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Coagulation Day 2010: an Austrian survey on the routine of thromboprophylaxis in intensive care

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Abstract Purpose: Venous thromboembolism (VTE) is a common but often overlooked life-threatening complication of critical illness. The aim of this cross-sectional survey was to assess current practice of thromboprophylaxis as well as adherence to international guidelines. **Methods:** After ethics committee approval, all intensive care units in Austrian hospitals treating adult patients were invited to participate in this web-based survey. Anonymized data on each patient treated at the participating intensive care units on Coagulation Day 2010 were collected using an electronic case report form. Risk assessment, choice and monitoring of anticoagulants, means of mechanical prophylaxis, and demographic data were recorded. **Results:** Data from 325 critically ill patients were collected. Patients had a median of four

risk factors for thrombosis and 6 % suffered from VTE. Of the 325 patients, 80 % received low molecular weight heparins subcutaneously, 10 % received unfractionated heparin intravenously, 1 % received alternative anticoagulants and 9 % received no pharmacological prophylaxis. Mechanical prophylaxis was used in 49 % with a predominant use of graduated compression stockings. In 39 % a combination of pharmacological and mechanical prophylaxis was applied and 5 % received no prophylaxis at all. Overall guideline adherence was 40 % on Coagulation Day 2010. **Conclusion:** Current practice of thromboprophylaxis is predominantly based on the administration of low molecular weight heparins prescribed at rather arbitrary doses without a discernible relationship to drug monitoring, thromboembolic risk factors, vasopressor use or fluid balance. The use of mechanical prophylaxis, evaluation of risk scores and overall guideline adherence must be further encouraged by education, training and communication.

Keywords Critical illness · Prevention of thromboembolism, low molecular weight heparin · Compression stockings, intermittent pneumatic compression devices

Introduction

Venous thromboembolism (VTE) with its clinical manifestations of deep venous thrombosis (DVT) and pulmonary embolism (PE) is common in intensive care patients [1]. Despite prophylaxis, more than 15 % of critically ill patients suffer from VTE [2]. This alarming prevalence of VTE in critical illness may in part be caused by the simultaneous occurrence of multiple risk factors such as age, immobilization, sepsis, trauma and/or decreased bioavailability of subcutaneous (s.c.) low molecular weight heparins (LMWH) [3–6]. VTE is life-threatening and DVT, even if initially asymptomatic, may provoke post-thrombotic syndrome as an irreversible life-long consequence [4, 7]. These clinical manifestations without doubt decrease quality of life after surviving critical illness and contribute to increased overall health-care costs [8]. Despite their impact on patient safety and patient outcome, intensive care physicians appear to be more concerned about bleeding than thrombotic events [9].

International and interdisciplinary recommendations exist on the prevention of VTE in critical illness [2]. Management should include an individualized risk assessment and pharmacological thromboprophylaxis—if not contraindicated—using unfractionated heparin (UFH) or LMWH (level of recommendation grade 1, level of evidence A). For critical care patients who are at high risk of bleeding, the optimal use of mechanical thromboprophylaxis with graduated compression stockings (GCS) and/or intermittent pneumatic compression (IPC) at least until the bleeding risk decreases is recommended (level of recommendation grade 1, level of evidence A). When the high bleeding risk decreases, pharmacological thromboprophylaxis should be substituted for or added to the mechanical thromboprophylaxis (level of recommendation grade 1, level of evidence C). Adherence to guidelines in general is known to be low but adherence to guidelines on thromboprophylaxis in critically ill patients nationwide is unknown. Accordingly, the aim of this cross-sectional survey in Austrian intensive care units (ICU) was to assess current practice of VTE risk assessment, methods and monitoring of thromboprophylaxis as well as the degree of guideline adherence.

Methods

The survey was endorsed as a national observational network trial by the Task Force of Perioperative Coagulation and by the Intensive Care section of the Austrian Society of Anaesthesiology, Resuscitation and Intensive Care (OEGARI). The questionnaire was created by members of the Task Force in the German Language and formatted into a personalized electronic Case Report

Form (e-CRF) by an IT expert. The study was approved by the Ethics Committee of the Medical University of Vienna and the General Hospital of Vienna (no. 828/2010, date of vote 12.11.2010).

We invited all ICUs and intermediate care units in Austrian hospitals treating adult patients (independent of their primary specialty) to participate in the web-based survey. As the decision to initiate VTE prophylaxis in children is still made on a case-by-case basis, paediatric and neonatal units were excluded. First we generated a list including electronic contact details of medical directors of all Austrian ICUs. In an email we informed the medical directors about the project, and asked them for their approval and assignment of an intensive care physician on their wards as our contact person. These contact persons were informed about the purpose of the survey and were instructed how to fill in the e-CRF. Contact persons were requested to deliver anonymized data on each patient who was treated at their ICU on Coagulation Day 2010, which was 1 December 2010. The term Coagulation Day was our creation for dedicating one specific day to the topic of coagulation in Austrian ICU patients. After an announcement by email 1 week in advance, an email with the link to the personal e-CRF was sent to each contact person on Coagulation Day 2010. The deadline for data input was 8 December; 2 days before this date a gentle reminder was sent by email.

Questionnaire items

In addition to demographic data the following items were evaluated in the questionnaire:

- Anticoagulants: drugs administered for pharmacological thromboprophylaxis, dosing of anticoagulants and, if any, laboratory tests used for monitoring during pharmacological thromboprophylaxis.
- Mechanical prophylaxis: means of mechanical prophylaxis.
- Risk assessment: underlying and actual diseases, known coagulation disorders and the use of risks scores. For every patient the individual risk profile was determined, including age >40 years, sex, body mass index (BMI) >30 kg/m², severity of illness by the simplified acute physiology score (SAPS) II and the sequential organ failure assessment score (SOFA), presence of heart failure, active cancer, varicose veins, fractures, surgery in the past 2 weeks, central venous line, mechanical ventilation with PEEP.
- Confounding factors: use of vasopressors and positive fluid balance were also evaluated because of their potential inhibiting effect on the bioavailability of s.c. anticoagulants [5, 6]. The size of the respective hospital and the number of beds in the ICU as well as the medical discipline (anaesthesia, internal medicine,

surgery, neurosurgery, neurology) were also documented.

The degree of guideline adherence was assessed by comparing actual practice with international and interdisciplinary recommendations on the prevention of VTE in critical illness [2].

Statistics

Data were analysed using the R software environment (R version 2.13.0, 2011-04-13). Descriptive data are given as number or percentage of the total number of patients if not otherwise stated. For the purpose of readability numbers and percentages were rounded up to whole numbers. For questions with multiple possible answers, each answer was analysed separately in regard to the percentage of positive and negative responses. Due to the descriptive character of the study, no *p* values were computed.

Results

From 186 contacted medical directors of ICUs 101 responded to the invitation to participate in this national survey. Finally, 59 contact persons completed the e-CRF, which gives a response rate of 32 %. Five contact persons were internists, and 91 % were specialists in anaesthesia and intensive care working in ICUs with a median of eight beds (range 6–12 beds). More than half of the patients (54 %) were admitted to ICUs in hospitals with more than 600 beds.

Data from 325 critically ill patients were collected. The patients' characteristics are shown in Table 1. The most common admission diagnoses were postoperative state in 22 %, sepsis in 19 %, brain trauma or craniotomy in 15 %, trauma in 8 %, respiratory failure in 8 %, and cardiac disease in 6 %. Bleeding complications were the reason for admission in 2 % of patients.

Table 2 summarizes the risk factors for VTE. Patients exhibited a median of four risk factors for thrombosis (range one to five). None of the responders reported the use of a score to assess individual patients' risk of thrombosis. On the day of the survey, only 4 % of patients (*n* = 11) suffered from thrombosis and PE was diagnosed in 2 % (*n* = 5).

Figure 1 shows the use of anticoagulants and non-pharmacological thromboprophylaxis in the cohort. Of the 325 patients, 80 % received LMWH and 10 % received UFH. Two patients received alternative anticoagulants (argatroban and danaparoid) for thromboprophylaxis. Overall, 39 % of all patients received GCS and 10 % received IPC. In 39 % of patients a combination of

Table 1 Characteristics of the study population

Characteristics	Value
Patients (<i>n</i>)	
Total	325
Male/female	176/149
Age (years, mean ± SD)	64.0 ± 18.3
BMI ^a (kg/m ² , mean ± SD)	26.8 ± 5.9
SAPS II (median, interquartile range)	33.3 (22.0–44.0)
SOFA (median, interquartile range)	7 (4–10)

^a Reference range 18.5–25 kg/m²

Table 2 Risk factors for VTE in the study population, based on [3, 4]

Factor	% of patients
Age >40 years	88
Central venous line	76
Surgery in the past 2 weeks	58
Mechanical ventilation with PEEP	45
Heart failure (NYHA stage 2–4)	26
BMI >30 kg/m ²	23
Active cancer	20
Sepsis	19
Varicose veins	17
Brain trauma/craniotomy	15
Fractures	13

pharmacological and mechanical prophylaxis was applied. In 83 % of these patients, LMWH or UFH was combined with GCS, in 16 % with IPC, and in 1 % with GCS and IPC. Of the 9 % of patients not receiving any pharmacological prophylaxis, 49 % used GCS, 2 % received IPC, and 1 % both GCS and IPC. Thus overall 5 % of patients received neither pharmacological nor mechanical thromboprophylaxis. Of these patients, 25 % had brain trauma and/or craniotomy.

Of the patients diagnosed with thrombosis or PE, 19 % received no thromboprophylaxis, 31 % received only pharmacological prophylaxis, 44 % received a combination of pharmacological prophylaxis and GCS, and 6 % used GCS only. In none of the patients with a known thrombotic event was IPC applied.

The LMWH administration route was s.c., the reported doses varied considerably with no relationship to drug monitoring, risk factors, vasopressor use and/or fluid balance. UFH was administered as a continuous intravenous (i.v.) infusion, with the dose adjusted according to the aPTT results. LMWH was monitored using aPTT in 20 % and using anti-Xa levels in 25 % of patients on LMWH. Thirty seven percent of these had a creatinine clearance below 30 ml/min. Conversely, 17 % of patients with a creatinine clearance below 30 ml/min received LMWH without anti-Xa monitoring. Anti-Xa was monitored in 36 % of patients with brain trauma/craniotomy who received LMWH.

Fig. 1 Use of pharmacological and mechanical thromboprophylaxis alone or in combination (LMWH low molecular weight heparin, UFH unfractionated heparin, GCS graduated compression stockings, IPC intermittent pneumatic compression)

There was no relevant difference between hospitals with more or fewer than 600 beds regarding the use of pharmacological prophylaxis (LMWH 52 % vs. 48 %, UFH 63 % vs. 37 %) and GCS (44 % vs. 56 %), but 71 % of patients receiving IPC were treated in hospitals with more than 600 beds. Regarding LMWH monitoring, 84 % of those patients in whom anti-Xa was used were in big hospitals with more than 600 beds, while 71 % of those in whom aPTT was used were in smaller hospitals with fewer than 600 beds.

Discussion

The present cross-sectional survey in Austrian ICUs addressed the current practice of VTE risk assessment as well as methods and monitoring of thromboprophylaxis. Confirming and extending previous surveys, guideline

adherence was moderate [10, 11]. A combination of pharmacological and mechanical methods for thromboprophylaxis is recommended for critically ill patients at high risk of bleeding and/or DVT [2]. Despite the presence of a median of four risk factors, the Coagulation Day 2010 survey showed the implementation of this particular recommendation in only 39 % of patients. A previous survey performed in France and Canada in 2003 found that combined prophylactic modalities were used in less than 10 % [10]. We can only speculate on the reasons for this attitude but it may—at least in part—be due to insufficient communication and knowledge of published guidelines, as well as limited recognition of expert panels and their consensus statements.

The most severe violation of the VTE prophylaxis guidelines was observed in 5 % of patients in our survey who received neither pharmacological nor mechanical prophylaxis. Our questionnaire did not assess the reasons for therapeutic decisions, but not implementing anticoagulation could be explained by missed opportunities for prescription, combined contraindications against the use of anticoagulants and mechanical thromboprophylaxis, or the perceived risk of bleeding in these patients. In fact, guidelines do not define “safe” time-points for starting anticoagulants and these are left to the clinician’s discretion. The limited use of mechanical devices was particularly pronounced in patients with brain trauma/craniotomy. Although there is strong evidence for the use of especially IPC in neurosurgical patients (level of recommendation grade 1, level of evidence A) [2], only five of these patients in our survey received mechanical prophylaxis. Cochrane analyses have shown that IPC is beneficial in preventing VTE in high-risk patients and have revealed an additional benefit of IPC if combined with pharmacological prophylaxis [12]. IPC can also be used easily in obese patients. In none of the patients diagnosed with a thrombotic event in our survey was IPC provided. It has to be taken into account that a recent DVT is a contraindication to the use of IPC.

Another Cochrane review has shown that GCS is beneficial in various groups of hospitalized patients [13]. Despite this evidence, only about a third of the patients in our survey received (additive) mechanical prophylaxis. The limited use may be due to educational, economic and logistic issues [14]. Nursing personnel are often concerned about patient discomfort and adverse events of GCS such as blisters and pressure sores [11, 14]. However, in the studies included in the above-mentioned Cochrane review no serious adverse events were documented [13]. In a recent study in orthopaedic surgery, comfort during IPC was rated by the patients as good (7.6 on a scale from 1 to 10) [15]. Adequate dosing of IPC has been reported to be more than 6 h per day, and this needs to be acknowledged [15]. Given the scientific evidence of the efficacy and patient satisfaction, more efforts are needed to increase the acceptance of mechanical

thromboprophylaxis among health-care providers—both intensivists and nurses.

There is an ongoing debate regarding the bioavailability of LMWH administered s.c. in critically ill patients receiving vasopressors and/or high amounts of fluids [5, 6]. Robinson et al. [16] have recently suggested that the dose of s.c. enoxaparin should be increased to achieve anti-Xa activities in the recommended range [17]. In this context it needs to be born in mind that target ranges are different for different LMWHs, and that it is still unknown if targets derived from pharmacological studies in healthy volunteers are indeed applicable to the critically ill population with major, heterogeneous and unpredictable modifications in pharmacokinetics and pharmacodynamics, as well as changes in haemostatic competence. Another problem is the only weak relationship between anti-Xa activity and clinical occurrence of symptomatic and asymptomatic VTE [18–20]. However, determination of anti-Xa activity is recommended if renal elimination of LMWH is impaired [2]. Also in patients at risk of bleeding into delicate regions (e.g. the central nervous system), drug monitoring could be useful. The uncertainty of clinicians regarding the utility and practicability of the anti-Xa testing is reflected by its limited use in our survey (25 % of patients on LMWH), even among those critically ill patients with renal insufficiency and brain trauma/craniotomy. In 20 % of patients who received LMWH, aPTT was analysed, although it is not sensitive enough for quantifying the biological effects of LMWH thromboprophylaxis. Only severe overdosing or accumulation of LMWH prolongs aPTT. The prescribed doses of LMWH varied considerably among patients, obviously as a result of lack of targeting based on the laboratory results for adequate drug monitoring, and without a clear relationship to risk factors, vasopressor use or fluid balance.

According to our survey, some clinicians in Austria try to avoid all these obstacles linked to s.c. LMWH by continuous prophylactic i.v. administration of UFH, although there is no evidence supporting this approach for primary VTE prevention. Apart from that, the usually targeted aPTT prolongation in Austria of 1.5–2.5 times the control value fulfils the criterion for therapeutic anticoagulation, and may contribute to an increased bleeding risk. Further limitations of conventional coagulation tests have to be considered. In an acute phase response with elevated factor VIII levels, aPTT may be inappropriate for monitoring the effects of UFH [21]. Some alternative anticoagulants as well as the new direct thrombin inhibitors modify the results of conventional coagulation tests such as aPTT [22]. Altogether, alternative laboratory methods may help to quantitatively assess the effects of anticoagulant drugs [23].

The risk profile of intensive care patients in our study arises from a combination of multiple risk factors. The patients displayed a median of four risk factors. A combination of risk factors is considered to be associated with an increased risk of VTE; e.g. patients heterozygous for

factor V Leiden have a three- to sevenfold increased risk. Oral contraceptives confer a two- to threefold increased risk. In the presence of both risk factors, the relative risk is increased 34-fold [4]. Critically ill patients exhibit mainly temporary risk factors such as sepsis, fractures, surgery, or central venous catheterization (Table 2). The magnitude of individual risk elevation due to combinations of temporary risk factors is not clear; however, despite the respective recommendation (level of recommendation grade 1, level of evidence A) [2] individual risk scores were not determined.

Interestingly, the incidence of clinical thrombosis was very low in our patients. It is unclear whether VTE did not occur or was simply not diagnosed. Our survey data were based on clinical observations only and not on sophisticated laboratory or sonographic techniques. VTE can be clinically inapparent. In a study of 261 ICU patients, 9.6 % had sonographically proven proximal DVT, and in all but one patient this was clinically unsuspected [24]. It needs to be considered that both silent and overt DVT are risk factors for the potentially life-threatening event of PE, which is also often overlooked and only found after death [4]. DVT with or without clinical symptoms can be complicated by post-thrombotic syndrome which usually develops months later—out of sight; learning from cause and effect is therefore not possible for intensivists. However, the rate of post-thrombotic syndrome is suggested to be high and may represent a chronic severe residue after surviving critical illness. It is noteworthy that post-thrombotic syndrome can be prevented by consistent use of GCS [4, 7].

We obtained our survey data from ICUs with a median of eight beds which is the size of an average Austrian ICU (range 6–12 beds). According to our survey, hospital size is relevant for management strategies in the ICU. Anti-Xa testing was mainly performed in big hospitals with more than 600 beds, whereas aPTT was mainly used in smaller hospitals. Almost three-quarters of patients receiving IPC were treated in big hospitals. It can be speculated that the costs and the provision of materials and qualified personnel determine the availability of mechanical prophylaxis and laboratory testing.

A limitation of our survey was that some aspects, e.g. concerning the general haemostatic management, were not included. We tried to keep the survey short and user-friendly. Furthermore, the results of the survey mirror current practice of thromboprophylaxis in 325 critically ill patients treated in 2010 in Austria, and should not be transferred directly to other settings and countries. Nevertheless, compared to previous surveys [10, 11], our results may indicate an improvement in overall adherence to VTE prophylaxis guidelines over the last decade. The response rate was higher than in Italy (17 %) but lower than in France (45 %) and Germany (50 %) [10, 11, 25]. However, we believe that opinion polls concerning guidelines in wards, departments or hospitals do not reflect reality regarding putting of these recommendations

into practice. We hope that the Austrian ICU data bank created by the Austrian Society of Anaesthesiology will receive more input from our future network trials among all disciplines involved in intensive care therapy.

Finally, unclear questions in our e-CRF and errors in data reporting could have contributed to unexpected responses. This is a potential limitation of any survey—paper-based or web-based.

Conclusion

Inherent problems in diagnosing VTE and its complications may nourish the general underestimation of its high

clinical relevance and need for adequate prevention. Increasing awareness by education, training and communication may improve quality of care and guideline adherence which was 40 % in our 2010 Austrian survey. Especially the use of mechanical prophylaxis combined with anticoagulants and appropriate drug-monitoring should be encouraged.

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