported long-term complications such as HAEC, fecal incontinence, soling. This study was an interesting short-term outcome after surgery.

Objectives: Aim of this study was to examine early postoperative complications within 30-days after TERPT and to identify risk factors at perioperative, intraoperative, and postoperative characteristics, associated with the development of early surgical complications.

Methods: A retrospective chart review was performed on the patient with Hirschsprung disease who was treated with TERPT/ abdominal assisted TERPT at Siriraj Hospital from January 2009 to December 2019.

Results: 43 of 163 patients developed complications with thin 30 days after the operation, Abdominal assist TERPT has higher complications than TERPT (n = 24, 55.8% and n = 19, 44.2%). Anastomosis stricture (n = 14, 32.6%), Abscess at anastomosis (n = 5, 11.6%), GI obstruction (n = 4, 9.3%) occurred most frequently. Most common signs and symptoms who have complications after surgery were abdominal distension (46.5%) and vomiting (18.6%). The risk factor associated with early surgical complications was enteritis before surgery (n = 13, 30.2%, $P = 0.069$), Inpatient with enteritis should irrigated bowel 5 days before surgery. Although pack glycerin before surgery may decrease early complication (n = 15, 12.5% $P = 0.072$). Nutritional status, Colostomy before the operation, Volume of NSS irrigation were not associated with complications.

Conclusions: There is no significant risk factor associated with early surgical complications after TERPT. However, we know NSS 10 ml/Kg were the minimum volume of NSS for irrigating rectum and the shortest period rectal irrigation after enteritis were safely for surgery. Surgeons should be cautious in postoperative time, the patient who has abdominal distention may develop a complication.

Keywords: Transanal endorectal pullthrough, TERPT, Rectal irrigation, Enteritis, Transitional zone

FACTORS AFFECTING LONG-TERM PSYCHOSOCIAL OUTCOMES AFTER HYPOSPADIAS REPAIR

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Background: Congenital hypospadias is one of the most common genital malformations. Despite current progress in surgical techniques in hypospadias repair, their long-term psychosocial outcomes received little attention.

Objective: To evaluate long-term psychosocial outcomes after hypospadias repair and to analyze the root causes regarding satisfactory outcomes.

Methods: Patients who underwent hypospadias repair during childhood period were recruited. Regarding psychosocial outcomes, the patients were invited for evaluation by the modified SIGHT questionnaire (developed by previous German publication in pediatric urology) and the Strength and Difficulty questionnaire in Thai version form. Then demographic data of patients was collected. Data was analyzed by STATA program. Univariate analysis and multiple linear regression were used for statistical analysis.

Results: There were 38 hypospadias patients, median age =14 years (range 11-27) participating in the study. The patients underwent first hypospadias repair at median 3.5 years of age (range 1-14). The types of hypospadias were glandular type (1/38), corona type (5/38), midshaft type (10/38) and penoscrotal type (22/38). The overall average score of satisfactory psychosocial outcomes was 25.31 ± 5.86 (range 14-37, maximal score =39). Using simple linear regression analysis, factors affecting psychosocial outcomes ($p < 0.05$), were older age at first hypospadias surgery, mild type of hypospadias, technique of hypospadias repair, current urethro-cutaneous fistula, conduct problems, and abnormal peer difficulty problems.

However, when applying multiple linear regression analysis, only 3 factors were significantly associated with psychosocial outcomes; severe type of hypospadias when compared with corona and mid-shaft type (r = 7.94 and 5.16, $p = 0.001$ and 0.005, respectively), current urethro-cutaneous fistula (r = -4.38, $p = 0.02$) and high peer difficulty problems, (r = -5.88, $p = 0.04$).

Conclusion: From the study, factors which affected long-term decreasing psychosocial satisfactory outcomes were penoscrotal hypospadias, current urethro-cutaneous fistula, and high peer difficulty problems. However, further studies are needed to elucidate causes of long-term satisfactory psychosocial outcome after hypospadias repair.

Keywords: Hypospadias, Long term, Psychosocial, Outcome, Urethro-cutaneous fistula

OUTCOMES OF EARLY SURVEILLANCE ESOPHAGOGASTRODUODENOSCOPY FOR ESOPHAGEAL VARICES AT THE AGE OF 1-YEAR IN BILIARY ATRESIA PATIENTS

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Background: Portal hypertension is a common consequence of progressive liver cirrhosis secondary to biliary atresia (BA) patient. Bleeding from ruptured esophagogastric varices (EV) is a catastrophic complication which relates to a high mortality rate. Surveillance esophagogastroduodenoscopy (EGD) and primary prophylaxis play a key role for early management of EV. Since 2012, our institution conducted an early surveillance EGD protocol in all 1-year-old BA patients.

Objectives: The aim is to determine the outcomes of patients, who underwent surveillance EGD in terms of EV bleeding rate, mortality rate, and procedure-related complications, compared to those of patients who did not have surveillance EGD.

Methods: A retrospective chart review was performed for all BA patients, aged between 1 and 18 years old, who visited Division of Pediatric Surgery, Siriraj Hospital during 2008-2019.

Results: One hundred and eight BA patients were included. Protocoled surveillance EGD starting at 9-18 months were conducted in 42 patients. Non-protocol EGD was performed in 54 patients, which consisted of 36 surveillances and 18 therapeutic purposes.

All of protocoled surveillance EGD were performed under general anesthesia. EV requiring primary prophylaxis were identified in 9 cases (22%). Among these, prompt endoscopic sclerotherapy was administered. GIH requiring blood transfusion was found later in 21.4% (21.4% VS 33.3%; $P = 0.18$), however most of them recovered soon. There was no mortality related to GIH in protocol group.

Post-procedural ICU admission was required in 2 patients among protocol group. (4.8% VS 16.7%; $P = 0.1$) One was for closed monitoring, another one was due to her pulmonary infection. There was no early complications related to procedure. Nevertheless, 8 GIH-related ICU admissions and 1 serious GIH requiring surgery were identified among non-protocol patients.

Late Kasai's operation (> 3 months) and low albumin level (< 3.5 g/dL) were identified as significant factors for presence of EV requiring treatment (OR = 4.4, $P = 0.036$; OR = 4.0, $P = 0.04$ respectively).

Conclusion: Early surveillance EGD protocol could identify and provide primary prophylaxis for EV in almost one-fourth of BA patients. The benefit of early detection of patients with EV requiring endoscopic treatment may outbalance the risk related to the procedure.

PREDICTIVE RISK FACTORS FOR POST-OPERATIVE ENTEROCOLITIS IN HIRSCHSPRUNG'S PATIENTS

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Background: Hirschsprung's associated enterocolitis (HAEC) remains potentially life-threatening complication even after surgically treated by definite pullthrough procedure.

Objective: This study aimed to identify risk factors for the development of post-pullthrough HAEC.

Methods: We retrospectively reviewed patients with Hirschsprung's disease who underwent pullthrough procedure from 2007 through 2018 at

our institute. HAEC was diagnosed by clinical record of HAEC. Patients were categorized into 2 groups; 1) Control group who had no HAEC episode after pullthrough, 2) Post-pullthrough HAEC group. Risk factors of post-operative HAEC were then examined. Data were analyzed using simple logistic regression for univariate analysis. *P*-value < 0.05 was considered statistical significance.

Results: There were 91 patients of Hirschsprung's patients underwent pullthrough procedure. The median of age at diagnosis of Hirschsprung's disease was 112 days. The median of age at pullthrough procedure was 364 days. The incidence of post-pullthrough HAEC was 26% (24/91). The risk factors of post-pullthrough HAEC included pre-operative HAEC (OR = 5.78, 95% CI: 2.11-15.81; *P* = 0.001) and post-operative anastomosis stricture (OR = 8.13, 95% CI: 1.36-48.66; *P* = 0.022).

Conclusion: Our study demonstrates that pre-operative HAEC and post-operative anastomosis stricture are risk factors of post-pullthrough HAEC in Hirschsprung's disease. Hirschsprung's patients with these factors are recommended to be closely monitored for early detection and treatment of post-pullthrough HAEC.

Keywords: Hirschsprung's disease, Enterocolitis, Risk factors

PREVALENCE AND FACTORS ASSOCIATED WITH POST OPERATIVE STRICTURE IN ANORECTAL MALFORMATION

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Background: Anal stricture is one of serious complications of anorectal surgery, it's depending on the nature of the disease and type of operation. Postoperative dilatation is prescribed to avoid anal stricture. If stricture still occur, the currently described treatment of anal stricture is surgical correction.

Objectives: The purpose of this study was to find the prevalence and factors associated with anal stricture after postoperative surgery. Secondary objective was to compare about type of ARM, operative type, complications and postoperative anal dilatation between stricture and non-stricture group.

Methods: Medical records of 204 patients with anorectal malformation who underwent surgical treatments in the Siriraj hospital January 2003 to December 2019 were reviewed. Data were collected including demographic data, type of ARM, operative records, anal dilatation practice, complications and redosurgery.

Results: 204 patients were identified. 128 (62.7%) were male. Types of ARM were as follows; without fistula (31), perineal fistula (49), vestibular fistula (34), rectobulbar fistula (26), rectoprostatic fistula (30), rectobladder neck fistula (17), cloaca (16) and rectal atresia (1).

In total, the stricture was reported about 19.6% (40/204). Post operative stricture that required resurgery were more common in rectobladder neck (*P* = < 0.001). Stricture incidence was differed according to operative type. PSARP was the most commonly performed procedure, with 17.65% developing stricture. 55.56% of abd-assist PSARP patients and 50% of children who had PSARVUP developed a stricture. Stricture also occurred in 16.22% of anal transposition patient and 25% in lap-assist PSARP respectively. Abd-assist PSARP and PSAVUP increase in stricture formation rate (*P* < 0.001, *P* = 0.009).Common complication that may lead to anal stricture include wound infection, dehiscence, retraction, and colonic necrosis.

Postoperatively, 160 underwent routine dilatation by parents which develop stricture (28/204). Routine anal dilatation by parent and dilate under GA seem to decrease rate of stricture, but no significance in statistic (*P* = 0.583). The duration of dilatation do not significantly reduced stricture formation (*P* = 0.123). The redo operation after anal stricture are anoplasty (11.2%), PSARP (3.4%), abd-assist PSARP (1.9%) and lap-assist PSARP (2.9%).

Conclusions: The prevalence of anal stricture was reported 19.6%. Factors associated anal stricture include wound infection, dehiscence, retraction, and colonic necrosis. Type of malformation and operative procedure are associated with rate of anal stricture which were common in high type malformation. There were no significance difference in stricture rate between case which were dilate and not dilated.

Keywords: Anorectal malformation, Anal stricture, PSARP, Redosurgery, Anal dilatation

RADIOLOGICAL PARAMETERS DETERMINING SURGICAL OUTCOMES IN PEDIATRIC HEPATOBLASTOMA

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Objective: Hepatoblastoma is the most common hepatic epithelial cancers in childhood. To evaluate survival outcomes after major hepatic resections for hepatoblastoma and analyse for radiological parameters associating with poorer survival as they may suggest additional treatment or more intensive follow-up.

Methods: Cases of histologically proven hepatoblastoma who were operated on at Songklanagarind Hospital during the period from May 2004 to April 2021 were retrospectively review. Focus was on sequential radiological findings and survival outcomes.

Results: During the study period, 42 cases of hepatoblastoma were operated on in our institute. Excluding 3 cases with incomplete radiological materials, 39 (13 females and 26 males) were included in the analysis. Median age at diagnosis was 19.5 months (interquartile range 10.8 - 38.4 months). Of 39 cases, 17 (43.6%) were in PRETEXT 3-4 when 20 (51.3%) were in PRETEXT 1-2 and 2 had not enough data for staging. Except for 2 cases in PRETEXT 1, all received preoperative chemotherapy according to the THAI-POG regimen. A majority of cases (30 cases, 76.9%) underwent extended right hepatic resection. Median follow-up period was 51.4 months (IQR 10.5 - 95.0 months). Two- and five-year overall survival were 80.4% and 73.6%, respectively. Post-operative alfa-fetoprotein (AFP) level was a strong independent parameter associated with survival. AFP more than 5,000 U/L was associated with poorer survival at the Odds ratio 11.2 (95% CI 2.2 - 55.8). On log-rank analysis, radiological parameters that were associated with poorer survival included presence of metastasis, post-chemotherapy tumor diameter and presence of residual tumor after surgery. Of these, presence of residual tumor was the only independent factor determining worse outcome as none of those with residual tumor survived longer than the first post-operative year, despite of intensive adjuvant chemotherapy. In non-metastatic hepatoblastoma cases without residual tumor after surgery, survival probability was 86.1% (95% CI 67.1 - 94.6%).

Conclusion: In non-metastatic hepatoblastoma, curative outcome is expectable when there was no residual tumor shown in post-operative imaging and the patient receives standard adjuvant treatment. Post-operative AFP higher than 5,000 ng/dL may indicate poorer outlook.

Keywords: Hepatoblastoma, Survival outcome, Radiology

SURGERY FOR PRIMARY LIVER TUMORS IN CHILDREN: A RETROSPECTIVE STUDY OF CONSECUTIVE 76 CASES

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Background: Primary liver tumors in children are rare. Multidisciplinary approach was used including surgery.

Objective: The objective of this study was to retrospectively review cases of primary liver tumors in children undergoing surgical resection.

Methods: Children (0-15 years old) undergoing surgery for primary liver tumors between 2006 and 2019 were retrospectively studied from 2 University Hospitals. Demographic data, types of procedures, operative time, pathology and post-operative complications were described. Data are expressed as mean ± SD.

Results: There were 76 children (M/F = 39/37), undergoing resection for primary liver tumors. Their average age was 27.9 ± 32.0 months and average weight was 11.7 ± 6.7 kgs. The most common presenting symptoms were asymptomatic abdominal mass. Ultrasonography, CT scan or MRI was used to confirm diagnosis and plan the surgery. The tumors were assessed to be initially unresectable in 57 of 76 (75%) patients who received preoperative chemotherapy and became resectable later.

The type of surgery included 51 lobectomies (67.1%), 9 extended hepatic lobectomies (11.8%), 7 multiple segmentectomies (9.2%). 6 segmentectomies (7.9%), and 3 wedge resections (4.0%). The mean operative time was 204.1 ± 82.1 minutes. The mean intraoperative blood loss was 274.1 ± 440.4 ml. The mean ICU stay was 2.1 ± 3.1 days. There was no statistical difference between 2 hospitals in terms of age, weight, types of procedure, intra-operative blood loss, and ICU stay ($P > 0.05$). Histopathology revealed 63 hepatoblastomas (82.9%), 4 mesenchymal harmatomas and one of endodermal sinus tumor, mature teratoma, immature teratoma, adenoma, hepatoma, undifferentiated embryonal sarcoma, focal nodular hyperplasia, glomus tumor, and undetermined benign liver tumor. The most common intraoperative complication was massive bleeding in 12 cases, with cardiac arrest in one case. Post-operative complication was found in 16 cases (21.05%) including chylous ascites, atelectasis, intra-abdominal collection, surgical site collection, C-line infection, ileus, gut obstruction, bleeding and bile leakage. Re-operation was required to correct complications in 3 patients. There was no mortality in this series. Recurrent hepatoblastoma occurred in 6 cases within 120 days.

Conclusions: The most common primary liver tumor in children requiring surgical therapy is hepatoblastoma. Abdominal mass is a common symptom. Serious complications occurred in 20% of patients with a small chance of re-operation.

Keywords: Liver tumors, Hepatoblastoma, Children

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