Prevention of Venous Thromboembolism

Adherence to the 1995 American College of Chest Physicians Consensus Guidelines for Surgical Patients

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Background: The American College of Chest Physicians addressed the dilemma of identifying optimal therapy for venous thromboembolism (VTE) prophylaxis and published their Fourth Consensus Conference on Antithrombotic Therapy in 1995, with recommendations for prophylactic therapy. Despite these recommendations, appropriate VTE prophylactic therapy is underused.

Objectives: To examine routine practices in the prevention of VTE in high-risk surgical patients and to determine the extent of adoption of grade A prophylactic therapies as recommended by the American College of Chest Physicians.

Methods: Retrospective medical record review in 10 teaching or community-based hospitals located in the United States. Medical charts of 1907 patients were randomly selected for review from the population of patients who underwent high-risk major abdominal surgery, total hip replacement, hip fracture repair, or total knee replacement between January 1, 1996, and February 28, 1997.

Results: Of 1907 patients, VTE prophylaxis was used in 89.3%; use was 93.7% in each of the 3 orthopedic surgery groups and 75.2% in the high-risk major abdominal surgery group. The percentage of patients receiving grade A therapy was highest in the hip replacement group (84.3%) vs the other groups (knee replacement, 75.9%; hip fracture repair, 45.2%; abdominal surgery, 50.3%).

Conclusions: The use of grade A prophylaxis was related to the type of surgery, with the highest use seen in total hip replacement and the lowest in hip fracture repair. One in 4 patients who underwent high-risk major abdominal surgeries failed to receive any form of VTE prophylaxis. Publication of consensus statements alone may be insufficient to ensure the incorporation of important new clinical information into routine practice.


VENOUS thromboembolism (VTE) is known to be a major cause of morbidity and mortality among hospitalized patients. Pulmonary embolism (PE) is estimated to cause death in more than 100 000 patients each year in the United States and may be a contributing factor in the deaths of another 100 000. In the United States alone, approximately 250 000 hospitalized patients every year will need therapy for symptomatic deep vein thrombosis (DVT). Moreover, since VTE is most often clinically silent, the actual frequency of PE and DVT is probably much greater.

Even though there have been significant advances in understanding the pathogenesis of DVT and PE, and some specific recommendations for prophylaxis and treatment have been identified, VTE remains a serious problem in hospitalized patients because of the inconsistency with which clinical research findings have been applied clinically. In one study conducted in 1986, only 32% of 2017 high-risk hospitalized patients received adequate prophylaxis. When physicians participated in a continuing medical education program on the prevention of VTE, the use of prophylaxis increased to 52%. While this study showed the potential for acceptance of prophylaxis, it also demonstrated considerable room for improvement in clinicians’ acceptance of recommendations for VTE prophylactic therapy.

Further, several studies have shown benefit of various prophylactic measures, and clinicians have faced the dilemma of identifying optimal therapy. The American College of Chest Physicians (ACCP) addressed this dilemma and published their Fourth Consensus Conference on Antithrombotic Therapy in 1995, with recommendations for prophylactic therapy. Recommendations were graded, with the highest grade, grade A, given to those therapies supported by the most rigorously designed studies. Despite these recommendations, appropriate VTE prophylactic therapy is underused.
PATIENTS AND METHODS

PATIENT SELECTION

Ten acute care hospitals representing various geographic areas in the United States participated in this retrospective study. Total number of beds in each institution ranged from 350 to 747. Nine of the 10 hospitals were considered teaching hospitals. Five of the 10 were university-based hospitals, while 4 were considered private and 1 was considered a county facility. At each site a physician or clinical pharmacist was actively involved in medical staff decisions and/or policy development regarding VTE prophylaxis.

The major criterion for inclusion of a chart for review was an admitting diagnosis of 1 of the following 4 surgical procedures between January 1, 1996, and February 28, 1997: high-risk major abdominal surgery (MAS), total hip replacement (THR), hip fracture repair (HFR), and total knee replacement (TKR). Patients were identified by means of preselected International Classification of Diseases, Ninth Revision (ICD-9) codes. Patients in the high-risk MAS group had to be older than 40 years, have required general anesthesia for at least 45 minutes, and have at least 1 additional risk factor for VTE at the time of surgery. These risk factors were lower-extremity paralysis or prolonged immobility, active congestive heart failure, previous VTE, history of cancer or current cancer, varicose veins, obesity (if ≥30% above ideal body weight), and hematologic abnormalities (activated protein C resistance, antithrombin III deficiency, protein C deficiency, protein S deficiency, dysfibrinogenemia, disorders of plasminogen and plasminogen activation, antiphospholipid antibodies and lupus anticoagulant, myeloproliferative disorders such as polycythemia vera, and hyperviscosity syndromes). Patients in the 3 orthopedic surgery groups had to be older than 18 years. Patients were excluded for insufficient data, if the patient had been participating in a clinical trial related to anticoagulation therapy, or if the patient had a history of heparin-induced thrombocytopenia, hemophilia, or hypersensitivity to any anticoagulant agent. At each participating site, a target of 50 patients for each surgical procedure was randomly selected from the charts meeting the above criteria.

DATA COLLECTION

A standard form was developed for data collection from the medical records. The recorded information included surgical procedure; demographic data; admission and discharge dates; location to which the patient was discharged; prehospital use of aspirin, estrogen, or warfarin sodium; and presence of risk factors for VTE at the time of surgery. Risk factors to be identified from the medical records were consistent with those summarized by the ACCP.1 Risk factors for myocardial infarction and stroke were not a part of the data collection protocol because of the difficulty in extracting this information as preexisting risks from the charts. All drug and nondrug regimens for VTE prophylaxis during hospitalization and at discharge, as well as duration of prophylaxis, were recorded.

DATA ANALYSIS

Recommended grade A therapies were as follows: for high-risk MAS, low-molecular-weight heparin (enoxaparin sodium, 30 mg twice daily, or dalteparin sodium, 2500 Ud, at least 1 injection during hospitalization), low-dose unfractionated heparin (any dose every 8 hours, initiated during hospitalization), or intermittent pneumatic compression (initiated during hospitalization); for THR, low-molecular-weight heparin, warfarin (any dose initiated during hospitalization), or adjusted-dose unfractionated heparin (any dose initiated during hospitalization); for HFR, low-molecular-weight heparin or warfarin; and for TKR, low-molecular-weight heparin or intermittent pneumatic compression. For the purposes of this study, therapies were defined as conforming to ACCP recommendations if they were administered in the dosing regimens given above. Although the ACCP consensus statement included recommendations regarding time for initiating therapies, the retrospective study design has inherent limitations regarding the accurate recording of this type of information. Therefore, initiating therapy during hospitalization, without regard to preoperative or postoperative period, satisfied the criteria for grade A therapy in this study.

Descriptive statistics were used to describe the study sample. The association of variables with the use of grade A prophylactic therapies was analyzed by means of logistic regression. Three main variables were tested first for association: surgical procedure, clinical site, and risk factors. Results of these variables and χ² goodness-of-fit tests determined the model for further analyses of association with the use of grade A therapies. A therapies for other variables, including patient characteristics, number of VTE prophylactic therapies, and length of hospital stay. A type I error (P value) of .05 or less was considered statistically significant.

RESULTS

PATIENT CHARACTERISTICS

A total of 1907 patients were included in the chart review. Eight of the 10 centers contributed at least 93% of their target 200 charts. The deficit in patients was mainly from 2 centers. However, these 2 centers contributed at least 80% of their targeted 200 patient charts. Three of the 10 hospitals had some method in place for VTE prophylaxis, which included a pocket guide for house staff, a critical pathway, and a policy developed by service. The other 7 hospitals did not have a policy in place but instead met inclusion criteria by having a physician or clinical pharmacist involved in VTE prophylaxis decisions.

The 4 surgical groups were generally similar in patient characteristics. Men and women were fairly balanced in the high-risk MAS group, while women outnumbered men within the orthopedic surgery groups (range, 1.33-1.70 to 1). Mean age was similar in all groups,
but more individuals younger than 40 years and older than 75 years were in the HFR group than in the other 3 groups, probably reflecting the presence of younger trauma patients and older patients with osteoporosis. Mean body weight and Quetelet index\(^{10}\) (index of body mass calculated as body weight in kilograms divided by the square of height in centimeters times 1000) were higher in the TKR group.

Age greater than 40 years, obesity, and a current diagnosis of cancer were the most common presurgical risk factors (Table 1). Obesity was a more common presurgical risk factor in the TKR group (35.7%) than in the other groups (range, 12.1% to 25.4%). A current diagnosis of cancer was much more prevalent in the high-risk MAS group (71.3%) than in any orthopedic surgery group (range, 0.2% to 2.7%). The majority of patients in the orthopedic surgery groups had 2 or fewer risk factors, whereas most cases in the high-risk MAS group had 3 or more risk factors, because of the entry criterion of at least 2 risk factors for this group. While MAS patients were selected to meet at least the criteria for high risk, 74% actually met the criteria for very-high-risk MAS (patient &gt;40 years old with additional risk factor of malignant disease or previous VTE).\(^{3}\)

Prehospitalization use of estrogen, aspirin, or warfarin, any of which could have represented a confounding factor in this study, ranged from 3% to 15% for all surgical groups. Because of the relatively low rate of usage, these drugs were not further analyzed as factors in the use of VTE prophylaxis.

### VTE PROPHYLAXIS

The proportion of cases that received some form of VTE prophylaxis during hospitalization was 89.3%; 93.7% in the orthopedic surgery groups compared with 75.2% in the high-risk MAS group (Table 2). However, the proportion of patients receiving VTE prophylaxis that met the study definition for grade A therapy varied from 45.2% in the HFR group to 84.3% in the THR group. Whereas VTE prophylaxis was absent in only 1.5% of TKR patients, it was absent in 24.8% of high-risk MAS patients and accounted for 50% of patients who did not receive grade A therapy in that group. Because 74% of the high-risk MAS group met the criteria for very high risk, for which grade A recommendations include warfarin as an option, the use of grade A prophylaxis was examined with respect to the patient’s risk

### Table 1. Summary of Risk Factors\(^*\)

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>% of Patients</th>
<th>High-Risk MAS (n = 495)</th>
<th>THR (n = 464)</th>
<th>HFR (n = 478)</th>
<th>TKR (n = 470)</th>
<th>Total (N = 1907)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt;=40 y</td>
<td>99.2</td>
<td>91.4</td>
<td>79.4</td>
<td>97.9</td>
<td>91.8</td>
<td></td>
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<tr>
<td>Obesity</td>
<td>23.0</td>
<td>25.4</td>
<td>12.1</td>
<td>35.7</td>
<td>24.1</td>
<td></td>
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<tr>
<td>Current cancer†</td>
<td>71.3</td>
<td>1.7</td>
<td>2.8</td>
<td>0.2</td>
<td>19.0</td>
<td></td>
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<tr>
<td>Active CHF</td>
<td>8.7</td>
<td>2.6</td>
<td>6.7</td>
<td>2.3</td>
<td>5.1</td>
<td></td>
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<tr>
<td>Previous venous thromboembolism</td>
<td>4.6</td>
<td>1.5</td>
<td>2.6</td>
<td>3.0</td>
<td>2.9</td>
<td></td>
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<tr>
<td>Varicose veins</td>
<td>1.0</td>
<td>1.5</td>
<td>0.6</td>
<td>3.6</td>
<td>1.7</td>
<td></td>
</tr>
<tr>
<td>Lower extremity paralysis</td>
<td>2.2</td>
<td>0.6</td>
<td>1.5</td>
<td>0.6</td>
<td>1.2</td>
<td></td>
</tr>
<tr>
<td>Hemostatic abnormalities</td>
<td>1.0</td>
<td>0.4</td>
<td>0.4</td>
<td>0</td>
<td>0.4</td>
<td></td>
</tr>
<tr>
<td>No. of risk factors</td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>0</td>
<td>7.3</td>
<td>19.0</td>
<td>1.9</td>
<td>7.1</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>1.0</td>
<td>57.8</td>
<td>54.6</td>
<td>55.3</td>
<td>42.2</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>79.6</td>
<td>31.2</td>
<td>22.0</td>
<td>35.7</td>
<td>42.1</td>
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</tr>
<tr>
<td>4</td>
<td>18.2</td>
<td>3.0</td>
<td>4.2</td>
<td>5.7</td>
<td>7.8</td>
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</tr>
<tr>
<td>5</td>
<td>1.2</td>
<td>0.6</td>
<td>0.2</td>
<td>1.3</td>
<td>0.8</td>
<td></td>
</tr>
</tbody>
</table>

* MAS indicates major abdominal surgery; THR, total hip replacement; HFR, hip fracture repair; TKR, total knee replacement; and CHF, congestive heart failure.

† Skin cancer, which was present in 0.4% or less in each of the subgroups, was not considered a risk factor and was excluded from this tabulation.

### Table 2. Number of Patients Receiving VTE Prophylaxis\(^*\)

<table>
<thead>
<tr>
<th>Type of Prophylaxis</th>
<th>No. (%)</th>
<th>High-Risk MAS (n = 495)</th>
<th>THR (n = 464)</th>
<th>HFR (n = 478)</th>
<th>TKR (n = 470)</th>
<th>Total (N = 1907)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A: Conforming prophylaxis</td>
<td></td>
<td>249 (50.3)</td>
<td>391 (84.3)</td>
<td>216 (45.2)</td>
<td>357 (76.9)</td>
<td>1213 (63.8)</td>
</tr>
<tr>
<td>(grade A therapy as inpatient)</td>
<td></td>
<td>262 (52.9)†</td>
<td></td>
<td></td>
<td></td>
<td>262 (52.9)†</td>
</tr>
<tr>
<td>B: Inpatient prophylaxis not</td>
<td></td>
<td>123 (24.8)</td>
<td>39 (8.4)</td>
<td>222 (46.4)</td>
<td>106 (22.6)</td>
<td>490 (25.7)</td>
</tr>
<tr>
<td>conforming to criteria</td>
<td></td>
<td>110 (22.2)†</td>
<td></td>
<td></td>
<td></td>
<td>110 (22.2)†</td>
</tr>
<tr>
<td>C: No prophylaxis as inpatient</td>
<td></td>
<td>123 (24.8)</td>
<td>34 (7.3)</td>
<td>40 (8.4)</td>
<td>7 (1.5)</td>
<td>204 (10.7)</td>
</tr>
<tr>
<td>A + B: Total inpatient prophylaxis</td>
<td></td>
<td>372 (75.1)</td>
<td>430 (92.7)</td>
<td>438 (91.6)</td>
<td>463 (98.5)</td>
<td>1703 (89.3)</td>
</tr>
<tr>
<td>B + C: Total nonconforming prophylaxis</td>
<td></td>
<td>246 (49.7)</td>
<td>73 (15.7)</td>
<td>262 (54.8)</td>
<td>113 (24.0)</td>
<td>694 (36.4)</td>
</tr>
</tbody>
</table>

*VTE indicates venous thromboembolism; MAS, major abdominal surgery; THR, total hip replacement; HFR, hip fracture repair; and TKR, total knee replacement.

† Including warfarin sodium as grade A therapy in patients defined as undergoing very-high-risk MAS.
category. The extent of use was slightly increased when warfarin was considered grade A therapy in very-high-risk MAS patients (52.9% vs 50.3%) (Table 2).

Patients were categorized as having received grade A therapy if they received at least 1 VTE prophylactic therapy meeting the criteria for grade A, and they may have received combinations with other grade A or non-grade A therapies. Most patients in all surgical groups received 2 or more VTE prophylactic therapies (Table 3). More therapies were used in combination in the TKR group, with 31.7% of patients (149/470) receiving 4 or more therapies. The mean number of therapies per patient was 2.3 and was highest in the TKR group and lowest in the high-risk MAS group. The proportion of patients receiving grade A therapies was higher than the proportion of those not receiving grade A therapies in the THR and TKR groups regardless of the number of therapies received. In contrast, a higher proportion of patients not receiving grade A therapy was observed in single-, double-, or triple-drug therapies in the HFR group, as well as for the group as a whole, and with monotherapy in the high-risk MAS group.

More patients in the high-risk MAS group than in the orthopedic surgery groups were hospitalized for more than 10 days (Table 4). Within each surgical group, the ratio of patients receiving grade A therapy to those not receiving grade A therapy was similar regardless of length of hospital stay, with exceptions primarily at the extremes of very short or very long stays, where small numbers created large shifts in ratios, and with the exception of HFR, where the ratio was reversed on the basis of duration, with more patients not receiving grade A therapy with short stays and more patients receiving grade A therapy with longer stays.

**NONCONFORMING PROPHYLAXIS**

Of the 694 patients who did not receive grade A VTE prophylactic therapy, 204 did not receive any form of therapy, and 490 had VTE prophylactic therapy that did not meet the criteria for grade A. The most common therapy in these 490 patients was elastic stockings. Intermittent pneumatic compression foot pump was frequently used in patients without grade A therapy who underwent THR and HFR and was less prevalent in TKR or high-risk MAS patients. Low-dose unfractionated heparin was a common therapy in HFR and high-risk MAS patients; in the latter group, low-dose unfractionated heparin did not meet the dosing criterion of every 8 hours for grade A therapy. Warfarin...
and continuous passive motion machine were common in TKR patients who did not receive grade A therapies.

**DISCHARGE VTE PROPHYLAXIS**

A total of 1373 VTE prophylactic therapies were given to 951 of the 1907 patients at the time of discharge from the hospital (Table 5). Nearly two thirds of the discharge therapies were given as single therapies, and about one third were given as combination therapies. The number of discharge therapies was highest in the TKR group and lowest in the high-risk MAS group. Continuous passive motion machines were prescribed 3 times more often in the TKR group than in each of the other 3 groups and, in part, account for the high total number of therapies for that group. Low-molecular-weight heparin, elastic stockings, and aspirin were also prescribed more often in the orthopedic surgery groups.

Prophylactic therapies for VTE were prescribed at discharge more often to patients who underwent TKR (70.2%) than to patients who underwent the other surgical procedures (THR, 58.2%; HFR, 53.3%; high-risk MAS, 19.4%) (Table 6). In the orthopedic surgery groups, about two thirds of the patients received VTE prophylaxis when they were discharged to a skilled nursing home or rehabilitation hospital, with a higher percentage (83.6%) of TKR patients receiving therapies when sent to nursing homes. Of orthopedic patients sent home without health care assistance, the proportion of patients given VTE prophylactic therapy was also about two thirds for THR and TKR, but only one third for HFR. High-risk MAS patients were more often discharged to their homes without health care and without VTE prophylactic therapy, compared with the orthopedic surgery patients. In the high-risk MAS group, the percentage of patients discharged to their homes with VTE prophylaxis was 17.2%. The percentage of high-risk MAS patients receiving VTE therapy when discharged to a skilled nursing or rehabilitation facility was also lower than that of orthopedic patients. We did not record the number of patients in whom prophylactic therapy failed (ie, who had a documented DVT or PE), as this was not an objective of the study.

**FACTORS ASSOCIATED WITH THE USE OF GRADE A PROPHYLAXIS**

The use of VTE prophylaxis meeting the study criteria for grade A therapy was associated significantly and independently with 2 factors: the surgical group of the patient and the clinical site from which the patient was selected (P<.001;
Venous thromboembolism is a potentially fatal complication of surgery for which the ACCP has provided specific and well-founded recommendations for prevention in high-risk MAS, THR, HFR, and TKR, among others. This retrospective chart review was conducted during the year after publication of the ACCP grade A recommendations. Of 1907 patients who underwent 1 of these 4 surgical procedures, most received some form of VTE prophylaxis during hospitalization. The use of VTE prophylaxis in 93.7% of the orthopedic surgery patients reflects the widespread awareness of the serious risk in these patients, but the risk appeared to be less appreciated in high-risk MAS patients, where 50.3% received grade A VTE prophylaxis, 24.8% received non-grade A prophylaxis, and 24.8% received no prophylaxis at all.

The type of surgical procedure was found to be a significant factor in the use of grade A prophylactic therapy. Grade A therapies were used in 84.3% of patients who underwent THR, 75.9% of those who had TKR, 50.3% of those who underwent high-risk MAS, and 45.2% of those who had HFR. Contributing to a large proportion of patients not receiving grade A therapies in HFR was the use of low-dose unfractionated heparin, which suggests a less-than-complete awareness of the recommended grade A therapies for VTE prophylaxis in these patients at the time of the study. The proportion of patients receiving grade A prophylactic therapy was only 50.3% in high-risk MAS patients, and this proportion was only marginally increased (52.9%) when warfarin was included as grade A therapy for patients who met the criteria for very-high-risk MAS. In addition to the 25% of high-risk MAS patients who received no form of VTE prophylaxis at all, several patients received low-dose unfractionated heparin at intervals other than every 8 hours, again possibly reflecting less-than-complete adoption of the ACCP recommended dose for this therapy in this indication.

Another suggestion of less-than-complete adoption of grade A recommended therapies during the time frame of this study was the use of warfarin in TKR. Warfarin has been commonly used for VTE prophylaxis in orthopedic surgery, including TKR. An extensive review of randomized studies showed warfarin to be effective in THR and HFR but relatively ineffective in TKR. These findings by the ACCP led to the exclusion of warfarin as grade A therapy in TKR in 1995. However, the 1998 recommendations for TKR include warfarin as a grade A1 recommendation.

The use of grade A prophylactic therapy was significantly associated with a larger number of prophylactic therapies administered to a single patient. This association simply reflected chance. It should be pointed out that, while multiple therapies were used, there is no evidence that they are more effective than a single grade A recommendation, and they certainly add to the cost of therapy. An inverse relationship was observed between the length of hospital stay and the use of grade A prophylactic therapy; higher use was seen with shorter stays. This association might be a reflection of the 4 surgical groups and their differences in hospitalization durations.

At the time of discharge, 49.8% of patients received some form of VTE prophylaxis, and the proportion was highest in TKR (70.2%) and least in high-risk MAS (19.4%). One possible explanation for this finding might be that TKR patients tended to have short hospital stays (68.3% stayed ≤5 days) and to be sent to care facilities, warranting continued VTE prophylaxis after discharge. In contrast, the high-risk MAS patients had a larger proportion hospitalized for longer than 10 days and were usually sent home without care; these patients may have achieved relative independence and ambulation by the time of their discharge and were considered at less risk for VTE.

The ACCP consensus statement and guidelines were developed in the spring of 1994 and published in October 1995. They represented the highest standards of scientific evidence available at that time. Although these recommendations guide treatment of most patients, they are not unequivocal answers in the choice of appropriate prophylaxis in every patient. The possibility exists that some cases in this chart review did not receive grade A therapies because of individual patient variables that were beyond the scope of examination by this retrospective study. The reader is referred to the most recent guidelines for additional guidance for prophylaxis in these procedures and recommendations regarding length of therapy.

In conclusion, this retrospective study in 4 surgical procedures associated with high risk of developing VTE found that most patients received VTE prophylaxis, but the proportion of patients receiving therapies in agreement with the ACCP-recommended grade A therapies varied with the surgical procedure, with the highest use seen in THR and the lowest in HFR. Approximately 1 in 4 patients who underwent high-risk abdominal operations failed to receive any form of VTE prophylaxis. Publication of consensus statements alone may be insufficient to ensure the incorporation of important new clinical information into routine practice.

COMMENT

Venous thromboembolism is a potentially fatal complication of surgery for which the ACCP has provided specific and well-founded recommendations for prevention in high-risk MAS, THR, HFR, and TKR, among others. This retrospective chart review was conducted during the year after publication of the ACCP grade A recommendations. Of 1907 patients who underwent 1 of these 4 surgical procedures, most received some form of VTE prophylaxis during hospitalization. The use of VTE prophylaxis in 93.7% of the orthopedic surgery patients reflects the widespread awareness of the serious risk in these patients, but the risk appeared to be less appreciated in high-risk MAS patients, where 50.3% received grade A VTE prophylaxis, 24.8% received non-grade A prophylaxis, and 24.8% received no prophylaxis at all.

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REFERENCES


