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# THE THAI JOURNAL OF SURGERY

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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.

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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. doi:10.21037/gs.2019.10.06.
- 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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Randomized controlled trials should be analyzed using the intention-to-treat principle, and as treated analysis should be applied as well if there are significant cross-overs. Further details of statistical issues are available here (http://www.icmje.org/icmje-recommendations.pdf).

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*(see Format https://bit.ly/3IaP4ZB)*

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**Main text:** should be written in a structured format, including the following headings. **Introduction** should describe the rationale of the study within the context of current knowledge; the gap in knowledge with which the research study will fill must be clearly pointed out and a research question explicitly stated. **Methods (and patients, if applicable)** should clearly describe the details of research methodology and patient or research volunteer recruitment according to Guidelines for each type of research as listed above (…), and how the data was collected and analyzed. A short description of statistics used, and the software and references if appropriate, must be provided. A note on Ethics Committee approval, if applicable, must be given. **Results** should include data or summaries of patient or volunteer characteristics, summaries of risk factors or covariates and outcomes, presented in tabular, graphical or descriptions in the text as appropriate, without significantly duplicating one another. Results of statistical analyses must be clearly displayed and should include point estimates, standard errors, statistical tests, *p*-values, and 95% confidence intervals as detailed (…). Analyses not shown but

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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**Abstract:** A brief description of aims and content is sufficient.

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# Editorial

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

We begin this year's issue with a new look, with more consistent color scheme and more modern design. We hope readers and members of The Royal College of Surgeons of Thailand will appreciate that visual appeal might attract more readers and motivate more contributions!

The current issue is packed with research articles of considerable interest. The first article reviews the management of an increasingly common, severe, life-threatening condition of necrotizing enterocolitis (NEC) of the new born, at a major Northeastern Institution, Khon Kaen Hospital. The 10-year study revealed that while most neonates with NEC could be managed by medical means, those requiring surgery still have considerable mortality and are still an open challenge for pediatric surgeons everywhere.

The second article demonstrates the use of a scoring system to help manage severe traumatic colon injury. This was part of a series of such studies from Maharat Nakhon Ratchasima Hospital. The scoring system may help surgeons with limited experience and without means to consult experienced colleagues to decide whether a colonic diversion, as opposed to primary repair and anastomosis, is better for the patient, and conversely.

The next article reports one surgeon's 10-year experience, from Chonburi Hospital, of performing parathyroidectomy in patients with renal hyperparathyroidism, an often-frustrating operation for many surgeons. The author's choice of total parathyroidectomy with autotransplantation, with virtually no postoperative hypoparathyroidism, would seem to be well-suited for patients on the waiting list for renal transplantation. However, as the author mentioned, the experience of the surgeon is paramount in the success of parathyroidectomy for renal hyperparathyroidism.

Continuing the authors' series on infective endocarditis (IE) is the next article focusing on valve surgery. This study from Maharat Nakhon Ratchasima Hospital was a 12-year review of the results of replacing diseased native valves of patients with active IE, with prosthetic valves. Long-term, 5-year results seemed to be good for whatever prosthetic valve used, but patients who had mechanical valve replacement had higher survival in the short term, as compared with those who had tissue valve replacement. However, this might have been due to better preoperative clinical status of IE patients who had mechanical valve replacement.

The next article is a randomized controlled trial comparing ultrasound (US)-guided percutaneous nephrolithotomy (PCNL) with a more widely-used fluoroscopic PCNL, from Suratthani Hospital. This study showed that US was similarly as effective as fluoroscopy for guiding PCNL in terms of time-to-access tract and stone clearance rate. With some practice, the urologist can perhaps avoid the use of imaging modalities requiring the much-feared ionizing radiation, in PCNL.

The last article is from Pakkred Community Hospital dealing with the use of small bore (18-gauge) core needle biopsy (CNB) as compared with the standard 18-gauge fine needle aspiration biopsy in thyroid nodules. There was evidently a much higher rate of adequate diagnosis, in terms of the Bethesda Classification, when CNB is used, without additional complications. The author is to be commended for advocating the use of the more effective CNB when the majority of institutions are still not convinced of its safety.

We trust the reader will find these articles interesting and thought-provoking. Surgeons all over Thailand are doing a wonderful job of translating their clinical work into generalizable knowledge that may change how Thai surgeons, and perhaps surgeons elsewhere, can improve the outcomes of managing their patients.

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*Original Article*

# *Outcomes of Surgical Management for Necrotizing Enterocolitis: an 11-year Experience*

**Sithichok Laohawilai, MD**[1]
**Thetiya Wirifi, MD**[1]
**Benjaporn Silaruks, Pharm.D**[2]

[1] *Department of Surgery, Khon Kaen Hospital, Khon Kaen, Thailand*
[2] *Department of Pharmacy, Khon Kaen Hospital, Khon Kaen, Thailand*

***Abstract***

***Background:*** Necrotizing enterocolitis (NEC) is a serious disease in neonates and requires surgical treatment in cases with complications. The purpose of this study was to review outcomes of NEC patients treated by various procedures during an 11-year period.

***Patients and Methods:*** A retrospective cohort study of patients with NEC treated at Khon Kaen Hospital between January 2009 and December 2019 was conducted. Medical records of patients were abstracted for clinical characteristics and presentations, laboratory findings, radiologic studies and results of treatment.

***Results:*** Seventy-three NEC patients (40 males and 33 females) was available for the study. Sixty-one cases (84%) were managed by medical treatment and 12 cases (16.4%) required surgery because of complications due to intestinal perforation and peritonitis. Of the 12 surgical NEC, 10 cases (83%) were premature (median gestational age, 29 weeks) and 10 were low birth weight infants (median birth weight, 1263 grams). Nine cases (75%) had a serious condition treated by primary peritoneal drainage (PPD) and 4 cases survived (44%). Three cases underwent primary exploratory laparotomy (PEL) – 2 had necrotic bowel resection with enterostomy, and one had primary anastomosis – and only one survived. The overall mortality of surgical NEC was 60% (7 of 12 cases), and the mortality rate of medical NEC was 12% (7 of 61 cases).

***Conclusion:*** NEC patients with serious complications including intestinal perforation and peritonitis require surgical treatment. PPD was done more common than PEL because of severely – ill patients with extremely and very low birth weight. The overall mortality of surgical NEC remains high, at 50%.

***Keywords:*** Necrotizing enterocolitis, Primary peritoneal drainage, Primary exploratory laparotomy, Necrotic bowel resection, Enterostomy

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***Corresponding author:*** Sithichok Laohawilai, MD, Department of Surgery, Khon Kaen Hospital, Khon Kaen, 40000, Thailand; Telephone: +6681 975 9065; E-mail: S.laohawilai@cpird.in.th

## Introduction

Necrotizing enterocolitis (NEC) is the most common gastrointestinal surgical condition leading to death in neonates with prematurity and low birth weight. This condition is an acquired disorder of the intestines, commonly found in infants born before 36 weeks of gestation.[1,2] NEC is a severe inflammation of all layers of the gastrointestinal wall, which can lead to ischemic necrosis.[3-6] In 1978 Bell[6] categorized NEC into three-stages for the purposes of diagnosis and treatment. The Bell staging criteria have been modified by Kliegman[7] in 1987 (Table 1). Although most patients with NEC improve with medical treatment, some cases require surgical management. The best surgical procedure for advanced diseases with extensive intestinal necrosis and perforation remains controversial. We reviewed our experience of treating NEC during an 11-year period at a tertiary hospital in the Northeastern Thailand.

## Patients and Methods

The present retrospective cohort study was conducted at the Department of Surgery, Khon Kaen Hospital (KKH). The study was approved by the Hospital's Ethics Committee. All patients with NEC who were admitted to KKH between January 2009 to December 2019 were identified from the electronic medical records, using ICD-10 Code 77.9. Patients who had incomplete medical record data were excluded. Data collected included clinical characteristics, presentation, laboratory and radiologic findings, and results of the treatment. The outcomes of survivors were finalized on December 31, 2020. Data were analyzed using the software STATA version 11.0 (Stata Corp, College Station, TX, USA). Differences between categorical variables were evaluated by Chi-square or Fisher's exact test, and between continuous variables by Wilcoxon rank-sum or Kruskal – Willis test. *P*-values less than 0.05 were considered statistically significant.

**Table 1** Modified Bell staging criteria for necrotizing enterocolitis[8]

| Stage* | Clinical findings | Abdominal findings | Roentgenographic findings |
|---|---|---|---|
| I A | Temperature instability, apnea, bradycardia, lethargy | Gastric retention, gastric distention, heme-positive stool | Normal or intestinal dilatation, mildileus |
| I B | Temperature instability, apnea, bradycardia, lethargy | Grossly bloody stool | Normal or intestinal dilatation, mildileus |
| II A | Temperature instability, apnea, bradycardia, lethargy | Moderate abdominal distention, bloody stool, absent bowel sound | Intestinal dilatation, ileus, pneumatosis intestinalis |
| II B | Temperature instability, apnea, bradycardia, lethargy, metabolic acidosis, thrombocytopenia | Moderate abdominal distention, bloody stool,absent bowel sound, definite tenderness with or without cellulitis or right lower quadrant mass | Intestinal dilatation, ileus, pneumatosis intestinalis, portal vein gas |
| III A | Temperature instability, bradycardia, lethargy metabolic acidosis, thrombocytopenia, hypotension, apnea combined respiratory and metabolic acidosis, DIC, neutropenia, oliguria | Marked abdominal distention, bloody stool, absent bowel sound, marked tenderness with or without cellulitis or right lower quadrant mass, signs of peritonitis | Intestinal dilatation, ± pneumatosis intestinalis, ± portal vein gas, ascites |
| III B | Temperature instability, bradycardia, lethargy metabolic acidosis, thrombocytopenia, hypotension, apnea combined respiratory and metabolic acidosis, DIC, neutropenia, oliguria | Marked abdominal distention, bloody stool, absent bowel sound, marked tenderness with or without cellulitis or right lower quadrant mass, signs of peritonitis | Intestinal dilatation, ± pneumatosis intestinalis, ± portal vein gas, ascites, pneumoperitoneum |

* IA, IB = suspected NEC,
II A = definite NEC, mildly ill; II B = definite NEC, moderately ill,
III A = advanced NEC, severely ill, intact bowel; III B = advanced NEC, severely ill, bowel perforation

## Results

Ninety-seven NEC patients were admitted at KKH during the study period. Only 73 patients had complete records. There were 40 boys and 33 girls. Of the 73 patients, the median gestational age (GA) was 31.5 weeks (range, 24 to 41 weeks) and the median birth weight (BW) was 1,510 grams (range, 620 to 3,390 grams). Thirty-six patients (49%) were classified as having very low birth weight (VLBW), and 13 (18%) were classified as having extremely low birth weight (ELBW). The median onset time of NEC was 11 days (range, 2 to 43 days). Sixty-one cases (84%) were categorized as Bell stages I and II, and medically treated. The remaining 12 cases (16%) were classified as advanced NEC (Bell stage III) and required surgical treatment. Patient characteristics in both medical and surgical treatment groups were similar (Table 2).

Patients in the surgical treatment group had more severe symptoms than those in the medical treatment group, which included significantly more frequent lethargy and abdominal erythema ($p < 0.05$). Presence of leukocytosis white blood cell (> 10,000/mm$^3$), or neutropenia (absolute neutrophil count < 1,500/mm$^3$) or thrombocytopenia (platelet < 150,000/mm$^3$) was not significantly different between the medical and surgical groups (see Table 3). On radiographic examination, there was greater degree of intestinal dilatation in patients in the medical treatment group, while pneumoperitoneum, an indication for surgery, was found in 10 of the 12 (83%) patients in the surgery group (see Figure 1).

The 61 patients with stages I and II NEC were conservatively treated by NPO, nasogastric or orogastric intubation, antibiotics, and total parenteral nutrition.

**Table 2** Comparison of clinical characteristics of patients with NEC (n = 73) between those undergoing medical treatment (n = 61) and those undergoing surgical treatment (n = 12)

| Clinical Characteristics | Medical NEC (n = 61) | Surgical NEC (n = 12) | *P*-value |
|---|---|---|---|
| **Gender** | | | |
| Male (no.): Female (no.) | 33 : 28 | 7 : 5 | 0.788 |
| **Gestational age (weeks)** | | | |
| Median (range) | 32 (29.3 to 37.0) | 29.1 (26.0 to 35.5) | 0.091 |
| < 28 (no.) | 9 | 5 | |
| 28-32 (no.) | 24 | 3 | |
| 32-36 (no.) | 12 | 2 | |
| > 36 (no.) | 16 | 2 | |
| Prematurity: no. (%) | 45 (74) | 10 (83) | 0.384 |
| Maturity: no. (%) | 16 (26) | 2 (17) | |
| **Birth weight (grams)** | | | |
| Median (range) | 1,520 (620 to 3,390) | 1,260.5 (720 to 3,350) | 0.190 |
| < 1,000 *: no. (%) | 8 (13) | 5 (42) | |
| 1,000-1,500 **: no. (%) | 21 (34) | 2 (17) | |
| 1,500-2,000: no. (%) | 11 (18) | 2 (17) | |
| 2,000-2,500: no. (%) | 6 (10) | 1 (9) | |
| > 2,500: no. (%) | 15 (24) | 2 (17) | |
| Low birth weight | 46 (76) | 10 (83) | 0.490 |
| Normal birth weight | 15 (24) | 2 (17) | |
| **Age at onset of symptoms (days)** | | | |
| Median (range) | 13 (2 to 44) | 9.5 (3 to 45) | 0.704 |
| **Risk factors: no. (%)** | | | |
| Birth asphyxia | 52 (80) | 12 (100) | 0.204 |
| Congenital heart disease (PDA) | 9 (15) | 4 (33) | 0.132 |
| Previous sepsis | 49 (80) | 10 (83) | 0.585 |
| Administration of NSAID | 3 (5) | 3 (25) | 0.052 |

* < 1,000 grams = extremely low birth weight; 1,000-1,500 grams = very low birth weight; no. = number

**Table 3** Comparisons of symptoms, laboratory and radiologic findings between NEC patients undergoing medical and those undergoing surgical treatment

| | Medical NEC (n = 61) | Surgical NEC (n = 12) | *P*-value |
|---|---|---|---|
| **Symptom: no. (%)** | | | |
| Hypothermia | 29 (48) | 9 (75) | 0.116 |
| Fever | 25 (41) | 6 (50) | 0.751 |
| Bradycardia | 16 (26) | 4 (33) | 0.725 |
| Lethargy | 17 (28) | 8 (67) | 0.017 |
| Apnea | 28 (43) | 5 (42) | 0.999 |
| Hypotension (shock) | 36 (59) | 9 (75) | 0.350 |
| Pregarvage residuals | 36 (59) | 7 (58) | 0.999 |
| Grossly bloody stool | 9 (15) | 1 (8) | 0.999 |
| Abdominal distension | 52 (85) | 12 (100) | 0.339 |
| Abdominal erythema | 7 (12) | 8 (67) | 0.001 |
| **Laboratory findings** | | | |
| Hemoglobin (gm/dL) | | | |
| Mean ± sd | 14.1 ± 3.13 | 12.8 ± 3.94 | 0.666 |
| White blood cell count (cell/mm3) | | | |
| Median (range) | 11,500 (2,000 to 39,600) | 21,485 (6,100 to 46,800) | 0.052 |
| Neutropenia*: no. (%) | 61 (100) | 12 (100) | NA |
| Thrombocytopenia**: no. (%) | 11 (18.0) | 5 (41.7) | 0.120 |
| **Radiographic findings: no. (%)** | | | |
| Intestinal dilatation | 52 (85) | 6 (50) | 0.013 |
| Ascites | 3 (5) | 2 (17) | 0.187 |
| Pneumatosis intestinalis | 10 (16) | 2 (17) | 0.999 |
| Pneumoperitoneum | 0 | 10 (83) | 0.001 |

* absolute neutrophil count < 1,500/mm$^3$; ** platelet count < 150,00/mm$^3$; no. = number; sd = standard deviation

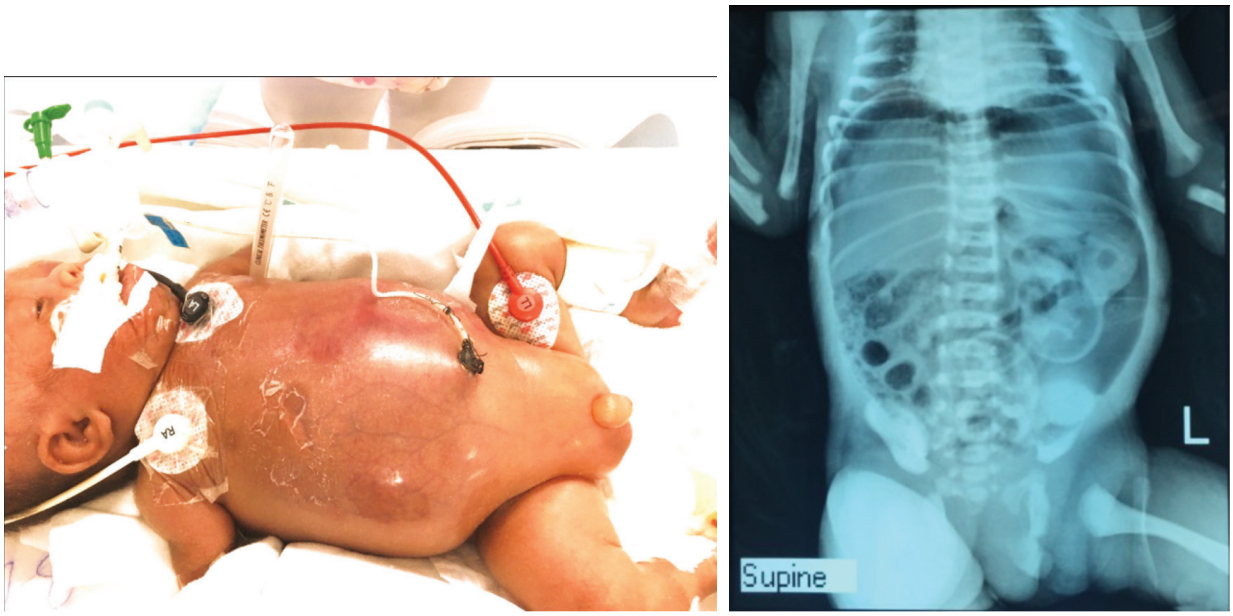


**Figure 1** A very low birth weight infant with signs of peritonitis (abdominal distension, erythema and guarding) and abdominal film showing free air in the abdomen (pneumoperitoneum)

**Table 4** Clinical characteristics, operative procedures and outcomes of NEC patients undergoing surgery

| Case No. | GA (weeks) | BW (grams) | Age at operation (days) | Symptomatologes and indications for surgery | Operative procedures* | Results |
|---|---|---|---|---|---|---|
| 1. | 25 | 770 | 6 | • Birth asphyxia, pneumonia<br>• Bowel perforation | PPD | • Survived<br>• Umbilical hernia<br>• Delayed development |
| 2. | 28 | 990 | 7 | • Birth asphyxia, ET-intubation<br>• Bowel perforation | PPD | • Survived<br>• Later Dx Hirschsprung's disease and treatment by Soave pull-through operation<br>• Patho; Absence of ganglion cells in the rectum<br>• Lysis of adhesion due to postop. obstruction<br>• Doing well |
| 3. | 27 | 890 | 8 | • Birth asphyxia, ET-intubation, PDA, jaundice platelet 5400/$mm^3$<br>• Signs of peritonitis | PPD | Survived<br>• Lost to follow-up |
| 4. | 24 | 720 | 8 | • Birth asphyxia, ET-intubation, abnormal color of abdomen<br>• Bowel perforation | PPD | Dead |
| 5. | 30 | 1600 | 10 | • Respiratory distress, septicemia, shock, abnormal color of abdomen, platelet 52000/$mm^3$<br>• Bowel perforation | PPD | Dead |
| 6. | 39 | 3350 | 11 | • Sepsis, PDA, got NSAID, platelet 20000/$mm^3$<br>• Bowel perforation | PPD | Dead |
| 7. | 29 | 1085 | 11 | • Birth asphyxia, ET-intubation, lethargy,sepsis<br>• Bowel perforation | PPD+EL, NBR and primary anastomosis | Dead |
| 8. | 35 | 1755 | 9 | • Birth asphyxia, ET-intubation, lethargy,sepsis, platelet 36000/$mm^3$<br>• Signs of peritonitis<br>Bowel perforation | PPD+EL, NBR and enterostomy | • Survived<br>• Lost to follow-up after closure of enterostomy 8 months |
| 9. | 30 | 1600 | 10 | • Birth asphyxia, sepsis<br>• Bowel perforation | PPD+EL, NBR and enterostomy | Dead |
| 10. | 37 | 2090 | 22 | • Birth asphyxia, sepsis, shock<br>• Bowel perforation | PPD+EL, NBR and enterostomy | Dead |
| 11. | 29 | 1440 | 19 | • Twins, birth asphyxia, ET atbirth, lethargy, sepsis,<br>• Signs of peritonitis | PEL, NBR and enterostomy | • Survived<br>• Lost to follow-up after closure of enterostomy 3 months |
| 12. | 35 | 2660 | 3 | • Birth asphyxia,abnormal color abdomen<br>• Bowel perforation | PPD+EL, NBR and enterostomy | Dead |

| | | |
|---|---|---|
| PPD (6) | Survived 3 | Dead 3 |
| PPD+EL, NBR and enterostomy (3) | Survived 1 | Dead 2 |
| PEL, NRB and enterostomy /anastomosis (3) | Survived 1 | Dead 2 |

* Abbreviation: PPD = primary peritoneal drainage, EL = exploratory laparotomy, PEL = primary exploratory laparotomy, NBR = necrotic bowel resection

Fifty-four patients (89%) survived and 7 (11%) died due to respiratory distress, persistent pulmonary hypertension and septicemia. Five patients with respiratory distress were intubated since birth. The 12 patients with advanced NEC required surgical intervention. Indications for surgery included intestinal perforation in 10 (83%) and obvious peritonitis (abdominal erythema and guarding) in the remaining 2 patients. Nine of the 12 cases (75%), who were severely ill, underwent primary peritoneal drainage (PPD) or bedside peritoneal drainage (BPD) in the Neonatal Intensive Care Unit (NICU) under local anesthesia (Figure 2). Six patients underwent PPD and 3 (50%) survived. Three patients initially underwent PPD and later required exploratory laparotomy because of complications, and one (33%) survived (Table 4). The remaining 3 patients with advanced NEC underwent primary exploratory laparotomy (PEL), bowel resection and enterostomy (Figure 3). Two patients died, while one survived and later underwent closure of the enterostomy. Causes of death in the surgical NEC group included severe sepsis, respiratory failure and congestive heart failure, in the presence of congenital heart diseases and extensive intestinal necrosis. The overall survival rate of advanced NEC in the present study was 42% and mortality rate was 58%.

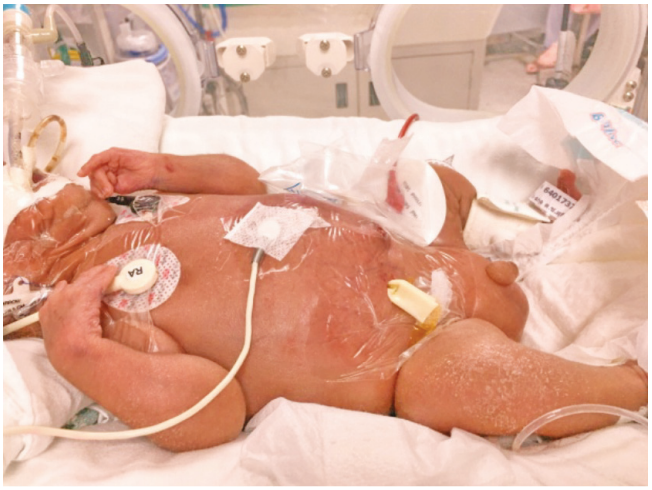

**Figure 2** Primary peritoneal drainage by placement of Penrose drains at both sides of lower abdomen; done under local anesthesia

## Discussion

At present, the incidence of NEC is increasing. The Increasing NEC incidence relates to decreasing birth weight and gestational age.[9,10] Worldwide, the incidence of NEC is approximately 1 to 3 per 1,000 live births, and over 90% of cases are seen in infants with body weight less than 1,500 grams and gestational age less than 32 weeks.[2,6,9] The incidence of NEC seen at Queen Sirikit National Institute of Child Heath was 1.04 per 1,000 live births in the period between 1993-1994, which increased to 2.7 per 1,000 live births at Rajavithi Hospital in 2004.[11,12] The Ministry of Public Health of Thailand reported the incidence of NEC as 3.7 to 11 per 1,000 live births, using data of all hospitals in the country.[13] The increasing NEC incidence may be partly explained by the increasing frequency of teenage pregnancy, which

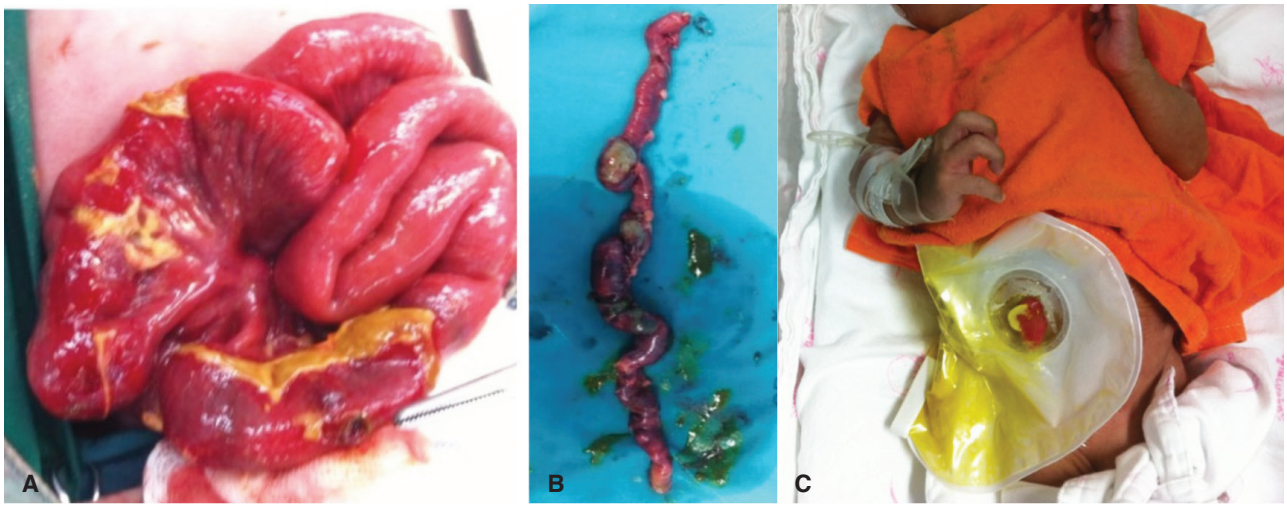


**Figure 3** Primary exploratory laparotomy in a premature infant: bowel necrosis and perforation (A); segmental resection of necrotic bowel (B); and creation of a stoma or enterostomy (C)

is a risk factor for premature deliveries and VLBW or ELBW babies.[11,12] Most NEC patients seen at KKH, especially those with severe conditions, were transferred from the other provinces.

In the present study, NEC occurred slightly more frequently in the male than in the female (1.2:1). The majority occurred in premature infants (75%) and in those with VLBW and ELBW, which constituted 50% of the cases. These findings were similar to those of previous reports.[6,11-13] We also found that major risks for NEC included birth asphyxia, sepsis, patent ductus arteriosus (PDA) and administration of non-steroid anti-inflammatory drugs (NSAID) for closure of PDA.

The Bell staging criteria[6,7] for the diagnosis and management of NEC is the international standard. The majority of NEC patients categorized as having stages I and II disease are usually conservatively or medically treated, whereas the minority with stage III or advanced NEC require surgical treatment. In general, 20% to 50% of NEC patients will require surgery.[14-16] In the present study, 16% of NEC patients were surgically treated. There is some controversy regarding the timing of and decision-making during surgery, and the various surgical procedures. The absolute indication for surgery is evidence of pneumoperitoneum detected by abdominal x-rays which indicates intestinal perforation.[17,18] Signs of peritonitis, intestinal obstruction (fixed bowel loops from abdominal imaging due to non-movable necrotic bowels), palpable abdominal mass and clinical deterioration (failure of medical treatment) are relative indications for surgery. Decision making and timing of surgery will depend on the surgeon and his or her experience.[19] In the present study, NEC patients required surgery due to evidence of intestinal perforation in 10 cases and due to signs of peritonitis in 2 cases.

Primary exploratory laparotomy with resection of necrotic bowel, while trying to preserve as much viable intestine as possible, and the creation of a stoma or enterostomy, is the traditional operation of choice.[19] Closure of the enterostomy should be done after 3 months to ensure complete resolution of the inflammatory process.[17-19] Prior to the enterostomy closure, colonic or small bowel strictures should be excluded with a barium or other contrast study, administered through the enterostomy.[18] Bowel resection with primary anastomosis is not generally recommended as the process of ischemic necrosis might be ongoing, with a high risk of anastomotic leakage.[6] Primary intestinal anastomosis is acceptable in cases of focal NEC, and intestinal perforation and necrosis at the upper jejunum. We have seen one patient with jejunal perforation close to the duodenojejunal junction. It was necessary to perform segmental jejunal resection and primary anastomosis in order to avoid high-output enterostomy. This patient died due to severe sepsis, but without evidence of anastomotic leakage (Table 4, patient no.7).

Primary peritoneal drainage (PPD), recommended by Ein in 1977,[20] is an alternative surgical procedure for advanced NEC. It is suitable for severely ill VLBW and ELBW infants with clinical instability, unable to be transferred to the operating room or unable to tolerate general anesthesia. This procedure can be done in the NICU or ordinary neonatal ward, as a bed-side peritoneal drainage.[14,20,21-23] PPD can reduce pneumoperitoneum and bowel inflammation.[14,20,21-23] The survival rate of patients with advanced NEC treated by PPD is approximately 30%,[14,20,21] similar to that of the present study. Currently, PPD is a standard procedure for advanced NEC.[22] Other operative procedures, such as the "patch, drain and wait technique" proposed by Moore in 1989,[23] and the "clip-and-drop-back technique" proposed by Voughan in 1996,[24] are suitable for NEC with multi segmental necrosis. We have no experience with these operative interventions.

The outcome of surgery for NEC is not entirely satisfactory compared with the outcome of medical treatment. Medical treatment of NEC carries a mortality of about 20%, whereas the mortality of surgical treatment is probably in excess of 35% and may be as high as 50%.[10,16,25-27] In the present study the mortality in the medical treatment group was 12% and the mortality in the surgical treatment group was 60%. For the survivors of surgical treatment, some degree of neurodevelopmental impairment, delayed growth development, adhesive small bowel obstruction and intestinal failure may occur.[22] These survivors should be followed in the long-term in order to detect and treat these problems.

The present study has some limitations. Data collection might be unreliable or incomplete due to loss of documentation after a long period of time, such as information on as laboratory findings, radiographic imagings, risk factors, or milk formula feeding after birth. These defects will be corrected by systematic planning of data gathering for a future prospective study.

## Conclusion

Most patients with NEC can be managed by medical treatment. In the present study, the ratio of NEC patients managed by medical to surgical treatment was 5:1. Indications for surgery included intestinal perforation (83%) and peritonitis (17%). PPD was more common performed than PEL, at a ratio of 3:1, because of severely-ill patients with VLBW and ELBW. The overall mortality of surgical treatment for NEC patients remained high, at 50%.

## Acknowledgement

The authors would like to thank the Department of Surgery, Khon Kaen Hospital for the allowing the use of Hospital records, and Dr. Rangsan Niramis for editing the manuscript.

## Conflict of Interest

None

## Funding

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## *บทคัดย่อ* ผลของการรักษาโดยการผ่าตัดภาวะลำไส้เน่าในเด็กทารก: ประสบการณ์ในระยะเวลา 11 ปี

**สิทธิโชค เล่าหะวิลัย พบ.[1], เทตียา วิริไฟ พบ.[1], เบญจพร ศิลารักษ์ ภบ.[2]**

*[1]กลุ่มงานศัลยกรรม โรงพยาบาลขอนแก่น*

*[2]กลุ่มงานเภสัชกรรมโรงพยาบาลขอนแก่น*

***ความเป็นมา:*** ลำไส้อักเสบรุนแรงจนเกิดการลำไส้เน่าในเด็กทารก (necrotizing enterocolitis – NEC) เป็นโรคที่มีอาการรุนแรงมากและต้องการการรักษาโดยการผ่าตัดในผู้ป่วยบางรายที่มีภาวะแทรกซ้อน วัตถุประสงค์ของการศึกษาครั้งนี้ เพื่อทบทวนผลการรักษาผู้ป่วยโรคนี้ที่รักษาโดยการผ่าตัดชนิดต่างๆ ในช่วงระยะเวลา 11 ปี

***วัสดุและวิธีการศึกษา:*** เป็นการศึกษาย้อนหลังในผู้ป่วย NEC ที่รับการรักษาในโรงพยาบาลขอนแก่นตั้งแต่เดือนมกราคม 2552 ถึง เดือนธันวาคม 2562 ข้อมูลผู้ป่วย NEC ถูกนำมาวิเคราะห์เกี่ยวกับข้อมูลทั่วไป ลักษณะทางคลินิก ผลการตรวจทางห้องปฏิบัติการ ภาพถ่ายรังสี และผลการรักษา

***ผลการศึกษา:*** ผู้ป่วย NEC ที่นำมาทำการศึกษาทั้งสิ้น 73 ราย เป็นเพศชาย 40 ราย เพศหญิง 33 ราย ผู้ป่วย 61 ราย (ร้อยละ 84) ได้รับการรักษาโดยการใช้ยาและ 12 ราย (ร้อยละ 16) ได้รับการรักษาโดยการผ่าตัดเพราะมีภาวะแทรกซ้อนจากลำไส้ทะลุและเยื่อบุช่องท้องอักเสบ ในผู้ป่วย NEC 12 รายที่ได้รับการผ่าตัด 10 ราย (ร้อยละ 83) เป็นเด็กที่คลอดก่อนกำหนด (ค่ามัธยฐานของอายุครรภ์มารดา 29 สัปดาห์) และ 10 รายเป็นทารกน้ำหนักแรกเกิดน้อยกว่าปกติ (ค่ามัธยฐานของน้ำหนักแรกเกิด 1,263 กรัม) ผู้ป่วย 9 ราย (ร้อยละ 75) ที่มีอาการหนักมาก ได้รับการรักษาโดยการใส่ท่อระบายน้ำออกจากช่องท้องและมีชีวิตรอด 4 ราย (ร้อยละ 44) ผู้ป่วยอีก 3 ราย ได้รับการรักษาโดยการผ่าตัดเปิดหน้าท้อง ตัดเอาลำไส้เน่าออก พร้อมทั้งเปิดลำไส้ไว้หน้าท้องเป็นทวารเทียม (2 ราย) และเย็บต่อลำไส้ในครั้งเดียว (1 ราย) มีเพียงผู้ป่วย 1 รายที่ผ่าตัดเปิดหน้าท้องมีชีวิตรอด อัตราการเสียชีวิตทั้งหมดในผู้ป่วย NEC ที่ผ่าตัดคือร้อยละ 60 (7 ใน 12 ราย) เปรียบเทียบอัตราการเสียชีวิตร้อยละ 12 (7 ใน 61 ราย) ในผู้ป่วยที่ได้รับการรักษาโดยการใช้ยา

***สรุปผลการศึกษา:*** ผู้ป่วย NEC ที่มีภาวะแทรกซ้อนรุนแรงต้องการรักษาโดยการผ่าตัด จากข้อบ่งชี้มีการทะลุของลำไส้และเยื่อบุช่องท้องอักเสบ การผ่าตัดใส่ท่อระบายน้ำออกจากช่องท้องได้รับการทำมากกว่าการผ่าตัดเปิดหน้าท้อง เพราะเหตุที่ผู้ป่วยมีอาการหนักมากและมีน้ำหนักน้อยมากอัตราการเสียชีวิตในผู้ป่วย NEC ที่ผ่าตัดยังคงสูงถึงร้อยละ 50

The THAI Journal of SURGERY 2022;43(1):12-17.
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Original Article

# *Santichatngam's Colonic Injury Prediction Score (SCOPES) for Decision Making in Colonic Injury Due to Trauma*

**Prinya Santichatngam, MD**

*Department of Surgery, Maharat Nakhon Ratchasima Hospital, Nakhon Ratchasima, Thailand*

***Abstract***

***Objective:*** Santichatngam's Colonic Injury PrEdiction Score (SCOPES), which was developed in 2017, can assist in surgical decision making for colonic injury, i.e., whether primary repair can be performed or diversion is needed. The aim of the present study was to demonstrate the validity and utility of SCOPES for appropriate surgical decision making in at least grade 3 colonic injury.

***Patients and Methods:*** Medical records of patients with colonic injury who were treated at Maharat Nakhon Ratchasima Hospital from October 1st, 2013 to September 30th, 2019, were reviewed. Two versions of SCOPES were created. Both versions consisted of four factors. In SCOPES version I, if only 1 factor were present, then primary repair is recommended. In SCOPES version II, in the presence of at least 2 major factors, or 1 major factor plus at least 1 minor factor, then a diversion procedure is recommended. The SCOPES recommendation was compared to a reference standard, which was determined by successful operative management and peer review.

***Result:*** The SCOPES version I has a sensitivity of 81%, specificity of 86%, positive likelihood ratio of 5.7, positive predictive value of 96%, and accuracy of 82% for primary repair. The SCOPES version II has a sensiti-vity of 43%, specificity of 100%, positive likelihood ratio over 10, positive predictive value of 100%, and accuracy of 90% for colonic diversion. Application of SCOPES was useful in decision making in 74% of patients.

***Conclusions:*** The present study demonstrated that SCOPES has good validity and utility in terms of recommending appropriate management. The use of SCOPES in clinical practice may have some advantages over clinical judgment alone.

***Keywords:*** Clinical prediction score, Colonic injury

## Introduction

One of the most common abdominal injuries is colonic injury.[1-5] Recent scientific evidence supports routine primary repair for nondestructive colonic injury (AAST Colon Injury Scale Grade I-II) irrespective of the presence or absence of risk factors.[2,6-8] Colonic diversion is performed based on the principles of damage control surgery in hemodynamically unstable patients. However, many surgeons still consider colonic diversion as a safer procedure in most high-risk colonic injury.[9,10]

Santichatngam's Colonic Injury PrEdiction Score (SCOPES), which was developed in 2017, can assist in surgical decision making in colonic injury.[11] SCOPES can help decide whether primary repair or diversion

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***Corresponding author:*** Parinya Santichatngam, MD, General Surgery Unit, Department of Surgery, Maharat Nakhon Ratchasima Hospital 49, Chang Phueak Rd, Mueang District, Nakhon Ratchasima Province; Telephone: +66 4423 5469, Fax: +66 4424 6389; Email: s_parinya@hotmail.com

procedure should be performed based on four factors: delayed time to surgery (greater than 6 hours); left sided colonic injury, gross fecal contamination, and presence of concomitant duodenal or ureteral injury. If at least 2 of these factors are present, colonic diversion is recommended. SCOPES (with a cut-off of at least 2 positive factors or score greater than 4.87) was shown to have a sensitivity of 88%, and specificity of 83% for predicting colonic diversion. The post-test probability of diversion for a positive SCOPES was 84% for the sample studied, and the post-test probability of diversion for a negative SCOPES was 12% for the same sample.[11]

Wattakawanch and Santichatgnam studied colonic injury patients of all severity at Maharat Nakhon Ratchasima Hospital from 2013 through 2017 (4 years), and found SCOPES to have low positive predictive value but high sensitivity, specificity, negative predictive value in predicting primary repair.[12] From multicenter studies and meta-analyses, routine diversion is not recommended.[5,13] The aim of the present study was to determine the validity and utility of SCOPES for appropriate surgical decision making in colonic injury.

## Patients and Methods

In the present retrospective study, information from the medical records of patients who were diagnosed with colonic injury (ICD 10th ed.; S365), at Maharat Nakhon Ratchasima Hospital (MNRH) between October 1st, 2013 and September 30th, 2019 (6 years) was obtained. The study was approved by Ethical Committee of the MNRH. Patients were included if they were over 15 years and underwent exploratory laparotomy for abdominal trauma during the same admission with findings of colonic injury grade 3 or higher.[8] They were excluded if they underwent damage control surgery or if the injury was iatrogenic.

Information abstracted included baseline demographic data and clinical characteristics including type of injury, underlying diseases, time to operation, colonic injury score (CIS) according to the American college of surgeons (ACS),[8] degree of fecal contamination, sites of colonic injury, grade of duodenal or ureteral injury,[14-15] damage control surgery, details of operative procedure, and operative complications.

Patients were categorized into two groups according to initial operative management and postoperative complications. The first group included patients who were treated with primary repair (including primary closure of defects and/or resection with re-anastomosis) with no postoperative complications, i.e. anastomotic leakage or intraabdominal abscess. The second group included patients who were treated with primary repair but had postoperative complications and patients who were treated by diversion. The patient's condition and operative notes were reviewed by two certified trauma surgeons.

The peer review process with consensus agreement between both surgeons was used to establish the reference standard for decision-making in the present study: patients were categorized into proper or appropriate primary repair and diversion groups. Patients who had successful primary repair, by definition, had correctly underwent proper management. When both peer reviewers disagreed with the actual operative decision, the peer reviewers' opinion was considered more appropriate.

Two versions of SCOPES were created. SCOPES version I consisted of four risk factors: delayed time to surgery (i.e., greater than 6 hours); left sided colonic injury (grade 3 or higher); gross fecal contamination; and concomitant duodenal or ureteral injury (grade 3 or higher). If only one risk factor were present, primary repair is recommended. SCOPES version II consisted of the same four risk factors, but with an added hierarchy. Gross fecal contamination and concomitant duodenal or ureteral injury are considered major risk factors. Delayed time to surgery and left side colonic injury are considered minor risk factors. Colonic diversion is recommended in the presence of 2 major risk factors, or 1 major plus at least 1 minor factor.

Operative management as recommended by both versions of SCOPES was compared to the reference standard. The "accuracy" (agreement) indices of SCOPES were in terms of sensitivity, specificity, positive likelihood ratio and overall accuracy, with corresponding 95% confidence intervals (95% CI).

## Results

From October 1st, 2013 to September 30th, 2019 (6 years), there were 250 patients who were diagnosed with colonic injury. Of these, 39 patients were deemed eligible for the study by the inclusion and exclusion criteria. Two of 32 patients in the actual primary repair group developed anastomotic leakage. Two of 7 patients in the actual diversion group developed intraabdominal collection (See Table 1).

**Table 1** Clinical characteristics of patients (N = 39)

| Characteristics | Summary |
|---|---|
| **Age (years): mean (SD)** | 36.8 (16.0) |
| **Sex (male : female): number (%)** | 4 (10) : 35 (90) |
| **Underlying disease: number** | |
| Hypertension | 4 |
| Diabetes mellitus | 1 |
| Chronic obstructive pulmonary disease | 2 |
| Human immunodeficiency virus infection | 1 |
| **Colonic management: number (%)** | |
| Primary repair | 32 (82) |
| Diversion procedure | 7 (18) |

Peer review was done on 9 patients (7 in the actual diversion group and 2 in the actual primary repair group who had complications). Thus, the reference standard categories consisted of 32 appropriate primary repairs: 30 actual successful primary repairs and 1 actual repair with complications, along with 1 actual diversion in which peer review suggested primary repair; and 7 appropriate diversions: 6 actual diversions with 1 in which peer review suggested diversion in an actual primary repair with complications (See Table 2).

The accuracy indices for SCOPES version I were as follows. The sensitivity was 82% (95% CI: 63.6% to 92.8%); the specificity was 86% (95% CI: 42.1% to 99.6%); the positive likelihood ratio was 5.7 (95% CI: 0.92 to 35), which is a moderate effect; the positive predictive value was 96% (95% CI: 81.0% to 99.9%); and the accuracy 82% (95% CI: 66.5% to 92.5%) (See Table 3).

**Table 2** Comparison between actual management of patients and peer review (N = 39)

| | | Actual Colonic management | |
|---|---|---|---|
| | | Diversion procedure | Primary repair |
| Reference Standard (peer review) | Diversion procedure | 6 | 1 |
| | Primary repair | 1 | 31 |

**Table 3** SCOPES version I for primary repair (N = 39)

| | | Reference standard | | Sensitivity (for primary repair) | Specificity (for primary repair) | Accuracy (for primary repair) | Positive predictive value | LR+ |
|---|---|---|---|---|---|---|---|---|
| | | Diversion | Primary repair | | | | | |
| SCOPES version I | Diversion Procedure | 6 | 6 | 81% | 86% | 82% | 96% | 5.7 (moderate effect) |
| | Primary repair | 1 | 26 | | | | | |

LR+: positive likelihood ratio

The accuracy indices for SCOPES version II were as follows. The sensitivity was 43% (95% CI: 9.89% to 81.6%); the specificity was 100% (95% CI: 89.1% to 100%); the positive likelihood ratio was greater than 10 (i.e., not calculable due to 0 value in one cell); the positive predictive value was 100% (95% CI: 29.2% to 100%); and the accuracy 90% (95% CI: 75.8% to 97.1%). (See Table 4).

Both versions may potentially help surgeon make appropriate decisions in 74% of all patients (95% CI: 57.9% to 87.0%). This was the proportion of patients with only one factor present, or those with 2 or more major factors or with 1 major factor and at least 1 minor factor. The remaining 26% of patients were those with exactly 2 minor factors, in whom the decision to perform primary repair or colonic diversion may both be appropriate.

**Table 4** SCOPES version II for diversion procedure (N = 39)

| | | Reference standard | | Sensitivity (for diversion) | Specificity (for diversion) | Accuracy (for diversion) | Positive predictive value | LR+ |
|---|---|---|---|---|---|---|---|---|
| | | Diversion | Primary repair | | | | | |
| SCOPES version II | Diversion Procedure | 3 | 0 | 43% | 100% | 90% | 100% | > 10 (strong effect) |
| | Primary repair | 4 | 32 | | | | | |

LR+: positive likelihood ratio

## Discussion

The aim of the present study was to present accuracy indices (i.e., the agreement with peer-reviewed decisions) of SCOPES to aid in decision making in the treatment of patients with colonic injury due to trauma. Currently, meta-analyses and multicenter studies do not recommend routine diversion.[5,13,14,16-20] Colonic injuries are often managed on an individual-patient basis, with a wide variation in results, which may be due to the absence of management guidelines.[21] If these injuries are not treated appropriately, severe complications and even death can occur.

Controversy exists regarding the standard treatment for colonic injury in trauma.[20] SCOPES version I consisted of four factors: delayed time to surgery (greater than 6 hours), left sided colonic injury (grade 3 or more), gross fecal contamination, and concomitant duodenal or ureteral injury (grade 3 or more). If only one factor is present, primary repair is recommended. In the present study, SCOPES version I using this criterion had a sensitivity of 81%, specificity 86% for (peer-reviewed) primary repair, and a positive likelihood ratio of 5.7, which is a moderate increase in the likelihood of primary repair. The probability of an appropriate decision for primary repair for SCOPES version I when only one factor is present was 96%. Decision making using SCOPES version I was consistent with previous studies.[5,13,14,16]

SCOPES version II consisted of the same four factors as in SCOPES I, but delayed time to surgery and left sided colonic injury were considered minor factors, while gross fecal contamination and concomitant duodenal or ureteral injury were considered major factors. In the presence of 2 major factors or 1 major factor plus at least 1 minor factor, colonic diversion is recommended. SCOPES version II using these criteria had high specificity (100%), and possibly high positive likelihood ratio for the appropriate decision to perform colonic diversion. The probability of appropriate decision to perform colonic diversion using the SCOPES II criteria was 100%. Decision making using SCOPES II was also consistent with previous studies.[1,5,17-20]

Thus, SCOPES version I may assist in the decision to perform primary colonic repair, whereas SCOPES version II may assist in the decision to perform diversion procedures. Both versions may assist in correct decision making in 74% of all patients. However, 26% of patients will not be covered by both versions of SCOPES (i.e., those with 2 minor factors). Surgeons need to make their

own decisions by themselves in this situation, which is consistent with current recommendations.[14,21-22] SCOPES versions I and II are valid and possibly a useful and reliable tool for decision making in colonic injury due to trauma, perhaps more so than using clinical judgment alone.

## Conclusion

SCOPES versions I and II are expected to help surgeons make appropriate surgical decisions in colonic injury due to trauma. The present study also recommends that routine colostomy should not be performed.

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*บทคัดย่อ*

## Santichatngam's Colonic Injury Prediction Scores เพื่อช่วยตัดสินใจรักษาการบาดเจ็บของลำไส้ใหญ่

**ปริญญา สันติชาติงาม, พบ.**

*กลุ่มงานศัลยกรรม โรงพยาบาลมหาราชนครราชสีมา จังหวัดนครราชสีมา*

***ความเป็นมา:*** ภาวะการบาดเจ็บของลำไส้ใหญ่พบได้บ่อย การศึกษาในปัจจุบันไม่แนะนำให้ผ่าตัด routine colostomy การศึกษาของปริญญา สันติชาติงาม เผยแพร่ในปี 2560 ใช้ Santichatngam's Colonic Injury PrEdiction Score (SCOPES) ช่วยในการตัดสินใจในการผ่าตัดรักษา primary repair หรือ diversion การศึกษาต่อมาพบว่า SCOPES มี positive predictive value ต่ำ แต่มี sensitivity, specificity และ negative predictive value สูงในการแนะนำผ่าตัด primary repair วัตถุประสงค์ของการศึกษานี้มีขึ้นเพื่อศึกษาประโยชน์ของการใช้ SCOPES ทั้ง versions I และ II สำหรับผู้ป่วยที่มีการบาดเจ็บของลำไส้ใหญ่เกรด 3 หรือมากกว่า

***วิธีการศึกษา:*** ศึกษาย้อนหลังในผู้ป่วยที่ได้รับการรักษาที่โรงพยาบาลมหาราชนครราชสีมา ช่วงเวลา 1 ตุลาคม 2556 ถึง 30 กันยายน 2562 โดยนำ SCOPES ทั้ง 2 versions มาวิเคราะห์ ซึ่งพิจารณาจากปัจจัย 4 ประการ สำหรับ SCOPES version I หากพบว่ามีเพียง 1 ปัจจัย จะแนะนำ primary repair สำหรับ SCOPES versions II ถ้าพบว่ามีมากกว่า 1 major factor หรือพบ 1 major factor ร่วมกับ 1 minor factor หรือมากกว่า จะแนะนำผ่าตัด diversion

***ผลการศึกษา:*** สำหรับ SCOPES version I มีค่าความไว 81%, ความจำเพาะ 86%, positive likelihood ratio 5.7, positive predictive value 96%, ความแม่นยำ 82% สำหรับการผ่าตัด primary repair ส่วน SCOPES version II มีค่าความไว 43%, ความจำเพาะ 100%, positive likelihood ratio มากกว่า 10, positive predictive value 100%, ความแม่นยำ 90% สำหรับผ่าตัด diversion การใช้ SCOPES อาจช่วยตัดสินใจในการรักษาผู้ป่วยบาดเจ็บลำไส้ใหญ่ได้ถึง 74%

***สรุปผลการศึกษา:*** ผลการศึกษานี้แสดงให้เห็นว่า SCOPES อาจเหมาะสมและได้ประโยชน์ สำหรับนำไปใช้ประกอบการตัดสินใจผ่าตัดการบาดเจ็บลำไส้ใหญ่ โดยอาจมีข้อดีเหนือกว่าการใช้วิจารณญาณทางคลินิกเพียงอย่างเดียว

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Original Article

# *Outcome of Parathyroidectomy for Renal Hyperparathyroidism : a Single-Center Experience*

**Kreangsak Chainapapong, MD**

*Department of Surgery, Chonburi Hospital, Chonburi, Thailand*

***Abstract***

***Objective:*** To evaluate and compare early and long-term outcomes and of total (TPTX) and partial parathyroidectomy (PPTX) operations in the management of patients with resistant renal hyperparathyroidism (rHPT) at Chonburi Hospital, Thailand.

***Methods:*** A single center retrospective medical record review of parathyroidectomy, with or without autotransplantation (AT), from 1 January 2012 to 31 March 2021 was performed.

***Results:*** A total of 110 patients were operated on for rHPT during the study period. The preoperative parathyroid hormone (PTH) levels were markedly high in both groups. Preoperative parathyroid localization was performed in less than 50% of cases. Eighty-four received TPTX, with or without AT, and 26 received PPTX. The average post-operative PTH levels at 24 hours, at 1, 3, 6 and 12 months after operation in TPTX group were significant lower compared with those of the PPTX group. Postoperative blood calcium levels (48 hours after operation) were found to be very low in both groups. Postoperative phosphate level (48 hours after operation) in the TPTX group returned to normal, while it remained elevated in PPTX group. Overall complications of either operation were very low. Eight patients in the PPTX group required reoperation for persistent hyperparathyroidism resistant to non-operative treatment. Five patients had successful primary operations. The remaining 18 PPTX cases continued medical treatment. Sixty patients received TPTX without AT and 24 patients received TPTX with AT. The blood PTH levels of those who had TPTX with AT tended to be higher than that of those who had TPTX without AT at 1, 3, 6 and 12 months after operation, but without statistical significance. Five of 24 patients (20%) who had TPTX with AT experienced recurrent HPT, while none of those who had TPTX without AT did. Two patients with recurrent HPT received autografectomy. Persistent hypoparathyroidism (PTH < 10 pg/mL) was found 10 patients (16%) who had TPTX without AT, but did not occur in any case of TPTX with AT, with a follow up of more than 12 months.

***Conclusion:*** Total parathyroidectomy with or without autotransplantation is the operation of choice for rHPT. The experience of the surgeon is the most important factor for operative success.

***Keywords:*** Secondary hyperparathyroidism, Renal hyperparathyroidism, Total parathyroidectomy, Partial parathyroidectomy, Autotransplantation, Outcome

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***Corresponding author:*** Kreangsak Chainapapong, MD, Surgical Unit of Chonburi Hospital, 69 Moo 2 Sukhumvit Rd, Tambon Ban Suan, Amphoe Mueang Chonburi, Chonburi Province, Thailand 20000; Telephone (office): +66 3893 1203, Mobile phone: +66 93 102 9554; E-mail: kreangsakchainapapong@gmail.com

## Introduction

End-stage renal disease (ESRD) is a common condition. Most patients with ESRD develop renal hyperparathyroidism (rHPT). Renal HPT results from long-term parathyroid hyperplasia, which can become functionally independent adenomas. Renal HPT can lead to high-turnover bone disease, interstitial and vascular calcifications and as well as cardiovascular diseases. The current treatment of rHPT is mainly medical, by using oral calcimimetic drugs.[1-3] However, some patients will develop resistance to medications.

Approximately 1 to 2% of patients with ESRD require parathyroidectomy. Surgical treatment is recommended for patients with parathyroid hormone (PTH) levels higher than 800 pg/mL, those with severe symptoms (bone pain, pruritus, calciphylaxis), serum calcium level over 11 mg/dL, and soft tissue calcification.[4,5] One study of rHPT showed significantly improvement in bone density after parathyroidectomy,[5] and a few studies showed benefit of surgery for patients with calciphylaxis.[3] In a study of patients with rPTH who underwent parathyroidectomy, the average hemoglobin level also increased from from 8.6 g/mL to 9.4 g/mL.[6]

Types of parathyroidectomy include: subtotal parathyroidectomy (removal of 3½ glands) with or without bilateral cervical thymectomy (BCT), total parathyroidectomy (TPTX) with or without autotransplantation (AT) at the nondominant forearm and with or without BCT.[7,8] There is no consensus on the best procedure. TPTX with AT by an experienced surgeon is an effective long-term treatment, which can stabilize PTH, calcium and phosphate levels. The incidence of recurrent hyperparathyroidism at the site of implantation is 7 to 9%. Autografectomy may be needed when the PTH level is greater than 800 pg/mL, with lack of response to medical therapy, and detectable hypertrophy of the implanted tissue.[5]

Preoperative sestamibi (MIBI) scanning of the parathyroid glands in rHPT varies greatly in sensitivity and specificity. A 2012 meta-analysis reported 58% sensitivity and 93% specificity. More recent studies have showed 43% to 88% sensitivity and 60 to 75% specificity.[9,10] Combined sestamibi/CT has greater sensitivity than sestamibi alone, but performs poorly in identifying ectopic glands.10 Many surgeons also use ultrasonography to help identify parathyroid glands in the neck, but its accuracy is extremely variable and likely user-dependent.[9-11]

## Patients and Methods

A single-center medical record review of patients who underwent parathyroidectomy for rHPT with or without AT, from 1 January 2012 to 31 March 2021, was performed. All patients were operated on by the author. Patients who were candidates for kidney transplantation received TPTX with AT. Patients who required life-long dialysis received TPTX without AT. A total of 110 patients were included in the present study. Preoperative MIBI scan, computerized tomography (CT) or unltrasonography of the neck were not routinely performed. Data collected included preoperative and postoperative PTH, serum calcium, and phosphate levels, as well as operative complications.

Surgical indications for parathyroidectomy followed existing guidelines as well as expert opinions. These included severe hyperparathyroidism (HPT) refractory to medical treatment (e.g., PTH level greater than 800 pg/mL, hypercalcemia and hyperphosphatemia), intolerance to medical therapy, severe symptomatic HPT including intractable bone pain, pruritus, osteoporosis, calciphylaxis, erythropoietin-resistant anemia and dilated cardiomyopathy.[12-14]

Adequate hemodialysis was performed 24 hours before surgery. Intraoperative frozen section examination of the all parathyroid glands was performed in all cases. All patients received bilateral neck exploration and at least 4 parathyroid glands were removed. Intraoperative serum PTH level measurement was not performed due to lack of availability in this hospital setting. Parathyroid tissue which was normal in appearance was minced into smaller pieces 1 mm to 3 mm in size, and reimplanted intramuscularly into the non-dominated forearm (usually the brachioradialis muscle). Cryopreservation of parathyroid tissues was not performed.

PTH levels were obtained for all patients on the first postoperative day, and calcium and phosphate levels were checked 24, 48, and 72 hours after operation. Recurrent HPT was defined as a new onset of PTH level 9 times the upper limit of normal during follow-up, and permanent hypoparathyroidism was defined as postoperative PTH level less than 10 pg/mL for over 6 months. Indication for autografectomy was based on a PTH level greater than 800 pg/ml without responding to medical treatment, and hypertrophy of the implanted parathyroid tissue.

Data analysis was done using STATA version 15.0

(Stata Corp, College Station, TX, USA). Quantitative data were contrasted using unpaired t test, while Chi-square or Fisher's exact test was used for categorical data. A *p*-value of less than 0.05 was considered statistically significant.

## Results

There were 110 patients who were operated on for rHPT during the years 2011 to 2021 in our hospital. TPTX was performed on 84 patients (4 glands were removed) and 26 patients underwent PPTX (less than 4 glands removed). In the PPTX group, 8 patients underwent re-exploration of the neck, and 5 were successful. The remaining (18 PPTX patients) received medical treatment (see Figure 1). Patients in both TPTX and PPTX groups were similar in terms of gender, age, preoperative PTH, calcium and phosphate levels (see Table 1). Preoperative PTH levels were markedly high in both groups. The average postoperative PTH level at 24 hours after operation was significantly lower in

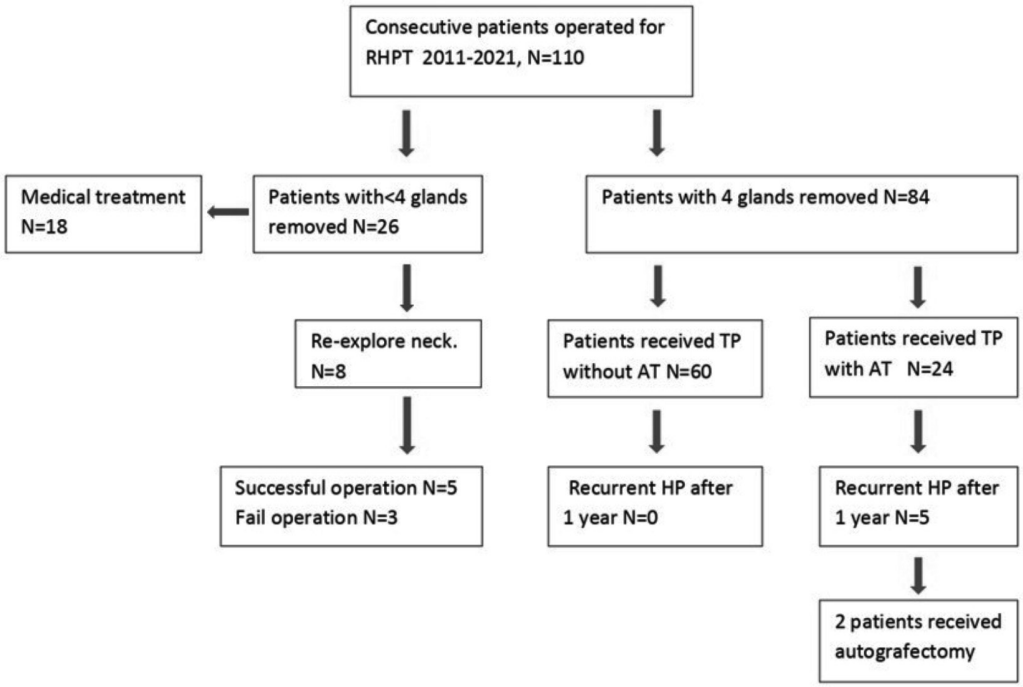


**Figure 1** Chart of patient flow in the study; RHPT: renal hyperparathyroidism; TP: total parathyroidectomy; AT: autotransplantation; HP: hyperparathyroidism

**Table 1** Comparing preoperative baseline characteristics of patients undergoing total parathyroidectomy (TPTX) and partial parathyroidectomy (PPTX).

| | TPTX N = 84 | PPTX N = 26 | *p*-value |
|---|---|---|---|
| Men: no. (%) | 34 (40) | 12 (46) | 0.608 |
| Women: no. (%) | 50 (60) | 14 (54) | |
| Age (years): mean ± sd | 50.7 ± 12.8 | 49 ± 14.3 | 0.566 |
| Hemodialysis: no. (%) | 79 (94) | 26 (100) | 0.337 |
| Pre-PTH (pg/mL): mean ± sd | 1527.1 ± 621.4 | 1593.9 ± 836.2 | 0.809 |
| Pre-calcium (mg/dL): mean ± sd | 9.7 ± 0.92 | 9.5 ± 0.46 | 0.289 |
| Pre-phosphate (mg/dL): mean ± sd | 6.5 ± 1.9 | 6.6 ± 1.9 | 0.815 |

Pre-PTH: preoperative parathyroid hormone level; Pre-calcium: preoperative calcium level; Pre-phosphate: preoperative phosphate level; no.: number; sd: standard deviation

Normal range of serum parathyroid hormone level is 16-65 pg/mL; calcium level is 8.6-10.2 mg/dL; phosphate level is 3.5-5.2 mg/dL.

the TPTX group. Average postoperative PTH levels at 1, 3, 6 and 12 months were also significantly lower in the TPTX group (see Table 2). Postoperative calcium levels at 48 hours were very low in both groups and some patients had symptoms of hypocalcemia which required intravenous infusion of calcium. Postoperative phosphate levels in the TPTX group returned to normal, but were more likely to remain high in the PPTX group. Very few operative complications occurred in either group (see Table 2).

Sixty patients underwent TPTX without AT and 24 patients underwent TPTX with AT. There were no significant differences in terms of gender, age, type of dialysis, preoperative PTH and postoperative PTH levels. The average PTH levels in the TPX with AT group were higher than those in the TPX without AT group at 1, 3, 6 and 12 months after operation, but these differences were not statically significant. Patients in the TPTX without AT group had no recurrence of HPT, whereas 5 of 24 patients (20%) in the TPX with AT group had recurrent HPT within 12 months of the operation. Two patients received autografectomy under local anesthesia. Persistent hypoparathyroidism was seen in 10 cases in the TPTX without AT group, but none in the TPTX with ATgroup within a follow up time of more than 12 months (see Tables 3 and 4).

**Table 2** Comparing postoperative laboratory values between patients undergoing total parathyroidectomy (TPTX) and partial parathyroidectomy (PPTX).

| | TPTX N = 84 | PPTX N = 26 | *p*-value |
|---|---|---|---|
| Post-PTH (24 hours) | 40.9 ± 40.3 | 564.9 ± 439.3 | < 0.001 |
| 1 month-PTH | 104 ± 289.6 | 618 ± 707.7 | < 0.001 |
| 3 months-PTH | 122 ± 456.4 | 666 ± 919.1 | < 0.001 |
| 6 months-PTH | 104 ± 218.1 | 1010 ± 2653.3 | 0.002 |
| 12 months-PTH | 219 ± 872.1 | 786 ± 1538.2 | 0.019 |
| Post-calcium (48 hours) | 6.7 ± 1.0 | 6.9 ± 1.3 | 0.410 |
| Post-phosphate (48 hour) | 3.5 ± 1.5 | 5.0 ± 2.2 | < 0.001 |
| Post-operative complications | | | |
| RLN injury: number | 1 | 0 | |
| Neck hematoma: number | 1 | 0 | |
| Intrahospital mortality: number | 0 | 0 | |

Post-PTH (24 hours): parathyroid hormone level at 24 hours after operation; post-calcium (48 hours): calcium level at 48 hours after operation; RLN = recurrent laryngeal nerve; units for PTH levels are pg/dL; units for calcium and phosphate levels are mg/dL; all are displayed as mean ± standard deviation unless stated otherwise.

**Table 3** Comparing preoperative baseline characteristics of patients undergoing total parathyroidectomy (TPTX) with and without autotransplantation (AT).

| | TPTX without AT N = 60 | TPTX with AT N = 24 | *p*-value |
|---|---|---|---|
| Men: no. (%) | 20 | 14 | 0.035 |
| Women: no. (%) | 40 | 10 | |
| Age (years): mean ± sd | 51.7 ± 13.4 | 48.3 ± 13.7 | 0.230 |
| Hemodialysis: no. (%) | 54 | 24 | 0.176 |
| Pre-PTH (pg/dL): mean ± sd | 1506.9 ± 652.8 | 1577.5 ± 544.8 | 0.641 |
| Pre-calcium (mg/dL): mean ± sd | 9.7 ± 0.77 | 9.5 ± 0.88 | 0.305 |
| Pre-phosphate (mg/dL): mean ± sd | 6.5 ± 2.2 | 6.6 ± 1.4 | 0.837 |

Pre-PTH: preoperative parathyroid hormone level; Pre-calcium: preoperative calcium level; Pre-phosphate: preoperative phosphate level; no.: number; sd: standard deviation

Normal range of serum parathyroid hormone level is 16-65 pg/mL; calcium level is 8.6-10.2 mg/dL; phosphate level is 3.5-5.2 mg/dL.

**Table 4** Comparing laboratory values of patients undergoing total parathyroidectomy (TPTX) with and without autotransplantation (AT)

| | TPTX without AT N = 60 | TPTX with AT N = 24 | *p*-value |
|---|---|---|---|
| Post-PTH (24hours) | 43.1 ± 45.9 | 35.3 ± 21.8 | 0.429 |
| 1 month-PTH | 54.9 ± 94.9 | 171.4 ± 341.1 | 0.017 |
| 3 months-PTH | 63.7 ± 159.6 | 240.1 ± 692.6 | 0.065 |
| 6 months-PTH | 78.4 ± 199.1 | 137.6 ± 214.1 | 0.232 |
| 12 months-PTH | 167.0 ± 928.4 | 289.7 ± 773.5 | 0.569 |
| Post-calcium (48 hour) | 6.9 ± 1.0 | 6.4 ± 1.1 | 0.063 |
| Post-phosphate (48 hour) | 3.4 ± 1.6 | 3.9 ± 1.6 | 0.199 |
| Recurrent HPT: number | 0 | 5 | |
| Persistent Hypo-PT: number | 10 | 0 | |
| Autografectomy: number | 0 | 2 | |

Post-PTH (24 hours): parathyroid hormone level at 24 hours after operation; post-calcium (48 hours): calcium level at 48 hours after operation; HPT: hyperparathyroidism; Hypo-PT: hypoparathyroidism; units for PTH levels are pg/dL; units for calcium and phosphate levels are mg/dL; all are displayed as mean ± standard deviation unless stated otherwise

Preoperative parathyroid localization including MIBI scan, CT scan and ultrasonography of the neck was not routinely performed, and was used in less than half of patients. Most of these investigations were requested by the consultant nephrologist or endocrinologist. There were only 5 patients for whom imaging studies could detect 4 parathyroid glands. In no patient was any ectopic parathyroid gland detected (see Table 5).

**Table 5** Preoperative parathyroid gland localization

| Imaging procedure | All patients: Number | Identified 4 glands: Number | Identified < 4 glands: Number |
|---|---|---|---|
| Ultrasonography | 26 | 3 | 23 |
| CT scan | 23 | 2 | 21 |
| MIBI scan | 1 | 0 | 1 |
| None | 60 | - | - |

## Discussion

As mentioned previously, parathyroid surgery for rHPT includes PPTX with or without bilateral cervical thymectomy (BCT), TPTX with or without autotransplantation (AT) at the nondominant forearm and with or without BCT.[3,14,15] At Chonburi Hospital, TPTX with or without AT is routinely performed. BCT was done in cases of PPTX (less than 4 parathyroid glands removed). A previously reported randomized controlled trial showed that TPTX with AT significantly decreases the rate of HPT recurrence, normalizes the serum calcium, and improves clinical signs such as pruritus when compared with subtotal PTX.[16]

Several retrospective case series and cohort studies found that the rate of recurrent or persistent HPT and permanent hypoparathyroidism ranged between 0 to 12% and 2 to 17% for PPTX, respectively. For TPTX with AT, these rates varied between 0 to 10% and 0 to 85% respectively. The actual rates of persistent HPT (defined as occurring within 6 months of surgery) and recurrent HPT (occurring over 6 months after surgery) are very difficult to estimate as studies have used variable cutoffs in defining these conditions. These cutoffs are significantly more conservative than those of the Kidney Disease Improvng Global Outcomes (KDIGO) guideline that only requires the PTH level to be maintained under 9-fold the upper limit of normal (at Chonburi hospital, a 9-fold upper limit would be 614.7 pg/mL, since the upper

limit of normal is 68.3 pg/mL) and persistent postoperative hypoparathyroidism to have values of PTH levels less than 10 pg/mL after 6 months.[17,18] In the present study the rate of recurrent HPT was 20% (5 cases) in the TPTX with AT group, but there was no recurrence in the TPTX without AT group after 1 year follow up. However, there was a high incidence of hypoparathyroidism (16%). Therefore, patients who are candidates for kidney transplantation should be recommended TPTX with AT to avoid permanent hypoparathyroidism.

In a review of anatomic and functional studies, supernumerary parathyroid glands occur in up to 33% of patients, especially in men.[19] A study recommended more extensive operation including all 4 parathyroid gland removal, bilateral thymectomy and bilateral central neck dissection (level VI).[20] The results of this study showed the disease did not persist in 91% of patients and the operation had low complications. The present author would consider performing more extensive operations, especially including bilateral cervical thymectomy, for further improvement of results.

Postoperative hypocalcemia almost always occur after TPTX, but only some patients will have symptoms and signs of hypocalcemia. These patients would require calcium supplement by oral and intravenous route. Calcium level should normalize within 2 to 3 months after surgery. Phosphate levels usually return to normal within 24-72 hours.

## Conclusion

From the present case series of rHPT at a single tertiary hospital, total parathyroidectomy with or without autotransplantation has remained the operation of choice. The operation is safe, with good results. Routine preoperative localization of the parathyroid glands does not appear necessary. An experienced surgeon is still the most important factor in a successful parathyroidectomy.

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## *บทคัดย่อ* ผลการรักษาโรคพาราไทรอยด์ฮอร์โมนสูงจากภาวะไตวายระยะสุดท้ายด้วยการผ่าตัดต่อมพาราไทรอยด์ของโรงพยาบาลชลบุรี

**เกรียงศักดิ์ ชัยนาภาพงษ์, พบ.**
*กลุ่มงานศัลยกรรม โรงพยาบาลชลบุรี จังหวัดชลบุรี*

***ความเป็นมา:*** ภาวะพาราไทรอยด์ฮอร์โมนสูงจะพบร่วมกับไตวายเรื้อรังระยะสุดท้าย การรักษาหลักคือการล้างไตและการให้ยาเพื่อลดระดับฮอร์โมน จะมีผู้ป่วยบางรายที่ล้มเหลวจากการให้ จำเป็นต้องผ่าตัดเอาต่อมพาราไทรอยด์ออกหมดเพื่อลดระดับฮอร์โมน

***วัตถุประสงค์:*** เพื่อศึกษาผลการรักษาการผ่าตัดต่อมพาราไทรอยด์ ผู้ป่วยภาวะไตวายเรื้อรังระยะสุดท้ายของโรงพยาบาลชลบุรี

***ผลการศึกษา:*** ผู้ป่วยพาราไทรอยด์ฮอร์โมนสูงจากไตวายทั้งหมด 110 คน ได้รับการผ่าตัดระหว่างปี 2011-2020 ผู้ป่วย 84 คนได้รับการผ่าตัดเอาต่อมพาราไทรอยด์ออกทั้งหมด (4 ต่อม) และ 26 คน ได้รับการผ่าตัดต่อมพาราไทรอยด์ออกบางส่วน (น้อยกว่า 4 ต่อม) ในกลุ่มนี้มี 8 คนได้รับการผ่าตัดซ้ำ และพบว่ามี 5 คนที่ผ่าตัดสำเร็จ ส่วนผู้ป่วยที่เหลือ (18 คน) ได้รับการรักษาแบบให้ยา กลุ่มที่ผ่าต่อมพาราไทรอยด์ออกทั้งหมดพบว่ามีระดับฮอร์โมนพาราไทรอยด์หลังผ่าตัดต่ำกว่าอย่างมีนัยสำคัญทางสถิติ ระดับแคลเซียมของทั้งสองกลุ่มต่ำมากหลังผ่าตัด 48 ชั่วโมง ส่วนระดับฟอสเฟตพบกลับมาเป็นปกติในกลุ่มที่ผ่าตัดต่อมพาราไทรอยด์ออกได้หมด พบภาวะแทรกซ้อนจากการผ่าตัดอยู่ในระดับต่ำ

ผู้ป่วย 60 คนได้รับการผ่าตัดต่อมพาราไทรอยด์ออกทั้งหมดและไม่ได้รับการฝังเนื้อเยื่อ และ 24 คนได้รับการผ่าตัดต่อมพาราไทรอยด์ออกทั้งหมดร่วมกับการฝังเนื้อเยื่อพาราไทรอยด์ที่แขน ระดับพาราไทรอยด์หลังผ่าตัดในกลุ่มที่ฝังเนื้อเยื่อที่แขน มีค่าเฉลี่ยสูงกว่ากลุ่มที่ไม่ฝังเนื้อเยื่อที่แขนที่ระยะเวลา 1, 3, 6 และ 12 เดือน แต่ไม่มีนัยยะสำคัญทางสถิติ และพบการกลับมาเป็นใหม่ของโรคพาราไทรอยด์ฮอร์โมนสูงในกลุ่มที่ฝังเนื้อเยื่อที่แขน 5 ราย (20%) และพบภาวะพาราไทรอยด์ฮอร์โมนต่ำ 16% (10 ราย) ในกลุ่มที่ไม่ได้ฝังเนื้อเยื่อที่แขนหลังจากติดตามอาการมากกว่า 12 เดือน

การหาตำแหน่งต่อมพาราไทรอยด์ก่อนการผ่าตัดพบว่ามีโอกาสพบทั้ง 4 ต่อมหรือต่อมที่อยู่ผิดที่ (ectopic) น้อยมาก

***สรุปผลการศึกษา:*** การผ่าตัดต่อมพาราไทรอยด์ออกหมดร่วมกับการฝังและไม่ฝังเนื้อเยื่อที่แขนให้ผลการรักษาที่ดีในผู้ป่วยไตวายที่มีภาวะพาราไทรอยด์ฮอร์โมนสูง มีภาวะแทรกซ้อนต่ำ การหาตำแหน่งต่อมพาราไทรอยด์ก่อนการผ่าตัดไม่มีความจำเป็น

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Original Article

# *Outcomes of Tissue versus Mechanical Valve Replacement for Infective Endocarditis*

**Komkrit Komuttarin, MD**
**Nisit Poolthananant, MD**
*Cardiothoracic Unit, Department of Surgery, Maharat Nakhon Ratchasima Hospital, Nakhon Ratchasima, Thailand*

***Abstract***

***Objective:*** There is no consensus regarding the best prosthetic valve for patients with infective endocarditis (IE). The aim of the present study was to compare short and long-term outcomes of tissue versus mechanical valve replacement in patients with left-sided severe IE.

***Methods:*** A retrospective medical chart review of IE patients treated between January 1st, 2008 and September 30th, 2020 was performed. Patients were categorized into two groups according to the type of prosthetic valve used (tissue or mechanical). Outcomes included in-hospital mortality, recurrent infection, reoperation and long-term survival.

***Results:*** There were 147 patients. The overall in-hospital mortality was 17%. The in-hospital mortality rate was 27% and 14% for patients undergoing tissue and mechanical valve replacement, respectively. The recurrent infection rate was 3% and reoperation rate was 1%. The 5-year survival for patients in the tissue valve group was 71.4% (95% CI: 53.4% to 83.5%) and for the mechanical valve group, 81.5% (95% CI: 72.4% to 87.8%).

***Conclusion:*** Mechanical prosthetic valve replacement in left-sided active endocarditis had better in-hospital mortality and long-term survival than tissue valve replacement, although the preoperative status of patients in the tissue valve group was worse. However, the recurrence rate was low and long-term survival was good for both groups.

***Keywords:*** Infective endocarditis, Prosthetic valve, Tissue valve, Mechanical valve

## Introduction

The choice of prosthetic valve for patients with active infective endocarditis (IE) is controversial. Long-term results are unknown. In Thailand, the incidence of IE is 5.7 per 1,000 admissions.[1] The incidence is 4 per 1000 admissions in the Northeastern region of Thailand.[2] In hospital mortality for active IE is 15% to 20%, and can be as high as 40%.[3] Modern management focuses on early surgery without 4 to 6 weeks of antibiotics. Although preoperative antibiotics did not affect in-hospital mortality and recurrence,[4] the placement of foreign body in patients who have active infection,[5] which may prevent further infection, can also increase the risk of reinfection and mortality.[6-8] Early mortality of surgery in active IE is 5% to 26%.[9-14]

The principle of surgery is radical debridement,

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***Corresponding author:*** Komkrit Komuttarin, MD, Cardiothoracic unit, Department of Surgery, Maharat Nakhon Ratchasima Hospital 49, Chang Phueak Rd, Mueang District, Nakhon Ratchasima Province; Tel: :+66 4423 5469, Fax: +66 4424 6389; Email: tuo2323@hotmail.com

which decreases the possibility of valve repair, and most patients end up with valve replacement. Guidelines from the American Association for Thoracic Surgery (AATS), the American College of Cardiology/American Heart Association (ACC/AHA) and the European Society of Cardiology (ESC) recommend mechanical valves in patients younger than 60 to 65 years and tissue valves in those 60 to 65 years or older. There is a gray zone between 50 to 70 years where there is no conclusion regarding the most suitable choice of prosthetic valve.[3,15-17] Theoretically, tissue valve is more likely to be infected whereas the mechanical valve is more resistant to infection. Tissue valves also has a tendency towards early degeneration.[18,19]

Most studies of active IE are observational and conducted at single centers in European countries and North America, and are less likely to involve Asian populations.[20] Different regions of the world have different patient characteristics and risk factors. Many reports were from over 10 years ago. Several of these included both active IE and healed IE. The aim of the present study was to determine more recent short and long-term outcomes of mechanical and tissue valve replacement in patients with left-sided active infective endocarditis of the native valve.

## Patients and Methods

Patients over 18 years who were diagnosed with left-sided native valve active infective endocarditis according to the modified Duke's criteria who underwent valve replacement at Maharat Nakhon Ratchasima hospital between Jan 1st, 2008 and Sep 30th, 2020 were included in the study. The definition of active endocarditis included the presence of wet vegetation, presence of valvular abscesses seen on echocardiogram or during surgery, presence of fever, leukocytosis, positive blood culture or tissue culture, valvular inflammation with PMN predominance and duration of antibiotics use of less than 4 to 6 weeks.[21-24] Patients with prosthetic valve infection or those who had both tissue and mechanical valve replacement were excluded.

This study was approved by the Maharat Nakhon Ratchasima Institutional Review Board (MNRH IRB). Patients were categorized into two groups according to the type of prosthetic valve received (mechanical or tissue). Early outcomes included in-hospital mortality, ICU stay, postoperative stay and complications. Long term outcomes included 5-year survival, the reinfection rate and reoperation rate. All survivors were followed from hospital discharge after surgery till Oct 31th, 2020. The cause of mortality was determined from medical records or from the civil registration.

All patients were managed by an IE Multidisciplinary Team. Preoperative echocardiography (transthoracic or transesophageal, TTE or TEE, respectively) was performed on every patient. Preoperative coronary angiography was performed in patients who were 40 years or older. We performed surgery via full sternotomy with standard cardio-pulmonary bypass under mild to moderate hypothermia. Cold blood cardioplegia was used for myocardial protection. The prosthetic valves used were selected according to patient preference or the decision of the surgeon. Patients were transferred to the ICU for postoperative care. Antibiotics was used under supervision of infectious disease specialists.

Quantitative variables were summarized as mean and standard deviation (SD), or median and interquartile range (IQR) as appropriate. Categorical data were summarized as frequency and percentage. Average survival was estimated using the Kaplan-Meier method, along with 95% confidence intervals. Stata statistical software (Stata Corp, College Station, TX, USA) was used for data analysis.

## Results

There were 147 patients in the study, with 37 patients in the tissue valve group and 110 patients in mechanical valve group. Table 1 shows the characteristics of patients in the study. Most patients had definite IE (99%) and received TTE (88%). The average age was 45.4 years, and was higher in the tissue valve group than the mechanical valve group. Most patients in both groups were male. Associated diseases included: hypertension (HT; 13%), rheumatic heart disease (10%), and diabetes mellitus (DM; 6%). The prevalence of HT, coronary artery disease, renal failure, and stroke was higher in the tissue valve group, whereas the prevalence of DM, rheumatic heart disease, previous cardiac surgery and congenital heart disease was higher in mechanical valve group.

Two patients in mechanical valve group had end-stage renal disease (ESRD) requiring long-term hemodialysis before surgery. Two patients in the mechanical valve group had previous cardiac surgery (PBMV and MVR), and 4 had associated congenital heart disease (mostly VSD).

**Table 1** Patient and disease characteristics, operations and complications

| Characteristics / Operations | Total (n = 147) | Mechanical (n = 110) | Tissue (n = 37) |
|---|---|---|---|
| **Age (years): mean (SD)** | 45.4 (13.6) | 41.9 (12.2) | 55.9 (12.4) |
| **Men: number (%)** | 103 (70) | 76 (69) | 27 (73) |
| **Comorbid: number (%)** | | | |
| DM | 9 (6) | 7 (6) | 2 (5) |
| HT | 19 (13) | 10 (9) | 9 (24) |
| Serum Cr > 2 mg/dL | 3 (2) | 2 (2) | 1 (3) |
| Coronary artery disease | 5 (3) | 1 (1) | 4 (11) |
| Stroke | 5 (3) | 3 (3) | 2 (5) |
| COPD | 4 (3) | 2 (2) | 2 (5) |
| Rheumatic | 15 (10) | 14 (13) | 1 (3) |
| Previous cardiac surgery | 2 (1) | 2 (2) | 0 |
| Congenital heart disease | 6 (4) | 5 (5) | 1 (3) |
| **Laboratory finding: number (%)** | | | |
| WBC > 15,000 | 5 (3) | 4 (4) | 1 (3) |
| Albumin < 3 gm/d | 75 (52) | 56 (51) | 19 (53) |
| Hct < 30% | 68 (47) | 47 (43) | 21 (57) |
| Cr clearance < 50% | 48 (33) | 26 (24) | 22 (60) |
| EF < 40% | 5 (3) | 3 (3) | 2 (5) |
| **Euroscore II: median (IQR)** | 6.9 (3.6-16) | 5.8 (2.9-12) | 13.5 (5.1-25) |
| **Echocardiography: number (%)** | | | |
| TEE | 18 (12) | 14 (13) | 4 (11) |
| TTE | 129 (88) | 107 (87) | 33 (89) |
| **Vegetation size (mm): mean (SD)** | 13.7 (7.1) | 14.3 (7.6) | 12.2 (5.6) |
| < 10 | 26 (20) | 19 (20) | 7 (22) |
| 10 - 15 | 63 (50) | 46 (48) | 17 (53) |
| > 15 | 38 (30) | 30 (32) | 8 (25) |
| **Microorganisms: number (%)** | 86 (63) | 68 (67) | 18 (50) |
| Staphylococcus aureus | 10 (7) | 9 (8) | 1 (3) |
| Staphylococcus epidermidis | 2 (1) | 2 (2) | 0 |
| Coagulase-neg staphylococci | 5 (3) | 4 (4) | 1 (3) |
| Streptococcal group | 58 (40) | 45 (41) | 13 (35) |
| Enterococcus species | 3 (2) | 2 (2) | 1 (3) |
| **Positive tissue culture: number (%)** | 13/77 (17) | 11/60 (18) | 2/17 (12) |
| **Diagnosis of IE: number (%)** | | | |
| Definite IE | 145 (99) | 108 (98) | 37 (100) |
| Possible IE | 2 (1) | 2 (2) | 0 |
| **Site of infection: number (%)** | | | |
| AV | 74 (50) | 54 (49) | 20 (54) |
| MV | 40 (27) | 32 (29) | 8 (22) |
| AV+MV | 28 (19) | 20 (18) | 8 (22) |
| MV+TV | 3 (2) | 3 (3) | 0 |
| AV+TV | 1 (1) | 1 (1) | 0 |
| AV+MV+TV | 1 (1) | 0 | 1 (3) |

**Table 1** (cont.) Patient and disease characteristics, operations and complications

| Characteristics / Operations | Total (n = 147) | Mechanical (n = 110) | Tissue (n = 37) |
|---|---|---|---|
| **Operation procedure: number (%)** | | | |
| AVR | 49 (33) | 38 (35) | 11 (30) |
| MVR | 38 (26) | 31 (28) | 7 (19) |
| AVR+MVR | 29 (20) | 21 (19) | 8 (22) |
| AVR+TV repair | 2 (1) | 2 (2) | 0 |
| MVR+TV repair | 14 (10) | 11 (10) | 3 (8) |
| AVR+MV repair | 10 (7) | 3 (3) | 7 (19) |
| AVR+MVR+TV repair | 3 (2) | 3 (3) | 0 |
| AVR+MVR+TVR | 2 (1) | 1 (1) | 1 (3) |
| **Complication: number (%)** | | | |
| Stroke | 15 (10) | 12 (11) | 3 (8) |
| Transient ischemic attack | 3 (2) | 2 (2) | 1 (3) |
| Prolong fever | 10 (7) | 7 (6) | 3 (8) |
| Acute renal failure | 35 (24) | 24 (22) | 11 (30) |
| Splenic abscess | 1 (1) | 1 (1) | 0 |
| Pericardial effusion | 1 (1) | 0 | 1 (3) |
| Limb ischemia | 7 (5) | 5 (5) | 2 (5) |
| Post-op bleeding | 5 (3) | 4 (4) | 1 (3) |
| Arrhythmia | 38 (26) | 29 (26) | 9 (24) |
| Pleural effusion | 16 (11) | 10 (9) | 6 (16) |
| Pneumonia | 18 (12) | 11 (10) | 7 (19) |

SD: standard deviation; DM: diabetic mellitus; HT: hypertension; EF: ejection fraction; WBC: white blood cell count; Cr: creatinine; TEE: transesophageal echocardiography; TTE: transthoracic echocardiography; IQR: interquartile range; Hct: hematocrit; AV: aortic valve; MV: mitral valve; TV: tricuspid valve

In the tissue valve group, hypoalbuminemia, anemia and severe renal impairment was more frequent and the median Euroscore II was higher. Most vegetation size was 10 mm or larger. In the mechanical valve group, vegetation size was larger than in the tissue valve group.

Positive blood culture was present preoperatively in 86 patients (63%). There was no record of preoperative blood cultures in 10 patients. Streptococcus group is the most common pathogen in both groups. Intraoperative tissue culture was performed on 77 patients, of which 13 were positive (17%). In the mechanical valve group, 11 (18%) cultures were positive, which was more than in the tissue valve group (2 patients, 12%). The infection mostly involved a single valve. The most common site of infection was the aortic valve. There were multivalvular involvement in 33 cases (22%). There was trivalvular involvement in one patient in the tissue valve group.

The most common operation was a single valve operation (59%). The most common was aortic valve replacement (AVR; 33%), followed by mitral valve replacement (MVR; 26%). AVR and MVR were more common in the mechanical valve group. In the tissue valve group, multiple valve operations were necessary in 51%, which included AVR and MVR, AVR plus mitral valve repair (MV repair), and combined AVR, MVR plus tricuspid valve surgery (TV surgery). TV surgery was required in 15% of patients in the mechanical valve group, and in 11% in the tissue valve group.

The most common arrhythmia was atrial fibrillation. Twenty-two patients required postoperative dialysis, most of which was peritoneal dialysis. Five patients had postoperative bleeding requiring reoperation. The incidence of postoperative transient ischemic attack, prolonged fever, acute renal failure, pericardial effusion, limb ischemia, pleural effusion and pneumonia was higher in the tissue valve group, whereas the incidence of stroke, splenic abscess, postoperative bleeding, and arrhythmia was higher in mechanical valve group.

Table 2 compares the early outcomes between the two groups. In the mechanical valve group, cross clamp time and bypass time were slightly longer, as well as the length of hospital stay. However the length of ICU stay was shorter. There were 25 in-hospital deaths (17%). Intraoperative mortality occurred in 5 patients. The tissue valve group had higher in-hospital mortality (27%) than the mechanical valve group (14%).

Table 3 shows the long-term outcomes. In tissue valve group, there was no recurrent infection or reoperation. In the mechanical valve group, there was 3% recurrent infection and 1% reoperation. Overall, 122 patients survived until hospital discharge (95 patients in mechanical valve group and 27 patients in tissue valve group). At the last follow up, 113 of 122 patients survived (93%), including 88 in the mechanical valve group (93%) and 25 in the tissue valve group (93%). The average 5-year survival was 81.5% (95% CI: 72.4 to 87.8) in mechanical valve group, which was better than the 71.4% (95% CI: 53.4 to 83.5) in the tissue valve group (see Figure 1).

**Table 2** Early outcomes

| Outcome | Total (n = 147) | Mechanical (n = 110) | Tissue (n = 37) |
|---|---|---|---|
| CCU stay (day): median (IQR) | 4 (2 to 7.5) | 4 (2 to 8) | 5 (1 to 7) |
| Hospital stay (day): median (IQR) | 14 (8 to 27) | 15 (9 to 27) | 11 (7 to 20) |
| Clamp time (min): median (IQR) | 77 (54 to 108) | 79 (52 to 107) | 75 (60 to 108) |
| Bypass time (min) median (IQR) | 98 (73 to 133) | 99 (73 to 129) | 98 (71 to 146) |
| In-hospital mortality: number (%) | 25 (17) | 15 (14) | 10 (27) |

CCU: cardiac care unit; min: minutes; IQR: interquartile range

**Table 3** Long term outcomes

| Outcome | Mechanical (n = 110) | Tissue (n = 37) |
|---|---|---|
| Reinfection: number (%) | 3 (3) | 0 |
| Reoperation: number (%) | 1 (1) | 0 |
| 5-year survival, % (95% CI) | 81.5 (72.4 to 87.8) | 71.4 (53.4 to 83.5) |

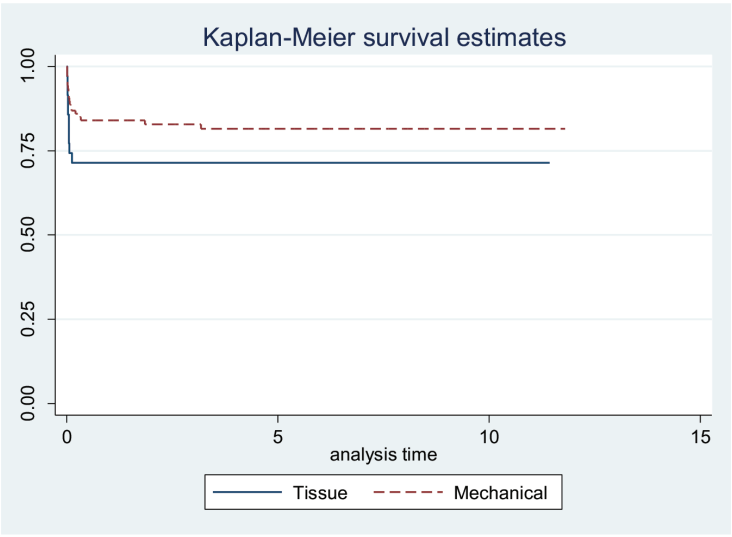


**Figure 1** Survival estimates of tissue vs mechanical valve replacement

## Discussion

In the present study of patients with left-sided native valve, active IE, we found that patients who had tissue valve replacement had higher in-hospital mortality than those who had mechanical valve replacement. Even though the mortality rate was high in the early postoperative period, long term outcomes, which included reinfection, reoperation and long-term survival, were good.

Baseline characteristics of patients in the present study were similar to those of previous studies, in which the average age was 36 to 60 years,[25-28] male patients were twice as many as female patients,[29] and common associated medical conditions included renal impairment (28%), anemia (38%), heart block (12%), hematuria (25%), and splenomegaly (11%).[9-11,29,30] In developing countries, active IE is commonly associated with rheumatic heart disease and poor dental hygiene. Common sites of involvement included the aortic valve (42%), mitral valve (34%), or multiple valves (24%). Common pathogens included streptococcus group (34%), staphylococcus aureus (27%), and staphylococcus coagulase negative (21%).[9,33-35]

In the present study, the prevalence of positive blood culture and tissue culture was low. The percentage of positive blood culture is usually from 83% to 92%, but positive tissue culture could be much lower, from 25% to 34%.[22,24,36] The reason for this might be due to antibiotic treatment before taking culture. Also, a negative blood culture is associated with low positive tissue culture, in the range of 5% to 15%.[22,25,29,30] In the present study, 5 patients developed stroke, which might be related to large mobile valvular vegetation, with higher chance of systemic embolization and cerebral complication in 15% to 20% of patients prior to operation, especially at 1 to 2 weeks after antibiotics administration.[3,4,20,29]

In the present study, patients who underwent tissue or mechanical valve replacement had similar operative time and length of hospital stay, which were similar to those of previous studies. For example, cross-clamp time was 78.8 ± 41.5 minutes, cardio-pulmonary bypass (CPB) time was 117.8 ± 58.3 minutes, ICU stay was 4.6 ± 5.3 days and length of hospital stay was 15.3 ± 14.7 days.[24,25]

From previous studies, postoperative complications included reoperation (15%) due to postoperative bleeding (6%) and deep sternal wound infection (1%), atrial fibrillation (AF; 20%), prolonged ventilation (28%), new stroke (3%), transient ischemic attack (1%) and coma (1%). Other complications included acute renal failure (ARF), cardiac tamponade, heart block, sepsis, cholecystitis, mesenteric ischemia, recurrent IE and low cardiac output.[5,20] In the present study, common complications were ARF requiring dialysis and cardiac arrhythmia.

Moon *et al*. found that in left-sided, active or healed IE, mechanical valve replacement had an operative mortality of 19% and tissue valve replacement 17%, which were not significantly different.[19] Nguyen *et al*. found that aortic valve replacement in active IE had an early mortality of 10% in the mechanical valve group, and 19% in the tissue valve group.[27] Bauernschmitt *et al*. found that early mortality of mechanical valve replacement in active IE was 12%.[5] Musci *et al*. found that 30-day overall survival of tissue valve replacement in active IE was 77%.[21] in the present study, the in-hospital mortality in the tissue valve group was 27%, which was higher than the 14% in the mechanical valve group.

Risk factors of postoperative mortality include advanced age, pulmonary embolism, large valvular vegetation, DM, critical status, prolonged ICU stay, previous cardiopulmonary bypass graft (CABG), emergency operation, active IE, previous valve surgery, renal dialysis, drug abuse, fungal infection, moderate to severe ischemic stroke, cerebral hemorrhage, double valve endocarditis, myocardial infarction, valvular abscess formation, CPB time longer than 120 minutes, massive blood transfusion, aortic valve involvement, Left ventricular ejection fraction less than 35%, WBC greater than 15,000 $mm^3$, creatinine level greater than 2 mg/dL, body temperature greater than 38 °C, hemoglobin level less than 10 g/dL, low serum albumin and high EuroSCORE.[7,19,20, 25, 32-34, 35-41]

Delahaye *et al*. found that tissue valve replacement had higher 1-year in hospital mortality than that of mechanical valve replacement.[42] This result is similar to that of the present study, but we also found that patients in the tissue valve group had higher EuroSCORE, older age, and required multiple valve operations. The reinfection and reoperation rate was low, especially in the mechanical valve group which is reported to be 3% to 9%, and in the tissue valve group, 7% to 29%.[43] In another study, in the first 5 years, the recurrence rate of native valve IE in the mechanical valve group was 2% and in the tissue-valve group was 1%; both rates were not significantly different.[19]

In another study of active IE, tissue valve replace-

ment has a reoperation rate of 7% and a reinfection rate of 9%.[21] Toyoda et al. found that recurrence rates of IE in mechanical and tissue valve groups were not statistically different. In aortic valve replacement, the rate of recurrent IE in the mechanical valve group was 10% and in the tissue valve group, 9%, whereas in mitral valve replacement, the rates of recurrent IE were 9% and 10% respectively.[33] At 1 to 2 years after surgery, reinfection, reoperation, and mortality rates gradually decrease.[18,22] In the present study the rate of recurrent IE was 3%, and the reoperation rate was 1%, all found in the mechanical valve group. These rates were lower than those of previous studies.

Factors influencing long-term survival include presence of coronary artery disease, renal disease, DM, and ejection fraction less than 40%.[44] Reul and Sweeny reported a 85% survival rate at 4 years in the mechanical valve group, which was higher than the 79% rate of the tissue valve group.[18] Delay et al. found a 71% 5-year survival rate in the mechanical valve group and 61% in the tissue valve group, and these rates were not significantly different.[45] This result was similar to that of a study by Saide et al., with 5-year survival rates of 75% and 62% in the mechanical and tissue valve groups, respectively.[46] Musci et al., in patients with active IE, found that by using tissue valves the survival rates at 1, 3 and 5 years were 60%, 53%, and 47%, respectively.[21] Flynn et al. conducted a meta-analysis comparing the results of tissue and mechanical valves, and found that the survival rates at 1, 3 and 5 years in the mechanical valve group was 73%, 57% and 49% and in the tissue valve group, 72%, 57% and 49%, respectively.[47]

In the present study, long-term survival rates of the two groups were similar and better than those of previous studies. Survival in the mechanical valve group was better than that in the tissue valve group, at 81.5% (95% CI: 72.4% to 87.8%) and 71.4% (95% CI: 53.4% to 83.5%), respectively. Flynn et al. found similar results and proposed that the choice of prosthetic valve replacement in IE should be based on age, co-morbidity and preference of patients and surgeons.[47]

The present study has many limitations. The design was retrospective and observational, conducted at a single center. The criteria for prosthetic valve selection were unclear. However, long-term follow-up was reasonably complete because all data were collected from medical records and civil registration, though there was some discrepancy in the cause of death.

## Conclusion

In patients with left-sided native valve active endocarditis, tissue valve replacement was associated with higher in-hospital mortality than mechanical valve replacement. However, the preoperative status of patients undergoing tissue valve replacement was worse. Long-term recurrence and survival rates were good in both groups.

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## *บทคัดย่อ* ผลลัพธ์ในระยะยาวของลิ้นหัวใจแบบเนื้อเยื่อและโลหะในผู้ป่วยลิ้นหัวใจติดเชื้อในระยะรุนแรง

**คมกฤษณ์ โกมุทรินทร์, พบ., นิสิต พูลธนะนันท์, พบ.**
*หน่วยศัลยกรรมทรวงอก กลุ่มงานศัลยกรรม โรงพยาบาลมหาราชนครราชสีมา*

***ความเป็นมา:*** ยังไม่มีข้อสรุปว่าลิ้นหัวใจชนิดใดเหมาะสมที่สุดสำหรับผู้ป่วยลิ้นหัวใจติดเชื้อ ซึ่งเป็นโรคที่มีความรุนแรงและโอกาสเสียชีวิตสูง ปัจจุบันการรักษามุ่งเน้นในการทำ early surgery โดยไม่รอให้ยาฆ่าเชื้อจนครบกำหนด ทำให้มีโอกาสติดเชื้อซ้ำส่งผลต่อการรอดชีวิตในระยะยาว ผู้วิจัยจึงทำการศึกษาผลลัพธ์ในระยะสั้นและระยะยาวของลิ้นหัวใจแบบเนื้อเยื่อและโลหะในผู้ป่วยลิ้นหัวใจติดเชื้อด้านซ้ายในระยะรุนแรง

***วิธีการศึกษา:*** เป็นการศึกษาแบบย้อนหลัง ระหว่าง 1 มกราคม 2551 ถึง 30 กันยายน 2563 มีผู้ป่วย 147 ราย แบ่งเป็น 2 กลุ่ม คือ กลุ่มได้รับการใส่ลิ้นแบบเนื้อเยื่อและแบบโลหะ เก็บข้อมูลอัตราการเสียชีวิตในโรงพยาบาล การติดเชื้อซ้ำ การผ่าตัดซ้ำ และการรอดชีวิตในระยะยาวของผู้ป่วย ทั้ง 2 กลุ่ม

***ผลการศึกษา:*** อัตราการเสียชีวิตในโรงพยาบาลอยู่ที่ร้อยละ 17 กลุ่มลิ้นแบบเนื้อเยื่อมีอัตราการเสียชีวิตร้อยละ 27 กลุ่มลิ้นแบบโลหะมีอัตราการเสียชีวิตร้อยละ 14 พบมีการติดเชื้อซ้ำร้อยละ 3 และผ่าตัดซ้ำร้อยละ 1 เฉพาะในกลุ่มลิ้นแบบโลหะ อัตราการอยู่รอดที่เวลา 5 ปี (5-yer Survival) ของลิ้นแบบเนื้อเยื่ออยู่ที่ร้อยละ 71.4 (95% CI : 53.4 – 83.5) และลิ้นแบบโลหะอยู่ที่ร้อยละ 81.5 (95%CI : 72.4 – 87.8)

***สรุปผลการศึกษา:*** การทำผ่าตัดเปลี่ยนลิ้นหัวใจในผู้ป่วย Lt. side native valve active endocarditis พบว่ากลุ่ม mechanical valve จะมี in-hospital mortality และ long term survival ที่ดีกว่ากลุ่ม tissue valve โดยทั้ง 2 กลุ่ม มีอัตราการเสียชีวิตในโรงพยาบาลค่อนข้างสูง ทั้งนี้ผู้ป่วยในกลุ่ม tissue valve มีสภาพก่อนผ่าตัดที่แย่กว่าแต่เมื่อติดตามในระยะยาวพบว่ามีอัตราการติดเชื้อและการผ่าตัดซ้ำต่ำ รวมถึงมีอัตราการรอดชีวิตที่ยืนยาว

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Original Article

# *A Randomized Controlled Trial of Ultrasound versus Fluoroscopic Guidance for Percutaneous Nephrolithotomy*

**Tanongsak Hathaivasiwong, MD**

*Division of Urology, Department of Surgery, Suratthani*

***Abstract***

***Objective:*** To compare the success rate of ultrasound (US) versus fluoroscopic guidance in entering the target calyx from a proper entry site and in the direction of renal pelvis during percutaneous nephrolithotomy (PCNL), and to determine their relative advantages and disadvantages.

***Methods:*** The present randomized controlled study was conducted between May 2020 and March 2021. Just before PCNL, patients were randomly assigned to undergo either US guidance access (group A) or fluoroscopic guidance access (group B). A needle placed on the patient's flank in the prone position was used to identify the preselected target. The needle was advanced through a needle holder and helped guide percutaneous tract dilation. Data on patient characteristics, tract length, tract access time, and the stone free rate were collected for analysis. Data were analyzed using *t*-test, chi-square test and Fisher's exact test.

***Results:*** There were a total of 40 patients in the trial with 20 patients in each group. There were no statistically significant differences between patients in groups A and B in terms of age, gender, ASA status, BMI, stone size and stone location. The average length of the access tract was 7.7 cm in group A and 7.6 cm. in group B ($p$ = 0.672). The tract access time was 15 minutes in group A and 13 minutes in group B ($p$ = 0.288). The frequencies of location of the access tract at the upper pole in groups A and B were 11 and 12, respectively ($p$ = 0.252). The stone free rate was 45% (9/20) in group A and 55% (11/20) in group B ($p$ = 0.853).

***Conclusions:*** The present study showed that PCNL under US guidance had similar success as PCNL under fluoroscopic guidance. US can be used as an alternative to fluoroscopy in PCNL. The present randomized trial might help convince some endourologists to use US rather than fluoroscopy in their management of renal stones, in order to minimize exposure to ionizing radiation.

***Keywords:*** Ultrasound, Fluoroscopic Guidance, Percutaneous Nephrolithotomy

## Introduction

Percutaneous nephrolithotomy (PCNL) is the treatment of choice for staghorn and large renal stones. A perfect percutaneous access tract to the pelvicalyceal system should be made through the tip of renal papilla in the targeted calyx and to be along the axis of the renal calyx.[1-8] It is traditionally guided by fluoroscopy and may pose a radiation risk to patients and staff. The use of ultrasonography in PCNL was first described as early as the 1970's. Although ultrasound (US) guidance renal access for PCNL is a safe, effective, and low-cost procedure, it is underused by urologists.

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***Corresponding author:*** *Tanongsak Hathaivasiwong, MD, Division of Urology, Department of Surgery, Suratthani Hospital, 56 Mu 2, Makham Tia Subdistrict, Mueang Surat Thani District, Surat Thani 84000; Telephone: +66 7795 2900; Email: beuy029@hotmail.com*

The use of fluoroscopy at Suratthani Hospital is limited by the availability of the equipment, which must be shared among all Departments of the Hospital. This was a motivation for the present study. We want to compare the success, the advantages and disadvantages of PCNL under ultrasound guidance to those of PCNL under fluoroscopy, and to determine factors related to difficulty of access.

## Patients and Methods

Patients who were admitted for PCNL at Suratthani Hospital by one urologist from May 2020 to March 2021 were enrolled into the study. Inclusion criteria included patients with renal or proximal ureteral stone; large renal stones (2 cm or larger) detected by computerized tomography (non-contrast); and age greater than 18 years. All participants gave informed consent. No participants were excluded from the analysis. Randomization was done using a table of random numbers. Participants were randomized into two groups after induction of anesthesia. Participants in group A underwent PCNL under US guidance. Participants in group B underwent PCNL under fluoroscopic guidance. All operative procedures were performed by one surgeon. All clinical information was collected prospectively. Data were summarized as mean and standard deviation or counts and percentage as appropriate. Quantitative variables were contrasted between groups using unpaired *t*-test while categorical variables were contrasted using chi-square test or Fisher's exact test as appropriate.[9] Statistical significance was defined as a *p*-value less than 0.05. The study was approved by Research Ethics Committee of Suratthani Hospital (no. 54/2563).

After induction of general anesthesia, an open-ended 5-French ureteral catheter was inserted into the ipsilateral ureter up to approximately 20 centimeters, under cystoscopic guidance, from a lithotomy position with the patient on the operating table. The patient was then moved to a prone position. In group A, percutaneous renal access was obtained under US guidance with a needle guide. We used the US (BK medical Flex Focus 500) to locate the stone as well as to identify an ideally suited posterior calyx for puncture (Figure 1). An 18-gauge needle was advanced under real-time ultrasound monitoring (Figure 2). In group B, we performed all the above steps but with fluoroscopic guidance. Tract access was chosen according to the location of the stone in both groups. In the absence of hydronephrosis, normal saline solution was injected in a retrograde fashion through the ureteral catheter to dilate the collecting system for easier imaging, though this was not routinely done for every patient. Entry into the collecting system was confirmed when either aspiration or efflux of urine through the puncture needle was seen, or when clear visualization of the needle tip within the urinary space

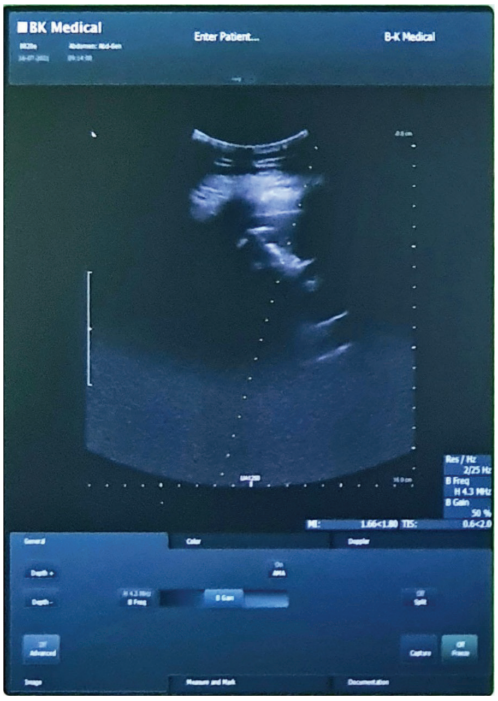


**Figure 1** Ultrasonography used for locating the stone and guiding instrumentation.

**Figure 2** Placing a needle under US guidance

or touching the stone can be demonstrated. After entry into the collecting system was confirmed, a J-tip coaxial guide wire was inserted into the renal pelvis or down the proximal ureter. We then sequentially passed a coaxial rod metal dilator, increasing the dilator by 3-French each time, starting from 9-French, and placed a safety wire introducer over the guide wire (Figure 3). The tip of each instrument was marked and visualized using either the US or fluoroscope. The images of instruments entering the collecting system were obtained to prevent perforation. A 30-French Amplatz sheath was advanced over the 27-French metal dilator. After removal of the coaxial rod metal dilator, nephroscopy was performed with a 27-French rigid offset nephroscope. Stone fragmentation was accomplished using an ultrasonic lithotripter. Flexible nephroscopy was performed to look for residual fragments and to perform additional holmium laser lithotripsy. At the end of the procedure, a nephrostomy tube was placed in all patients. The position of the tubes was checked by retrograde injection of saline solution through the ureteral catheter. A 24-French Foley catheter was routinely used for this purpose.

Length of the access tract was measured from the skin to the calyx. Evidence of any residual stone in the urinary tract, and size of residual stones, were assessed by computerized tomographic scan. Access time was measured from the time of US or fluoroscope use until the nephroscope was successfully inserted.

**Figure 3** Introducing the safety wire

## Results

From May 2020 to March 2021, 40 patients were enrolled into the study. There were 20 participants in group A and 20 participants in group B. Clinical characteristics of participants are shown in Table 1. All characteristics including age, gender, ASA status, and body mass index were similar between groups. Characteristics of the stone including location, side and size were similar as well. Most of the stones were located in the renal pelvis and at the lower pole. Finally, the degree of hydronephrosis was also similar between groups, the most common being grades II and III.

Comparison of outcomes of the operation between the two groups is shown in Table 2. Most of the operation required only one attempt at puncture, and this was similar between groups. Length of the access tract, time to access, and stone free rate were all similar between both groups. The length of the access tract was from 7 to 8 cm, and the access time was less than 15 minutes, on average. The stone-free rate was about 50%.

## Discussion

Percutaneous nephrolithotomy (PCNL) is the procedure of choice for patients with large renal stones not amenable to ureteroscopy or shockwave lithotripsy. In the United States of America and around the world, fluoroscopy had been the primary imaging method used to guide percutaneous renal access and establish a working tract for PCNL. However, there are concerns that long-term use of ionizing radiation may increase the incidence of cancer.[11-13] For patients with nephrolithiasis, reducing their exposure to ionizing radiation is important, as these patients are at high risk for cumulative radiation exposure. Surgical staff are at risk for intraoperative radiation exposure as well. While some studies have shown that radiation exposure during PCNL may be relatively low, this might not be so everywhere. The use of radiation protective equipment may not be effective, or unreliable. The surgeon generally receives more ionizing radiation exposure, especially to the legs and eyes.[14,15]

Several methods have been proposed to help reduce radiation exposure during PCNL. One method is to use endoscopic guidance, commonly known as Retrograde Intra Renal Surgery (RIRS).[16] This method can access the renal collecting system by the use of a flexible ureteroscope. After positioning the ureteroscope in the target calyx, fluoroscopy is used to guide a needle into the kidney in an antegrade percutaneous fashion.

**Table 1** Clinical characteristics of patients

| Characteristics | Ultrasound guidance (N = 20) | Fluoroscope guidance (N = 20) | *p*-value |
|---|---|---|---|
| **Age (years): mean (SD)** | 59.9 (11.6) | 58.5 (9.4) | 0.677 |
| **Gender: number (%)** | | | |
| Women | 7 (35) | 9 (45) | 0.519 |
| Men | 13 (65) | 11 (55) | |
| **ASA Status: number (%)** | | | |
| I | 8 (40) | 11 (55) | 0.342 |
| II | 12 (60) | 9 (45) | |
| **Body mass index (kg/m2): number (%)** | | | |
| < 25 | 13 (65) | 14 (70) | 0.796* |
| 25 to 29.9 | 4 (20) | 2 (10) | |
| > 30 | 3 (15) | 4 (20) | |
| **Site of stone: number (%)** | | | |
| Left | 10 (50) | 10 (50) | 0.999 |
| Right | 10 (50) | 10 (50) | |
| **Stone size (cm): mean (SD)** | 3.96 (1.34) | 4.03 (1.35) | 0.870 |
| **Stone location: number (%)** | | | |
| Renal pelvis/ Lower pole | 8 (40) | 6 (30) | 0.898* |
| Full staghorn calculus | 7 (35) | 7 (35) | |
| Renal pelvis | 2 (10) | 5 (25) | |
| Renal pelvis /Upper pole | 1 (5) | 1 (5) | |
| Upper /Lower pole | 1 (5) | 1 (5) | |
| Renal pelvis /Middle pole | 1 (5) | 0 | |
| **Hydronephrosis grade: number (%)** | | | |
| II | 5 (25) | 4 (20) | 0.827* |
| III | 11 (55) | 13 (65) | |
| IV | 4 (20) | 3 (15) | |

*Fisher's exact test; ASA: American Society of Anesthesiologists; SD: standard deviation

The needle enters the collecting system under direct vision of the ureteroscope. Although fluoroscopy is still needed for caliceal puncture, compared to standard PCNL this technique may lower fluoroscopic screening time and increase stone clearance.[17,18]

Real-time US is becoming accepted as an imaging modality for directing PCNL in a dilated renal collecting system.[19] The overall success rate is likely comparable to that of standard fluoroscopic PCNL.[20] US is free of ionizing radiation and is highly portable. US can provide additional imaging information as well. It can identify important structures locating between the skin and kidney that might be in the path of the access tract. The depth of penetration of the puncture needle relative to the target calyx can be estimated. The orientation of calyceal anatomy during PCNL can be correctly established. Thus, US can help prevent adjacent and visceral organ injury. In addition, US eliminates the need for a retrograde ureteral catheter if retrograde ureteral catheterization was unsuccessful.[21] US is ideal for patients who are sensitive to radiation exposure, including pediatric and pregnant patients. Finally, US can help visualize non-opaque or semi-opaque stones not seen radiographically, and thus help improve the stone-free rate.[22]

Table 2 Operative outcomes

| Outcome | Ultrasound guidance (N = 20) | Fluoroscope guidance (N = 20) | *p*-value |
|---|---|---|---|
| **Numbers of puncture attempt: number (%)** | | | |
| One attempt | 14 (70) | 13 (65) | 0.938 |
| Two attempts | 5 (25) | 6 (30) | |
| Three attempts | 1 (5) | 1 (5) | |
| **Location of tract: number (%)** | | | |
| Lower pole | 1 (5) | 4 (20) | 0.252* |
| Lower/ Upper pole | 0 | 1 (5) | |
| Upper pole | 11 (55) | 12 (60) | |
| Middle pole | 2 (10) | 0 | |
| Upper /Lower pole | 4 (20) | 1 (5) | |
| Upper /Middle pole | 2 (10) | 2 (10) | |
| **Length of tract (cm): mean (SD)** | 7.7 (0.72) | 7.6 (0.76) | 0.672 |
| **Access time (min): mean (SD)** | 14.7 (6.3) | 12.7 (5.4) | 0.288 |
| **Residual stone: number (%)** | | | |
| No residual stone (stone-free) | 9 (45) | 11 (55) | 0.853* |
| Lower pole, 10 mm | 1 (5) | 0 | |
| Lower pole, 2 mm | 1 (5) | 0 | |
| Lower pole, 3 mm | 3 (15) | 5 (25) | |
| Lower pole, 4 mm | 2 (10) | 1 (5) | |
| Lower pole, 8 mm | 1 (5) | 0 | |
| Middle pole, 10 mm | 1 (5) | 1 (5) | |
| Middle pole, 4 mm | 1 (5) | 0 | |
| Upper pole, 4 mm | 0 | 1 (5) | |
| Upper pole, 6 mm | 1 (5) | 0 | |
| Upper pole, 8 mm | 0 | 1 (5) | |

* Fisher's exact test; SD: standard deviation

The disadvantages of US include additional training for the operator to gain the required skills, although successful puncture of the collecting system can be confirmed by the appearance of urine following removal of the needle obturator. There is the difficulty of percutaneous access when there is no or only mild hydronephrosis. But this can be overcome by administration of diuretics or the retrograde injection of saline solution to transiently dilate the calyces. Finally, there is the difficulty of visualizing the guide wire during its manipulation following renal access, as well as the poor echogenicity of the Amplatz dilatator and Amplatz sheath.[23-25]

The success rate in achieving access tract in our study was 100 % for both groups. The ability to gain access to the collecting system under US guidance was similar to that under fluoroscopic guidance. Some studies have shown that the primary stone-free rate with US guided PCNL was from 49% to 79%.[26,27] In the present study the stone-free rate was 45% to 50%, which was similar to those of previous studies, and was not significantly different between US and fluoroscope guidance. The average access time under US guidance was slightly longer than that under fluoroscope guidance, due to cases with difficult dilatation requiring retrograde fluid irrigation to facilitate US visualization, as compared with fluoroscopy which can visualize the process directly. Also, US guidance is more difficult in obese patients, due to the longer length of the access tract. US guidance is sometimes a "blind technique" when compared with fluoroscopy, which is a real-time image guidance.

Finally, higher degree of hydronephrosis is easier for access by US, so if minimal hydronephrosis is present, then more time or more preparation is required for access.

## Conclusion

The present randomized controlled study showed that US guidance had similar outcomes as fluoroscope guidance for PCNL. Thus, US is an equally effective alternative to fluoroscopy in PCNL, and will help reduce exposure to radiation.

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Original Article

# *Ultrasound-Guided Core Needle Biopsy versus Fine-Needle Aspiration Biopsy for Thyroid Nodules*

**Chollada Suwannachod, MD**

*Department of Surgery, Pakkred Community Hospital*

***Abstract***

***Objective:*** The use of core needle biopsy (CNB) may help overcome limitations of fine needle aspiration biopsy (FNAB) for thyroid nodules. The aim of the present study was to compare ultrasound-guided (US-G) CNB with US-G FNAB in terms of diagnostic adequacy based on the 2017 Bethesda System for Reporting Thyroid Cytopathology (the 2017 Bethesda System).

***Patients and Methods:*** A retrospective cohort study of two groups of patients with thyroid nodules who underwent US-G FNAB and CNB at Pakkred Community Hospital between January 1, 2017 to December 31, 2020 was performed. The two groups were compared in terms of diagnostic adequacy.

***Results:*** There were 31 patients in each group. In the CNB group, adequate results in terms of the 2017 Bethesda System were obtained in 77% of patients, while FNAB yielded only 26% adequacy, a statistically significant difference ($p < 0.001$). Size of the thyroid nodule greater than 2 cm was significantly related to increased adequacy. Cystic or solid or mixed composition of nodules did not significantly impact adequacy.

***Conclusion:*** Ultrasound-guided CNB performed better than FNAB in terms of adequate biopsy results based on the 2017 Bethesda System.

***Keywords:*** Core needle biopsy, Fine needle aspiration biopsy, Thyroid nodule

## Introduction

Thyroid nodules are a common clinical problem. The prevalence of thyroid nodules is 4% to 7% of the population.[1,2] The incidence of thyroid nodules is 0.8% annually, commonly found in women.[1,2] The probability of thyroid cancer in thyroid nodules is 7% to 15% depending on age, gender, previous radiation exposure, family history, and other factors.[3] Thyroid ultrasound (US) plays a key role in determining characteristics of thyroid nodules in terms of size, solid or cystic composition, as well as to help guide biopsy.

US-guided biopsy can help diagnose whether a thyroid nodule is benign or malignant.[3] The more tissue sample is obtained, the more accurate the diagnosis. The diagnosis of thyroid nodule is usually based on the 2017 Bethesda System for Reporting Thyroid Cytopathology (the 2017 Bethesda System). There are six categories of diagnosis: B1: nondiagnostic (ND) or unsatisfactory (UNS); B2: benign; B3: atypia of undetermined significance (AUS) or follicular lesion of undetermined significance (FLUS); B4: follicular neoplasm (FN) or suspicious for follicular neoplasm (SFN); B5: suspicious for malignancy (SUS); and B6: malignancy.[4,5]

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***Corresponding author:*** *Chollada Suwannachod, MD, Department of Surgery, Pakkred Community Hospital, 345 Rd., Pakkred, Nonthaburi, Thailand, 11120; E-mail: Suwannachod.c@gmail.com*

In terms of adequacy, benign, FN/SFN, SUS, and malignant categories (B2, B4-6) are considered adequate biopsy results, representing enough tissue to make a definitive diagnosis. Inadequate results consist of ND/UNS and AUS/FLUS categories (B1, B3), which may require re-biopsy or excision.

Fine needle aspiration biopsy (FNAB) is a biopsy method using an 18-gauge needle under negative pressure to collect cellular tissue from different parts of the thyroid nodule, usually done under US guidance. It is a simple procedure with few complications and is recommended as a first-line biopsy method when a thyroid nodule is suspected of being cancerous. However, results of FNA are often inadequate.[1,6] When a finding is inadequate or indeterminate, FNA can be repeated until a determinate result is obtained.[4-5] In some cases, surgeons may need to perform excisions because of persistent inadequate FNA results.

Core needle biopsy (CNB) is an alternative biopsy method using a biopsy gun, and an 18 gauge needle, to enable more tissue to be removed, also usually done under US guidance. It is commonly used for solid tumors, providing higher diagnostic accuracy than FNAB. CNB can often obtain adequate tissue to determine whether the nodule is benign or malignant. It is expected to be more accurate than FNAB.[8-19]

The aim of the present study was to compare the diagnostic effectiveness between CNB and an FNAB, under US guidance, in terms of adequate biopsy results for thyroid nodules, based on the 2017 Bethesda System. A secondary aim is to identify factors related to obtaining adequate biopsy results.

## Patients and Methods

The present study is a retrospective cohort study of patients with thyroid nodules seen at the surgical clinic of Pakkred Community Hospital, Nonthaburi, Thailand. The data is collected from medical records of patients who underwent an ultrasound-guided FNA and/or CNB from January 1st, 2017 to December 31st, 2020, obtaining diagnosis based on the 2017 Bethesda System. Under a type I error of 5% and type II error of 20%, and the assumed proportion of adequate biopsy for of 67% and 33% for CNB and FNAB respectively, the sample size is at least 29 patients per group. Thus, a sample size of 31 patients per group or 62 patients overall is sufficient.

Biopsies were obtained under local anesthesia using a portable US machine, an 18-gauge needle, and a 10-mL syringe for FNAB (Figure 1), or a biopsy gun with an 18-gauge biopsy gun needle for CNB (Figure 2). All patients were placed in a supine position with hyperextended neck and a pillow under the shoulders. Lidocaine was used for local anesthesia. For FNAB, an 18-gauge needle under manual negative pressure was placed in the thyroid nodules for tissue sampling. If a cystic nodule is found, all fluid in the cyst was removed. When a solid nodule is found, samples were drawn from 2 to 3 different directions. Tissue samples from FNAB were smeared onto glass slides and fixed in 95% alcohol to be examined under the microscope. For CNB, a biopsy gun and an 18-gauge biopsy gun needle were used for obtaining tissue samples. Tissue obtained from CNB were fixed in formalin for microscopic examination.

Data collected included age, gender, thyroid function test, size of thyroid nodules, and solid/cystic composition of thyroid nodules as seen on US.


**Figure 1** An 18-gauge needle and a 10 mL syringe

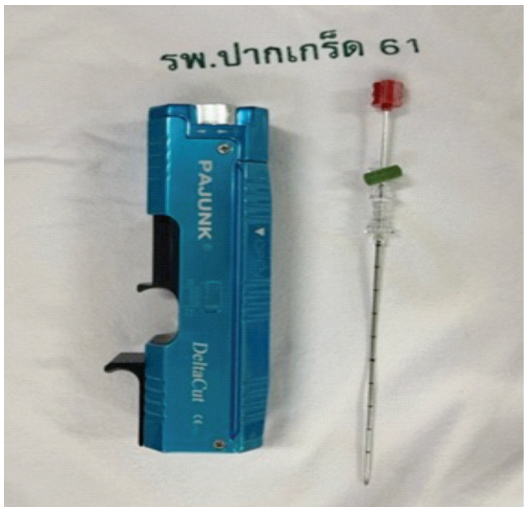


**Figure 2** A biopsy gun and an 18-gauge biopsy gun needle

The outcome was categorized as adequate or inadequate biopsy result, as previously defined. Data were compared between the two biopsy methods. Summary statistics were in terms of frequency and percentage or mean and standard deviation (SD) as appropriate. Chi-squared test or Fisher's exact test was used for categorical data and unpaired *t*-test for quantitative data. Statistical significance was defined as a *p*-value less than 0.05.

## Results

Sixty-five patients underwent US-guided biopsy of the thyroid nodule during the period under study. Three were excluded due to loss to follow-up and lack of US results. A total of 62 patients were included in the study, with 31 patients in each of the CNB and FNAB groups. Clinical characteristics of 62 patients are shown in Table 1. The majority of patients were women (84%). The average age was 50.4 ± 16.4 years (range, 12 to 78 years). The average thyroid stimulating hormone (TSH) level was 1.43 ± 1.04 uIU/mL and the average free thyroxine (FT4) level was 1.16 ± 0.28 ng/dL. There were no significant differences between the CNB and FNAB groups in terms of age, gender, TSH and FT4 levels.

Characteristics of all 62 thyroid nodules are also shown in Table 1. The average size of thyroid nodules was 2.9 ± 1.2 cm (range, 1 to 7 cm). The composition of thyroid nodules on US examination included pure solid component in 29 (47%), mixed solid and cystic components in 17 (27%), and pure cystic lesion in 16 patients (26%). None of these characteristics were significantly different between the two groups.

Overall, B1, B2, B3, B4, B5 and B6 categories were seen in 29 (47%), 28 (45%), 1 (2%), 1 (2%), 2 (3%), and 1 (2%) patients, respectively. The major differences between CNB and FNAB in terms of these outcomes were that for CNB, 6 (19%) and 20 (65%) patients were in categories B1 and B2, respectively, while for FNAB 23 (74%) and 8 (26%) were in categories B1 and B2. Thus, there was a significantly higher proportion of adequate biopsy results in the CNB group (28/31 or 77%) than in the CNB group, (7/31 or 23%) ($p < 0.001$; see Table 2).

**Table 1** Clinical characteristics of patients

| Characteristic | Overall (N = 62) | CNB (N = 31) | FNA (N = 31) | *p*-value |
|---|---|---|---|---|
| **Women: number (%)** | 52 (84) | 27 (87) | 25 (81) | 0.490 |
| **Age (years): mean ± SD** | 50.4 ± 16.4 | 50.4 ± 17.9 | 50.5 ± 15.0 | 0.981 |
| **TSH (uIU/mL): mean ± SD** | 1.43 ± 1.04 | 1.51 ± 1.11 | 1.35 ± 0.99 | 0.552 |
| **FT4 (ng/dL): mean ± SD** | 1.16 ± 0.28 | 1.16 ± 0.32 | 1.16 ± 0.24 | 0.999 |
| **Size (cm): mean ± SD** | 2.9 ± 1.2 | 3.0 ± 1.2 | 2.7 ± 1.2 | 0.329 |
| **Composition of thyroid nodule:** | | | | |
| Solid: number (%) | 29 (47) | 18 (58) | 11 (36) | 0.135 |
| Solid-cystic: number (%) | 17 (27) | 8 (26) | 9 (29) | |
| Cystic: number (%) | 16 (26) | 5 (16) | 11 (36) | |

SD: standard deviation; TSH: thyroid stimulating hormone; FT4: free thyroxine; CNB: core needle biopsy; FNA: fine needle aspiration

**Table 2** Diagnosis of thyroid nodules according to the 2017 Bethesda System

| Diagnosis: number (%) | Overall (N = 62) | CNB (N = 31) | FNA (N = 31) | *p*-value |
|---|---|---|---|---|
| B1: ND/UNS | 29 (45) | 6 (19) | 23 (74) | < 0.001* |
| B2: Benign | 28 (45) | 20 (65) | 8 (26) | |
| B3: AUS/FLUS | 1 (2) | 1 (3) | 0 | |
| B4: FN/SFN | 1 (2) | 1 (3) | 0 | |
| B5: SUS | 2 (3) | 2 (7) | 0 | |
| B6: Malignant | 1 (2) | 1 (3) | 0 | |
| Adequate results (B2 & B4-6) | 32 (52) | 24 (77) | 8 (26) | < 0.001 |

*Fisher's exact test; ND: nondiagnostic; UNS: unsatisfactory; AUS: atypia of undetermined significance; FLUS: follicular lesion of undetermined significance; FN: follicular neoplasm; SFN: suspicious for follicular neoplasm; SUS: suspicious for malignancy; CNB: core needle biopsy; FNA: fine needle aspiration

Overall, the only factor significantly associated with adequate biopsy result was size of thyroid nodule larger than 2 cm. US findings of cystic and/or solid component did not significantly relate to adequacy (Table 3). In the CNB group, the nodule size (larger than 2 cm) was also significantly related to adequate biopsy results, but cystic/solid components were of borderline significance (Table 4). In the FNAB group, neither nodule size nor cystic/solid components were significantly related to adequate biopsy results. While solid nodules were more likely to yield adequate biopsy in the FNAB group, as might be expected, this seemed not to be the case in the CNB group.

**Table 3** Factors related to adequate biopsy results: all patients

| Factor | Overall (N = 62) | Inadequate results (N = 30) | Adequate results (N = 32) | *p*-value |
|---|---|---|---|---|
| **Size > 2 cm: number (%)** | **44 (71)** | **17 (57)** | **27 (84)** | **0.016** |
| **Composition: number (%)** | | | | 0.395 |
| Solid | 29 (47) | 12 (40) | 17 (53) | |
| Solid-cystic | 17 (27) | 8 (27) | 9 (28) | |
| Cystic | 16 (26) | 10 (33) | 6 (19) | |

**Table 4** Factors related to adequate biopsy results: core needle biopsy (CNB)

| Factor | CNB (N = 31) | Inadequate results (N = 7) | Adequate results (N = 24) | *p*-value |
|---|---|---|---|---|
| **Size > 2 cm: number (%)** | 22 (71) | 2 (29) | 20 (83) | 0.012* |
| **Composition: number (%)** | | | | 0.043* |
| Solid | 18 (58) | 7 (100) | 11 (46) | |
| Solid-cystic | 8 (26) | 0 | 8 (33) | |
| Cystic | 5 (16) | 0 | 5 (21) | |

*Fisher's exact test

**Table 5** Factors related to adequate biopsy results: fine needle aspiration (FNA)

| Factor | FNA (N = 31) | Inadequate results (N = 23) | Adequate results (N = 8) | *p*-value |
|---|---|---|---|---|
| **Size > 2 cm: number (%)** | 22 (71) | 15 (65) | 7 (88) | 0.379* |
| **Composition: number (%)** | | | | 0.052* |
| Solid | 11 (31) | 5 (21) | 6 (75) | |
| Solid-cystic | 9 (29) | 8 (35) | 1(13) | |
| Cystic | 11 (31) | 10 (44) | 1 (13) | |

*Fisher's exact test

## Discussion

The aim of the present study was to compare the rate (proportion) of adequate biopsy results between CNB and FNAB under US guidance for thyroid nodules, based on the 2017 Bethesda System. There were no significant differences between the CNB and FNAB groups in terms of baseline characteristics, which included gender, age, and TSH and FT4 levels. There were more women than men in both CNB and FNAB groups, which was related to the generally higher prevalence of thyroid nodules in women.[1,2]

There were also no significant differences between CNB and an FNAB groups in terms of size and solid/cystic components of the thyroid nodules. CNB was able to obtain more thyroid tissue for more adequate diagnosis as compared to FNAB. This result is similar to those of other studies.[9,13,14,16-18] CNB can reduce false negative results, or prevent unnecessary excision after FNAB.[9,13,14,16-18]

CNB can be safely performed in the outpatients department, with few complications.[13,14] Pain during the procedure, tolerability, and complications were similar between the two biopsy methods.[20,21] Some studies recommend using CNB instead of a repeat FNAB after a prior inadequate FNAB result.[13-16] Other studies recommend using CNB as a first-line biopsy method for high risk solid thyroid nodules.[18] The present study seemed to affirm the use of CNB as a first-line biopsy method.

Overall, without regards to biopsy methods, patients with thyroid nodules larger than 2 cm were more likely to have adequate biopsy. On the other hand, presence of cystic/solid components did not significantly affect biopsy adequacy. In the CNB group, both larger nodule size and cystic/solid components were related to adequate biopsy. But, for CNB, solid nodules were less likely to obtain adequate biopsy, a counterintuitive result. This could be explained by the small size of the nodule. That is, for the 7 patients with inadequate CNB result, 5 had nodules smaller than 2 cm (Table 4). In the FNAB group, while both size and components of the nodules were not strictly significantly related to adequate biopsy, the cystic/solid component were of borderline significance. For FNAB, solid nodules were more likely to obtain adequate biopsy. This was as expected, since solid nodules should yield more cells. Also, size of the nodule might be important: it can be seen that in the 8 patients with adequate FNAB, 7 had nodules larger than 2 cm (Table 5).

In the present study, the rate of non-diagnostic FNAB results was higher when compared with to other studies. Experience of the US operator, FNA technique, and cytological preparation may also affect the non-diagnostic rates. As our hospital has no cytologist, the slides obtained from FNAB are sent for outside examination. Also, a nodule that is cystic and of size smaller than 2 cm tends to increase the chance of non-diagnostic results.

The present study has several limitations. The retrospective design, the small sample size, and operator-dependent procedures might make the study less valid and less reliable. Pakkred Community Hospital also lacks radiologists and pathologists, and needs to co-ordinate diagnosis and treatment with other provincial hospitals whose services include these specialists. Some patients chose to receive treatment at other hospitals and were lost to follow-up. Finally, with only one US operator who also does the biopsy, the experience of the operator and the technique used may not be generalizable.

## Conclusion

CNB under US guide is associated with higher rate of adequate biopsy than FNAB, for thyroid nodules, with adequacy defined by the 2017 Bethesda System. Size of nodules greater than 2 cm was the most consistent predictive factor for adequate biopsy. US-guided CNB is recommended as a first-line biopsy method, in place of FNAB.

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## Funding

None

## Conflict of Interest

None

## Ethical Approval

The study was approved by the Institutional Ethics Committee.

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*บทคัดย่อ* **การเปรียบเทียบการเก็บตัวอย่างส่งตรวจสำหรับก้อนที่ต่อมไทรอยด์ ระหว่างการทำ Fine needle aspiration และการทำ Core needle biopsy ร่วมกับการใช้อัลตร้าซาวด์**

**ชลลดา สุวรรณะชฎ, พบ.**

*กองศัลยกรรม, โรงพยาบาลปากเกร็ด จังหวัดนนทบุรี*

*วัตถุประสงค์:* การทำ Core Needle Biopsy (CNB) ก้อนที่ต่อมไทรอยด์ (thyroid nodule) ถูกนำมาใช้แทนการทำ Fine Needle Aspiration (FNA) ที่มักมีข้อกำจัดคือได้เซลล์ไม่เพียงพอต่อการวินิจฉัยแปลผลตาม Bethesda Classification System (2017) การทำ CNB เป็นการเก็บตัวอย่างที่มักจะได้เซลล์เพียงพอในการแปลผลสามารถแยกวินิจฉัยได้ว่าเป็นก้อนที่ไม่ร้ายแรง (Benign) หรือเป็นก้อนที่มีความเสี่ยงเป็นมะเร็ง (Malignant) วัตถุประสงค์ของการวิจัยนี้คือ การเปรียบเทียบประสิทธิผลของวิธีเก็บตัวอย่างก้อนที่ต่อมไทรอยด์ระหว่าง CNB และ FNA ร่วมกับการใช้อัลตร้าซาวด์ กับการแปลผลตาม Bethesda System

*วิธีการศึกษา:* การวิจัยนี้เป็นรูปแบบ retrospective cohort study โดยการเก็บข้อมูลจากเวชระเบียนผู้ป่วยที่มีการเก็บตัวอย่างก้อนที่ต่อมไทรอยด์ด้วยวิธีการทำ FNA และ/หรือ CNB ร่วมกับการใช้อัลตร้าซาวด์ที่โรงพยาบาลปากเกร็ด ตั้งแต่วันที่ 1 มกราคม พ.ศ. 2560 ถึงวันที่ 31 ธันวาคม พ.ศ. 2563 ผู้ป่วยถูกแบ่งออกเป็น 2 กลุ่ม คือ กลุ่ม CNB (N = 31) และกลุ่ม FNA (N = 31)

*ผลการศึกษา:* ผู้ป่วยที่ได้รับการเก็บชิ้นเนื้อตัวอย่างที่เพียงพอในการแปลผลตาม Bethesda System พบในกลุ่ม CNB มากกว่าในกลุ่ม FNA (ร้อยละ 77 และ 26 ตามลำดับ) อย่างมีนัยสำคัญทางสถิติ (p-value < 0.001) ปัจจัยที่มีความสัมพันธ์อย่างมีนัยสำคัญทางสถิติ กับความสำเร็จในการเก็บตัวอย่างก้อนที่ต่อมไทรอยด์ได้แก่ขนาดก้อนที่มากกว่า 2 ซม. ส่วนลักษณะของก้อนที่ต่อมไทรอยด์ ไม่มีผลต่อความสำเร็จในการเก็บชิ้นเนื้อตัวอย่างและการแปลผล อย่างมีนัยสำคัญทางสถิติ

*สรุปผลการศึกษา:* ในการเก็บชิ้นเนื้อตัวอย่างก้อนที่ต่อมไทรอยด์ การทำ CNB มีประสิทธิผลดีกว่า FNA