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地域医療基盤開発推進研究事業

肺血栓塞栓症／深部静脈血栓症の院内発症予防ガイドライン

公開後の評価ならびに改定と普及・推進に関する研究

平成19年度～20年度 総合研究報告書

主任研究者 中野 赴

平成21(2009)年3月

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「肺血栓塞栓症／深部静脈血栓症の院内発症予防ガイドライン公開後の評価ならびに改定と普及・推進に関する研究」

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(研究要旨)

2004 年に発刊されたわが国の初版の肺血栓塞栓症／深部静脈血栓症(静脈血栓塞栓症:VTE) 予防ガイドラインの改訂を進めるための作業を行った。VTE 予防領域での種々の進捗があり、一般外科領域、産婦人科領域、整形外科領域では、種々の取り組みが進み、情報も集積した。新しい抗凝固薬も使用可能となっている。また、モデルとなる米国胸部疾患学会の予防ガイドラインの改訂も行われた。今回、より診療科横断的な VTE 予防ガイドラインへの改訂のための組織や進め方が整った。さらに、各領域間の共通の問題点の解決を通じて意識の統一を行った。

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A. 研究目的

2004 年に発刊されたわが国の初版の肺血栓塞栓症／深部静脈血栓症(静脈血栓塞栓症:VTE) 予防ガイドラインの改訂を進めるための作業を行う。

B. 研究方法

VTE 予防ガイドラインの改定に必要となる下記の事項に関して検討した。

- ① VTE の臨床・研究の現状と進歩の評価
- ② 各種診療科における VTE 予防の現状と進歩の検討
- ③ わが国の VTE 予防ガイドラインの改訂作業の進め方ならびに組織編成に関する検討
- ④ 米国胸部疾患学会(ACCP)の VTE 予防ガイドラインの改訂点に関する検討

⑤ VTE 予防ガイドライン改訂に関するアンケート調査

C. 結果と考察

①VTE の臨床・研究の現状と進歩の評価

わが国における VTE の発生率は年々増加しており、最近の 10 年間で 2.3 倍となっている。高齢化社会を背景に、VTE リスクを有する人口が増加し、また食生活の欧米化により肥満人口が増えたことなどが一因である。日本人と欧米人との遵守的な VTE 頻度の違いは未だ解明されていないが、日本人に特異性が高い遺伝子変異も見つかっており、例えば Protein S 徳島変異は VTE の 10%に見られる頻度の高い異常である。

VTE の予防に関しては、関連学会の活動などにより理学的予防法に対する理解は深まっている。麻酔学会などの調査では、VTE 予防ガイドラインが発刊された 2004 年以降、明らかに周術期の VTE 発症率は減少している。しかし、周術期の薬物的予防への抵抗は依然高く、その施行率は低いとの報告が多い。

VTE に対する画像診断では、深部静脈血栓症に対しては静脈エコーが主流となり、検査技師の養成も進んでいる。また、肺血栓塞栓症の診断検査は肺動脈造影 CT が中心となり、多検出器型 CT の発達により診断能力も著しく向上した。しかし、VTE に対する簡便なスクリーニング法がないことが問題である。血液検査では D ダイマーを初期検査に使用する施設も増えているが、その使用法は統一されていない。

一方、VTE の治療法に関しては、中枢型の深部静脈血栓症に対するカテーテル的治療が一定の成果をあげている。しかし、無症候性の下腿静脈血栓の対処法は意見の集約が不

十分である。肺血栓塞栓症に対しては、組織プラズミンノーゲンアクチベータであるモンテプラゼがようやく保険適応となり、重症例への治療選択肢が増えたが、予後改善効果は明らかではない。一方、下大静脈フィルターは発展を続けており、最近では回収可能型フィルターが主流となっている。その挿入適応には確立していないが、最も確実な VTE 治療法として期待されている。

②各種診療科における VTE 予防の現状と進歩の検討

2004 年の VTE 予防ガイドラインの発刊以降、診療報酬に「肺血栓塞栓症予防管理料」が記載されたこともあり、全国の一般外科領域、産婦人科領域、整形外科領域の多くの施設で VTE 予防が積極的に行われるようになった。一般外科においては、多施設前向き試験にて腹部手術後 VTE の発生率の検討が行われており、20%以上と欧米と同程度の VTE 発生がみられている。産婦人科領域においては 2001 年から 2005 年に新たに発症した VTE の全国調査が行われている。婦人科の VTE 発症数は 2000 年以前と比して増加しているが、特に卵巣癌術前発症例が一段と増加していた。一方、産科の VTE 発症数は減少しており、他の領域と比較して VTE 予防対策が浸透していると考えられた。整形外科領域は VTE 予防が最も進んでいる領域である。新しい抗凝固薬の治験などからエビデンスとなるデータが多く発表されており、例えば、膝関節置換術においては VTE の発生率は 60%以上であり、欧米の報告とほとんど同程度である。リスクの高い手術では日本人と欧米人の VTE 発生率はほとんど相違ない可能性が示唆される。

注射ならびに経口の新しい抗凝固薬の

開発が積極的に行われている。抗 Xa 因子阻害薬の注射薬であるフォンダパリヌクスが 2007 年に下肢整形外科手術で保険適応となり、さらに 2008 年には腹部手術にも適応拡大となった。また、低分子量ヘパリンであるエノキサパリンの保険適応も 2008 年に股関節置換術・膝関節置換術・股関節骨折手術に対して適用となり、さらに 2009 年には腹部手術にも適応拡大されている。一方、ワルファリンに代わる新しい経口抗凝固薬の開発も進んでおり、近い将来、使用可能となる可能性がある。

2008 年にはわが国の VTE 予防ガイドラインのモデルになった ACCP の VTE 予防ガイドラインが改訂となっている。また、わが国の VTE 予防ガイドラインの作成協力学会である日本整形外科学会の VTE 予防ガイドラインも 2008 年に発刊されている。これらのガイドラインは、わが国の VTE 予防ガイドラインの改訂において大いに参考にすべきものである。一方、2007 年には米国整形外科学会 (AAOS) から股関節および膝関節置換術後の症候性肺塞栓症予防ガイドラインが公開されている。ACCP ガイドラインは一線を画するものであり、AAOS の予防ガイドラインの内容をどの様にわが国の VTE 予防ガイドラインに反映させるかは、更なる検討を要する。

2004 年のわが国の VTE 予防ガイドラインの発刊とほぼ時期を同じくして、2004 年の診療報酬改訂で「肺血拴塞症予防管理料」が加えられた。日本麻酔科学会の周術期の調査などでも明らかであるように、2004 年以降に周術期 VTE の発生率は明らかに低下しており、また全国の医療機関において VTE 予防の取り組みが拡大している。一方で、薬物予防を行った場合は、包括医療制度のもとでは診療報酬に反映されずむしろ減収となるため、これら

の診療報酬に関する点も、今後の検討課題である。

日本麻酔科学会の周術期肺血拴塞症調査の結果では、2004 年以降は有意な肺血拴塞症の減少が認められているが、2006 年以降は下げ止まっている可能性がある。VTE 予防ガイドライン発刊以降、一気に VTE 予防が広がり、一定の効果が得られたが、十分な予防効果を得るには、さらにレベルの高い予防法を確立する必要がある。

③わが国の VTE 予防ガイドラインの改訂作業の進め方ならびに組織編成に関する検討

2004 年の初版 VTE ガイドラインへの参加学会である日本血拴止血学会、日本産科婦人科学会、日本産婦人科・新生児血液学会、日本集中治療医学会、日本静脈学会、日本心臓病学会、日本整形外科学会、日本泌尿器科学会、日本麻酔科学会、肺塞栓症研究会には改訂委員会への参画を依頼し、了解を得た。また、本研究班が中心となって作業を進めることに対しても承諾を得た。そのほかに協力要請が必要な学会を検討し、依頼を行った。その結果、日本救急医学会、日本胸部外科学会、日本外科学会、日本呼吸器学会、日本循環器学会、日本精神神経学会、日本内科学会、日本脳神経外科学会から、参加協力の承諾を得た。上記の学会・研究会と本研究班とで「肺血拴塞症/深部静脈血拴症(静脈血拴塞症)予防ガイドライン改訂委員会」を組織した。初版の VTE 予防ガイドラインの検証や新しい情報の収集を行い、下記の手順で改訂作業を進めていく。

1. クリニカルクエスチョン (CQ) の設定。

↓

2. 疾患名および CQ の内容に基づき選定されたキーワードを元に、文献を網羅的に検索。

↓

3. 検索で収集した文献のタイトルと著者抄録を査読し、フルテキストを取り寄せる文献を採択。

↓

4. フルテキストを査読し、文献のエビデンスレベルを判定してアブストラクトフォームを作成。

↓

5. 作成したアブストラクトフォームのなかから本文に採用するものを選択し、サイエンティフィック・ステートメントを執筆。

↓

6. サイエンティフィック・ステートメントに基づき、背景、推奨文を執筆。

↓

7. アブストラクトフォームと本文の照合・校正。

↓

8. ガイドライン本文の最終案を、外部評価委員に校閲依頼。

↓

9. 評価を受けて、修正等につき委員会にて検討、適宜修正。

↓

10. 出版社編集部と、初校、再校などの工程を経て刊行。

④米国胸部疾患学会の VTE 予防ガイドラインの改訂点に関する検討

大きな変更点は、リスク分類が 4 段階から 3 段階となったことである。特に、エビデンスが乏しかった年齢や手術の大小による分類が削除

され、臨床医にとってより使い易くなった。理学的予防は、出血リスクが高い場合は積極的に使用することが推奨されている。したがって、①低リスク=早期離床および⁷⁾積極的な歩行、②中～高リスク:薬物予防、③出血リスクの高い中～高リスク:理学的予防の大きく 3 つのグループに分類されたことになる。また、病院全体での VTE 予防対策の推進を、Grade 1A として積極的に推奨している。

⑤VTE 予防ガイドライン改訂に関するアンケート調査

1) リスク分類、推奨予防法に関して: 第 8 版 ACCP ガイドラインにおける予防の推奨は、より薬物に傾斜し簡便な分類へと変更していた。一方、わが国の VTE 予防は歴史が浅く、早急な変更や薬物的予防への傾斜は時期尚早との意見も少なくなかった。一方で、新しい抗凝固薬の安全な使用も推進する必要があるとの意見があった。

2) VTE スクリーニングや VTE 発生時の対処法の記載に関して: スクリーニングや周術期 VTE の治療に関するエビデンスはないので、ガイドラインでの推奨としての記載はするべきでないとの意見が多かった。

3) 特定の院外発症領域への言及の必要性に関して: 旅行者血栓症や災害被災者関連血栓症は社会的にニーズの高い分野であり、関連学会などとも十分協議の上、前向きに検討すべきとの意見が半数ほどあった。

4) ガイドラインの公開方法に関して: 他の診療ガイドラインと同じように出版社から発刊した方が、広く普及できるとの意見が多かった。また、WEB で公開し、必要な場合は WEB 上で微修正を行ってはどうかとの意見もあった。

研究成果の刊行に関する一覧表

書籍

著者氏名	論文タイトル名	書籍全体の編集者名	書籍名	出版社名	出版地	出版年	ページ
Mashio Nakamura, Takeshi Nakano, Satoshi Ota, Norikazu Yamada, Masatoshi Miyahara, Naoki Isaka, Masaki Ito	Current Clinical Status of Venous Thromboembolism in Japan	K. Tanaka, E.W. Davies	Recent Advances in Thrombosis and Hemostasis 2008	Springer	Japan	2008	563-573

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K. Tanaka · E.W. Davie
Editors

Y. Ikeda · S. Iwanaga · H. Saito · K. Sueishi
Associate Editors

**Recent
Advances in
Thrombosis and
Hemostasis
2008**

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Current Clinical Status of Venous Thromboembolism in Japan

MASHIO NAKAMURA, TAKESHI NAKANO, SATOSHI OTA,
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Summary. Venous thromboembolism (VTE) is the third most common cardiovascular disease for which many clinical guidelines have been published in the Western world. In Japan, VTE has recently been recognized as a common disease and has received increased social as well as medical attention; however, the clinical diagnostic yield is still low. The most effective means of reducing unexpected death from VTE is to implement a comprehensive institutional policy of primary prophylaxis in patients at risk. Although it is difficult to prepare Japanese guidelines for prophylaxis of VTE based on reliable evidence, epidemiological information is available in the general surgical, orthopedic, and gynecological areas of practice. Finally, the first Japanese guidelines for prophylaxis of VTE were published in the spring of 2004. In addition, the diagnostic and management strategies have changed along with improvement in modalities and coverage by thrombolytic agents. The next goal is to gather evidence that provides the foundation for guidelines on treatment and prophylaxis. Large-scale research studies similar to those performed in the West should be conducted to elucidate the pathological mechanisms of VTE and improve its management.

Key words. Anticoagulation therapy · Prophylaxis · Thrombolytic therapy · Vena cava filters · Venous thromboembolism

Introduction

Venous thromboembolism (VTE), manifesting as either deep vein thrombosis (DVT) or pulmonary thromboembolism (PTE), is an extremely common medical problem in the Western world, occurring either in isolation or as a complication of other diseases or procedures. Many clinical guidelines for VTE have been published, such as "Guidelines on diagnosis and management of acute pulmonary embolism" (2000) by the European Society of Cardiology [1]; "Guidelines for the management of suspected acute pulmonary embolism" (2003) by the British Thoracic Society [2]; "Prevention of venous thromboembolism" (2004) by the American College of Chest Physicians [(3)]; and "Prevention and treatment of venous thromboembolism" (2006) by the Internal Union of Angiology [4]. At the same time, the incidence of VTE in Japan was considered to be minimal, and it was not a focus of attention in most Japanese medical

societies. Nonetheless, a few researchers suspected that VTE might be common in Japan and could be responsible for some unexplained sudden deaths. The lower diagnostic yield of VTE in Japan was also thought to be a contributor because the disorder is observed in multiple medical areas, including cardiovascular and respiratory medicine and surgery, and information on these cases was not disseminated systematically.

The Japanese Society of Pulmonary Embolism Research was established in 1994 [5], and international symposiums on pulmonary embolism in Japan took place in Mie in 1998 [6] and in Chiba and Sendai in 2003 and 2000, respectively [7]. These efforts were aimed at raising awareness of VTE and compiling data on Japanese cases. As a result, awareness in the medical profession has improved, diagnostic techniques have advanced, and the number of cases of VTE reported in Japan has increased rapidly. Furthermore, because of the increase in venous thromboembolic risk factors, such as continuing westernization of Japanese life and social aging, and of postoperative sudden death and travelers' thrombosis (so-called economy-class syndrome), as well as the high incidence of VTE noted following the recent mid-Niigata Prefecture earthquake, it has recently received a lot of attention, both medically and socially. In 2004, Japanese guidelines for VTE [8, 9] were published, and the increasing awareness of this disorder in Japan is changing the perception of VTE from that of a rare disease to a common one. However, large-scale studies that would help provide evidence of VTE have not been conducted in Japan. Moreover, Japan lags behind Western countries in clinical management of this disease.

Incidence and Prognosis of Venous Thromboembolism

Although VTE is diagnosed and treated in as many as 260 000 patients in the United States each year, it is estimated that more than half the cases that actually occur are never diagnosed. Thus, the true incidence may be as high as 600 000 cases [10, 11]. At the same time, the incidence of PTE in serial autopsy cases in Japan and the United States was reported as 0.8% and 23.8%, respectively, according to a previous international collaboration [12]. Moreover, the annual reports of the pathological autopsy cases in Japan noted a rate of 1.41%–1.72% [13, 14]. These results indicated that the incidence of VTE was extremely low in Japan. However, more recent reports have indicated that the incidence of DVT after joint replacement in Japan is the same as in Western countries [15, 16], and the incidence of PTE in serial autopsy cases ranged from 11% to 24% [17–20]. Consequently, the incidence of VTE in Japan is no longer considered low. Despite this evidence, data compiled from recent questionnaire surveys showed that the number of clinically diagnosed cases of PTE in Japan was only 28–32 per 1 million people [21, 22], which is 1/15th that of Western countries. We must therefore conclude that Japanese clinicians are still not entirely familiar with VTE.

Racial and environmental factors may contribute to the differences in incidence reported among Japanese and Westerners. Reports that show a higher incidence of PTE in black Americans than in black Africans [23] and no differences between white and nonwhite South Africans [24] suggest that an environmental factor is involved in

the incidence of PTE. On the other hand, the factor V Leiden mutation with activated protein C resistance, which has drawn attention as a new coagulation abnormality, is a high-frequency gene mutant that appears in 30%–50% of Caucasians with VTE [25]. No Japanese patients were found with this mutation. Similarly, no Japanese patient has the prothrombin G20210A mutation, which is associated with VTE in Caucasians [26, 27]. These findings suggest that a racial factor is also involved in the incidence of PTE. Studies among races in the United States also show that the incidence of VTE among Asians is one-fifth to one-quarter that of whites [28, 29]. Meanwhile, in our study that investigates coagulopathy in detail, only 5 of 61 consecutive patients (8%) with PTE did not have an inherited coagulopathy or a secondary risk factor for VTE [30]. These results suggest that Japanese patients might have unknown inherited coagulopathies.

In the United States, widespread prevention of VTE in hospitals led to a significant decline in the incidence of PTE beginning during the mid-1980s, although the incidence had been increasing before that period [31]. On the other hand, deaths from PTE in Japan were projected to increase by 10 times over the 50 years from 1951 to 2000 according to the vital statistics of the Ministry of Health, Labor, and Welfare [32]. The PTE rate in autopsy cases from the annual reports of the pathological autopsy cases in Japan also increased 3.5-fold from 1958 to 1997 [13, 14, 33]. These increases in PTE reflect both an "increase in appearance" and a "true increase." The "increase in appearance" indicates improved accuracy of diagnosis, such as the rising awareness among health care professionals, increasing visibility of VTE, and advances in modalities. The recent rapid increase in the incidence of this disease stems largely from these factors, which has resulted from educational campaigns in various quarters. Among the factors contributing to the "true increase" of VTE are, first, the aging of the Japanese population, which itself confers a risk of VTE; and the elderly are likely to have other risks for VTE. The second factor is change in life style. In recent decades, eating habits in Japan have become westernized, and the percentage of the population that is overweight is growing. Although the relation between VTE and metabolic syndrome is unknown, it should be considered. The third factor is advances in medical care. The risk of VTE at an inpatient setup rises according to the complexity of treatment, and the number of patients at risk further increases because the prognosis has improved for conditions such as malignancy that increase the risk of VTE. In addition, many medicines, such as oral contraceptives and drugs used in hormone replacement therapy, may increase the risk of VTE (Fig. 1).

From the point of view of prognosis, the hospital mortality rate was 14% for 309 patients diagnosed with PTE from 1994 to 1997 according to a collaborative study conducted by the Japanese Society of Pulmonary Embolism Research [34]. Among those who died, mortality among patients with shock at presentation was 30%, and it was 20% except for cases diagnosed by an autopsy, and 6% for those who presented without shock. In addition, the mortality after discharge was 3%. These results indicate that patients with PTE who are correctly diagnosed have a relatively good prognosis. However, in the following decade, the prognosis of severe cases did not improve [35] (Table 1). In addition to underdiagnosis of PTE, the high frequency of sudden death, which afflicts 25% of severe cases, and death due to recurrent PTE affect the mortality rates [36] (Fig. 2). In particular, many patients with unexpected circulatory

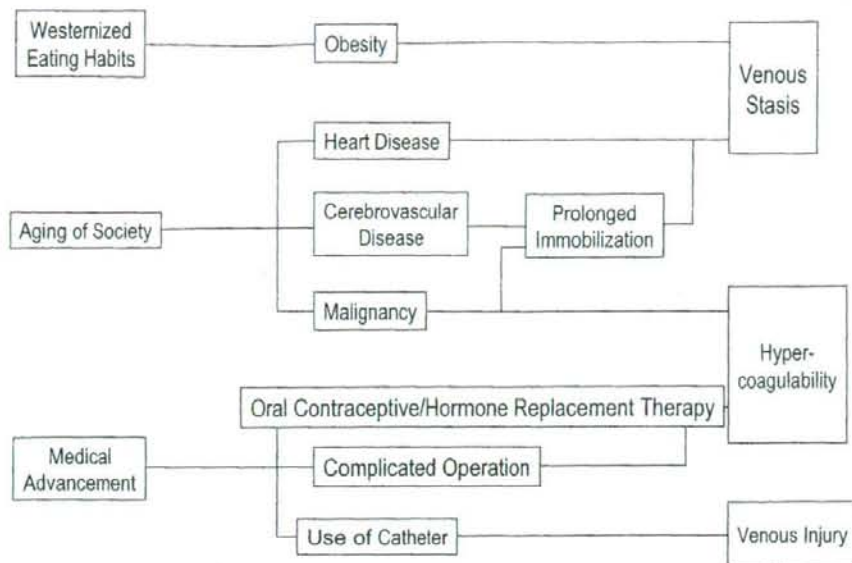


FIG. 1. Change in social structure and increasing risk of pulmonary thromboembolism

TABLE 1. Change in the mortality rate of pulmonary thromboembolism in Japan

Subjects	Change in mortality (%)		
	1/1994–10/1997 (n = 309)	11/1997–10/2000 (n = 257)	11/2000–8/2003 (n = 461)
Total	14	12	8
Cases with arrest or shock	30	32	27
Other mild cases	6	3	2

Data are from Sakuma et al. [35]

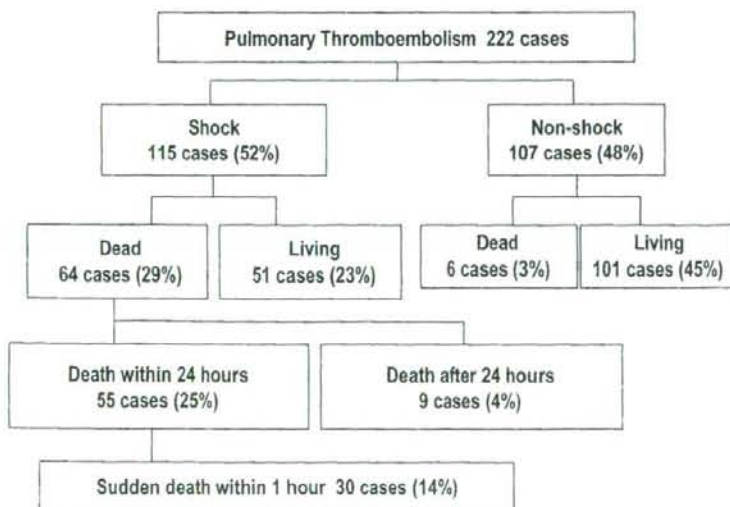


FIG. 2. In-hospital mortality of 222 patients with pulmonary thromboembolism. Sudden deaths within 1 h from onset account for 43% of total deaths with pulmonary thromboembolism

arrest succumb even with percutaneous cardiopulmonary support. Consequently, it is important to prevent PTE.

Development of Diagnostic Methods and Management of Pulmonary Thromboembolism

Many guidelines on the diagnosis and management of PTE have been published and reported at Western scientific meetings. Guidelines for the diagnosis and management of PTE have also been developed by the Japanese Society of Circulation in cooperation with other societies in Japan [9] (Fig. 3). Application of Western guidelines for PTE in Japan, as for other disorders, was uncertain because of unknown differences in the incidence of PTE in Caucasian and Japanese populations and the differences in medical care among countries. In addition, guidelines for diagnosis that are based on the situation in each country are necessary because of differences in the development of diagnostic modalities and cost.

Traditionally, the gold standard for diagnosis of PTE has been pulmonary angiography. However, efforts have been made to restrict the indications for use of pulmonary angiography, which is invasive; currently, the diagnosis of PTE tends to rely on noninvasive modalities [34, 35, 37] (Table 2). Although the main noninvasive diagnostic modality for PTE in Western countries is the perfusion lung scan, contrast-enhanced multislice computed tomography (CT) is useful in Japan. Current machines can evaluate a thromboembolism even in segmental arteries except in patients who cannot hold their breath for the necessary imaging interval. Multislice CT has the additional

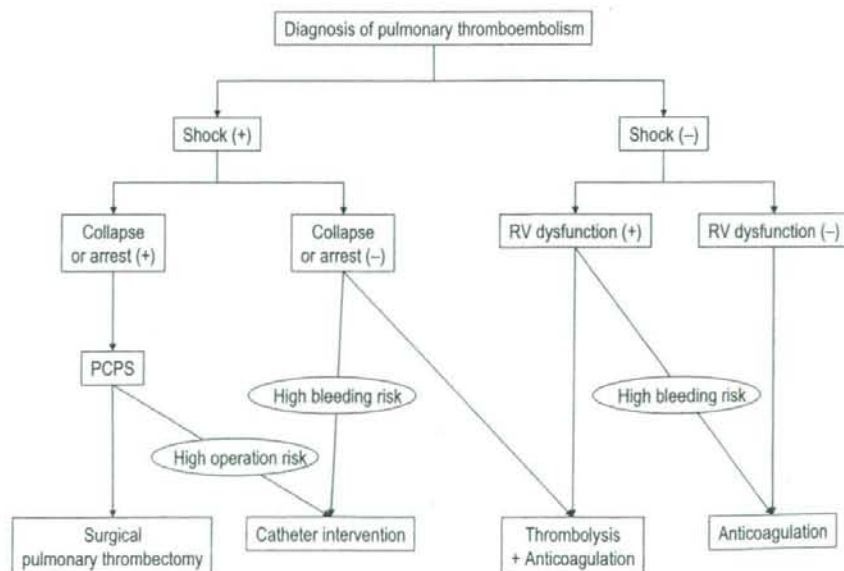


FIG. 3. Management strategy in pulmonary thromboembolism. PCPS, percutaneous cardiopulmonary support; RV, right ventricle

TABLE 2. Development of diagnostic methods of pulmonary thromboembolism in Japan

Diagnostic methods	Development of methods (%)		
	1/1994-10/1997 (n = 309)	11/1997-10/2000 (n = 257)	11/2000-8/2003 (n = 461)
Perfusion lung scan	74	77	62
Pulmonary angiography	45	57	37
Contrast-enhanced CT	14	58	62
MRI	2	6	2

Data are from Nakamura et al. [34] and Sakuma et al. [35, 37] CT, computed tomography; MRI, magnetic resonance imaging

TABLE 3. Development of diagnostic methods for DVT after the occurrence of pulmonary thromboembolism in Japan

Diagnostic method	Development (%)		
	1/1994-10/1997 (n = 309)	11/1997-10/2000 (n = 257)	11/2000-8/2003 (n = 461)
Operation rate of examination for DVT	61	65	83
Venous ultrasonography	18	24	55
Venography	81	73	41
Radio nuclear angiography	13	12	2

Operation rate indicates the ratio of patients examined for operation during each interval to the total number of patients diagnosed with DVT during that interval.

DVT, deep vein thrombosis

Data are from Nakamura [34] and Sakuma [35, 37]

advantage of being able to examine veins in the abdomen, pelvis, and legs after scanning the pulmonary arteries. The efficacy of multislice CT in PTE has been examined, and this modality is now included in the diagnostic algorithm for PTE. In addition, because of the importance of diagnosing DVT as a source of thromboembolism, venous ultrasonography, which is convenient and can be used noninvasively at the bedside, is recommended. Implementation of this modality has nevertheless been inadequate [34, 35, 37] (Table 3), and it is important to train sonographers and physicians to perform venous ultrasonography.

In the West, management guidelines for anticoagulation and thrombolysis based on a wealth of evidence are being released. No clinical trials are planned or underway to gather such evidence in Japan [38]. With regard to thrombolytic agents, which are used commonly for PTE, Alteplase, mutant tissue plasminogen activator (t-PA), has been permitted for use in patients by the Japanese government only since autumn 2005. At the same time, the effect of thrombolysis on the prognosis of patients with PTE is not clear, even in Western countries [39]. In many randomized controlled trials for PTE therapy, although thrombolysis has been shown to bring about more rapid thrombolytic and hemodynamic effects than anticoagulation, there have been no

reports that thrombolysis reduces PTE-related mortality. Therefore, the ability of thrombolysis to improve the prognosis is unknown, and its indications have not been sufficiently established. In addition, it is arguable whether thrombolysis has an effect on prognosis in severe cases. Recently, right ventricular dysfunction was identified as an important factor linked to prognosis. In the most recent randomized controlled trial of PTE in normotensive patients with right ventricular dysfunction, t-PA was found to improve the clinical course and prevent clinical deterioration; it requires an escalation of treatment compared with heparin, although the differences in mortality were not significant [40]. Therefore, thrombolytic therapy might be recommended for PTE patients with right ventricular dysfunction; however, the choice of this therapy has little scientific basis and needs further research.

Over the past few years, the use of catheter intervention for various kinds of vascular diseases has progressed, and catheter thrombolysis and catheter fragmentation are now used in patients with VTE. These techniques are being used to dissolve a thromboembolus and reduce right ventricular overload in PTE, rapidly restore a venous valve, and decrease the frequency of postthrombotic syndrome. Although it is often difficult to dissolve an obstructive DVT using conventional pharmacotherapy, a recent Japanese study reported that catheter-directed thrombolysis achieves a high dissolution rate of DVT and a reduction in the incidence of postthrombotic syndrome [41]. Thus, this technique appears to be promising.

The development of inferior vena cava (IVC) filters constitute a marked advance in the prevention of primary and recurrent PTE with DVT. When the technique was initially introduced, only permanent filters were used, and the recurrence rate of PTE after IVC filter implantation was reported to be 2% [42]. However, results of a French prospective multicenter study indicated that the long-term prognosis was worse after IVC filter implantation than after anticoagulation [43]. As a result, prophylactic use of permanent IVC filters for stable patients is not recommended. On the other hand, when anticoagulation alone is performed as PTE management, it may lead to massive recurrent PTE, a critical complication. To avoid such cases of recurrent, severe PTE, nonpermanent IVC filters have recently come into use. These filters are implanted only during the acute phase when a venous thrombus can easily migrate and the pulmonary vascular bed is small. The filter can then be removed after thrombus dissolution, decreasing the risk of embolism. Temporary IVC filters [44] and retrievable IVC filters [45] can now be used as nonpermanent IVC filters. Although temporary filters carry a risk of infection and bleeding, because they are joined to an external catheter they fare better in younger subjects and women of child-bearing age because they can be readily removed. At the same time, retrievable IVC filters are implanted as permanent filters and can be retrieved with a catheter after use. They impose fewer limitations of patient activities, and the risk of infection and bleeding is small. Moreover, they can be implanted permanently. Although the indications for use of these IVC filters have not yet been determined, the decision to use these devices should be based on the severity of the right ventricular overload and the size and ease of migration of the DVT. The trend in Japan, more so than in the West, is toward increased use of IVC filters. Once the utility of anticoagulation has been confirmed, indications for use of IVC filters should be determined carefully, especially when considering the use of permanent IVC filters (Table 4).

TABLE 4. Development of methods of management of pulmonary thromboembolism in Japan

Methods of management	Development (%)		
	1/1994-10/1997 (n = 309)	11/1997-10/2000 (n = 257)	11/2000-8/2003 (n = 461)
Anticoagulation	74	82	92
Thrombolytic therapy	50	48	58
Catheter intervention	6	6	10
Surgical pulmonary thrombectomy	2	3	2
Vena cava filter	18	34	35

Data are from Nakamura [34] and Sakuma [35, 37]

Current Status of Prophylaxis of Venous Thromboembolism

In-hospital prophylaxis of VTE is important for the following reasons: (1) the incidence of VTE is remarkably high in hospitals; (2) early diagnosis of DVT is difficult because it produces few symptoms; (3) PTE has a high fatality rate; and (4) prophylaxis of VTE is cost-efficient. Many Western medical societies have developed guidelines for the prevention of VTE based on extensive evidence. Sudden death from PTE after surgery and in other conditions is an increasing problem in Japan, and medical malpractice litigation is becoming more frequent when an appropriate treatment for PTE has not been provided. Until now, it was difficult to estimate the incidence of PTE accurately because of the difficulty of its diagnosis. However, adequate diagnosis and management of PTE is currently regarded as a matter of course, and an inadequate response by health care providers could be judged a lack of due diligence. For these reasons, a guideline for prophylaxis of VTE was anxiously awaited in Japan. As previously noted, it was impossible to use Western guidelines without modification because of differences in the incidence and use of prophylactic agents between Japan and the West. In response to this situation, the "Japanese Guideline for Prevention of Venous Thromboembolism" [8] was published in the spring of 2004 by the Editorial Committee organized by the Japanese Society of Anesthesiologists, Japanese Society of Phlebology, Japanese Society of Pulmonary Embolism Research, Japan Society of Obstetrics and Gynecology, Japanese College of Cardiology, Japanese Orthopaedic Association, Japanese Society of Intensive Care Medicine, Japanese Society of Thrombosis and Homeostasis, Japanese Urological Association, and Japan Society of Obstetrical Gynecological and Neonatal Hematology. Because few clinical studies are available that provide evidence specific to Japanese patients, the guideline remains incomplete. Even so, the participation of numerous medical societies in the development of the Japanese guideline is a significant step that is unprecedented elsewhere in the world. At about the same time, a PTE prophylaxis management fee was listed in the revised health insurance as a part of medical treatment fees in the spring of 2004. As a result, in-hospital VTE prophylaxis is starting to be implemented in many institutions. In the future, collection