Venous thromboembolism prophylaxis and the impact of a thrombosis service at a Canadian level 1 trauma centre

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Background: Venous thromboembolism (VTE) is a common and serious complication seen in patients with trauma. Guidelines recommend the routine use of pharmacologic prophylaxis; however, compliance rates vary widely. The aim of this study was to describe the clinical practice related to VTE prophylaxis in the first 24 hours after injury at our level 1 Canadian trauma centre and the impact of a thrombosis consultation service.

Methods: We performed a retrospective review of the health records of adult patients with trauma admitted between Jan. 1, 2012, and June 30, 2013. The rate of VTE was ascertained. The use of an initial prophylactic regimen, potential contraindications to prophylaxis and involvement of the thrombosis service were determined.

Results: A total of 633 patients were included, 459 men and 174 women with a mean age of 47.4 years. The mean Injury Severity Score was 15.8. The overall VTE rate was 2.8%. A total of 514 patients (81.2%) received VTE prophylaxis, mechanical in 302 (47.7%) and pharmacologic in 231 (36.5%) (19 patients received both types). The thrombosis service was involved in the care of 164 patients (25.9%). Patients seen by the thrombosis service were more likely to receive VTE prophylaxis than those not seen by the service (145 [88.4%] v. 369 [78.7%], $p < 0.01$).

Conclusion: Compliance with VTE prophylaxis administration was suboptimal, and opportunities for improvement exist. The involvement of a thrombosis consultation service appears to improve compliance with VTE prophylaxis, and augmented use of this service may improve clinical outcomes.

Contexte : La thromboembolie veineuse (TEV) est une complication grave et fréquente chez les patients vus en traumatologie. Les lignes directrices recommandent l'utilisation systématique d'une prophylaxie pharmacologique; par contre, les taux de conformité aux lignes directrices varient beaucoup. Le but de cette étude était de décrire la pratique clinique en matière de thromboprophylaxie dans notre centre de traumatologie canadien de niveau 1 au cours des 24 premières heures suivant un traumatisme et l'impact d'un service de prévention des thromboses.

Méthodes : Nous avons procédé à une revue rétrospective des dossiers médicaux de patients adultes hospitalisés en traumatologie entre le 1^{er} janvier 2012 et le 30 juin 2013. Le taux de TEV a été mesuré et nous avons vérifié si un schéma prophylactique initial avait été utilisé, s'il y avait des contre-indications potentielles à la prophylaxie et si le service de prévention des thromboses avait été mis à contribution.

Résultats : En tout, 633 patients ont été inclus, 459 hommes et 174 femmes âgés en moyenne de 47,4 ans. L'indice moyen de gravité de la blessure (IGB) était de 15,8. Le taux global de TEV a été de 2,8 %. En tout 514 patients (81,2 %) ont reçu une thromboprophylaxie (mécanique chez 302 [47,7 %] et pharmacologique chez 231 [36,5 %]; 19 patients ont reçu les 2 types de prophylaxie). Le service de prévention des thromboses a été impliqué dans 164 dossiers (25,9 %). Les patients vus par le service de prévention des thromboses étaient plus susceptibles que les autres patients de recevoir une thromboprophylaxie (145 [88,4 %] c. 369 [78,7 %], $p < 0,01$).

Conclusion : La conformité aux lignes directrices sur la thromboprophylaxie a été sous-optimale, et il est possible de l'améliorer. L'implication d'un service de prévention des thromboses semble améliorer la conformité aux lignes directrices sur la thromboprophylaxie et y faire appel plus souvent pourrait améliorer les résultats cliniques.

Venous thromboembolism (VTE) is a common complication seen in patients who experience trauma.¹ Venous thromboembolism includes deep vein thrombosis and pulmonary emboli, both of which are associated with substantial morbidity and mortality. Pulmonary embolism is associated with mortality rates ranging from 10% to 50%^{1,2} and is the third-leading cause of death in patients with trauma who survive beyond the first 24 hours.³ The American College of Surgeons Committee on Trauma reported rates of deep vein thrombosis and pulmonary embolism of 1.4% and 0.6%, respectively, in patients with trauma.⁴ Life-threatening VTE events can occur at any point during the hospital stay but tend to occur early in this population.^{5,6}

It is estimated that 50% of patients with trauma experience VTE without the use of prophylaxis.³ A Cochrane review of VTE prophylaxis in this population showed that patients who received prophylaxis had a lower risk of deep vein thrombosis and recommended the use of any method of deep vein thrombosis prophylaxis for people with severe trauma.⁷ As a result, routine use of VTE prophylaxis for all admitted patients with major trauma is recommended.³

Prophylaxis can be mechanical, consisting of sequential compression devices, or pharmacologic, in the form of administered medications. Pharmacologic prophylaxis has been shown to significantly reduce the risk of deep vein thrombosis and pulmonary embolism and is therefore recommended for all patients with major trauma.⁸ Low-dose unfractionated heparin has historically been preferred over low-molecular-weight heparin (LMWH) for pharmacologic prophylaxis, perhaps because of the perceived increase in risk of bleeding and difficulty in reversing the effect of the latter compared to unfractionated heparin.⁹ However, studies have shown the superiority of LMWH compared to unfractionated heparin in prevention of VTE after major trauma.⁹⁻¹¹

Despite strong evidence and guidelines advocating for the routine use of pharmacologic prophylaxis, compliance rates vary widely. Currently, to our knowledge, there are no reported Canadian studies looking at compliance with the use of VTE prophylaxis within the first 24 hours in patients with trauma. In addition, our trauma centre has a clinical thrombosis service, novel to our site, which is frequently involved in managing VTE prophylaxis in our patients with trauma. The aim of this study was to describe the clinical practice related to the ordering and administration of VTE prophylaxis within the first 24 hours at our level 1 Canadian trauma centre. In addition, we aimed to determine the incidence of VTE in our trauma population and the impact of the thrombosis consultation service.

METHODS

This was a retrospective review of the health records of adult patients with trauma who presented to the Hamilton

General Hospital, Hamilton Health Sciences between Jan. 1, 2012, and June 30, 2013. The hospital is a regional level 1 trauma centre that serves a population of 2.5 million in southern Ontario. Based on its long-standing history of leading hematologic research,¹²⁻¹⁶ it also has a clinical thrombosis service, which is available to any hospital patient and is commonly involved in the care of inpatients with trauma.

We identified patients through the Hamilton Health Sciences Trauma Registry, which contains data for all patients with an Injury Severity Score (ISS) of 12 or higher and those with an ISS less than 12 with trauma team activation. We included consecutive patients aged 16 years or more who were admitted to the trauma service. Exclusion criteria were hospital length of stay less than 1 day, death within 24 hours of arrival, direct admission bypassing the emergency department and admission to services other than trauma (e.g., orthopedics, neurosurgery). We obtained demographic data, mechanism of injury, ISS, Maximum Abbreviated Injury Scale (MAIS) for head score, hospital length of stay and information on in-hospital death directly from the trauma registry. We used a chart review to ascertain whether a prophylactic regimen was ordered for the patient, whether any regimen (pharmacologic or mechanical) was received by the patient and the involvement of the hospital thrombosis service. We defined VTE positivity as deep vein thrombosis or pulmonary embolism diagnosed on leg ultrasonography, chest computed tomography or ventilation/perfusion scan during the index admission. A random sample of 5% of the cases was drawn and reabstracted by a second abstractor to assess agreement. The overall percent agreement exceeded 95% for selected data elements.

We analyzed the data using descriptive statistics. Categorical variables were expressed as frequencies and percentages, and continuous variables as means with standard deviation. We assessed practice differences between patients with a brain injury (defined as MAIS score ≥ 2) versus no brain injury (MAIS score ≤ 1) using the χ^2 test and Fisher exact test for categorical variables, and the Student *t* test for continuous variables. We carried out all statistical analyses using SPSS version 22.0 (IBM Corp.). We considered *p* values < 0.05 statistically significant.

Ethics approval

The study received ethics approval from the Hamilton Integrated Research Ethics Board.

RESULTS

Of the 1138 patients entered in the Hamilton Health Sciences Trauma Registry between Jan. 1, 2012, and June 30, 2013, 477 were excluded from analysis (179 with length of stay < 1 d, 175 with direct admissions, 123

admitted to other services), and an additional 28 charts were unavailable for review. Thus, our study cohort consisted of 633 patients. The patients' baseline characteristics are presented in Table 1. The mean age was 47.4 years. Most patients were male (459 [72.5%]) and experienced blunt trauma (585 [92.4%]). The mean ISS was 15.8. The mean hospital length of stay was 12.4 days. Sixty-five patients (10.3%) were receiving antiplatelet or anticoagulation medication on admission. The incidence of VTE was calculated at 2.8% (18 patients), and the crude in-hospital mortality rate was 3.9% (25 deaths).

Venous thromboembolism prophylaxis was ordered for 528 patients (83.4%) within the first 24 hours after admission. Despite the orders, 14 (2.6%) of these patients did not receive any prophylactic measures. Of the 633 patients, 302 (47.7%) received mechanical devices, 231 (36.5%) received pharmacologic agents, 19 (3.0%) received both pharmacologic and mechanical measures, and 100 (15.8%) received no prophylaxis (Table 2). In total, 402 patients (63.5%) received no pharmacologic prophylaxis. Potential contraindications were documented for 336 (83.6%) of these patients, in most cases signs of extravasation or active bleeding (287 [85.4%]). Other contraindications related to surgical or angiographic procedures (56 [16.7%]) or blood transfusion requirements (16 [4.8%]).

Of the 268 patients with a brain injury, 54 (20.1%) received pharmacologic prophylaxis, compared to 182/365 (49.9%) of those with no brain injury ($p < 0.001$). Potential contraindications for patients who received no pharmacologic prophylaxis differed significantly between the 2 groups: a contraindication was identified for 242 patients (90.3%) in the brain-injured group, compared to 256 (70.1%) in the group without a

brain injury ($p < 0.001$). There was no difference in the frequency of VTE between the 2 groups (3% v. 3%).

Fig. 1 presents the pharmacologic agents administered to patients. Heparin (5000 units given subcutaneously every 12 h) was most commonly administered (110 patients [47.6%]). The remaining patients received LMWH medications: dalteparin (5000 units administered subcutaneously daily) (97 patients [42.0%]), or enoxaparin (30 mg given subcutaneously twice daily or 40 mg given subcutaneously daily) (24 patients [10.4%]).

The thrombosis service consulted on 164 patients (25.9%) (Table 3). Compared to patients who did not receive a consultation, those who received a consultation

Table 2. Early venous thromboembolism prophylaxis ordered and received

Variable	No. (%) of patients <i>n</i> = 633
Venous thromboembolism prophylaxis ordered	528 (83.4)
Venous thromboembolism prophylaxis received	514 (81.2)
Type of prophylaxis received*	
Mechanical	302 (47.7)
Pharmacologic	231 (36.5)
None	100 (15.8)
Potential contraindication for cases with no pharmacologic prophylaxis†	336 (53.1)
Signs of active bleeding (including radiographic)	287 (85.4)
Surgical or angiographic procedure	56 (16.7)
Blood transfusion	16 (4.8)
Thrombosis service recommended against initiation	24 (7.1)
No potential contraindication documented for cases with no pharmacologic prophylaxis	66 (10.4)

*Nineteen patients received both pharmacologic and mechanical prophylaxis.

†Some patients had more than 1 contraindication.

Table 1. Demographic and clinical characteristics of patients with trauma admitted to a trauma service

Characteristic	No. (%) of patients* <i>n</i> = 633
Age, yr, mean $\pm$ SD	47.4 $\pm$ 20
Male sex	459 (72.5)
Injury Severity Score, mean $\pm$ SD	15.8 $\pm$ 9
Mechanism of injury	
Blunt	585 (92.4)
Penetrating	46 (7.3)
Unknown	2 (0.3)
Antiplatelet or anticoagulation medication on admission	65 (10.3)
Admitted to intensive care unit from emergency department	316 (49.9)
Intensive care unit length of stay, d, mean $\pm$ SD	8.9 $\pm$ 10
Hospital length of stay, d, mean $\pm$ SD	12.4 $\pm$ 17
Venous thromboembolism	18 (2.8)
Died in hospital	25 (3.9)

SD = standard deviation.

*Except where noted otherwise.

Fig. 1. Pharmacologic agents administered for venous thromboembolism prophylaxis. Q = every; SC = subcutaneously.

Table 3. Comparison of patients with and without thrombosis service consultation

Variable	No. (%) of patients*		p value
	Seen by thrombosis service n = 164	Not seen by thrombosis service n = 469	
Age, yr, mean $\pm$ SD	51.2 $\pm$ 21.0	46.4 $\pm$ 20.0	< 0.05
Male sex	108 (65.8)	351 (74.8)	< 0.05
Injury Severity Score, mean $\pm$ SD	15.7 $\pm$ 8.0	15.8 $\pm$ 10.0	0.8
Head MAIS score $\geq$ 2	60 (36.6)	208 (44.3)	0.08
Head MAIS score $\leq$ 1	104 (63.4)	261 (55.6)	0.08
Mean head MAIS score $\pm$ SD	1.1 $\pm$ 1.6	1.5 $\pm$ 1.8	< 0.05
Mechanism of injury			
Blunt	160 (97.6)	425 (90.6)	< 0.01
Penetrating	3 (1.8)	43 (9.2)	
Unknown	1 (0.6)	1 (0.2)	
Antiplatelet or anticoagulation medication on admission	34 (20.7)	31 (6.6)	< 0.001
Intensive care unit length of stay, d, mean $\pm$ SD	9.5 $\pm$ 9.0	9.0 $\pm$ 8.0	0.7
Hospital length of stay, d, mean $\pm$ SD	13.1 $\pm$ 22.0	12.2 $\pm$ 16.0	0.6
Venous thromboembolism	5 (3.0)	13 (2.8)	0.8
Died in hospital	4 (2.4)	21 (4.5)	0.2
Venous thromboembolism prophylaxis ordered	147 (89.6)	381 (81.2)	< 0.05
Venous thromboembolism prophylaxis received	145 (88.4)	369 (78.7)	< 0.05
Type of prophylaxis received†			
Mechanical	82 (56.6)	220 (59.6)	0.6
Pharmacologic	65 (44.8)	166 (45.0)	0.97
No pharmacologic prophylaxis received	99 (60.4)	303 (64.6)	0.3
Potential contraindication for cases with no pharmacologic prophylaxis‡	92 (92.9)	244 (80.5)	< 0.01
Signs of active bleeding	72 (78.3)	204 (83.6)	0.2
Surgical or angiographic procedure	14 (15.2)	42 (17.2)	0.7
Blood transfusion	5 (5.4)	11 (4.5)	0.7
Thrombosis service recommended against initiation	22 (23.9)	2 (0.8)	< 0.001
No potential contraindication documented for cases with no pharmacologic prophylaxis	7 (7.1)	59 (19.5)	< 0.01

MAIS = Maximum Abbreviated Injury Scale; SD = standard deviation.
 *Except where noted otherwise.
 †Nineteen patients, 2 seen by the thrombosis service and 17 not seen by the thrombosis service, received both mechanical and pharmacologic prophylaxis.
 ‡Some patients had more than 1 contraindication.

were significantly older (mean 51.2 yr v. 46.4 yr, $p < 0.05$) and were more likely to have experienced blunt trauma (160 [97.6%] v. 425 [90.6%], $p < 0.01$) and to have been receiving antiplatelet or anticoagulation medication on admission (34 [20.7%] v. 31 [6.6%], $p < 0.001$). No differences were observed in the proportion of brain-injured patients, ISS, hospital length of stay, in-hospital mortality rate or rate of VTE occurrence between the 2 groups. Patients who received a thrombosis service consultation were more likely to receive VTE prophylaxis than those without a consultation (145 [88.4%] v. 369 [78.7%], $p < 0.01$). However, no differences were observed in administration of pharmacologic prophylaxis between the 2 groups (65 [39.6%] v. 166 [35.4%], $p = 0.3$). Overall, there was no difference in VTE occurrence between patients seen and not seen by the thrombosis service (5 [3.0%] v. 13 [2.8%], $p = 0.8$).

DISCUSSION

Patients with multisystem injuries and traumatic brain injuries (TBIs) are at high risk for VTE events.^{6,17} Two-thirds of VTEs identified on screening venous duplex ultrasonography are asymptomatic,¹⁸ but these patients remain at increased risk for illness and death. This emphasizes the importance of routine, standardized VTE prophylaxis in patients with trauma. Overall, the rate of VTE events among admitted patients with trauma at our centre, 3%, is in keeping with the published literature.^{2,4,11} However, in the current study, we identified important areas of potential improvement that may lead to decreasing this number even further.

One out of 5 patients did not receive any VTE prophylaxis within 24 hours of admission to the trauma service, and only one-third received pharmacologic prophylaxis.

The goal is to initiate VTE prophylaxis as soon as is considered safe, with a target of initiation within 48 hours of presentation, as life-threatening VTE events occur more commonly early during the hospital stay of patients with trauma.⁹ Furthermore, a higher risk of pulmonary embolism in these patients was shown when initiation of VTE pharmacologic prophylaxis occurred beyond the first day of admission.¹¹

Interestingly, not all patients for whom any type of VTE prophylaxis was ordered received it. Our study was not able to provide information on the cause of this; however, Machado-Aranda and colleagues¹⁹ showed that a regimen of single daily dosing of LMWH is less likely to have challenges with missed doses. Missed VTE prophylaxis doses are associated with a higher rate of VTE.²⁰ Once-daily dosing of LMWH was the least common form of pharmacologic prophylaxis in the current study, and unfractionated heparin was the most common. The initiation of VTE prophylaxis with LMWH appears to be delayed compared to unfractionated heparin,⁹ possibly a result of a perceived increased risk of bleeding or concerns regarding the reversibility of LMWH compared to unfractionated heparin. Alternatively, it has been noted in our institution (despite lack of evidence) that initiation of pharmacologic prophylaxis in clinical practice may be held if surgical procedures are planned in the following 24 hours. It is possible that, in the present study, the ordered prophylaxis was not administered for this reason. Identification of causes of the lack of administration of ordered prophylaxis remains an important part of future studies.

Lower rates of pulmonary embolism have been reported by trauma centres with the greatest use of LMWH,¹¹ and standardization of VTE prophylaxis in patients with trauma has been shown to decrease the rate of VTE events.¹⁹ Furthermore, once-daily dosing regimens of enoxaparin are associated with greater risk reduction than twice-daily dosing.⁹ Implementation of standardized prescribing of LMWH prophylaxis in certain patients with trauma — those who do not have any predefined contraindications — may aid us in improving our rate of VTE events. However, 30% of our patients with no brain injury did not have an identified contraindication to pharmacologic prophylaxis. This indicates that further education is required for prescribers to identify when no contraindications are present. Education measures to improve the implementation of VTE prophylaxis in the absence of contraindications could include use of a VTE “default” prophylaxis order set on admission, which would identify the presence or absence of contraindications. The absence of contraindications would trigger implementation of VTE prophylaxis, whereas the presence of contraindications would trigger thrombosis service consultation.

One in 5 patients treated for major injury at trauma centres have a TBI.²¹ These patients are at increased risk for VTE events secondary to prolonged immobilization

and systemic hypercoagulability.¹⁷ Concerns regarding exacerbating intracranial bleeding with the initiation of LMWH prophylaxis in patients with intracranial hemorrhage have limited its use in this population, with only 18.1% of patients receiving LMWH prophylaxis in 1 multicentre report.²² Studies have shown a wide range of hemorrhagic progression following administration of LMWH prophylaxis, from 1% to 14.5%.^{22,23} This has led to concerns about administration of pharmacologic prophylaxis before 7 days.²² However, Byrne and colleagues²⁴ showed that patients with severe TBI who received LMWH prophylaxis within 72 hours had significantly lower rates of VTE events than those who received prophylaxis after 72 hours. Furthermore, there was no association between early prophylaxis and increased risk of late neurosurgical interventions or death. Phelan and colleagues²⁵ showed that, in patients with TBI who had repeat head computed tomography showing stable intracranial hemorrhage, pharmacologic prophylaxis could be initiated as early as 24 hours after injury. These studies suggest that LMWH should be the preferred pharmacologic prophylaxis for patients with severe TBI. Randomized controlled trials, including the PROTEST (PROphylaxis for Venous ThromboEmbolism in Severe Traumatic Brain Injury) study (<https://clinicaltrials.gov/ct2/show/NCT03559114?term=trauma&cond=vte&rank=9>), are ongoing to determine the safety of pharmacologic prophylaxis in patients with TBI. Given the existing data, there is room for improvement in our management of this population with regard to VTE prophylaxis.

Only one-quarter of patients admitted to our trauma service were seen by the thrombosis service. Patients who were receiving anticoagulants/antiplatelet medications on admission and those who were older were more likely to be referred to the thrombosis service. There was also a trend toward more consultations for brain-injured patients, which may reflect the more complicated decision-making involved in VTE prophylaxis in these patients and a need for support in clinical decision-making.

In the current study, higher rates of any type of VTE prophylaxis and pharmacologic VTE prophylaxis were observed among patients seen by the thrombosis service than among those not seen by the service. There is a paucity of evidence in the literature regarding the use or impact of thrombosis service involvement on the use of VTE prophylaxis in patients with trauma. Historically, thrombosis services have been used mainly for patients requiring long-term prophylactic anticoagulation (i.e., for atrial fibrillation) or treatment of VTE. The use of multidisciplinary anticoagulation-management teams results in shorter length of hospital stay,²⁶ fewer bleeding events^{26–28} and improved therapeutic dosing.^{26,28} More recently, a study looking at the impact of a dedicated thrombosis service for cancer-associated thrombosis showed an improvement in consistent management of cancer-associated

thrombosis, improved adherence to guidelines and improved access to LMWH.²⁹ In the current study, patients who were seen by the thrombosis consultation service and had prophylaxis ordered received it at a higher rate than those who had prophylaxis ordered but were not seen by the thrombosis service. The cause of this increased rate of administration of ordered VTE prophylaxis is unclear and may represent a Hawthorne effect, but this result shows another potential benefit of the involvement of the thrombosis service in this high-risk population. Interestingly, our study failed to show any outcome benefit of the involvement of the thrombosis service, with equivalent VTE event rates among patients who were seen by the service and those who were not, despite increased efficacy for prescribing any type of VTE prophylaxis when the thrombosis service was involved. This may, however, have been influenced by the small number of patients who were seen by the thrombosis service overall.

These studies, combined with our results, suggest that standardization of involvement of the thrombosis service for admitted patients with multisystem injuries and trauma may aid in improving prescribing practices for pharmacologic and all-type VTE prophylaxis. However, further, high-quality prospective research is needed to determine whether involvement of the thrombosis service will improve not only prescribing practices but also clinically relevant outcomes. Furthermore, mandatory involvement of the thrombosis service for admitted patients with trauma may vastly affect the service's workload and be unsustainable in the long term. One option may be to implement mandatory triggers for involvement of the service, such as preadmission use of anticoagulation or presence of TBI. One-quarter of patients in the current study were seen in consultation by the thrombosis service. Use of the criterion of presence of TBI (indicated by an MAIS head score ≥ 2) would have triggered consultation for 268 patients (42%), an increase of 104 consultations. The feasibility and sustainability of this increase in workload would require further assessment and investigation. Alternative strategies may include the use of standardized VTE prophylaxis order sets, which would trigger referral to the thrombosis service based on the presence or absence of contraindications to prophylaxis, or the use of a thrombosis pharmacist on trauma rounds for review of VTE prophylaxis.

Limitations

This study is limited by its retrospective nature, and, as such, we were unable to capture real-time clinical decision-making. In addition, the retrospective review captured only patients symptomatic from VTE events, as patients with trauma are not routinely screened for VTE at our centre. We inferred potential contraindications to VTE prophylaxis based on the presence of predefined characteristics.

Furthermore, we did not assess longitudinal VTE prophylaxis administration; rather, we focused on the first 24 hours after admission. This may have led us to miss other clinical practices that could affect VTE occurrence, such as discontinuation of prophylaxis based on the results of repeat head computed tomography for brain-injured patients. In addition, we did not account for the presence of contraindications to mechanical VTE prophylaxis, such as lower extremity fractures. Last, we did not capture complications of VTE prophylaxis, including bleeding complications or progression of hemorrhage, in patients with TBI.

CONCLUSION

Our VTE event rates were low and are consistent with the reported rates in the literature, but opportunities exist to improve processes of VTE prophylaxis administration at our trauma centre. Future quality-improvement initiatives focusing on expansion of the involvement of the thrombosis service for patients with trauma, standardization of routine LMWH use as first-line prophylaxis in this population and mandatory default use of mechanical prophylaxis may help to improve patient care and outcomes.

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