

Cost Effectiveness of Combined CT Pulmonary Angiography (CTPA) and Indirect CTV in Patient with Intermediate to High Probability for Pulmonary Embolism

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Objective: Evaluate the cost effectiveness of combined CTPA and indirect CTV for evaluation of patients with intermediate to high probability for pulmonary embolism using Wells criteria.

Material and Method: One hundred cases with moderate to high probability for pulmonary embolism according to Wells criteria were prospectively collected between December 2007 and January 2010. Combined CTPA and indirect CTV were performed. Positive findings were including the visualization of filling defect within the pulmonary artery and/or deep venous system of the lower extremities. Negative findings were including no demonstrable of filling defect within pulmonary artery and deep venous system of lower extremity plus absence of clinical manifestation of pulmonary embolism and deep vein thrombosis during 3-month follow-up.

Results: One hundred cases including 31 men and 69 women with age range 16 to 95 years (mean = 61.8) were collected. Four cases were excluded according to non-opacified of the lower extremities veins. The authors found that 36 cases (38%) had pulmonary embolism, while 60 cases (62%) were negative for pulmonary embolism. For the group with positive pulmonary embolism, 11 cases (31%) did not have DVT while 25 (69%) case also had DVT as well. In the negative pulmonary embolism group, 49 (82%) did not have DVT but 11 (18%) were shown to have DVT.

Conclusion: For 96 cases with intermediate to high probability of PE, the authors needed to spend 70,909 baht more per case for the extra-investigation (combined CTPA and indirect CTV) for early detection of DVT. By comparison of two work-up strategies, combined CTPA and indirect CTV of the lower extremities and CTPA with direct CTV of the lower extremities, the expense for detecting DVT in patients who also have PE will be 31,200 baht per case. Clinicians can use this value to judge between the cost effectiveness of this investigation and the expense of longer hospitalization and medical expense for late complication of DVT, which was frequently found in patients with PE. In additional, indirect CTV can increase diagnosis of deep vein thrombosis in non-PE case up to 30% in the present study.

Keywords: Combined CT pulmonary angiography (CTPA) and indirect CTV, Cost effectiveness, Pulmonary embolism

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Pulmonary embolism is one of the lethal conditions that are commonly a complication from the deep vein thrombosis (DVT). Patients with pulmonary embolism usually come with symptoms of chest pain, dyspnea, or shortness of breath, which are not specific to diagnose pulmonary embolism. Even if there are many non-invasive diagnostic strategies included serum d-dimer level help to predict the likelihood ratio of the pulmonary embolism but negative result of d-dimer is most valid when the test was done in patients with low-risk. The positive result suggested

of follow-up or lead to further investigation. The innovation of multidetector CT (MDCT) scan that provided faster scan time with less artifact made pulmonary CT angiography as a common first line investigation for pulmonary embolism. Moreover, the authors can evaluate both pulmonary artery and deep venous system of the lower extremities, which is the most common source of the emboli in the same setting by using the protocol of combined CTPA and indirect CT venography. With this technique patient will receive only single contrast injection and get both CTPA and CTV in the same study, which will provide a prompt diagnosis and early treatment in case the patient has pulmonary embolism. Although the patient will expose to radiation in CT study but the radiation dose in CT is below the threshold doses for the induction of

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deterministic effects such as epilation and skin erythema. Patient risks from CT examinations are therefore restricted to the stochastic processes of carcinogenesis and the induction of genetic effects⁽¹⁾. The aim of the present study was to evaluate the cost effectiveness of combined CTPA and indirect CTV of both thighs for diagnosing pulmonary embolism in patient with intermediate to high probability for pulmonary embolism.

Material and Method

One-hundred cases with clinical data of intermediate to high probability of pulmonary embolism were prospectively collected based on Wells criteria (Table 1)⁽²⁾.

Low probability, moderate/intermediate probability and high probability were related to Wells score < 2, 2-6 and > 6 points, respectively. CT pulmonary angiography (CTPA) with indirect CT venography (CTV) of lower extremities was performed after the consent forms were signed. The present study was approved by Human Ethic Committee of Siriraj Hospital (SiEC protocol No: 247/2550(EC2)).

Two 64-slices CT scanner machines were used in this study included GE lightspeed VCT machine and Siemens somatom definition machine. For GE lightspeed VCT machine, CTPA was scan from diaphragmatic dome to lung apex with a standard collimation of 1.25 mm, pitch = 0.9, kV = 120, and care dose with reference mA = 315 while the indirect CTV was scan from knees to distal IVC. For Siemens somatom definition, CTPA was scan with standard collimation of 1.5 mm, pitch = 1.35, kV = 120 and automate mA. The scan direction was the same as former machines. The authors used 100 cc of non-ionic contrast media with flow rate 5cc/second. The delay time for CTPA in GE light speed machine was performed using the

smart preparation technique, but Siemens somatom definition machine used the bolus tracking with the automate trigger of 100 HU. The regions of interest in both techniques were placed within the main pulmonary trunk. The delay time for indirect CTV is 180 seconds. The CTPA was scan in caudocranial direction.

All CT images were reviewed independently by two chest radiologists from picture archive and communication system (PACS) and the final decision was reached by consensus. The diagnostic criterion for pulmonary embolism was defined by detection of filling defect within the pulmonary artery lumen (Fig. 1). While diagnostic criteria for diagnosing DVT were an intravascular filling defect or localized non-enhancement of a vascular segment (Fig. 2).

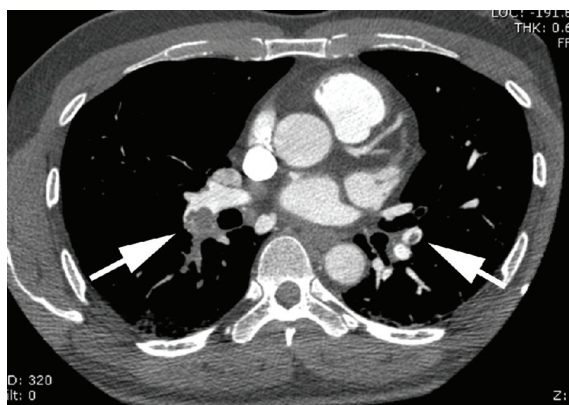


Fig. 1 CT pulmonary angiography of 42 year-old man with clinical intermediate probability for pulmonary embolism show filling defect within the superior segmental branch of right and left lower lobe pulmonary arteries (arrows)

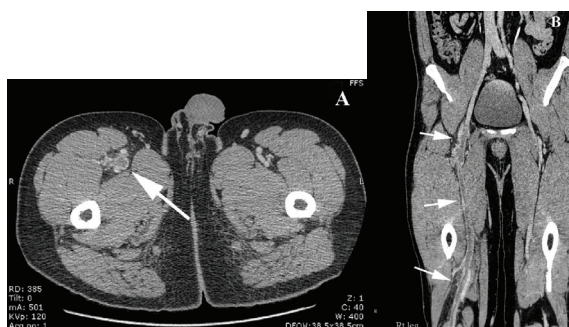


Fig. 2 Axial view of indirect CTV (A) of 42 year-old man with clinical intermediate probability for pulmonary embolism shows filling defect within the right common femoral vein (arrow). In the coronal view (B), the filling defect is seen from right common femoral down to right popliteal vein (arrows)

Table 1. Wells criteria for pulmonary embolism

Clinical sign and symptom of deep vein thrombosis	3
An alternative diagnosis less likely than PE	3
Heart rate > 100 beats/min	1.5
Recent surgery in past 4 weeks	1.5
Previous DVT or PE	1.5
Malignancy during the past 6 months	1
Hemoptysis	1

Low probability, moderate/intermediate probability and high probability were related to Wells score < 2, 2-6 and > 6 points, respectively

Additional ancillary findings of DVT including venous expansion, wall enhancement, and perivenous edema were noticed. The criterion used to exclude PE and DVT was the absence of intraluminal filling defects either intrapulmonary artery or intravenous of the lower extremities. In the negative cases, the clinical follow-up was performed every 3 months by asking about symptoms that suggested of pulmonary embolism or DVT including dyspnea, chest discomfort, and legs swelling.

Results

Between December 2007 and January 2010, one hundred cases with intermediate to high probability of pulmonary embolism according to Wells criteria were collected. Thirty-one men and 69 women with age range 16-95 years (mean = 61.8). Four cases were excluded because the non-opacification of the lower extremities venous system. The authors found that 36 cases (38%) had pulmonary embolism, while 60 (62%) were negative for pulmonary embolism. For the group with positive pulmonary embolism, 11 cases (31%) did not have DVT while 25 (69%) cases had DVT. In the negative pulmonary embolism group, 49 (82%) did not have DVT but 11 (18%) shown to have DVT (Fig. 3). Among cases that had neither pulmonary embolism nor DVT, the 3-month clinical follow-up was done. Twenty-one (43%) cases had no abnormal symptom, 11 (22%) cases died, and 17 (35%) appeared to have some of these clinical symptoms including dyspnea, chest discomfort, or leg(s) edema (Table 2). The medical record review of 11 cases with negative PE and DVT who died during the 3-month follow-up showed that none of them died from PE (Table 3).

Discussion

As CTPA was commonly used as a first line for diagnosis of acute pulmonary embolism in our institute, the high negative cases were found. In the present study, the authors excluded case with low probability for pulmonary embolism as the authors expected to get more positive pulmonary embolism in the authors' population.

Wells criteria was used to predict the presence of pulmonary embolism based on clinical manifestation and found that more than half of the cases (62.5%) had negative CTPA. Among this group, 97% (58/60) had intermediate probability for pulmonary embolism and 3% (2/60) had high probability for pulmonary embolism. For patients with intermediate probability for pulmonary embolism, nearly all of them had

Table 2. The 3-month follow-up cases in negative cases (49)

Clinical manifestation	Cases (%)
Normal	21 (43)
With clinical symptoms of dyspnea, legs edema, chest discomfort	17 (35)
Dead	11 (22)

Table 3. Causes of death during 3-month follow-up in 11 patients without PE and DVT

Cause of death	Number
Sepsis/pneumonia	5
Cardiac arrest	2
DIC	1
Acute renal failure	1
Lymphangitic metastasis	1
Bony metastasis	1

criteria of "alternative diagnosis is less likely than PE", which had important impact for this scoring system and caused a higher score than what it should be. This result shown to be nearly the same as a study by Mohammad MM et al⁽²⁾.

The present study shows that 69% of the presented cases with pulmonary embolism had DVT. This data supports the concept of which pulmonary embolism and deep venous thromboembolism are the same complex and common process, which has a wide spectrum of clinical presentations and consequences, ranging from no symptoms or sequelae to a lethal outcome⁽³⁾. However, the number of cases might increase if the authors scanned the lower extremities more distally.

Even the combination of CT pulmonary angiography and indirect venography creates a unique, comprehensive baseline study for thromboembolism, but for patient with underlying heart disease like four of the presented cases who were excluded from our study; this technique might have some limitation from poor opacification of venous system of the lower extremities.

Another investigation such as color Doppler ultrasound also had a role for diagnosis DVT in patient with PE. Lower extremity sonography has high accuracy in symptomatic patients, involves no contrast medium or ionizing radiation, and is portable. On the other hand, this technique is operator dependent and limited in obese patients. The accuracy of ultrasound is high for the large vein that are easily compressed

such as the thigh but less reliable small overlapping veins of the calf plexus and in non-compressible pelvic veins^(4,5). When compared with CTV technique, the only con for this investigation is the radiation exposure. While the accuracy for DVT diagnosis is higher when compared with ultrasound. Nowadays, the combination protocol of CTPA and indirect CTV used in patients who had clinical manifestation suspected of pulmonary embolism is referred as non-invasive and time saving since this technique can evaluate filling defect in both pulmonary artery and deep venous system of the lower extremities at the same time.

In our institute, the cost of CTPA is 14,000 Baht per study and CTV of the lower extremity is 27,000 Baht. The combined CTPA and indirect CTV is 39,000 Baht. The combined technique was 2000 Baht cheaper than the two separate studies since only one time contrast media was injected.

Thirty-six cases had DVT and 30% (11/36) of these cases did not have pulmonary embolism, which means indirect CTV also increased diagnosis of DVT about 30% in the present study.

As shown in result, 11 cases had negative pulmonary embolism but patient appeared to have deep vein thrombosis. The authors calculate the expense for early detection of DVT in this group (11 cases) in the following equation:

$$\begin{aligned}
 &= (\text{cost of combined CTPA and indirect CTV of the legs of 96 cases}) - (\text{cost of CTPA of 96 cases} + \text{cost of direct CTV of the legs of 60 cases}) \text{ Baht} \\
 &= (39,000 * 96) - ((14,000 * 96) + (27,000 * 60)) \text{ Baht} \\
 &= 780,000 \text{ Baht}
 \end{aligned}$$

From this result, the authors showed that for 96 cases with intermediate to high probability of PE, we need to spend 70,909 (780,000/11) Baht more per case for the extra-investigation (combined CTPA and indirect CTV) for early detection of DVT.

The authors calculated the extra expense for detecting 11 cases of DVT patients who did not have pulmonary embolism in the following equation:

$$\begin{aligned}
 &= (\text{cost of combined CTPA and indirect CTV of the legs of 96 cases}) - (\text{cost of CTPA of 96 cases}) \text{ Baht} \\
 &= (39,000 * 96) - (14,000 * 96) \text{ Baht} \\
 &= 2,400,000 \text{ Baht}
 \end{aligned}$$

Therefore, the authors need to spend 218,182 (2,400,000/11) Baht more per case for extra-investigation to detect a patient who had DVT without pulmonary embolism. This amount of expense should be valuable when compared with the expense that will occur if these individuals are untreated DVT cases,

which came back with complications that will also need long-term hospitalization, ICU care, or patient death in severe case.

In the result seen in the flow chart of Fig. 3, if the authors perform two work-up strategies to detect pulmonary embolism and DVT, the result will be as Table 4. The first line is combined CTPA and indirect CTV of the lower extremities for 96 cases with intermediate to high probability of PE. With this line, the authors can detect 36 PE cases, 25 DVT cases (with PE), and 11 DVT cases (without PE). The second line is performed CTPA for 96 cases with intermediate to high probability of PE, and then only patients who did not have PE will go on to do direct CVT of the lower extremities to rule out DVT. According to the later line, the authors can detect 36 PE cases and 11 DVT cases without PE. The expense for the first line is 3,744,000 (which is derived from 96 * 39,000) Baht. While the expense for second line is 2,964,000 (which is derived from (96 * 14,000) + (60 * 27,000)) Baht.

As seen in Table 4, the difference of the diagnosis outcome is that the authors can detect 25 DVT with PE from the first line diagnosis, which is not demonstrated by use this second line work-up. The difference of expense used of these two work-up strategies is 780,000 (which derived from 3,744,000-2,964,000) Baht. Therefore, to detect 25 DVT cases in patients with PE the authors spend 31,200 baht/case (which derived from 780,000/25) by performing combined CTPA and indirect CTV of the lower extremities.

In the authors' study group, only four cases have high probability for PE. The data for this specific group is shown in Table 5. The additional expense of doing combined CTPA and indirect CVT compared with sequential CTPA followed by direct CVT study for detecting one miss DVT case is 46,000 Baht (the number derived from the equation below).

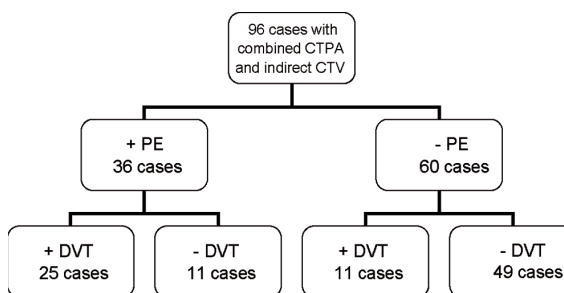


Fig. 3 The result of CTPA and indirect CTV in 96 patients

Table 4. Comparison of diagnosis out come and work-up cost of two work-up strategies

	Combined CTPA + indirect CTV		Sequential CTPA followed by direct CTV for negative PE cases	
Diagnose	PE	36 cases	PE	36 cases
	DVT	25 cases (found with PE)	DVT	11 cases (without PE)
	DVT	11 cases (without PE)		
Cost		3,744,000 baht		2,964,000 baht

Table 5. The patients data in high probability group for PE

Case No.	PE	DVT
1	-	+
2	-	-
3	+	+
4	+	-

Combined CTPA and indirect CVT for four case
 = 4 * 39,000
 = 156,000 Baht

Sequential CTPA follow by direct CTV
 = (4 * 14,000) + (2 * 27,000)
 = 110,000 Baht

The additional expense for detecting 1 miss DVT case
 = 156,000 - 110,000
 = 46,000 Baht

There are two limitations of this study. The first one is that we do not have any gold standard investigation to confirm the diagnosis of negative DVT case but we use 3-month clinical follow-up instead. As seen in result, less than half (43%) of patients with negative CTV appeared to have normal symptom during 3 months follow-up but 35% had symptom which suggested of DVT included dyspnea, legs edema, chest discomfort. While the rest, 22% of negative DVT cases, dead during 3-month follow-up. Therefore, this could be a false negative CTV since our protocol evaluated vein of lower extremities from IVC to both knees level therefore the thrombus may locate distal to this level. The second one is that we used two different CT scanner machines for investigation, which had a little bit difference in protocol. However, with the very thin slice thickness, this should not cause any impact for interpretation both PE and DVT.

Conclusion

For 96 cases with intermediate to high probability of PE, the authors need to spend 70,909 Baht more per case for the extra-investigation (combined CTPA and indirect CTV) for early detection of DVT. By comparison of two work-up strategies, combined

CTPA with indirect CTV of the lower extremities and CTPA with direct CTV of the lower extremities, the expense for detecting DVT in patients who also have PE will be 31,200 Baht per case. For patients with high probability for PE, the additional cost for detecting DVT in patients who had PE is 46,000 Baht per case. Clinicians can use these values to judge between the cost effectiveness of this investigation and the expense of longer hospitalization and medical expense for late complication of DVT, which was frequently found in patients with PE. In addition, indirect CTV can increase the diagnosis of deep vein thrombosis in non-PE cases up to 30% in the authors' study.

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Potential conflicts of interest

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ความคุ้มค่าของการตรวจเอกซเรย์คอมพิวเตอร์ของหลอดเลือดแดงปอดร่วมกับหลอดเลือดดำของ ต้นขาในคราวเดียวกันในผู้ป่วยที่มีโอกาสเกิดภาวะลิ่มเลือดอุดตันในหลอดเลือดแดงของปอดระดับ ปานกลางถึงสูง

นิตา เมืองแมน, กัญยรัตน์ โตรนะรุ่งโรจน์

วัตถุประสงค์: เพื่อศึกษาความคุ้มค่าของการตรวจเอกซเรย์คอมพิวเตอร์ของหลอดเลือดแดงปอดร่วมกับหลอดเลือดดำของต้นขา
ในคราวเดียวกัน ในผู้ป่วยที่มีโอกาสเกิดภาวะลิ่มเลือดอุดตันในหลอดเลือดแดงของปอดระดับปานกลางถึงสูงโดยใช้ Wells criteria
วัสดุและวิธีการ: ทำการศึกษาในผู้ป่วย 100 ราย ที่มีโอกาสเกิดภาวะลิ่มเลือดอุดตันในปอดระดับปานกลางถึงสูงโดยใช้ Wells
criteria และได้รับการตรวจเอกซเรย์คอมพิวเตอร์ของหลอดเลือดแดงปอดร่วมกับหลอดเลือดดำของต้นขาในคราวเดียวกันระหว่าง
เดือนธันวาคม พ.ศ. 2550 ถึงเดือนมกราคม พ.ศ. 2553 ผลการตรวจที่เป็นบวกคือการที่พบลิ่มเลือดอุดตันในหลอดเลือดแดงของ
ปอดหรือหลอดเลือดดำของต้นขา ผลการตรวจที่เป็นลบคือการที่ไม่พบลิ่มเลือดอุดตันในหลอดเลือดแดงของปอดหรือหลอดเลือด
ดำของต้นขา ร่วมกับการที่ไม่มีอาการแสดงของภาวะลิ่มเลือดอุดตันในหลอดเลือดแดงของปอดหรือหลอดเลือดดำของขาภายใน
3 เดือน ของการตรวจติดตาม

ผลการศึกษา: ในผู้ป่วย 100 ราย พบว่าเป็นผู้ป่วยชาย 31 คน ผู้ป่วยหญิง 69 คน มีอายุระหว่าง 16-95 ปี (เฉลี่ย 61.8 ปี)
ผู้ป่วย 4 ราย ถูกคัดออกเนื่องจากเห็นสารทึบรังสีในหลอดเลือดดำของต้นขาไม่ชัดเจน ในการศึกษาพบว่ามีผู้ป่วย 36 ราย (38%)
พบลิ่มเลือดอุดตันในปอด ที่เหลืออีก 60 ราย (62%) ไม่พบลิ่มเลือดอุดตันในปอด ในกลุ่มผู้ป่วย 36 ราย ที่พบลิ่มเลือดอุดตันใน
ปอด 11 ราย (31%) ไม่พบลิ่มเลือดอุดตันในหลอดเลือดดำของต้นขาแต่อีก 25 ราย (69%) พบลิ่มเลือดอุดตันในหลอดเลือดดำ
ของต้นขา ในกลุ่มผู้ป่วย 60 ราย ที่พบไม่พบลิ่มเลือดอุดตันในปอด 49 ราย (82%) ไม่พบลิ่มเลือดอุดตันในหลอดเลือดดำของต้นขา
แต่อีก 11 ราย (18%) พบลิ่มเลือดอุดตันในหลอดเลือดดำของต้นขา

สรุป: ในผู้ป่วย 96 รายที่มีโอกาสเกิดภาวะลิ่มเลือดอุดตันในหลอดเลือดแดงปอดระดับปานกลางถึงสูงโดยใช้ Wells criteria ต้อง
เสียค่าใช้จ่ายมากขึ้น 70,909 บาทต่อราย สำหรับการตรวจเอกซเรย์คอมพิวเตอร์ของหลอดเลือดแดงปอดร่วมกับหลอดเลือดดำของ
ต้นขาในคราวเดียวกันเพื่อที่จะตรวจพบลิ่มเลือดอุดตันในหลอดเลือดดำของต้นขาได้อย่างรวดเร็ว ถ้าเปรียบเทียบแนวทางการตรวจ
2 แบบ ได้แก่ การตรวจเอกซเรย์คอมพิวเตอร์ของหลอดเลือดแดงปอดร่วมกับหลอดเลือดดำของต้นขาในคราวเดียวกันกับการแยก
ตรวจเอกซเรย์คอมพิวเตอร์ของหลอดเลือดแดงปอดกับหลอดเลือดดำของต้นขาทีละครั้ง ค่าใช้จ่ายในการตรวจพบลิ่มเลือดอุดตัน
ในหลอดเลือดดำของต้นขาในผู้ป่วยที่พบลิ่มเลือดอุดตันในหลอดเลือดแดงปอดคิดเป็น 31,200 บาทต่อราย แพทย์ผู้รักษาอาจใช้
ข้อมูลนี้เพื่อเปรียบเทียบถึงความคุ้มค่าของการตรวจเอกซเรย์คอมพิวเตอร์วิธีนี้กับค่าใช้จ่ายที่เกิดจากการที่ผู้ป่วยต้องนอนโรงพยาบาล
นานขึ้น รวมทั้งค่ารักษาพยาบาลของภาวะแทรกซ้อนจากภาวะลิ่มเลือดอุดตันในหลอดเลือดดำของต้นขาที่มักพบในผู้ป่วยที่พบลิ่ม
เลือดอุดตันในหลอดเลือดแดงปอด นอกจากนี้การตรวจเอกซเรย์คอมพิวเตอร์ของหลอดเลือดดำของต้นขาในคราวเดียวกันยังช่วย
วินิจฉัยภาวะลิ่มเลือดอุดตันในหลอดเลือดดำของขาในผู้ป่วยที่ไม่พบลิ่มเลือดอุดตันในหลอดเลือดแดงปอดถึงร้อยละ 30
