ISSN 0125-6068

The Thai Journal of SURGERY

Official Publication of the Royal College of Surgeons of Thailand
www.rcst.or.th

Volume 39 January-March 2018 Number 1

ORIGINAL ARTICLES

Secretariat Office :
Royal Golden Jubilee Building, 2 Soi Soonvijai, New Petchaburi Road, Huaykwang, Bangkok 10310, Thailand
Tel. +66 2716 6141-3 Fax +66 2716 6144 E-mail: frcst@rcst.or.th www.rcst.or.th

Royal College of Surgeons of Thailand

Secretariat Office :
Royal Golden Jubilee Building, 2 Soi Soonvijai, New Petchburi Road,
Bangkok 10310, Thailand

OFFICERS 2017 - 2019

President	:	**Tanaphon Maipang**
President-Elect	:	**Paisit Siriwittayakorn**
Vice President	:	**Pramook Mutirangura**
Secretary General	:	**Vitoon Chinswangwatanakul**
Assistant Scretary	:	**Charnvate Satthaputh**
Treasurer	:	**Preecha Siritongtaworn**
Past Presidents	:	**Udom Poshakrisna**
		Sem Pring-Puang-Geo
		Kasarn Chartikavanij
		Charas Suwanwela
		Thira Limsila
		Kijja Sindhvananda
		Arun Pausawasdi
		Kitti Yensudchai
		Thongueb Uttaravichien
		Chomchark Chuntrasakul
		Prinya Sakiyalak
		Vithya Vathanophas
		Naronk Rodwarna
		Nopadol Wora-Urai
		Soottiporn Chittmittrapap
		Vajarabhongsa Bhudhisawasdi
		Parinya Thavichaigarn

BOARD OF DIRECTORS

Songchai Simaroj	*Representative of General Surgeons*
Monawat Ngerncham	*Representative of Pediatric Surgeons*
Sirachai Jindarak	*Representative of Plastic & Reconstructive Surgeons*
Sompop Prathanee	*Representative of Thoracic Surgeons*
Yodruk Prasert	*Representative of Neurosurgeons*
Chaiyong Nualyong	*Representative of Colorectal Surgeons*
Nopdanai Chaisomboon	*Representative of Urological Surgeons*
Thana Turajane	*Representative of Orthopedic Surgeons*
Thanyadej Nimmanwudipong	*Member*
Pornchai O-Charoenrat	*Member*
Supakorn Rojananin	*Member*

The THAI *Journal of* SURGERY

Official Publication of Royal College of Surgeons of Thailand

ISSN 0125-6068

Editorial Board

Published quarterly by : Royal College of Surgeons of Thailand

The THAI *Journal of* SURGERY

Official Publication of the Royal College of Surgeons of Thailand

INFORMATION FOR AUTHORS

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

The Thai Journal of Surgery invites concise original articles in the field of clinical and experimental surgery as well as surgical education. Articles must be contributed solely to The Thai Journal of Surgery and when published become the property of the Royal College of Surgeons of Thailand. The Royal College of Surgeons of Thailand reserves copyright on all published materials and such materials may not be reproduced in any form without the written permission.

The Royal College of Surgeons of Thailand accepts no responsibility for opinions expressed by contributors. Manuscripts submitted for publication should be sent to :

Pornchai O-charoenrat, M.D.
The Thai Journal of Surgery
Royal College of Surgeons of Thailand
Royal Golden Jubilee Building
2 Soi Soonvijai, New Petchburi Road
Huay Kwang, Bangkok 10310, Thailand
Tel. : +66 2716 6141-3 Fax : +66 2716 6144
E-mail : frcst@rcst.or.th

Manuscripts

Manuscripts should be typewritten on one side of A4 paper only with double spacing and at least one inch margins. Separate pages: title page, text, acknowledgments, references, individual tables, abstract in Thai, and legends (as the format in this journal). Number pages consecutively, beginning with the title page. Type the page number in the upper right-hand corner of each page. An orginal and one additional copy of all materials including figures and tables, using *the Microsoft Words* Program, must be submitted for editorial review. Metric measurements should be used. Generic names for drugs should be used and if trade name is mentioned, it should be put in parenthesis.

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

1. Title of the paper
2. Name of Author(s), including first name(s) with academic degree(s)
3. Name of department and institution in which the work was done
4. Index word(s)
5. Short running title

Illustrations and Tables

Glossy, black and white photographs of illustration are requested. Original drawing should be professionally drawn in black India ink. Typewritten or freehand lettering is not acceptable. Illustration should be numbered, the tops indicated and the title of the article and the authors name in brief typed on a label pasted on its back. Do not mount the illustrations in the manuscripts. Each table should be prepared on a separate sheet and should be numbered consecutively as mentioned in the text and each must have a heading. Illustrations are accepted with color prints or color slide (not the negatives).

References

References must be listed on a separate sheet in numeric order as referred to in the article, not alphabetically. Only references mentioned in the text should be listed and should be selective with not more than 30 references except under unusual circumstances. Number references consecutively in the order in which they are first mentioned in the text. Identify references in text, tables, and legends by arabic numerals (in superscript).

The references must be verified by the author(s) against the original documents.

Example forms of references are given below.

Journal

1. *Standard Journal Article :*
   List all authors when six or less; when seven or more, list only first three and add et al.
   Soter NA, Wasserman SI, Austen KF. Cold urticaria: release into the circulation of histamine and eosinophil chemotactic factor of anaphylaxis during cold challenge. N Engl J Med 1976; 294:687-90.
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.

Books and Other Monographs

3. *Personal Author (s) :*
   Osler AG. Complement: mechanisms and functions. Englewood Cliffs: Prentice - Hall, 1976.
4. *Corporate Author :*
   American medical Association Department of Drugs. AMA drug evaluations. 3rd ed. Littleton: Publishing Sciences Group, 1977.
5. *Editor, Compiler, Chairman as Author :*
   Rhooder AJ, Van Rooyen CE, comps. Textbook of virology: for students and practitioners of medicine and the other health sciences. 5th ed. Baltimore: Williams & Wilkins, 1968.
6. *Chaper in Book :*
   Weinstein L, Swartz MN. Pathogenic properties of invading microorganisms. In: Sodeman WA Jr. Sodeman WA, eds. Pathologic physiology: mechanisme of disease. Philadelphia: WB Saunders, 1974:457-72.
7. *Agency Publication :*
   National Center for Health Stastistics. Acute conditions: incidence and associated disability, United States, July 1968-June1969. Rockville. Md.: National Center for Health statistics, 1972. Vital and health statistics. Series 10: Data from the National health Survey, No. 69 : (DHEW publication no. (HSM) 72-1036).

Other Articles

8. *Newspaper Article :*
   Shaffer RA. Advances in chemistry are starting to unlock mysteries of the brain: discoveries could help cure alcoholism and inso mnia, explain mental illness. How trhe messengers work. Wall Street Journal 1977 Aug 12:(col. 1), 10(col.1).
9. *Magazine Article :*
   Roueche B. Annals of medicine: the Santa Claus culture. The New Yorker 1971 Sep 4:66-81.

Abbreviations

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

SUBSCRIPTION INFORMATION

Subscription rate : B 200.00. single issue B 60.00
International : Individual US$ 35.00, Institutional US$ 45.00
Postage and handling - Surface mail included.
Air mail added US$ 15.00 for each or US$ 40.00 for bulk of 4 copies.
Combined subscriptions > 4 copies available for institutional only at US$ 35.00 each subscription.
Medical Students, Intern and Residents : B 100.00

Business Address : Subscriptions, advertising, and all business communications should be addressed to:

THE THAI JOURNAL OF SURGERY
Royal Golden Jubilee Building
2 Soi Soonvijai, New Petchburi Road
Bangkok 10310, Thailand

Change of Address : Please allow 30 days before date of issue for change of address. Notification should include the old as well as the new address, with indication of whether the change is temporary or permanent.

The THAI *Journal of* SURGERY

Official Publication of the Royal College of Surgeons of Thailand

Vol. 39 January - March 2018 No. 1

Original Article

Renal Tumors in Children: Outcomes of Treatment in a 10-year Period

Siripuk Sawetchaikul, MD
Suranetr Laorwong, MD
Rangsan Niramis, MD

Department of Surgery, Queen Sirikit National Institute of Child Health, Bangkok, Thailand

Abstract

Background: **Renal tumors are the second most common intraabdominal tumor in children and Wilms' tumor is mostly mentioned. Other renal tumors have a small number and also have different clinical characteristics, treatment and prognosis comparing with Wilms' tumor.**

Purpose: **The aim of this study was to determine characteristics and outcomes of treatment of renal tumors in children.**

Materials and Methods: **A retrospective chart review of patients with renal tumors who were surgically treated at Queen Sirikit National Institute of Child Health from January 2006 to December 2015 was conducted. Patients' data were collected and analyzed for demonstration of treatment outcomes of the various renal tumors.**

Results: **Sixty-four patients, 30 males and 34 females, were available for the study. Age at diagnosis ranged from 2 months to 14.5 years (average 3.2 years). The three most common clinical manifestations were palpable abdominal mass, hematuria and abdominal pain in 47 (73.4%), 17 (26.6%) and 12 cases (18.8%), respectively. The principal preoperative imaging was computerized tomographic scan which was done in 62 cases (96.9%). Benign and malignant renal tumors were noted in 7 (10.9%) and 57 cases (89.1%). Benign renal tumors including mesoblastic nephroma (4 cases) and others (3 cases) were treated by total nephrectomy and all of the 7 cases survived. Malignant renal tumors included Wilms' tumor (42 cases), clear cell sarcoma (6 cases), renal cell carcinoma (5 cases) and others (4 cases). Primary nephrectomy could be done in 80% of all malignant renal tumors. Adjuvant chemotherapy and radiotherapy were used to treat malignant renal tumors. Four patients died in this study, Wilms' tumor (2 cases), renal cell carcinoma (1 case) and mesenchymal chondrosarcoma (1 case). There was no mortality in the benign group.**

Conclusion: **Wilms' tumor was the most common renal tumor in children with good prognosis. Mesoblastic nephroma was the most common benign renal tumor and had a 100% survival rate.**

Keywords: **Renal tumors, children, Wilms' tumor, mesoblastic nephroma, outcome**

Correspondence address: *Rangsan Niramis, MD, Department of Surgery, Queen Sirikit National Institute of Child Health, 420/8 Rajavithi Road, Bangkok 10400, Thailand; Telephone/Fax: +66 2354 8095; E-mail: rniramis@hotmail.com*

Introduction

Renal tumors are the second most common solid intraabdominal tumor in children that represent malignant more common than benign tumors. Wilms' tumor is the most common pediatric renal tumor approximately 90% of the malignant group[1-5]. The other malignant renal tumors include clear cell sarcoma, malignant rhabdoid tumor and renal cell carcinoma. Benign renal tumor is the minority group including congenital mesoblastic nephroma, cystic renal tumor and angiomyolipoma. Renal tumors in children have different identities and manifestations. Prognosis of each tumor is depended on histology, stage, age of the patients, tumor weight, response to therapy and chromosomal abnormalities. However, it is not possible to definitely identify the difference between each type with clinical manifestation and preoperative imaging[6,7]. Herein, we are interested to review our experience in management of the renal tumors in a-10- year period. The objective of the study was to determine the characteristics and outcomes of the treatment of the renal tumors in children at our institute.

Materials and Methods

After the proposal was approved by the Ethic Committees of the institute (Document No. 59-065), medical records of children (age 0-15 years) with the diagnosis of renal tumors from January 2006 to December 2015 at Queen Sirikit National Institute of Child Health (QSNICH) were reviewed. Patients who had been surgically treated from other hospitals were excluded from this study. Data collection included demographics, clinical manifestations, underlying diseases, preoperative imaging, metastasis work up, staging, types of management and results of treatment. Follow-up time was determined by the last contact at QSNICH until December 31, 2016 by review of the medical records. We contacted some patients in order to update clinical data by telephone and letter. Patients' data were analyzed using descriptive statistic.

Results

Sixty-six patients were treated with renal tumors during the study period. Two patients with Wilms' tumor were excluded from this study. One was sent from the other hospital after tumor recurrence and the other was transferred after primary surgery from the rural hospital to continue chemotherapy. Therefore, 64 patients were available for the study.

Pathological diagnosis

Malignant renal tumors were identified in 57 of the 64 patients (89.1%) and Wilms' tumor had the most common incidence (42 cases or 65.5% of all renal tumors and 73.8% of malignant renal tumors). The other malignant renal tumors were clear cell sarcoma (6 cases or 9.4% of all renal tumors), renal cell carcinoma (5 cases or 7.8% or all renal tumors), rhabdoid tumor (2 cases) and others (mesenchymal chondrosarcoma and malignant round cell tumor in one case, each). The remaining 7 patients (10.9%) had benign renal tumors including mesoblastic nephroma (4 cases) and others (metanephric adenoma, cystic partial differentiated nephroblastoma and angiomyolipoma in one case, each).

Demographic data

Of the 64 patients with renal tumor there was no difference of sex incidence between male and female (30 vs 34) (Table 1). For analysis of each type of the tumors, male was more common than female in malignant non-Wilms' tumor (2:1) and benign renal tumor (2.5:1), whereas female are more predominant than male in Wilms' tumor (1:1.8).

Age of the patients with renal tumor ranged from 2 months to 14 years. Each type of tumor was found in different age groups (Figure 1). Median age of rhabdoid tumor, mesoblastic nephroma and Wilms' tumor was 1.08, 1.12 and 1.45 years, where as median age of clear cell sarcoma and renal cell carcinoma was 4.58 and 7.83 years, respectively.

Associated anomalies

Four patients had associated anomalies. Three patients with Wilms' tumor were noted to have association with Denys-Drash syndrome, autosomal recessive polycystic kidney disease and hypospadias with bilateral undescended testes. One patient with angiomyolipoma was previously diagnosed with tuberous sclerosis.

Clinical manifestations

The most common presentation of these patients

Table 1 Gender and type of renal tumors

Gender	Wilms' tumor (n=42)	Malignant non -Wilms' tumors (n=15)	Benign renal tumor (n=7)	Total (N=64) (%)
Male	15	10	5	30 (46.9)
Female	27	5	2	34 (53.1)
Male: Female	1:1.8	2:1	2.5:1	1:1.1

Table 2 Clinical manifestations of patient with renal tumors

Type of renal tumors	Abdominal mass	Abdominal pain	Hematuria	Fever	Weight loss	Hypertension
Wilms' tumor (n=42) (%)	32 (76.2)	9 (21.4)	11 (26.2)	4 (9.5)	2 (4.8)	6 (14.3)
Clear cell sarcoma (n=6) (%)	5 (83.3)	-	2 (33.3)	-	-	-
Renal cell carcinoma (n=5) (%)	2 (40)	1 (20)	2 (40)	2 (40)	2 (40)	-
Rhabdoid tumor (n=2) (%)	1 (50)	-	2 (100)	1 (50)	-	-
Mesoblastic nephroma (n=4) (%)	4 (100)	-	-	-	-	-
Other (n=5) (%)	3 (60)	2 (40)	-	2 (40)	-	-
Overall (N=64) (%)	47 (73.4)	12 (18.8)	17 (26.6)	9 (14.1)	4 (6.3)	6 (9.4)

with renal tumor was palpable abdominal mass (Table 2). Gross hematuria was found in every type of malignant renal tumors. Only 6 patients (14.3%) with Wilms' tumor developed hypertension. There were two patients who did not have any symptoms. One patient with angiomyolipoma was found during screening ultrasonography of tuberous sclerosis. One with Wilms' tumor was incidental finding during exploratory laparotomy due to splenic injury.

Preoperative imaging

Plain film of abdomen was done in 41 patients (64.1%) and mostly revealed soft tissue mass density in the kidney. Abdominal ultrasound was done in 42 patients (65.6%) and could differentiate between solid and cystic renal tumors. Computerized tomographic (CT) scan was done in 62 patients (96.9%). Two patients was not investigated with the CT scan because of incidental diagnosis of Wilms' tumor during operation of ruptured appendicitis (one case) and using intravenous pyelography (IVP) instead of the CT scan (one case). The CT scan could not differentiate the definite type of renal tumors.

Location of the renal tumors

Table 3 showed the renal sides involved by primary renal tumors. Tumors originated more often in the right kidney than the left one, both benign and malignant tumors (56.3% vs 40.6%). Only two cases with Wilms' tumor involved bilaterally.

Operative procedures

All of the patients were treated along with National Wilms' Tumor Study Group-5 (NWTSG-5)[2] and Thai Pediatric Oncology Group 2014 (Thai POG 2014)[8]. Primary nephrectomy was the recommended procedure. If nephrectomy was not possible, tumor biopsy for tissue diagnosis should be done. All of 7 patients with benign renal tumor (100%) and approximately 80% of the malignant renal tumors could undergo primary nephrectomy (Table 4). Nine malignant renal tumors were primarily treated with open tissue biopsies. Needle biopsy was performed in one case and open biopsy was repeated after pathological report of inadequate tissue. Eight of 10 patients with primary tumor biopsy underwent nephrectomy after treatment with chemotherapy and radiation. Other two patients were lost to follow-up, one with renal cell carcinoma and one with undifferentiated malignant round cell tumor.

Chemotherapy and radiation

All of the patients with benign tumor underwent only nephrectomy, no other additional treatment. All

Table 3 Location of the primary renal tumors (n=42)

Type of renal tumor	Right kidney	Left kidney	Bilateral kidneys
Malignant renal tumors			
Wilms' tumor	25	15	2
Renal cell carcinoma	2	3	0
Clear cell sarcoma	3	3	0
Rhabdoid tumor	0	2	0
Mesenchymal chondrosarcoma	1	0	0
Malignant roumd cell tumor	0	1	0
Benign renal tumors			
Mesoblastic nephroma	3	1	0
Metanephric adenoma	0	1	0
Angiomyolipoma	1	0	0
Cystic partial differentiated Nephroblastoma	1	0	0
Total (%)	**36 (56.3)**	**26 (40.6)**	**2 (3.1)**

Table 4 The first operative procedure

Operative procedures	Wilms' tumor (n=42)	Malignant Non-Wilms' tumors(n=15)	Benign renal tumors (n=7)	Total (N=64)
Primary nephrectomy (%)	35 (83.3)	12 (80)	7 (100)	54 (84.4)
Tumor biopsy				
Open (%)	7 * (16.7)	3 (20)	-	10 (15.6)

*Initial needle biopsy in one case and open biopsy later because of inadequate tissue in the first procedure

Table 5 Outcome of patients with Wilms' tumor (n =42)

Patients' data	Follow-up time after nephrectomy				
	3 months	6 months	1 year	2 years	3 years
Follow-up	39	39	38	34	33
Lost to follow-up	3	3	4	7	7*
Death	0	0	0	1	2*
Tumor recurrence	0	2	2	3	4*

*accumulative number

of the patients with malignant tumor were treated by chemotherapy and radiation after nephrectomy or tumor biopsy, based on the guideline of NWTSG-5[2] and Thai POG 2014[8].

Outcomes

Mean follow-up time was four years. Of the total 64 patients, 42 cases (65.6%) had contact with the hospital over 3 years after nephrectomy.

Malignant renal tumors

Wilms' tumor: Table 5 showed patients' data of Wilms' tumor after surgical treatment in a 3-year period. Tumors recurred after nephrectomy in 4 cases (9.5%) within 6 months (2 cases), 2 years (1 case) and 3 years (1 case), respectively. All of the recurrence cases were treated with chemotherapy and tumor resection. Two cases died after nephrectomy within one and three years in one case, each. Therefore, the patients were

alive more than 2 years in at least 34 cases (81.0%) and more than 3 years in at least 33 cases (78.6%) of the total 42 cases after nephrectomy.

Clear cell sarcoma: Four of the 6 patients were doing well after 3-year follow-up. Other two patients had recurrence diseases at one and two years after nephrectomy. One case was in the process of treatment and another case received a palliative care.

Renal cell carcinoma: Two of the 5 patients were doing well without any recurrence after 3-year follow-up. Two patients were transferred to the rural hospital after surgical treatment, one case died a few weeks later and there was no information on another case. The remaining one case was lost to follow-up six months after tumor biopsy.

Rhabdoid tumor: All of the two patients were lost to follow-up within one year after nephrectomy and chemotherapy.

Other malignant renal tumors: One case with chondrosarcoma had recurred within 1.5 years and died within 3 years after primary nephrectomy. One patient with undifferentiated malignant round cell tumor was lost to follow-up within three months after tumor biopsy.

Benign renal tumors

Mesoblastic nephroma: Four patients were alive over 3-year follow-up. One of the 4 patients had recurrence at 1.5 years after nephrectomy. He underwent tumor resection once again and was doing well after that.

Other benign renal tumors: Three patients with angiomyolipoma, cystic partial differentiated nephroblastoma and metanephric adenoma were alive over 3-year follow-up without any recurrence.

Discussion

Wilms' tumor is the most common renal tumor in children. Approximately 94% of childhood renal tumors was reported in the United States[7,9,10]. Our experience from the present study revealed that Wilms' tumor was found in only 65.6% of all renal tumors. Rhabdoid tumor and clear cell sarcoma of the kidney were previously classified in a variant of Wilms' tumor. Clear cell sarcoma and renal cell carcinoma in this study were found to have a higher incidence than those in the report of Ying[11] (9.4% vs 2.8% and 7.8% vs 2.5%). In other previous study, there is no sexual predominance in any group of the renal tumor, except slightly higher of female in Wilms' tumor[9,12,13], whereas our present study revealed female predominance in Wilms' tumor and male predominance in malignant non-Wilms' tumor and benign renal tumors. Age group of each renal tumor is different but overlapped in some types. Wilms' tumor, rhabdoid tumor and mesoblastic nephroma were present in infant and early childhood, but renal cell carcinoma was commonly found in adolescent. Clear cell sarcoma was present in early childhood period (Figure 1). Regarding associated abnormality, although tuberous sclerosis is found in angiomyolipoma, it may be associated with renal cell carcinoma as the report of Kida et al.[14]. Asymp-tomatic abdominal mass is the main problem to seek for

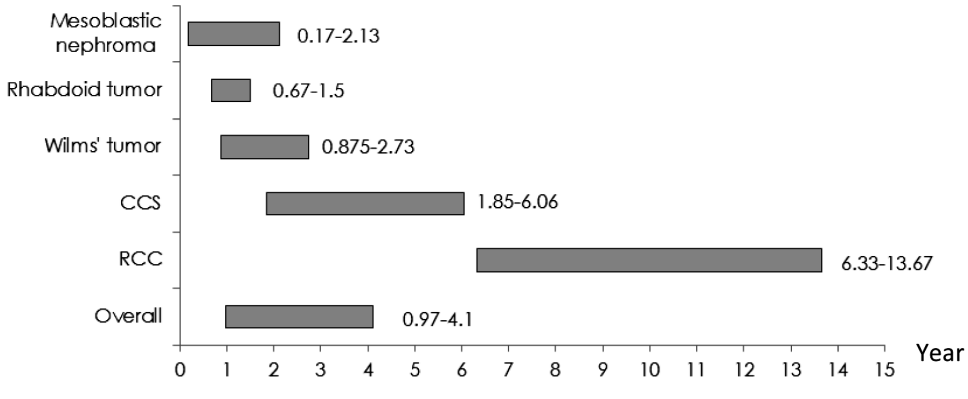

Figure 1 Age distribution of renal tumors (25^{th} -75^{th} percentile)
Abbreviation: CCS = clear cell sarcoma
RCC = renal cell carcinoma

medical service. Preoperative imaging by a CT scan has unique features but limited value in differentiate type of the renal tumors[6,7]. Previously an IVP was done for demonstration of renal tumors[15]. One patient in our study was investigated by an IVP instead of a CT scan to differentiate renal tumor and hydronephrosis.

Management of renal tumors at our institute was based on NWTSG-5[2] and Thai POG 2014[8]. Primary nephrectomy could be performed in 100% of benign renal tumors and approximately 80% of malignant renal tumors. There was no difference in primary nephrectomy between Wilms' and malignant non-Wilms' tumor (83.3% vs 80%). In the patients with initial treatment by tumor biopsy, every case with Wilms' tumor underwent nephrectomy after chemotherapy, whereas nephrectomy was not done in two of three cases with malignant non- Wilms' tumor because of loss to follow-up.

Improved outcomes of Wilms' tumor management in our institute revealed from the previous studies in two periods of time. The first period was between 1986 and 1995 with the 2-year survival rate of 50%[16]. The second one was between 1999 and 2009 with the 2-year survival rate of approximately 90%[17]. Five-year overall survival rate in the United States[18,19], Siriraj Hospital[20] and 4-year overall survival rate at Songklanagarind Hospital[21] were 95%, 77.40% and 65.20%, respectively. Malignant-non Wilms' tumor group had poorer prognosis than Wilms' tumor. Clear cell sarcoma had better prognosis than renal cell carcinoma and rhabdoid tumor[11]. There were more recurrences in clear cell sarcoma but the patients survived. All of rhabdoid tumor was lost to follow-up within one year with unknown reason. Benign renal tumor had good prognosis. It might recur in the case with remaining residual tumor and successfully treated by redo-surgical resection.

The present study had some limitations because it was a retrospective review and had a short time for clinical follow-up of the patients. We could not compare a long-term outcome with other institutes.

REFERENCES

1. Ehrich PF, Shamburger RC. Renal tumors. In: Holcomb GW III, Murphy PJ, Ostlie DJ, eds. Ashcraft's pediatric surgery. 6th ed. Philadelphia: Elsevier- Saunders; 2014. p. 859-82.
2. Ehrich PF, Shamburger RC. Wilms' tumors. In: Coran AG, Caldamone A, Adzick NS, editors. Pediatric surgery. 7th ed. Philadelphia : Elsevier-Saunders; 2012. p. 423-40.
3. Ritchey ML, Shamburger RC. Pediatric urologic oncology: renal and adrenal. In : Wein AJ, Kavoussi LR, Partin AW, eds. Campbell-Walsh Urology. 11th ed. Philadelphia: Elsevier-Saunders; 2016. p. 3559-81.
4. Hanif G. Intra-abdominal tumors in children. J Coll Physicians Surg Pak 2004;14(8):478-80.
5. Brok J, Treger TD, Gooskens,et al. Biology and treatment of renal tumors in childhood. Eur J Cancer 2016;68:179-95.
6. Miniati D, Gay AN, Parks KV, et al. Imaging accuracy and incidence of Wilms' and non-Wilms' tumors in children, J Pediatr Surg 2008;43:1031-7.
7. Lowe LH, Isnuani BH, Heller RM, et al. Pediatric renal masses: Wilms tumor and beyond. Radiographics 2000;20(6):1585-603.
8. The Thai Pediatric Oncology Group. Renal tumor. National protocol for the treatment of childhood cancer 2014. Bangkok: M-Print Corporation; 2014. p. 227-44(in Thai).
9. Bernstein L, Linet M, Smith MA, et al. Renal tumors. In : Ries LAG, Smith MA, Gurney JG, et al, eds. Download a report : Cancer Incidence and Survival Among Children and Adolescents: United States SEER Program 1975-1995. Bethesda: National Cancer Institute; NIH Pub, No. 99-4649; 79-90; SEER Program.
10. Ali AN, Diaz R, Shu HK, et al. Surveillance, epidemiology and end results (SEER) comparison of adult and pediatric Wilms' tumor. Cancer 2012;118:2541-51.
11. Ying Z, Cheung MC, Yang R, et al. Pediatric non-Wilms renal tumors: subtypes, survival and prognostic indicators. J Surg Research 2010;163:257-63.
12. Indolfi P, Terenziani M, Casale F. Renal cell carcinoma in children: a clinicopathologic study. J Clin Oncol 2003;21(3): 530-5.
13. Tomlinson GE, Breslow NE, Dome J, et al. Rhabdoid tumor of the kidney in the National Wilms' Tumor Study: age at diagnosis as a prognostic factor. J Clin Oncol 2005;23:7641-5.
14. Kida Y, Yamaguchi K, Suzuki H, et al. Tuberous sclerosis, associated with renal cell carcinoma and angiomyolipoma, in a patient who developed end stage renal failure after nephrectomy. Experiment Nephrol 2005;9(2):179-82.
15. Lister J, Levick RK. Errors in diagnosis in Wilms' tumor. J Pediatr Surg 1966;1(5):488-97.
16. Naprasert L. Wilms' tumor in Queen Sirikit National Institute of Child Health. A thesis submitted in partial fulfillment of the requirement for the Diploma of the Thai Board of Pediatrics of the Medical Council of Thailand 1996.
17. Pattarakunwiwat P. Wilms' tumor in Queen Sirikit National Institute of Child Health. A thesis submitted in partial fulfillment of the requirement for the Diploma of the Thai Board of Pediatrics of the Medical Council of Thailand 2011.
18. Hamilton TE, Shamberger RC. Wilms tumor: recent advances in clinical care and biology. Semin Pediatr Surg 2012;21:15-20.
19. Howlader N, Noone AM, Krapcho M, et al. SEER Cancer Statistics Review, 1975-2014, National Cancer Institute.

Bethesda, MD, https://seer.cancer.gov/csr/1975_2014/ , based on November 2016 SEER data submission, posted to the SEER website, April 2017.
20. Sanpakit K, Triwatanawong J, Sumboonnanonda A. Long-term outcome in pediatric renal tumor survivors: experience of a single center. J Pediatr Hematol/Oncol 2014;35 (8):610-3.
21. Sangkhathat S, Chotsampanvharaen T, Kayasut K, et al. Outcomes of pediatric nephroblastoma in Southern Thailand. Asian Pacific J Cancer Prev 2008;9:643-7.

บทคัดย่อ

เนื้องอกของไตในเด็ก: ผลของการรักษาในระยะเวลา 10 ปี

ศิริพักตร์ เศวตชัยกุล, พ.บ.*, สุรเนตร ลออวงศ์, พ.บ.*, รังสรรค์ นิรามิษ, พ.บ.*
**กลุ่มงานศัลยศาสตร์ สถาบันสุขภาพเด็กแห่งชาติมหาราชินี กรุงเทพฯ*

ความเป็นมา: เนื้องอกของไตพบได้บ่อยเป็นอันดับที่สองของเนื้องอกในช่องท้องในเด็ก และส่วนใหญ่จะกล่าวถึงแต่ Wilms' tumor เนื้องอกของไตชนิดอื่นๆ พบเป็นจำนวนน้อย และมีคุณลักษณะแตกต่างกันในแต่ละชนิด รวมทั้งการรักษาและการพยากรณ์โรคก็แตกต่างกัน เมื่อเทียบกับ Wilms' tumor

วัสดุและวิธีการ: เป็นการศึกษาย้อนหลังจากการทบทวนเวชระเบียนของผู้ป่วยที่เป็นโรคเนื้องอกของไตที่ได้รับการรักษาโดยการผ่าตัดที่สถาบันสุขภาพเด็กแห่งชาติมหาราชินี ตั้งแต่เดือนมกราคม 2549 ถึง เดือนธันวาคม 2558 ข้อมูลของผู้ป่วยถูกรวบรวมและวิเคราะห์ เพื่อแสดงถึงผลของการรักษาของเนื้องอกของไตแต่ละชนิด

ผล: ผู้ป่วย 64 ราย (เพศชาย 30 ราย เพศหญิง 34 ราย) ที่มีข้อมูลเหมาะสมในการศึกษา อายุเมื่อให้การวินิจฉัย ตั้งแต่ 2 เดือน ถึง 14.5 ปี (อายุเฉลี่ย 3.2 ปี) ลักษณะทางคลินิกที่สำคัญ 3 อย่างที่พบในผู้ป่วยได้แก่ ก้อนที่คลำได้ในท้อง ถ่ายปัสสาวะเป็นเลือดสีแดง และปวดท้อง พบในผู้ป่วย 47 ราย (ร้อยละ 73.4), 17 ราย (ร้อยละ 26.6) และ 12 ราย (ร้อยละ 18.8) ตามลำดับ ภาพรังสีที่สำคัญตรวจก่อนการผ่าตัดคือ การสแกนด้วยคอมพิวเตอร์ (CT scan) ทำในผู้ป่วย 62 ราย (ร้อยละ 96.9) เนื้องอกของไตชนิดไม่ร้ายแรง และเนื้องอกชนิดร้ายแรงหรือมะเร็ง พบได้ 7 ราย (ร้อยละ 10.9) และ 57 ราย (ร้อยละ 89.1) เนื้องอกของไตชนิดไม่ร้ายแรง ได้แก่ mesoblastic nephroma (4 ราย) และเนื้องอกไม่ร้ายแรงชนิดอื่นๆ (3 ราย) เนื้องอกของไตชนิดร้ายแรงประกอบด้วย Wilms' tumor (42 ราย), clear cell sarcoma (6 ราย), renal cell carcinoma (5 ราย) และเนื้องอกร้ายแรงอื่นๆ (4 ราย) การรักษาครั้งแรกโดยการผ่าตัดเอาไตออก สามารถทำได้ร้อยละ 100 ในผู้ป่วยเนื้องอกของไตชนิดไม่ร้ายแรง และสามารถตัดไตออกได้ประมาณร้อยละ 80 ในเนื้องอกของไตชนิดร้ายแรง การรักษาด้วยเคมีบำบัดและการฉายแสงร่วมด้วยใช้ในเนื้องอกไตชนิดร้ายแรง ในการศึกษาครั้งนี้มีผู้ป่วยเสียชีวิต 4 ราย จาก Wilms' tumor 2 ราย, renal cell carcinoma และ mesochymal chondrosarcoma อย่างละ 1 ราย ไม่มีผู้ป่วยเสียชีวิตในกลุ่มเนื้องอกของไตชนิดไม่ร้ายแรง

สรุป: Wilms' tumor เป็นเนื้องอกของไตชนิดร้ายแรงที่พบได้บ่อยที่สุดในเด็ก และมีการพยากรณ์โรคที่ดี mesoblastic nephroma เนื้องอกของไตชนิดไม่ร้ายแรงที่พบบ่อยที่สุด และมีอัตราการมีชีวิตรอดร้อยละ 100

The THAI Journal of SURGERY 2018;39:8-14.
Official Publication of the Royal College of Surgeons of Thailand

Original Article

Tumor Markers and Pediatric Intraabdominal Solid Tumors

Pimsiri Pungsuk, MD
Suranetr Laorwong, MD
Achariya Tongsin, MD
Department of Surgery, Queen Sirikit National Institute of Child Health, Bangkok, Thailand

Abstract

Background: **There are many tumor markers for initial investigation and diagnosis of pediatric intraabdominal solid tumors (ISTs). However, some types of ISTs cannot be diagnosed by tumor marker examinations because of no specific relationship between the tumor markers and these ISTs.**

Purpose: **The aim of this study was to analyse the relationships between tumor markers and pediatric ISTs.**

Materials and Methods: **A retrospective study of patients with ISTs who were initially treated at Queen Sirikit National Institute of Child Health form June 2015 to December 2016 was conducted. Patient data were collected from the medical records and were selected only among those with the definite diagnosis of ISTs. Tumor markers included neuron-specific enolase (NSE), 24-hour urine of vanillymandelic acid (VMA), serum ferritin, lactase dehydrogenase (LDH), serum alpha-fetoprotein (AFP), beta-human chorionic gonadotrophin (beta-hCG) and cancer antigen 125 (CA125). Information of the tumor markers and each type of ISTs were studied in order to demonstrate the relationships by using statistical analysis with SPSS program. The level of p-value less than 0.05 was considered significant.**

Results: **Thirty-six patients with ISTs were available for the study. The ISTs were finally definite diagnosis based on pathological reports including neuroblastoma, hepatoblastoma, hematologic tumors and retroperitoneal teratoma in 12 (33.3%), 6 (16.7%), 5 (13.9%) and 4 (11.1%), respectively. The 9 remaining ISTs were Wilms' tumor (3), ovarian dysgerminoma (2) and others (4). NSE over 130 ng/ml and urine VMA over 2 mg/day were statistically significant for definite diagnosis of neuroblastoma (p = 0.033, 0.034). NSE level might elevate in ovarian dysgerminoma, Wilms' tumor, lymphoma and leukemia but it was not statistically significant ($p > 0.05$). Increased NSE, 24-hour urine VMA and serum ferritin levels demonstrated a relationship to the severity of neuroblastoma both advanced stage and poor prognosis but no statistical significance. An elevation of LDH level might be found in many ISTs, but it revealed a significant relationship to ovarian dysgerminoma and N-myc amplification of neuroblastoma. High level of beta-hCG and CA 125 were observed in ovarian dysgerminoma. Marked elevation of average AFP level of 653,538 ng/ml was strongly indicated in diagnosis of hepatoblastoma (p = 0.01).**

Conclusion: **NSE over 130 ng/ml and urine VMA over 2 mg/day had a significant relationship to diagnosis of neuroblastoma. Marked elevation of LDH level was significantly demonstrated N-myc amplification of neuroblastoma and ovarian dysgerminoma. Marked elevation of AFP level was a strong indicator for diagnosis of hepatoblastoma in pediatric patient with ISTs.**

Keywords: **Tumor markers, intraabdominal solid tumors**

Correspondence address: *Suranetr Laorwong, MD, Department of Surgery, Queen Sirikit National Institute of Child Health, 420/8 Rajavithi Road, Bangkok 10400, Thailand; Telephone/Fax: +66 2354 8095; E-mail: netr028@yahoo.com*

Introduction

Three most common intraabdominal solid tumors (ISTs) include neuroblastoma, Wilms' tumor and hepatoblastoma. Incidences of these tumors are 1:75,000-100,000, 7.9:1,000,000 and 0.6-1.2:1,000,000 populations in neuroblastoma, Wilms' tumor and hepatoblastoma, respectively[1-3]. Most of the patients present the symptomatologies with abdominal mass, abdominal distension, weight loss, etc. Investigations with blood examinations, radiological procedures and tissue biopsy for histopathology are performed in order to confirm the definite diagnosis. In this era, tumor markers are influenced in diagnosis of various types of malignant tumors. A tumor marker is a biomarker found in blood, urine and body tissues that can be elevated by the presence of one or more types of cancer[4,5]. Therefore, tumor markers are used to help diagnosis of malignant tumors instead of tissue biopsy in some types of tumor.

However, we had an experience in misdiagnosis of ISTs due to confidence in a tumor marker. An infant with ISTs had mild elevation of serum alpha-fetoprotein (AFP) and moderate elevation of serum neuron specific enolase (NSE) and 24-hour urine vanillylmanadelic acid (VMA) levels. She was diagnosed with neuroblastoma without tissue biopsy and initially treated with chemotherapy. The patient did not improve and the tumor became larger. The diagnosis was changed from neuroblastoma to hepatoblastoma after confirmation of tissue biopsy and pathological report. Herein, we were interested to study the relationships between tumor markers and various types of ISTs in pediatric patients at our institute.

Materials and Methods

This was a retrospective study of all pediatric patients, aged 0-15 years, with ISTs, who were initially treated at Queen Sirikit National Institute of Child Health from June 2015 to December 2016. Patient data were collected from the medical records and were selected only among those with the diagnosis of ISTs and tumor markers including NSE, 24-hour urine VMA, serum ferritin, lactase dehydrogenase (LDH), AFP, beta-human chorionic gonadotrophin (beta-hCG) and cancer antigen 125 (CA 125). We excluded patients who had indefinite diagnosis from the pathological reports and patients surgically treated from other hospitals. Normal levels of tumor markers mentioned in this study were the normal levels used at our institute.

Information of the tumor markers and each type of ISTs were studied in order to demonstrate the relationships by using SPSS version 20 (IBM® SPSS statistic). Correlations between categorical variables were evaluated by Chi-square test and ANOVA. A *p*-value of less than 0.05 was considered significant.

The study was approved by the Ethic Committees of our institute, Document No. 60-041.

Results

During the study period, 48 new patients with intraabdominal tumors admitted for investigation and treatment. Twelve cases were excluded because of presence of cystic abdominal tumors (10) and indefinite diagnosis (2). Therefore, 36 cases with intraabdominal solid tumors were enrolled in the study (Figure 1).

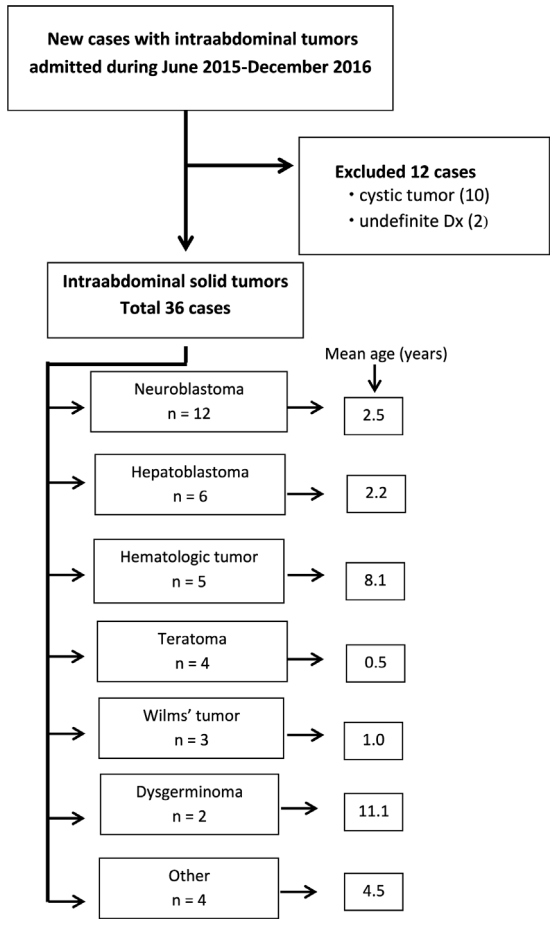

Figure 1 Schematic diagram of patients with intraabdominal solid tumors

These tumors included neuroblastoma 12 cases, hepatobastoma 6 cases, hematologic tumors 5 cases (lymphoma = 4 and acute lymphoblastic leukemia = 1), retroperitoneum teratoma 4 cases (mature =3, immature = 1), Wilms' tumor 3 cases, dysgerminoma 2 cases and others 4 cases (liver sarcoma, rhabdoid tumor of the kidney, rhabdomyosarcoma of urachus and inflammatory myofibroblastic tumor of the pancreas, one case each).

Mean age of the patients varied along with each type of tumors (Figure 1). Teratoma, Wilms' tumor, hepatoblastoma and neuroblastoma occurred in infants and young children with the mean age of 0.5, 1.0, 2.2 and 2.5 years, respectively. Hematologic tumors, rhabdomyosarcoma and dysgerminoma were present in older children with mean age of 8.1, 9.5 and 11.1 years.

Common clinical presentations of these ISTs were palpable abdominal mass in 15 cases and (41.7%), abdominal pain 7 cases (19.4%), and abdominal distension in 9 cases (25%). Three patients (8.3%) had a history of fever and 2 patients had a diagnosis of myocarditis and bony metastasis from neuroblastoma.

Normal level of each tumor marker at our institute and mean tumor marker level of each type of ISTs were shown in Table 1. Of the 12 patients with neuroblastoma, mean levels of serum NSE and urine VMA elevated more than normal levels with statistical significance ($p = 0.020$ and $p = 0.010$). Serum NSE and 24-hour urine VMA levels were the tumor markers

Table 1 Mean levels of various tumor markers for each type of intraabdominal solid tumors (N = 36)

Tumor markers / Types of tumor (n)	NSE Normal 16.3 ng/ml	AFP Normal 12 ng/ml	LDH Normal 344 U/L	Ferritin Normal 10-160 ng/ml	urine VMA Normal 2-7 mg/day
Neuroblastoma (12)					
Mean (sd)	662.9 (717.1)	7.7 (13.4)	3,305.5 (4270.8)	346.8 (286.7)	23.5 (23.9)
p-value*	0.020	0.312	0.350	0.160	0.010
Hepatoblastoma (6)					
Mean (sd)	31.7 (12.7)	652,528 (997,030)	541.3 (66.4)	102.5 (90.4)	2.3 (2.4)
p-value*	0.128	0.001	0.121	0.104	0.310
Hematologic tumor (5)					
Mean (sd)	187.8 (153.6)	1.2 (0.48)	2956.6 (3027.4)	135.2 (128.3)	1.5 (0.21)
p-value*	0.640	0.590	0.770	0.260	0.450
Teratoma (4)					
Mean (sd)	42.3 (33.0)	539.1 (18.0)	722 (239.5)	163.3 (39.8)	0.6 (0.14)
p-value*	0.330	0.590	0.340	0.550	0.410
Dysgerminoma (2)					
Mean (sd)	474.7 (23.0)	1.9 (0.36)	8,667 (6448.8)	695.4	3.2 (0.42)
p-value*	0.660	0.710	0.008	-	0.530
Wilms' tumor (3)					
Mean (sd)	190.6 (36.9)	7 (8.7)	2,435.6 (328.6)	191.6 (191.1)	2.9 (1.64)
p-value*	0.650	0.900	0.850	0.290	0.590
Rhabdoid tumor (1)					
Mean	88.2	5.5	1,678	299.6	-
Liver sarcoma (1)					
Mean	21.3	0.89	580	628.3	0.2
IMT (1)					
Mean	48.5	1.97	620	38	1.7
RMS (1)					
mean	21.4	1.8	1,424	491.2	2.6

*p-value by unpaired t-test; compared with other tumors grouped together

Table 2 Levels of NSE and 24-hour urine VMA for the diagnosis of neuroblastoma (12 cases) compared with non-neuroblastoma (24 cases)

Levels of tumor marker	Sensitivity (%)	Specificity (%)
NSE (ng/ml)		
16.3	100 (12/12)	0 (0/24)
120	66.7 (8/12)	70.8 (17/24)
130	66.7 (8/12)	75.0 (18/24)
24- hour urine VMA (ng/day)		
1.5	91.6 (11/12)	58.3 (14/24)
2	83.3 (10/12)	70.8 (17/24)
7	53.3 (7/12)	100 (24/24)

used for diagnosis of neuroblastoma. For analysis of our 36 ISTs, serum NSE level over normal limit (>16.3 ng/ml) had the sensitivity of 100% for neuroblastoma, but there was no specificity for other tumors because serum NSE level elevated over 16.3 ng/ml in every type of ISTs. Serum NSE level step up to 130 ng/ml was statistically significant for definite diagnosis of neuroblastoma (sensitivity 66.7%, specificity 75.0%, $p = 0.033$).

Evaluation of 36 patients with ISTs, an upper normal limit of 24-hour urine VMA (> 7 mg/day) had the sensitivity of 58.3% for patients with neuroblastoma and specificity of 100% with other tumors ($p = 0.000$). If we chose the lower limit of 24-hour urine VMA (>2 mg/day) for analysis, there were 83.3% sensitivity and 70.8% specificity ($p = 0.034$) (Table 2).

Therefore, significant value for diagnosis of neuroblastoma were serum NSE level over 130 ng/ml ($p = 0.033$) and 24-hour urine VMA over 2 ng/day ($p = 0.034$). Serum NSE level might elevate in ovarian dysgerminoma, Wilms' tumor, lymphoma and leukemia, but it was not statistically significant ($p > 0.05$). The level of 24-hour urine VMA might elevate in hepatoblastoma, dysgerminoma and Wilms' tumor but it was not significantly different ($p > 0.05$). AFP level markedly elevated in hepatoblastoma with the mean level of 652, 528 ng/ml ($p < 0.001$), while LDH level elevated in ovarian dysgerminoma with the mean level of 8,667 U/L ($p = 0.008$). Every tumor marker had no significant relationship to definite diagnosis of Wilms' tumor, rhabdoid tumor of kidney, retroperitoneal teratoma, liver sarcoma, rhabdomyosarcoma, lymphoma, leukemia and inflammatory myofibroblastic tumor of pancreas ($p > 0.05$).

Table 3 showed correlation of tumor markers

Table 3 Mean levels of tumor markers and clinical risks of neuroblastoma

Tumor markers / Neuroblastoma (N =12)	NSE Normal 16.3 ng/ml	AFP Normal 12 ng/ml	LDH Normal 344 U/L	Ferritin Normal 10-160 ng/ml	Urine VMA Normal 2-7mg/day
Stage					
2 (n=1) Mean	29.7	1.4	442	88.5	1.2
3 (n=4) Mean (sd)	633.2 (1037)	7.9 (5.2)	3942.5 (6385.3)	128.7 (111.5)	12.7 (17.3)
4 (n=7) Mean (sd)	770.4 (569.3)	10.4 (18.8)	3350.7 (3378.5)	477.2 (279.4)	32.9 (25.1)
p-value*	0.839	0.668	0.798	0.130	0.270
Risk					
Low (n=1) Mean	29.7	1.4	442	88.5	1.2
Intermediate (n=4) Mean (sd)	309.1 (398.1)	8.2 (3.9)	1344.2 (1216.1)	213.2 (257.9)	17.5 (16.7)
High (n=7) Mean (sd)	955.5 (783.1)	9.6 (19.1)	4835.2 (5102.9)	441.0 (290.5)	30.1 (27.3)
p-value*	0.250	0.885	0.328	0.366	0.477
N-myc					
non-amplification (n= 7) Mean (sd)	334.7 (349.8)	6.0 (4.6)	1221.2 (931.2)	326.3 (325.5)	19.7 (20.4)
Amplification (n=4) Mean (sd)	1282.4 (1081.5)	17.1 (27.2)	6970.3 (6552)	286.7 (136.7)	23.3 (34.5)
p-value*	0.058	0.332	0.039	0.885	0.837

***p-value by one-way ANOVA**

with clinical risks of neuroblastoma. NSE, ferritin and 24-hour urine VMA levels trended to elevate without statistical significance in neuroblastoma stage 3 and 4, intermediate and high risk groups and patients with positive N-myc amplification. LDH level elevated in advanced stages, intermediate and high risk groups of neuroblastoma, especially marked elevation of LDH level in N-myc amplification ($p = 0.039$). Elevation of serum ferritin level had the relationship to all stages of neuroblastoma by 72% sensitivity and increased to 100% sensitivity in stage 4 neuroblastoma. High ferritin level was noted in every case of neuroblastoma stage 3 and stage 4. Ferritin level elevated over 150 ng/ml in all 7 cases with neuroblastoma stage 4.

Special tumor marker investigations of ovarian dysgerminoma were beta - hCG (normal level < 5 m IU/ml) and CA 125 (normal level < 35 U/ml). Of our 2 patients with dysgerminoma, beta - hCG were 117.8 and 53.3 m IU/ml and mean level 85.5 m IU/ml. While, CA 125 was 81 and 470 U/ml, mean level 275.5 U/ml.

Discussion

This study showed the incidence of ISTs at our institute which neuroblastoma, hepatoblastoma and hematologic cancers were the three most common tumors. These findings were contrast from the previous studies[1-3] because this study was done in a short period of time and did not represent large amounts of ISTs. However, age incidences of each type of tumors were similar to the previous studies[1-3].

NSE is a neuronal form of glycolytic enzyme which was originally extracted from bovine brain. It was later found in endocrine (APUD - amine precursor uptake and carboxylation) cells of the central and peripheral divisions of the diffuse neuroendocrine system. Tumors of the APUD system or APUDomas, that can produce NSE, are islet cell tumor, pheochromocytoma, medullary thyroid tumor, neuroblastoma and APUD tumors of gut and lung[6].

NSE was detected in small cell lung cancer[6]. High serum level of this tumor marker had relationship to stage and disease course of neuroblastoma[7,8]. Nowadays, NSE is the principal tumor marker for diagnosis and prognostic predictor of neuroblastoma[8,9]. Zeltzer[8] chose a cutoff point of 100 ng/ml of NSE level to show the difference in survival of neuroblastoma, while the level of NSE over 15 ng/ml was defined as abnormal. Patients with NSE levels between above and below 100 ng/ml were significantly different. From this study, we choose the cutoff point of NSE level at 130 ng/ml to have the relationship to diagnosis and survival ($p = 0.033$), while NSE level over 16.3 ng/ml, at our institute, was defined as abnormal but not significant. Serum NSE level in patient with neuroblastoma was proven to have relationship to stage and disease course. Zeltzer[9] revealed elevation of serum NSE level correlation to high staging with significance and decreased NSE level in patients with response to therapy. In patients with stage IV-S disease, serum NSE level was significantly lower than those in stage IV. This result might confirm that stage IV-S had a more benign clinical course. Our present study revealed high NSE level in stage 3 and 4 of neuroblastoma and there was significantly higher NSE level in N-myc amplification than those with non-amplification.

From the present study, serum NSE level elevated over 100 ng/ml in the patients with ovarian dysgerminoma, Wilms' tumor, lymphoma and leukemia without statistical significance. Odelstad[10] used NSE to be a marker for differential diagnosis of neuroblastoma and Wilms' tumor. Tsuchida[11] suggested that serial determination of serum NSE could be differential diagnosis of neuroblastoma and other pediatric tumors because of its specificity and sensitivity.

VMA is one of intermediate products of catecholamine which excretes in the urine. Elevation of 24-hour urine VMA level has relationship to adrenal tumors, especially neuroblastoma and pheochromocytoma. Approximately 90-95% of patients with neuroblastoma showed high level of 24-hour urine VMA[12,13]. This study demonstrated that almost all of our patients with neuroblastoma had elevation of 24-hour urine VMA (range 1.2-63.2 ng/day and mean level 23.5 ng/day, $p = 0.010$). It slightly elevated in dysgerminoma, Wilms' tumor and rhabdomyosarcoma, but no significance. We used the cutoff level of 24-hour urine VMA of over 2 mg/day for significant diagnosis of neuroblastoma (sensitivity 83.3%, specificity 70.8%, $p = 0.034$).

Zeltzer[8] reported elevation of serum NSE in children with metastatic neuroblastoma. Our study revealed serum NSE, ferritin, LDH and 24-hour urine VMA levels elevated in neuroblastoma with high stage,

high risk and N-myc amplification, but no significance, except correlation of high LDH level to N-myc amplification ($p = 0.039$).

Serum AFP level was significantly high in our six cases with hepatoblastoma. It also elevates in normal infants under eight months of age and malignant germ cell tumors. However, small cell undifferentiated hepatoblastoma does not associate with elevated serum AFP[3]. Elevation of LDH level is not specific to diagnose any ISTs, but it demonstrated a high level with statistical significance in our two cases with ovarian dysgerminoma. LDH level usually elevates in tumors with high turnover rate, such as dysgerminoma, malignant hematologic tumors, seminoma and advanced stages of neuroblastoma[14,15].

Tumor markers for ovarian tumors are beta-hCG and CA 125 that correlates to epithelial cell type of ovarian malignancy. Both tumor markers elevated in our two patients with dysgerminoma. Beta - hCG level slightly elevates in dysgerminoma, but it markedly elevates in choriocarcinoma[16].

Ferritin level was found to increase significantly in our both cases of dysgerminoma and had a trend to elevate in high stage and high risk neuroblastoma. Our 7 patients with stage 4 neuroblastoma had the ferritin level increased over 150 ng/ml. Silber[17] reported that ferritin level over 150 ng/ml had a relationship to metastatic neuroblastoma and prediction of a poor prognosis.

This study has some limitations because it was a retrospective study conducted in a short period of time. Only 36 patients were enrolled in the study. Some types of ISTs had a small amount so patient data could not be well analyzed. Further study should be performed.

Conclusion

The present study revealed serum NSE level over 130 mg/ml and 24-hour urine VMA level over 2 mg/day had a relationship to diagnosis of neuroblastoma with statistical significance. Both tumor markers trended to increase levels in high stage and high risk neuroblastoma but there was no statistical significance. Serum NSE level also elevated in dysgerminoma, Wilms' tumor, lymphoma and leukemia. Marked elevation of AFP level had significant relationship to hepatoblastoma. AFP level slightly elevated in teratoma and normal infant. LDH level was significantly high in ovarian dysgerminoma and N-myc amplification neuroblastoma. Ferritin level elevated in every case of stage 3 and stage 4 neuroblastoma. Beta-hCG and CA125 levels were higher than normal limit in ovarian dysgerminoma.

REFERENCES

1. Rich BS, La Quaglia MP. Neuroblastoma. In: Coran AG, Adzick NS, Krummel TM, et al, editors. Pediatric surgery. 7th ed. Philadelphia: Elsevier; 2012. p. 441-62.
2. Ehrlich PF, Shamberger RC. Wilms' tumor. In: Coran AG, Adzick NS, Krummel TM, et al, editors. Pediatric surgery. 7th ed. Philadelphia: Elsevier; 2012. p. 423-40.
3. Meyers RL, Aronson DC, Zimmermann A. Malignant liver tumors. In : Coran AG, Adzick NS, Krummel TM, et al, editors. Pediatric surgery. 7th ed. Philadelphia : Elsevier; 2012. p. 463-90.
4. Bigbee W, Herberman E, Grubb R, et al. Tumor markers and immunodiagnosis. In : Bast RCJr, Kufe DW, Pollock RE, et al, eds. Cancer medicine. 6th ed. Hamilton, Ontario, Canada: BC Decker; 2003.
5. National Cancer Institute. Tumor markers. https://www.cancer.gov/about-cancer/diagnosis-staging/diagnosis/tumor-markers-fact-sheet. Reviewed : November 4,2015.
6. Tapia FJ, Polak JM, Barbosa AJA. Neuron-specific enolase is produced by neuroendocrine tumours. Lancet 1981; 1:808-11.
7. Carney DN, Marangos PJ, Ihde DC, et al. Serum neuron-specific enolase: a marker for disease extent and response to therapy of small-cell lung cancer, Lancet 1982; 1: 583-5.
8. Zeltzer PM, Marangos PJ, Parma AM. Raised neuron-specific enolase in serum of children with metastatic neuroblastoma. Lancet 1983;2:361-3.
9. Zeltzer PM, Marangos PJ, Evans AE. Serum neuron-specific enolase in children with neuroblastoma. Cancer 1986;57: 1230-2.
10. Odelstad L, Pahlman S, Lackgren G, et al. Neuron specific enolase: a marker for differential diagnosis of neuroblastoma and Wilms' tumor. J Pediatr Surg 1982;17:381-5.
11. Tsuchida Y, Honna T, Iwanaka T, et al. Serial determination of serum neuron-specific enolase in patients with neuroblastoma and other pediatric tumors. J Pediatr Surg 1987;17:419-4.
12. Laug WE, Siegel SE, Shaw KNF, et al. Initial urinary catecholamine metabolite concentrations and prognosis in neuroblastoma. Pediatrics 1978;62:77-83.
13. Smith SJ, Diehl NN, Smith BD, et al. Urine catecholamine levels as diagnostic markers for neuroblastoma in a defined population: implications for ophthalmic practice. Eye (Lond) 2010;24:1792-6.

14. Sokoll LJ, Rai AJ, Chan DW. Tumor markers. In: Burtis CA, Ashwood ER, Bruns DE, eds. Tietz textbook of clinical chemistry and molecular diagnosis. Missouri: Elsevier; 2012: 627.
15. Allmen DV, Fallat ME. Ovarian tumors. In: Coran AG, Adzick NS, Krummel TM, et al, editors. Pediatric surgery. 7th ed. Philadelphia: Elsevier; 2012. p. 529-48.
16. Perkins GL, Slater ED, Sanders GK. Serum tumor markers. Am Fam Physic 2003;68:1075-82.
17. Silber JH, Evans AE, Fridman M. Models to predict outcome from childhood neuroblastoma: the role of serum ferritin and tumor histology. Cancer Res 1991;51:1426-33.

บทคัดย่อ **สารส่อมะเร็งและก้อนเนื้องอกในช่องท้องของเด็ก**

พิมสิริ พึ่งสุข, พ.บ.*, สุรเนตร ลออวงศ์, พ.บ.*, อัจฉริยา ทองสิน, พ.บ.*
**กลุ่มงานศัลยศาสตร์ สถาบันสุขภาพเด็กแห่งชาติมหาราชินี กรุงเทพฯ*

ความเป็นมา: มีสารส่อมะเร็งหลายชนิดที่ใช้ตรวจเบื้องต้นเพื่อวินิจฉัยก้อนเนื้องอกในช่องท้องของเด็ก อย่างไรก็ตาม เนื้องอกบางชนิดไม่สามารถให้การวินิจฉัยได้โดยการตรวจจากสารส่อมะเร็งเพราะว่าไม่มีความสัมพันธ์เฉพาะระหว่างสารส่อมะเร็งกับชนิดของเนื้องอกเหล่านี้

วัตถุประสงค์: เพื่อวิเคราะห์หาความสัมพันธ์ระหว่างสารส่อมะเร็งกับก้อนเนื้องอกในช่องท้องของเด็ก

วัสดุและวิธีการ: เป็นการศึกษาย้อนหลังในผู้ป่วยเด็กที่ป่วยเป็นโรคก้อนเนื้องอกในช่องท้องที่รักษาครั้งแรกในสถาบันสุขภาพเด็กแห่งชาติมหาราชินี ตั้งแต่เดือนมิถุนายน 2548 ถึง ธันวาคม 2549 ข้อมูลของผู้ป่วยถูกรวบรวมจากเวชระเบียนและเลือกเฉพาะผู้ป่วยที่ได้รับการวินิจฉัยได้ถูกต้อง สารส่อมะเร็งที่ศึกษาได้แก่ neuron specific enolase (NSE), vanillylmandelic acid (VMA) ในปัสสาวะที่เก็บใน 24ชั่วโมง serum ferritin lactic dehydrogenase (LDH), alpha-fetoprotein (AFP) beta-human chorionic gonadotrophin (beta-HCG) และ cancer antigen 125 (CA125) ข้อมูลของสารส่อมะเร็งและก้อนเนื้องอกในช่องท้องแต่ละชนิดถูกนำมาศึกษาเพื่อแสดงให้เห็นถึงความสัมพันธ์ระหว่างกันโดยการวิเคราะห์ทางสถิติด้วยโปรแกรม SPSS กำหนดให้ p-value น้อยกว่า 0.05 มีนัยสำคัญทางสถิติ

ผล: ผู้ป่วย 36 รายที่มีก้อนเนื้องอกในช่องท้องถูกนำมาศึกษาในครั้งนี้ ก้อนเนื้องอกที่ได้รับการวินิจฉัยขั้นสุดท้ายยืนยันจากรายงานผลการตรวจทางพยาธิวิทยา ประกอบด้วย neuroblastoma 12 ราย (ร้อยละ33.3), hepatoblastoma 6 ราย (ร้อยละ16.7), hematologic tumors 5 ราย (ร้อยละ13.9) ก้อนเนื้องอกในช่องท้องที่เหลืออีก 9 ราย ได้แก่ Wilms' tumor (3 ราย), ovarian dysgerminoma (2 ราย) และเนื้องอกอื่นๆ (4 ราย) ระดับ NSE ที่สูงกว่า 130ng/ml และ VMA ในปัสสาวะ 24 ชั่วโมงสูงกว่า 2 mg/day สามารถใช้ในการวินิจฉัย neuroblastoma อย่างมีนัยสำคัญทางสถิติ ($p = 0.033$ และ $p = 0.034$) ระดับของ NSE อาจสูงขึ้นใน ovarian dysgerminoma, Wilms' tumor, lymphoma และ leukemia แต่ไม่มีนัยสำคัญทางสถิติ ($p > 0.05$) การสูงขึ้นของระดับ NSE, VMA และ serum ferritin แสดงให้เห็นถึงความสัมพันธ์กับความรุนแรงของ neuroblastoma ทั้งระยะที่แพร่กระจาย และบอกถึงการพยากรณ์โรคที่ไม่ดี แต่ไม่มีนัยสำคัญทางสถิติ การเพิ่มขึ้นของระดับ LDH อาจจะพบในผู้ป่วยก้อนเนื้องอกของช่องท้องหลายชนิด แต่จะมีความสัมพันธ์อย่างมีนัยสำคัญกับ ovarian dysgerminoma และ neuroblastoma ชนิดที่พบ N-myc amplification การสูงขึ้นของค่า beta-HCG และ CA125 พบใน ovarian dysgerminoma ระดับ AFP ที่สูงค่าขึ้นอย่างมาก โดยมีค่าเฉลี่ย 653,538 ng/ml ในการศึกษาครั้งนี้เป็นการบ่งชี้ยืนยันการวินิจฉัยโรค hepatoblastoma อย่างเด่นชัด ($p = 0.01$)

สรุป: ค่า NSE ที่สูงกว่า 130 ng/ml และ VMA ในปัสสาวะ 24 ชั่วโมงสูงกว่า 2 mg/day มีความสัมพันธ์ในการวินิจฉัย neuroblastoma อย่างมีนัยสำคัญ ค่า LDH ที่สูงมาก แสดงถึงความสัมพันธ์กับ neuroblastoma ชนิดที่มี N-myc amplification และ ovarian dysgerminoma การสูงขึ้นอย่างมากของระดับ AFP เป็นเครื่องบ่งชี้ถึงการวินิจฉัย hepatoblastoma ในผู้ป่วยที่มาด้วยก้อนเนื้องอกในช่องท้องเด็ก

The THAI Journal of SURGERY 2018;39:15-20.
Official Publication of the Royal College of Surgeons of Thailand

Original Article

Evaluation of Knee Arthroscopy with Concomitant Reconstruction of Anterior and Posterior Cruciate Ligament

Nguyen Manh Khanh*
Nguyen Hoang Quan*
**Institute of Orthopedies and Traumatology, Viet Duc Hospital, 40 Trang Thi, Ha Noi, Vietnam*

Abstract

Objective: **The Aim of the study is to evaluate the outcome of knee arthroscopy with concomitant reconstruction of anterior cruciate ligament (ACL) and posterior cruciate ligament (PCL).**

Materials and Methodology: **From November 2013 to December 2016, the Institute of Trauma and Orthopedics, Viet Duc University Hospital has conducted a study in 33 patients who had a knee injury.**

Results: **Ages ranged from 20 to 45 (mean 34.9). There was no difference between injuries of the left knee and right knee. Chief complaints included swelling, pain and limited movement. The sensitivity of MRI in diagnosis was 100%, 91.9%, and 78% for the ACL, PCL, and meniscus, respectively. Nineteen of 33 patients had other types of injury. Two materials preferred in surgery were autologous graft (Hamstrings) (72.2%) and homologous graft, postsurgical mean Lyscholm score: 88.1 ± 10.1, 12.5% of patients has g18 of 32 patients returned for follow-up on time and had very good outcome without any complications such as loose knee, joint stiffness, significant pain or atrophy of the quadriceps femoris muscle, good outcome, 6.2% of patients has bad outcome and required reoperation.**

Conclusions and Recommendations: **Concomitant injury of ACL and PCL is a serious injury and significantly affects patients' quality of life. Successful surgery can markedly improve patients' function and quality of life, and enable them to resume daily activities.**

Keywords: **Concomitant injury of ACL and PCL, knee trauma arthroscopy for knee**

Introduction

Knee injuries are common in daily activities but do not usually receive attention from patients because of the mild symptoms. Concomitant injury of the anterior cruciate ligament and (ACL) the posterior cruciate ligament (PCL) is rare but its complication is severe if not promptly diagnosed and treated[1,2].

The injury mechanisms include direct and indirect trauma, but mostly are due to an indirect twisting force causing the concomitant injury to both ligaments[2]. Ligament injuries are often transient and missed, however, if patients do not pay attention and it causes the instability of the knee joint if not treated[3].

Following many patients up who have been operated in Viet Duc University Hospital (VDUH), we have noticed many patients with severe sequelae, which seriously impacted the quality of life. Therefore, we conducted a study to research this problem.

Correspondence address: *Dr. Nguyen Hoang Quan, Institute of Orthopedies and Traumatology, Viet Duc Hospital, 40 Trang Thi, Ha Noi, Vietnam; Telephone: +84 9 7819 4434; Email: hoangquan9987@gmail.com*

Materials and Method

It is a combination of retrospective and prospective observational study of 33 patients diagnosed with knee injuries.

Retrospective study

Patients diagnosed with close knee trauma with ACL and PCL were treated in the Institue of Traumatology and Orthopedies (ITO) by reconstruction arthroscopy from November 2013 to November 2014.

Prospective study

Patients were operated on in ITO from December 2014 to December 2016.

Inclusion criteria

Patients admitted to the Institute of Trauma and Orthopedics (ITO), VDUH for treatment of rupture of both ACL and PCL caused by trauma, both female and male included, and aged between 16 and 60 years old.

Exclusion criteria

Patients with other concomitant injuries such as head trauma, chest trauma, abdominal trauma or the medical record is not completed.

Lysholm Knee Scoring Scale is used to evaluate outcomes of knee ligament surgery in patients. First version of this was published in 1982. The present scale includes 8 items: Limp, support, locking, instability, pain, swelling, stair climbing, squating. Maximum score is the sum of each response to the 8 items, of a possible score of 100. Computer scoring is not necessary[4].

RESULTS

Outcome

- **Demographic of patients**

Mean age 34.9. Max 57, min 20. Male 57.6%, female 42.4%, no statistical difference.

Among 33 patients, 15 (45.5%) had injury in the left kneeand 18 (54.5%) had injury in the right knee. No statistical difference.

Table 1 Age distribution (n=33)

Gender \ Age	20-45	>46	Total	%
Male	16	3	19	57.6
Female	10	4	14	42.4
Total	26	7	33	
%	78.8	21.2	100	

Table 2 Site of lesions (n=33)

Site of injury	Number	%
Left knee	15	45.5
Right knee	18	54.5

Table 3 Construction material (n=33)

	Material	Number	%
Autologous	Lateral fibularis longusand hamstring	16	48.5
	Hamstring	4	12.1
	Hamstring (bilateral)	2	6.1
Homologous	Achilles	7	21.2
	Lateral fibularis longus	1	3.0
	Achillesand patella	1	3.0
Autologous hamstring and homologous lateral fibularis longus		2	6.1
	Total	**33**	**100**

Table 4 Associated injuries (n=33)

Injury	Number	%
Lateral meniscus	5	15.2
Medial meniscus	8	24.2
Lateral ligament	2	6.1
Both menisci	5	15.2
Lateral ligament + meniscus	1	3.0

Among 33 patients, 19 (57.5%) had associated injuries, including 5 (15.2%) with injury of both menisci, 2 (6.1%) patients with lateral ligament injury, and 1 patient with lateral ligament and meniscus.

After surgery, no patients had infection of the knee or site of material harvesting. Two out of 33 patients had knee effusion. To treat this, knee aspiration and buccellation were done.

Table 5 Complication (n=32)

Complications		Yes	No
Infection	Knee	0	32
	Site of material harvesting	0	32
Knee effusion		2	30
Numbness at site of material harvesting		0	32

The minimal postsurgical follow-up duration was 3 months, the longest duration was 28 months.

Among 33 patients, 32 patients were followed up and examined after surgery, these patients were assessed by the 1993 IKDC Subjective Knee Evaluation Form and Lyscholm Knee Score.

- **Patients returning for follow-up**

32/33 patients were followed up after surgery, there were:

- 20 patients returned on time for follow-up.
- 12 patients returned late for follow-up (37.5%).

- **Postsurgical Lyscholm knee score**

Postsurgical mean Lyscholm score: 88.1 ± 10.1; min 31 (1 patient); max: 95 (4 patients). Lyscholm score improved significantly after surgery compared to before surgery.

- **Knee function evaluation by Lyscholm score**

- 4 (12.5%) patients had very good outcome.
- 2 (6.2%) patients had bad outcome and required reoperation.

Table 6 Lyscholm knee score (n=32)

	Mean ± SD	Min-Max
After surgery	88.1 ± 10.1	31-95
Before surgery	32.6 ± 17.34	18-78

$p < 0.001$

Table 7 Knee function evaluation (n=32)

Lyscholm score	Very good (95-100đ)	Good (84-94đ)	Average (65-83đ)	Bad (<65đ)	Total
Number	4	16	10	2	32
%	12.5	50	31.3	6.2	100

Factors affecting treatment outcome (by Lyscholm score)

Age

Among the patients, 61.1% with very good/good outcome were > 31 of age; 64.3% with very good/good outcome were ≤ 30 age. No statistical difference, $p > 0.05$.

Relationship between gender and outcomes

Among the patients, 66.7% with very good/good outcome were male, 57.1% with very good/good outcome were female. No statistical difference, $p > 0.05$.

Reconstruction material

- 14 (66.67%) patients with autologous material had very good/good outcome.
- 55.6% of patients with homologous material had very good/good outcome.

Follow-up visit

- 18 of 32 patients that returned for follow-up were on time, and 17 of them had very good/good outcome.

Table 8 Age and treatment outcome (n=32)

Age	Very good and good	Average and bad	Total
> 31	11	7	18
≤ 30	9	5	14
Total	**20**	**12**	**32**

Table 9 Gender and treatment outcome (n=32)

Age	Very good and good	Average and bad	Total
Male	12	6	18
Female	8	6	14
Total	**20**	**12**	**32**

Table 10 Reconstruction material (n=32)

Ligament	Very good and good	Average and bad	Total
Autologous	14	7	21
Homologous	5	4	9
Both	1	1	2
Total	**20**	**12**	**32**

Table 11 Associated injury (n=32)

Associated injury	Very good and good	Average and poor	Total
Presence	8	10	18
Absence	12	2	14
Total	**20**	**12**	**32**

- 14 of 32 patients that returned for follow-up were late, only 1 had very good result and 11 (78.6%) patients had average and poor outcome.

Associated injury

- 85.7% of patients without associated injuries had very good/good outcome.

- 44.4% of patients with associated injuries had very good/good outcome.

Discussion

Most people have had a minor knee problem at one time or another. Most of the time our body movements do not cause problems, but it is not surprising that symptoms develop from everyday wear and tear, overuse, or injury. Knee problems and injuries most often occur during sports or recreational activities, work-related tasks, or home projects.

Most dislocated knees involved tears in the two cruciate ligaments and were often accompanied by other collateral ligament complexes. Surgical repair or reconstruction seems to achieve results superior to conservative treatment. Various methods of reconstructing anterior cruciate ligament (ACL) and posterior cruciate ligament (PCL) after knee dislocation have been described.

The age of the patients in our study ranged from 20 to 57 (Table 1), with a mean age of 34.9. Most patients were in within the age of 20-30 (42.4%) or 31-45 (36.4%) (together 78.8%); only 21.2% were above 45. Therefore, knee injuries often occurred in patients at the working age who are physically active. The result was the same as when Phùng Văn Tuân in 2010 conducted on patients with isolated PCL injury[1]. Recently, 15 patients in a study conducted by Nguyên Manh Khánh[2] had a mean age of 36.1.

The injured knee was not associated with leg dominance (Table 2). Among 33 patients, the number of patients with left knee and right knee injury did not show any significant difference (15 and 18, respectively; $p > 0.05$).

Eighteen patients had meniscal injury, 8 had medial meniscus tear (44.4%), 5 had lateral meniscus tear (27.8%), and 5 had both. Medial meniscus tear appears more common than lateral meniscus tear, probably because medical meniscus is less mobile, and hence is more at risk for trauma. The similar result was observed by Trân Trúng Dâng (2011) where 26.4% and 11.8% of patients had medial and lateral meniscus injury, and by Nguyên Manh Khánh (2015)[2] with 46.7% of 15 patients.

In addition, the force that can cause trauma to both ligaments is often relatively high, or twisting; hence the high incidence of both meniscus injury.

Two patients had lateral ligament and one patient had both lateral ligaments and two menisci; these are severe associated injury in a complex knee injury, leading to low recovery ability and even the need for multiple surgeries. Among 35 patients, Fanelli[4] found 19 with injury of associated posterolateral angle, 9 with injury of medical collateral ligament (MCL), and 6 with injury of both ligaments. Phùng Vân Tuân[1] found 4 of 11 patients having associated MCL injury.

In addition, four patients had a history of knee dislocation and were treated with knee fixation or vascular grafting. These patients are often severe and likely to have more sequelae. Our patients followed a preoperative exercise regimen to restore normal range of movement of the knee joint to optimize the operation outcome[2].

Two materials preferred in surgery were autologous graft (tendon of gracillis or semitendonosus muscle, 23 (72.2%) patients) and homologous graft (Achilles tendon, 10 (27.8%) patients) (Table 3). In concomitant reconstruction of ACL and PCL, use of hamstring tendon was not adequate, therefore we had to use the ipsilateral lateral fibularis longus tendon or contralateral hamstring tendon. In VDUH, reconstruction with homologous tendon had been performed since 2008 and the result was very positive (88.2% with very good/good outcome). However, despite advantages (shorter duration of surgery, adequate graft for reconstruction, less postsurgical pain), there is an increase in the risk for infection, graft rejection, high cost, and unavailability of the material. Fanelli[4] only used homologous Achilles tendon for

reconstruction of 6 ACL injuries and 26 PCL injuries, and homologous patellar tendon for 6 ACL injuries. Lysholm Knee Scoring Scale is a patient completed questionnaire where each possible response to each of the eight items has been assigned an arbitrary score on an increasing scale. Apart from knee ligment injury, the score can be used for meniscal tears, knee cartilage lesions, osteochondritis dissecans, traumatic knee dislocation, patellar instability, patellofemoral pain, and knee osteoarthritis[4]. Postsurgical Lyscholm score was 31-95 (mean 88.1) (Table 7) and 4 (12.5%), 16 (50%), 10 (31.3%), and 2 (6.2%) patients had a very good, good, average, and bad outcome, respectively (Table 8). Strobel MJ (2006)[8], Fanelli GC (2002)[4], Zhao J (2006)[5], and Dentil M (2015)[6] found a mean Lyscholm score of 71.8, 91.2, 91.8, and 93.8, respectively.

There are few domestic studies on ACL and PCL injuries. The study of Nguyên Manh Khánh (2015)[2] on 15 patients showed a remarkable improvement on knee function, with a mean Lyscholm score of 89.4, 8 patients had very good outcome, 6 good outcome, 1 average outcome, and no bad outcome. Phùng Vân Tuân, [1] found the mean Lyscholm score were 82.4 in 7 patients with reconstruction of both ligaments (out of 10 patients in total).

Age and sex were not associated with treatment outcome, however, in our study, age range was 20-54 and the sample size was small, so it was possible that the study did not have enough power to demonstrate a difference. However, we do not favor PCL reconstruction for patients over 60.

In our study, 8 out of 32 patients used homologous tendons; among those, 4 patients had loose knee, 2 patients still had pain, and 1 patient required reoperation due to degeneration of both ligaments after 2 years. In 2014, this patient's ACL was reconstructed with autologous tendon and the outcome was favorable. The degeneration could be attributed to graft rejection or storage condition in the previous hospitals. Twenty-four patients used autologous tendons, and only one required reoperation due to wrong tunnel position.

Eighteen of 32 patients returned for follow-up on time and had very good outcome without any complications such as loose knee, joint stiffness, significant pain or atrophy of the quadriceps femoris muscle. But among 14 patients that returned late for follow-up, 11 had complications (7 loose knee). Among retrospective patients, there was a patient that had only one follow-up visit.

Therefore, rehabilitation assumes an important role in recovery. Patients without regular and timely follow-up visits are often associated with less positive outcomes. Besides, during our survey with patients who used homologous tendons, we found some patients who did not want to come back for follow-up due to the fear of reoperation.

Many factors might affect treatment outcome, including duration of surgery, surgical methods, timing of surgery, associated injuries, and timing of postsurgical rehabilitation. However, since these are rare injuries, our study did not have an adequate sample for profound discussion on this issue.

In total, 44.4% of patients with associated injuries and 85.7% of patients without associated injuries had a very good or good outcome, this difference was statistically significant ($p < 0.05$). Concomitant ACL and PCL injury might be associated with meniscal tear, medial and lateral collateral ligament injury, and knee degeneration if surgery is late. In our study, patients with associated injuries had a worse outcome, and it also affected the efficiency of pre- and postsurgical rehabilitation. Among 18 patients with associated injuries, 10 had an average or bad outcome, and one patient with bad outcome had four associated injuries. Hence, associated injuries can affect the treatment outcome in patients with concomitant ACL and PCL reconstruction.

Conclusion

Concomitant injury of ACL and PCL is a serious injury and significantly affects patients' quality of life. Successful surgery can markedly improve patients' function and quality of life, and enable them to resume daily activities.

REFERENCES

1. Phung Van Tuan, Le Hong Hai, Nguyen Quoc Dung and partner. Arthroscopic Reconstruction of the Posterior Cruciate Ligament With Use of a Hamstring Tendon Graft. Orthopedic Magazine of Vietnam, Special 2013;99-105.
2. Nguyen Manh Khanh. Evaluation of knee arthroscopy with concomitant reconstruction of anterior and posterior cruciate ligamentuse Hamstrings tendon autograft and peroneus

tendon autograft. Vietnam Medecin 2015;2:131-4.

3. Michael J. Strobel (2006). Combined. Anterior. Cruciate. Ligament, Posterior Cruciate. Ligament, and Posterolateral Corner Reconstruction With. Autogenous.Hamstring.Grafts.in. Chronic.Instabilities. Arthroscopy 2006;22(2):182-92.
4. Briggs KK, Lysholm J, Tegner Y, Rodkey WG, Kocher MS, Steadman JR. The reliability, validity, and responsiveness of the Lysholm score and Tegner activity scale for anterior cruciate ligament injuries of the knee: 25 years laterAm J Sports Med 2009;37(5):890-7. doi: 10.1177/036354650 8330143. Epub 2009 Mar 4.
5. Fanelli GC. Arthroscopically assisted combined anterior and posterior cruciate ligament reconstruction in the multiple ligament injured knee: 2- to 10-year follow-up. 2002;18(7):703-14.
6. Zhao J. Simultaneous arthroscopic reconstruction of the anterior and posterior cruciate ligaments with autogenous hamstring tendons. Arthroscopy 2006;22(5):497-504.
7. Denti M. Combined chronic anterior cruciate ligament and posterior cruciate ligament reconstruction: functional and clinical results, Knee Surg Sports Traumatol Arthrosc 2015;23(10):2853-8.

The THAI Journal of SURGERY 2018;39:21-29.
Official Publication of the Royal College of Surgeons of Thailand

Original Article

Outcomes of a Structured Program for Bowel Preparation in Patients Scheduled to Undergo Colonoscopy: A Randomized Controlled Trial

Nisa Ruangkitudom*
Vathinee Thiensukon*
Pathomporn Bunnag†
Rojsirin Chaiwong†
Varayu Prachayakul‡
Somchai Amornyotin¶
Thawatchai Akaraviputh§

*Professional Nurse (Senior Professional Level), Gastroenterology Unit, Nursing Work, Siriraj Hospital, Mahidol University, Bangkok, Thailand

†Professional Nurse, Gastroenterology Unit, Nursing Work, Siriraj Hospital, Mahidol University, Bangkok, Thailand

‡Division of Gastroenterology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok ,Thailand

¶Department of Anastasia Physiology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand

§Minimally Invasive Surgery Unit, Department of Surgery, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand

Abstract ***Objectives:*** **An important element that affects the diagnosis and procedure ofcolonoscopy is the cleanliness of the bowel preparation.**

Methods: **This study was to investigate the incidence of repeated endoscopy. The intestinal preparation is not clean, and to assess knowledge and practice in patients receiving colonoscopy compares between the two groups. Randomized controlled trial of 63 control subjects. Get regular care. The experimental group received 67 structured bowel preparation programs. The instrument used to collect data was a questionnaire using standard deviation, chi-square, independent *T*-test, relative risk.**

Results: **The results showed that repeated endoscopy was not found in the two groups. However, in the experimental group, colorectal intestinal disease was fair level 0.81 times that of the control group ($p = 0.1540$), which is approximately a 13% difference. With regard to subjects' understanding before and after giving knowledge, both groups had a similar percentage of correct responses at 80%. Regarding the suitable diets for the first and second day, the correct response rate differed with 5% correct in the pre-test and 1.9% correct in the post-test. On the topic of drinking water following defecation, there was a statistically significant difference where the results of the group that drank water ($p < 0.05$) was 13.5 times that of the group that did not ($p = 0.02$).**

Conclusions: **Although the results were not statistically significant, the experimental group that received a structured bowel preparation program had a tendency to have a very good level of cleanliness, higher than that of the control group. Patients should also self-assess their intestinal cleanliness. It is recommended that this be studied further in these subgroups.**

Keywords: **Enhancement program, bowel preparation, colonoscopy**

Correspondence address: *Nisa Ruangkitudom, Gastroenterology Unit, Nursing Work, Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand; Email: ning2601@hotmail.com*

Introduction

An important factor that affects the effectiveness of colonoscopy and a clinician's ability to diagnose abnormality is the cleanliness of the patient's bowel. Inappropriate bowel preparation may hide or obscure signs of disease and the presence of tumors. Examination of the cecum may be difficult (or impossible), which increases the risk of complications, such as diverticular diseases, infection, and gas. Patients who undergo a failed colonoscopy have to endure a repeat procedure. Data from the Siriraj Hospital GI Endoscopy Center from 2011 (B.E. 2554)[1] revealed that 28% of patients had to undergo repeat colonoscopy, which resulted in increased risk of complications (e.g., flatulence), and increased operative time to perform the procedure, because repeat patients have to receive a higher dose of anesthesia. Moreover, increased expense was incurred by both patients and the hospital.

Our review of the literature relative to bowel preparation for colonoscopy revealed two approaches to bowel preparation - split dose regimen and same day regimen[2,3,4]. Both approaches have advantages and disadvantages. Split-dose regimen requires patients to take laxatives on both the day before and on the day of the procedure. The same day regimen requires patients to take a laxative in the morning for a colonoscopy that is scheduled for the afternoon. Both approaches have studies that support their efficacy. Moreover, two different bowel preparation strategies allow for more choice relative to patient convenience and preference. Increased patient awareness regarding the importance of bowel preparation will increase the rate of successful colonoscopy, improve the detection of present tumor or other abnormalities, and decrease the rate of repeat colonoscopy.

This study therefore developed a structured bowel preparation program by adapting the split dose regimen to fit into the organizational culture. This program consisted of providing advice, a bowel preparation manual, telephone calls, and monitoring preparation for the colonoscopy. The population was separated into two groups: a group that received the structured bowel preparation program, and a group that received regular care. The researchers hypothesized that the group that underwent the program would result in high levels of cleanliness or higher than that of the statistics collected by the Siriraj Gastrointestinal Endoscopy Center. Expected benefits of the research are to help reduce repeated colonoscopies.

Research Objectives

The primary objective is to study the incidence of repeated colonoscopies from unclean bowel preparation by comparing the control group and experimental group. The secondary objectives are to assess the knowledge and practice of colonoscopy patients between the aforementioned two groups, and to find other causes of unclean bowel preparation.

Hypothesis

A structured bowel preparation program for patients scheduled to undergo colonoscopy will help to reduce the incidence of repeat colonoscopy.

Materials and Methods

This study is experimental procedure/intervention using a structured bowel preparation program, which has minimal risk. The allocation of the study population is through randomized controlled trial by using a computer program to randomly sequence relevant documents into sealed opaque envelopes. After explaining the study to the patients, they selected an opaque envelope in the order given by the computer program to see if they were in the control or experimental group.

Population and Samples

The population consisted of Siriraj Hospital GI Endoscopy Center colonoscopy patients aged 18-75 years. The method of recruitment of the study population was from patients who had appointments at the center. Patients who met the research participation qualifications were given information by the researchers and gave their consent to participate. The duration of data collection was from November 2015 (B.E. 2558) to March 2017 (B.E. 2560). The inclusion criteria were: patients who came for their first colonoscopy aged 18-75 years, are able to take care of themselves, and can communicate and understand Thai. The exclusion criteria were: patients with gastrointestinal bleeding, emergency patients, patients with chronic renal failure, patients who are unable to take care of themselves, and patients who did not want to participate.

Data Collection

The research process was as follows: Recruitment of the study population was undertaken through a randomized controlled trial from a computer program's random sequencing in sealed opaque envelopes. After explaining the study details to patients, they selected an envelope to determine which of the two groups they would be part of, namely, 1) the control group which received advice and guidance documents from nurses on bowel preparation using the regular approach, a guidance for colonoscopy patients, and undertook a pre-test and post-test after receiving information, as well as evaluation; and 2) the experimental group, which received advice and guidance documents from nurses using the new approach, with advice from nurses on how to prepare bowels using flip charts, and undertook a pre-test and post-test after receiving information, as well as received further information on their areas of inquiry, evaluation, and telephone calls to remind patients to prepare two days before their colonoscopy and give them more information on the study.

If patients consented to participating in the study, the researcher asked them to sign their consent and select a sealed brown envelope to be put into their group. The study participant would then be given advice and guidance documents from nurses specific to their group, be evaluated by the practitioner who performed the colonoscopy on the cleanliness, and be determined on whether a repeat colonoscopy is necessary and for what reason.

Assessment of Research Tools

The research tools were questionnaires and evaluation forms with content inspection by three experts.

This study received approval from the Siriraj Institutional Review Board of the Faculty of Medicine Siriraj Hospital (Project Code: 501/2558(EC3)).

Data Analysis

Demographic data analysis used descriptive statistics by frequency distribution and percentages of correct answers to the pre-test and post-test.

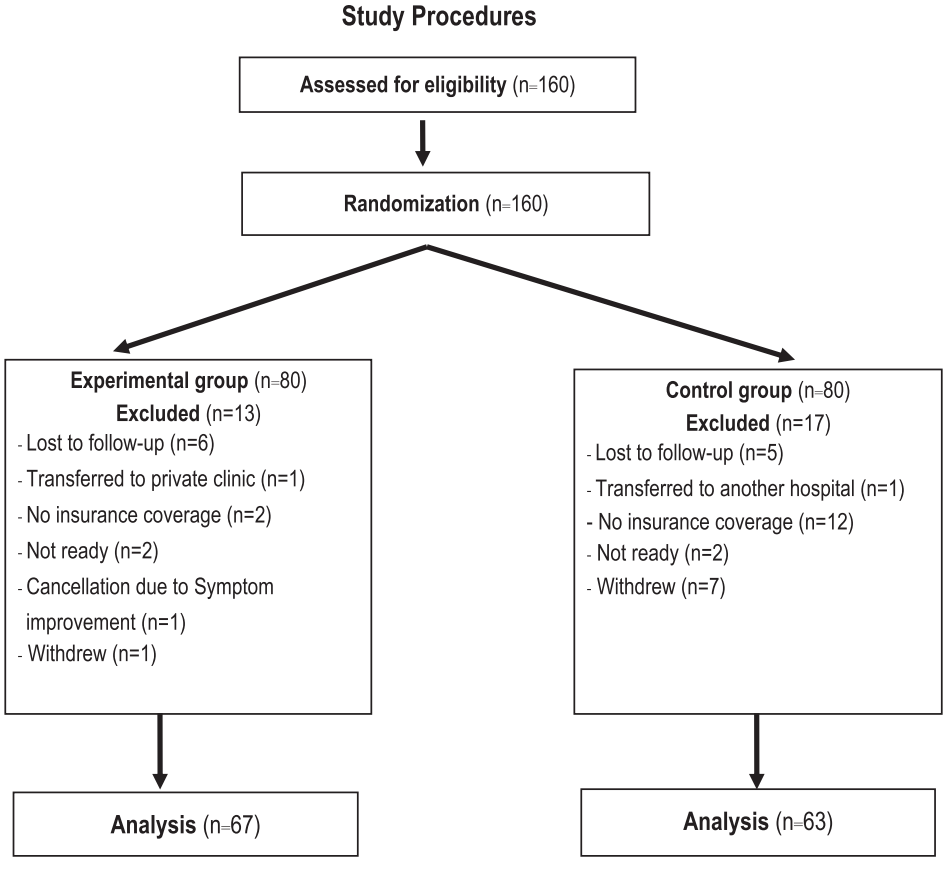

Figure 1 Flow diagram of study protocol

The difference in the need for a repeated colonoscopy following unclean bowel preparation was assessed using the chi-squared test. The different scores in the correct answers to the pre-test and post-test on patient knowledge before and after receiving advice and guidance was compared using independent t-test. Testing factors, such as gender, age, education level, chronic disease, correct answers on post-tests, and bowel preparation prior to colonoscopy in the experimental group to see whether it affected cleanliness was done using relative risk and 95% confident interval, which is the risk of developing an incident (or disease) from exposure to the factors.

Results

There is no difference between the general information of the experimental group and the control group (Table 1).

Even though the characteristics of people who received bowel cleanliness and repeat colonoscopy assessments by Aronchick bowel preparation scale (ABPS)[8] in the experimental group and control group did not differ, it was found that in the experimental group, the number of fair and poor intestinal cleanliness levels was 0.81 times that of the control group, which is approximately an absolute 13% difference. There was an inclination to do another bowel preparation, but the practitioner in charge tried to cleanse the intestinal tract to perform a diagnosis, so it took a long time, but did not affect the work plan.

It was found that for question 5 on food that can be eaten on the first and second day (soft foods, such as porridge (no vegetables), bread, fish, eggs, soy milk) was answered correctly by only 1.3% in the experimental

Table 1 Demographic and clinical characteristics of study population

Characteristics	Group	
	Experimental (n=67) n (%)	Control (n=63) n (%)
Gender		
Male	25 (37.3)	21 (33.3)
Female	42 (62.7)	42 (66.7)
Age (years), mean±SD	56.1 ± 9.9	53.6 ± 10.6
Education level		
Primary education	9 (13.4)	13 (20.6)
Secondary education	7 (10.4)	6 (9.5)
Higher education	32 (47.8)	30 (47.6)
Other	19 (28.4)	14 (22.2)
Chronic disease		
Hypertension/cardiovascular	25 (37.3)	14 (22.2)
Dyslipidaemia	16 (23.9)	12 (19.0)
Diabetesmellitus	9 (13.4)	4 (6.3)
Cancer	4 (6.0)	0 (0.0)
Gastrointestinal	5 (7.5)	7 (11.1)
Respiratory	0 (0.0)	1 (1.6)
Orthopaedics	3 (4.5)	2 (3.2)
Allergy	5 (7.5)	5 (7.9)
Other	4 (6.0)	2 (3.2)

Table 2 Intestinal cleanliness level and colonoscopy status (repeat vs. no repeat) in 130 colonoscopy patients

	Group		Total n (%)	*p-value*	RR (95% CI)
	Experimental (n=67) n (%)	Control (n=63) n (%)			
Intestinal cleanliness level					
Excellent	6 (9.0)	4 (6.3)	10 (7.7)		
Good	25 (37.3)	17 (27.0)	42 (32.3)		
Fair	32 (47.8)	36 (57.1)	68 (52.3)		
Poor	4 (6.0)	6 (9.5)	10 (7.7)		
Inadequate	0 (0.0)	0 (0.0)	0 (0.0)	0.1540	0.81 (0.61-1.07)
Colonoscopy					
No repeat colonoscopy	67 (100.0)	63 (100.0)	129 (100.0)		
Repeat colonoscopy	0 (0.0)	0 (0.0)	0 (0.0)		

A *p*-value < 0.05 indicates statistical significance

Abbreviations: ABPS, Aronchick Bowel Preparation Scale; RR, risk ratio; CI confidence interval

group and 2.5% in the control group (Table 3). Additionally, for question 2 on bowel preparation not needing laxatives but needing food that is easily digestible without fibers, the experimental group answered correctly more than the control group by 93.8% to 87.5% respectively. For other questions, the percentage of correct answers was over 80% similar (Table 3).

The average score of knowledge before and after receiving advice between the experimental and control group did not differ (Table 4).

For bowel preparation of patients in the experimental group, the actions that were followed by less than 90% are those relating to the preparation 1 day before the colonoscopy, namely only taking in fluids, which was at 80.3% (Table 5).

Table 3 Percentage of correct answers on the post-test

	Group		Total n (%)
	Experimental (n = 67) n (%)	Control (n = 63) n (%)	
Clean bowel preparation will make colonoscopy easier and make diagnosis and treatment easier	67 (100)	63 (100)	130 (100)
For bowel preparation, no laxatives have to be taken - only food that is easily digestible without fiber should be eaten	64 (95.5)	54 (85.7)	118 (90.8)
For bowel preparation before colonoscopy on days 1, 2 and 3, no vegetables and fruits should be eaten	63 (94.0)	58 (92.1)	121 (93.1)
For bowel preparation before colonoscopy, no meat should be eaten except for fish and crab	66 (98.5)	59 (93.7)	125 (96.2)
Food that can be eaten on day 1 and 2 of bowel preparation should be soft, easily digestible food, such as porridge (no vegetables), bread, fish , eggs, and soy milk	1 (1.5)	2 (3.2)	3 (2.3)
Food that can be eaten on day 3 of bowel preparation should be fluid, such as soup, boiled rice water, Ovaltine, milk, and sweet drinks without coloring	65 (97.0)	61 (96.8)	126 (96.9)
For bowel preparation for colonoscopy, patients do not need to take laxatives	67 (100)	63 (100)	130 (100)
After taking laxatives, milk and other food should not be eaten	60 (89.6)	58 (92.1)	118 (90.8)
Clean bowel preparation can help reduce risk of complications	65 (97.0)	59 (93.7)	124 (95.4)
No fluids and food of any kind should be taken after midnight before undergoing the colonoscopy	67 (100)	63 (100)	130 (100)

Table 4 Average knowledge score before and after receiving advice

Score	Group				*p*	p^{δ}
	Experimental		Control			
	Mean ± SD	(n = 67) Median (min-max)	Mean ± SD	(n=63) Median (min-max)		
Average score before advice	7.8 ± 1.1	8.0 (5-9)	7.7 ± 1.2	8.0 (4-10)	0.600	0.557
Average score after advice	8.7 ± 0.7*†	9.0 (6-10)	8.6 ± 0.8*†	9.0 (6-10)	0.225	0.229

Abbreviation: SD, standard deviation

A *p*-value < 0.05 indicates statistical significance

p-value by independent t-test; p^{δ} by Mann-Whitney U test; **p*-value < 0.001 paired *t*-test , †*p*-value < 0.001 Wilcoxon signed ranks test;

Table 5 Bowel preparation for colonoscopy in the experimental group

Preparation parameter	Able to n (%)	Reason not able to
2 days before - no fruits	66 (100)	
2 days before - only soft, easily digestible food	64 (97.0)	
1 day before - only fluid	53 (80.3)	Accidentally ate 1 piece of bread (n=1)
Taking laxatives	58 (87.9)	Vomiting (n=1)
Taking all laxatives	60 (90.9)	
Drank water after defecating	54 (81.8)	Nauseous (n=2) Forgot (n=1) Queasy (n=1)
Able to refrain from all food and fluid	65 (98.5)	
Score of actions undertaken before endoscopy, median (min-max)	7.0 (4-7)	

Table 6 Analysis for factors that significantly affect bowel cleanliness prior to colonoscopy

Factors	Poor bowel cleanliness		
	n (%)	RR (95% CI)	*p*-value
Gender			
Male (n=46)	2 (4.3)	1.000	0.308
Female (n=84)	8 (9.5)	2.1905 (0.48-9.89)	
Age range			
24-50 years (n=38)	2 (5.3)	1.000	0.512
51-75 years (n=92)	8 (8.7)	1.65 (0.37-7.42)	
Education level			
Higher than bachelor's degree (n=62)	3 (4.8)	1.000	0.258
Lower than bachelor's degree (n=68)	7 (10.3)	2.13 (0.58-7.87)	
Gastrointestinal tract disease			
Yes (n=12)	2 (16.7)	1.000	0.218
No (n=118)	8 (6.8)	2.46 (0.59-10.20)	
Diabetes			
Yes (n=13)	2 (15.4)	1.000	0.270
No (n=117)	8 (6.8)	2.25 (0.53-9.49)	
Hypertension/cardiovascular disease			
Yes (n=39)	4 (10.3)	1.000	0.474
No (n=91)	6 (6.8)	1.56 (0.46-5.2)	
Programs for experimental and control group			
Experimental group (n=67)	4 (6.0)	1.000	0.4522
Control group (n=63)	6 (9.5)	1.60 (0.47-5.39)	
Eating only fluids 1 day before colonoscopy			
Unable to do (n=13)	2 (15.4)	1.000	0.1394
Able to do (n=53)	2 (3.8)	4.08 (0.63-26.29)	
Drinking water every time after defecting			
Done (n=53)	1 (1.9)	1.000	0.020
Not done (n=13)	3 (25.0)	13.5 (1.53-118.8)	
Time between intervention and colonoscopy			
≤ 30 days	2 (5.0)	1.000	0.447
> 30 days	8 (9.0)	1.80 (0.40-8.09)	

A *p*-value < 0.05 indicates statistical significance
Abbreviations: RR, risk ratio; CI, confidence interval

The reason they were unable to follow the prescribed action was because they accidentally ate 1 piece of bread, drank water every time after defecation (81.8%), felt nauseous (2 persons), forgot (1 person), and vomited (1 person). With regard to taking laxatives, it was 87.9%.

There are factors that can affect the cleanliness of the bowel, namely gender, age, education level, chronic diseases such as digestive tract diseases, diabetes, hypertension, cardiovascular disease, and different programs for the control and experimental group (Table 6).

In the time from intervention to colonoscopy, it was found that none of the factors affected bowel cleanliness except for on drinking water after defecating. Those who were unable to do so were 13.5 times more likely to have unclean bowels compared to those who are able to ($p = 0.020$).

Discussion

From the results of the study on a structured bowel preparation program for patients who received bowel cleanliness assessments in the experimental group and control group, it was found that there was no difference in the cleanliness and need for repeat colonoscopies in both groups. In the experimental group, 46.3% had cleanliness levels of good or very good, while in the control group it was 33.3% ($p = 0.132$). There was also no difference in the average score for knowledge before and after receiving advice between the experimental group and control group. In addition, the researcher used the general information collected to analyze the relative risk (RR) for developing incidents (or disease) from exposure to factors in the general information. It was found that women have a higher risk of less clean bowels than men. Patients aged 51-75 years were also more likely to have less clean bowels than patients in the 24-50 years range. For education level, it was found that those who had an education level at less than a bachelor's degree had less clean bowels than those with higher than a bachelor's degree. It was also found that in the experimental and control group, chronic diseases affected bowel cleanliness. In order from high to low level of effects are digestive tract disease, diabetes, hypertension and cardiovascular disease.

When considered jointly with the results of the previous study, it can be seen that existing literatures on bowel preparation for colonoscopies have two approaches to bowel preparation, namely split dose regimen and same day regimen. Each regimen has their advantages and disadvantages. In the case of split dose regimen, patients have to take laxative the day before and morning of the colonoscopy. For the same day regimen, patients take laxative the morning before an afternoon colonoscopy. Both regimens have supporting studies saying that they are better than the other. This study cannot be used as data for the same day regimen, but may help increase the effectiveness of the split dose regimen. Nevertheless, more research is needed[5,6,7].

Although there was no difference in the results, the experimental group which received a structured bowel preparation program had a higher rate of good to very good bowel cleanliness assessments as compared to the control group that did not have such a program. The researcher believes that there are two key factors that affect bowel cleanliness. The first is related to the patient, namely their age, gender, education level, and chronic diseases. The second is the format of the program. Upon reviewing the research of Wei-Fan Hus[9], it was found that VDO and pictures illustrating the cleanliness of bowels made the cleanliness of bowel preparation in the very good level (21.8%-35.9%) and bad level (18.2%-15.9%).

The researcher agrees with the notion to adapt the aforementioned program and to have patients do self-assessments on whether they are ready for colonoscopy. From the study, it was also found that the control group did not see the importance of bowel preparation, and did not appreciate that a clean bowel is important in allowing doctors to perform diagnoses. This is a problem that requires further information and study.

Conclusion

Although there was no significant difference in the results, the experimental group that received a structured bowel preparation program was more likely to have very good or good levels of bowel cleanliness, higher than that of the control group that did not receive the structured bowel preparation program. These results can therefore be used to enhance the quality of bowel preparation. This study found that, for

bowel preparation before colonoscopy, each patient had different individual characteristics, making them more responsive to particular laxatives and bowel treatments. However, it remains that raising awareness in patients of the importance of bowel preparation for successful colonoscopies, increases the chances of finding tumors. On reducing the need for repeat colonoscopies resulting from unclean bowels, information is still insufficient from questioning patients on their defecation, such as a history of chronic constipation, and elderly patients having more difficulty digesting food with fiber than younger patients.

The limitation of this research is the low number of participants resulting from 30 patients not attending the scheduled colonoscopy after receiving advice in the experimental and control group.

Following analysis, the research team has the recommendations for a further study. The number of the control group and increasing follow up on patients about drinking water after taking laxatives. Some did not drink water due to experiencing abdominal discomfort, or drank water but only a small amount. Increasing follow up will help lead to cleaner bowel preparation for the next study.

Acknowledgements

This study is supported by Siriraj Research Development Fund, Faculty of Medicine Siriraj Hospital, Mahidol University, (managed by the Routine to Research: R2R).

REFERENCES

1. Agerskov U. Statistical Yearbook 2011 of Vijay Virabudin.115th ed. Denmark: Published by Statistics Denmark; 2011.
2. Chiwisalpong P, Rattanakosan Sukishi T. Colorectal Cancer Screening and Diagnosis. Bangkok: Bangkok University Press; 2003.
3. Pongchai S, Akaraviput T. Colonoscopy 1. Bangkok: Bangkok Medical Journal; 2011.
4. Chaiyapongchai S, Akaraviput T, Chinchitorn U. Gastrointestinal bleeding, 1st ed. Bangkok: Bangkok Medical Journal; 2010.
5. Gurudu SR1, Ratuapli S, Heigh R, Di Baise J, Leighton J, Crowell M. Quality of bowel cleansing for afternoon colonoscopy is influenced by time of administration. Am J Gastroenterol 2010;105:2318-22.
6. American Society for Gastrointestinal Endoscopy(ASGE). Bowel preparation before colonoscopy. Gastrointest Endosc 2015;81:781-94.
7. Gurudu SR1, Ratuapli S, Heigh R, Di Baise J, Leighton J, Crowell M. Quality of bowel cleansing for afternoon colonoscopy is influenced by time of administration. Am J Gastroenterol 2010;105:2318-22.
8. Kastenberg D, Bertiger G, Brogadir S.Bowel preparation quality scales for colonoscopy. World J Gastroenterol 2018; 24:2833-43.
9. Wen CC, Jao SH, Hsiao CW. A modified bowel preparation regimen for colonoscopy providing the patients' satisfaction and convenience. Med Sci Monit 2017;23:3123-9.

บทคัดย่อ **ผลของโปรแกรมการเตรียมลำไส้อย่างมีแบบแผนในผู้ป่วยที่มารับการส่องกล้องลำไส้ใหญ่: การศึกษาแบบสุ่ม**

พว. นิษา เรืองกิจอุดม*, พว.วาทินี เธียรสุคนธ์*, พว.ปฐมพร บุนนาค†, พว.รจศิรินทร์ ชัยวงศ์†,
รศ.นพ.วรายุ ปรัชญกุล‡, รศ.นพ.สมชาย อมรโยธิน¶, ศ. นพ.ธวัชชัย อัครวิพุธ§
**พยาบาลวิชาชีพชำนาญการพิเศษ หน่วยส่องกล้องระบบทางเดินอาหาร งานการพยาบาลผ่าตัด โรงพยาบาลศิริราช*
†พยาบาลวิชาชีพ หน่วยส่องกล้องระบบทางเดินอาหาร งานการพยาบาลผ่าตัด โรงพยาบาลศิริราช
‡ภาควิชาอายุรศาสตร์ โรคระบบทางเดินอาหาร คณะแพทยศาสตร์ศิริราชพยาบาล
¶ภาควิชาวิสัญญีวิทยา คณะแพทยศาสตร์ศิริราชพยาบาล
§ภาควิชาศัลยศาสตร์ คณะแพทยศาสตร์ศิริราชพยาบาล

วัตถุประสงค์: สิ่งสำคัญที่มีผลต่อการวินิจฉัยและการทำหัตถการของการส่องกล้องลำไส้ใหญ่คือ ความสะอาดของลำไส้ การวิจัยนี้เพื่อศึกษาอุบัติการณ์การส่องกล้องซ้ำเนื่องจากเตรียมลำไส้ไม่สะอาดและประเมินความรู้ และการปฏิบัติตัว

วิธีการศึกษา: การศึกษานี้เป็นการศึกษาอุบัติการณ์ของการส่องกล้องซ้ำ การเตรียมลำไส้ไม่สะอาด และประเมินความรู้และการปฏิบัติในผู้ป่วยที่ได้รับการส่องกล้องลำไส้ใหญ่ เปรียบเทียบระหว่างสองกลุ่ม โดยใช้การทดลองแบบสุ่มแบ่งเป็นกลุ่มควบคุมจำนวน 63 คน ได้รับการดูแลตามปกติ ส่วนกลุ่มทดลองได้รับโปรแกรมเตรียมลำไส้ใหญ่จำนวน 67 คน เครื่องมือที่ใช้ในการเก็บรวบรวมข้อมูลคือแบบสอบถาม โดยใช้ค่าเบี่ยงเบนมาตรฐานไคสแควร์ การทดสอบค่าทีอิสระ ค่าความเชื่อมั่น

ผลการวิจัย: ไม่พบการส่องกล้องซ้ำในสองกลุ่ม แต่พบว่าในกลุ่มทดลองมีการประเมินความสะอาดของลำไส้ใหญ่ในระดับพอใช้และแย่น้อยกว่าคิดเป็น 0.81 เท่าเมื่อเทียบกับกลุ่มควบคุม (p = 0.1540) ซึ่งต่างกันประมาณร้อยละ 13 และคะแนนความรู้ความเข้าใจก่อนและหลังให้ความรู้ ตอบถูกใกล้เคียงกันคือมากกว่าร้อยละ 80 แต่มีประเด็นหัวข้อเรื่องอาหารที่รับประทานในวันที่ 1 และ 2 นั้น ตอบถูกเพียงร้อยละ 5 ใน Pretest และ Posttest ร้อยละ 1.9 ตามลำดับ แต่ในหัวข้อการปฏิบัติตัวเรื่องการดื่มน้ำตามทุกครั้งหลังถ่ายอุจจาระในกลุ่มที่ทำไม่ได้นั้น มีความแตกต่างกันอย่างมีนัยสำคัญทางสถิติ (p < 0.05) คิดเป็น 13.5 เท่า เมื่อเทียบกับกลุ่มที่ทำได้ (p = 0.02)

สรุป: ถึงแม้ผลการทดลองที่ได้จะไม่มีความแตกต่างกัน แต่กลุ่มทดลองที่ได้รับโปรแกรมการเตรียมลำไส้อย่างมีแบบแผน มีแนวโน้มจะมีผลการประเมินการตรวจความสะอาดในระดับดีถึงดีมาก สูงกว่ากลุ่มควบคุมที่ผู้วิจัยเห็นว่าการให้คำแนะนำกับผู้ป่วยเพียงอย่างเดียวอาจไม่เพียงพอ ควรให้ผู้ป่วยประเมินระดับความสะอาดของลำไส้ด้วยตัวเอง จึงเป็นเรื่องที่จะเสนอแนะให้ผู้สนใจศึกษาในกลุ่มย่อยนี้ต่อไป

The THAI Journal of SURGERY 2018;39:30-37.
Official Publication of the Royal College of Surgeons of Thailand

Original Article

Clinical Efficacy of Endoscopic Ultrasound-guided Fine Needle Aspiration (EUS-FNA) Performing in Upper Abdomen: A Single Center Experience

Kannikar Laohavichitra, MD
Thawee Ratanachu-ek, MD
Department of Surgery, Rajavithi Hospital, College of Medicine, Rangsit University, Bangkok, Thailand

Abstract

Background: **Endoscopic ultrasound with fine needle aspiration (EUS-FNA) is a useful procedure for the evaluation and tissue acquisition of lesions located in organs close to the upper gastrointestinal tract, such as the pancreas, periceliac lymph nodes, aortocaval lymph nodes, left lobe of liver, bile duct, retroperitoneal masses or lesions located in the wall of upper gastrointestinal tract itself, and also masses located in mediastinum. EUS-FNA can provide tissue samples for cytological or pathological analysis that is helpful for the diagnosis, tumor staging, and management of many surgical conditions. The authors conducted the present study to evaluate the accuracy of EUS-FNA performed at Rajavithi Hospital.**

Objective: **To evaluate the results of diagnostic accuracy, sensitivity, specificity, positive predictive value and negative predictive value of EUS-FNA performed at a tertiary gastrointestinal endoscopic center of the Department of Surgery, Rajavithi Hospital.**

Material and method: **The authors retrospectively reviewed the EUS-FNA database obtained between October 2014 and September 2016. Data obtained, including demographics, organ of examination, results of cytological and/or pathological reports, size of the needles and follow-up data, were analyzed and reported.**

Results: **EUS-FNA was performed in 172 patients (90 males, 82 females), with a mean age of 54.8 years (range 17-89 years). The overall diagnostic accuracy was 91.9%, with a sensitivity of 88.1%, specificity of 100%, positive predictive value (PPV) of 100% and negative predictive value (NPV) of 81.8%. Patients were divided into four groups according to anatomical location, i.e., pancreas, stomach, lymph nodes and other locations. The majority of the EUS-FNA was performed on the pancreas, which included 124 patients. There were 15 patients with stomach lesions, 19 with lymphadenopathy and 14 with other lesions. The sensitivity of EUS-FNA for each group varied from 84.6% to 93.7%. The specificity was 100% for every group due to no false positive result, and the accuracy ranged from 86.7 to 94.7%. No serious complications occurred in all patients.**

Conclusion: **EUS-FNA performed at the Gastrointestinal Endoscopic Center, Department of Surgery, Rajavithi Hospital, is a safe and accurate diagnostic procedure which is very useful for management planning.**

Keywords: **Endoscopic ultrasound, fine needle aspiration, efficacy, EUS-FNA**

Correspondence address: *Kannikar Laohavichitra, MD, Department of Surgery, Rajavithi Hospital, 2 Phyathai Road, Ratchathewi, Bangkok, Thailand; Telephone: +668 1396 2535; Fax: +66 2354 8080; E-mail: niphangnga@yahoo.com*

Background

Endoscopic ultrasound guided-fine needle aspiration (EUS-FNA) is recently a very useful procedure for evaluation and tissue acquisition of the lesions located in the wall of upper gastrointestinal tract itself such as subepithelial mass or thickening wall of esophagus or stomach following a negative biopsy in esophago-gastroscopy, and many organs located close to upper gastrointestinal tract such as pancreas, periceliac lymph nodes, aortocaval lymph nodes, left lobe of liver, bile duct,ampulla, retroperitoneal mass, and mass in mediastinum. EUS-FNA can provide tissue samples for cytological and/or pathological analysis which is very helpful for making diagnosis, tumor staging and leads to proper management. As EUS-FNA is a diagnostic tool that requires good sensitivity, specificity and accuracy and there are many factors involved in the effectiveness of the procedure, the authors conduct this study to evaluate the result of EUS-FNA performing at the gastrointestinal endoscopic center, Department of Surgery, Rajavithi Hospital.

Objective

To evaluate the effectiveness of EUS-FNA in diagnostic accuracy, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and safety performing at a single-tertiary gastrointestinal endoscopic center of the Department of Surgery, Rajavithi Hospital.

Material and Methods

Retrospective data collection was carried out from all patients who were sent to gastrointestinal endoscopic center of the Department of Surgery, Rajavithi Hospital to perform EUS-FNA from October 2014 to September 2016. Patient characteristics, indications for EUS-FNA, anatomical locations, size of needle, cytological and/or pathological results of FNA, surgical pathology if available and clinical follow-up were recorded and analyzed.

Results

One hundred and eighty-five consecutive patients were sent to perform EUS-FNA on various indications. Thirteen patients were excluded from the study due to loss to follow-up (2 patients), loss of data (5 patients), EUS for intervention without tissue acquisition (5 patients) and error of tissue processing (1patient). One hundred and seventy-two patients (90 males and 82 females) were included in this study, mean age was 54.8 years (range 17-89 years). EUS-FNA was performed mainly on pancreas for 124 patients, 15 patients on stomach, 19 patients on intra-abdominal lymph nodes, and on other 6 organs which had small numbers of patients, i.e., 5 patients from liver, 2 from ampulla, 1 from mediastinal mass, 2 from bile duct,1 from esophagus and 3 from retroperitoneal mass. The patients were classified into four groups due to anatomical locations of FNA such as pancreas, gastric, intra-abdominal lymph nodes and others, including all 6 organs which had small number of patients as described in Table 1.

Indications of tissue acquisition from pancreas are to confirm diagnosis of unresectable pancreatic cancer planned for chemo-radiation, mass forming chronic pancreatitis, solid or cystic pancreatic lesions which had inconclusive diagnosis from other imaging modalities and small number of cystic fluid analysis for cytology from pancreatic pseudocyst. Major indications of FNA from stomach were subepithelial mass for diagnosis of gastric GIST and some of thickening gastric wall suspicious of gastric lymphoma or adenocarcinoma but had negative result from ordinary

Table 1 Characteristic of the patients

Character	Number (%)
Age (mean, range)	54.8 (range 17-89)
Sex	
Male	90 (52.3)
Female	82 (47.7)
Organs	
Pancreas	124
Stomach	15
Intra-abdominal lymph node	19
Others	14
Liver	5
Ampulla	2
Mediastinal mass	1
Bile duct	2
Esophagus	1
Retroperitoneal mass	3

gastroscopy with mucosal biopsy. Two most common indications of FNA from intra-abdominal lymph nodes were for staging of metastasis cancers and tissue diagnosis of lymphomas. The other indications are tissue diagnosis of retroperitoneal tumors, suspicious of left lobe liver metastasis or tumor of biliary system that had negative tissue biopsy or brush cytology from performing of endoscopic retrograde cholangiography (ERC).

The results were classified into true positive when cytological and/or pathological report identified the disease correctly; false positive when the positive result incorrectly identified the disease after clinical follow-up of the patient or when the result did not correspond to the surgical pathological report; true negative when the cytological report was not the same as provisional diagnosis but same as the clinical follow-up result and false negative when the negative result incorrectly rejected the disease clinically and/or was in contrast to the pathological report.

Total correct classification rate (accuracy) ranged from 87% to 95% (combining true positive and true negatives) and false negative rates of each organ varied from 6% to 15%. The highest false negative rate was for the stomach (15%) which could be due to relatively small number of this group and no false positive of every group (Tables 2 and 3).

As there was no false positive, the specificity and positive predictive value (PPV) of FNA from every organ were 100%. Overall sensitivity, accuracy and negative predictive value (NPV) were 88.1%, 91.9% and 79.4%, respectively. The results of each anatomical location were also in good range, e.g., pancreas had sensitivity 87%, accuracy 92%, NPV 82%, stomach had sensitivity of 85%, accuracy 87% but had lowest NPV of only 50%. Intra-abdominal lymph nodes and the other organs also had excellent sensitivity (94%, 90%), high accuracy (95%, 93%) and good NPV (75%, 80%) (Table 3).

Considering each anatomical location (except the other group), there were variety of indications and characteristics of conditions and/or mass that probably influence the efficacy of EUS-FNA, so we made subgroup analysis of sensitivity, specificity, accuracy, PPV and NPV of each anatomical location, i.e., pancreas, stomach and intra-abdominal lymph nodes.

Among 124 cases of the pancreas group, 10 EUS-FNA was performed in pancreatic pseudocyst for routinely fluid analysis of amylase, culture for bacteriologic study, and cytology which all negative for malignancy cell corresponded to primary diagnosis, so subgroup analysis was only done on the unresectable

Table 2 Results of EUS-FNA for cytological and /or pathological examination of each organ

Organs	Results (Number)			
	True positive	True negative	False positive	False negative
Pancreas	69	45	0	10
Stomach	11	2	0	2
Lymph node	15	3	0	1
Others	9	4	0	1
Overall	104	54	0	14

Table 3 Sensitivity, specificity, accuracy PPV and NPV of each anatomical location

Organs	Results				
	Sensitivity (%)	Specificity (%)	Accuracy (%)	PPV (%)	NPV (%)
Pancreas	87.3	100.0	91.9	100.0	81.8
Stomach	84.6	100.0	86.7	100.0	50.0
Lymph node	93.7	100.0	94.7	100.0	75.0
Others	90.0	100.0	92.8	100.0	80.0
Overall	88.1	100.0	91.9	100.0	79.4

Table 4 Sensitivity, specificity, accuracy, PPV and NPV of pancreatic lesions (N=124)

Disease/condition	Number	Results				
		Sensitivity (%)	Specificity (%)	Accuracy (%)	PPV (%)	NPV (%)
Unresectable pancreatic cancer	46	44/46 (96)	NA	NA	NA	NA
Provisional diagnosis of solid/cystic pancreatic lesion	48	16/24 (67)	(100)	40/48 (83)	(100)	24/32 (75)
Chronic pancreatitis	20	9/20 (45)	NA	NA	NA	NA
Pancreatic pseudocyst	10	10/10 (100)	NA	NA	NA	NA

NA: not applicable

pancreatic cancer to confirm diagnosis and plan for chemo-radiation, inconclusive diagnosis of solid/cystic pancreatic lesions, and mass forming chronic pancreatitis (Table 4).

Among 46 patients with unresectable pancreatic cancer, 44 patients had cytological diagnosis of adenocarcinoma of pancreas (true positive) which could have palliative chemo-radiation as planned. There were 2 false negative cases; one patient was sent to surgery and intraoperatively found advanced pancreatic cancer and received enterobiliary bypass, another died from liver metastasis after follow-up. Thus the sensitivity was 96%, and false negative rate was 4%.

There were 48 patients who had a provisional diagnosis of solid/cystic pancreatic lesions on the imaging studies and were sent for EUS-FNA. Sixteen patients had positive cytological reports (true positive) and were diagnosed of adenocarcinoma of pancreas (6), intraductal papillary mucinous neoplasm (IPMN) (3), pancreatic neuroendocrine tumor (pNET) (3), serous neoplasm of the pancreas (SCN) (2), tuberculosis (1) and lymphoma (1). Twenty-four patients had (true) negative malignancy cell and lived well on clinical follow-up. Eight patients (6 solid lesions and 2 cystic lesions) had false negative. There were 4 adenocarcinoma of pancreas (3 were diagnosed after operation and 1 by repeat EUS-FNA), 3 pNET and one solid pseudopapillary epithelial neoplasm (SPEN) also diagnosed by pathological report after operation. There was no false positive. False negative was relatively high and lowered the sensitivity to 66.7% but other parameters were still in good range, i.e., specificity 100%, accuracy 83.3%, PPV 100%, and NPV 75%.

For the 20 cases of mass forming chronic pancreatitis, cytological report revealed 9 cases of true positive of inflammatory cell confirming the diagnosis of chronic pancreatitis. Thus the sensitivity was 45%.

Eleven patients with subepithelial mass at stomach suspicious of gastric GIST were sent for tissue acquisition, nine patients had confirmed diagnosis by pathological reports (true positive). Two false negative cases were confirmed diagnosis of gastric GIST after surgery. Thus the sensitivity was 82% with a false negative rate of 8% (Table 5).

Among four patients with thickening gastric wall, two patients were diagnosed of gastric lymphoma by EUS-FNA same as primary diagnosis (true positive), another two had true negative results of cytological reports; one who was suspicious of infiltrative gastric cancer but with negative result on FNA showed improvement after being followed up clinically and received repeated esophagogastroduodenoscopy (EGD) while another with carcinomatosis from advanced ovarian cancer with negative FNA cytology confirmed no gastric involvement after follow-up as well. As there were only true positive and true negative cases of this group, all sensitivity, specificity, accuracy, PPV and NPV were 100%.

Eight patients were suspicious of advanced intra-abdominal cancer with metastasis to celiac lymph nodes or aortocaval lymph node (3 cholangiocarcinoma, 2 pancreatic tumor and 3 of carcinoma unknown primary). Six patients were confirmed diagnosis by positive of malignant cell of the lymph nodes (true positive) and two of malignant cell negative cytology (true negative) was confirmed diagnosis by following up the patients clinically and/or imaging. All sensitivity, specificity, accuracy, PPV and NPV were 100% (Table 6).

Table 5 Sensitivity, specificity, accuracy, PPV and NPV of stomach lesions (N=15)

Disease/condition	Number	Results				
		Sensitivity (%)	Specificity (%)	Accuracy (%)	PPV (%)	NPV (%)
Gastric GIST	11	9/11 (82)	NA	NA	NA	NA
Provisional diagnosis of gastric malignancy	4	2/2 (100)	2/2 (100)	4/4 (100)	(100)	(100)

NA: not applicable

Table 6 Sensitivity, specificity, accuracy, PPV and NPVof intra-abdominal lymphadenopathy (N=19)

Disease/condition	Number	Results				
		Sensitivity (%)	Specificity (%)	Accuracy (%)	PPV (%)	NPV (%)
Cancer metastasis to lymph nodes	8	6/6 (100)	2/2 (100)	8/8 (100)	(100)	(100)
Lymphoma	11	9/10 (90)	1/1 (100)	10/11 (91)	(100)	1/2 (50)

Eleven patients suspicious of malignant lymphomas had confirmed diagnosis by pathological report in nine patients (true positive). One true negative case was diagnosed with SLE and another one false negative case was still diagnosed with a high suspicion of lymphoma by repeated CT scan and MRI. He died later. There was no false positive case in this group and sensitivity, specificity, accuracy, PPV and NPV were 90%, 100%, 91%, 100% and 50 %, respectively.

There were three sizes of needle used to perform EUS-FNA which were 25G, 22G and 19G. Practically, 25G and 22G needle are used in almost every location if the tissue acquisition indicated cytology. In situation that core tissue is needed for pathological examination or special stain such as thickening of gastric wall with negative biopsy, diagnosis of gastrointestinal stromal tumor (GIST) or other subepithelial tumor in gastrointestinal tract, or special immunohistochemistry stain were needed for diagnosis such as lymphoma both in stomach or intra-abdominal lymph nodes, we usually prefer to use 19G needle or special design of 22G needle that could get core tissue or request for cell block if 19G needle could not be used in some situations. So, the needles mainly used for FNA of pancreas are 22G needle (46%) and 25G needle (31.5%), and less frequently used is 19G needle (22.6%) but 46.7% of both 19G needle and 22G needle were used for stomach. Both 19G and 22G needles are also frequently used to get tissue in intra-abdominal lymph nodes which is 47.4% and 31.6%, respectively. For six organs from the other group (liver, ampulla, mediastinal mass, bile duct, esophagus, retroperitoneal mass) every size of needle is used varying widely, i.e., 28.6% of 25G needle, 21.4% of 22G needle and 50% of 19G needle (Table 7).

Table 7 Type of needle used for each organ

Organs	Type of Needle (N, %)		
	25G	22G	19G
Pancreas	39 (31.5)	57 (46.0)	28 (22.6)
Stomach	1 (6.7)	7 (46.7)	7 (46.7)
Lymph node	4 (21.1)	6 (31.6)	9 (47.4)
Others	4 (28.6)	3 (21.4)	7 (50.0)

Discussion

Endoscopic ultrasound (EUS) has been used for diagnosis and treatment in various clinical contexts. Numerous studies demonstrated that EUS has an important role in the diagnosis and staging of GI malignancy[1]. For pancreatic solid tumors, EUS-FNA has a high diagnostic accuracy. Comparing with ultrasound-guided or computed tomography (CT)-guided FNA, EUS-FNA seems to have a higher diagnostic accuracy, particularly for small lesions (smaller than 2-3 cm) of which its sensitivity reaches

99 %[1-2] and also has shown superiority in pancreatic tumor detection and staging compared with CT[1]. EUS has a very high negative predictive value (NPV), and thus EUS can reliably exclude pancreatic cancer[1].

Previous studies have shown that EUS-FNA for pancreatic cancer has sensitivity, specificity of 80.3-95%, 92.3-96%, PPV 94-100% and NPV 75-85% in range respectively[3-5] and most of our results were within these ranges.EUS-FNA for unresectable pancreatic cancer and pancreatic pseudocyst yielded over 95% sensitivity. For solid/cystic pancreatic lesions, the sensitivity was only 66.7% in the diagnosis of pancreatic tumors, with an accuracy of 83% due to false negative cases, more for solid compared to cystic lesions (6:2). In these 8 cases, there was no variation in the needle size used (2 patients using 25G needle, 3 patients using 22G needle and 3 patients using 19G needle for FNA), but 5 out of 8 procedures were performed by less experienced endosonographer. Although the sensitivity of diagnosing mass-forming chronic pancreatitis was 45% (9/20), in all 20 cases pancreatic cancer could be excluded by FNA.

Three quarters of gastric subepithelial tumor larger than 2 cm are GISTs and EUS-FNA can be omitted in most of cases, except for poor surgical candidates, for tumors located at areas which are difficult to resect such as the cardia, or for unresectable GIST. Data on diagnostic yield of EUS-FNA and EUS-true cut biopsy (TCB) in diffuse gastric wall thickening are limited and diagnostic accuracy of EUS-FNA was significantly lower for diffuse GI wall thickening as compared with other conditions[2]. In a multicenter study, the sensitivity, specificity and accuracy for the diagnosis of cancer for 115 gastrointestinal wall lesions were 61%, 79%% and 67%, respectively[6]. One recent study on performed EUS-FNA for gastric subepithelial tumor using 19, 22, 25 G needles found that 62% had a definite diagnosis with IHC, and 22% yielded results suspicious for GIST using side-port needle[7]. Another recent study reported EUS-FNA in the diagnosis of all types of gastric lesions such as lymphoma, adenocarcinoma, and most of submucosal tumors (SMT) such as gastrointestinal stromal tumor (GIST) and leiomyoma found a sensitivity of 87.3%, specificity of 100%, PPV of 100%, NPV of 85.2%, and accuracy of 92.7%[8]. In our study, all 11 gastric subepithelial masses were GISTs, and the sensitivity of EUS-FNA was 82% (9/11). In the 4 cases with gastric wall thickening, cancer was correctly diagnosed in 2 cases and correctly excluded in another 2 cases, achieving a sensitivity, specificity and accuracy of 100% for this condition. But because of a very small number of cases, the high accuracy rates must be interpreted with caution.

EUS-FNA allows accurate determination of the nature of lymph nodes of unknown origin both from intra-abdomen and mediastinum. EUS-FNA is thus recommended if the lymph nodes are easily accessible via EUS, as pathological results would be helpful for management planning[2]. Reports of sensitivity, specificity, and accuracy of EUS-FNA for various diseases and conditions were within the ranges of 89.7-97.1%, 98.3-100% and 93.5-98%, respectively, and no serious complications occurred with the procedure[9-12]. In our study EUS-FNA was performed in 19 cases of intra-abdominal lymphadenopathy; in patients with proven cancer metastasis (8 patients) and those suspicious of having lymphoma (11 patients). The results were comparable to those of previous studies.

Standard upper GI endoscopy carries a risk of perforation of 0.03%, while for upper EUS, according to a prospective study, cervical esophageal perforation rate was 0.06% (3 of 4,894 patients, with curvilinear-array devices used in all). A systematic review of EUS-FNA adverse events found that the risk of these events was highest among patients with ascites, liver lesions and perirectal lesions. Various adverse events included infection (e.g., bacteremia, sepsis), pancreatitis, hemorrhage, bile peritonitis, and malignant seeding[13]. A study of EUS-FNA for various anatomical locations demonstrated a 1.3% complication rate (3 of 233 patients)[14]. In our study, no serious complications were observed.

Conclusion

EUS-FNA is a safe and effective diagnostic tool for tissue acquisition and has high diagnostic yield which can affect management planning. The accuracy and safety of EUS-FNA in our center were comparable with those reported in the literature, despite the small number of patients with certain conditions or organ involvement. The acquisition of more data should allow more accurate assessment in the future.

REFERENCES

1. Murad FM, Komanduri S, Abu Dayyeh BK, Chauhan SS, Enessvedt BK, Fujii-Lau LL, et al. (ASGE TECHNOLOGY COMMITTEE). Echoendoscopes. GastrointestEndosc 2015; 82:189-202.
2. Dumoceau JM, Polkowski M, Larghi A, Wilmann P, Giovannini M, Frossard JL, et al. Indications, results, and clinical impact of endoscopic ultrasound (EUS)-guided sampling in gastroenterology: European Society of Gastrointestinal Endoscopy (ESGE) Clinical Guideline. Endoscopy 2011; 43:897-909.
3. Chen G, Liu S, Zhao Y, Dai M, Zhang T. Diagnostic accuracy of endoscopic ultrasound-guided fine-neeedle aspiration for pancreatic cancer. A meta-analysis. Pancreatology 2013;13:298-304.
4. Houshang A, Alizadeh M, Shahrokh S, Hadizadeh M, Padashi M, Zali MR. Diagnostic potency of EUS-guided FNA for the evaluation of pancreatic mass lesions. Endosc Ultrasound 2016;5(1):30-4.
5. Eloubeidi MA, Jhala D, Chheing DC, Chen VK, Eltoum I, Vickers S, et al. Yield of endoscopic ultrasound-guided fine-needle aspiration biopsy in patients with suspected pancreatic carcinoma. Cancer 2003;99:285-92.
6. Wiersema MJ, Vilmann P, Giovannini M, Chang KJ, Weirsema LM. Endosonography-guided fine-needle aspiration biopsy: diagnostic accuracy and complication assessment. Gastroenterology 1997;112:1087-95.
7. Webb K, Hwang JH. Endoscopic ultrasound-fine needle aspiration versus core biopsy for the diagnosis of subepithelial tumors. Clin Endosc 2013;46:441-4.
8. Okasha HH, Naguib M, Nady ME, Ezzat R, Gemeie EA, Nabawy WA, et al. Role of endoscopic ultrasound and endoscopic-ultrasound-guided fine-needle aspiration in endoscopic biopsy negative gastrointestinal lesions. Endoscopic Ultrasound 2017;6:156-61.
9. Jorenblit J, Anantharaman A, Loren DE, Kowalski TE, Siddiqui AA. The role of endosopicuitrasound-guided fine needle aspiration (eus-fna) for the diagnosis of intra-abdominal lymphadenopathy of unknown origin. J Interv Gastroenterol 2012;2:172-6.
10. Dhir V, Mathew P, Bhandari S, Kwek A, Doctor V, Maydeo A.Endosonography-guided fine needle aspiration cytology of intra-abdominal lymph nodes with unknown primary in a tuberculosios endemic region. J Gastroenterol Hepatol 2011;26(12):1721-4.
11. Korenblit J, Anantharaman A, Loren DE, Kowalski TE, Siddiqui AA. The role of endoscopic ultrasound-guided fine needle aspiration (eus-fna) for the diagnosis of intra-abdominal lymphadenopathy of unknown origin. J Interv Gastroenterol 2012;2(4):172-6.
12. Yasuda I, Tsurumi H, Omar S, Iwashita T, Kojima Y, Yamada T, et al. Endoscopic ultrasound-guided fine-needle aspiration biopsy for lymphadenopathy of unknown origin. Endoscopy 2006;38(9):919-24.
13. Early DS, Acosta RD, Chandrasekhara V, Chathadi KV, Decker GA, Evans JA, et al. (ASGE STANDARDS OF PRACTICE COMMITTEE). Adverse events associated with EUS and EUS with FNA. Gastrointest Endosc 2013;77:839-43.
14. Yang SS, Liao SC, Ko CW, Tung CF, Peng YC, Lien HC, et al, The clinical efficacy and safety of EUS-FNA for diagnosis of mediastinal and abdominal solid tumors-A single center experience. Advances in Digestive Medicine 2015;2:61-6.

บทคัดย่อ **ประสิทธิภาพของการตรวจวินิจฉัยด้วยการส่องกล้องระบบทางเดินอาหารด้วยคลื่นความถี่สูงร่วมกับการใช้เข็มเจาะเพื่อนำเซลล์ไปตรวจทางเดินอาหารส่วนบนและอวัยวะต่าง ๆ ใกล้เคียง ของศูนย์ส่องกล้องทางเดินอาหารศัลยกรรม โรงพยาบาลราชวิถี**

แพทย์หญิงกรรณิการ์ เลาหวิจิตร, นายแพทย์ทวี รัตนชูเอก

ศูนย์ส่องกล้องทางเดินอาหาร กลุ่มงานศัลยศาสตร์ โรงพยาบาลราชวิถี คณะแพทยศาสตร์ มหาวิทยาลัยรังสิต กรุงเทพฯ

หลักการและเหตุผล: การส่องกล้องระบบทางเดินอาหารด้วยคลื่นความถี่สูงร่วมกับการใช้เข็มเจาะเพื่อนำเซลล์มาตรวจเมื่อมีข้อบ่งชี้ (endoscopic ultrasound with fine needle aspiration: EUS-FNA) จัดเป็นหัตถการที่ขณะนี้เป็นที่ยอมรับโดยทั่วไปในการตรวจเพื่อการวินิจฉัยและวางแผนการรักษา โดยส่วนใหญ่มักใช้ในการวินิจฉัยโรคในอวัยวะต่าง ๆ ที่อยู่ใกล้เคียงทางเดินอาหารส่วนบน อาทิ ตับอ่อน ต่อมน้ำเหลืองที่อยู่โดยรอบหลอดเลือดแดง celiac (peri-celiac lymph nodes) หรือต่อมน้ำเหลืองที่อยู่ใกล้หลอดเลือดแดงใหญ่และหลอดเลือดดำใหญ่ (aortocaval lymph nodes) ตำแหน่งตับกลีบซ้าย ท่อน้ำดี ก้อนที่อยู่บริเวณช่องท้องด้านหลัง (retroperitoneal mass) ตลอดจนการตรวจความผิดปกติของก้อนที่อยู่ใต้ผนังทางเดินอาหารส่วนบน (subepithelial tumor) ได้แก่ หลอดอาหาร กระเพาะอาหาร และลำไส้เล็กส่วนต้น หรือใช้เข็มเจาะผนังทางเดินอาหารส่วนบนที่หนาตัวผิดปกติ แต่ตรวจชิ้นเนื้อไม่พบความผิดปกติจากการส่องกล้องทางเดินอาหารทั่วไป และยังสามารถใช้ตรวจก้อนหรือต่อมน้ำเหลืองที่อยู่บริเวณช่องอก (mediastinum) ได้อีกด้วย และเนื่องจากการทำ EUS-FNA นี้เป็นหัตถการที่ต้องการความไว ความจำเพาะ และความแม่นยำในการตรวจสูง และประสิทธิภาพของการตรวจขึ้นอยู่กับหลายปัจจัย ดังนั้นผู้เขียนจึงต้องการทำงานวิจัยนี้เพื่อประเมินประสิทธิภาพของหัตถการดังกล่าวที่ทำโดยศูนย์ส่องกล้องทางเดินอาหาร กลุ่มงานศัลยศาสตร์โรงพยาบาลราชวิถี

วัตถุประสงค์ของการวิจัย: เพื่อศึกษาความแม่นยำ (accuracy) ความไว (sensitivity) ความจำเพาะ (specificity) ค่าทำนายผลบวก (positive predictive value : PPV) และค่าทำนายผลลบ (negative predictive value : NPV) ของการทำ EUS-FNA ที่ทำโดยศูนย์ส่องกล้องทางเดินอาหาร กลุ่มงานศัลยศาสตร์ โรงพยาบาลราชวิถี

วิธีการดำเนินการ: ผู้เขียนได้เก็บข้อมูลย้อนหลังของการทำ EUS-FNA ในช่วงเวลาระหว่าง ตุลาคม พ.ศ. 2557 ถึง กันยายน พ.ศ. 2559 โดยเก็บข้อมูลลักษณะทางคลินิกของผู้ป่วย อวัยวะที่ทำการตรวจ ผลการตรวจทางเซลล์วิทยาและหรือพยาธิวิทยา ขนาดของเข็มที่ใช้ในการทำ FNA และข้อมูลการติดตามผู้ป่วยทางคลินิก ตลอดจนผลชิ้นเนื้อจากการผ่าตัดถ้ามี เพื่อนำมาวิเคราะห์ข้อมูลในแง่มุมต่าง ๆ ดังกล่าวข้างต้น

ผลการศึกษา: ผู้ป่วยที่ได้รับการทำ EUS-FNA จำนวน 172 คน (ชาย 90 คน หญิง 82 คน) อายุเฉลี่ย 54.8 ปี (ช่วงอายุ 17-89 ปี) โดยมีความแม่นยำของการตรวจโดยรวมร้อยละ 91.9 ความไวร้อยละ 88.1 ความจำเพาะร้อยละ 100 ค่าทำนายผลบวกร้อยละ 100 และค่าทำนายผลลบร้อยละ 81.8 และเมื่อแบ่งผู้ป่วยเป็น 4 กลุ่มย่อยตามตำแหน่งของอวัยวะที่ทำการตรวจ ได้แก่ กลุ่มตับอ่อน กระเพาะอาหาร ต่อมน้ำเหลือง และอื่น ๆ พบว่าตับอ่อนเป็นกลุ่มที่มีจำนวนผู้ป่วยมากที่สุด ได้แก่ 124 ราย และกระเพาะอาหาร 15 ราย ต่อมน้ำเหลือง 19 ราย และ กลุ่มอื่น ๆ ซึ่งรวบรวมจาก 6 อวัยวะที่มีจำนวนผู้ป่วยน้อยรวมกันเป็นจำนวน 14 ราย โดยความไวของแต่ละกลุ่มสูงอยู่ในช่วงระหว่างร้อยละ 84.6 ถึง 93.7 ความจำเพาะของทุกกลุ่มร้อยละ 100 เท่ากัน เนื่องจากไม่มีผลบวกลวง (false positive) และความแม่นยำอยู่ในช่วงระหว่างร้อยละ 86.7 ถึง 94.7 และค่าทำนายผลบวกของทุกกลุ่มเท่ากับร้อยละ 100 เนื่องจากไม่มีผลบวกลวงเช่นกัน และไม่พบภาวะแทรกซ้อนรุนแรงจากการทำหัตถการ EUS-FNA ในผู้ป่วยทุกราย

สรุป: การทำ EUS-FNA ของศูนย์ส่องกล้องทางเดินอาหารศัลยกรรม โรงพยาบาลราชวิถีมีความปลอดภัยและประสิทธิภาพสูง และมีประโยชน์มากในการให้การวินิจฉัยและวางแผนการรักษา