



Review Article

Treating pulmonary embolism in Pacific Asia with direct oral anticoagulants



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ABSTRACT

Pulmonary embolism (PE) is the principal preventable cause of in-hospital deaths. Prevalence of PE in Asians is uncertain but undoubtedly underestimated. Asians and Caucasians have similar non-genetic risk factors for PE, and there is mounting evidence that PE affects Asians much more commonly than previously supposed; incidence, especially among high-risk patients, may approach that in Caucasians. Furthermore, PE incidence in Asia is increasing, due to both increased ascertainment, and also population ageing and growing numbers of patients with predisposing risk factors. Despite being warranted, thromboprophylaxis for high-risk patients is not routine in Pacific Asian countries/regions. There also appears to be scope to implement venous thromboembolism (VTE) management guidelines more assiduously.

Anticoagulants, primarily heparins and warfarin, have been the mainstays of VTE management for years; however, these agents have limitations that complicate routine use. The complexity of current guidelines has been another barrier to applying evidence-based recommendations in everyday practice. Updated management approaches have considerable potential to improve outcomes. New oral anticoagulants that are easier to administer, require no, or much less, monitoring or dose-adjustment and have a favourable risk/benefit profile compared with conventional modalities, may offer an alternative with the potential to simplify VTE management. However, more information is required on practical management and the occurrence and treatment of bleeding complications.

Increasing recognition of the burden of PE and new therapeutic modalities are altering the VTE management landscape in Pacific Asia. Consequently, there is a need to further raise awareness and bridge gaps between the latest evidence and clinical practice.

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Abbreviations: PE, Pulmonary Embolism; VTE, Venous Thromboembolism; DVT, Deep-Vein Thrombosis; ACCP, American College of Chest Physicians; RIETE, Computerized Registry of Patients with Venous Thromboembolism; ESC, European Society of Cardiology; US, United States; UFH, Unfractionated Heparin; LMWH, Low Molecular Weight Heparin; VKA, Vitamin K Antagonists; NOACs, Non-Vitamin K Oral Anticoagulants; FDA, Food and Drug Administration; CrCl, Creatinine Clearance; aPCC, Activated Prothrombin Complex Concentrate; PCC, Prothrombin Complex Concentrate.

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Venous thromboembolism (VTE) is a blanket term designating the related disorders of deep-vein thromboses (DVT) of the limbs and body, and pulmonary embolism (PE). These medical complications are common and incur substantial morbidity, mortality and related healthcare expenditure [1]. Although sometimes idiopathic, PE results primarily consequent to a precipitating DVT and is a serious, potentially life-threatening, cause of complications associated with surgery, illness and trauma; it is the principal preventable cause of in-hospital fatalities, accounting for up to 10% [1–3]. The prevalence of PE, especially in Asians, is uncertain and probably underestimated because PE is often clinically silent, being diagnosed antemortem in a minority of patients with fatal PEs [4–7]. VTE, especially PE, was once considered rare in Asians, but mounting evidence to the contrary suggests not only that it affects Asians much more commonly than was previously supposed, but also that its incidence is increasing [8].

Notwithstanding advances in VTE prophylaxis and treatment that have improved patient outcomes, the conventional treatment paradigm has limitations. Moreover, some practice guidelines in widespread current use, such as those by the American College of Chest Physicians (ACCP) [9], are complicated, and most are based on predominantly Caucasian data. Pacific Asia has no regional VTE treatment guideline. Concurrently, greater appreciation of the impact of PE in Pacific Asian populations and the recent advent of new therapeutic modalities are rapidly changing the management landscape in the region. In this context, concerted efforts are warranted to further raise awareness of PE across disciplinary boundaries and to bridge remaining gaps between the latest evidence and everyday clinical practice. To these ends, a panel of experts drawn from Australia, Hong Kong, Malaysia, Indonesia, South Korea, Taiwan, Thailand and the United Kingdom met with the specific objectives to: 1) Review epidemiology and evidence gaps in the Pacific Asia region¹; 2) Take stock of current PE treatment and emerging data and trends; 3) Offer practical advice on new oral anticoagulants, including monitoring, managing bleeding complications and reversing anticoagulation; 4) Assess the potential of novel therapeutic options to reduce the burdens of disease and its treatment. This review summarises contemporary issues in PE treatment

and key barriers and opportunities to refining practice in the Pacific Asian region.

PE Epidemiology and Trends in Pacific Asia

Most data on VTE epidemiology derive from predominantly Caucasian populations and the prevalence of VTE, particularly PE, in other races or ethnic groups has not been studied comprehensively [10]. While reported overall VTE prevalence in Asian populations has generally appeared lower than in Caucasians, evidence from numerous studies indicates that VTE is certainly not uncommon [7,11–14], with incidence, especially among high-risk patient groups, that may not be dissimilar to that in Caucasians [8,15–20].

The historic supposition that VTE is much rarer in Asians than Caucasians probably largely reflects lower clinical suspicion among Asian physicians in the past, as well as limited diagnostic capabilities and access to healthcare [4,21,22]. Underdiagnosis of PE due to comparatively lower autopsy rates in Asian countries for practical, cultural and religious reasons, also contributes to relatively lesser ascertainment that belies its true prevalence [21]; indeed data from Hong Kong, India, Japan and Singapore suggest a similar incidence of autopsy-detected PE to that in Caucasians [7,23–26].

Furthermore, reported DVT and PE rates have risen steeply over recent decades in countries/regions across Pacific Asia (Table 1) [10, 12,13,27–29]. Underlying upward trending PE rates in Asian populations are likely driven by rising numbers of patients with risk factors that include: advanced age; obesity; diseases predisposing to PE, particularly cancer and chronic obstructive pulmonary disease [30,31]; or who are old and/or ill and undergo major surgery [1,20,21,29]. Another important factor contributing to rising incidence is increased ascertainment due to greater cognisance and vigilance among physicians coupled with growing use of sensitive modern diagnostic modalities, such as duplex ultrasound and advanced computed tomography techniques [4,10,12,13,19,20]. For example, following implementation of a nationwide VTE prevention and treatment initiative in 2001, annual incidence of PE in 60 hospitals across China doubled from 0.07% to 0.14%, probably reflecting increased awareness and diagnosis; after 2005, incidence stabilised at 0.14%. The case fatality rate declined concurrently, probably as a result of improved medical management [10]. Others with similar findings likewise attributed declining PE mortality to improved survival as a result of earlier diagnosis and better prophylaxis and management [13,32]. Conversely, recent studies in the

¹ Due to sparse Asian data, the scope of this review is largely limited to Pacific Asian countries/regions including Australia, Hong Kong, Indonesia, Malaysia, Singapore, South Korea, Taiwan and Thailand, for which exist robust data as well as expert knowledge of the panel members. Nevertheless, for other Asian countries with less reliable data, the situation is likely to be no better and probably worse.

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