

# Venous thromboembolism prophylaxis in the critically ill: a point prevalence survey of current practice in Australian and New Zealand intensive care units

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Venous thromboembolism (VTE), comprising deep vein thrombosis (DVT) and pulmonary embolism, is a well-recognised life-threatening complication for critically ill patients admitted to intensive care units.<sup>1-3</sup> A number of risk factors encourage the development of VTE, including pre-morbid conditions, prolonged immobility, invasive intravascular catheters and surgical procedures.<sup>3-8</sup> Most thromboses are asymptomatic and confined to the deep veins of the leg. However, if untreated, calf vein thromboses may extend proximally into the thigh, where they pose a greater risk of pulmonary embolism if untreated.<sup>9,10</sup>

VTE has been shown to occur in 10%–28% of ICU patients who do not receive prophylaxis,<sup>4,11-15</sup> and post-mortem studies have reported pulmonary emboli in 7%–27% of patients who died in the ICU.<sup>1,16</sup> DVT has been associated with longer durations of mechanical ventilation, longer ICU and hospital stays, and increased mortality in medical–surgical ICU patients.<sup>4</sup> Importantly, prophylaxis with unfractionated heparin (UFH) and low molecular weight heparin (LMWH) has been shown in randomised studies to substantially reduce the incidence of VTE in critically ill patients.<sup>11,13,17</sup> However, despite concerted efforts to provide appropriate prophylaxis, the incidence of VTE in critically ill patients admitted to the ICU for over 48 hours remains high, with estimates ranging from 9.6% to 33%.<sup>18-22</sup>

As part of an international research program to investigate the efficacy of VTE prophylaxis in critically ill patients, a survey was conducted to determine clinical practice in Australian and New Zealand ICUs in 2005.<sup>20</sup> In this self-administered email survey of 21 ICUs, 19 reported routine use of subcutaneous low-dose UFH for VTE prophylaxis in critically ill patients, and the remaining two reported routine use of LMWH.<sup>20</sup> All surveyed ICUs used mechanical prophylaxis measures (antithrombotic stockings and/or sequential calf compressors) in patients with contraindications to anticoagulation.<sup>20</sup>

## ABSTRACT

**Background:** Critically ill patients are at high risk of morbidity and mortality caused by venous thromboembolism (VTE). In addition to pre-morbid predisposing conditions, critically ill patients may be exposed to prolonged immobility, invasive intravascular catheters and frequent operative procedures, and further may have contraindications to pharmaceutical prophylactic measures designed to attenuate VTE risk. There are limited data describing current VTE prophylaxis regimens in Australia and New Zealand.

**Objective:** To document current Australian and New Zealand management of VTE prophylaxis in a large mixed cohort of critically ill patients.

**Design:** Prospective, multicentre point prevalence survey endorsed by the Australian and New Zealand Intensive Care Society Clinical Trials Group (ANZICS CTG).

**Setting:** 30 public hospital ICUs in Australia and New Zealand surveyed on Wednesday 9 May 2007.

**Methods:** For all patients in each ICU on the study day, demographic data, admission diagnosis and information on VTE prophylaxis were prospectively collected.

**Results:** 502 patients were included in the survey, and 431 of these (86%) received VTE prophylaxis. Of these, 64% (276/431) received pharmacological prophylaxis and 80% (345/431) received mechanical prophylaxis, with 44% (190/431) receiving both. Of those receiving pharmacological prophylaxis, unfractionated heparin was used in 74%, and enoxaparin (low molecular weight heparin) in 23%. Contraindications to pharmacological prophylaxis were reported in 122 patients. Overall, pharmacological prophylaxis was administered to 87% of potentially suitable patients.

**Conclusions:** We observed a high prevalence of VTE prophylaxis, with many critically ill patients receiving two or more modalities of prophylaxis. These results show that the potential risk of VTE in critically ill patients is recognised in Australia and New Zealand, and strategies to mitigate this serious complication are widely implemented.

\*The VTE Point Prevalence Study committees and investigators are listed in Appendix 1.

Although the survey helped document clinicians' attitudes to VTE prophylaxis in critically ill patients, it did not assess actual, rather than self-reported, practice. Utilisation campaigns in critically ill patients have had variable success in implementing universal VTE prophylaxis. Although the average compliance with some form of VTE prophylaxis outside Australia and New Zealand has been reported as 69%, compliance in individual studies ranged from 33% to 100%.<sup>16</sup>

This study aimed to document current Australian and New Zealand management of VTE prophylaxis across a broad sample of general (mixed medical–surgical) ICU patients. This type of ICU population has not previously been surveyed by international multicentre VTE utilisation studies.

## Methods

The study was endorsed by the Australian and New Zealand Intensive Care Society Clinical Trials Group (ANZIC-CTG), and Australasian ICUs were invited to participate.

The study was a prospective epidemiological observational audit and, where required, was approved by the institutional ethics committee of each participating hospital; the need for participant consent was waived. Data were de-identified before submission to the coordinating centre.

The point prevalence survey was performed on a single day, Wednesday 9 May 2007. All adult patients (aged 16 years or older) in the participating ICUs at any time on that day were recorded. Demographic data included age, sex, admission diagnosis categorised as for APACHE III, weight, APACHE II score in the 24 hours before the study day, and whether the patient was admitted or discharged from the ICU on the study day. Information on VTE prophylaxis for the study day included pharmacological prophylaxis (type administered), mechanical prophylaxis (type and location), presence of contraindications to pharmacological VTE prophylaxis, and, if VTE prophylaxis was not required, the reason. Administration of anticoagulant and antiplatelet agents for purposes other than VTE prophylaxis was also recorded.

## Statistical analysis

Analysis was undertaken using SAS version 9.1 (SAS Institute Cary, NC, USA). Variables that were approximately normally distributed were reported as mean (standard deviation), and non-normally distributed data as median (interquartile range). Proportions (n/N) were reported as percentages.

## Results

Thirty public hospital ICUs (26 in Australia, four in New Zealand) participated in the study: 26 were Level III tertiary ICUs, and four were Level II. All were closed multidisciplinary

**Table 1. Patient demographic characteristics**

Characteristic	Percentage of patients (n = 502)*
Age (years), mean (SD)	58.7 (17.7)
Sex, male	62.2%
Weight (kg), mean (SD)	77.7 (19.8)
APACHE II score, mean (SD)	14.52 (6.99)
ICU length of stay (days), median (IQR) †	2 (1–8)
ICU admission ‡	22.5%
ICU discharge §	17.5%
Postoperative	43.2%
APACHE III diagnostic categories	
Cardiovascular	24.5%
Respiratory	16.9%
Gastrointestinal	14.3%
Neurological	13.3%
Sepsis	9.2%
Trauma	11.8%
Other	10.0%

SD = standard deviation. IQR = interquartile range.

\* Unless otherwise indicated. † ICU length of stay before study day.

‡ Patients admitted to ICU on the study day.

§ Patients discharged from ICU on the study day.

ICUs, with patient management supervised by accredited ICU specialists. A total of 502 adult patients were in one of these ICUs at some time on the study day; their characteristics are summarised in Table 1.

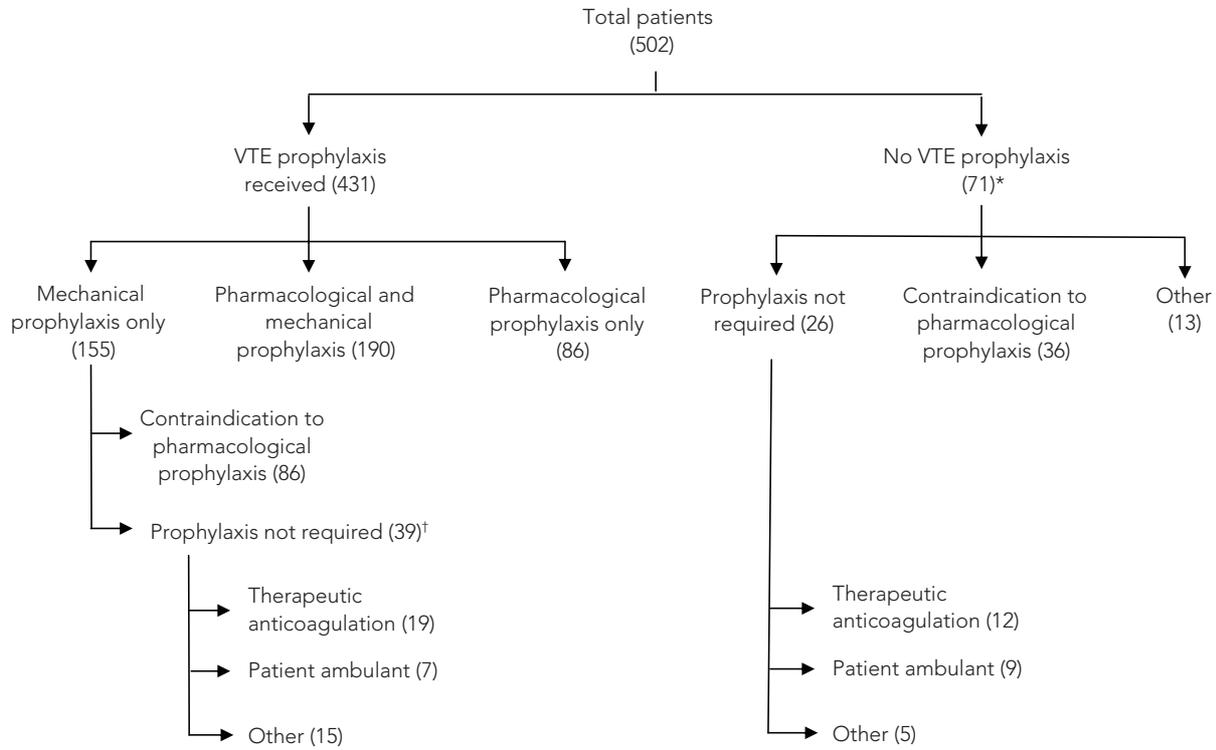
VTE prophylaxis was received by 86% (431/502) of participants: 64% (276/431) received pharmacological prophylaxis, and 80% (345/431) received mechanical prophylaxis, with 44% (190/431) receiving both modalities (Figure 1).

UFH was the most common pharmacological agent used for VTE prophylaxis (74%, 204/276). Enoxaparin was the only form of LMWH used (23%, 63/276). Other prophylactic agents used included warfarin (7 patients) and danaparoid (1 patient); in four patients the prophylactic agent was not specified (Figure 2) (some patients received more than one type of pharmacological prophylaxis on the study day).

The most common form of mechanical prophylaxis used was antiembolic stockings (87%, 301/345), followed by pneumatic compression devices (34%, 117/345); 21% of patients received more than one mode of mechanical prophylaxis (Figure 2). Use of inferior vena caval filters was reported in three patients. Among the 155 patients who received mechanical prophylaxis only, 86 (56%) were reported to have a contraindication to pharmacological prophylaxis (Table 2).

No VTE prophylaxis was received by 14% (71/502) of survey participants. Of these, 51% (36/71) had a reported

**Figure 1. Mechanisms of venous thromboembolism (VTE) prophylaxis used and reasons for those who did not receive prophylaxis**



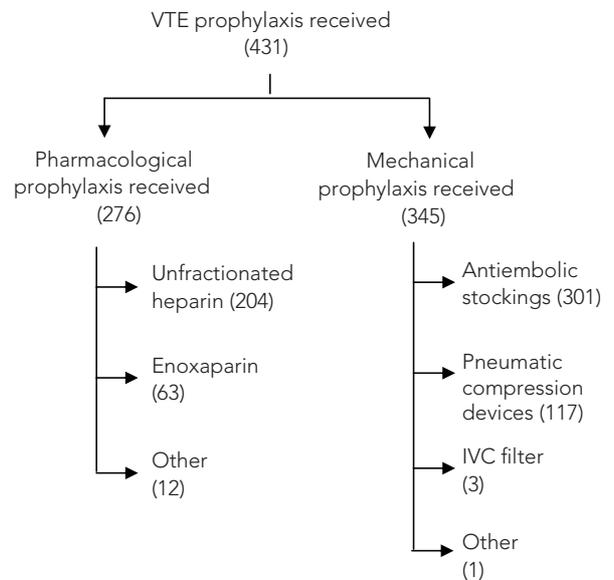
\*Some patients had more than one reason for not receiving VTE prophylaxis. † Some patients had more than one reason for not requiring VTE prophylaxis.

contraindication to pharmacological prophylaxis (Table 2), 37% (26/71) were considered not to require prophylaxis (12 were receiving therapeutic anticoagulants, 9 were ambulant, and 5 did not require prophylaxis for other reasons), and 13 did not receive prophylaxis for other (5) or unknown (8) reasons (Figure 1).

Contraindications to pharmacological prophylaxis were reported in 122 patients who did not receive pharmacological prophylaxis; 86 of these received mechanical prophylaxis, and 36 received no prophylaxis (Table 2). Of the 370 patients with no documented contraindication to pharmacological prophylaxis, 276 (75%) received that prophylaxis. Sixty-one of the patients who did not receive pharmacological prophylaxis had a documented reason for not requiring prophylaxis. Thus, 43 patients (9%, 43/502) did not receive pharmacological VTE prophylaxis despite having no reported contraindication and a possible need for prophylaxis. Of these 43, 30 received mechanical prophylaxis, but 13 received neither mechanical nor pharmacological prophylaxis. Overall, pharmacological prophylaxis was administered to 87% (276/319) of potentially suitable patients.

Anticoagulant and antiplatelet agents were administered for reasons other than VTE prophylaxis to 20% (102/502) of

**Figure 2. Types of venous thromboembolism (VTE) prophylaxis used**



IVC = inferior vena caval.

**Table 2. Contraindications to pharmacological prophylaxis, by VTE prophylaxis group**

Contraindication	No. with contraindication	
	Mechanical prophylaxis only (n = 155)	No prophylaxis (n = 71)
Recent neurosurgery	15 (10%)	1 (1%)
Ischaemic stroke	2 (1%)	0
Intracranial haemorrhage	21 (14%)	1 (1%)
Major haemorrhage	12 (8%)	3 (4%)
Coagulopathy	21 (14%)	14 (20%)
Thrombocytopenia	13 (8%)	7 (10%)
Other not specified	20 (13%)	17 (24%)
<b>Total no. of patients with a contraindication*</b>	<b>86 (55%)</b>	<b>36 (51%)</b>

VTE = venous thromboembolism.

\* Some patients had more than one contraindication to VTE prophylaxis.

patients, with aspirin (95/102) being the most common agent prescribed.

## Discussion

This Australian and New Zealand point prevalence study showed that most critically ill patients included in the audit received some form of VTE prophylaxis on the study day. Mechanical measures, including antiembolic stockings and pneumatic compression devices, were the most common modes of prophylaxis, used in 69% of participants overall and 80% of those receiving VTE prophylaxis. Pharmacological prophylaxis was used overall in 55% of all participants and 64% of patients documented as requiring VTE prophylaxis. Excluding patients with contraindications, three-quarters of those eligible received pharmacological prophylaxis. Further excluding patients documented as not requiring DVT prophylaxis, pharmacological VTE prophylaxis was administered to 87% of all potentially appropriate ICU patients.

These results must be seen in the light of recent studies that have benchmarked international practice. A previous large international multicentre cross-sectional survey of 1222 medical ICU patients reported 64% received heparin VTE prophylaxis; when patients with a contraindication to heparin were excluded, appropriate heparin VTE prophylaxis was reported for 92% of medical ICU patients.<sup>23</sup> In contrast, a multicentre study of VTE prophylaxis in 89 surgical ICU patients found that, although only two patients received no VTE prophylaxis, heparin VTE prophylaxis was used in only 48%.<sup>24</sup> Furthermore, a survey of 1827 patients

in three ICUs found that VTE prophylaxis was used in 98% of patients following intensive education of staff and computer medication-entry support, compared with 62% with only intensive education, and 38% in the control ICU with no educational intervention.<sup>25</sup> These findings suggest that the current use of pharmacological VTE prophylaxis in Australia and New Zealand in a mixed cohort of medical and surgical ICU patients is comparable to that found by previous international studies.

Although some areas of hospital practice, such as trauma and orthopaedic surgery, have moved predominantly to use LMWH in preference to UFH for VTE prophylaxis, LMWH has not yet been shown to be beneficial in medical and general surgical ICU patients. Hence, prescribing practice varies both internationally and within Australia and New Zealand. In a binational VTE prophylaxis study, Lacherade et al showed that LMWH was used significantly more often in French ICUs (90%), while UFH was used predominantly in Canadian ICUs (88%).<sup>23</sup>

In a previous survey of first-line VTE prophylaxis in Australian and New Zealand ICUs conducted before 2005, Cooper et al reported that fewer than 10% used LMWH as routine VTE prophylaxis.<sup>20</sup> However, in the current 2007 study, although UFH remained the most commonly used pharmacological VTE prophylactic agent, 23% of critically ill patients who received pharmacological prophylaxis received the LMWH enoxaparin. This level of LMWH use suggests that, in the absence of a randomised controlled trial to guide practice, prescription of pharmacological VTE prophylaxis by Australian and New Zealand intensive care clinicians is changing, but at present continues to resemble Canadian rather than European practice. The publication of the PROTECT study results, expected in 2011 (NCT00182143; a large international randomised controlled trial comparing UFH and LMWH in critically ill medical patients), should provide important guidance in this area.

Our study reported that mechanical prophylaxis was the most commonly used form of VTE prophylaxis in Australia and New Zealand ICUs. More than one in five patients given mechanical prophylaxis received more than one form simultaneously, and almost a third of all ICU patients received only mechanical prophylaxis. This is particularly interesting, given that little is known about the safety or effectiveness of mechanical prophylaxis in ICU patients,<sup>26</sup> with evidence that graduated compression stockings may be less effective than pharmacological prophylaxis.<sup>27,28</sup> Recent recommendations suggest that use of these devices should be confined primarily to patients at high risk of bleeding, or possibly as an adjunct to pharmaceutical measures, and that careful attention should be directed towards their proper use to prevent complications.<sup>3</sup> Although few would argue against the use of mechanical devices when pharmaceutical VTE

prophylaxis is contraindicated, it appears that clinicians in Australia and New Zealand favour the use of mechanical devices as adjuncts to pharmaceutical prophylaxis, and frequently use more than one mechanical device in individuals despite a lack of supporting evidence. Future trials are needed to determine whether this approach is beneficial in reducing the complications of VTE or actually increase morbidity in the critically ill.

Recently, several authors have cautioned against the routine use of inferior vena caval filters as VTE prophylaxis.<sup>29-31</sup> Consistent with this guidance, our survey reported that very few patients received these filters. Their appropriateness in these patients (eg, for treating large proximal thrombi with a high chance of embolisation or in the presence of an absolute contraindication to pharmaceutical prophylaxis) cannot be judged from the data available through our survey.

In our study, the main reason for patients not receiving pharmaceutical prophylaxis was a perceived risk of bleeding complications (Table 2). Some authors have recently suggested that many ICU patients are perceived to have a high risk of bleeding despite the fact that fatal bleeding is very rare in the ICU, while DVT and pulmonary embolism are common.<sup>32</sup> This has resulted in a call for clinicians to frequently re-evaluate the real risk of bleeding in their patients and to consider pharmaceutical measures to prevent the real threat of VTE-associated morbidity and mortality. This advice is echoed in our findings, which showed that 49% of patients who received no VTE prophylaxis and 45% of those who received only mechanical prophylaxis had none of several identified contraindications (Table 2). However, our survey did not specifically collect data on clinically relevant contraindications (eg, previous heparin-specific reactions). Furthermore, a few patients did not appear to receive any form of VTE prophylaxis despite a probable need and no recorded contraindications. This highlights the need for daily consideration of VTE prophylaxis in all critically ill patients.

The strengths of our study were the large number of participating ICUs across two countries, the varied population of critically ill medical and surgical patients, including trauma, neurosurgical and cardiothoracic subgroups. Its limitations include the point prevalence design, with practice documented on a single audit day, which may not reflect overall practice. Secondly, as all participating ICUs are associated with the ANZICS CTG, the results may not represent practice in other Australasian ICUs. Finally, data collection was preceded by a study planning period with extensive academic discussions of VTE prophylaxis in the critically ill, which may have changed routine practice.

In conclusion, this study showed that Australian and New Zealand ICUs implement therapies in an attempt to mitigate

potentially serious VTE complications in most critically ill patients. Mechanical prophylaxis was widely used in patients with contraindications to pharmaceutical VTE prophylaxis. A small proportion of ICU patients were judged not to require prophylaxis, and an even smaller proportion seemed to lack prophylaxis when no contraindication was identified. Future studies are required to explore the clinical decisions behind these categories, and document the frequency with which clinicians reassess their patients' requirements and contraindications to VTE prophylaxis.

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