A cross-sectional evaluation of venous thromboembolism risk and use of venous thromboembolism prophylaxis in hospitalized patients in Senegal

Évaluation du risque de maladie thromboembolique veineuse et de sa prophylaxie chez les patients hospitalisés au Sénégal

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KEYWORDS
Venous thromboembolism; Prophylaxis

Summary
Background. — Venous thromboembolism is a common and preventable cause of morbidity and mortality in hospitalized patients. There is a lack of data on the distribution of risk factors and prophylaxis practices in sub-Saharan Africa.

Abbreviations: ACCP, American College of Chest Physicians; CI, confidence interval; DVT, deep vein thrombosis; ENDORSE, Epidemiologic International Day for the Evaluation of Patients at Risk for Venous Thromboembolism in the Acute Hospital Care Setting; LMWH, low-molecular-weight heparin; PE, pulmonary embolism; TROMBUS, Table ronde de mobilisation pour le bon usage des antithrombotiques (Round Table of Mobilization for the Best Use of Antithrombotics); UFH, unfractionated heparin; VTE, venous thromboembolism.

Background

VTE is a common complication that affects patients hospitalized for a variety of medical and surgical conditions. It contributes to longer duration of hospitalization stay, morbidity and mortality, with PE accounting for 5–10% of deaths in hospitalized patients [1]. VTE is often asymptomatic, misdiagnosed and unrecognized at death, as there is a lack of routine postmortem examinations. These factors are thought to result in a marked underestimation of VTE incidence [2].

VTE in hospitalized patients is often thought of as a consequence of surgery, as major surgery is a risk factor, but medical patients also are at risk. Non-surgical patients account for 70–80% of fatal PE cases and 50–70% of symptomatic thromboembolic events [3]. In an 8-month prospective screening study, DVT was detected by ultrasound in 33% of adults admitted to a medical intensive care unit [4]. The high incidence of DVT in medical patients and the high percentage of patients with VTE who are asymptomatic underscore the importance of identifying and assessing the risk of VTE in hospital patients, so that prophylactic strategies can be implemented [5]. Up to 10% of hospital deaths are caused by PE, suggesting that there is room for improvement in identifying patients at risk of VTE and providing VTE prophylaxis [3].

Risk factors for VTE are well established. Overall, VTE risk should be perceived as the combined result of constitutional risk factors and the added risk attributable to the patient’s current medical situation and/or surgical procedure [6]. The most common personal risk factors include age > 75 years, cancer (history or current), history of VTE,
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and UFH) [1]. New oral anticoagulants are available in
and/or pharmacological prophylaxis (LMWH, fondaparinux
guidelines recommend prophylaxis for patients at moderate-
have been available for almost 20 years [12]. The ACCP
ulation.

This is the most recent study on VTE risk in an African pop-
[11]. The most frequent risk factors for PE were malignancy
mortem reports in Nigeria found a prevalence of PE of 2.9%
was included in this global ENDORSE study.

A possible effect of race and ethnicity on the incidence
VTE has been reported [9]. Some authors have suggested
that a higher prevalence of VTE in Caucasians is due to the
fact that factor V Leiden is more prevalent in Caucasian than
in African-American or Asian populations [10]. However,
a recent review of the subject by White and Keenan concluded
that African-American patients have a significantly higher
incidence of first-time VTE exposure and are more likely to
manifest a PE compared with other racial groups, although
the incidence of recurrent VTE is similar across racial groups
[9].

There is a relative paucity of studies on the prevalence
of VTE and its associated risk factors in sub-Saharan African
populations. A retrospective analysis of nearly 1000 post-
mortem reports in Nigeria found a prevalence of PE of 2.9%
[11]. The most frequent risk factors for PE were malignancy
(38%) and immobility for >4 days (28%). To our knowledge,
this is the most recent study on VTE risk in an African pop-
ulation.

Evidence-based consensus guidelines for VTE prophylaxis
have been available for almost 20 years [12]. The ACCP
guidelines recommend prophylaxis for patients at moderate-
to-high risk of VTE, using either mechanical prophylaxis
and/or pharmacological prophylaxis (LMWH, fondaparinux
and UFH) [1]. New oral anticoagulants are available in
western countries, even if they have not yet shown their
superiority and safety against LMWH in diverse situations.
However, prophylaxis with these new oral anticoagulants
must only be given in labelled indications (total hip arthro-
plasty and total knee arthroplasty).

Despite this evidence and the guidelines, physicians often
fail to use this important therapy in a variety of high-risk
situations, including the perioperative period, during critical
illness and among other high-risk medical patients [2].

On the basis of the ENDORSE study methodology [8], a
multidisciplinary group of Senegalese experts (the TROM-
BUS committee) conducted a country-wide assessment of
the prevalence of VTE risk and VTE prophylaxis coverage
in the acute-care setting in Senegal. The aim of the survey
was to acquire accurate prospective data on VTE risk and
VTE prophylaxis in developing countries to support national
disease management.

Methods

The methodology was adapted from the ENDORSE study [8].
Hospitals were considered eligible for enrolment if they con-
tained more than 50 beds: in Senegal, this amounted to
18 functioning hospitals and private clinics with a total of
2084 eligible beds. Stratified sampling was done to ensure
that at least two hospitals were included from each of the
four geographic zones identified in the country. Included
hospitals were randomly selected using a random table. At
hospital level, wards were eligible if they were occupied by
acute medical and surgical patients. All eligible wards within
enrolled hospitals were included in the study.

To comply with the international ENDORSE study, the
following wards were not included: psychiatric; paedi-
atriac; palliative; maternity and obstetric; neonatal; burns
units; ophthalmologic; ear, nose and throat; dermatologic;
alcohol/drug treatment; rehabilitation; accident and emer-
gency.

In eligible wards, the inclusion criteria for patients were
the same as for the ENDORSE study [8]: age ≥40 years in
medical wards or age ≥18 years in surgical wards. In medi-
cal wards, eligible patients included those who were acutely
ill; in surgical wards, eligible patients included those who
had undergone a surgical intervention requiring general or
epidural anaesthesia for at least 45 mins or who were admit-
ted due to a major trauma.

Patients were not eligible if they would have normally
been admitted to an ineligible ward, if they were admitted
for treatment of VTE or for a minor procedure, if their chart
was unavailable or missing or if they refused to give informed
consent. All patients in all eligible wards were screened.

Data collection

After obtaining informed consent from patients, data were
collected using a standardized questionnaire adapted from
the ENDORSE study case report form. Data collected
included: patient demographics; date of admission; medical
history, including risk factors for VTE; surgical interven-
tion; risk factors for bleeding during hospitalization; risk factors
for VTE manifested immediately before admission or in the
first 14 days of hospitalization; type, dose and frequency of
VTE prophylaxis and start or stop date; presence or absence
of anticoagulation therapy and start or stop date; and condi-
tion of patient upon discharge.

Enrolled patients were assessed for VTE risk as per the
ACCP 2004 guidelines ([8], web tables 1 and 2). Patients
considered as being at risk of VTE were classified as being
at moderate, high or highest risk.

Types and use of VTE prophylaxis received by patients
were recorded from their hospital charts. Evaluation of
prophylaxis was done according to both the type and the
dose prescribed. Patients were classified as receiving pro-
phylaxis if a predefined prophylaxis method was prescribed
by a physician during hospitalization. Prophylaxis methods
included antithrombotic drugs (heparins, vitamin K antago-
nists, direct thrombin inhibitors, factor Xa inhibitors) given
for prevention of DVT and PE or mechanical prophylaxis (intermittent pneumatic compression, graduated compression stockings, foot pump).

Clinical situations defined as contraindications to anticoagulant prophylaxis were: intracranial haemorrhage; hepatic impairment; bleeding at hospital admission; active gastroduodenal ulcer; or known bleeding disorder [13].

Statistical analysis

To assess the true occurrence of VTE risk at 10% with a margin of error of 4%, a minimum of 216 patients per analysis group were required.

Collected data were double checked and double entered into Epi Info software, version 6.04. Quantitative data were summarized using the median. Categorical data were summarized using number and percentage. Ninety-five percent CI were calculated.

The proportion of at-risk patients was calculated as the number of patients at moderate, high or highest risk of VTE/number of patients included. The proportion of patients receiving prophylaxis was calculated as the number of patients who received a prescription for prophylaxis/number of patients at risk of VTE.

The study was approved by the Senegalese Ethics Committee (Ministry of Health).

Results

Between October 2008 and November 2008, 943 patients were screened and of these 520 were enrolled for VTE risk assessment in 12 hospitals across Senegal; 306 of these patients were enrolled in Dakar and 214 from the surrounding regions. The number of beds assessed and the reasons for exclusion of patients are shown in Fig. 1. Demographics and reasons for admission of patients are shown in Table 1. The median age of patients on medical wards was 62 years, 150 (54.0%) were men and the median duration of hospitalization was 7 days. The median age of patients on surgical wards was 49 years, 155 (55.8%) were men and the median duration of hospitalization was 8 days.
More than 40% of medical patients but less than 20% of surgical patients had at least one risk factor for VTE prior to admission (Table 2). The most prevalent VTE risk factor present at admission for both groups of patients was long-term immobility. The most prevalent risk factors among women differed between groups: among the 128 female medical patients the most common VTE risk factor was contraceptive use (n = 5, 3.9%), while among the 87 female surgical patients, the most common VTE risk factor was pregnancy (n = 6, 6.9%). Post admission, the most prevalent risk factors for VTE in both groups were immobility with bathroom privileges and complete immobilization.

Of the 520 enrolled patients, 298 (57%) were identified to be at risk of VTE according to the ACCP guidelines [3]. For patients in medical wards, 152 (57.4%, 95% CI 48.8–60.5%) were deemed to be at risk of VTE according to ACCP guidelines, 38% due to heart failure or severe respiratory disease and 17% due to immobility or reduced mobility combined with at least one other risk factor (Fig. 2A).

The proportion of patients in medical wards, regardless of risk, who received prophylaxis was 20.9% (n = 58); of those deemed to be at risk for VTE, the proportion who received prophylaxis was 31.6% (n = 48); 10 patients received prophylaxis despite a lack of indication. Nearly 50% of patients at risk in cardiovascular wards were given prophylaxis, whereas only 11% of patients at risk due to infectious diseases received prophylaxis (Fig. 2A). No patients in the intensive care units or neurology wards who were at risk received prophylaxis. The only anticoagulant prescribed in all cases was the LMWH enoxaparin, at a median dose of 40 mg per day.

Among surgical patients, 146 (60.3%, 95% CI 54.2–66.5%) were considered to be at risk of VTE and requiring prophylaxis, the majority (33%) having moderate risk (Fig. 2B). Overall, 86 patients (35.5%) received VTE prophylaxis; of those who were at risk, 52 (35.6%) received effective prophylaxis. Thirty-four patients received prophylaxis despite not being considered at risk according to the 2004 ACCP guidelines. All patients (n = 18) who had undergone hip surgery received prophylaxis, whereas only 36.4% of patients with head trauma received prophylaxis. The highest coverage of prophylaxis in surgical wards was found on orthopaedic wards, with 82.3% of at-risk patients receiving prophylaxis, followed by surgical intensive care units, with 50.0% of patients receiving prophylaxis (Fig. 3). None of the patients in neurology or urology units received prophylaxis for VTE. Enoxaparin 40 mg once daily represented 94% of all prescriptions for prophylaxis for VTE. Enoxaparin 20 mg once daily (2.5%) and enoxaparin 60 mg once daily (3.5%) were the other prescriptions.

Overall, 51 patients (9.8%) had a contraindication to pharmacological prophylaxis (Table 3). The most common contraindications were hepatic impairment in nine (41%) medical patients and bleeding upon admission in 14 (48%) surgical patients. Among the population at risk of VTE, 16 (10.5%) medical patients and 18 (12.3%) surgical patients were considered to have a contraindication to pharmacological prophylaxis. Among patients at risk of VTE who had no contraindication to anticoagulant therapy, the proportions who received prophylaxis were 33.8% (46/136; CI 95% 25.9–41.8%) in the medical wards and 37.5% (48/128; CI 95% 29.1–45.9%) in the surgical wards.

Discussion

This study is the first survey to measure VTE risk and use of VTE prophylaxis coverage in patients hospitalized for medical or surgical conditions in West Africa. The methodology was based on the ENDORSE study methodology [8], with minor adaptations. Our survey showed that more than half of
Table 1 Characteristics of patients and reasons for admission to medical and surgical wards.

<table>
<thead>
<tr>
<th></th>
<th>Medical patients (n = 278)</th>
<th>Surgical patients (n = 242)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years)</strong></td>
<td>62 (40—90)</td>
<td>49 (18—90)</td>
</tr>
<tr>
<td><strong>Men</strong></td>
<td>150 (54.0)</td>
<td>155 (64.0)</td>
</tr>
<tr>
<td><strong>Length of hospitalization (days)</strong></td>
<td>7</td>
<td>8</td>
</tr>
<tr>
<td><strong>Hospitalized &gt; 10 days</strong></td>
<td>89 (32.0)</td>
<td>100 (41.3)</td>
</tr>
<tr>
<td><strong>Reason for admission to medical ward</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute heart failure</td>
<td>42 (15.1)</td>
<td></td>
</tr>
<tr>
<td>Other cardiovascular disease</td>
<td>65 (23.4)</td>
<td></td>
</tr>
<tr>
<td>Acute non-infectious respiratory diseases</td>
<td>12 (4.3)</td>
<td></td>
</tr>
<tr>
<td>Pulmonary infection</td>
<td>43 (15.5)</td>
<td></td>
</tr>
<tr>
<td>Infection (non-respiratory)</td>
<td>37 (13.3)</td>
<td></td>
</tr>
<tr>
<td>Ischaemic stroke</td>
<td>18 (6.5)</td>
<td></td>
</tr>
<tr>
<td>Cerebral haemorrhage</td>
<td>6 (2.2)</td>
<td></td>
</tr>
<tr>
<td>Haematological diseases</td>
<td>10 (3.6)</td>
<td></td>
</tr>
<tr>
<td>Malignancy (active)</td>
<td>13 (4.7)</td>
<td></td>
</tr>
<tr>
<td>Rheumatological or inflammatory disease</td>
<td>13 (4.7)</td>
<td></td>
</tr>
<tr>
<td>Neurological diseases</td>
<td>19 (6.8)</td>
<td></td>
</tr>
<tr>
<td>Renal diseases</td>
<td>14 (5.0)</td>
<td></td>
</tr>
<tr>
<td>Endocrine/metabolic disease</td>
<td>43 (15.5)</td>
<td></td>
</tr>
<tr>
<td>Other medical condition</td>
<td>18 (6.5)</td>
<td></td>
</tr>
<tr>
<td><strong>Reason for admission to surgical ward</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Major trauma</td>
<td>81 (33.5)</td>
<td></td>
</tr>
<tr>
<td>Surgery with anaesthesia &gt; 45 minutes</td>
<td>162 (66.9)</td>
<td></td>
</tr>
<tr>
<td>Under observation</td>
<td>27 (11.2)</td>
<td></td>
</tr>
<tr>
<td>Awaiting surgery</td>
<td>52 (21.5)</td>
<td></td>
</tr>
</tbody>
</table>

Data are median, median (range) or number (%); percentages may add up to more than 100% as patients could have more than one medical condition.

Figure 3. Proportion of at-risk patients receiving prophylaxis. ICU: intensive care unit.
Table 2  Risk factors for venous thromboembolism.

<table>
<thead>
<tr>
<th></th>
<th>Medical patients (n = 278)</th>
<th>Surgical patients (n = 242)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Before admission</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients with ≥ 1 risk factor present before admission</td>
<td>123 (44.2)</td>
<td>41 (16.9)</td>
</tr>
<tr>
<td>Previous venous thromboembolism</td>
<td>4 (1.4)</td>
<td>0</td>
</tr>
<tr>
<td>Obesity</td>
<td>21 (7.5)</td>
<td>12 (5.0)</td>
</tr>
<tr>
<td>Varicose veins or venous insufficiency</td>
<td>2 (0.7)</td>
<td>1 (0.4)</td>
</tr>
<tr>
<td>Thrombophilia</td>
<td>1 (0.4)</td>
<td>1 (0.4)</td>
</tr>
<tr>
<td>Hormone replacement therapy</td>
<td>1 (0.8)a</td>
<td>1 (1.1)b</td>
</tr>
<tr>
<td>Chronic pulmonary disease</td>
<td>42 (15.1)</td>
<td>4 (1.7)</td>
</tr>
<tr>
<td>Long-term immobility</td>
<td>52 (18.7)</td>
<td>13 (5.4)</td>
</tr>
<tr>
<td>Pregnancy (within 3 months)</td>
<td>2 (1.6)a</td>
<td>6 (6.9)b</td>
</tr>
<tr>
<td>Contraceptives</td>
<td>5 (3.9)a</td>
<td>3 (3.4)b</td>
</tr>
<tr>
<td>Chronic heart failure</td>
<td>32 (11.5)</td>
<td>4 (1.7)</td>
</tr>
<tr>
<td><strong>Post admission</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Admitted to critical or intensive care unit</td>
<td>1 (0.4)</td>
<td>3 (1.2)</td>
</tr>
<tr>
<td>Central venous catheter</td>
<td>0</td>
<td>1 (0.4)</td>
</tr>
<tr>
<td>Mechanical ventilation</td>
<td>0</td>
<td>1 (0.4)</td>
</tr>
<tr>
<td>Immobile with bathroom privileges</td>
<td>38 (13.7)</td>
<td>15 (6.2)</td>
</tr>
<tr>
<td>Complete immobilization</td>
<td>35 (12.6)</td>
<td>14 (5.8)</td>
</tr>
<tr>
<td>Cancer therapy</td>
<td>2 (0.7)</td>
<td>3 (1.2)</td>
</tr>
<tr>
<td>Heparin-induced thrombocytopenia</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Data are number (%).
a n = 128 women.
b n = 87 women.

all hospitalized patients examined in eligible wards were at risk of VTE, according to the 2004 ACCP risk definition. Surgical patients were slightly more at risk than medical patients (60.3% vs 57.4%). These findings are similar to that of a study examining VTE risk worldwide [8].

However, among all patients at risk, less than a third of medical patients and just over a third of surgical patients were receiving prophylaxis. A large multinational study found rates ranging anywhere from 4 to 80% and from 0.4 to 94% for any type of prophylaxis among at-risk medical and surgical patients, respectively [8]. Within Senegal, at the various hospitals examined, rates of coverage for at-risk patients varied greatly, from 0 to 50% and from 0 to 83% for medical and surgical patients, respectively.

Prophylaxis in hospitalized medically ill patients was very low in our survey. Less than one third of patients at risk received a prescription for prophylaxis, regardless of duration. This result is consistent with that reported in the subgroup analysis of medically ill patients from the ENDORSE study: Bergmann et al. concluded that ACCP-recommended prophylaxis was underused worldwide in the medical patient population and was provided to < 40% of those at risk [14]. This under usage of VTE prophylaxis in medical wards may reflect a low level of perception of the risk of VTE among some hospital physicians, combined with a lack of awareness of the benefits of VTE prophylaxis [15].

Surprisingly, prophylaxis coverage in surgical patients was also low in our survey. Less than 40% of at-risk VTE patients received prophylaxis, which was not statistically different to the rate of usage of prophylaxis in medical patients. This is in contrast to the ENDORSE global survey, where the rate of prophylaxis was reportedly significantly higher.

Table 3  Contraindications to pharmacological venous thromboembolism prophylaxis.

<table>
<thead>
<tr>
<th></th>
<th>Medical patients (n = 22)</th>
<th>Surgical patients (n = 29)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intracranial haemorrhage</td>
<td>6 (27.3)</td>
<td>3 (10.3)</td>
</tr>
<tr>
<td>Unknown bleeding syndrome</td>
<td>2 (9.1)</td>
<td>2 (6.9)</td>
</tr>
<tr>
<td>Hepatic impairment</td>
<td>9 (40.9)</td>
<td>9 (31.0)</td>
</tr>
<tr>
<td>Bleeding upon admission</td>
<td>2 (9.1)</td>
<td>14 (48.3)</td>
</tr>
<tr>
<td>Active duodenal ulcer</td>
<td>3 (13.6)</td>
<td>1 (3.4)</td>
</tr>
</tbody>
</table>

Data are number (%).
in surgical patients, ranging from 50 to 88% [8]. In our survey, prophylaxis coverage was higher in orthopaedic patients than in other surgical patients, suggesting that orthopaedic surgeons are more aware of VTE risk and are more convinced about the necessity of VTE prophylaxis than other surgeons. A survey in Togo has found that only 16% of anaesthesiologists and surgeons considered that VTE was as common in their country as in western countries [16]. There is an urgent need for awareness and training of physicians regarding the burden of VTE. In the context of low-income countries without social security or insurance coverage, cost of drugs may have impacted negatively on the prescription of VTE prophylaxis and patients’ adherence to treatment. In the participating hospitals, patients pay for the drugs themselves; the average price of one syringe of LMWH is €4.5.

Only one anticoagulant was prescribed, namely enoxaparin. Despite the fact that almost 10% of patients had a contraindication to pharmacological prophylaxis, no mechanical prophylaxis was used to prevent VTE. It should be noted that some local practices in surgical wards are considered as mechanical prophylaxis (early mobilization and shorter hospital stays).

By excluding medical patients aged < 40 years, we may have excluded some potential groups who are known to be at risk for VTE, such as those with poststreptococcal cardiopathy, which is known to be more frequent in patients aged 15—25 years and is also known to lead frequently to VTE [17]. Some other risk factors frequent in the African population, such as sickle cell disease [18], have not been captured in our study. This may have led to an underestimation of the proportion of patients at risk who need VTE prophylaxis. Given the cross-sectional design of this study, only the quality of treatment up to the date of the survey was recorded and assessed. Adherence to prophylaxis through to the end of a patient’s hospital stay was not recorded, which may have led to an overestimation of prophylaxis rates.

Means to improve VTE prophylaxis coverage should include increasing physicians’ awareness through training and the implementation of procedures to assess VTE risk during hospitalization, along with the application of evidence-based guidelines for VTE prophylaxis and treatment in both medical and surgical patients [5]. Three types of strategy may be used to improve VTE risk assessment and the use of VTE prophylaxis when it is warranted [5]: risk assessment scoring systems; risk recognition systems; and prophylaxis default systems. Risk assessment scoring systems categorize a patient’s risk based on their risk factors for VTE [5]. It should be noted that there are no local guidelines for the prevention of VTE in Senegal. Considering that VTE is a serious clinical situation that may lead to patient death, VTE is usually asymptomatic and VTE prevention is more cost-effective than treatment, we do recommend the assessment of VTE risk (using a risk model assessment form, locally adapted) for all hospitalized patients at admission and during hospitalization. Patients found to be at risk for VTE will be candidates for the most adequate thromboprophylaxis (taking socioeconomics into consideration). Other means of VTE prevention, such as mechanical prophylaxis, are scarce in our country; the low level of education of patients in our setting might be a major constraint regarding their utilization in a public health approach.

Conclusion

VTE is a major clinical concern with a substantial risk of morbidity and mortality in patients hospitalized for acute medical and surgical illnesses. This hospital-based country-wide study in Senegal shows that large proportions of medical and surgical patients are at risk of VTE but that the recommended VTE prophylaxis is not prescribed in the majority of cases. A nationwide strategy to assess patients at VTE risk, along with measures to educate and inform physicians about appropriate forms of VTE prophylaxis, should be undertaken in Senegal. Efforts need to be made by all levels of stakeholders (Ministry of Health, pharmaceutical industry, physicians) to increase access to high quality medications and other appropriate interventions at the appropriate prices, in order to ensure the safe and widespread use of VTE prophylaxis.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

Acknowledgments

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