Original Article

Prevalence of Occult Cancer in Acute Unprovoked Lower Extremities Deep Vein Thrombosis in Thai Patients

Pruekprasert K, MD[1], Banthawatanarak K, MD[1], Ruangsetakit C, MD[1], Wongwanit C, MD[1], Chinsakchai K, MD[1], Hahtapornsawan S, MD[1], Hongku K, MD[1], Puangpanngam N, MD[1], Sermsathanasawadi N, MD, PhD[1]

[1] Division of Vascular Surgery, Department of Surgery, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand

Objective: To determine the prevalence of occult malignancy in Thai patients with the first episode of unprovoked deep vein thrombosis, and to identify the methods leading to the diagnosis of occult cancer.

Materials and Methods: The medical records of 369 consecutive patients with symptomatic proximal DVT of the lower extremity were retrospectively reviewed. The patients' demographic data, sites of occult cancer, and the screening methods utilized for the detection of occult cancer were recorded.

Results: Among the 369 acute DVT patients enrolled in this study, there were 104 (28.2%) unprovoked DVT cases, 106 (28.7%) DVT provoked by transient risk factors, and 159 (43.1%) cancer-associated DVT. Among the 104 patients with unprovoked DVT, occult malignancies were identified in 26 (25%) patients, with 13 (50.0%) of the occult cancers being in the metastatic stage. The methods leading to the diagnosis of occult cancers were limited screening by history taking and physical examination with a routine blood test and chest x-rays in 21 (80.8%) patients, by serum tumor markers screening in 3 (11.5%) patients, and by abdominal computed tomography screening in 2 (7.7%) patients.

Conclusion: The prevalence of occult cancer in acute unprovoked DVT in the present study was 25%, with most of the occult cancers detected by a limited screening strategy.

Keywords: Venous thromboembolism, Unprovoked deep vein thrombosis, Occult malignancy, Cancer-associated deep vein thrombosis

J Med Assoc Thai 2020;103(Suppl. 5): 82-5
Website: http://www.jmatonline.com

Patients with acute deep venous thrombosis (DVT) of the lower extremity can be categorized into three groups: those provoked by transient risk factors (e.g., pregnancy, recent surgery or trauma, hormone use, prolonged immobilization), those without any transient risk factors (unprovoked DVT), and those with cancer-associated DVT[1]. However, the first episode of unprovoked DVT can also be a warning sign leading to the diagnosis of occult malignancy, with more than 60% of occult cancers identified shortly after the diagnosis of venous thromboembolism (VTE) in a previous study[2]. The prevalence of occult cancer in those patients was estimated to be 4 to 10%, with most diagnosed by limited screening, including a basic blood test, chest x-rays, and standard screening for breast, cervical, and prostatic cancer after the episode of unprovoked DVT[3,4].

Since these findings have not been studied in Thai patients, the objectives of the present study were to determine the prevalence of occult malignancy in Thai patients with the first episode of unprovoked deep vein thrombosis, and to identify the method leading to the diagnosis of occult cancer in each case.

Correspondence to:

Sermsathanasawadi N.

Division of Vascular Surgery, Department of Surgery, Faculty of Medicine Siriraj Hospital, Mahidol University, 2 Wanglang Road, Bangkok Noi, Bangkok 10700, Thailand.

Phone: +66-2-4198021

E-mail: nuttawut@gmail.com

Materials and Methods

Patients and data collection

The medical records of patients who were diagnosed with acute symptomatic proximal DVT of the lower extremity as evidenced by imaging study, including duplex ultrasonography or computer tomographic venography, and who visited the Division of Vascular Surgery, Department of Surgery, Siriraj Hospital, Thailand, from January 1, 2012 to December 31, 2013 were retrospectively reviewed. Patients were classified into 3 groups: provoked DVT with presentation of one or more of the transient risk factors, unprovoked DVT without transient risk factors, and cancer-associated DVT.

In the unprovoked DVT group, the patients' medical records were reviewed for any cancer subsequently diagnosed after the diagnosis of acute DVT up to 31 September 2016. The patients' demographic data, site of occult cancer, and the diagnostic methods leading to the

How to cite this article: Pruekprasert K, Banthawatanarak K, Ruangsetakit C, Wongwanit C, Chinsakchai K, Hahtapornsawan S, Hongku K, Puangpanngam N, Sermsathanasawadi N. Prevalence of Occult Cancer in Acute Unprovoked Lower Extremities Deep Vein Thrombosis in Thai Patients. J Med Assoc Thai 2020;103(Suppl.5): 82-5.

diagnosis of occult malignancy, i.e., medical history, physical examination, laboratory findings, and any specific diagnostic investigations, were recorded. Medical records without the certified method utilized for the diagnosis of acute DVT, or with incomplete information, were excluded.

In our center, patients with acute unprovoked DVT were routinely screened for occult malignancy by focused history-taking for malignancy, physical examination (including pelvic vaginal examination and PAP smear in female patients), routine blood test (including complete blood count, blood chemistry, and renal function test), and chest x-rays. Patients suspected with malignancy were sent for further specific investigations for a definite diagnosis of malignancy as appropriate.

Some patients were also requested to undergo serum tumor markers screening or abdominal computed tomography screening at the time of acute unprovoked DVT diagnosis, with such decisions dependent on the physicians' judgement and patients' preference. The authors documented all the investigations leading to the diagnosis of occult cancer.

In the present study, we categorized the methods leading to the diagnosis or guiding toward further specific investigations for occult malignancy into three groups. The first group involved a limited screening protocol with history taking, physical examination, routine blood test, and chest x-rays; the second group involved additional serum tumor markers screening; and the third group involved additional abdominal computed tomography screening.

The ethics committee of the Siriraj Institutional Review Board approved the present study, No. 347/2558 (EC2).

Statistical analysis

Continuous variables are reported herein as the mean and standard deviation (SD) or the median and range, as appropriate. Categorical variables are reported as the number and percentage. Data were recorded and analyzed using PASW Statistics 18.0 software (SPSS Inc., Chicago, IL, USA).

Results

In total, 369 patients with acute symptomatic proximal DVT were included in this study; of whom, 261 (70.7%) were female. The average age was 59.3±17.3 years old. The mean body mass index (BMI) was 23.5±4.7. There were 166 (45%) inpatients and 203 (55%) outpatients (Table 1).

There were 104 (28.2%) patients with unprovoked DVT, 106 (28.7%) DVT provoked by transient risk factors, and 159 (43.1%) cancer-associated DVT (Figure I). Among the 159 patients with cancer-associated DVT, there were 54 (34.0%) cases of gynecologic cancer, 18 (11.3%) colorectal cancer, 15 (11.3%) head neck breast cancer, 10 (6.3%) hepato-pancreatico-biliary cancer, 2 (1.3%) cancer of unknown origin, 19 (11.9%) urologic cancer, 6 (3.8%) soft tissue tumor cancer, 14 (8.8%) hematologic cancer, 8 (5.0%) lung cancer, 8 (5.0%) upper gastrointestinal cancer, and 5 (3.1%) brain cancer (Table 1). Also, 84 patients (52.8%) had metastatic cancer.

Among the 104 patients with unprovoked DVT, occult malignancy was subsequently identified in 26 (25.0%) patients. Among these 26 patients with occult malignancy, there were 6 (23.1%) cases of gynecologic cancer, 4 (15.4%) colorectal cancer, 3 (11.5%) head neck breast cancer, 3 (11.5%) hepato-pancreatico-biliary cancer, 3 (11.5%) cancer of unknown origin, 2 (7.7%) urologic cancer, 2 (7.7%) soft tissue tumor cancer, 2 (7.7%) hematologic cancer, and 1 (3.8%) lung cancer, while 13 (50.0%) of the occult cancers were found to be metastatic disease (Table 1).

The authors found that limited screening with history taking and physical examination with a routine blood test and chest x-rays led to the diagnosis of occult cancers in 21 (80.8%) of the 26 occult malignancy patients, while occult cancers were detected by serum tumor marker screening in 3 (11.5%) patients, and by abdominal computed tomography screening in 2 (7.7%) patients (Figure 2).

Table 1. Primary sites of cancer in patients with cancer-associated DVT and unprovoked DVT

Sites	Known cancer (cancer-associated DVT) Number (%)	Occult cancer in unprovoked DVT Number (%)
Gynecologic cancer	54 (34.0)	6 (23.1)
Colorectal cancer	18 (11.3)	4 (15.4)
Head neck breast cancer	15 (9.4)	3 (11.5)
Hepato-pancreatico-biliary cancer	10 (6.3)	3 (11.5)
Cancer of unknown origin	2 (1.3)	3 (11.5)
Urologic cancer	19 (11.9)	2 (7.7)
Hematologic cancer	14 (8.8)	2 (7.7)
Soft tissue tumor cancer	6 (3.8)	2 (7.7)
Lung cancer	8 (5.0)	1 (3.8)
Upper gastrointestinal cancer	8 (5.0)	0
Brain cancer	5 (3.1)	0
Total	159	26

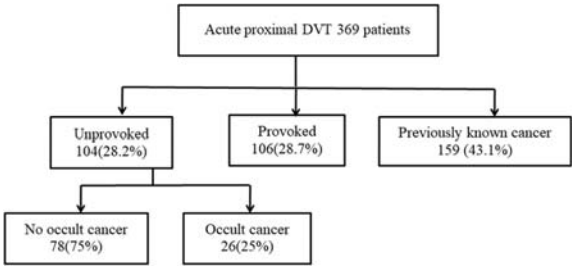

Figure 1. Categorization of patients with acute symptomatic proximal DVT.

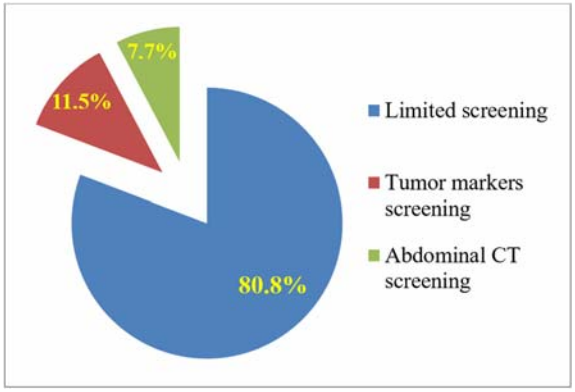

Figure 2. Methods leading to the diagnosis of occult cancer in patients with acute unprovoked symptomatic proximal DVT.

Discussion

The prevalence of occult malignancy in our study was 25% of our patients with acute symptomatic unprovoked proximal DVT, which is higher than reported in previously published studies[3,4]. Carrier et al[3] reported an overall prevalence of 3.9% of occult malignancy in unprovoked DVT patients in their randomized controlled trials performed in a Canadian population, while Prandoni et al[4] reported an overall prevalence of 9.2% in an Italian randomized controlled trial. The high prevalence of occult cancer in our study was possibly from the lack of an effective cancer screening program in our country, and a lack of awareness of the overall population of the need to enter into a cancer screening program. Further evidence for this finding can be gleaned from the fact that half of our patients with occult cancers were found to be in the metastatic stage.

In the present study, the most common primary sites of the occult cancers were gynecological cancer followed by colorectal cancer, which is consistent with the findings from the Canadian study mentioned above[3]. However, in the Italian population from the other study mentioned above, kidney and lung cancers were the most common[4].

From the present study, the authors found that limited screening with history taking, physical examination, a routine blood test, and chest x-rays were the most common methods leading to the diagnosis of occult cancers, accounting for the diagnosis of more than 80% of the occult cancers in patients with the first episode of unprovoked DVT. This result is consistent with the results from previously published randomized controlled trials, which demonstrated that routine screening with chest or abdominal computed tomography did not provide a clinically significant benefit for occult cancer detection[3,4].

There were some limitations of our study to report; for instance, due to its retrospective nature, whereby some information was missing, so that we had to exclude some medical records. Also, there was no definite protocol for occult cancer screening in patients with unprovoked venous thromboembolism in our hospital; thus the screening strategies varied among physicians' judgement and patients' preference. Some physicians used only a limited screening protocol, while some preferred additional screening with serum tumor markers or computed tomography. Also, our study was a single center study.

Conclusion

The prevalence of occult cancer in acute unprovoked DVT in Thai patients in the present study was 25%. Most of the occult cancers were gynecologic malignancies. Most of the occult cancers were detected by a limited screening strategy, including history taking, physical examination, routine blood testing, and chest radiography, which led to further specific investigations.

What is already known on this topic?

The unprovoked lower extremity deep vein thrombosis can be the first sign leading to the diagnosis of occult malignancy. From the previous studies in Caucasian population, the prevalence of occult cancer was estimated to be 4 to 10%, with most diagnosed by limited screening.

What this study adds?

Estimated at 25%, this study found a higher prevalence of occult malignancy in Thai patients with acute unprovoked deep vein thrombosis. Limited screening strategy can lead to the diagnosis of most of the occult cancers.

Acknowledgements

The authors would like to thank Miss Wannaporn Paemueang for her assistance with the collection of data.

Potential conflicts of interest

The authors declare no conflicts of interest.

References

1. Kearon C, Akl EA, Comerota AJ, Prandoni P, Bounameaux H, Goldhaber SZ, et al. Antithrombotic therapy for VTE disease: Antithrombotic therapy and prevention of thrombosis, 9th ed. American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest 2012;141:e419S-96S.

2. Carrier M, Le Gal G, Wells PS, Fergusson D, Ramsay T, Rodger MA. Systematic review: the Trousseau syndrome revisited: should we screen extensively for cancer in patients with venous thromboembolism? Ann Intern Med 2008;149:323-33.
3. Carrier M, Lazo-Langner A, Shivakumar S, Tagalakis V, Zarychanski R, Solymoss S, et al. Screening for occult cancer in unprovoked venous thromboembolism. N Engl J Med 2015;373:697-704.
4. Prandoni P, Bernardi E, Valle FD, Visona A, Tropeano PF, Bova C, et al. Extensive computed tomography versus limited screening for detection of occult cancer in unprovoked venous thromboembolism: A multicenter, controlled, randomized clinical trial. Semin Thromb Hemost 2016;42:884-90.

อุบัติการณ์ของโรคมะเร็งแอบแฝง ในผู้ป่วยไทยที่เป็นโรคหลอดเลือดดำชั้นลึกของขาอุดตันเฉียบพลันจากลิ่มเลือดที่ไม่มีปัจจัยกระตุ้น

คณินท์ พฤกษ์ประเสริฐ, กมล บรรพวัฒนรักษ์, เฉนียน เรืองเศรษฐกิจ, ชุมพล วองวานิช, คามิน ชินศักดิ์ชัย, สุธีคณิต หัถพรสวรรค์, เกียรติศักดิ์ หงษ์คู, ณัฐวุฒ พ่วงพันธุ์งาม, ณัฐวุฒิ เสริมสาธนสวัสดิ์

วัตถุประสงค์: เพื่อศึกษาอุบัติการณ์ของโรคมะเร็งแอบแฝง ในผู้ป่วยโรคหลอดเลือดดำชั้นลึกของขาอุดตันเฉียบพลันจากลิ่มเลือดที่ไม่มีปัจจัยกระตุ้น และหาวิธีการสืบค้นที่นำไปสู่การวินิจฉัยโรคมะเร็งแอบแฝงในผู้ป่วย

วัสดุและวิธีการ: ใช้วิธีการสืบค้นเวชระเบียนย้อนหลัง ในผู้ป่วยไทย 369 ราย ที่เป็นโรคหลอดเลือดดำชั้นลึกของขาอุดตันเฉียบพลันจากลิ่มเลือด เพื่อบันทึกข้อมูลทางประชากรศาสตร์ ตำแหน่งของโรคมะเร็งที่ตรวจพบ และกระบวนการตรวจคัดกรองที่นำมาสู่การวินิจฉัยโรคมะเร็งซ่อนเร้นในผู้ป่วย

ผลการศึกษา: ผู้ป่วยโรคหลอดเลือดดำชั้นลึกของขาอุดตันเฉียบพลันจากลิ่มเลือด 369 รายจากการศึกษานี้ประกอบด้วยผู้ป่วยที่เกิดโรคโดยไม่มีปัจจัยกระตุ้น 104 ราย (ร้อยละ 28.2) เกิดโรคโดยมีปัจจัยกระตุ้น 106 ราย (ร้อยละ 28.7) และเกิดในผู้ป่วยที่ทราบว่าเป็นโรคมะเร็งอยู่เดิม 159 ราย (ร้อยละ 43.1) ในกลุ่มผู้ป่วย 124 รายที่เป็นโรคหลอดเลือดดำชั้นลึกของขาอุดตันเฉียบพลันจากลิ่มเลือดโดยไม่มีปัจจัยกระตุ้น ตรวจพบโรคมะเร็งซ่อนเร้นในผู้ป่วยจำนวน 26 ราย (ร้อยละ 25) โดย 13 ราย (ร้อยละ 50) เป็นมะเร็งที่อยู่ในระยะลุกลาม กระบวนการสืบค้นที่นำมาสู่การวินิจฉัยมะเร็งซ่อนเร้น ในผู้ป่วย 21 ราย (ร้อยละ 80.8) ตรวจพบจากการคัดตรวจกรองเบื้องต้นด้วยการซักประวัติ การตรวจร่างกาย การตรวจเลือดทั่วไป และการตรวจวินิจฉัยภาพเอกซเรย์ทรวงอก ในผู้ป่วย 3 ราย (ร้อยละ 11.5) ตรวจพบจากการตรวจคัดกรองสารบ่งชี้มะเร็งในเลือด และในผู้ป่วย 2 ราย (ร้อยละ 7.7) ตรวจพบจากการตรวจคัดกรองโดยเอกซเรย์คอมพิวเตอร์ช่องท้อง

สรุป: อุบัติการณ์ของโรคมะเร็งซ่อนเร้นในผู้ป่วยไทยที่เป็นโรคหลอดเลือดดำชั้นลึกของขาอุดตันเฉียบพลันจากลิ่มเลือดที่ไม่มีปัจจัยกระตุ้นอยู่ที่ร้อยละ 25 โดยการตรวจคัดกรองเบื้องต้นสามารถนำไปสู่การวินิจฉัยโรคมะเร็งซ่อนเร้นส่วนใหญ่ได้