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Incidence and associated factors of negative appendectomy and ruptured appendicitis in PMSMC

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Introduction : *Acute appendicitis is the most common acute surgical condition. Too early operation may reduce the chance of appendiceal perforation but increases negative appendectomy cases. These two outcomes must be weighted carefully before the surgical treatment is performed.*

Objective : *To find out negative appendectomy rate, perforation rate, and clinical factors associated with negative appendectomy and ruptured appendicitis in Princess Maha Chakri Sirindhorn Medical Center (PMSMC).*

Setting : *PMSMC tertiary care setting.*

Study design : *Retrospective descriptive study.*

Patients : *All patients who were diagnosed as acute appendicitis at PMSMC from 2003 to 2008. Incidental appendectomy, interval appendectomy, and patients' age under 6 years were excluded from the study.*

Methods : *Medical records, operative notes, and pathological reports of patients with acute appendicitis who underwent appendectomy during the study periods were reviewed. Variables of interest were, namely: age, gender, stage of appendix described by the surgeon and pathological reports. Migratory pain, anorexia, vomiting, right lower quadrant rebound (RLQR) and tender (RLQT), fever, leucocytosis, and shifting to the left were collected. Statistical analysis was performed using descriptive statistics, student t test, and Chi square test.*

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Result : *There were 454 patients. Their mean age was 30.61 years old. Appendicitis was diagnosed equally in male and female patients. Negative appendectomy rate of 13.40 % was reported. The female patients were were more likely to be diagnosed negative appendectomy than the male with statistically significant (P = 0.02). Perforation rate in our series was 15.64 %. Being female (P = 0.02) without fever (P < 0.01), no migratory pain (P < 0.001), no anorexia (P = 0.005), no nausea/vomiting (P < 0.001), no leucocytosis (P < 0.001), and having no tender or rebound at the right lower area of the abdomen, these were significantly associated with negative appendectomy (P < 0.001). Factors associated with ruptured appendectomy were right lower quadrant tender (P = 0.04), duration of RLQ pain prior to operation (P<0.001), rebound (P < 0.01) and leucocytosis especially WBC more than 15,000 /mm^3 (P < 0.001).*

Conclusion : *Negative appendectomy rate in our institute was the same as the generally accepted rate (13.40 % and 10 - 15%, respectively. However, perforation rate was quite low (15.64%). Factors associated with negative appendectomy in our study including females gender, no fever, no migratory pain, no anorexia, no nausea/vomiting, no leucocytosis and no tender or rebound at the right lower area of the abdomen. Factor associated with ruptured appendectomy were tender and rebound at the right lower quadrant area, duration of RLQ pain prior to operation, and leucocytosis.*

Keywords : *Negative appendectomy, Acute appendicitis, Ruptured appendicitis.*

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เฉลิมพร โรจน์รัตน์ศิริกุล. อุบัติการณ์และปัจจัยที่เกี่ยวข้องของการผ่าตัดไส้ติ่งแล้วไม่พบพยาธิสภาพและการแตกของไส้ติ่งในโรงพยาบาลศูนย์การแพทย์สมเด็จพระเทพรัตนราชสุดา ฯ จุฬาลงกรณ์เวชสาร 2552 ก.ค. – ส.ค.; 53(4): 279 - 92

บทนำ : *ภาวะไส้ติ่งอักเสบเฉียบพลันเป็นภาวะที่พบได้บ่อยที่สุดในภาวะฉุกเฉินทางศัลยกรรม การผ่าตัดที่เร็วเกินไป จะช่วยลดโอกาสที่จะเกิดไส้ติ่งแตก แต่จะเป็นการเพิ่มโอกาส ที่จะไม่พบพยาธิสภาพของไส้ติ่งอักเสบได้ ดังนั้นการตัดสินใจผ่าตัดไส้ติ่งอักเสบจึงต้องระวังการผ่าตัดแล้วไม่พบพยาธิสภาพของไส้ติ่งอักเสบ และการแตกของไส้ติ่งที่อาจเกิดขึ้นได้*

จุดประสงค์การศึกษา : *เพื่อศึกษาหาอัตราการผ่าตัดไส้ติ่งแล้วไม่พบพยาธิสภาพ อัตราการแตกของไส้ติ่งและปัจจัยที่มีผลในโรงพยาบาลศูนย์การแพทย์สมเด็จพระเทพรัตนราชสุดา ฯ*

รูปแบบการศึกษา : *เป็นการศึกษาแบบเก็บข้อมูลย้อนหลัง ในผู้ป่วยทุกรายที่ได้รับการวินิจฉัยเป็นไส้ติ่งอักเสบเฉียบพลัน (ยกเว้นการผ่าตัดไส้ติ่งพร้อมการผ่าตัดอย่างอื่น ๆ การนัดผู้ป่วยไส้ติ่งเรื้อรังมาผ่าตัด และในผู้ป่วยที่อายุต่ำกว่า 6 ปี) ณ โรงพยาบาลศูนย์การแพทย์สมเด็จพระเทพรัตนราชสุดา ฯ ระหว่างปี พ.ศ. 2546 – พ.ศ. 2551*

สถานที่ทำการศึกษา : *โรงพยาบาลศูนย์การแพทย์สมเด็จพระเทพรัตนราชสุดา ฯ สยามบรมราชกุมารี คณะแพทยศาสตร์ มหาวิทยาลัยศรีนครินทรวิโรฒ*

วิธีการศึกษา : *เก็บข้อมูลจากเวชระเบียน รายงานการผ่าตัด และผลชิ้นเนื้อ ตัวแปรที่สนใจศึกษาประกอบด้วยอายุ เพศ อาการที่มาโรงพยาบาล (อาการปวดท้องที่ย้ายตำแหน่ง คลื่นไส้อาเจียน ปวดหรือกดเจ็บที่ท้องด้านขวาล่าง อาการไข้) รวมทั้งผลเลือดทางห้องปฏิบัติการ และนำข้อมูลวิเคราะห์ทางสถิติ*

ผลการศึกษา : *จากจำนวนผู้ป่วยทั้งสิ้น 454 คน มีอายุเฉลี่ยที่ประมาณ 30.61 ปี พบเป็นผู้ชายใกล้เคียงกับผู้หญิง อัตราการผ่าตัดไส้ติ่งแล้วไม่พบพยาธิสภาพเท่ากับ 13.40% ผู้หญิงมีโอกาสเกิดการผ่าตัดไส้ติ่งแล้วไม่พบพยาธิสภาพมากกว่าผู้ชายอย่างมีนัยสำคัญทางสถิติ ($P < 0.05$) อัตราการแตกของไส้ติ่งเท่ากับ 15.64% ปัจจัยที่มีผลต่อการเกิดการผ่าตัดไส้ติ่งแล้วไม่พบพยาธิสภาพ ได้แก่ เพศหญิง ($P = 0.02$) การไม่มีไข้ ($P < 0.01$) ไม่มีอาการปวดท้องที่ย้ายตำแหน่ง ($P < 0.001$) ไม่มีเบื่ออาหาร ($P = 0.005$)*

ไม่มีคลื่นไส้อาเจียน (P < 0.001) ไม่มีอาการกดเจ็บที่ท้องน้อยขวาล่าง (P < 0.001) และ ไม่มีเม็ดเลือดขาวสูงกว่าปกติ (P < 0.001) ส่วนปัจจัยที่มีผลต่อการเกิดไส้ติ่งแตก ได้แก่ มีอาการเจ็บที่ท้องน้อยขวาล่าง (P = 0.04) ระยะเวลาของอาการปวดท้องจนกระทั่งได้รับการผ่าตัด (P <0.001) กดเจ็บที่ท้องน้อยขวาล่าง (P < 0.01) และมีเม็ดเลือดขาวสูงกว่าปกติ (P < 0.001)

สรุป : *ในโรงพยาบาลศูนย์การแพทย์ ฯ ที่ทำการศึกษาพบว่า มีอัตราการผ่าตัดไส้ติ่งแล้วไม่พบพยาธิสภาพเท่ากับ13.40% ซึ่งอยู่ในช่วงที่ใกล้เคียงกับอัตราที่พบในรายงานอื่น ๆ ส่วนอัตราการแตกของไส้ติ่งเท่ากับ15.64% ซึ่งค่าที่ได้อยู่ในระดับที่เป็นที่ยอมรับได้ในการรักษาไส้ติ่งอักเสบ โดยปัจจัยที่มีผลต่อการเกิดการผ่าตัดไส้ติ่งแล้วไม่พบพยาธิสภาพ ได้แก่ เพศหญิง การไม่มีไข้ ไม่มีอาการปวดท้องที่ย้ายตำแหน่ง ไม่เบื่ออาหาร ไม่มีคลื่นไส้และอาเจียน ไม่มีอาการกดเจ็บที่ท้องน้อยขวาล่าง และไม่มีเม็ดเลือดขาวสูงกว่าปกติ ส่วนปัจจัยที่มีผลต่อการเกิดไส้ติ่งแตก ได้แก่ มีอาการเจ็บหรือกดเจ็บที่ท้องน้อยขวาล่าง ระยะเวลาของอาการปวดท้องและมีเม็ดเลือดขาวสูงกว่าปกติ*

คำสำคัญ : *ไส้ติ่งอักเสบ, การผ่าตัดไส้ติ่งแล้วไม่พบพยาธิสภาพ, ไส้ติ่งแตก.*

Appendicitis is the most common cause of acute abdominal condition.[1,2] Its incidence is around 7 to 11/10,000 population per year.[3,4] The life-time risk for appendicitis is approximately 8.6% and 6.7% for male and female, respectively.[3] This makes appendectomy the most common performed surgical operation. Approximately, 300,000 appendectomies are performed each year in the USA.[5]

It has been believed that appendicitis progresses steadily from early inflammation to later gangrene and perforation; therefore, appendectomy, in timely fashion, is the treatment of choice for acute appendicitis in order to control the source of infection, reduce morbidity and mortality.[5] The problem is the diagnosis of acute appendicitis, especially in the early stage, is not easy even in the hand of an experienced surgeon. Incorrect diagnosis of acute appendicitis leads to unnecessary operation (negative appendectomy) while delayed diagnosis and treatment increases the risk for appendiceal perforation, prolonged hospital length of stay, and increases overall complications.[6]

The objectives of this study were to calculate the negative appendectomy rate and the rate of perforation at our institute, Princess Mahachakri Sririndhorn Medical Center (PMSMC), which is a teaching school hospital and to investigate the significance of clinical predictors contributing to negative appendectomy and ruptured appendicitis which would be beneficial in many ways, e.g., for educational purposes, such as the findings are as an evidence-based study for improving the clinical guidelines at our institute as well as for hospital quality-control (i.e., to determine whether the hospital's negative appendectomy rate is within the acceptable rate).

Materials and Methods

Patients: We collected all cases of patients who were diagnosed as acute appendicitis and were treated by appendectomy at our institute between 2003 and 2008. There were all together 454 cases of appendectomy cases within this period. Incidental appendectomy, interval appendectomy, and patients younger than 6 years old were excluded because children younger than 6 years old are difficult to obtain history and assess physical examination.

Medical records, operative notes, and pathological reports were systematically retrospectively reviewed. The variables of interest were age, gender, stage of appendix described by the surgeon as well as pathological reports. In negative appendectomy and perforation group, the additional data that complied with Alvarado score which were migratory pain, anorexia, vomiting, right lower quadrant tenderness (RLQT) and Rebound tenderness (RLQR), fever, leucocytosis, and shifting to the left were also collected.

Currently, the clinical guidelines for appendicitis of our institute has been implemented for few months. Therefore, all acute appendicitis patients are managed along with the clinical guidelines (see appendix). Basic laboratory tests such as CBC, urianalysis, etc., are commonly used whereas imaging investigations such as ultrasoungraghy or CT scan are reserved for unusual cases.

All data were analyzed by SPSS software version 16. Patients' demographic data were analyzed by descriptive statistics and presented in frequency table, mean and standard deviation (SD). Negative appendectomy rate and perforation rate were expressed in percent. Student t test was used for

calculating P-value for continuous, normal distribution variables. Chi-square test was used for analyzing variables which was not normal distribution. P value of less than 0.05 is considered statistically significant.

Results

There were 454 patients who were diagnosed as acute appendicitis and underwent appendectomy operation between the year 2003 and 2008 at our institute. The mean age of patients was 30.61 years (range 7 - 85 years old). More than half of patients' age was younger than 30 years (260 patients, 51.1%). There was no significant difference between the number of male and female (225 and 229, respectively; P = 0.296). Patients' demographic data are shown in table 1.

Table 1. Patient demographic data.

Age group	Sex		Total
	Male	Female	
1-10	14	9	23
11-20	79	59	138
21-30	47	52	99
31-40	35	38	73
41-50	25	34	59
51-60	16	17	33
≥60	9	20	29
Total	225	229	454
Mean age	28.39	32.79	30.61
SD	15.61	16.61	16.25

The overall negative appendectomy rate was 13.40% while overall perforation rate was 15.6%. Perforation cases were found nearly equally in both genders; male (35), female (36). On the other hand, female patients had a significantly higher incidence of negative appendectomy than their male counterpart (39 and 22, respectively; P = 0.02) (Table 2).

The female patients were more likely to be diagnosed as negative appendectomy in every age group except in age group 1-10. Almost half of the female patients had age less than 30 years old (21 out of 39). On the contrary, there was no difference of incidence between genders in perforation group. Perforation seems to distribute equally in every age group (Table 3).

As for negative appendectomy group, 17 patients (4 males and 13 females) had specific diagnosis. Nine of 13 female patients had gynecologic disease. Gastro-enteric diseases were responsible for all the male patients and the rest of the female patients (Table 4).

The pathological reports of the excised appendixes were categorized into 3 groups, namely: normal, perforation, and acute inflammation. The overall rate of these reports was 13.40%, 15.6% and 70.92%, respectively. No statistical significance was detected between the male and female patients, except in negative appendectomy where the female had more significant chance than their male counterpart (Table 5).

Usually, negative appendectomy was found in female patients who had no fever, no migratory pain, no anorexia, no N/V, no RLQT/RLQR, and no leucocytosis (Table 6).

Table 2. Negative appendectomy and perforation rate grouped by gender.

	Male (n = 225)	**Female (n = 229)**	**Total (n = 454)**	**P value**
Negative appendectomy	22 (9.78%)	39 (17.0%)	61 (13.40%)	0.021
Perforation rate	35 (15.56%)	36 (15.7%)	71 (15.6%)	0.660

Table 3. Age group distribution of negative appendectomy and appendiceal perforation group.

Age group	**Negative appendectomy**		**Appendiceal perforation**	
	Male	**Female**	**Male**	**Female**
1 - 10	2	1	3	1
11 - 20	5	11	7	9
21 - 30	5	9	6	6
31 - 40	4	6	5	6
41 - 50	4	6	6	5
51 - 60	2	4	5	5
≥60	0	2	3	4
Total	22	39	35	36

Table 4. Specific causes in negative appendectomy group.

Male (4)		**Female (13)**	
PU perforation	1	Ruptured ovarian cyst	4
Ileal perforation	1	Twisted ovarian cyst	2
Segmental enteritis	1	TOA, Salpingitis	2
Diverticulitis	1	Tubal pregnancy	1
		Segmental enteritis	2
		Diverticulitis	2

Table 5. Type of appendiceal pathology.

	Male (n = 225)	**Female (n = 229)**	**Total (n = 454)**	**P value**
Negative appendectomy	22 (9.78%)	39 (17.0%)	61 (13.40%)	0.021
Perforation rate	35 (15.56%)	36 (15.7%)	71 (15.6%)	0.660
Acute appendicitis	168 (74.66%)	154 (67.24%)	322 (70.92%)	0.143
Total	231 (100%)	254 (100%)	454 (100%)	

Table 6. Significant factors in negative appendectomy group.

Variable	**OR**	**95%CI**	**p value**
Female	1.93	1.06- 3.58	0.02
Migratory pain	37	9.9-250	<0.001
anorexia	6.25	1.56-5.55	0.005
N/V	2.94	1.58-5.55	<0.001
RLQT	7.69	2.77-20.0	<0.001
RLQR	4.34	2.32-8.33	<0.001
Fever	3.12	1.63-6.25	<0.01
Leukocytosis	6.66	2.32-16.94	<0.001

Ruptured appendectomy was usually found in patient with RLQT/RLQR, long duration of RLQ pain prior to operation, and leucocytosis especially when WBC more than 15,000/mm^3 ($P < 0.001$) (Table 7).

The longer the duration of RLQ pain prior to the operation, the higher is the chance of the patient to be diagnosed as ruptured appendicitis. (Table 8)

Table 7. Significant factors in ruptured appendectomy group.

Variable	**OR**	**95%CI**	**p value**
RLQT	4.76	0.61-50.0	0.04
RLQR	3.57	1.92-6.25	<0.01
Leukocytosis (>15,000)	7.14	2.77-17.24	<0.001
Duration of pain > 24 hours	1.88	1.30-2.70	<0.001

Table 8. The association of duration of pain and ruptured appendicitis.

Variable	OR	95%CI	p value
0 - 24 hours	1		
25 - 48 hours	2.55	1.26 - 5.16	<0.05
49 - 72 hours	3.06	1.38 - 6.77	<0.05

Discussion

The overall appendectomy cases during our study period were 454 cases. From our results, the male and female proportion was around 1:1. This was slightly different from other studies that were around 1.3 - 1.4:1.[7, 8] The figure may be explained by the geographical location of our institute which was set in the rural area. Men might have moved into more urban areas, leaving more women in the area.

In the past, the rate of negative appendectomy was 20% which was acceptable [9] but, because of new imaging technologies such as ultrasonography and computerized tomography. This rate is now unacceptably high. Peck *et al.*[10] reported only 5% of negative appendectomy rate in their study which used non-contrast helical computed tomography for assisting diagnosis of appendicitis. In general, the overall acceptable negative appendectomy rate is 10 - 15 %.[8, 9, 11] Nevertheless, in some regions, negative appendectomy rate as high as 85% has been reported.[4]

The rate of negative appendectomy in our study was 13.4%. It was equal as in the generally acceptable rate range (10 - 15%). Women had higher chance of negative appendectomy with statistical significance (P < 0.02) which was consistent with earlier studies, regarding the influence of gender on negative appendectomy.[7, 12] Women's higher chance

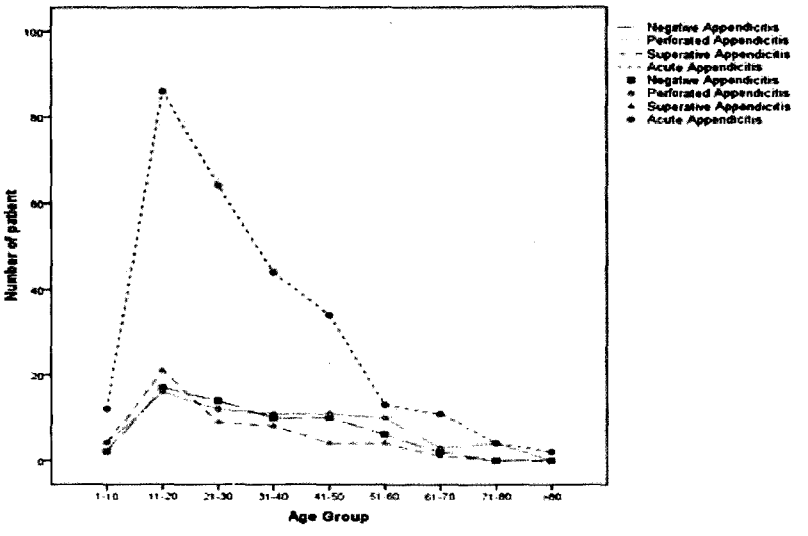

Figure 1. Number of patients in each stage of appendicitis grouped by age group.

for negative appendectomy was found in every age group. The highest incidence was found in child-bearing age group (66%). Gynecological diseases such as salpingitis, were claimed for the causes of high negative appendectomy rate as their symptoms usually mimic appendicitis leading to incorrect diagnosis and unnecessary operation.[13] Out of the 13 female patients in our series who had specific diagnosis for negative appendectomy, 9 of them had gynecologic diseases. Furthermore, the concept that delayed treatment for appendicitis may increase the chance for tubal occlusion, leading to secondary infertility, may increase negative appendectomy rate in women, especially in the child-bearing age group.[14]

The overall appendiceal perforation rate was around 14 - 40%.[15] In one large series with 63,707 appendectomy cases, perforation rate of 25.8% was reported.[16] Our perforation rate was 15.6% which was lowest when compared to the studies mentioned earlier. Regarding the gender ratio, we found that men and women had the same incidence of appendiceal perforation. This finding was different from earlier studies in which men had more chance of perforation than women.[3, 17]

When compared within their own groups, cases of negative appendectomy were usually female who had no fever, no migratory pain, no anorexia, no nausea/vomiting, no leucocytosis, and no tendernessness or Rebound tenderness at the right lower area of the abdomen were significantly associated with negative appendectomy ($P < 0.001$). Factors associated with ruptured appendectomy were the right lower quadrant tenderness ($P = 0.04$), duration of RLQ pain ($P<0.001$), Rebound tenderness at the right lower abdominal area ($P < 0.01$) and leucocytosis, especially when WBC was more than 15,000 /mm^3 ($P < 0.001$).

Women had more chance to have negative appendectomy because of the difficulty to distinguish between appendicitis and gynecological diseases as well as the concept of early treatment in order to prevent tubal occlusion as discussed above. Anorexia was found in only 5 cases out of 73 patients. As mentioned earlier, gynecological causes pay a dominant role in cases of negative appendectomy. GI symptoms in gynecologic diseases were usually presented in later stage.[18] Leucocytosis, especially WBC more than 15,000 /mm^3, and shift to the left were statistically reduced the chance of negative appendectomy ($P < 0.001$). However, Anderson reported in his meta-analysis study that laboratory examination of the inflammatory response such as leucocytosis alone was a weak discriminator for excluding appendicitis. Clinical peritoneal irritation signs, history of migration pain, and laboratory examinations of the inflammatory responses are the best tools for the diagnosis of acute appendicitis.[7]

Conclusion

Acute appendicitis is the most common surgical condition and appendectomy is the treatment of choice. However, the diagnosis of acute appendicitis is sometime difficult leading to unnecessary operations (negative appendectomy). We have collected appendectomy cases in our institute between 2003 and 2008. There were 454 cases with 13.4% of negative appendectomy and 15.6% of appendiceal perforation. The mean age for appendicitis was 30.61 years old. Both genders had

equal chance of appendicitis as well as appendiceal perforation.

On the contrary, women were more likely to have negative appendectomy than men. A female patient without fever, no migratory pain, no anorexia, no nausea/vomiting, no leucocytosis, and no Rebound tenderness /tenderness at the right lower area of the abdomen were the significant predicting factors for negative appendectomy. Factors associated with ruptured appendicitis in our institute were tenderness/ Rebound tenderness at the right lower area of the abdomen, duration of RLQ pain and leucocytosis especially when WBC was more than 15,000 /mm.^{3}

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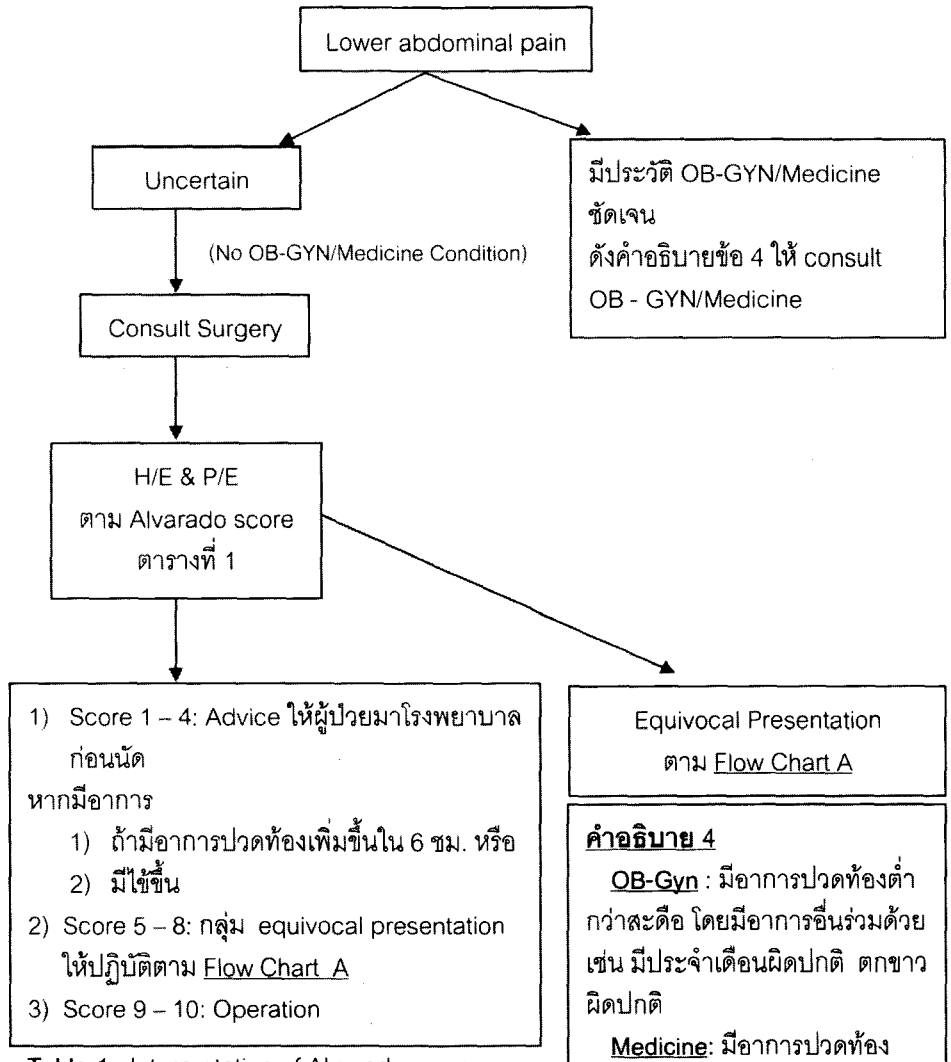
Appendix



คำอธิบาย 4

OB-Gyn : มีอาการปวดท้องต่ำกว่าสะดือ โดยมีอาการอื่นร่วมด้วย เช่น มีประจำเดือนผิดปกติ ตกขาวผิดปกติ

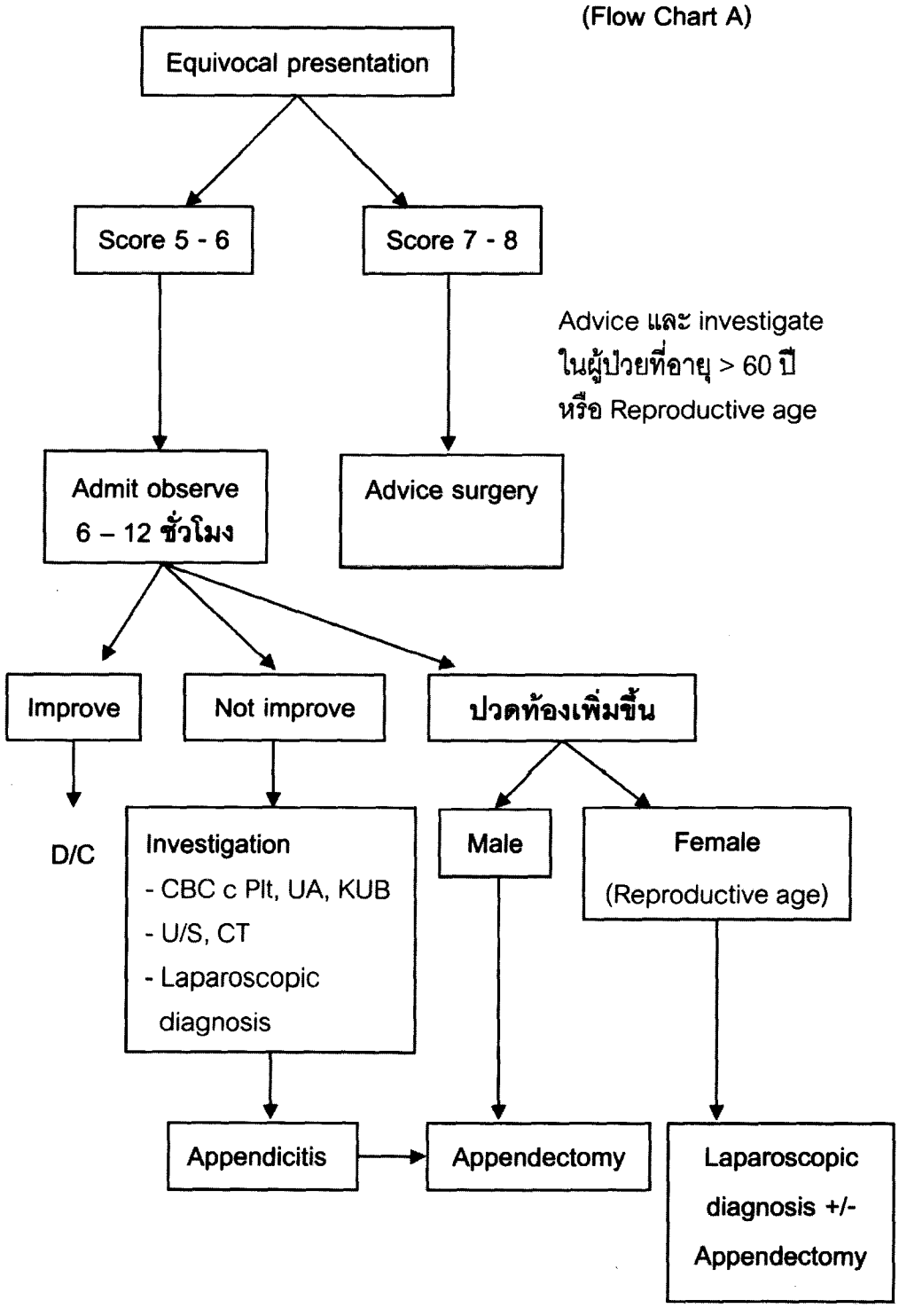
Medicine: มีอาการปวดท้องร่วมกับอาการอาหารเป็นพิษ เช่น มีคลื่นไส้ อาเจียน นำมาก่อนปวดท้อง มีอาการถ่ายเหลว หรือมีไข้นำมาก่อน ปวดท้อง และต้องไม่มี sign หน้าท้อง

ศัลยกรรม: ปวดท้องก่อนมีไข้ มี sign หน้าท้อง (localize tenderness) มา ER 2 ครั้งในคืนเดียวกัน หลังจากได้ยารับประทานแล้วไม่ดีขึ้น ภายใน 24 ชั่วโมง

Table 1. Interpretation of Alvarado score.

Characteristics	Score
M = migration of pain to the RLQ	1
A = anorexia	1
N = nausea and vomiting	1
T = tenderness in RLQ	2
R = rebound pain	1
E = elevated temperature	1
L = leukocytes	2
S = shift of WBC to the left	1
Total	10

(Flow Chart A)


Equivocal presentation
Score 5 - 6
Score 7 - 8
Advice และ investigate
ในผู้ป่วยที่อายุ > 60 ปี
หรือ Reproductive age
Admit observe
6 – 12 ชั่วโมง
Advice surgery
Improve
Not improve
ปวดท้องเพิ่มขึ้น
D/C
Investigation
- CBC c Plt, UA, KUB
- U/S, CT
- Laparoscopic diagnosis
Male
Female
(Reproductive age)
Appendicitis
Appendectomy
Laparoscopic diagnosis +/- Appendectomy