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

Aim & Scope

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 surgical trainees 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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2. Corporate Author:

- The Committee on Enzymes of the Scandinavian Society for Clinical Chemistry and Clinical Physiology. Recommended method for the determination of gamma glutamyltransferase in blood. Scand J Clin Lab Invest 1976; 36:119-25.
- American Medical Association Department of Drugs. AMA drug evaluations. 3rd ed. Littleton: Publishing Sciences Group, 1977.

3. Personal Author(s):

- Osler AG. Complement: mechanisms and functions. Englewood Cliffs: Prentice - Hall, 1976.

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- o Chirappapha P, Arunnart M, Lertsithichai P, et al. Evaluation the effect of preserving intercostobrachial nerve in axillary dissection for breast cancer patient. Gland Surg 2019;8:599-608. doi:10.21037/gs.2019.10.06.

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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All statistical analyses and the statistical software used must be concisely described. Descriptive statistics for quantitative variables must include an appropriate central tendency measure (e.g., mean or median) as well as a corresponding measure of spread (e.g., standard deviation or range or interquartile range). Categorical variables must be summarized in terms of frequency (counts) and percentage for each category. Ordinal variables can be summarized in terms of frequency and percentage, or as quantitative variables when appropriate. Statistical tests must be named and p-values provided to 3 decimal places. P-values less than 0.001 should be written "< 0.001" and p-values approaching 1 should be written "0.999".

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referred to must not change the conclusions or outcomes. **Discussion,** which must fully describe the implications of the research results, should include a concise literature review of previous published, related results. These related results must be compared with those of the authors' study, and the differences clearly stated along with plausible explanations. New unexpected findings, especially from subgroup analyses or those for which the research was not designed, should be considered hypothetical and stated as such. Any plausible, relevant clinical application should be indicated. Finally, any significant limitations of the study must be mentioned and possible extensions of research should be briefly provided. **Conclusion,** which should be concerned with answering the research question posed by the current study, should not be summarizing results of previous studies or recommendations. An **Acknowledgement** section can be added at the end of the article. The Reference list should be in the format as described previously.

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Use the common format. Emphasis is on clinician comprehension. The **Abstract** uses the same common structured format. In the **Main text,** the **Introduction,** in addition to the usual context setting and rationale, should also contain explanations and descriptions of basic science concepts at the level of the educated layman. The **Methods** section should still be concise with sufficient detail for others to replicate the experiment, but one or two paragraphs in between explaining basic processes in plain English would be helpful. In the **Results** section, similar conciseness is still the rule, but a brief simplified summary of the findings should be provided. In the **Discussion,** clinical implications should be clearly stated. The **Conclusion,** again, should answer the research question.

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We encourage publication of case series or case reports if a comprehensive review of the literature is included, with the aim of helping the clinician manage rare and challenging diseases or conditions based on best available evidence in conjunction with practical, local experience. For the Thai Journal of Surgery, this implies that the case report format differs somewhat from that of the common format for research articles.

Abstract: Need not be structured. State objective of the case presentation, present a summary of the case, the outcome and learning points in one concise paragraph.

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Main text: An **Introduction** to set the aims of the article. The **main content** can be structured in any way. A **Conclusion** to summarize the content should be helpful, as well as to place some personal reflections.

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Retracted Article

Notice of Retraction

Naravejsakul K. Primary Adrenal Tuberculosis: A Case Report. Thai J Surg 2021;42(4):174-9.

Author: Krittin Naravejsakul
Division of Urology, Department of Surgery, School of Medicine,
University of Phayao, Thailand 56000

Retraction date: 26 September 2022

The Thai Journal of Surgery (ISSN: 0125-6068 / E-ISSN: 2697-5858) hereby announces the formal retraction of the article titled "Primary Adrenal Tuberculosis: A Case Report", which was published in The Thai Journal of Surgery Vol. 42 No. 4 (October - December 2021),[1] due mainly to clear-cut evidence of plagiarism. Parts of the retracted article contain direct translation, from Thai to English, of the content of an online article[2] without providing due credit. The overall plagiarized material constitutes over 20% of the total word count of the retracted article in its original manuscript form. Twelve of the 19 references in the retracted article are identical to those of the online article, and almost all in the same order of reference. Some other events of concern surrounding the article also played a role in the decision to retract. The author agreed to the retraction.

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1. Naravejsakul K. Primary Adrenal Tuberculosis: A Case Report. Thai J Surg 2021;42(4):174-9.
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Review Article

Current Surgical Role in Pediatric Gastroesophageal Reflux

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Abstract Reflux of gastric content into the esophagus is a physiologic event that mostly disappears with body growth. However, infants and children with gastroesophageal reflux may develop pathologic consequences, from esophagitis, failure to thrive to airway problems. Such gastroesophageal reflux with a pathologic consequence is known as a gastroesophageal reflux disease (GERD). Certain groups of pediatric patients, including children with neurological impairment, congenital esophageal malformation or congenital diaphragmatic hernia, have increased risk of GERD and these groups of patients have poorer response to non-surgical management. Wrapping the gastric fundus around the distal esophagus, fundoplication, is a surgical technique that has long been practiced to treat GERD. Although the procedure has been proven to support the shutter mechanism of the esophagogastric junction, it comes with potential complications such as swallowing difficulty, gas bloating syndrome or dumpling syndrome. Smart patient selection, detailed pre-operative evaluation, precise technical tailoring and post-operative follow-up are key success factors that a care team should develop when considering this procedure. In addition, frontier technologies, such as transoral endoscopic fundoplication, robotic-assisted fundoplication and magnetic bead esophageal supporting device, are on their way to this arena.

Keywords: Gastroesophageal reflux disease, Fundoplication, Esophagus

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Introduction

Regurgitation of gastroesophageal content from the stomach to the esophagus, known as gastroesophageal reflux (GER) can be a physiologic condition occurring normally in neonates and an occasional event in all age groups. In cases in which the GER results in a pathologic condition or a complication such as reflux esophagitis, respiratory tract symptoms or nutritional problems, the condition is termed as gastroesophageal reflux disease (GERD), although demarcation between GER and GERD can be unclear in real clinical practice.[1,2]

It has been estimated that physiologic reflux occurs in about 25-40% of infants 4-6 months of age.[3-6] Spontaneous resolution occurs in a majority of these children, as the anti-reflux mechanisms mature, usually by 12 months of age.[7] Premature birth, congenital esophageal anomalies (e.g. esophageal atresia), congenital diaphragmatic hernia or neurological impairment increase risk the of developing GERD in childhood.[8,9] According to a primary care data from the UK, the population-based overall incidence of GERD in children aged 1-17 years was estimated at 0.84/1,000 person-years.[10] This finding was consistent with a large population-based cohort study from New Zealand which reported that about 1% of infants aged less than 12 months were admitted to a hospital with a diagnosis of GERD-related complications.[2]

Surgeons are often consulted to participate in the management of pediatric patients with reflux symptoms. Failed medical treatment is a mainstay indication for anti-reflux surgery.[11] In addition, an anti-reflux procedure is considered to be a part of a gastrostomy operation in children with neurological impairment who require a feeding gastrostomy.[12] This paper aimed to review up-to-date data on physiologic fundamentals, surgical indications, surgical technique and expectable outcome that are essential for a surgeon to understand as a team member in pediatric GERD management.

1. Anti-reflux mechanisms and natural history of pediatric GER

Immaturity of anti-reflux mechanisms and a predominantly liquid diet explain the high incidence of GER in the neonatal period. A recent cohort study from France used a parent-reported questionnaire to assess the incidence of GER in 157 full-term neonates and reported that 72% had GER related symptoms at 1 month age and the figures reduced to 56% and 14% at the ages of 6 month and 12 month, respectively.[13] The anatomical components of anti-reflux mechanisms include the lower esophageal sphincter, mucosal folding at the esophagogastric junction, diaphragmatic crura, length of intraabdominal esophagus and angulation between the lower esophagus and the gastric fundus (angle of His). Maturation of these structures together with the esophageal peristalsis and the gastric emptying function explain the decreasing incidence of GER as age increases. The change from liquid food to a semi-solid baby diet also help reduce splashing events. The lower esophageal sphincter and its surrounding organs keep a positive intraesophageal pressure gradient in relation to the intragastric pressure. After one year of age, GERD is an uncommon symptom, and is it occurs, defects in the anti-reflux mechanisms should be sought out through clinical evaluation and investigations.[14]

Certain pediatric surgical diseases are associated with an increased risk of GERD. In an infant with a congenital esophageal anomaly, a surgery itself may cause upward migration of the intra-abdominal esophagus to the chest, hence losing the pressure tone positivity at the lower esophageal sphincter mechanism. GER following an esophagoesophagostomy was reported in 15-50% of infants with esophageal atresia, depending on the method of evaluation; the same study hypothesized that acid reflux may have been related to anastomotic stricture.[15] Using pH monitoring, Vergouwe and colleagues reported 17.5% of 57 children previously treated with esophageal atresia had abnormal gastroesophageal reflux index.[16] Patients with spastic cerebral palsy often have a higher risk of GER due to increased intraabdominal pressure. In addition, patients forced to maintain a long-term supine position and chronic use of anticonvulsants may contribute to GERD.[17] Children with morbid obesity also have a higher risk of GERD.[18]

2. Clinical manifestation and diagnostic approach

GERD is literally defined as 'troublesome GER' but drawing a clear line between such pathologic conditions and physiologic variations is difficult. Regurgitation and vomiting are the most common problems that bring a child to medical attention. In general, regurgitation of not more than 6 times a day in an infant who accepts feeding and thrives well can be regarded as within normal limits and does not require intervention beyond observation to ensure the condition does not worsen.[19]

Chronic vomiting might lead to esophagitis, pain and food aversion. Failure-to-thrive can be a consequence of GERD. Apart from the gastrointestinal symptoms, a child with GERD may present with extraesophageal manifestations, from respiratory wheezing, intractable asthma or recurrent pneumonia to apparent life-threatening events such as food aspiration. Sinusitis, sleep disturbance, otitis media and dental erosion can be related to GERD. In neurologically impaired children, a typical form of posturing called the Sandifer syndrome including arching of the back, torsion of the neck and left-up chin is highly specific to GERD.[19]

Differential diagnosis of GER/GERD is broad and consists of a variety of disease entities, ranging from allergy, infection/inflammation, inborn errors of metabolism, cyclic vomiting, and increased intracranial pressure to anatomical obstruction of the upper gastrointestinal tract (Table 1). Red-flag symptoms that are indications for investigations in a vomiting child include late onset of persistent vomiting (> 6 months age) and prolonged symptoms of longer than 12-18 months, weight loss/failure-to-thrive, abnormal head circumference, seizure and long-term constipation. In a child with non-alarming vomiting symptoms, time is allowed for therapeutic trials which should focus on diet modification and a cow's milk withholding trial in infants and gastric acid suppression in older children. Diet modification in infants includes such things as division of feeding into smaller volume meals and addition of thicker food such as congee (rice porridge) or cereal. Obesity management is advisable in older obese children with reflux symptoms.

On surgical consultation, before planning for a surgery, a surgical team should play an active role in excluding other anatomical obstructions of the gastrointestinal tract. A thorough clinical evaluation focusing on feeding history, bowel habits and growth usually provide clues to select appropriate investigations. In young infants, intractable vomiting can be caused by pyloric stenosis or duodenal web or midgut malrotation/volvulus. Chronic constipation and abdominal distension may indicate low gut obstruction as in Hirschsprung disease. The choice of investigative approach depends on the relevant clinical information.

There is no gold standard investigation in a pediatric case who is suspected to have GERD.[9] Barium swallowing (upper gastrointestinal tract study, UGIS) is the most widely used radiologic study to look for refluxing events. A UGIS is useful to study the anatomy of the esophagus and the stomach in relation to the diaphragm and other mediastinal structures. Anatomical obstructions at the pylorus and/or duodenum can be excluded by this type of study. When performed under real-time video fluoroscopy, the swallowing mechanism can also be evaluated, especially in a child with neurological impairment. The main limitation of UGIS is that it is performed over a very short time, hence it may miss refluxing events occurring during the rest of the day. Also, although UGIS can demonstrate a reflux event, it cannot tell the acidity of the refluxed content.[20]

Table 1 Differential diagnosis of gastroesophageal reflux disease in pediatric age group

Physiologic change	- Physiologic reflux in infants - Overfeeding
Neurological problems	- Increased intracranial pressure caused by intracranial hemorrhage or a mass - Hydrocephalus
Metabolic disorders	- Inborn errors of metabolism e.g., galactosemia, urea cycle defects, organic acidemia, adrenal crisis - Toxic substance, e.g., lead poisoning
Gastrointestinal tract disorders	- Gastrointestinal obstruction e.g., pyloric stenosis, malrotation, duodenal web, superior mesenteric artery syndrome, foreign body ingestion - Motility disorders, e.g., achalasia cardia, gastroparesis - Inflammation, e.g., eosinophilic esophagitis, food allergy
Others	- Cyclic vomiting - Psychological, e.g., self-induced vomiting

Direct monitoring of esophageal pH is an investigation that provides an advantage in fulfilling some limitation gaps of UGIS. This instrument monitors pH at the lower esophagus over a long enough duration to detect acid regurgitation, usually a 24-hour period. The percentage of the time that the pH falls lower than 4, calculated as reflux index (RI), is the most reliable measurement of esophageal exposure to acid. An RI of less than 3% is within normal limits, while 3% - 7% is equivocal and > 7% can be regarded as abnormal. Although 24-hour pH monitoring provides high sensitivity to detect GER, the tool detects only acid reflux and may not correlate well with the reflux-related pathology. A more advanced investigative tool for GER is a multiple intraluminal impedance with pH monitoring (MII-pHM), which detects all refluxing events and can distinguish between solid, liquid and gas refluxes. A study that used nuclear scintigraphy as a reference reported sensitivity of 24-hour MII-pHM at 87.2%, which was much higher than that of 24-hour pH monitoring alone (53.2%).[21] In cases with significant GER, esophageal and gastric mucosa can be further studied through esophagogastroduodenoscopy (EGD). EGD may also detect associated anatomical anomalies such as an esophageal, hiatal hernia.

3. Management of pediatric GERD

One of the common indications for anti-reflux surgery in children with GERD is GERD in children with cerebral palsy. Typical clinical features in these children are a swallowing handicap, generalized motor spasms, and/or recurrent pulmonary infection. Some authors suggest adding a fundoplication as a part of a feeding gastrostomy operation, if indicated following pre-operative evaluation of the reflux using UGIS and 24-hour pH monitoring.[22,23] In children without neurological impairment, there are 2 categories of surgical indication for GERD: failed non-operative treatment and severe reflux consequences.

Most GERD cases in children can be successfully managed with lifestyle modifications and acid-suppressing medications. In the infant age group, feeding volume splitting, formula thickening and feeding in a semi-erect posture are recommended when body weight control and avoiding caffeine or spicy food are advisable in older age group. GERD associated with severe pulmonary consequences, apparent life-threatening events or failure-to-thrive are common indications for anti-reflux surgery in infants while esophageal stricture and Barrett's esophagus are more common in teenage children.[24,25] The main objectives of anti-reflux surgery are to correct any anatomical risks of GER and to re-create a high pressure zone at the lower esophagus.[11]

Surgical Techniques

Fundoplication has long been a standard anti-reflux procedure. The technique was developed by Rudolph Nissen (1896-1981), a German-trained surgeon who was working in the University of Basel, Switzerland, when he published the very first report on 'A simple operation for control of reflux esophagitis' in 1956,[26] and now laparoscopic Nissen fundoplication is the most common anti-reflux operation in both adults and children. The most important step in Nissen fundoplication is using the gastric fundus to wrap around the lower esophagus in its total circumference (360 degree), with a wrap length of around 2 centimeters. Before undertaking this procedure, the intraabdominal esophagus must be mobilized from its diaphragmatic attachment by means of dividing the phrenoesophageal membrane. Care should be taken at this step to keep the vagus nerves on the surface of the esophagus intact. Such mobilization not only helps increase the length of the intraabdominal esophagus and correct a hiatal hernia, division of the phrenoesophageal membrane makes the diaphragmatic crura become clear enough for approximation. On gastric fundus mobilization, the short gastric vessels do not always need to be sacrificed. Laparoscopy provides a magnificent view for fundoplication and has become a surgical standard for Nissen fundoplication (Figure 1).

Multiple versions of fundoplication have been developed with an aim to reduce complications of the total wrap, especially swallowing difficulty or dysphagia.[27] Table 2 summarizes the principles of each technique.[28-33] Apart from these methods, novel fundoplication techniques are being developed in adult patients including the transoral rotational esophagogastric fundoplication, which is a total endoscopic approach.[34] In older children, the transoral technique was reported to be feasible although, of unclear efficacy.[35] Currently, although there is no consensus technique for fundoplications, all technical modifications seem to be towards less invasive procedures.

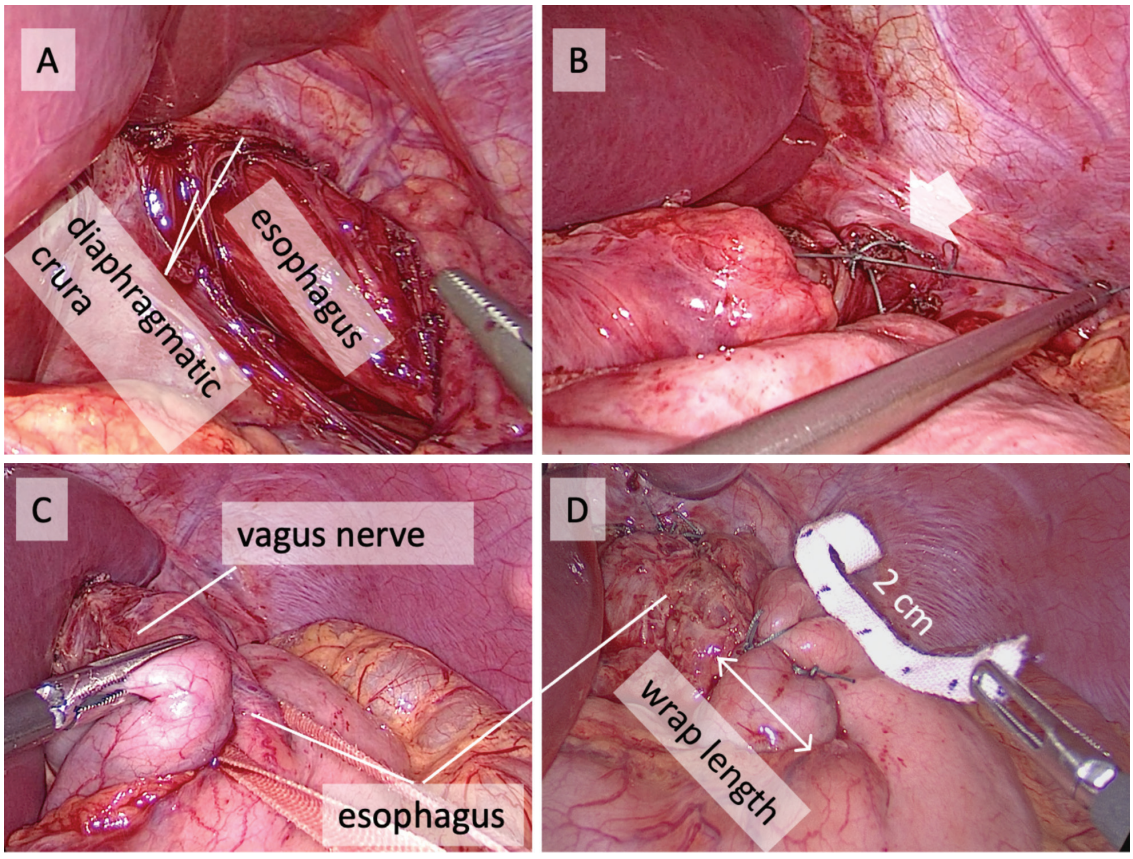

Figure 1 Laparoscopic view of a Nissen fundoplication in a child. A) Mobilization of the distal esophagus by dissecting into the phrenoesophageal membranes, B) Closure of the diaphragmatic crura with anchoring stitches to hold the esophagus, C) Mobilizing the gastric fundus to the left of the distal esophagus, D) Completion of the fundoplication, which was a 360-degree (complete) wrap of 2 cm length in this case

In children with recurrent respiratory tract infection, pre-operative preparation is important as an existing infection can increase the risk of post-operative complications. However, it might not possible to wait until a patient is absolutely clear of respiratory symptoms. Cooperation among pediatricians, anesthesiologists and the surgical team is one of the keys to operative success. An intensive care facility should be prepared for the post-operative period. Usually, enteral feeding can be resumed as soon as hemodynamic stability is restored. Feeding volume titration may be necessary at the early post-operative period.

Complications

A fundoplication in children, especially in neurologically impaired children, is not a low-risk procedure. One study reported that up to 50% of children undergoing a fundoplication experienced one or more early post-operative complications[36] (Table 3). While pulmonary complications were prevalent in patients with neurological impairment, feeding problems were more common among those without a neuronal condition. Serious complications at the early post-operative period include wrap disruption, gastrostomy leakage, and gastric necrosis. On Nissen fundoplication, excessively tight wrapping can be very problematic as it will lead to dysphagia and aspiration. A large bore nasogastric tube should be in place during the wrap. Unintended suturing of the nasogastric tube to the wrap is possible and it should be checked by the anesthesiologist before commencement of the operation. Also, the condition of 'gastric inlet obstruction' caused by and overly tight wrapping may cause a gas-bloat syndrome which is defined as the inability to burp gas out of the stomach when there is acute gastric distension. When a fundoplication is performed without a gastrostomy, this condition can even be so serious that gastric overdistension leads to stimulation of the vagovagal reflex.

Table 2 Technical variants in fundoplication used in the pediatric age group

Technique	Technical principles	Remarks
Nissen[28]	Abdominal approach, complete (360° wrap) with a bougie in place, diaphragmatic crura approximation	Current standard
Toupet[29]	Abdominal approach, posterior partial wrap (270°)	Less dysphagia[27]
Thal[30]	Abdominal approach, Anterior partial wrap (270°), Angle of His reconstruction[32]	
Dor	Abdominal approach, Anterior partial wrap (180°, fundus laid-over)	Optimum choice following Heller myotomy for achalasia cardia[33]
Boix-Ochoa[31]	Abdominal approach, Restoration of the normal anti-reflux anatomy and fundus unfolding	

Recurrence of GERD has been reported in around 7-15% of neurologically impaired patients following an anti-reflux procedure and 2-10% of neurologically normal patients.[36-38] Transthoracic migration of the wrap is among the most common anatomical reasons for recurrence. Therefore, a contrast study is recommended in cases with recurring reflux symptoms. In a systematic review of laparoscopic fundoplication in children, pooled mortality in neurologically impaired cases was at 18% and most of the mortalities were associated with progression of the underlying condition(s).[39,40]

Associated esophageal atresia or diaphragmatic hernia are predictors of failed anti-reflux surgery.[41] One study reported that redo-operations were required in 13% and 8% of patients following primary fundoplication in patients with and without esophageal atresia, respectively.[42] Poorer esophageal motility and a short esophagus explain the risk in this group of patients. Partial fundoplication or loose Nissen fundoplication are recommended for correcting intractable GERD in patients with esophageal malformation.[43-46]

Injury to the vagal trunks may lead to decreased gastric emptying time, thus more rapid passage of food from the stomach into the small intestine. High osmolarity chyme absorbs fluid into the intestinal lumen and stimulate secretion of various gut hormones including serotonin, bradykinin, enteroglucagon, cholecystokinin and vasoactive intestinal peptide.[47] In addition, a rapid surge of insulin may result in hypoglycemia. Dumping syndrome following a fundoplication is usually transient and can be managed by adjusting the formula and rate of feeding.

4. Surgical outcomes

Surgical outcome measures of anti-reflux surgery in children usually focus on improvement of reflux associated consequences, including episodes of pneumonia that requires hospitalization, feeding tolerance, physical growth and quality of life. Significant weight gain following fundoplication has been reported and this effect is even clearer in neurologically impaired children[48]. Contrarily, evidence did not support an impact of fundoplication on reducing reflux-related admissions due to respiratory problems in neurologically impaired children.[49] However, a large study in 182 neurologically intact children showed that partial (Thal) fundoplication significantly improved airway symptoms and reduced the need for medications.[50] In general, recurrence rates have been reported at around 2% - 12%[51-53] and redo-operations around 15%.[54] Neurologically impaired children had higher rate of recurrence when compared to their counterparts.

5. New technologies

Robotic assisted fundoplication in children

Case series reporting technical success in robotic assisted fundoplication in children began to appear in the medical literature at the beginning of the 2000s[55-60] and there was a meta-analysis in 2014.[61] According to the meta-analysis, the overall conversion rate was 3% and operative times ranged from 127-186 minutes.

Table 3 Potential complications of fundoplication

Intraoperative complications
- Hypercapnia and respiratory acidosis
- Iatrogenic adjacent organs injury (left lobe of liver, spleen, diaphragm, vagal trunks, pneumothorax, hemothorax)
Immediate post-operative complications
- Respiratory complications (pneumonia, atelectasis)
- Gastrostomy related complications (intraperitoneal leak, bleeding, dislodgement)
- Fundoplication related complications (sewn gastric tube, gastric necrosis, wrap disruption)
Medium and long-term complications
- Recurrent gastroesophageal reflux symptoms
- Transthoracic migration of the wrap
- Gas bloat syndrome
- Dumping syndrome

Although the data have proven technical feasibility and shown a trend toward shorter operative times, there was no significant difference in short term outcomes when comparing robotic assisted surgery and conventional laparoscopic fundoplication.[61]

Magnetic bead esophageal sphincter augmentation device

An esophageal sphincter augmentation device is an alternative treatment for patients who respond only partially to the acid-reducing medications and whose parents are still reluctant for their child to undergo a fundoplication.[62] A prototype of this instrument is the LINX (Ethicon, Johnson & Johnson, Inc.). This device is composed of a string of magnetic beads held together in a ring shape. When surgically applied to the lowermost part of the intraabdominal esophagus, the ring enhances the tone of the lower esophageal sphincter which opens when there is a passage of esophageal content from the upper esophagus but remains closed in prevention of gastric content splashing. Studies in adult patients have shown the safety and efficacy of the device and have suggested it as a first-line surgical anti-reflux procedure.[63-66] Up to the time of this review, there has been no reports of its use in the pediatric age group.

Conclusion

Reflux of gastric content into the esophagus can be pathogenic when it occurs long and frequently enough. Although most pediatric patients with GER can be managed conservatively, surgical therapy has a role in specific groups of patients including children with neurological impairment and infants born with esophageal atresia. Although the current surgical standard is laparoscopic Nissen fundoplication, there are trends toward minimal dissection and avoiding a tight wrap. Surgeons should be aware of post-procedure complications as they are not uncommon. Long term care by multi-disciplinary team is essential.

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Original Article

Survival Rate in Curative Resection of Pancreatic Cancer Patients at Maharat Nakhon Ratchasima Hospital

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Abstract

Objective: Pancreatic cancer is difficult to diagnose and treat. Survival rate of pancreatic cancer is also dismal and many clinicopathologic factors are related to survival. The aims of the present study were to determine the 5-year survival rate and prognostic factors associated with survival in pancreatic cancer patients undergoing curative resection.

Patients and Methods: Pancreatic cancer patient data were collected from medical records between January 1, 2009 and June 30, 2012. The primary outcome was overall survival by Kaplan-Meier method. Univariate and multivariate Cox proportional hazard regression analysis was used to determine independent prognostic factors.

Results: Median survival time was 14.3 months and 5-year survival rate was 10.3%. From Cox univariate regression analysis, independent and significant factors predicting the survival of these patients included tumor size, intraoperative blood loss, pathological margin, and lymph node involvement ($p < 0.05$). From Cox multivariate regression analysis only pathological margin, and intraoperative blood loss were significantly associated with survival ($p < 0.05$).

Conclusion: In this study, pathological margin and intraoperative blood loss significantly affected overall survival

Keywords: Pancreatic cancer, Survival rate, Prognostic factors

Introduction

Although the incidence of pancreatic cancer is low, the mortality rate of this lethal disease is high. Because the pancreas is a retroperitoneal organ, it is difficult to make an early diagnosis of pancreatic cancer. The relative incidence of newly diagnosed pancreatic cancer was 2.5% of all cancers. Age-standardized rates (ASRs) per 100,000 person-years was 7.7 in Europe and 7.6 in North America.[1] The Thai National Cancer Institute reported the incidence of pancreatic cancer in 2019 was higher in women. Pancreatic cancer was in the top ten highest ranking causes of cancer-related deaths (8th for males, 9th for females).[2]

Pancreatic cancer is categorized into 2 main types: Pancreatic adenocarcinoma, which is found in 85% of all pancreatic cancer patients, and pancreatic neuroendocrine tumor (PanNET), which is found in less than 5%.[3] There are 4 stages of pancreatic cancer (American Joint Committee on Cancer 7th editon). Curative resection in pancreatic cancer can be performed in all stage 1 and

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some stage 2 patients.[4] Tumors located in the head of pancreas should be be surgically removed by pancreaticoduodenectomy, while cancer located in the body and tail of pancreas is removed by distal pancreatectomy. Only 18 % of pancreatic cancer patients are eligible for curative resection.[5]

Pancreatic cancer has 1-year and 5-year survival rates of 24% and 9%, respectively.[6] In Thailand, 1-year and 3-year survival rates were 24% and 6 %, respectively.[7] From a study of pancreatic cancer survival rates by stage, stages 1 and 2 (localized pancreatic cancer) has a 5-year survival rate of 32% to 39 %. For stage 3 disease (regional pancreatic cancer), the 5-year survival rate was 12% to 13%, and in stage 4 disease (distant metastasis), the 5-year survival rate was 3 %.[8-9]

One study found some clinicopathological factors which may affect survival rates. These include involvement of resection margins, major vascular ingrowth, site of origin, and perioperative blood transfusion.[10] A study reported that, with pancreatic lesions less than 3 cm in size, preoperative EUS -FNA (endoscopic ultrasonography- fine needle aspiration) was able to determine T staging, vascular invasion and resectability with some accuracy.[11] Also, many studies showed that lymph node involvement was related to survival.[12,13] In this study, we aim to determine the survival rates and the clinicopathological factors associated with survival of resectable pancreatic cancer.

Patients and Methods

After approval by the Ethics Committees of the Institute (Document No112/2021), data were collected retrospectively from medical records at Maharat Nakhon Ratchasima Hospital of patients with pancreatic cancer (ICD10 codes: C250, C251, C252, C253) treated between January 1, 2009 to June 30, 2012 (3 years and 6 months). All patients were followed until June 30, 2017. All patients had pathologically confirmed pancreatic adenocarcinoma and all underwent successful curative surgery. Those with recurrent pancreatic cancer or metastatic cancers to the pancreas were excluded.

All statistical analyses were performed with STATA, version 11.0, software (StataCorp LP, College Station, Texas). Histograms, boxplots, and descriptive methods were used to examine data for errors, outliers, and missing values. The primary outcome was overall survival by Kaplan-Meier method, calculated in months from the date of diagnosis to the date of death. Non-deaths or deaths from other causes were censored at the time of the last follow-up. Clinical factors examined included age, gender, tumor size (< 3 cm or ≥ 3 cm),[11] lymph node involvement (negative or positive), pathological margin (positive margin was defined as cancerous cells detected < 1 mm from resection margin; otherwise the margin was negative),[14] and intraoperative blood loss (< 700 mL or ≥ 700 mL).[15]

Comparison of survival curves was done using the log-rank test. Independent prognostic factors were identified using multivariable Cox proportional hazards regression models. In one model, variables with a p-value < 0.1 on univariable analysis were included in analysis, with backward stepwise selection. In another, all variables of a priori interest, which included tumor size, lymph node involvement, pathological margin, and intraoperative blood loss were forced into the model. The results were expressed as hazard ratios with p-values and 95% confidence intervals. A p-value of < 0.05 was considered statistically significant.

Results

There were 177 patients diagnosed with pancreatic cancer in the present study. Only 29 patients (16%) underwent successful curative resection. The mean age was 55.4 years with a range from 40 years to 74 years. There were slightly more men (52%) than women (48%). Classical pancreaticoduodenectomy (38%) was the most common operation, and distal pancreatectomy (35%) was the second most common. Among 29 patients, stage 1a (38%) disease was most commonly found, followed by stage 2b (31%). Median intraoperative blood loss was 750 mL. Ten patients (35%) developed postoperative complications (Table 1). The most common postoperative complication was pancreatic anastomosis leakage seen in 5 patients (17 %), defined as fluid amylase > 3 times the upper limit of serum amylase. Three patients had grade B pancreatic leakage, and 2 patients had grade C leakage based on the 2016 update of the International Study Group (ISGPS).[16] Delayed gastric emptying was seen in 3 patients (10%). Two patients developed wound infection (7%). There were 2 postoperative deaths (7%). Causes of death were sepsis and multiorgan failure following pancreatic anastomosis leakage.

The overall survival is presented in Figure 1. The median survival time was 14.3 months (95% CI: 7.2 to 20 months) and the 5-year survival rate was 10.3%. There was no statistical difference in survival between

Table 1 Clinical and laboratory characteristics of patients.

Characteristics	Summary (N = 29)
Age (year): mean, SD (range)	55.4, 8.9 (40 to 74)
Gender: number (%)	
Male	15 (52)
Female	14 (48)
Operations: number (%)	
Classical pancreaticoduodenectomy	11 (38)
PPPD*	8 (28)
Distal pancreatectomy	10 (34)
Stage: number (%)	
1a	11 (38)
1b	7 (24)
2a	2 (7)
2b	9 (31)
Intraoperative blood loss (mL): median (interquartile range)	750 (500 to 900)
Postoperative complication: number (%)	10 (35)
Postoperative deaths: number (%)	2 (7)
Total bilirubin: number (%)	
< 3 mg/dL	18 (62)
≥ 3 mg/dL	11 (38)
Serum albumin: number (%)	
≤ 3.5 g/dL	17 (59)
> 3.5 g/dL	12 (41)
CEA ≥ 5 ng/mL: number (%)	8 (28)
CA 19-9 ≥ 37 U/mL: number (%)	11 (38)

*PPPD: pylorus-preserving pancreaticoduodenectomy

the pancreatic head resection (combine classical pancreaticoduodenectomy and pylorus-preserving pancreaticoduodenectomy) and distal pancreatectomy ($p = 0.61$), as displayed in Figure 2.

On univariable analysis of clinicopathologic factors in Table 2, tumor size, pathological margins, blood lass and lymph node involvement were significantly related to survival at the 5% level. In particular, the mortality risk was increased for patients with positive pathological margin as compared with patients with negative pathological margin, with a hazard ratio (HR) of 9.5; 95% CI: 3.3 to 27.3; $p < 0.001$. The mortality risk was 6-fold higher in patients with positive lymph node involvement as compared with those with negative lymph node involvement (HR of 6.0; 95% CI: 2.1 to 16.8; $p = 0.001$). In addition, intraoperative blood loss of more than 700 mL increased the mortality risk when compared with intraoperative blood loss of less than 700 mL (HR of 3.7; 95% CI: 1.6 to 8.7; $p = 0.003$). Similarly, the mortality risk of patients who had tumor size greater than 3 cm was 3.2- fold higher than that of patients had tumor size smaller than 3 cm (HR of 3.2, 95% CI: 1.3 to 6.8; $p = 0.01$). Other clinicopathological factors, such as age and gender, had no significant association with survival.

On multivariable Cox regression analysis (Table 3), only pathological margin, and intraoperative blood loss were significantly associated with survival ($p < 0.05$). In detail, positive pathological margin increased 7.4-fold the mortality risk, as compared with negative pathological margin (HR of 7.4; 95% CI: 2.6 to 21.4; $p < 0.001$).

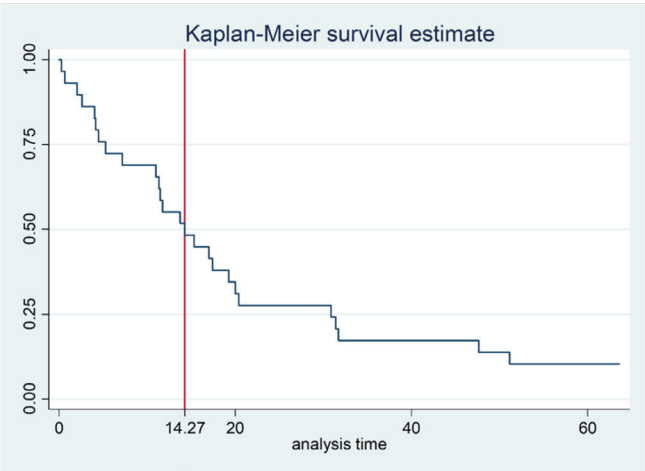

Figure 1 Overall survival of pancreatic cancer patients

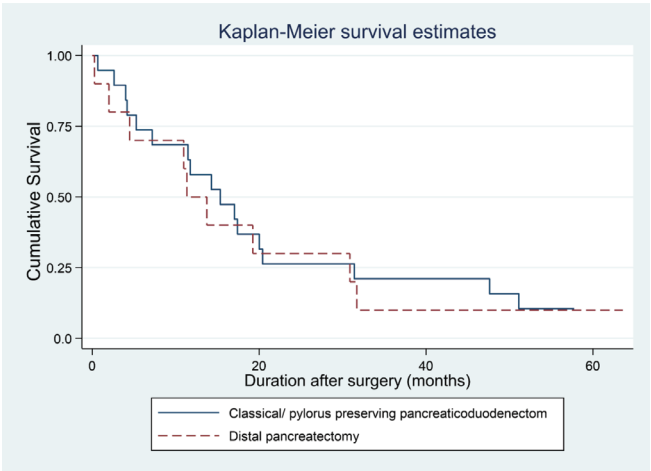

Figure 2 Comparison of survival between pancreatic head resection and distal pancreatectomy (log-rank test $p = 0.61$). See text

Table 2 Univariable Cox regression analysis of clinicopathologic factors

Factors	Number (%) N = 29	Median survival (months)	Time at risk	Incidence rate/100	Crude HR	95% CI	*p*-value
Age (years)						0.8 to 3.9	0.158
< 65	17 (59)	17.40	419.73	3.5	1		
≥ 65	12 (41)	11.33	162.13	6.7	1.8		
Gender						0.2 to 1.1	0.072
Men	15 (52)	13.73	206.33	7.2	1		
Women	14 (48)	17.03	375.53	2.9	0.5		
Tumor size						1.3 to 6.8	0.008
< 3 cm	14 (48)	20.4	404.69	2.9	1		
≥ 3 cm	15 (25)	7.16	177.16	7.9	3.2		
Intraoperative blood loss						1.6 to 8.7	0.003
< 700 mL	15 (52)	20.4	442.09	2.7	1		
≥ 700 mL	14 (48)	7.16	139.76	10.0	3.7		
Pathological margin						3.3 to 27.3	< 0.001
Negative	19 (65)	20	529.36	3.0	1		
Positive	10 (35)	4	52.49	19.0	9.5		
Lymph node involvement						2.1 to 16.8	0.001
Negative	21 (72)	19.23	531.99	3.3	1		
Positive	8 (28)	4.16	49.86	16.0	6.0		

HR: hazard ratio; CI: confidence interval

Table 3 Multivariable Cox regression analysis of clinicopathologic factors

Factors	Crude HR	Adjusted HR* (95% CI)	*p*-value	Adjusted HR* (95% CI)	*p*-value
Gender					
Male	1	-	-	-	-
Female	0.48	-	-	-	-
Tumor size				Ref. 1.64 (0.53 to 5.11)	0.392
< 3 cm	1	-	-		
≥ 3 cm	3.02	-	-		
Intraoperative blood loss		Ref. 2.88 (1.17 to 7.08)		Ref. 3.18 (1.14 to 8.85)	0.027
< 700 cc	1				
≥ 700 cc	3.7		0.023		
Pathological margin		Ref. 7.39 (2.55 to 21.4)		Ref. 6.24 (1.40 to 27.8)	0.016
Negative	1				
Positive	9.48		< 0.001		
Lymph node involvement				Ref. 0.79 (0.17 to 3.66)	0.759
Negative	1	-	-		
Positive	6.01	-	-		

*Each column represents a different cox regression model. Covariates not included in final models are indicated as (-); CI: confidence interval; HR: hazard ratio; Ref.: reference group

Patients with operative blood loss more than 700 mL also had increased mortality risk as compared with patients with operative blood loss less than 700 mL (HR of 2.9; 95% CI 1.2 to 7.1; $p = 0.023$). The result of a model with all *a priori* factors of interest included, also showed that only positive pathological margin and intraoperative blood loss more than 700 mL were significant risk factors, with similar HR's as those in the previous model, while other factors had no significant association with survival.

Discussion

Only 15% to 20% of all pancreatic cancers are resectable. These mostly include stage1 and 2 diseases.[5,17] Our study showed a similar resectability rate (16.4%). To improve resectability, early detection is important. We suggest that patients who have symptoms, including severe weight loss, chronic abdominal pain and jaundice, should be examined by a physician as soon as possible and appropriate investigations be done for detecting early stage pancreatic cancer. A study reported that preoperative EUS- FNA[11] and neoadjuvant chemotherapy may improve resectability.[18]

Operative morbidity and mortality reported in the present study were similar to those of other tertiary centers.[5,19] The 5-year survival rate of patients with resectable pancreatic cancer was comparable to those of some other reports (10% to 31%).[20] However, many recent studies showed better survival.[5,21] We believe that some of these differences may be due to treatment in specialized pancreatic care centers, treated by pancreatic disease specialists, with better treatment options, shorter cancer waiting time, and along with a higher frequency of negative surgical margin, and negative lymph nodes involvement, these can all improve treatment outcomes.

The present study clearly indicated that positive pathological margin was an independent risk factor for cancer-related death. There are 8 pancreatic resection margins: 4 in transection margins that include pancreas cut-end margin, bile duct cut-end margin, proximal gastric or duodenal resection margin, and distal jejunal or enteric margin; 3 in the dissected margins including posterior margin, portal vein (PV) or superior mesenteric vein (SMV) groove margin and superior mesenteric artery (SMA) margin; and the last margin at the anterior surface of the pancreas.[22] Some reports defined the posterior margin as the retroperitoneal margin or the uncinate margin, and the SMA margin as the uncinate margin.[23] One study demonstrated that margin clearance by at least 1.5 mm may improve long-term survival.[23] Another study reported that a margin clearance of 2 mm or greater were associated with increased overall survival.[24] At our Institution, we consider a surgical resection margin negative when at least 1 mm margin clearance is achieved.[14]

Intraoperative blood loss (IBL) is also associated with mortality risk in the present study. A study from Japan reported that operative blood loss was associated with the risk of pancreatic cancer mortality.[25] On the other hand, there are also studies showing that IBL was not an independent risk factor in patients with cancer.[15,26-27] Some studies reported that there was evidence for an association between blood transfusion and increasing risk of infectious complications,[28] and the risk of recurrence.[29] It remains unclear why IBL is associated with morbidity and low survival rate. Data from animal studies found that the activity or cytotoxicity of natural killer cells was depressed after blood loss.[30] In the present study, massive intraoperative blood loss occurred when pancreatic resection was combined with portal vein resection. To prevent massive IBL, we focused on preoperative preparation, especially in jaundice patients. Coagulopathy must be corrected. Moreover, we emphasized good surgical technique, identifying bleeding points and to secure bleeding sites around branches of the portal vein, at blood vessels around the uncinate area, and at the transection margin.

The presence of malignant cells in the lymph node (LN) was a predictor of poor survival in several studies.[12] Some studies demonstrated that patients with one to three involved nodes had better survival when compared with those with four to seven nodes.[31] Other reports also showed that patients with more than three involved LNs had worse survival in relation to those with less than three nodes.[13] Recent studies showed that the lymph node ratio (LNR) may be more useful than involved LN status as a prognostic factor in pancreatic cancer.[32-33] However, one study reported that LNR was not associated with survival.[34] In the present study, lymph node involvement was not associated with cancer-related mortality. This may be due to incomplete lymphadenectomy.

The present study has some limitations. Firstly, it was a retrospective study with a relatively small sample size. Larger-sized studies are needed. Secondly, there was selection bias in that patients who has severe underlying diseases such as severe cardiomyopathy, ischemic

heart disease or of very old age are often not operated on. Surgeons tend to treat these patients conservatively to avoid high operative morbidity and mortality.

Conclusion

In the present study, the 5-year survival rate of patients undergoing curative pancreatic resection for pancreatic cancer was 10.3%. Also, positive pathological margin and intraoperative blood loss of more than 700 mL were the only independent risk factors associated with increased cancer-related mortality. From the present study, we emphasize that patients with positive resection margin must be managed with aggressive treatment.

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บทคัดย่อ **อัตราการรอดชีวิตของผู้ป่วยมะเร็งตับอ่อนที่ได้รับการผ่าตัดหวังผลหายขาด (curative resection) ของโรงพยาบาลมหาราชนครราชสีมา**

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หน่วยศัลยกรรมทั่วไป กลุ่มงานศัลยกรรม โรงพยาบาลมหาราชนครราชสีมา

ความเป็นมา: มะเร็งตับอ่อนเป็นมะเร็งที่มีการวินิจฉัยได้ยากและมีความเสี่ยงสูงในการผ่าตัดทำให้มีอัตราการรอดชีพที่ต่ำ อีกทั้งยังพบว่ามีปัจจัยเสี่ยงอื่นๆ ต่อการรอดชีพ

วัตถุประสงค์: เพื่อศึกษาอัตราการรอดชีพในระยะเวลา 5 ปี และปัจจัยที่มีผลต่อการรอดชีพของผู้ป่วยมะเร็งตับอ่อนที่ได้รับการผ่าตัดหวังผลหายขาด

วิธีการศึกษา: ศึกษาข้อมูลจากเวชระเบียนย้อนหลังและข้อมูลทะเบียนราษฎร์ของผู้ป่วยมะเร็งตับอ่อนที่ได้รับการผ่าตัดหวังผลหายขาดที่โรงพยาบาลมหาราชนครราชสีมาในช่วงเวลา 1 มกราคม 2552 ถึง 30 มิถุนายน 2555 ศึกษาอัตราการรอดชีพในระยะเวลา 5 ปี โดยวิธี Kaplan-Meier และใช้วิธี Cox proportional hazard regression analysis ในการศึกษาถึงปัจจัยที่มีผลต่อการรอดชีพ

ผลการศึกษา: ผู้ป่วยเพียง 29 ราย (ชาย 15 รายและหญิง 14 ราย) เข้ารับการผ่าตัดหวังผลหายขาด มีอายุเฉลี่ย 55.4 ปี ผู้ป่วย 10 ราย (34.5%) เกิดภาวะแทรกซ้อนหลังผ่าตัด และมีผู้ป่วยเสียชีวิตหลังผ่าตัด 2 ราย (6.9%) พบว่ามีอัตราการรอดชีวิตเฉลี่ยอยู่ที่ 14.27 เดือน และอัตราการรอดชีวิต 5 ปี เท่ากับ 10.3% การวิเคราะห์ Cox univariate regression analysis พบว่าปัจจัยที่มีผลต่อการรอดชีพ ได้แก่ ขนาดของเนื้องอก การสูญเสียเลือดระหว่างการผ่าตัด ขอบพยาธิสภาพ และการมีส่วนร่วมของต่อมน้ำเหลือง ($p < 0.05$) และจากการวิเคราะห์ Cox multivariate regression analysis พบว่ามีเพียงระยะขอบทางพยาธิวิทยา และการสูญเสียเลือดระหว่างการผ่าตัดเท่านั้น มีความสัมพันธ์กับการรอดชีวิตอย่างมีนัยสำคัญ ($p < 0.05$)

สรุปผลการศึกษา: ในการศึกษานี้พบว่ามีอัตราการรอดชีวิตเฉลี่ยอยู่ที่ 14.3 เดือนและอัตราการรอดชีวิต 5 ปี เท่ากับ 12.5% และยังพบว่าระยะขอบทางพยาธิวิทยาและการสูญเสียเลือดระหว่างผ่าตัดมีผลต่อการรอดชีวิตโดยรวมอย่างมีนัยสำคัญ

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Original Article

The Safety of Lactobacillus Plantarum Extract Used as a Possible Adjuvant Treatment of Breast Cancer

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Abstract

Objective: *Lactobacillus plantarum* is one of the most interesting strains of probiotics with potential anticancer effects. However, few clinical studies have been done to demonstrate this. The objective of the present study was to evaluate clinical safety of *Lactobacillus plantarum* extract used as an adjuvant treatment for breast cancer.

Materials and Methods: This study was a prospective, randomized, double-blind, and placebo-controlled study of early-stage breast cancer patients who underwent surgical removal of tumor and given conventional chemotherapy. The treatment group received products containing *L. plantarum* extract, and the placebo group received only a placebo for the duration of six months. Evaluated clinical parameters include body weight, symptoms resulting from side effects from chemotherapy, quality of life and laboratory tests.

Results: There were 56 patients in the study, of whom 27 were randomly assigned to a treatment group and 29 to the placebo group. A significant difference in the WBC count between the two groups was found in the second month after chemotherapy ($P = 0.04$). The mean white blood cell (WBC) count in the treatment group was 7,641 cells/mm^3 and 5,108 cells/mm^3 in placebo group, respectively. The mean bodyweight in the placebo group decreased in the second month to an extent more than in the treatment group, and continue to decrease in the sixth month while in the treatment group the mean bodyweight increased.

Conclusions: The present study demonstrated that *L. plantarum* extract can be used safely as a possible adjuvant therapy for breast cancer patients. There was a trend towards better clinical and laboratory profiles in the treatment group, but mostly without statistical significance. Only the WBC count at the second month of chemotherapy showed a significant difference.

Keywords: Efficacy of *Lactobacillus plantarum* extract, Breast cancer

Introduction

Cancer is the second leading cause of mortality in the world, and the first leading cause of death in Thailand since 2000. Breast cancer is the most common malignancy among woman and an important cause of cancer related morbidity and mortality worldwide. Although the advancement in screening and treatment of breast cancer have decreased its mortality steadily, however, the clinical management of breast cancer using conventional chemotherapeutic agents are harmful to normal host cells. These cytotoxic drugs are associated with various types of life-threatening side-effects and adverse clinical outcomes.

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The term probiotics is defined by the Food Agricultural Organization (FAO) and the World Health Organization (WHO) as live microorganisms. When probiotics is administered in adequate amounts, it may provide healthful benefits to the host.[1] Probiotics can be found in a large quantity in fermented food and yogurt. Most of the probiotics consists of lactic acid producing, non-pathogenic bacteria, such as *Lactobacillus, Streptococcus, Bifidobacterium, Enterococcus* or non-pathogenic yeast. Gastrointestinal (GI) tracts of humans and animals contain a complex community of bacteria, which has an active interaction with host cells. These microorganisms are helpful in physiologic activities such as digestion, metabolism of bile acids, synthesis of vitamins B and K, and play a crucial role in the development of homeostasis of the innate and adaptive immune system.

Any disequilibrium in both composition and quantity of the gut microbiota can generate a condition known as dysbiosis. Dysbiosis could be linked to human pathology that includes metabolic disorders such as obesity, types 2 diabetes, autoimmune disease, asthma, inflammatory bowel disease, irritable bowel syndrome and cancer.[2-6] Furthermore, probiotics has been proven to be able to revert intestinal dysbiosis, which may play a role in the development of several diseases including cancer.[7] Numerous clinical studies have suggested that probiotics may have various benefits in cancer treatment including the reduction of serious side-effects associated with anticancer therapy,[8-11] improvement of efficacy of some anti-neoplastic drugs[12] and immunotherapies,[13] reduction of post-operative complications[14] and prevention the recurrence of cancer.[15]

Probiotics are mostly considered safe, affordable, and important microbes, which may have anti-carcinogenic activities in some cancers.[16] Dead probiotics and their metabolic products may provide similar beneficial effects in the prevention and treatment of cancer compared to live probiotics.[17-18] Molecules and metabolites such as lipopolysaccharide, exopolysaccharide extracted from various specific strains of probiotics could play an important role in prevent and treatment of colon cancer.[19-22]

In vitro and *in vivo* studies have provided some evidence that many specific strains of probiotics may display activity against breast cancer.[23-27] *Lactobacillus plantarum* is one of the most interesting strain of probiotics.[28] *Lactobacillus plantarum* may have anti-cancer property via multiple mechanisms of action such as inflammatory suppression via cytokines, induced apoptosis of tumor cell, activating T cell mediated and enhancing NK cell activity.[28-31] However, only a few clinical trials have been conducted in breast cancer patients. The objective of the present study was to determine the safety of using *Lactobacillus plantarum* as a probiotic supplement and possibly adjuvant treatment in breast cancer.

Patients and Methods

The present study was a prospective, randomized, double-blind, and placebo-controlled study. Early-staged breast cancer patients (Stages 1 to 3 by the American Joint Committee on Cancer (AJCC) TNM system) aged between 21 to 65 years with ECOG performance status 0 to 1 who had undergone surgical treatment and planned to receive further conventional chemotherapy at the Chemotherapy Unit, Lamphun Hospital, were recruited into the study. All patients provided written informed consent before participating.

All patients were enrolled by the investigator and assigned to a placebo group and treatment group by simple randomization, according to the randomization number obtained through a computer-generated randomization table. Information obtained from the patient included age, tumor stage, number of positive lymph nodes, and hormonal receptor status. The study products were pre-packaged by the sponsor as per the randomization codes and dispensed accordingly. Placebo and probiotics were prepared and labelled 'A' or 'B'. The capsules and their content were visually identical in both groups. Only a nurse not directly involved in the trial was able to break the treatment codes.

Chemotherapeutic regimens were standard anthracycline and cyclophosphamide (AC) or 5-FU with an anthracycline and cyclophosphamide (FAC), or with added taxane (AC-T) for more advanced stage cancers.

All patients received 5 capsules of products containing *L. plantarum* extract or placebo to be taken 4 times a day for a period of 6 months, covering the whole duration of chemotherapy. Patients underwent evaluation of clinical symptoms and signs and routine laboratory tests at every 3 weeks. Clinical parameters included body weight, symptoms of side effects from chemotherapy, and basic laboratory tests such as complete blood counts. Quality of life questionnaires such as WHOQOL-BREF-THAI and PHQ-9 were administered at the first month and 6 months later.

The preparation of the *L. plantarum* extract capsules began with inactive ingredients in powder form: turmeric (10%), lemon grass (10%), maize (10%), soybean (25%), ginkgo seed (25%) and Indian gooseberry (10%). All the ingredients were mixed thoroughly. Water was then added to the mixture, at up to 900 mL/kg of the mixed powder. The mixture was then sterilized by an autoclave. *Lactobacillus plantarum* was cultured overnight in 100 mL of the mixture mentioned above, then transferred into 800 mL of the residual mixture and subsequently fermented for one week. The bacterial extract was prepared from the *L. plantarum* cultured on solid medium plate for two days. Bacterial cells were scrapped and put into liquid detergent and incubated for 12 hours. Sodium chloride was added and was extracted with ethanol. Ten grams of this precipitate was added in the fermented *L. plantarum* mixture previously prepared and then sterilized once again by autoclave. Finally, the mixture was heat dried in an oven and packed in capsules. Each capsule contained 3 mg of *L. plantarum* extract.

The comparisons of clinical and laboratory characteristics and outcomes between the two groups were done separately at several time points during the trial. Unpaired t-tests, Wilcoxon rank-sum test, and Chi-square tests were used as appropriate. *P*-values of 0.05 or less were considered statistically significant. The data were analyzed by using STATA statistical software version 15.1.

Results

From January 2017 to February 2019, 65 patients were enrolled into the study, but only 56 patients had complete data for evaluation. Although the calculated sample size was planned for 100 patients, the study had to be completed within two years. Due to this schedule restriction, only 65 patients were obtained. Nine subjects were excluded (5 in treatment arm and 4 in the placebo arm) because of product discontinuation by these patients within 2 weeks after enrolment into the study. Some of these patients complained of taking too many pills, causing difficulty of ingestion. Others experienced some adverse side effects allegedly from the medication, such as the loss of appetite, nausea, and vomiting. The flow diagram showing randomization and follow-up of the trial is shown in Figure 1. Patient's baseline characteristics are summarized in Table 1.

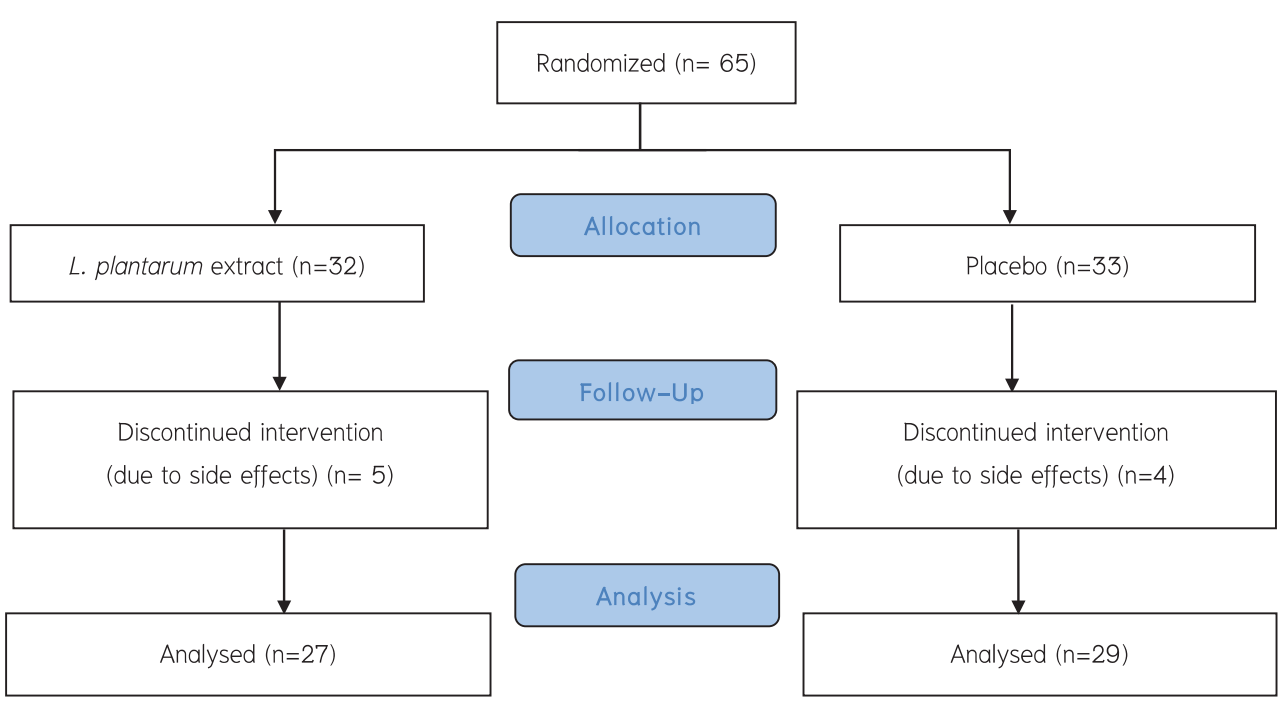

Figure 1 Flow diagram of the clinical trial

Table 1 Baseline characteristics of patients

Characteristic	*L. plantarum* (N = 27)	Placebo (N=29)	*p*-value
Age (years): mean (SD)	51.1 (9.5)	52.3 (10.9)	0.670
Weight (kg): mean (SD)	56.2 (10.9)	54.5 (9.2)	0.540
Underlying disease: number (%)	14 (52)	13 (45)	0.599
Stage 1: number (%)	14 (52)	15 (52)	0.093
Stage 2: number (%)	4 (15)	0	0.093
Stage 3: number (%)	9 (33)	13 (45)	0.093
Chemotherapy: number (%)			0.757
FAC/AC	11 (41)	13 (45)	
AC-T	16 (59)	16 (55)	
Alternative medicine: number (%)			0.279
Yes	22 (81)	25 (86)	
No	3 (11)	1 (3)	
ECOG status: mean (SD)	0.8 (0.4)	0.4 (0.2)	0.498
PHQ-9: mean (SD)	1.1 (1.1)	0.6 (0.7)	0.609
WHOQOL-BREF-THAI: mean (SD)	95.8 (11.2)	89.1 (20.8)	0.147

SD: standard deviation; stage refers to breast cancer staging (see text); chemotherapy regimen is as in text; ECOG, PHQ-9, WHOQOL-BREF-THAI are quality of life measures (see text)

The treatment and placebo groups were similar with regards to age, body weight, clinical staging of cancer, ECOG status, depression score, and quality of life by WHOQOL-BREF-THAI at the first visit. All patients received concurrent chemotherapy. There were some baseline laboratory test differences between the two groups, with the mean hematocrit and platelet count in the placebo group being slightly higher than those of the treatment group ($p = 0.013$ and $p = 0.03$, respectively); but the other laboratory values were not significantly different (Table 2).

Table 2 Baseline laboratory test results

Laboratory value	*L. plantarum* (N = 27)	Placebo (N = 29)	*p*-value
Hemoglobin (g/dL): mean (SD)	11.8 (1.3)	12.3 (1.0)	0.149
Hematocrit (%): mean (SD)	35.5 (3.2)	37.7 (2.9)	0.013
WBC (cells/mm^3): mean (SD)	7,124 (2,406)	7,033 (2,381)	0.891
Platelets (cells/mm^3): mean (SD)	285,560 (88,808)	332,348 (61,190)	0.028

SD: standard deviation; WBC: white blood cell count

At the second month after beginning of treatment (third visit), there were significant differences in the WBC count between two groups ($p = 0.04$). The mean WBC count in the treatment group was increased from 7,124 cells/mm^3 to 7,640 cells/mm^3, while the mean WBC count in placebo group was decreased from 7,034 cells/mm^3 to 5,108 cells/mm^3 (Table 3).

Table 3 Clinical and laboratory test results at the second month (third visit)

Value	*L. plantarum* (N = 27)	Placebo (N = 29)	*p*-value
Weight (kg): mean (SD)	56.1 (21.4)	53.4 (8.4)	0.362
Number of adverse symptoms from chemotherapy: mean (SD)	3.6 (1.0)	3.8 (1.7)	0.521
Hemoglobin (g/dL): mean (SD)	11.1 (1.3)	10.9 (1.4)	0.747
Hematocrit (%): mean (SD)	33.7 (3.8)	33.8 (4.1)	0.940
WBC (cells/mm^3): mean (SD)	7,640 (3,060)	5,108 (1,971)	0.046
Platelets (cells/mm^3): mean (SD)	365,143 (120,981)	397,640 (167,675)	0.340

SD: standard deviation; WBC: white blood cell count

The mean body weight of patients in both groups decreased in the second month compared to baseline (56.2 kg to 56.1 kg in treatment group and 54.5 kg to 53.4 kg in placebo group). At the sixth month, the mean body weight in the treatment group was increased compared to baseline (56.2 kg to 58.6 kg in treatment group) while the body weight in the placebo group continue to slightly decrease (54.5 kg to 54.4 kg). However, these changes were not significantly different between the two groups (Table 4).

Table 4 Clinical and laboratory test results at the sixth month (final visit)

Value	*L. plantarum* (N = 27)	Placebo (N = 29)	*p*-value
Weight (kg): mean (SD)	58.6 (12.8)	54.4 (8.5)	0.290
Hemoglobin (g/dL): mean (SD)	11.3 (1.4)	11.5 (1.2)	0.718
Hematocrit (%): mean (SD)	34.7 (4.1)	35.5 (3.2)	0.383
WBC (cells/mm^3): mean (SD)	7,181 (3,258)	6,889 (2,158)	0.693
Platelets (cells/mm^3): mean (SD)	377,778 (111,755)	435,517 (85,843)	0.034
ECOG status: mean (SD)	0.04	0.00	0.228
PHQ-9: mean (SD)	1.1 (1.1)	0.6 (0.7)	0.180
WHOQOL-BREF-THAI: mean (SD)	92.1 (23.4)	86.2 (26.6)	0.412

SD: standard deviation; WBC: white cell count; ECOG, PHQ-9, WHOQOL-BREF-THAI are quality of life measures (see text)

Other clinical and laboratory measures, including adverse symptoms from chemotherapy, values of the hemoglobin, hematocrit and platelet counts were similar in both groups at all visits. There were no statistically significant differences in terms of ECOG status, depression score, and quality of life by the WHOQOL-BREF-THAI questionnaire between two groups at the sixth month of visit.

Discussion

In a previous study, polynucleotide extracted from *L. plantarum* was demonstrated to have efficacy and safety as adjuvant treatment in HIV infected patients.[32-33] Thus, we conducted a similar study of *L. plantarum* extract in breast cancer patients. Although probiotics can be used safely in the general population,

in immunocompromised patients such as cancer patients receiving chemotherapy, probiotics may cause opportunistic infections.[9] Therefore, the use of dead probiotics would be safer in this group of patients.

The result of the present study demonstrated that at the third visit of follow up, or about two months after chemotherapy, when most patients were experiencing the side effects of chemotherapy, the clinical and laboratory profile of treatment group tended to be slightly better than those of the placebo group. This included body weight reduction, the reduction of hemoglobin and hematocrit levels, and the platelet count from baseline, and the number of chemotherapy adverse events, but none of these differences were statistically significant. Only the difference in the WBC count was of borderline significance.

We could not exactly explain why the platelet count increased in both groups at the second and sixth month, while the RBC and WBC counts decreased. We hypothesized that the increase in platelet counts was the result of reactive thrombocytosis from iron deficiency anemia caused by occult GI hemorrhage, which is a side effect of several chemotherapeutic drugs used in our protocol.[34-36] Of course, all of these minor differences could have been due to chance variation.

From several in vitro studies, several mechanisms of action of *L. plantarum* may be beneficial in cancer treatment. *L. plantarum* seems to demonstrate some chemopreventive efficacy in a rat model of breast cancer.[30] The oral supplement of a selenium nanoparticle enriched with *L. plantarum* may increase IFN-γ, TNF-α, IL-2 levels and increase NK cell activity in breast cancer-bearing mice.[29] One major limitation of the present study was that our current institution could not carry out any of the laboratory tests mentioned in these studies, and thus any biological link between these hypothetical mechanisms and the observed clinical and laboratory effects could not be directly verified.

Other limitations of the present study included the small sample size, the small effect differences, and the use of multiple statistical comparisons, which meant that any borderline significant results were likely to be due to chance. Finally, the study could not address the issue of cancer-adjuvant effects of *L. plantarum* as no cancer-related outcomes were obtained in the present study.

Conclusions

The present study showed that *L. plantarum* extract can probably be used safely as a possible adjuvant therapy in breast cancer. There seemed to be slightly better clinical and laboratory profiles in the treatment group as compared with the placebo group, but without statistical significance. Only one difference in the WBC counts at one time point seemed to be of borderline significance. Perhaps future studies including a larger number of patients performed in institutions with more detailed laboratory testing could be done to confirm and extend the findings of the present study.

Acknowledgement

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Conflicts of Interest

The authors declare no conflicts of interest.

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บทคัดย่อ

ความปลอดภัยของสารสกัดจากเชื้อแบคทีเรียไม่ก่อโรค (*Lactobacillus plantarum*) ที่นำมาใช้ร่วมในการรักษาผู้ป่วยโรคมะเร็งเต้านม

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ความเป็นมา: เชื้อแบคทีเรีย *Lactobacillus plantarum* เป็นเชื้อโปรไบโอติก ที่มีผลการวิจัยพบว่ามีกลไกหลากหลายในการต่อต้านเซลมะเร็งในห้องปฏิบัติการ แต่ยังมีการศึกษาในผู้ป่วยน้อย

วัตถุประสงค์: เพื่อทำการศึกษาความปลอดภัยของสารสกัดจากเชื้อแบคทีเรียไม่ก่อโรค (*Lactobacillus plantarum*) นำมาใช้ร่วมในการรักษาผู้ป่วยโรคมะเร็งเต้านม

วิธีการศึกษา: เป็นการศึกษาแบบ prospective, randomized, double-blind, placebo-controlled ในผู้ป่วยโรคมะเร็งระยะแรกจำนวน 56 ราย ซึ่งได้รับการผ่าตัดเรียบร้อย และเตรียมที่จะได้รับยาเคมีบำบัดสูตรมาตรฐาน ผู้ป่วยจำนวน 27 ราย ได้รับการสุ่มเป็นกลุ่มทดลอง และ 29 รายเป็นกลุ่มควบคุม ผู้ป่วยในกลุ่มทดลองจะได้รับยาแคบซูลที่บรรจุสารสกัดจากเชื้อ *Lactobacillus plantarum* ในขณะที่อีกกลุ่มจะได้รับยาหลอกเป็นระยะเวลา 6 เดือน โดยมีการเก็บข้อมูลทางคลินิก เช่น น้ำหนักตัว, ดัชนีคุณภาพชีวิต, อาการแพ้ยาเคมีบำบัด และค่าทางห้องปฏิบัติการ

ผลการศึกษา: พบว่าค่าเฉลี่ยของระดับเม็ดเลือดขาวของกลุ่มทดลอง 7,640.5 cell/ mm^3 และ 5,107.6 cell/ mm^3 ในกลุ่มควบคุม มีความแตกต่างกันอย่างมีนัยสำคัญทางสถิติ ($P = 0.04$) ในเดือนที่สองของการวิจัย ค่าเฉลี่ยของน้ำหนักตัวของผู้ป่วยในกลุ่มควบคุมจะลดลงมากกว่ากลุ่มทดลองในเดือนที่สองของการวิจัยเช่นเดียวกัน แต่ไม่มีนัยสำคัญทางสถิติ และยังคงลดลงในเดือนที่ 6 ในขณะที่กลุ่มทดลองมีค่าเฉลี่ยของน้ำหนักตัวที่เพิ่มขึ้น

สรุปผลการศึกษา: การศึกษานี้แสดงให้เห็นว่า สารสกัดจากเชื้อ *Lactobacillus plantarum* สามารถนำมาใช้ในการรักษาร่วมกับการรักษามาตรฐานในการรักษาโรคมะเร็งเต้านมได้อย่างปลอดภัย ผลการศึกษายังพบว่ามีตัวแปรทางด้านคลินิกหลายตัวที่ในกลุ่มทดลองจะมีผลดีกว่าในกลุ่มควบคุม แต่มีเพียงค่าเฉลี่ยของเม็ดเลือดขาวเพียงตัวแปรเดียวที่แสดงให้เห็นความแตกต่างอย่างมีนัยสำคัญทางสถิติ

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Case Report

Left Paraduodenal Hernia as a Cause of High Gut Obstruction in a Young Child: A Case Report

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Abstract Although a paraduodenal hernia is the most common intraabdominal herniation causing intestinal obstruction, the condition comprises less than 2% of intestinal obstructions in the pediatric age group. Accurate diagnosis of this condition may help in preparing for surgery and selection of the right surgical choice. Herein, we report a pediatric case of left paraduodenal hernia who presented with intractable vomiting and dehydration without abdominal distension. An upper gastrointestinal study demonstrated a narrow segment of the proximal jejunum with severely delayed passage of contrast media. Surgical exploration found a left paraduodenal hernia and subsequent narrowing of the herniated segment, which was managed by a segmental resection. The patient had an uneventful post-operative course and could regained healthy status within a month of treatment.

Keywords: Paraduodenal hernia, Pediatric gut obstruction, Vomiting

Introduction

During the neonatal and infantile periods, intestinal obstruction is not an uncommon condition. They are mostly caused by congenital malformations of the gastrointestinal tract itself, while intestinal obstruction in older children is rare and usually related to an acquired condition such as adhesion caused by previous abdominal surgery, infection/infestation, inflammatory bowel diseases or a foreign body.[1] Apart from an inguinal hernia, internal herniations caused by abnormal recesses within the abdominal cavity are rare events, but may cause obstruction in various parts of the intestine.[2,3]

According to a classic study by Hansmann and Morton, internal hernia can be categorized based on anatomical location into 7 groups, retroanastomotic, foramen of Winslow, paraduodenal, pericecal, intersigmoid, transmesenteric and transomental. Paraduodenal hernias are the majority of all internal hernias and are more frequent on the left side.[4] Paraduodenal hernias are often associated with abnormal intestinal rotation and/or a midgut volvulus.[5] Although a paraduodenal hernia is the most common form of internal hernia, it comprises less than 2% of intestinal obstructions and a correct diagnosis can be made only when the practitioner is aware of this potential diagnosis.[6,7]

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In this report, we report a case of a left paraduodenal hernia in a 3-year-old boy who had no history of any type of gastrointestinal event before this problem.

Case Report

A 3-year-old boy was referred to us with a problem of intractable vomiting for 5 days. The boy had been previously healthy until 2 weeks prior to the referral when the mother noticed that he began to have post-prandial vomiting with bile and food particles. The severity of vomiting increased over the next few days, and he eventually became weak and dehydrated. He was taken to a local hospital where a diagnosis of acute gastritis was made, and supportive care were given. The patient did not get better and was taken back to the same hospital 2 days before arrival at our hospital when serum electrolytes showed hyponatremia, hypokalemia, and severe metabolic alkalosis (Na 128.6 mmol/L, K 2.5 mmol/L, Cl 71.9 mmol/L, and CO2 40.1 mmol/L). The patient was resuscitated and transferred to our hospital for further management.

At the emergency department, vital signs were BT 38.1 C, RR 26/min PR 130/min, BP 95/72 mmHg and the SaO2 was 100%. His body weight on admission was 10.6 kg (10^{th} percentile for Thai Children) and the height was 100 cm (> 90th percentile for Thai children). The child was found to have upper abdominal distension with tympanic percussion. However, there were no signs of peritonitis. A rectal examination was unremarkable. The retained gastric tube was in-place and has drained 70 ml of green turbid fluid. Initial laboratory revealed Na 134.3 mmol/L, K 3.13 mmol/L, Cl 90.4 mmol/L, CO2 31.8 mmol/L, Ca 8.5 mmol/L, and PO4 2.8 mmol/L. A plain abdominal film showed a distended stomach and a duodenum with the presence of air in the colon (Figure 1). Abdominal ultrasonography reported no gross abdominal masses and no evidence suggestive of a midgut volvulus. The patient was admitted with a provisional diagnosis of incomplete obstruction of the proximal small bowel. During admission, the patient had no abdominal pain and could pass normal feces. The gastric output was about 90-140 ml/day and he still had occasional vomiting even on starvation.

An upper gastrointestinal study was performed on the second days of admission which showed distension from the stomach down to the third part of the duodenum and collapsed forth part of the duodenum (Figure 2). An esophagogastroscopy was then performed, during which the scope could be passed to the third part of the duodenum with unremarkable findings. The decision was made to perform an exploratory laparotomy which revealed that the distal part of the duodenum together with a short part of the proximal jejunum was trapped in a recess behind the inferior mesenteric vein (Figure 3).

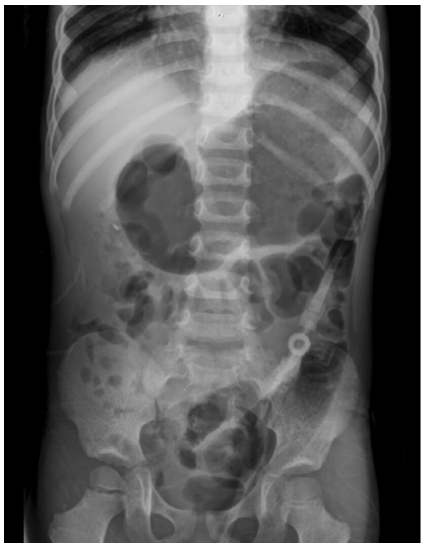

Figure 1 A plain abdominal radiograph of the patient, showing dilated stomach and duodenum

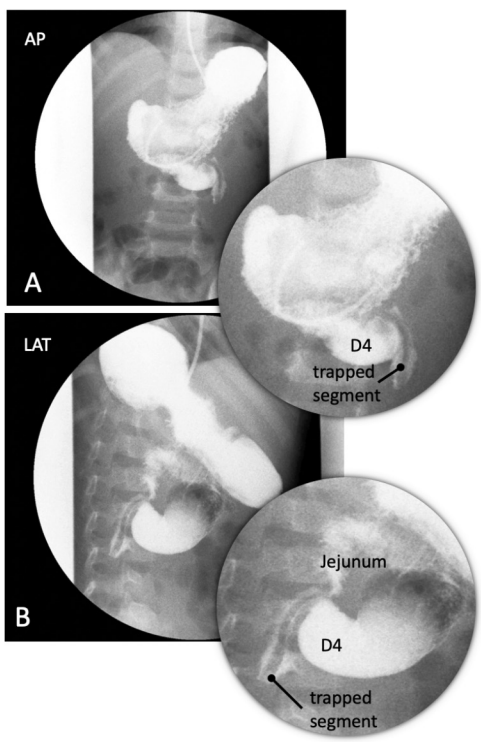

Figure 2 Upper gastrointestinal contrast study of the patient, showing the trapped segment of the proximal jejunum

There were spots of calcification on the mesentery of the trapped segment. The herniated segment was released from the pouch and was seen to be stiffly stenosed with severe proximal dilatation. The decision was made to resect the stenosed segment, followed by an end-to-end anastomosis.

The patient had an uneventful post-operative course and could be discharged on post-operative day 7. On a follow-up visit at one month, the patient had gained 4 kilograms of weight and was able to eat and defecate normally.

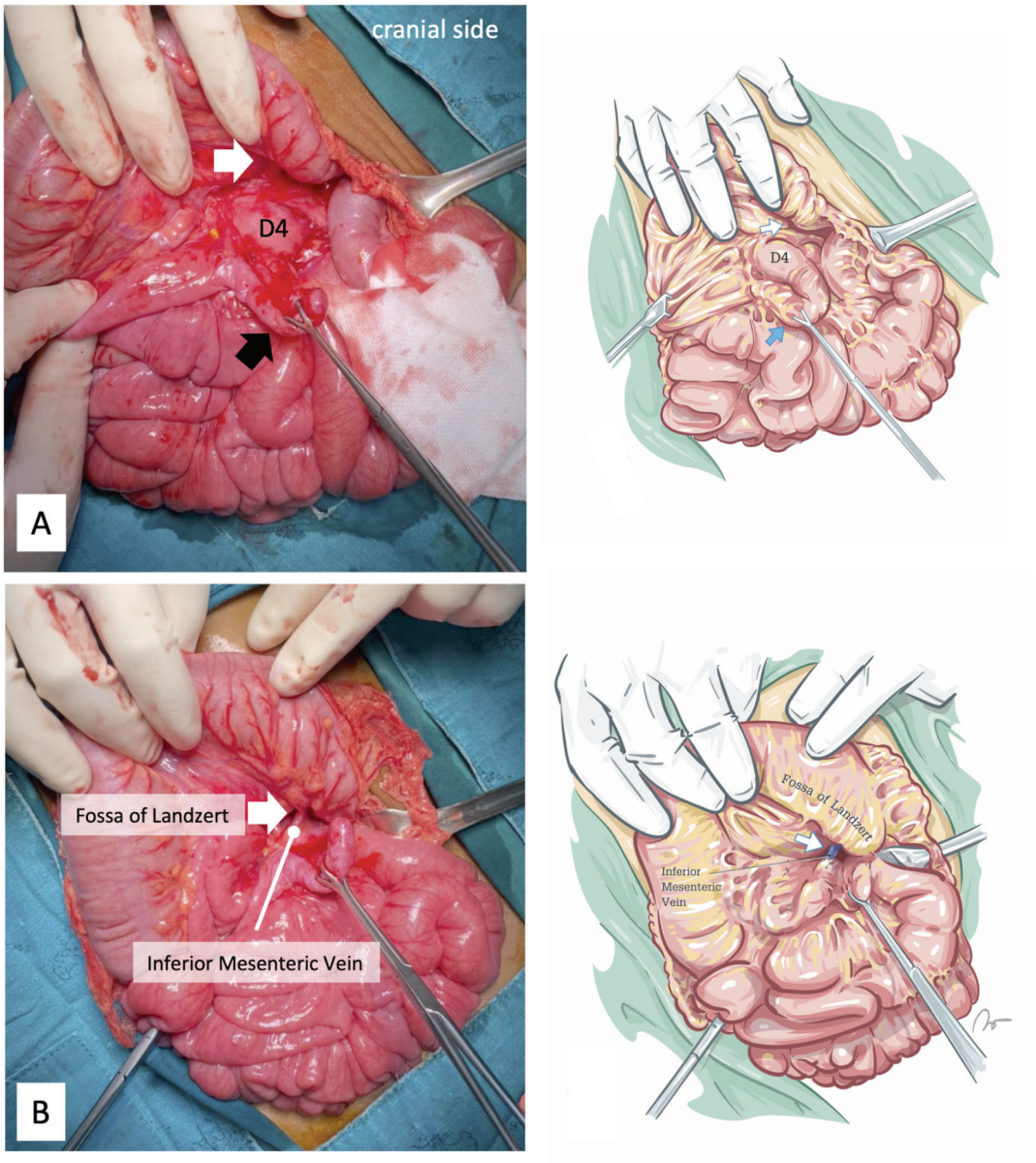

Figure 3 Operative findings A: Reduced bowel from the herniation, B: depicting the fossa of Landzert

Discussion

Although intestinal obstruction caused by a congenital anomaly of the gastrointestinal tract is not common in children older than 1 year of age, an acute obstructing event caused by a midgut volvulus or internal herniation can occasionally occur in this age group.[8] Other conditions that are more common in this age include intussusception, obstructing foreign body, adhesion in a case with previous abdominal surgery or trauma-related obstruction. When these acquired conditions can be ruled out and the symptoms of obstruction are apparent, a rotation abnormality and an internal hernia should be looked for. In our case, protracted vomiting, dehydration and electrolyte imbalance prompted the diagnosis of intestinal obstruction. Less severe abdominal pain and normal defecation suggested that the obstruction was unlikely to be a complete one, which indicated a contrast study with an aim to differentiate other causes of vomiting that might not require surgery. As the contrast study showed a significant delay at the duodenojejunal junction with severe size disparity, the decision was made to explore the abdomen.

A left paraduodenal hernia is defined as herniation of a part of the intestine through an internal defect of the mesentery, dorsal to the inferior mesenteric vein and lateral to the forth part of the duodenum.[9] The defect is named 'the fossa of Landzert', which is believed to be a result of abnormal rotation of the midgut, involving incomplete fixation of the mesocolon near the inferior mesenteric vein to the posterior peritoneum.[10] The herniated intestine is usually located at the proximal jejunum, which can be a short segment as in our case or a large cluster of bowel segments as reported in other studies.[11,12] An upper gastrointestinal study with a small bowel follow-through is a valuable tool for assessing location and nature of a proximal intestinal obstruction. In our case, the study nicely demonstrated a partial obstruction at the most distal part of the duodenum with a u-shaped streak of contrast passing through the trapped segment before entering the jejunum.

Considering the weight percentile of the patient and the evidence of a hard stricture of the trapped segment together with surrounding calcification, it seemed that the obstruction had occurred long before the symptoms developed. Although most reported cases presented with an acute intestinal obstruction, there have been several reports of chronic recurrent abdominal pain in adults as a result of intermittent obstruction by a left paraduodenal herniation.[13,14] Once this diagnosis is made, surgery is the only choice of treatment. Surgical abdominal exploration aims to confirm the diagnosis, reduce the herniated segment and resect the non-viable bowel, if present. Care should be taken not to injure the inferior mesenteric vessels to avoid ischemia of the descending colon. In uncomplicated cases, laparoscopic surgery has been reported to offer a better cosmetic outcome and quicker recovery.[15-17]

In conclusion, we report a case of a paraduodenal hernia in a child with radiological findings and corresponding operative findings that might increase awareness that this entity can be a cause of proximal intestinal obstruction. The condition should be one of differential diagnosis in a case of proximal intestinal obstruction in children.

Acknowledgement

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Case Report

Duct of Luschka Injury - The Biloma Dilemma: A Case Report

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Abstract Post-Operative bile leaks have been a major topic of discussion in the literature. These events lead to morbidity as well as increased mortality among patients. Injury to the 'Duct of Luschka' has increasingly been discussed in recent times. We present a case of post-open cholecystectomy complicated with bile leak attributed to injury to the subvesical duct, also known as the 'Duct of Luschka'. This case report discusses the origins of the term of the duct of Luschka as well as other aspects of tackling a case of bile leak from this duct.

Keywords: Duct of Luschka, Subvesical duct, Bile leakage, Cholecystectomy

Introduction

Bile leak post cholecystectomy is one of the most feared postoperative complications. The International Study Group of Liver Surgery has defined bile leakage as "bilirubin concentration in the drain fluid at least 3 times the serum bilirubin concentration" on or after postoperative day 3, requiring radiologic or operative intervention due to biliary collection or bile peritonitis.[1]

Post-operative bile leaks were observed to occur in 0.9% of patients after laparoscopic cholecystectomy, 4.2% in patients undergoing laparoscopic cholecystectomy but converted to open surgery, and 2.4% in patients undergoing open cholecystectomy. This complication significantly contributes to morbidity in 44% of the patients and boasts a mortality rate of 8.8%.[2]

The most common site contributing to postoperative bile leaks occurs at the cystic duct stump, followed by the duct of Luschka, and other sites.[3] The duct of Luschka, also known as the subvesical duct, was first described in detail by Hubert Von Luschka in 1963. He described the subvesical duct as a slender bile duct running along the gallbladder fossa, draining into the right hepatic duct or common hepatic duct.[4] A literature review conducted by Schnelldorfer revealed a prevalence of subvesical duct injury of only 4%.[5] We herein report the occurrence of bile duct leakage secondary to an injury to the duct of Luschka after open cholecystectomy for gallbladder empyema.

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Case Presentation

A 74-year-old man presented with a history of right upper quadrant for 2 days. There was nausea and vomiting. He had tenderness at the right hypochondrium with positive Murphy's sign. His white cell count (WCC) was raised (23,400/mm^3) and had slightly elevated serum bilirubin level (2.0 mg/dL). Abdominal ultrasonography (USG) showed features of gallbladder empyema with multiple gallstones. The patient underwent an emergency open cholecystectomy. The surgery was uneventful. A drain was left in the Morison's pouch.

The patient had an uneventful postoperative course until day 4 after surgery. There was significant bile fluid flowing from the drainage tube, and the patient had a mild right upper quadrant tenderness. A repeated abdominal ultrasonography (USG) showed a fluid collection at the gallbladder fossa measuring 2.2 cm × 2.2 cm × 2.0 cm, while Magnetic Resonance Cholangiopancreatography (MRCP) revealed a gallbladder fossa fluid collection communicating with segment VIII/V intrahepatic duct, likely through the duct of Luschka (Figure 1). Endoscopic Retrograde Cholangiopancreatography (ERCP) was performed in view of the persistent bile drainage, and established that there was contrast leakage from the duct of Luschka, with no leakage from the cystic duct (Figure 2). A 12 cm/7Fr plastic biliary stent was deployed. Over the next few days, the bile leakage decreased markedly, and the patient was discharged home, symptom free.

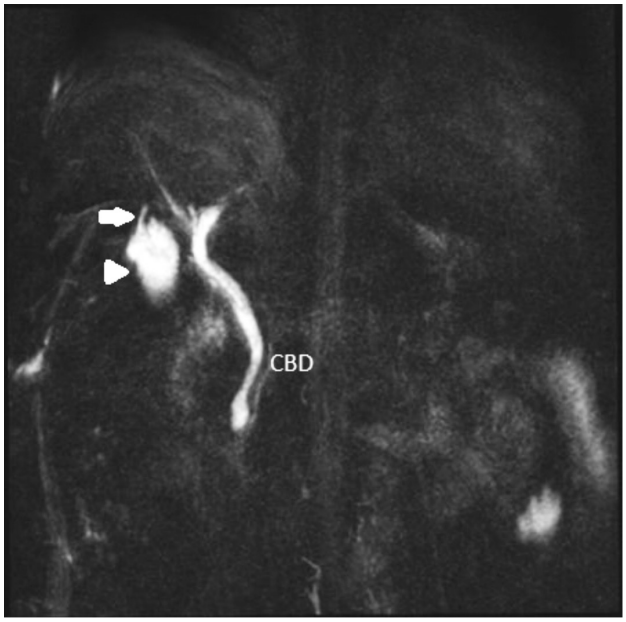

Figure 1 MRCP image showing contrast flow from subvesical duct (arrow) and contrast extravasation (arrow head)

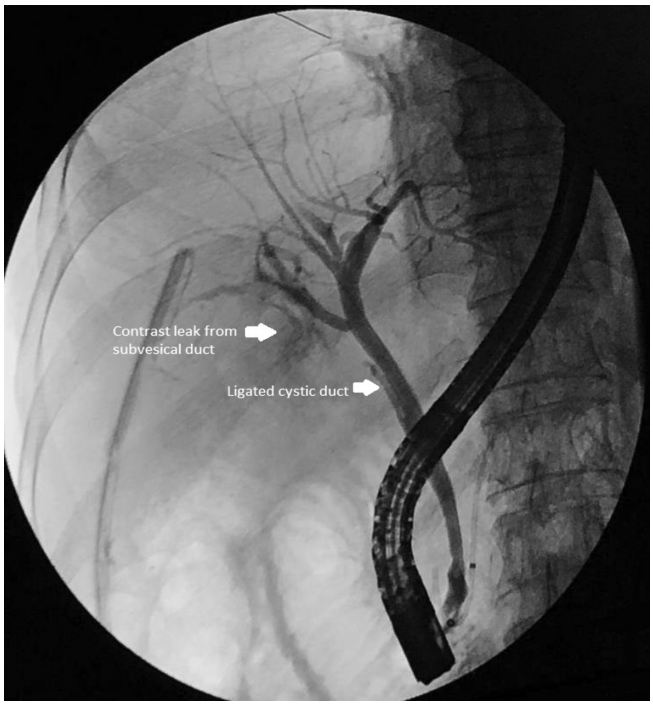

Figure 2 ERCP image demonstrating contrast leak from subvesical duct

Discussion

The duct of Luschka is a well-known anatomic variant that has been mentioned and discussed frequently in recent papers. Knowledge of the anatomy of this biliary tree variation is important from a clinical perspective, as it is at risk of injury during gallbladder and hepatic operations.

The name "duct of Luschka" originates from Hervert Von Luschka, who, in his anatomy book, describes the duct as an intra-mural gland draining into the gallbladder lumen or a network of microscopic ducts within the soft tissue surrounding the gallbladder.[4] The duct of Luschka have since been cited and referenced frequently without a clear definition. A literature review by Schnelldorfer in 2011, identified 13 articles, comprising 3996 patients, in an attempt to properly define the anatomy of the duct of Luschka. He concluded that this anatomic variant should be better termed the subvesical duct. In his review, the subvesical duct prevalence was 4%. He also revealed that the duct commonly had a mean diameter of 2 mm (range, 1 to 18 mm) and a mean length of 35 mm (range, 8 to 82 mm). These subvesical ducts originated mainly from the right lobe (69%). Drainage into the right lobe occurred in 40% of subvesical ducts, while majority drained into the gallbladder.[5] Being aware of the anatomical variants may go a long way in preventing biliary complications.

As expected, bile leaks carry some degree of morbidity and mortality. An analysis of 3,551 patients with bile leaks revealed that 2.4% of patients died within 1 year, which is 2-fold higher than that of patients with no bile leaks.[6] This mortality was observed despite adjusting for sepsis and cholangitis suggesting even in the absence of overt infection, bile leakage still had a detrimental effect on survival. Hence, clinical awareness remains crucial in detecting bile leakage. A retrospective study of patients who were referred for suspected bile leakage, revealed that the majority of patients with bile leakage was symptomatic (72%). A large proportion presented with abdominal pain (62%), as well as fever (37%) and jaundice (7%).[3]

Bile leakage from the duct of Luschka is a rare complication, reported in only 0.15% to 2% of patients undergoing cholecystectomy.[8] The duct of Luschka can be screened for its presence or injury in three phases, namely pre-operative, intra-operative and post-operative. Pre-operative detection uses drip-infusion cholangiography with computed tomography (DIC-CT). A study conducted by Kitami et al revealed that among 277 patients with cholelithiasis, the duct of Luschka was identified in 28 patients.[7] Intra-operative cholangiography to detect duct of Luschka injury during surgery could be technically challenging, and hence does not always detect such injury.[9] The most common period where an injury to the duct of Luschka is diagnosed is therefore post-operative. Radiologic imaging is an important modality in detecting postoperative bile leakage. There are many options available, such as fistulography, ERCP, or MRCP.[7] MRCP with contrast agents primarily excreted by the biliary tract in T1-weighed sequences results in 86% sensitivity and 83% specificity for the detection of bile leakage. It also offers the possibility to detect leaks not communicating with the central biliary tree and to differentiate bile from free fluid of different origin.[8] An example of contrast agent being used is Teslascan (intravenous mangafodipir trisodium) which is primarily excreted via the biliary tract.[7]

Treatment of bile leakage from the duct of Luschka depends on several factors, mainly taking into account the clinical condition of the patient. In most cases, patients who are asymptomatic with low output bile leakage should only require a simple percutaneous drain insertion. Spontaneous resolution of bile leakage is possible if the duct of Luschka does not drain bile from a significant portion of the liver parenchyma.[7] If there is clinical deterioration, or the bile leakage becomes high output, ERCP with sphincterotomy and biliary duct stenting would benefit the patient.

Conclusion

Bile leakage is a serious complication after cholecystectomy. Leaks from the duct of Luschka are an infrequent event, but should remain a possible complication after cholecystectomy in the surgeon's mind. Even in the hands of the most experienced surgeon, this complication may occur. ERCP and stenting is still the gold standard treatment for this injury. The name 'duct of Luschka' should be referred to as the subvesical bile duct.

Declarations

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

Authors' contributions

Hemanathan Praemanathan: Conceptualization, Data curation, Resources, Validation, Visualization, Writing-original draft, Writing-review & Editing

Ivan Ho Khor Ee: Conceptualization, Data curation, Resources, Validation, Visualization, Writing-original draft, Writing-review & Editing

Yeoh Aik Guan: Conceptualization, Resources Validation, Visualization, Writing-Review

Muhamad Izwan Ismail: Conceptualization, Resoures Validation, Visualization, Writing-Review, Supervision

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Resident Paper Award

3D PRINTABLE DEVICE FOR 3D FACIAL SCANNING USING IPHONE TRUE DEPTH SENSOR: PRECISION ACCURACY AND APPLICABILITY TESTING

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Background: 3D scanning technology has become more affordable and easy to access. Even in our most popular computerized hand held device, an iPhone (Apple, Inc., Cupertino, Calif.), is already equipped with high precision and accuracy 3D scanner. But the usage in medical field is still lower than as it should be. One part of this may be due to user experience and understanding requirement of the process to obtain reliable result.

Objective: The purpose of this study is to build a reliable device that helps decrease human factor error while using iPhone for scanning 3D facial file which can be used by any level of user and also provide 3D printable file that reader cloud recreate and use in one's own setting.

Methods: 3 inexperience user (trainee) and 4 live subject (2 male, 2 female) underwent 3D facial scan with the iPhone and the iPhone with 3D printed device and also Artec spider as a reference device. Accuracy and precision was calculate by surface to surface root mean square distance error (RMSE). Total number of attempt, failure rate, and incomplete rate was also record and report.

Results: All methods show high precision with average RMSE of 0.59 mm (manually), 0.56 mm (with 3D printed device), 0.51 mm (Artec scanner) and high accuracy with average RMSE of 0.82 mm (manually), 0.84 mm (with 3D printed device). No significant in precision and accuracy was found between devices using iPhone in combination with the device decrease failure rate from 31% to 0%, incomplete rate from 22% to 0% and a faster time used from 57 to 42 sec. p value = 0.01, 0.03, 0.003, 0.0003 respectively.

Conclusions: iPhone true depth sensor with or without device is a capable 3D scanner with a great precision and accuracy, but with the helps of device most errors can be reduce to zero with a faster time. Therefore, a real potential clinical used may be achieved this way.

Disclosure: This is a self-experiment of Joe Areejunthawat, MD. The authors have no financial disclosures and no funding was received for this work and have no association with any of the mentioned companies.

ACCURACY OF 2019 ASGE GUIDELINE AND PREDICTIVE PARAMETERS FOR CHOLEDOCHOLITHIASIS BEFORE ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY

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Background: In 2019, the American Society for Gastrointestinal Endoscopy (ASGE) revised guideline of endoscopic management for common bile duct stone (CBDS). This study aimed to evaluate accuracy of 2019

ASGE criteria in evaluation of CBDS and to identify additional predictive parameters which might improve accuracy of criteria.

Methods: The study design was retrospective cohort study. The patients who suspected CBDS and treated with ERCP in service of Surgery Department of Thammasat University Hospital since January 2017 to January 2020 were enrolled. Clinical, laboratory, radiological and endoscopic data were retrospectively collected by chart review.

Results: Total of 565 patients were enrolled with 85.8% in high risk group by ASGE criteria. CBDS were found in 75.4% by ERCP. Overall high-risk criteria have sensitivity 90.6%, and accuracy 75.4%. CBDS on imaging was the most powerful criteria (odds ratio = 3.36, $P < 0.01$) with the highest sensitivity (68.1%), specificity (61.2%), and accuracy (66.4%). Post-cholecystectomy, age, and elevated alkaline phosphatase (ALP) level were significant factors in finding of CBDS by multivariate analysis. Newly proposed high-risk condition of "TB 1.8-4.0 and elevated ALP and CBD dilatation" had improved sensitivity (92.3%), accuracy (76.4%) and odds ratio (4.65) compared to original high-risk criteria (odds ratio = 3.90).

Conclusions: The high-risk criteria of ASGE 2019 guideline was the effective evaluation for patients with clinically suspected CBDS. Adding a new criterion of "TB 1.8-4.0 and elevated ALP and CBD dilatation" could make the high-risk criteria more sensitive to CBDS and also higher accuracy.

ACCURACY OF MIRROR IMAGE MAPPING OF LYMPHATIC TRACT FOR HIGH STAGE AND REDO LYMPHATICOVENULAR ANASTOMOSIS: INTRAOPERATIVE ANALYSIS

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Background: ICG lymphography (ICGL) generally has a non-linear pattern in advanced-stage lymphedema. Despite the lack of ICGL, intraoperative lymphatic vessels have been discovered in several studies. The purpose of this work was to establish lymphatic mapping utilizing information from the contralateral limb and to illustrate the symmetry of lymphatic systems.

Methods: The data of 55 patients who underwent lymphaticovenular anastomosis (LVA) using contralateral mapping technique during 2018-2021 were retrospectively collected. The sensitivity, specificity, accuracy, negative predictive value, and positive predictive value of this technique were calculated and analyzed.

Results: Lymphatic vessels can be identified in 80.65% and 76.92% of the upper and lower limb presumed sites, respectively, using the contralateral mapping technique. The positive predictive value for successful one LVA anastomosis was 90.90% for the upper limb and 92.30% for the lower limb cases. This mirror image technique's accuracy was 91.67% and 93.55%, for upper limb and lower limb group, respectively. Between redo and new LVA cases, there was no statistically significant difference in the number of lymphatic vessels, type, diameter, or number of anastomoses.

Conclusions: For lymphedema patients with ICGL's non-linear pattern, LVA with contralateral mapping technique was an effective method.

Keywords: Lymphedema, Lymphaticovenular anastomosis, Lymphovenous bypass, Augmented reality

CORRELATION BETWEEN IMAGE-DEFINED RISK FACTORS AND SURGICAL COMPLICATIONS IN PATIENTS WITH NEUROBLASTOMA: A RETROSPECTIVE STUDY

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Background: Prognosis and treatment options of neuroblastoma (NB), the most common extracranial malignancy in children, depend on various factors used

for risk stratification. Currently, the International Neuroblastoma Risk Group classification system is used, which include tumor biology, pathology, and radiology called image-defined risk factors (IDRF). We speculated that anatomical evaluation by IDRF might be correlated with outcomes of surgery which meant surgical complications and the oncologic outcome.

Objectives: To investigate correlation between IDRF with surgical complications and oncologic outcomes in neuroblastoma patients.

Methods: The study retrospectively reviewed medical records and CT scans of neuroblastoma patients who underwent a surgery at Songklanagarind Hospital between 2002 and 2019. IDRF were analyzed for correlation with surgical complications, overall survival, progression free survival and local recurrence within 2 years. The study also analyzed for significance of IDRF change after neoadjuvant chemotherapy.

Results: There were 45 patients operated on in our institute during the study period, whose IDRF score at diagnosis ranged from 1-16 (median 8). For analysis, patients were divided into 2 groups according to the IDRF score: 16 (35%) in low IDRF (score 1-5) group and 29 (64%) in high IDRF (score 6-13) group. High IDRF group significantly had higher incidence of organ injury and more intraoperative blood loss. Upfront chemotherapy significantly reduced median IDRF score from 8 to 4 ($p < 0.01$). At post-chemotherapy, high IDRF was not only associated with higher operative complications, but also associated with 2-year overall survival and progress-free survival.

Conclusions: Neuroblastoma patients whose IDRF score, either at diagnosis or after neoadjuvant therapy, was 6 or higher had increased risk of surgical complication. In addition, IDRF score after neoadjuvant chemotherapy predicted oncologic outcomes. This evidence prompts pediatric surgeons to prepare more for safe surgery in this group of patient.

Keywords: Image-defined risk factors, Neuroblastoma, Surgical complications, Survival outcomes

DE NOVO HEPATITIS B VIRUS INFECTION AFTER LIVER TRANSPLANTATION FROM ANTI-HEPATITIS B CORE ANTIBODY POSITIVE DONOR: A 19-YEAR EXPERIENCE AT A SINGLE CENTER

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Background: Thailand is an endemic area of hepatitis B virus (HBV) infection, and there is a significant proportion of liver donors who were previously infected with HBV. These valuable organs are acceptable for liver transplantation to hepatitis B recipients. However, liver transplantation from anti-Hepatitis B core antibody (anti-HBc) positive donor to hepatitis B surface antigen (HBsAg) negative recipient is still controversial because there is currently no standard protocol in prophylaxis and long-term follow-up. The aim of this study is to evaluate the incidence of *de novo* HBV infection after liver transplantation from anti-HBc positive donor in non-hepatitis B recipient. Secondary outcome is to evaluate factors associated with *de novo* HBV infection in these recipients.

Methods: We retrospectively reviewed 388 patients who underwent liver transplantation between 2002 to 2020 at Siriraj Hospital. Among these, there were 67 HBsAg negative recipients receiving anti-HBc positive liver grafts. *De novo* HBV infection was defined as HBsAg positive detected after liver transplantation. Incidence of *de novo* HBV infection was calculated and associated factors, such as pre- and post-transplant hepatitis B immunoglobulin (HBIG) and antiviral, were evaluated.

Results: *De novo* HBV infection occurred in 11 recipients (16.4%). Median time to *de novo* HBV infection was 1,090 days. Post-transplant antiviral drug (lamivudine) was the only significant protective factor against *de novo* HBV infection ($p = 0.003$). There was no *de novo* HBV infection occurred in recipients who continuously received post-transplant lamivudine. While, 33.3% of recipients who did not receive and 27.8% of recipients who discontinued lamivudine during post-transplant period had *de novo* HBV infection. Recipients who received pre-transplant and post-transplant HBIG had a trend to have lower rate of *de novo* HBV infection (10.9% vs. 28.6%, $p = 0.070$ and 9.8% vs. 26.9%, $p = 0.065$, respectively). Pre-transplant anti-HBs and anti-HBc antibody status and pre-transplant antiviral were not significant factors related to *de novo* HBV infection.

Conclusions: Anti-HBc positive liver grafts are safe to be transplanted to HBsAg negative recipients

if they receive a suitable pre- and post-transplant prophylaxis especially post-transplant antiviral medication continuously.

Keywords: *De novo* hepatitis B infection, Anti-HBc positive donor, Liver transplantation

DEVELOPMENT AND VALIDATION OF AUTOMATED SUTURE QUALITY EVALUATION AND FEEDBACK GENERATION FOR END-PRODUCT IMAGES OF SUTURING PRACTICES

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Background: Onsite suturing skill teaching for medical student is fundamental and intelligible. During Covid pandemic, online teaching is adopted and applied to improve surgical skill.

Objectives: Self-training simple bench suturing model is an affordable method to improve suturing skill. An effectively progressive self-training requires objective feedbacks during the practice. Thus, this project aimed to develop an automated assessment tool of open wound sutures using a computer vision approach. This tool analyzed an image of the suture practice end-product and computed metrics relevant to suture quality.

Methods: Two datasets consisting of 240 images of suturing practice end-products were collected and annotated from both medical student and expert staff. A suture instance segmentation model, trained in this project, identified suture components (a wound, stitches, knots, and leftovers). Then a novel algorithm grouped components of a stitch together and computed the quality metrics. Both steps were evaluated for their precision at identifying suture components, and R^2 between the manually measured and predicted metrics, respectively.

Results: For the suture instance segmentation, 5-fold cross validation was conducted to obtain mean average precision. For both datasets, the best performing suture instance segmentation was the Mask R-CNN with the ResNet50-FPN backbone, pre-trained using the COCO instance segmentation dataset. The medians of mean average precisions were 43:45 and 52:76 respectively.

Conclusions: Automated quality assessment of the suture practice is achievable by analyzing an image of the sutured model. The suture segmentation models can learn to segment on silk and surgical nylon thread. This automated assessment tool may support self-training suturing skill improvement of medical students and enable further large-scale analysis.

Keywords: Suturing skill, Online teaching, Self-training, Automated assessment

EFFECTIVENESS OF PROKINETIC AGENTS IN IMPROVING ABDOMINAL DISCOMFORT AT PRE- AND POST- COLONOSCOPY

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Background: Taking large volume of Polyethylene glycol-electrolyte lavage (PEG-EL) solution for bowel preparation possibly leads to unpleasant GI symptoms. Prokinetic agents are used to promote GI motility in order to decrease undesirable abdominal symptoms. The aim of this study was to examine the effectiveness of different type of prokinetic in alleviating abdominal discomfort in patients who undergo colonoscopy and evaluate the incidence of abdominal discomfort between 3 groups; only colonoscopy, with intervention and with esophagogastroduodenoscopy (EGD).

Methods: This was a prospective randomized, double blind study conducted in Ramathibodi Hospital, Bangkok, Thailand between 1st March 2020 - 30th November 2021. All included patients were randomized into one of three trial arms (Placebo, Itopride or Domperidone). The patients were interviewed regarding the severity of abdominal discomfort during the preparation and post-colonoscopy period (at 1, 24, 48 and 72 hour) using a numeric pain rating scale (0-10 score).

Results: A total of 200 patients were included in the analysis (68 in Placebo, 77 in Itopride and 55 in Domperidone). The mean colonoscopy time was 18.46 minutes and most of the patients reported 0 pain score. The reported pain scores were comparable in all study

arms and different follow-up periods; preparation (p = 0.206), post-colonoscopy 1 hour (p = 0.206), post-colonoscopy 24 hour (p = 0.837), post-colonoscopy 48 hour (p = 0.129), post-colonoscopy 72 hour (p = 0.324). The incidence of abdominal discomfort at post-colonoscopy with intervention or EGD was higher but not statistically different from the other groups ($p > 0.05$).

Conclusions: Low incidence of abdominal discomfort during colonoscopy. Co-administration of prokinetic agents (Itropride or Domperidone) together with PEG-EL solution was not superior to the placebo in decreasing abdominal symptoms. The group of patients who underwent colonoscopy with intervention or EGD had higher incidence of abdominal discomfort but not statistically different. However, more sample size is needed in a further study.

EFFICACY OF USING MOSAPRIDE CITRATE WITH ORAL MECHANICAL BOWEL PREPARATION FOR COLONOSCOPY CLEANSING QUALITY IMPROVEMENT

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Background: Bowel preparation is an important factor for an optimal outcome of colonoscopy. Recently, polyethylene glycol (PEG) solution and sodium phosphate solution (SWIFF) has been in common use for bowel cleansing for colonoscopy, but some patients are intolerant of PEG or SWIFF because of taste or volume.

Objective: This study aimed to evaluate the efficacy and safety of adjunctive Mosapride citrate with oral mechanical bowel preparation for colonoscopy cleansing quality improvement.

Methods: We conducted a randomized, double-blind, Mosapride in addition to mechanical bowel preparation. Of 330 patients undergoing colonoscopy, 172 were randomized to an additional 10 mg of Mosapride citrate (Intervention group) to oral mechanical bowel preparation, and 158 received only oral mechanical bowel preparation (Control group). Patients completed questionnaires reporting the acceptability and tolerability of the bowel preparation process. The efficacy of bowel preparation was assessed by colonoscopists using a Boston Bowel Preparation Scale (BBPS).

Results: A total of 330 patients were included in the analysis. In the intervention group, optimal excellent bowel preparation rates were significantly higher compared with the control group (81.6% vs. 64.5%, $P < 0.05$). The incidence of adverse events was similar in both groups. Moreover, patients significantly favored Intervention group over control, reflected by less clinical symptoms of nausea, abdominal pain, abdominal distension and willingness to repeat the same regimen.

Conclusions: Mosapride citrate may be an effective and safe adjunct to oral mechanical bowel preparation for colonoscopy that leads to improve quality of bowel preparation and patient compliance.

Keywords: Mosapride citrate, Colonoscopy, Boston bowel preparation scale, Polyethylene glycol, Sodium phosphate solution

FACTORS AFFECTING AN ANASTOMOTIC LEAKAGE IN CURATIVE COLORECTAL CANCER SURGERY

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Background: Colorectal cancer is leading cause of cancer incidence and mortality in Thailand and worldwide. Surgery remains the mainstay treatment to achieved curative aim. Anastomotic leakage is the most dreadful complication following colorectal surgery because of increased risk of morbidity, mortality and overall impact in functional and oncologic outcomes. The etiology of anastomotic leakage is not clearly known; several factors were found associated with anastomotic leakage.

Objectives: This study aimed to find the incidence and factors affecting anastomotic leakage after curative colorectal surgery in Songklanagarind Hospital.

Methods: The retrospective cohort study was conducted, reviewed data from Hospital Information System (HIS). All patients who underwent curative colorectal surgery by a single colorectal surgeon between July 2003 and June 2021 were included. Patients who underwent emergency surgery and without a primary anastomosis, i.e. abdominoperineal resection, low anterior resection with end colostomy, total proctocolectomy with end ileostomy, transanal excision, were excluded. Clinical details in preoperative, intraoperative and postoperative period were recorded as risk factors. Primary outcome was an anastomotic leakage rate.

Results: In total, 968 patients were included in the study. The incidence of anastomotic leakage was 5.1%. To categorize by onset of leakage, there were 1.3% immediate leakage (positive air leak test), 2.6% early leakage (≤ 30 postoperative days) and 1.1% late leakage. By diagnosis, clinical leakage accounted for 3.2% and radiologic leakage for 0.5%. Among anastomotic leakage patients, there was 2.6% re-operation rate and 10% 30-day readmission rate. The factors significantly affecting anastomotic leakage were active smoking OR 2.77 (95% CI 1.34, 5.7), tumor location at rectum odd ratio (OR) 3.16 (95% CI 1.67, 5.98), distant metastasis OR 0.28 (95% CI 0.08, 0.91) and preoperative serum albumin < 3 g/dl OR 4.75 (95% CI 1.51, 14.97). Overall cancer-related survival (OS) with 5-year OS at 75.0% (95% CI 71.5%-78.2%) which is not different between those with and without leak (*p*-value by log-rank test 0.07).

Conclusions: This study, the incidence of anastomotic leakage was 5.1%. The factors affecting anastomotic leakage were active smoking, tumor location at rectum, distant metastasis and preoperative serum albumin < 3 g/dl. The adjustable factor was preoperative serum albumin which should be as assessed and improved to reduce risk of leakage.

Keywords: Anastomotic leakage, Factors, Colorectal surgery

PREDICTION SCORE FOR IN-HOSPITAL MORTALITY IN NECROTIZING FASCIITIS IN NAKORNPING HOSPITAL: DERIVATION AND INTERNAL VALIDATION

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Background: Necrotizing fasciitis (NF) is a rapidly progressive life-threatening skin and soft tissue infection. Currently, a risk score tool to predict in-hospital mortality in NF patients is not warranted.

Objectives: This study aimed to develop and internal validate a tool to predict in-hospital mortality in NF patients.

Methods: From January 2019 to December 2020, records of 293 NF patients were reviewed. Data including age, sex, location of lesion, laboratory results, comorbidity, pathogen organism, and in-hospital mortality were collected. Multivariable logistic regression was used to identify a set of prognostic factors. The results were weighed, assigned, and summed to a total risk score. Finally, three risk groups; low, moderate, and high for in-hospital mortality in NF patients were classified.

Results: A total of 293 patients with a diagnosis of NF, 8.4% (n = 25) died in hospital. From multivariable analysis, four factors were found significantly predicted in-hospital mortality including diabetic mellitus, cirrhosis, white blood cell count (WBC) > 20,000/uL, and blood lactate > 2 mmol/L. A total of risk score (possible range 1-12.5) explained 91.3% possibility of in-hospital mortality based on area under the receiver operating characteristic curve (AuROC) analysis. Likelihood ratio of positive among low risk (< 5), moderate risk (5-7), and high risk (> 7) were 0, 0.82 (95% CI 0.33-0.27, p = 0.672), 4.94 (95% CI 2.81-8.69, $p < 0.001$), respectively.

Conclusion: The proposed risk score groups contain simple-to-assess four prognostic factors with excellent performance to distinguish and can be applied to predict in-hospital mortality in NF patients in secondary to tertiary hospitals.

Keywords: Necrotizing fasciitis, Risk score of in-hospital mortality

PREVALENCE OF NONALCOHOLIC STEATOHEPATITIS AMONG PATIENTS UNDERGOING BARIATRIC SURGERY, A PROSPECTIVE DESCRIPTIVE STUDY

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Background: Obesity is one of the major health issues worldwide which has many consequences, including fatty liver. Diagnosis of nonalcoholic steatohepatitis (NASH) is crucial, since it harbors the risk of cirrhosis and ultimately, hepatocellular carcinoma. Non-invasive methods have proven to be useful despite depending on the liver biopsy to confirm the diagnosis. Little is known about the number of obese patients with NASH.

Objectives: This study primary aim is to find the prevalence of NASH in patients undergoing bariatric surgery. Secondary objective is to evaluate the utility of transient elastography (Fibroscan) as a screening test.

Methods: Data were prospectively gathered from 64 morbidly obese patients aged 18 to 60 years who undergoing bariatric surgery during 2019 and 2022 at Srinagarind Hospital. Patients with history of hepatitis from other causes were excluded. Transient elastography was performed and its values, Controlled attenuation parameter (CAP) and liver stiffness measure (LSM), were used to measure the hepatic steatosis and fibrosis respectively. If elastography is successful, intraoperative liver biopsy will be made. NASH is diagnosed based on the presence of hepatic steatosis (S) with lobular inflammation (L) or ballooning hepatocyte (B) on histology. Correlations between variables were calculated and displayed as Spearman's correlation coefficient (p). The accuracy of elastrography was evaluated by using time-dependent receiver operating characteristic (ROC) curve.

Results: 64 patients were included in the study. Elastrography was successfully performed in 48 patients and liver biopsy yielded in 46 patients. Lobular inflammation or ballooning hepatocyte were presented in 32 specimens, thus the prevalence of NASH in patients undergoing bariatric surgery was 50%. There was significantly moderate correlation between CAP and grading of steatosis ($p = 0.59$, $p < 0.001$). CAP cutoff points for S0 and S1-3 is 265.5 db/m (sensitivity 88.1%, specificity 50%, positive predictive value (PPV) 63.79%, and area under the receiver operating characteristic curve (AUROC) 0.87).

Conclusions: Patients with morbid obesity were presumed to have NASH. Transient elastrography showed a promising result in screening for NASH. However, this study included only obese patients who were candidates for bariatric surgery.

Keywords: Obesity, Bariatric surgery, Liver biopsy, NASH, Elastography

RAMA. FACIAL LACERATION TOOLBOX

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Background: Facial laceration is one of the most common problems that brought patients to the emergency room (ER) and many of them are simple lacerations. According to the literature review, there is no practical guideline for treatment of the facial laceration at the moment. And by our observations, sutures that are done by the non-facial trauma specialists (NFTS) are usually followed by unsatisfied results. In consequence, re-suturing by the facial trauma specialist (FTS) is likely required with the trade-off of the additional operations that may unnecessarily harm the patient once more. This study aims to create an application that contains guidelines for treatment of the facial laceration and analyze its efficacy whether it plays a role in improving the long term results of the wounds that are repaired by the NFTS.

Methods: The study consisted of two main phases, the application development (phase 1) and the research (phase 2). The application development was carried out from February of 2020 to May of 2021 in cooperation with MedEnsy Co., Ltd. After the application was firstly launched, it was applied into our institution's consultation protocol of facial laceration cases. The research started with the enrollment period which took place from May 21, 2021 to September 1, 2021. Patients with simple facial lacerations that were consulted by the emergency physicians (EP), using the application, were enrolled and randomized into 'ER' group (receive treatment from EP under the guidance of the application) and 'Plastic' group (receive treatment from plastic surgeons; PS). After treatment, the patients in both group were followed for 6 months. The patients who completed the 6-month follow-up in both group were compared. The primary outcome was the overall quality of the scar at 6 months after the suture. Secondary outcomes were early complication rate, patient satisfaction score, consult-to-approval time (CtA), consult-to-complete-treatment time (CtCT), and the user's review.

Results: A total of 27 patients with simple lacerations were enrolled and randomized. Eighteen patients gave their consent to join the research and had the application completed. A total of 9 cases in each group were followed and the same remaining 7 cases in each group completed the 6-month follow-up. Consult-to-approval time (CtA) and consult-to-complete-treatment time (CtCT) were lower in ER group (plastic, 24.4 min and 109.9 min, respectively; ER, 18.3 min and 86.9 min, respectively). Early complication rate on the 7-day follow- up was higher in ER group than in plastic group (plastic, 14.3%; ER, 42.9%). The final analysis at 6-month follow-up showed that the mean VSS score was slightly

lower in plastic group (plastic, 0.9; ER, 1.4) and the mean expert's rating score was slightly higher in plastic group (plastic, 4.5; ER, 4.2). However, the mean patient satisfaction score between 2 groups were the same (plastic, 9.6; ER, 9.6).

Conclusions: As far as our knowledge, "RAMA. Facial Laceration Toolbox" is the first application that provides practical guidelines of facial laceration management and may help equalizing the long term quality outcomes of the facial wounds between those that are repaired by the non-facial trauma specialists (NFTS) under the use of it and those that are repaired by the facial trauma specialists (FTS).

RESULTS OF TREATMENTS OF PELVIC RING FRACTURES WITH UNSTABLE HEMODYNAMICS IN THAMMASAT UNIVERSITY HOSPITAL, A RETROSPECTIVE COMPARISON STUDY

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Background: Patients with hemodynamic instability associated with pelvic ring fractures may have a severe hemorrhage. Emergent treatment included; pelvic external fixation (EF), angioembolization (AE), and preperitoneal pelvic packing (PPP). The mortality rate remained high at 30-40%. We aim to identify treatment results in pelvic ring fractures with hemodynamic instability in our institute. The result may reflect the quality of our treatment planning and guide us to create the best clinical practice guidelines in this condition.

Objectives: Evaluate the outcomes of treatments (mortality, length of hospital stays, length of ICU stays, ventilator days, disability after discharge), incidence of traumatic pelvic fracture with instability hemodynamics.

Methods: This study is a retrospective review of pelvic ring fractures with hemodynamic instability in patients admitted at our institute between 1st January 2014 to 31st December 2018. Age, sex, initial vital signs, laboratory data and imaging, mechanism of injury, organ-specific injury, abbreviated injury scales (AIS) and injury severity scores (ISS), operations, interventions, and results of treatment were collected and analyzed. Comparison data of treatment modalities were conducted to identify which treatment gave a better result.

Results: There were 321 patients diagnosed with pelvic ring fractures in this period, and 294 cases were excluded by age < 18 years (42 cases), hemodynamic stability in the ED (163 cases), diagnosed outside of the ED (39 cases), and associated torso injuries (50 cases). Most patients were male (74.1%) with a mean age of 38.7 ± 14.7 years. The most common mechanism was motorcycle crashes (51.9%). The mean initial systolic blood pressure was 83.6 ± 3.6 mmHg with a mean pulse rate of 116 ± 8 bpm. There was no mortality rate, with the mean hospital LOS of 14.3 ± 8.9 days. Twelve cases were treated with emergency procedures; EF, EF with PPP, and AE. Most of the emergency procedures were EF alone (6 patients). Three cases were treated with EF with PPP. Comparison data revealed significantly shorter transferred time, lower initial SBP, higher ISS, less required PRCs, shorter ICU LOS, and more extended hospital LOS in the EF with PPP group. There were zero mechanical ventilator days in the AE group. However, there was no significant difference in disability after treatment among treatment modalities.

Conclusions: There were good outcomes in treating the pelvic ring fractures with hemodynamic instability in TUH (0% mortality). There were significantly better outcomes (less PRCs requirement and shorter ICU LOS) in the EF with PPP group compared to others. However, we cannot state that EF with PPP is preferred over others because of the multifactorial effect.

Keywords: Pelvic fracture, Hemodynamic instability, Pelvic external fixation, Angioembolization, Preperitoneal pelvic packing, Pelvic trauma

ROLE OF PHASE ANGLE AS A PREDICTOR FOR SURGICAL COMPLICATIONS IN CRITICALLY ILL PATIENT

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Background: Bioelectrical impedance (BIA) is one of the modern ways to analyzing body composition which reflects nutritional status, cell death and inflammation

process. These conditions are well known to have affect the surgical outcome. But the use of BIA in predicting surgical complication is not widespread. This study was conducted to study the relationship between BIA and surgical complication so that it might lead to a new way for predicting surgical outcome and eventually find a way to improve it.

Objectives: To study the relationship between of postoperative phase angle and 30 days postoperative complications. And studying the relationship between phase angle changes in post operative day 1 and severity of complication in patient underwent surgery, in Intensive Care Unit of Surgery Department, Maharaj Nakorn Chiang Mai Hospital.

Methods: This research was conducted in prospective observational Study. Conducted between 2019-2021. Using InBodyS10 to measure post operative BIA. The duration of follow up for surgical complications was 30 days or at discharge date. The study group was Patient underwent surgery, in intensive care unit of surgery department.

Results: From the study and follow up of 103 patients underwent surgery and admitted to intensive care unit. There were 47 patients (45.6%) with no complication, and 56 patients (54.4%) with complication. The most occurred complication was in Clavien-Dindo Class 3 and Class 2 (34.04% and 31.91%) respectively. Phase angle was significantly lower in group of patient with complication (4.6 (4.08-5.3) vs 3.75 (3.1-4.6) $p = 0.001$). But in complication group the decrease or increase in phase angle in post-operative day 1 was not shown to be significant factor in prediction of severity of complication. ($p = 0.028$). Other factors that shown to be statistically significant between groups are preoperative albumin (3.6 (2.9-4) vs 3.75 (3.3-4.2) $p < 0.001$) and APACHE II score (9.39 ± 4.61 vs 11.66 ± 4.45 $p = 0.016$). The optimal cutoff value for phase angle is 6.22.

Conclusions: Post operative Phase angle was a safe and useful parameter in predicting postoperative complications. Patients whose phase angle are likely to have post operative complication. 1 point decrease in phase angle will raise the CCI by 6.67. Low phase angle low should prompt evaluation and re-assessment for postoperative complications especially patient whose phase angle is below 6.22.

Keywords: Bioelectrical impedance, Phase angle, Post-operative complication, Critical care patient

SEXUAL DYSFUNCTION BETWEEN LAPAROSCOPIC AND OPEN INGUINAL HERNIA REPAIR: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Sexual dysfunction after inguinal hernia complication is considered rare, however, its consequences impact one quality of life inevitably. Laparoscopic and open inguinal hernia repair may comparable in terms of recurrent rate, overall complication and chronic pain. The sexual dysfunction complication is still questionable between these approaches. We to compare sexual dysfunction and related complication between laparoscopic and open inguinal hernia repair.

Methods: Systematic review and meta-analysis of randomized controlled trials (RCTs) compared laparoscopic and open inguinal hernia repair. Risk ratio (RR) and 95% confidence intervals (CI) were used as pooled effect size measures.

Results: Thirty RCTs (12,022 patients) were included. Overall, 6,014 (50.02%) underwent laparoscopic hernia repair and 6,008 (49.98%) underwent open hernia repair. Laparoscopic approach provided non-significance benefit on pain during sexual activity (RR 0.57; CI 0.18-1.76), vas deferens injury (RR 0.46; CI 0.13-1.63), testicular pain (RR 1.37; CI 0.81-2.31), orchitis (RR 0.84; CI 0.61-1.17), scrotal hematoma (RR 0.99; CI 0.62-1.60) and testicular atrophy (RR 0.46; CI 0.17-1.20). Meanwhile, open inguinal hernia approach reduced cord seroma complication (RR 1.79; CI 1.13-2.86)

Conclusions: There is no advantage of laparoscopic inguinal hernia repair over open approach in term of sexual dysfunction. On the contrary, there is increasing risk of cord seroma after laparoscopic inguinal hernia repair with statistical significance.

THE EFFICACY OF TRANEXAMIC ACID IN SUBCUTANEOUS ADMINISTERED FOR DECREASING BLEEDING AND INFLAMMATION IN UPPER BLEPHAROPLASTY: A DOUBLE BLINDED RANDOMIZED CONTROL TRIAL

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Background: Eyelid surgery is one of the top five aesthetic procedures that preformed to improve both appearance and function. Intraoperative bleeding is important factor that leading to adverse event which concerned the patients. This study purposes to demonstrate the efficacy of TXA when combined with epinephrine in decreasing intraoperative blood loss and post-operative inflammation.

Methods: This study is prospective randomized control trial performed in 15 patients with 30 side of eyelids who undergo upper blepharoplasty. In each patient, his/her eyes were randomly divided into two groups. The first group (TXA group) were given 2% lidocaine with epinephrine (1:100000) mixed with TXA (50 mg/ml) in 1:1 mixture subcutaneously as local anesthetic drug and the second group (control group) received 2% lidocaine with epinephrine (1:100000) diluted with normal saline in 1:1 mixture. Intraoperative blood loss and post-operative swelling was evaluated and compared between two groups.

Results: Intraoperative blood loss was significantly higher in TXA group [4.86 (1.83) ml] compared with control group [2.53 (1.49) ml] ($p < 0.001$). There is no statistically significant difference in operative time ($p = 0.645$), pain score ($p = 0.498$), Lid crease ($p = 0.548$) and MRD1 ($p = 0.626$) between two groups. There is no difference in 7-day post-operative lid crease ($p = 0.879$), MRD1 ($p = 0.463$), pain score ($p = 0.934$) and ecchymosis ($p = 0.976$) between two groups.

Conclusions: TXA in lidocaine with epinephrine was found to increase intra-operative bleeding compared to lidocaine with epinephrine alone but no difference in postoperative swelling and ecchymosis. TXA combined with lidocaine and epinephrine injected subcutaneously should be avoided until additional relevant data are obtained. Further drug interaction study is needed.

THE PROPERTIES OF BIOCELLULOSE DRESSING IN VITRO STUDY AND CLINICAL SAFETY TEST IN HEALTHY VOLUNTEER: CLINICAL TRIAL PHASE I

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Background: Biocellulose wound dressing, wound dressing that had the flexibility and water-retained properties that lead to coolness and painless dressing but is limited due to high cost. In 2020, PTT Research and Development Department developed "Innaqua®", a Thai national biocellulose wound dressing with low cost for the Thai population that could assess.

Objectives: "Innaqua®" passed 2 preclinical studies in an animal model. But never studied in humans and never report In vitro studies compare with the original biocellulose product. This study aims to compare the property of Innaqua® with other wound dressings and to reassure that Innaqua® was safe for humans.

Methods: This study had 2 parts, In vitro studies which compare the capacity of the fluid absorption, desorption, wound dressing surface, and moisture analysis of Innaqua® with other dressings; Bactigras® and Bluribbon®. The clinical study was carried out on 63 healthy volunteers and applied both Innaqua® and Bactigars® on each side of the upper arm after randomization. Skin irritation and an allergic reaction were observed and evaluated using Acute Dermal Irritation/Corrosion GRADING OF SKIN REACTIONS from Organization for Economic Co-operation and Development 2015 and Modified scale for reading repeated open application test results from European Society of Contact Dermatitis PATCH TEST GUIDELINE 2015.

Results: Innaqua® and Bluribbon® had statistical significant higher fluid absorption ($p = 0.003$, $p = 0.001$) and desorption ($p = 0.039$, $p = 0.003$) than Bactigras®. From the scanning electron microscope, smaller non-homogenous pore sizes and morphologies of innaqua® and Bluribbon® were seen. Innaqua® had the most significant moisturization. In clinical safety studies showed non-inferior of erythema (4.8% vs 4.8%; $p = 0.012$) and allergic reaction (3.2% vs 4.8%; $p = 0.004$) in Innaqua® compared with Bactigras®. No oedema occurs in both wound dressings.

Conclusions: Innaqua® is biocellulose wound dressing which produce in Thailand, created an appropriate environment for wounds because of the small pore at the contact surface of wound dressing, high absorptive quality, and desorption which encourage moisturization for the wound as shown in moisture analysis. From in vivo study, it showed the safety of this wound dressing in human skin. Innaqua® was the new choice of biocellulose wound dressing, and come at a low price for population.

Keywords: Biocellulose, Innaqua, Allergy, Irritation, Safety

THE VERSATILITY OF ATHEROSCLEROTIC CARDIOVASCULAR DISEASE (ASCVD) RISK SCORE IN DETERMINATION OF POPLITEAL ARTERY BRANCHES PATENCY IN COMPUTED TOMOGRAPHY ANGIOGRAPHY

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Background: The atherosclerotic cardiovascular disease (ASCVD) risk score is commonly used for risk estimation of developing coronary artery disease and stroke. However, the atherosclerosis changes involve arteries throughout the body including the blood supply of legs, which are seen as peripheral arterial disease. The popliteal artery branches are affected by atherosclerosis and leads to luminal stenosis, which are crucial for operative decision among clinical practices such as vascular bypass procedure, intravascular surgery, and reconstruction of lower limb.

Objectives: To investigate the relationship between the ASCVD risk score and degree of stenosis among popliteal artery and its branches.

Methods: The data regarding all patients, who underwent computed tomography angiography (CTA) of the legs during 2016-2021 with complete data for ASCVD risk score assessment, was recruited. The 10-year and lifetime ASCVD risks were calculated, and association between ASCVD risk score and luminal stenosis from CTA was analyzed.

Results: There were 117 males and 81 females, and the average age was 66.5 years. The common comorbidities including hypertension (84.3%), diabetes mellitus (61.1%), and chronic kidney disease (34.3%). The average 10-Year ASCVD risks in ≥ 50% stenosis group of popliteal artery, anterior tibial artery, and posterior tibial artery were significantly higher than those < % stenosis ($p < 0.01$). The peroneal artery had no significant difference in 10-Year ASCVD risks between stenosis groups. For the Lifetime ASCVD risks, the popliteal artery had significantly higher ASCVD risks in in ≥ 50% stenosis group ($p < 0.01$) but the anterior tibial artery, posterior tibial artery, and peroneal artery showed no statistically significant difference between stenosis groups.

Conclusions: The 10-year ASCVD risks showed significant higher values in ≥ 50% stenosis group of popliteal artery, anterior tibial artery, and posterior tibial artery. These findings can establish the further study on how ASCVD risks can be applied to predict the stenosis of popliteal artery and its branches, and guide the rationale of preoperative leg CTA for FFF harvest.

Keywords: Atherosclerotic cardiovascular disease (ASCVD) risk score, Luminal stenosis, Popliteal artery

VDO Award

CONVERSION TO ROUX-EN-Y GASTRIC BYPASS WITH HIATAL HERNIA REPAIR AS THE TREATMENT OF INTRATHORACIC GASTRIC SLEEVE MIGRATION

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Background: Laparoscopic sleeve gastrectomy (LSG) is standard bariatric surgery. There is ongoing controversy regarding the potential of worsening and de novo gastrointestinal reflux disease (GERD) postoperatively. The altered anatomy of the esophagogastric junction and conversion to a high-pressure system makes LSG patients more likely to develop GERD symptom. The reported incidence of de novo GERD after LSG is up to 35%. There is little published data on diagnosis of hiatal hernia (HH) after LSG and its potential as the cause for the worsening or new-onset GERD symptoms. Current standard of care for intractable GERD status-post LSG indicates conversion to laparoscopic Roux-en-Y gastric bypass (RYGB).

Methods: This video presented the morbid obesity patient who underwent LSG and subsequently developed severe reflux symptom which not response to medication treatment. And concurrent hiatal hernia with intrathoracic gastric tube migration. Laparoscopic hiatal hernia repair with conversion sleeve to Roux-en-Y gastric bypass was performed.

Results: Laparoscopic hiatal hernia repair with conversion sleeve to Roux-en-Y gastric bypass can be done safely and was the treatment of choice.

Conclusions: The development of intractable GERD after laparoscopic sleeve gastrectomy (LSG) is a major concern as it affects the quality of life of the patients and potentially exposes them to the complications of GERD. Laparoscopic hiatal hernia repair with conversion sleeve to Roux-en-Y gastric bypass was the treatment of choice.

Keywords: Hiatal hernia, Intrathoracic gastric migration, De novo GERD, Sleeve gastrectomy, Conversion Roux-en-Y gastric bypass

HOW TO DEAL WITH SMALL BOWEL OBSTRUCTION CAUSED BY A PLUM SEED

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Background: Adhesive band is the most common cause of small bowel obstruction. However, an unusual cause as a foreign body has been rarely reported. Normally, this obstructed foreign body could pass through the gastrointestinal tract without further management. Nevertheless, some patients who have this issue need to be operated either open or minimally invasive approach. Although the latter approach carries more benefits to the patients, its technique is quite challenging. We demonstrated a small bowel obstruction caused by a plum seed which was treated successfully by minimally invasive approach.

Objectives: To demonstrate the technique of laparoscopic enterotomy and foreign body removal. Also, how to prevent the contamination during the surgery.

Methods: A 71-year-old Thai male who unintentionally swallowed a plum seed for 2 days. After that, he developed abdominal distension and obstipation. Abdominal CT scan showed diffuse small bowel dilatation and a 2.8-cm. impacted foreign body at distal ileum causing proximal small bowel dilatation. Surgical intervention as laparoscopic foreign body removal was planned. The video contained the operative room setup, port sites, and the step-by-step procedures, including how to prevent contamination and suture small bowel.

Results: The operative time was 1.30 hours with minimal blood loss. Postoperatively, the patient tolerated oral diet well and had regular bowel movement. He could be discharged home uneventfully on postoperative day 4. No early complication could be detected upon the postoperative follow-up.

Conclusions: A plum seed causing small bowel obstruction is a rare condition which probably requires surgery. Minimally invasive approach to fix this issue is safe and feasible in selected case. Standardization of surgical steps is crucial in order to prevent complications.

LAPAROSCOPIC TRANSABDOMINAL PREPERITONEAL REPAIR FOR LEFT FEMORAL HERNIA CONTAINING BLADDER DIVERTICULUM

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Femoral hernia is a protrusion of peritoneum into femoral canal which incidence is only 2-8% and more common in female. According to its rigid space, patient often presents with strangulation and requires emergency repair. Elective surgery remains only 14% in female. Operative approach could be performed by laparoscopic technique. Nowadays, we have the novel concept of critical view of myopectineal orifice. Following this concept would provide proper exposure of anatomy that must be achieved before mesh placement to reduce complication and recurrence. Our video demonstrated surgical procedure of laparoscopic transabdominal preperitoneal repair (TAPP) in a 93-year-old female who had chronic incarceration of left femoral hernia for 20 years. Abdominal computed tomography was requested to confirm diagnosis which revealed an outpouching lesion from bladder herniated into left femoral canal. The patient never complained any lower urinary tract symptom over the past 20 years. Operation was scheduled as elective setting. Under general anesthesia with indwelled urinary catheter, laparoscopic ports were placed as usual TAPP operation. We also used intravenous indocyanine green to enhance visualizing the nearby vascular structures to prevent injury during dissection.

After peritoneal flap creation, hernial sac and its content were reduced back to abdominal cavity. We followed all technical steps to accomplish the critical view of myopectineal orifice before mesh placement. Polypropylene mesh was placed to cover the myopectineal orifice including femoral defect properly and fixed by tacker. Peritoneal flap was closed by intracorporeal sutures. No postoperative complication happened. The patient was discharged uneventfully on postoperative day 2. No recurrence was observed at 6 months after surgery.

LAPAROSCOPIC VENTRAL RECTOPEXY WITH PELVIC FLOOR SUSPENSION: LEFT-SIDED APPROACH

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Pelvic floor descended disease has multifactorial etiology including aging, pelvic floor relaxation, sigmoid redundancy, rectal mobility, and deep cul-de-sac, which eventually cause obstructive defecation. Laparoscopic ventral rectopexy (LVR) has been reported for treatment of pelvic floor descended. The right-sided peritoneal dissection approach for rectal mobilization has been standardized, however there are some technical challenges in obesity, deep cul-du-sac, redundant sigmoid, and redo LVR. The aim of this study is to demonstrate the left-sided approach of rectal mobilization to overcome the redundant sigmoid and previous pelvic operation.

A case of 50-year-old woman presented with obstructive defecation symptom. She previously underwent pelvic organs suspension using a trans-sacral approach. The MRI defecography showed pelvic floor descended, anterior rectocele, and mucosal recto-rectal intussusception.

This video demonstrated a step-by-step approach of LVR and pelvic floor suspension using a novel left-sided rectal mobilization approach. The operation started at peritoneal dissection on the left side of rectosigmoid colon. The dissection continued downward to the rectovaginal space and the pelvic floor using mesorectal plane dissection. All pelvic autonomic nerve bundles was preserved. Superb visualization facilitated by gravity was the great advantage of the left-sided approach. The pelvic floor suspension was performed using prolene mesh sutured fixed to the pelvic floor muscle and tacked to S3-S4 with permanent fasteners. The ventral rectopexy was done using prolene mesh sutured to the anterior rectal wall and posterior vagina wall then the mesh was tacked to S3 with permanent fasteners. The peritoneum was closed with vicryl 3-0. This patient had an uneventful recovery and discharged on postoperative day 2.

The postoperative functional outcome was excellent. She reported dramatic improvement of obstructive defecation symptoms as well as an improvement in urinary symptom.

PERINEAL PROCTOSIGMOIDECTOMY WITH POSTERIOR LEVATORPLASTY (ALTEMEIER) PROCEDURE FOR RECTAL PROLAPSE

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Background: Altemeier's procedure is one of well-known perineal operations to treat full-thickness rectal prolapse; it removes the prolapse without a pexy and performs only a partial reconstruction of the pouch of Douglas. However, high recurrence rates relegate the procedure to a back-up role for elderly or other high-risk patients who are not candidates for an abdominal operation.

Objectives: To demonstrate perineal proctosigmoidectomy with posterior levatorplasty (Altemeier) technique for rectal prolapse.

Methods: This is a case of a 91-year-old woman with underlying of DM, HT and parkinson's disease who presented with persistent rectal prolapse about 10 cm in length. The rectum had been reducible itself for 20 years. The rectal prolapse was exteriorized and the dentate line was identified. A circumferential line, 2 cm proximal to the dentate line, was scored on the rectal mucosa with electrocautery. Full thickness rectal wall dissection was began anteriorly then laterally and finally posteriorly until peritoneum was divided. After complete disconnection, posterior levetor ani was identified and levatorplasty was performed with interrupted 2-0 prolene. the rectum and distal sigmoid were exteriorized and skeletonized the mesorectal fat and its vessel. Colostomy was started anteriorly and hanging suture of colon to anus was performed quadrant by quadrant. Coloanal anastomosis was performed with interrupted 3-0 vicryl.

Results: The patient was discharged home safely without complications. Her defecatory function improved without recurrence after 1 month follow-up.

Conclusions: Perineal proctosigmoidectomy with posterior levatorplasty (Altemeier) procedure is safe and feasible in elderly and comorbid patient.

POSTERIOR RETROPERITONEOSCOPIC ADRENALECTOMY: A NOVEL APPROACH FOR PATIENTS WITH PREVIOUS INTRA-ABDOMINAL SURGERY

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This video describes how we have performed the posterior retroperitoneoscopic right adrenalectomy in order to avoid abdominal adhesions in a 70 year old female with a history of whipple procedure for metastatic duodenal cancer. After the induction of general anesthesia the patient was placed in the prone position. The camera and working ports were created along the tip of 12th rib. The posterior retroperitoneal space was accessed through Gerota's fascia. The perinephric fat was identified and dissected until the kidney was visualized. Dissection was performed along the superior boarder of the kidney. The tumor was noted to abut the renal capsule. Subcapsular dissection of the kidney was accomplished. The right renal artery was visualized beside the kidney. A small adrenal vein close to the renal artery was identified and ligated. Further dissection was carried beyond the renal artery until the IVC was located. Dissection of all the tissue surrounding the IVC and the tumor was performed. A peritoniectomy was performed due to the adhesion of the tumor to the peritoneum. After the peritoneum was incised, the retroperitoneal and the intraperitoneal spaces became one continuous space. The tumor was then gently dissected along the IVC. From the upper lateral side, the falciform ligament was partially dissected to encircle it and achieve the resection margins. Then, the tumor was dissected medially and upwardly from the paraspinal muscle to the crus of diaphragm. A regional lymph node was incidentally encountered, and it was dissected altogether with the tumor. The superior aspect of the tumor was dissected from the diaphragm to complete the en bloc dissection. The specimen was removed via the endo bag in one piece. The camera was reinserted to check for bleeding before closing the patient. The pathology results showed metastatic adenocarcinoma into nearly entire adrenal gland with extensive extracapsular soft tissue extension. The patient received adjuvant chemotherapy. A repeat CT scan one year after surgery showed no signs of local recurrence. In conclusion, In order to avoid adhesions, the posterior retroperitoneoscopic adrenalectomy is an ideal approach for the patient with a history of previous abdominal surgery.

Keywords: Laparoscopic surgery, Adrenal gland, Metastatic cancer, Previous abdominal surgery, Retroperitoneoscopic adrenalectomy

ROBOTIC ASSISTED VATS BILATERAL ESOPHAGEAL DIVERTICULECTOMY WITH LONG MYOTOMY

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Background: Epiphrenic diverticulum is a rare type of pulsion esophageal diverticulum that occur in distal esophagus. The prevalence is varying ranging from 0.015 – 2%. Two esophageal diverticula had a little data, only in case reports. Most common etiology is an increase in intraluminal pressure, which associated with underlying esophageal motility disorder. Symptomatic patients are indication to operation. Surgical approaches can be transabdominal or transthoracic, depending on distance from diverticulum to esophagogastric junction. Minimally invasive procedure includes laparoscopic and robotic surgery had advantage in reducing postoperative pain, shorter length of hospital stay and lower rate of mortality. Robotic-assisted surgery may offer better visualization than traditional laparoscopic/thoracoscopic approaches. Due to high association of underlying motility disorders, routine myotomy should be performed to reduce postoperative leakage and recurrence.

Objectives: To demonstrate the surgical technique of transthoracic approach in case of bilateral epiphrenic diverticula.

Methods: This video demonstrate the operative steps of transthoracic bilateral epiphrenic diverticuluectomy. Starting from preoperative preparation with EGD and enteral tube placement for improve nutrition and diverticulum irrigation, especially in patients who had food retention.

How to localize and identify diverticulum safely. Combined intraoperative gastroscopy can give information to perform the procedure confidently. Finally, is the key step in long myotomy.

Results: Patient's clinical outcomes are improved, and can be discharged without any complication. Esophagogram demonstrates good passage, without leakage or stenosis.

Conclusions: Thoracoscopic approach in case of epiphrenic diverticulum can be performed safely. Knowing in operative steps and attention in surgical tricks can reduce the difficulty and avoid complications during the operation.

Keywords: Robot, VATS, Epiphrenic, Diverticulectomy

STEP-BY-STEP APPROACH WITH ANATOMICAL HIGHLIGHT IN SMV-FIRST LAPAROSCOPIC RIGHT COLECTOMY

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The concept of complete mesocolic excision (CME) and central vascular ligation (CVL) is consisted of the dissection between the mesocolic fascia and the retroperitoneal fascia, with ensuring an adequate lymph node harvesting at the vascular origins. This concept has been reported to have significant better oncological outcomes in many studies. However, laparoscopic right-side colectomy is technically challenge due to highly right-side vascular anatomy variations. Therefore, clearly understanding laparoscopic anatomy in right-side colon is essential to minimized serious complications and achieve better oncological outcomes.

The SMV-first approach aims to identify superior mesenteric vein (SMV) then dissects along the anterior surface of the SMV. This provides a clearer vascular origins identification, thus facilitates better lymphadenectomy. This video demonstrates the step-by-step approach with anatomical highlight in SMV-first approach laparoscopic right colectomy in locally advance hepatic flexure colon cancer with massive nodal metastasis. The procedure includes intra-abdominal set up for a good exposure, SMV identification, CME/CVL, lateral dissection, specimen extraction and anastomosis creation.

Keywords: Complete mesocolic excision, Central vascular ligation, Superior mesenteric vein, Right-side colon cancer, Laparoscopic

THE LAPAROSCOPIC HIATAL HERNIA REPAIR

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Background: Hiatal hernias occur when there is intrathoracic herniation of abdominal contents through the hiatal orifice of the diaphragm. Its pathophysiology remains unknown, stressors, such as obesity, chronic cough, and gastroesophageal reflux, may cause weakening of the hiatus and results in widening of the hiatal aperture, allowing for movement of the GEJ and herniation of abdominal contents into the thoracic cavity. The surgery for hiatal hernia is mandatory in the patients whose symptoms can't be controlled medically, or presented with complications. The laparoscopic approach has become preferred worldwide, since it has demonstrated to decrease postoperative pain, and enhance recovery when performed.

Objectives: To present the laparoscopic technique for hiatal hernia repair

Methods: This laparoscopic hiatal hernia repair was performed in 70-year-old female, who presented with dyspepsia which is not responded to medications. She underwent the physical examination, laboratory and imaging studies and the diagnosis was confirmed. The treatment options were discussed with the patient, and laparoscopic transabdominal hiatal hernia repair was planned. The patient was in supine position. After the generalized exploration, the liver was retracted upward. The herniated contents were reduced, and the hernial sac was carefully dissected. Right and left crura were identified, and the Penrose drain was used to hang around the esophagus, helping in sac dissection. When the sac was fully dissected and the 3-cm length of intra-abdominal esophagus was achieved, the hiatal defect was closed inferiorly and posteriorly. Then gastric fundus was mobilized to perform Nissen fundoplication, and the anterior gastropexy was done.

Results: Satisfactory repair using laparoscopic techniques was achieved. The patient experienced no postoperative complication. In the 4-week follow up appointment, she had no dysphagia, and could eat normally.

Conclusions: The laparoscopic approach is a safe and beneficial alternative for the surgeon in the treatments of hiatal hernia. The training and implementation of this technique would be useful for the patients with this condition.

Keywords: Hiatal hernia, Laparoscopic surgery, Surgical technique, Fundoplication

THE LAPAROSCOPIC STEP OF PEDICLED PERITONEAL FLAP VAGINOPLASTY IN MALE TO FEMALE GENDER AFFIRMATION SURGERY

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Background: In today's society, gender diversity is becoming more accepted globally, including in Thailand. Gender-affirmating surgery is consistently evolved to produce a better outcome and to decrease complications. Peritoneal vaginoplasty (Davydov-procedure) has been used for the reconstruction of vagina in females borned with congenital vaginal agenesis. The advantages of using the peritoneum for vaginal reconstruction are its abundant availability, the proximity to vagina, the mucosal-type surface and its self-lubricating property. Pedicled peritoneal vaginoplasty was adapted from Davydov-procedure. In male-to-female reassignment surgery, penile skin inversion (PSI) vaginoplasty remains the standard technique. This peritoneal flap technique has become an exciting procedure for augmenting neovaginal length and postsurgical transgender women who are unable to undergo the standard PSI.

Objectives: To present the technique of laparoscopic step in pedicled peritoneal flap vaginoplasty.

Methods: The procedure was contained in 2 steps; laparoscopic step and perineal step. In the laparoscopic step, the peritoneum, including transversalis fascia, was dissected down from abdominal wall to create the flap based on left inferior epigastric artery. The size of the neovaginal flap, mostly 12 cm for the circumference and 15 cm for the depth. Musculocutaneous perforators to the rectus abdominis were ligated and divided. The peritoneal branches of left inferior epigastric artery were preserved. Peritoneal flap was totally constructed (rolled and sewn) in peritoneal cavity, then delivered through the tunnel between rectovesical space toward the perineum. At last, in the perineal step, the flap and perineal skin were conjoined with the neovaginal opening by plastic surgeon.

Results: All wounds were healed within 3-4 weeks. The neovaginal depth was 13 cm at 6-month visit. The vaginoscopy revealed good neovaginal surface and its self-lubrication.

Conclusions: Laparoscopic pedicles peritoneal flap vaginoplasty is a minimal invasive procedure that can effectively reduce limitation of neovaginal depth in gender reassignment surgery.

Keywords: Gender reassignment, Sex change, Peritoneal flap, Neovaginal depth

Young Investigator Award

CLINICAL APPLICATION OF SIRIRAJ MOLECULAR NOMOGRAM FOR PREDICTION OF NON-SENTINEL LYMPH NODE METASTASIS: FINE TUNING OF ACOSOG Z0011

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Background: Axillary staging is an important prognostic factor that is frequently used to determine the course of treatment for breast cancer. To avoid unnecessary axillary lymph node dissection (ALND), a nomogram for predicting non-sentinel lymph node (NSLN) status using one-step nucleic acid amplification (OSNA) was developed.

Objectives: To evaluate clinical application of the nomogram for prediction of NSLN status using OSNA technique.

Patients and Methods: Breast cancer patients with clinical T1-T2 and negative axillary lymph node who underwent sentinel lymph node biopsy (SLNBx) at Siriraj Hospital were enrolled. Sentinel lymph nodes (SLNs) were examined by OSNA technique and the probability of positive NSLN was calculated. The patients who had

more than 2 positive SLNs or probability of positive NSLN > 20% underwent ALND while in the patients with probability ≤ 20%, ALND was omitted. Clinicopathological data was compared between the patients with negative and positive NSLN.

Results: There were 192 SLNBx performed and 54 patients had positive SLN. ALND was performed in 45 patients. NSLNs were negative in 23 patients and positive in 22 patients. In the patients with 1-2 positive SLNs, 21 (47.7%) out of 44 patients had positive NSLN and 29.5% had advanced disease in the axilla (N2-N3).

Conclusions: Determination of omitting ALND using Siriraj Molecular Nomogram for prediction of NSLN status identified the patients with NSLN involvement. This nomogram might be utilized to select the patients who suitable for omitting ALND.

Keywords: Axillary lymph node dissection, Breast cancer, One-step nucleic acid amplification, Sentinel lymph node biopsy

INSULIN RESISTANCE OUTCOMES FOLLOWING PREOPERATIVE ORAL CARBOHYDRATE LOADING IN BARIATRIC SURGERY PATIENTS: A RANDOMIZED CONTROLLED TRIAL

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Background: Enhanced Recovery After Surgery (ERAS) protocol in bariatric surgery is well-accepted worldwide. Preoperative oral carbohydrate loading is one of the components of ERAS protocol which has scarce data in bariatric patients. Preoperative fasting increases insulin resistance and inflammatory stress responses which can be reduced by preoperative oral carbohydrate loading.

Objectives: This study aimed to evaluate the effect of preoperative oral carbohydrate loading on insulin resistance and inflammatory outcomes compare with conventional fasting protocol.

Methods: We conducted this study between October 2021 to February 2022. Morbidly obese patients underwent bariatric surgery, either sleeve gastrectomy or Roux-en-Y gastric bypass were randomized to intervention group and control group. The intervention group received 2 doses of oral carbohydrate loading, the night before and 3 hours prior to surgery. In control group, patients received 2 doses of water in the same fashion as intervention group. Primary outcome was insulin resistance, measured by homeostasis model assessment-estimated insulin resistance (HOMA-IR) index. Secondary outcomes were interleukin-6 (IL-6) and C-reactive protein (CRP) level. We measured HOMA-IR index, IL-6 and CRP level at preoperative, postoperative day 1, 3 and 14.

Results: 20 patients were enrolled in this analyzes (10 patients in intervention group, 10 patients in control group). The median difference of HOMA-IR index from preoperative was 8.83 in intervention group and 8.32 in control group ($p = 0.36$) in postoperative day 1. In postoperative day 14, 5.52 in intervention group and 2.09 in control group ($p = 0.082$).

Conclusions: Preoperative oral carbohydrate loading has no difference in insulin resistance and inflammatory outcomes in bariatric surgery patients. Increasing in number of patients may alter the results. Further studies should be conduct for other clinical outcomes.

Keywords: Bariatric surgery, Oral carbohydrate loading, Insulin resistance

PATHOGENIC GERMLINE MUTATION IN 13 HEREDITARY CANCER-RELATED GENES IN BREAST CANCER PATIENTS: A CASE SERIES IN NARATHIWAT PROVINCE

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Background: Approximately 27% of breast cancer are hereditary, and germline pathogenic variants in *BRCA1* and *BRCA2* genes are known genetic causation as a carrier of the mutations have increased lifetime risk of breast cancer at 10–20 folds. Identification of inherited patients potentially reduce the risk of breast and/or ovarian cancer through early detection of the disease which may decrease the mortality rate. Three southern border provinces of Thailand have distinct population characteristics. Although a majority of the population is Thai-Malays trait, the area has population admixture. Genetic test for hereditary cancers is not common in the area.

Objectives: This study explored the frequency and distribution of genetic variants in unselected cases of breast cancer patients in Narathiwat province.

Methods: Non-selected consecutive 64 breast cancer patients undergoing treatments in two general hospitals in the province between 2021 and 2022 (12 cases from Sungaikolok Hospital and 52 cases from Naradhiwas Rajanagarindra Hospital). Molecular genetic study is performed using a whole exome study platform. Moderate to high penetrance variants recommended by National Comprehensive Cancer Network (NCCN) guidelines 2022 were annotated *(ATM, BARD1, BRCA1, BRCA2, CDH1, CHEK2, NF1, PALB2, PTEN, RAD51C, RAD51D, STK11, TP53)* and filtered for Pathogenic, Likely pathogenic, or High-impact variants.

Results: Of 64 cases pathogenic germline variants were found in 8 cases (12.5%) which included *BRCA1* in 3 (4.7%), *BRCA2* in 4 (6.3%), *ATM* in 1 (1.6%) and *PALB2* in 1 (1.6%). One patient had two concomitant germline mutations: in *BRCA2* and in *ATM*.

Conclusions: This is the first study on the frequency of germline mutations in *BRCA1/2* and other breast cancer predisposing genes in breast cancer in the southernmost borders of Thailand. In unselected breast cancer patients, at least one pathogenic germline mutation was identified in 12.5%, which suggested that genetic testing in this population has a high potential to provide benefit.

Keywords: Breast cancer, Germline variants, Hereditary cancer

American College of Surgeons Chapter Award

APPENDICITIS IN COVID-19 ERA

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Background: For more than two years since the COVID-19 pandemic, human lives have been changed worldwide, including in the health care system. Management of acute appendicitis, the most common emergency surgical disease, has been inevitably affected by the COVID-19 pandemic. This study aimed to assess the effect of the COVID-19 pandemic on the management of acute appendicitis, the incidence of complicated appendicitis, treatment outcome, and complications.

Objectives: The primary objective was to compare the incident rate of complicated appendicitis pre COVID-19 and during COVID-19 pandemic. The secondary objectives were to compare complication rate, length of hospital stay, time to surgery, and cost between pre COVID-19 and during COVID-19.

Methods: This study was a retrospective cohort study comparing 574 patients diagnosed with acute appendicitis before the COVID-19 outbreak (pre COVID-19) and 434 patients diagnosed with acute appendicitis during the COVID-19 outbreak (during COVID-19). Patient demographic data, type of appendicitis, type of treatment, time to surgery, length of hospital stay, cost and complications were collected and analyzed by multivariate regression analysis.

Results: During the COVID-19 pandemic, the number of patients diagnosed with acute appendicitis was reduced. CT scan usage for diagnosis was increased compared to pre COVID-19 (45.39% vs 32.75%, p-value < 0.001). Most patients diagnosed with acute appendicitis received operative treatment in both groups. Median time to surgery was significantly longer during

the COVID-19 pandemic, 11.93 hours compared to 9.62 hours pre COVID-19, *p*-value < 0.001 (relative risk 1.5, 95% CI 1.29-1.76, *p*-value 0.041). The incidence of complicated appendicitis was not higher during COVID-19. Compared to pre COVID-19, ICU admission rate, the use of a mechanical ventilator, length of stay and cost were increased in the univariate analysis but not statistically significant in the multivariate analysis. Other treatment complications had no statistically significant difference.

Conclusions: The incidence of complicated appendicitis did not increase during the COVID-19 pandemic. The operation waiting time significantly increased but did not increase the rate of treatment complications in a well-prepared hospital system.

Keywords: Acute appendicitis, Complicated appendicitis, Outcome, Coronavirus 2019, COVID-19