

Diagnosis of appendicitis: comparison of computed tomography (CT) scans using oral contrast material alone versus oral and intravenous (IV) contrast media

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Objectives The purpose of this study was to compare the diagnostic accuracy between computed tomography (CT) scans using oral contrast material alone (oral contrast CT) versus oral and intravenous (IV) contrast media (contrast-enhanced CT) in patients with equivocal symptoms and signs of appendicitis.

Methods This retrospective study had 103 patients, who were aged from 15 to 94 years, with equivocal symptoms and signs of appendicitis. All of the patients were given oral contrast material, and a CT scan was performed one hour later. Immediately thereafter, a repeated CT scan of the abdomen was performed following intravenous administration of contrast-enhanced media. Studies were separated and interpreted independently by two radiologists, who were blinded to medical records. The final outcome was based on operative and clinical findings, and follow-up data.

Results Of the 103 patients enrolled, seven underwent only oral contrast CT because they had contraindication for IV contrast media. Data analysis of the contrast-enhanced CT and oral contrast CT revealed sensitivity of 89.4% and 83.3% ($p=0.55$), specificity of 95.9% and 96.4% ($p=1.00$), PPV of 95.5% and 95.2% ($p=1.00$), NPV of 90.4% and 86.9% ($p=0.77$), and accuracy of 92.7% and 90.3% ($p=0.62$), respectively. An alternative diagnosis was established in 30 of the patients (29.1%), which included 12 with gastrointestinal abnormality, 10 with urinary tract abnormality, six with gynecologic abnormality, and two with other abnormalities.

Conclusions Patients presenting with suspected acute appendicitis had similar characteristics to those diagnosed as appendicitis when CT scans used either oral contrast material alone or oral and IV contrast media. **Chiang Mai Medical Journal 2014;53(4):157-65.**

Keywords: appendicitis, oral contrast CT, contrast-enhanced CT

Background

Acute appendicitis commonly causes acute abdominal pain, and is the most common con-

dition requiring abdominal surgery. Approximately 20-33% of patients suspected of having

appendicitis present with equivocal clinical findings and/or laboratory test results^[1,2]. In non-classic presentations of acute appendicitis, computed tomography (CT) scans have been shown as highly valuable in the diagnosis of appendicitis^[3-6]. CT protocol for patients with suspected appendicitis commonly includes the use of oral and intravenous (IV) iodinated contrast agents^[7-10]. However, CT protocols may vary, due to controversy over scanning techniques; e.g. radiation dose and use with or without oral, rectal and IV contrast media^[7,8]. Currently, institutions use different protocols to evaluate patients suspected of appendicitis, as there is no expert consensus of which CT protocol should be used^[11,12]. Each protocol has different advantages and disadvantages. One of the major problems in many institutions is the disadvantage of IV contrast media, which risks contrast-induced nephropathy and allergic reactions, and is contraindicated in many patients with poor renal function.

Due to the disadvantage and contraindication of IV contrast media, the purpose of this retrospective study was to compare the diagnostic accuracy of CT scans using oral and IV contrast media (contrast-enhanced CT), which is a widely used, versus CT scans using oral contrast material alone (oral contrast CT) in patients presenting with clinically equivocal symptoms of acute appendicitis.

Materials and methods

Patients

This retrospective study was approved by the institutional review board. All patients presenting with acute right lower quadrant pain and clinically suspected acute appendicitis, and requesting CT examination to evaluate acute appendicitis at Lamphun Hospital between February 2012 and March 2014, were included in this study. An emergency department or surgical attending physician made the decision to refer patients for a whole or lower abdominal CT scan if the clinical features were considered insufficient for diagnosis. Patients less than 15 years' old, pregnant women and patients without adequate follow-up were excluded.

The population in this study consisted of 103 patients; 61 female and 42 male (mean age, 45.75 years; age range 15-94 years). Seven patients had contraindication for IV contrast media (renal insufficiency, seafood allergy), and

they underwent oral contrast CT only. CT scans of the whole and lower abdomen were performed on 71 and 32 patients, respectively.

CT Technique

CT examinations were performed using a 16-slice multi-detector CT scanner (Activion 16, Toshiba). All of the patients received positive oral contrast preparation (1,000 cc of 2-3% iohexol [Omnipaque 300; Amersham Health, Princeton, NJ]). CT scans were performed 60 minutes after commencing oral contrast material administration. A single helical scan, while holding breath, was performed through the whole or lower abdomen, according to the request of the referring physician.

Immediately thereafter, a second helical scan was obtained after an IV injection of 100 mL of a contrast agent (Omnipaque [300 mg of iodine per milliliter]; Amersham Health, Princeton, NJ). The CT scan that covered the whole abdomen from the dome of the liver to the symphysis pubis and lower abdomen, scanned from the right renal lower pole to symphysis pubis. Both helical scans were performed with the same CT parameters as follows: tube voltage, 120 kVp; tube current time product, 250-300 mAs; pitch, 0.9; and slice collimation, 1 mm.

Image analysis

Two radiologists (PS and SK, with seven and four years experience, respectively) independently reviewed images from each CT examination. They were blinded to medical records (including the method of treatment, surgical and pathologic report, and final diagnosis), with the understanding that all of the examinations were performed in patients clinically suspected of having acute appendicitis. Firstly, the oral contrast CT was interpreted. Then, the contrast-enhanced CT in the same patients was reviewed. Reviewers interpreted the scans in any plane with the multiplanar reconstruction (MPR) display, and were free to adapt the window settings as preferred. Specific findings of appendicitis were evaluated and recorded on CT scans using both oral contrast CT and contrast-enhanced CT. The radiologists were asked at each reading to assess the presence or absence of appendicitis. The criteria for CT diagnosis of acute appendicitis included an outer-wall-to-outer-wall transverse diameter greater than 6 mm, appendicolith, wall thickening, wall hyperenhancement, periappendiceal inflammation, phlegmon, abscess or extraluminal air^[13,14]. CT scans were interpreted as negative for appendicitis if the appendiceal lumen filled completely with air or contrast material, if the appendix was less than or equal to 6 mm in maximum diameter, if the appendiceal wall was less than 2 mm thick^[15], or if no periappendiceal inflammation was present. When the appendix was not visible, absence of appendicitis was diagnosed on the basis of absent periappendiceal inflammation.

The scans were evaluated additionally for the presence of alternative diagnosis. If the reviewer suspected that an alternative diagnosis was present, its presumed cause would be recorded. Incidental findings that could not explain the pain presented by the patient were not considered in this study. Provisional diagnosis of acute appendicitis or alternative diseases or negative study was based on the decision and judgment of the radiologist after integrating all positive and negative findings on each study. A consensus on the result was determined for cases in which the initial interpretations by the radiologists differed.

Final diagnoses

The final diagnoses were determined at surgery and histopathologic examination in the patients who underwent an appendectomy. Two patients with negative CT findings underwent an appendectomy; and the appendix was found to be normal. The decision to perform surgery was based on clinical findings in both of them. The patients who had conservative treatment without appendectomy were follow-up by examinations at 24 hours and 2-4 weeks after discharge. In negative appendicitis patients, an alternative clinical diagnosis was recorded.

Statistical analysis

The Fisher's exact test was performed to compare the value between groups. A P value of 0.05 or less was considered to indicate a statistically significant difference. The kappa statistics was used for interobserver agreement. The levels of agreement were interpreted as follows: 0-0.20, poor agreement; 0.21-0.40, fair agreement; 0.41-0.60, moderate agreement; 0.61-0.80, good agreement; and 0.81-1.00, very good agreement.

Results

Results of CT scan interpretation compared

with clinical and/or histopathologic findings for oral contrast CT and contrast-enhanced CT are shown in Table 1 and 2, respectively. Forty-eight patients (46.60%) had a final diagnosis of appendicitis (Figure 1), and 47 of those underwent an appendectomy while one was treated conservatively with antibiotics for an appendiceal abscess. A retrospective review of two false positive cases found misinterpretation from both techniques in the same patients, as the radiologists thought that there were subtle positive findings of appendicitis. Slightly enlarged appendiceal mucosa, with questionable mild hyperenhancement, was interpreted in these cases, but there was lack of periappendiceal inflammatory change.

False negatives were found in CT scans for eight patients using oral contrast CT and five on contrast-enhanced CT. Finally, all of the former patients had surgical confirmation of appendicitis, whereas the latter five had negative findings (Figure 2). Discordant interpretations were revealed in three patients, with a negative study for appendicitis on oral contrast CT and a positive one on contrast-enhanced CT being interpreted (Figure 3). The false-negative findings in this study resulted from early appendicitis, paucity of intraabdominal fat, inflammation occurring only at the tip of the appendix, and severe inflammation at the right lower quadrant (RLQ) from appendiceal abscess.

Kappa value for inter-observer agreement for oral contrast CT and contrast-enhanced CT

Table 1. Result of oral contrast CT diagnoses compared with clinical and/or histopathologic findings

Oral contrast CT	Appendicitis positive	Appendicitis negative	Total
CT positive for appendicitis	40	2	42
CT negative for appendicitis	8	53	61
Total	48	55	103

Table 2. Result of contrast-enhanced CT diagnoses compared with clinical and/or histopathologic findings

Contrast-enhanced CT	Appendicitis positive	Appendicitis negative	Total
CT positive for appendicitis	42	2	44
CT negative for appendicitis	5	47	52
Total	47	49	96

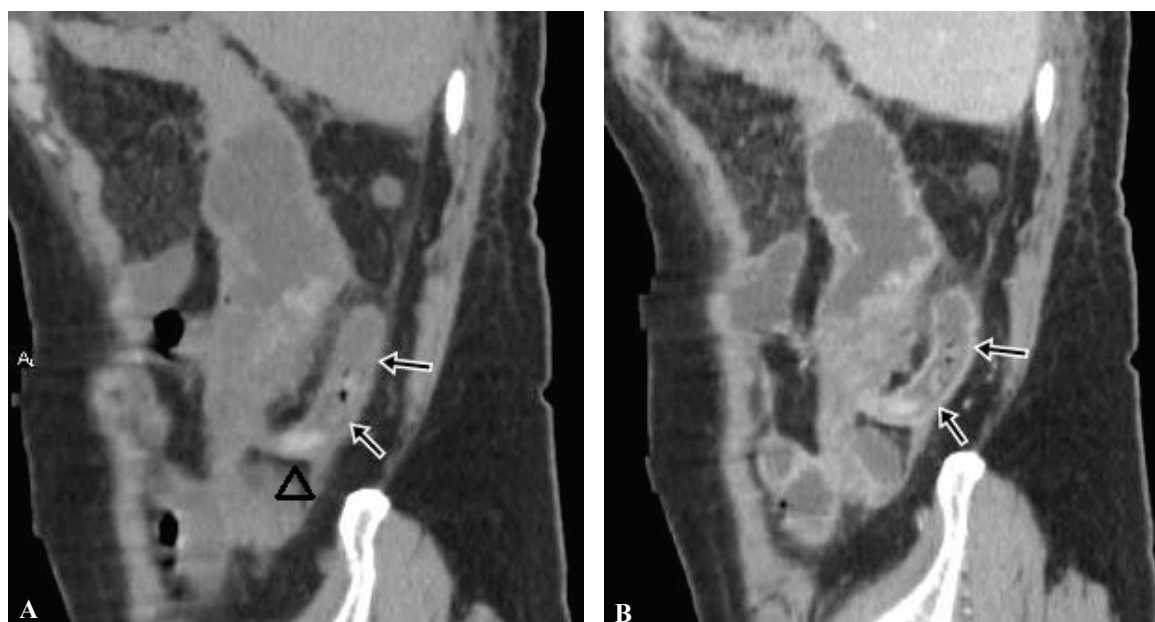


Figure 1. A 38-year-old man with acute appendicitis.

A and B, sagittal oral contrast CT image (A) and contrast-enhanced CT image (B) showing enlarged, thickened, fluid-filled appendix (arrow). Periappendiceal fat stranding and appendicolith (arrow head) are also seen

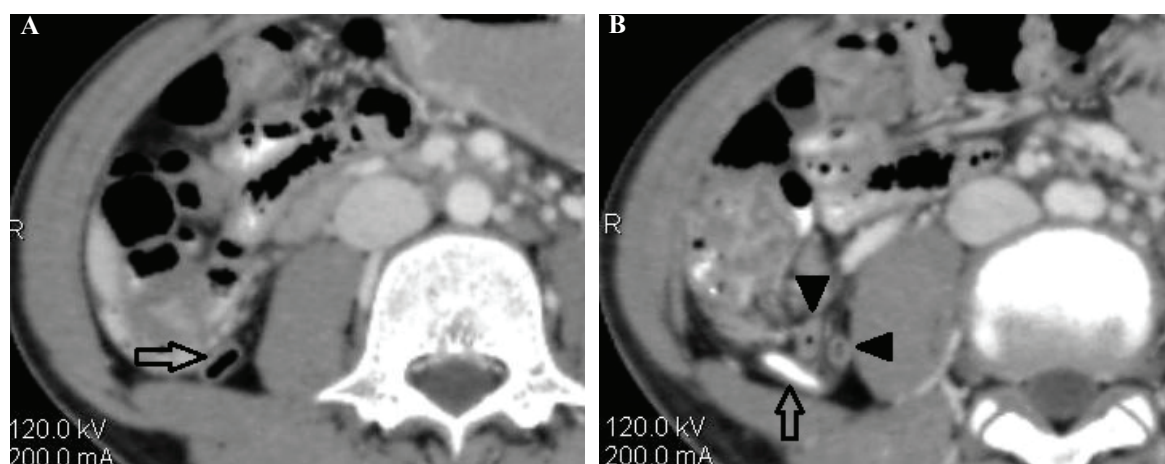


Figure 2. False negative interpretation of acute appendicitis in the case of surgical confirmation in a 15 year-old man.

A and B, axial contrast-enhanced images showing enteric contrast material and gas in the lumen of the appendix (arrow). Mild thickened and enhanced wall at the distal part is noticeable (arrow head)

was 0.88 and 0.90, respectively, which indicated very good agreement. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy for the diagnosis of acute appendicitis on both oral contrast CT and contrast-enhanced CT are listed in Table 3. No significant difference was observed in per-

formance between protocols. However, both reviewers agreed that contrast-enhanced CT interpretation provides a higher degree of diagnostic confidence than oral contrast CT.

Fifty-five patients (53.40%) did not have appendicitis. Two patients in the true-negative group underwent surgery, and a normal ap-

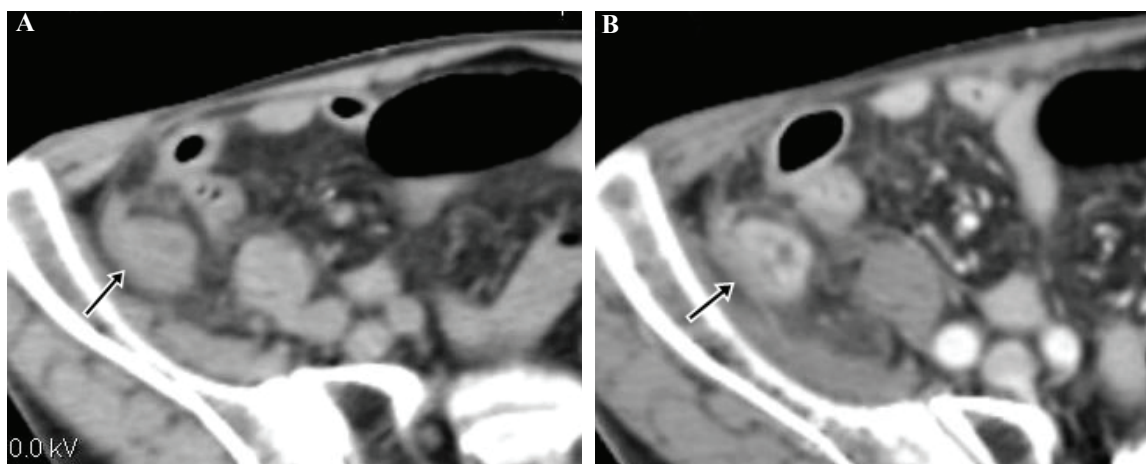


Figure 3. A 59-year-old man with suspected acute appendicitis.

A and B, oral contrast CT scans obtained before (A) and after (B) IV contrast administration, illustrating the benefit of IV contrast material in difficult cases. Oral contrast CT scan (A) is indeterminate because the appendix is not visualized, and seen as nonspecific soft-tissue mass (arrow) with surrounding fat stranding at the RLQ. Contrast-enhanced CT scan (B) showing dilated appendix with thickened, hyperenhancing wall (arrow).

Table 3. Comparison of accuracy in oral contrast CT and contrast-enhanced abdominal CT

	Oral contrast CT	Contrast-enhanced CT	<i>p</i>
Sensitivity	83.3	89.4	0.55
Specificity	96.4	95.9	1.00
PPV	95.2	95.5	1.00
NPV	86.9	90.4	0.77
Accuracy	90.3	92.7	0.62

pendix was found in both of them. Alternative diagnoses of the 55 patients without acute appendicitis included non-specific abdominal pain in 25 (45.45%), gastrointestinal abnormality in 12 (21.81%), urinary tract infection or calculi in 10 (18.18%), gynecologic abnormality in six (10.90%), and other conditions in two (3.63%) (Table 4).

Discussion

At present, multiple detector computed tomography (MDCT) is well developed. CT can scan faster with a very thin slice and achieve good image quality, leading to excellent diagnostic performance. Whether to administer both positive oral and IV contrast media and scan using a standard-radiation-dose CT technique,

Table 4. Alternative diagnoses in 55 patients without appendicitis

Alternate diagnosis	No. of cases*
1. Nonspecific abdominal pain	25 (45.45)
2. Gastrointestinal abnormality	12 (21.81)
Right-sided diverticulitis	2
Sigmoid diverticulitis	2
CA cecum	2
Colitis	2
Bowel gangrene	1
Intramural small bowel hge	1
Acute cholecystitis	1
Acute pancreatitis	1
3. Urinary tract abnormality	10 (18.18)
Ureteral calculi	5
Calculi with infection	4
Right pyelonephritis	1
4. Gynecologic abnormality	6 (10.90)
Ovarian cyst	6
5. Other	2 (3.63)

*Number in parentheses is the percentage

for patients with suspected appendicitis, raises the question of which is the most appropriate protocol. Many trials have been published reporting and comparing various CT protocols for evaluating patients with suspected appendicitis. Several studies have advocated unenhanced

CT protocols as a rapid and accurate method of establishing acute appendicitis^[14,16-19]. Lane *et al*^[14] examined 300 consecutive patients prospectively by using non-enhanced thin-section focused helical CT for detection in cases of suspected acute appendicitis. Their study yielded 96%, 99% and 97% sensitivity, specificity and accuracy, respectively. Other studies reported high diagnostic accuracy by using only IV contrast CT^[20], only rectal contrast CT^[21] and oral contrast CT alone^[13]. Mun *et al*^[20] reported 100% sensitivity and 97% specificity of IV contrast CT in suspected acute appendicitis. Similarly, Hershko *et al*^[21] found convincing evidence that CT using rectal contrast material only had excellent sensitivity, specificity and accuracy. A few studies reported that the low-dose technique also allowed excellent sensitivity, specificity, and negative and positive predictive value^[22,23].

Adverse reactions to IV contrast agents range from a mild inconvenience to a life-threatening condition. Renal toxicity is a well-known adverse reaction associated with the use of intravenous contrast material. Other forms of adverse events include delayed allergic reactions, anaphylactic reactions, and local tissue damage. Patients with impaired renal function are at risk of developing contrast-induced nephropathy. If a CT protocol without IV contrast material had accuracy similar to that of the traditional protocol, patients with suspected acute appendicitis would benefit. Positive contrast given orally achieved good cecal distension and appendiceal filling, allowing visualization of the entire appendix. A minor disadvantage of positive oral contrast ingestion is that patients must wait at least one hour after the commencement of oral contrast material administration before CT is performed, and they might be at risk of appendiceal perforation.

Contrast-enhanced CT scans (using both oral and IV contrast media) provide excellent diagnostic accuracy. The authors who proved that contrast-enhanced CT is a highly effective and an accurate means of diagnosing acute appendicitis include Anderson *et al*^[24], Kamel *et al*^[25], and Balthazar *et al*^[26] who reported 98-100%,

83-100% and 93-99% sensitivity specificity and accuracy, respectively. This study provided contrast-enhanced CT scans with a sensitivity of 89%, specificity of 96%, PPV of 95%, NPV of 90%, and accuracy of 93%.

Wijetunga *et al*^[13] examined 100 consecutive patients prospectively by using oral contrast material focused appendiceal CT in clinically equivocal cases of acute appendicitis, and achieved 93% sensitivity, 97% specificity, and 96% accuracy. The diagnostic accuracy of the oral contrast CT scan in this study revealed sensitivity of 83%, specificity of 96%, PPV of 95%, NPV of 84%, and accuracy 90%. Although the sensitivity of contrast-enhanced CT and oral contrast CT scans is lower in this study than in previous reports, it is an accurate and effective technique for diagnosing acute appendicitis. The specificity and accuracy on both techniques are closer to those in previous studies. Misinterpretation may occur in patients with mild incipient forms of acute appendicitis. There may be minimal dilatation of the appendix or absent periappendiceal inflammation in patients with a small amount of retroperitoneal fat, and those with ruptured appendix that is surrounded by a large amount of pericecal inflammation. However, the diameter threshold of 6 mm may be inappropriate. Brown *et al*^[27] showed normal appendix measurements of greater than 6 mm in 42% of asymptomatic adult outpatients, and they defined the upper limit of normal as 10 mm.

No marked difference was found between the diagnostic accuracy of oral contrast CT in this study when compared to that by Jacobs *et al*^[4]. Jacobs *et al*^[4] found that the focused technique with oral contrast material in suspected appendicitis revealed 71.4-83.3% sensitivity and 92.3-97.9% specificity. They (4) concluded that the use of oral and IV contrast material improved diagnostic accuracy when compared to oral contrast material alone. This differs from the results in this study, which concluded that oral contrast CT and contrast-enhanced CT had no effect on sensitivity, specificity, NPV, PPV, or accuracy. The protocol of Jacobs *et al*^[4] was slightly dif-

ferent from that in this study. They used thicker slices than those utilized in this study, and the regions scanned with and without IV contrast material were different. These authors performed focused appendiceal CT (15-cm coverage in the RLQ) on oral contrast CT, and scanned the entire abdomen following IV and oral administration.

Although the clinical symptoms may suggest appendicitis, this condition is often mimicked by various other gastrointestinal and genitourinary processes. Established alternative diagnoses (not including nonspecific abdominal pain) in most previous studies have ranged from 22-42%^[4,13-14,16], and are common conditions that include ovarian cyst, urinary calculi with or without infection, and cecum or sigmoid diverticulitis. In the results of this study, alternative diagnosis was at 27.58% and common findings were similar to those in other studies. Use of IV contrast material may improve the diagnostic confidence and visualization of the appendix, and correct alternative diagnosis.

The limitations of this study include patient selection and types of CT scan, as the inclusion criteria contained patients with clinically equivocal acute appendicitis, who underwent CT examination that was ordered by an emergency department or surgical attending physician. The judgment of each physician was different depending on their experience.

In conclusion, the use of oral contrast CT and contrast-enhanced CT scans achieved high levels of accuracy in the diagnosis of equivocal cases of acute appendicitis. The findings of this study suggest that there is no statistically significant difference between CT scans for diagnosing appendicitis after administration of oral and IV contrast media versus that of oral contrast material alone. Further studies are needed to evaluate unenhanced CT, limited scanning area, and the low-dose scanning technique. Simplified CT techniques that yield high levels of accuracy for radiologists and patients are still a challenge.

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การวินิจฉัยผู้ป่วยที่สงสัยโรคไส้ติ่งอักเสบด้วยการตรวจเอกซเรย์คอมพิวเตอร์โดยวิธีการกินและฉีดสารทึบรังสีเปรียบเทียบกับ การตรวจเอกซเรย์คอมพิวเตอร์โดยวิธีการกินสารทึบรังสี

พรทิพย์ สุทธิรัตน์ชัยชาญ, พ.บ., และ ศิริินภา คำพันธุ์, พ.บ.

กลุ่มงานรังสีวิทยา โรงพยาบาลลำพูน กระทรวงสาธารณสุข

วัตถุประสงค์ งานวิจัยฉบับนี้มีเป้าหมายเพื่อเปรียบเทียบความแม่นยำในการวินิจฉัยระหว่างการตรวจด้วยเครื่องเอกซเรย์คอมพิวเตอร์โดยวิธีการกินสารทึบรังสี และการตรวจด้วยเครื่องเอกซเรย์คอมพิวเตอร์โดยวิธีการกินและฉีดสารทึบรังสีในผู้ป่วยซึ่งอาการและอาการแสดงของโรคไส้ติ่งอักเสบไม่ชัดเจน

วิธีการศึกษา ผู้ป่วย 103 ราย (อายุระหว่าง 15-94 ปี) ซึ่งมีอาการและอาการแสดงของโรคไส้ติ่งอักเสบไม่ชัดเจนจะถูกวมเข้าในการศึกษาแบบย้อนหลัง ผู้ป่วยทุกรายจะได้กินสารทึบรังสีและได้รับการตรวจเอกซเรย์คอมพิวเตอร์ 1 ชั่วโมงหลังจากเริ่มกินสารทึบรังสี หลังจากนั้นผู้ป่วยจะได้รับการตรวจเอกซเรย์คอมพิวเตอร์ซ้ำอีกครั้งหลังจากฉีดสารทึบรังสีเข้าทางหลอดเลือดดำ การแปลผลภาพเอกซเรย์จะกระทำโดยรังสีแพทย์ 2 คน ซึ่งต่างแปลผลแยกกันและเป็นอิสระต่อกัน โดยรังสีแพทย์ทั้งสองจะไม่ทราบประวัติทางการแพทย์ของผู้ป่วย การวินิจฉัยสุดท้ายของผู้ป่วยพิจารณาจากผลการผ่าตัด อาการทางคลินิก และข้อมูลการติดตามของผู้ป่วย

ผลการศึกษา มีผู้ป่วยเข้าร่วมในการวิจัย 103 ราย ผู้ป่วย 7 ราย ได้รับการตรวจเฉพาะเอกซเรย์คอมพิวเตอร์โดยวิธีการกินสารทึบรังสี เนื่องจากมีข้อห้ามในการฉีดสารทึบรังสีเข้าทางหลอดเลือดดำ จากการวิเคราะห์ผลการตรวจเอกซเรย์คอมพิวเตอร์โดยใช้วิธีทั้งการกินและฉีดสารทึบรังสี กับเอกซเรย์คอมพิวเตอร์โดยวิธีการกินสารทึบรังสี พบว่า ให้ความไวเท่ากับ 89.4 และ 83.3 ($p=0.55$) ความจำเพาะเท่ากับร้อยละ 95.9 และร้อยละ 96.4 ($p=1.00$) คุณค่าการทำนายผลบวกเท่ากับร้อยละ 95.5 และร้อยละ 95.2 ($p=1.00$) คุณค่าการทำนายผลลบเท่ากับร้อยละ 90.4 และร้อยละ 86.9 ($p=0.77$) และ ความแม่นยำเท่ากับร้อยละ 92.7 และร้อยละ 90.3 ($p=0.62$) ตามลำดับ การวินิจฉัยโรคอื่นพบในผู้ป่วย 30 ราย (ร้อยละ 29.1) โดยพบความผิดปกติระบบทางเดินอาหาร (12 ราย) ความผิดปกติระบบทางเดินปัสสาวะ (10 ราย) ความผิดปกติระบบนรีเวช (6 ราย) อื่น ๆ (2 ราย)

สรุปผลการศึกษา การวินิจฉัยผู้ป่วยที่สงสัยโรคไส้ติ่งอักเสบด้วยการตรวจเอกซเรย์คอมพิวเตอร์โดยวิธีการกินสารทึบรังสี และโดยวิธีการกินและฉีดสารทึบรังสีให้ผลลัพธ์ที่เหมือนกัน **เชียงใหม่เวชสาร 2557;53(4):157-65.**

คำสำคัญ: โรคไส้ติ่งอักเสบ เอกซเรย์คอมพิวเตอร์โดยวิธีการกิน เอกซเรย์คอมพิวเตอร์โดยใช้สารทึบรังสี