Adequate Management of Venous Thromboembolism

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Venous thromboembolism (VTE), which includes deep venous thrombosis (DVT) and pulmonary embolism (PE), is a prevalent disease that has potentially serious complications. PE is a major life-threatening complication for patients with VTE because it can lead to the sudden collapse of circulatory dynamics and subsequent death. The incidence of chronic thromboembolic pulmonary hypertension (CTEPH) among survivors of acute PE is approximately 1%. CTEPH results from the obstruction of pulmonary arteries by unresolved, organized thrombi. In untreated patients, CTEPH may progress to right heart failure and death. A study of patients with inoperable CTEPH showed that prognosis was poor (5-year survival = 30%), especially for patients with a mean pulmonary artery pressure > 40 mmHg. Bosentan and sildenafil are used as modern oral therapy for patients with inoperable CTEPH. Medically treated patients with CTEPH have a better survival rate, and the use of bosentan and sildenafil contributes to this improved survival. The incidence of VTE is approximately 7 per 10,000 person-years among community residents, and it has recently become a common preventable cause of hospital death.

In Europe and the United States, VTE is already recognized as a common disease and even in Japan, the prevalence of VTE has been increasing in association with the increasing spread of a western lifestyle, aging, increased awareness of VTE, and advances in diagnostic techniques.

In the issue of this journal, Nakamara et al. report their results from the nationwide Japan Venous Thromboembolism Treatment (JAVA) observational study, including the incidence of VTE in Japan and the recent status of VTE management and outcomes. The authors found a low incidence of VTE, reflecting the results of previous studies. However, the JAVA study was not designed to assess the incidence of VTE. Hence, further investigation is still necessary to clarify the actual number of VTE cases in the general population of Japan. In addition, the authors found that the prognosis of VTE depended on background factors and the choice of therapy. Therefore, early detection of VTE and adequate management of risk factors for VTE are important to prevent serious complications.

The common independent risk factors for VTE are listed in Table. They include surgery, hospitalization for acute medical illness, trauma, active cancer, immobilization, superficial vein thrombosis, central venous catheter/transvenous pacemaker, and hormone therapy.

In the JAVA study, a medical history of cancer was observed to be the most common VTE risk factor, being present in 27.0% of patients with VTE. Concomitant acute medical illness was found in approximately 25% of patients, and the incidence of VTE was 10 times higher in patients with cancer compared to those without it. The incidence of VTE was also increased in patients with active cancer compared to those with previous cancer.

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20% of VTE cases. A history of recent surgery (within 3 months) was reported in 17.8% of VTE cases. In the guidelines for the Diagnosis, Treatment and Prevention of Pulmonary Thromboembolism and Deep Vein Thrombosis (JCS 2009), the recommended methods of VTE prevention vary according to the strata of various risk factors. Therefore, it is useful to investigate risk factors that could be important to VTE prevention among hospitalized patients.

As components of the treatment for VTE, acute- and chronic-phase anticoagulation play key roles in the overall prognosis of this disease. Even in recent years, the main drug treatments for VTE have been an initial course of unfractionated heparin or low-molecular-weight heparin (LMWH), followed by warfarin, a vitamin K antagonist. The JAVA Study demonstrated that 85% of patients achieved the target international normalized ratio (INR) of 2.0 (range, 1.5–2.5) with respect to chronic anticoagulation, which is in line with the Japanese guidelines. However, warfarin has a number of limitations: it has a narrow therapeutic window, requires close monitoring to ensure that the INR remains within 2–3, and has numerous drug interactions that can modify both its effects and adverse reactions to a remarkable extent. In addition, the level of anticoagulation that results from a fixed-dose regimen of warfarin remains difficult to predict during the initiation of therapy. Recently, Pirmohamed et al reported that genotype-guided dosing may be useful for patients who have atrial fibrillation or VTE and are starting warfarin therapy. Moreover, it has been reported that factor Xa inhibitors or direct thrombin inhibitors are also effective for preventing VTE recurrence. This is especially important because they are expected to lead to fewer hemorrhagic complications as new anticoagulant therapies.

In contrast, the JAVA study has highlighted the differences between the Japanese treatment guidelines and treatments occurring in clinical practice. The guidelines for VTE treatment in Japan strongly recommend that permanent inferior vena cava (IVC) filters be specifically indicated for patients who are contraindicated for anticoagulation therapy, exhibit treatment-related complications or adverse drug reactions to anticoagulation therapy, are unable to continue anticoagulation therapy, or experience recurrent VTE during adequate anticoagulation therapy. However, as observed in the JAVA Study, IVC filters were used in 40% of VTE cases, with the overall rate of use increasing to 60% for cases of PE+DVT. Although the JAVA study investigators did not examine the reasons why IVC filters were inserted, it is worth noting that only 9.9% of patients at a high risk of bleeding underwent IVC filter insertion. Accordingly, bleeding did not appear to be the main reason for IVC filter insertion in the JAVA study. Similarly, in a previous study of a small series of Japanese patients, the reasons for IVC filter insertion differed markedly from those in other countries. In deed, in that series, the most frequently reported indication was perioperative VTE prophylaxis (84.8%), followed by other prophylactic indications, thrombolytic therapy, and pregnancy with DVT. Based on these findings, it has been suggested that VTE management comprises highly aggressive strategies in Japan. The JAVA study has revealed the epidemiology of VTE in Japan, as well as the recent status of its clinical management. The observational findings of the JAVA study will help us optimize VTE management, thereby improving patients’ outcomes.

References