Incidences and Time Course of Thromboembolic Outcomes Following Total Hip or Knee Arthroplasty

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Background: Little is known about the incidence and time course of clinical thromboembolic events after total hip or knee arthroplasty, particularly after hospital discharge.

Methods: We used a linked hospital discharge database provided by the State of California to identify cases diagnosed as having deep vein thrombosis or pulmonary embolism within 3 months of unilateral total hip or knee arthroplasty. Also, we surveyed orthopedic surgeons to estimate the frequency of postoperative thromboprophylaxis during July 1991 through June 1993. Medical charts were audited to determine the accuracy of the coded records.

Results: Among 19,586 primary hip and 24,059 primary knee arthroplasties, the cumulative incidence of deep vein thrombosis or pulmonary embolism within 3 months of surgery was 556 (2.8%) after hip arthroplasty and 508 (2.1%) after knee arthroplasty. The diagnosis of thromboembolism was made after hospital discharge in 76% and 47% of the total hip and total knee arthroplasty cases, respectively (P < .001), with a median time of diagnosis of 17 days and 7 days after surgery, respectively (P < .001). Questionnaire results indicated that 95% of all cases received thromboprophylaxis and that the frequency, type, and duration of thromboprophylaxis was virtually identical after hip and knee arthroplasty.

Conclusions: There is a difference in the temporal patterns of clinically symptomatic thromboembolic complications after total hip and total knee arthroplasty, suggesting differences in pathogenesis or natural history. The findings suggest that to further reduce thromboembolic outcomes, earlier, more intense prophylaxis may be needed for total knee arthroplasty, and more prolonged prophylaxis may be required after total hip arthroplasty.

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It is widely appreciated that asymptomatic deep vein thrombosis (DVT) frequently develops after both total hip arthroplasty and total knee arthroplasty and that medical or mechanical prophylaxis significantly reduces the incidence of venographically defined thrombosis.17 Much less is known about the incidence and time course of symptomatic DVT or pulmonary embolism (PE), particularly after hospital discharge. A number of studies have provided evidence that asymptomatic venous thromboembolism develops in a significant proportion of patients after hospital discharge after either general or orthopedic surgery.8-16 Moreover, recent clinical trials have demonstrated that more prolonged medical prophylaxis after hospital discharge significantly reduces the incidence of venographically detected DVT after total hip arthroplasty.17,18

The objectives of this study were to determine the incidence and time course of clinically overt DVT and PE after unilateral total hip or knee arthroplasty using a large linked hospital discharge data set. In addition, we conducted a mail survey of a random sample of orthopedic surgeons to determine if there was a difference in the reported use of thromboprophylaxis after total knee arthroplasty and total hip arthroplasty during the period studied.

RESULTS

OVERVIEW

Linkage of records, using both encrypted social security numbers and dates of birth, was possible in 95.3% of all arthroplasty cases. The remainder either lacked a social security number or had 2 different dates of birth associated with the same social security number. Twelve hospitals met our criteria for performing screening venography or ultrasound testing; all cases
from these hospitals were excluded. The overall incidence of DVT during the initial hospitalization after hip or knee arthroplasty in these 12 hospitals was 4.3% (5.4% for knee and 3.0% for hip), considerably higher than the average incidence of 0.9% observed in the remaining 364 hospitals. The incidence of PE was not significantly different between the 12 excluded hospitals and the remaining hospitals (0.31% and 0.36%, respectively; P = .56).

In the 2-year study period, 19,082 patients underwent 19,586 first-time unilateral hip arthroplasties, 23,157 patients underwent 24,059 first-time unilateral knee arthroplasties, and 27,579 patients underwent 1 of the major gastrointestinal operations. There were 4198 revision hip arthroplasties and 2100 revision knee arthroplasties. The mean age, sex, race, and length of hospital stay, and the percentage of cases with cancer are shown in Table 1 for each type of surgery. After hip and knee arthroplasty, 22.9% and 20.2% of the cases were transferred to a rehabilitation or convalescence hospital, respectively.

The cumulative incidences of DVT, PE, and death during the first 91 days after surgery, categorized by hospitalization status, are shown in Table 2. The incidence of thromboembolic events was higher after primary total hip arthroplasty (556 [2.8%] of 19,586) than after primary total knee arthroplasty (508 [2.1%] of 24,579; difference, 0.7%; 95% confidence interval [CI], 0.4%-1.0%). Using logistic regression analysis, the factors independently associated with a thromboembolic complication developing within 3 months of surgery were total hip arthroplasty (odds ratio, 1.4; 95% CI, 1.2-1.6),
Cases with an associated diagnosis of cancer were identified using ICD-9-CM diagnosis codes 141 through 208 (except 173, nonmelanoma skin cancers). Specific codes were also used to identify coexisting major medical diseases.26

VALIDATION OF CODING

The validity of ICD-9-CM coding for DVT and PE was evaluated using (1) a random sample of 984 lumbar discectomy cases from 30 hospitals that were reabstracted as part of a separate study, (2) a review of the charts of 17 cases that underwent orthopedic or general surgery at 1 of 2 local hospitals and who were subsequently reabstracted with a principal diagnosis code for venous thromboembolism, (3) a sample of 92 cases at our hospital in whom a vena cava filter was placed, and (4) a review of the charts of 218 cases admitted to 1 of 4 local hospitals with a principal diagnosis of DVT.

DATA ANALYSIS

The cumulative incidence of DVT and PE was determined for arthroplasties performed between July 1, 1991, and June 30, 1993; potential follow-up of at least 6 months was available for all cases. We used procedures rather than patients as the unit of analysis, because only 3.9% of the patients underwent a second procedure within the study period. Outcomes were categorized as occurring during the initial hospitalization, during a contiguous hospitalization for rehabilitation, or after discharge leading to readmission to an acute-care facility with a principal diagnosis of DVT or PE.

The incidence of thromboembolic events over time was determined by assigning a date to each thromboembolic event, using the following assumptions. During the initial hospitalization, we used the date of the first objective test (eg, ultrasonography) as the date of occurrence of DVT or PE; if no test was coded (approximately 40% of cases), we selected a random date between the day after surgery and 3 days before discharge, assuming the last 3 days were required for initiation of anticoagulation therapy. Among cases that developed thromboembolism after hospital discharge, termed late events, we used the date of readmission if the principal diagnosis for that admission was DVT or PE (85% of late events). If DVT or PE was a secondary diagnosis on the readmission record, we used the date of objective testing (8% of late events) or, lacking this, the date of admission (7% of late events). We analyzed these data using survival techniques, censoring cases on the date of death or the date of any subsequent surgical procedure that might have required general anesthesia.

USE OF THROMBOPROPHYLAXIS

We contacted the offices of the chiefs of orthopedic surgery at each of the 75 hospitals that performed the greatest volume of total hip and knee arthroplasties in California during the study period. A questionnaire was sent to all surgeons who were identified as performing total joint arthroplasties at these hospitals, asking for (1) the estimated number of total hip arthroplasties and total knee arthroplasties performed between 1991 and 1993; (2) the percentage of cases given heparin sodium (fixed or adjusted), warfarin, pneumatic compression, aspirin, and thromboembolic stockings; and (3) the percentage of cases discharged on a regimen of warfarin sodium. To estimate statewide use of thromboprophylaxis, these percentages were weighted by each surgeon’s reported volume and then averaged. We also asked whether surgeons at each respondent’s hospital ordered routine ultrasonic testing to detect DVT postoperatively.

STATISTICAL METHODS

The primary outcomes were a principal or secondary diagnosis of DVT or PE within 3 months (91 days) of the day of surgery. The procedure-specific cumulative incidence of thromboembolism was calculated using survival techniques, using the log-rank and Wilcoxon methods to calculate the statistical significance of differences between arthroplasty procedures. Procedure-specific frequencies of categorical variables were compared using the χ² test. Incidence differences were compared using 2-sided 95% confidence intervals estimated from the normal approximation to the binomial distribution. Logistic regression was used to evaluate the association of age, sex, coexisting medical diseases, and type of primary arthroplasty with a diagnosis of either DVT or PE within 3 months of the day of surgery.

### Table 1. The Demographic Characteristics of Primary or Revision Total Hip or Knee Arthroplasty Cases

<table>
<thead>
<tr>
<th>Variable</th>
<th>Primary Total Hip (n = 19,586)</th>
<th>Primary Total Knee (n = 24,059)</th>
<th>Revision Total Hip (n = 4,198)</th>
<th>Revision Total Knee (n = 2,100)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean ± SD age, y</td>
<td>66.5 ± 13.0</td>
<td>69.6 ± 9.9</td>
<td>66.8 ± 14.2</td>
<td>68.3 ± 11.4</td>
</tr>
<tr>
<td>Sex, % female</td>
<td>59.6</td>
<td>62.1</td>
<td>60</td>
<td>56.3</td>
</tr>
<tr>
<td>Race, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>88.9</td>
<td>84.4</td>
<td>87.0</td>
<td>84.7</td>
</tr>
<tr>
<td>African American</td>
<td>3.8</td>
<td>4.7</td>
<td>5.8</td>
<td>6.4</td>
</tr>
<tr>
<td>Latino</td>
<td>4.9</td>
<td>8.3</td>
<td>4.7</td>
<td>7.3</td>
</tr>
<tr>
<td>Asian</td>
<td>1.6</td>
<td>1.9</td>
<td>1.9</td>
<td>1.0</td>
</tr>
<tr>
<td>Mean ± SD length of stay, d</td>
<td>6.9 ± 3.3</td>
<td>6.7 ± 3.0</td>
<td>8.0 ± 5.3</td>
<td>6.4 ± 3.2</td>
</tr>
<tr>
<td>Malignancy, %</td>
<td>1.6</td>
<td>0.7</td>
<td>1.4</td>
<td>1.0</td>
</tr>
</tbody>
</table>

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Figure 1 shows the incidence of thromboembolic complications over the first 3 months after surgery. Overall, we could confidently assign a date for 807 (75%) of 1074 of the cases with a thromboembolic event. The date of an objective diagnostic test during the initial hospitalization for surgery or subsequent rehabilitation, or the date of readmission with a principal diagnosis of DVT or PE, was noted in 453 (81.5%) of the hip cases and in 354 (69.7%) of the knee cases.

The median time of diagnosis for thromboembolic events was 7 days after knee arthroplasty, compared with 17 days after hip arthroplasty ($P < .001$). As seen in Figure 1, the incidence of thromboembolic events decreased to a stable rate approximately 4 weeks after knee arthroplasty, whereas the rate became stable approximately 10 weeks after hip arthroplasty. This difference in the temporal pattern of thromboembolic events between primary total hip arthroplasty and total knee arthroplasty was statistically significant using the log-rank test ($P < .001$). A significant difference was also found when we limited our analysis to cases that were coded as having an objective diagnostic test for DVT or PE during the hospitalization or were readmitted for thromboembolism.

The cumulative incidence of PE within 3 months of surgery was 1.1% after primary total hip arthroplasty and 0.8% after primary total knee arthroplasty (difference, $0.3\%$; 95% CI, $0.1\%$-$0.4\%$). Figure 2 shows when PE was diagnosed after primary hip and knee arthroplasty. Focusing only on the early postoperative period, there was no significant difference in the incidence of PE among cases undergoing primary total hip or primary total knee arthroplasty in the first 10 days after surgery ($P = .30$).

The cumulative incidence of thromboembolic events after revision total hip arthroplasty (1.8%) and revision total knee arthroplasty (1.4%) were not significantly different. However, 38 (49%) of 77 revision total hip arthroplasty cases were diagnosed after discharge, compared with just 6 (20%) of 30 revision total knee arthroplasty cases (difference, 29%; 95% CI, 11%-47%).

In the 27 579 cases that underwent major gastrointestinal surgery, 1.1% were diagnosed complications with

### Table 2. The Incidence of Deep Vein Thrombosis and Pulmonary Embolism During the First 3 Months After Total Hip or Total Knee Arthroplasty

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Primary Total Hip (n = 19 586)</th>
<th>Primary Total Knee (n = 24 059)</th>
<th>Primary Total Hip (n = 4198)</th>
<th>Primary Total Knee (n = 2100)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thromboembolic events</td>
<td>556 (2.8)</td>
<td>508 (2.1)</td>
<td>77 (1.8)</td>
<td>30 (1.4)</td>
</tr>
<tr>
<td>Deep vein thrombosis</td>
<td>354 (1.8)</td>
<td>326 (1.4)</td>
<td>45 (1.1)</td>
<td>25 (1.2)</td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td>202 (1.1)</td>
<td>182 (0.8)</td>
<td>32 (0.76)</td>
<td>11 (0.5)</td>
</tr>
<tr>
<td>Thromboembolic event by time of diagnosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>During the initial hospitalization</td>
<td>133 (0.7)</td>
<td>268 (1.1)</td>
<td>27 (0.6)</td>
<td>9 (0.4)</td>
</tr>
<tr>
<td>During rehabilitation hospitalization</td>
<td>94 (0.5)</td>
<td>57 (0.2)</td>
<td>12 (0.3)</td>
<td>15 (0.7)</td>
</tr>
<tr>
<td>Requiring readmission</td>
<td>329 (1.7)</td>
<td>183 (0.7)</td>
<td>38 (0.9)</td>
<td>6 (0.3)</td>
</tr>
<tr>
<td>Deaths</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-91 d after surgery</td>
<td>233 (1.2)</td>
<td>216 (0.9)</td>
<td>87 (2.1)</td>
<td>14 (0.7)</td>
</tr>
<tr>
<td>In-hospital</td>
<td>57 (0.3)</td>
<td>60 (0.2)</td>
<td>40 (0.6)</td>
<td>3 (0.1)</td>
</tr>
<tr>
<td>≤91 d after discharge</td>
<td>176 (0.9)</td>
<td>156 (0.6)</td>
<td>60 (1.4)</td>
<td>11 (0.5)</td>
</tr>
<tr>
<td>92-182 d after discharge</td>
<td>121 (0.6)</td>
<td>92 (0.4)</td>
<td>45 (1.1)</td>
<td>7 (0.3)</td>
</tr>
</tbody>
</table>

*All values other than $P$ values are presented as number (percentage). Cases diagnosed as both deep vein thrombosis and pulmonary embolism were categorized as pulmonary embolism.*
thromboembolism in the hospital, and 0.7% received the diagnosis after discharge within 45 days of surgery. The incidence of any thromboembolic event within 3 months after gastrointestinal surgery was 1.9%.

ACCURACY OF CODING

The sensitivity of coding for acute DVT or PE was 100% (4/4 cases) in the random sample of 984 diskectomy cases that were reabstracted. In our local audit of 92 cases in which an inferior vena cava filter was placed, 64 (93%) of 69 cases in which DVT was suspected or confirmed were correctly coded.

The positive predictive value of having a code for DVT or PE was 67% (4/6) for diskectomy cases, (100%) (17/17) for cases in which thromboembolism was the principal diagnosis at the time of readmission after orthopedic surgery, 98% (64/65) for cases treated with an inferior vena cava filter, and 92% (182/198) for cases admitted to 1 of 4 local hospitals for 3 or more days with a principal diagnosis of DVT. The 2 diskectomy cases that were miscoded would not have been included in our study, since both had a prior diagnosis of venous thrombosis within 6 months of the day of surgery, and such cases were excluded in our analysis.

THROMBOPROPHYLAXIS

Questionnaires were received from 199 (51%) of 388 surgeons who were identified as performing total hip or knee arthroplasty at the 75 highest-volume hospitals. Respondents estimated that they performed approximately 16 688 total hip or knee arthroplasties during the 2-year study period. Overall, use of thromboprophylaxis was similar for both procedures. Respondents estimated that 88% of all cases received either subcutaneous heparin, oral warfarin, pneumatic compression, or a combination of these (11.7% regular heparin, 54.1% warfarin, 60.4% pneumatic compression); only 5% were treated with compression stockings alone. Of the 128 surgeons who performed both total hip and knee arthroplasties, 90% reported that they used identical prophylaxis for both surgical procedures. Among surgeons who performed only hip or only knee surgery, the percentages of cases given prophylaxis in the hospital and after discharge were similar for both procedures. Approximately 32% of the cases that underwent total hip or total knee arthroplasty were treated with warfarin after hospital discharge, and the average duration of prophylaxis in these cases was 4 weeks.

The results of our questionnaire indicated that various thromboembolism remains a small but important problem in this era of widespread use of medical prophylaxis. Within 3 months of the day of surgery, 2.8% of the cases that underwent primary total hip arthroplasty and 2.1% of those that underwent primary total knee arthroplasty were diagnosed as having DVT or PE. The fact that these rates are much lower than the 30% to 45% incidence rates reported in studies that have used screening venography simply reflects the fact that in most cases the thromboembolism resolves without causing symptoms that either patients or physicians perceive as significant.

The most striking findings in this study were that 76% of the thromboembolic events after total hip arthroplasty and 47% of the events after total knee arthroplasty were diagnosed after discharge from the hospital. Of the cases that underwent total hip arthroplasty and that were eventually diagnosed as having thromboembolism, 50% received the diagnosis 17 days or more after the day of surgery. These findings are similar to those reported by Warwick et al., who noted that 64% of all thromboembolic complications that were diagnosed in 1100 total hip arthroplasty cases occurred after hospital discharge. Our findings certainly support the widely held belief that posthospitalization thromboembolism is an important clinical problem.

The results of our survey of California orthopedic surgeons make it unlikely that the high rate of posthospitalization thromboembolism, particularly after total hip arthroplasty, was due to inadequate use of thromboprophylaxis after surgery. Respondents indicated that approximately 88% of the cases that underwent hip or knee arthroplasty received 1 or more of the prophylaxis regimens that were recommended between 1991 and 1993, namely subcutaneous heparin, pneumatic compression, or oral warfarin. This estimate may be too high because nonresponding orthopedic surgeons may have used effective prophylaxis less often than responders. However, a recent review of more than 400 randomly selected charts in Massachusetts reported similar results: adequate prophylaxis was given in 93% of total hip arthroplasty cases. Because we had no information regarding the use or nonuse of thromboprophylaxis in each case, it is possible that the cases that developed DVT or PE either received no prophylaxis or were given prophylaxis for only a few days.

A noteworthy finding in this study was the difference in the time of diagnosis of DVT and PE between total hip and knee arthroplasty. Symptomatic thromboembolism occurred much earlier after total knee arthroplasty, with half of all clinical events developing within 7 days of surgery and few events occurring 4 or more weeks after the day of surgery. In comparison, the risk of DVT or PE remained moderately high for about 10 weeks after total hip arthroplasty. It is possible that the high frequency of thromboembolism shortly after total knee arthroplasty reflects a bias in detection. Assuming that nonspecific lower-extremity symptoms occur more frequently after knee arthroplasty, ultrasound testing would be expected to detect an appreciable number of DVT cases that are unrelated to the patient’s symptoms. On the other hand, there is considerable evidence that venous thrombosis does indeed start very early during total knee surgery.

The results of our questionnaire indicated that thromboprophylaxis regimens used after hip and knee arthroplasty were almost identical, suggesting that the observed difference in the temporal pattern of thromboembolic outcomes after total hip and total knee arthroplasty was not due to a difference in the frequency, type,
or duration of thromboprophylaxis. Indeed, concerns expressed in the orthopedic literature regarding posthospitalization thromboembolism have focused primarily on hip arthroplasty, making it likely that any difference in the frequency of posthospital discharge thromboprophylaxis would have favored greater use among the total hip arthroplasty cases. Such a bias should have led to a lower incidence of thromboembolism after hospital discharge among hip arthroplasty cases.

The sheer size and comprehensiveness of the linked data set that we used offers major advantages over small studies performed at 1 or a few hospitals. However, use of such an administrative data set raises appropriate concerns regarding the validity of the coded diagnoses as well as the assumptions involved in assigning a date to each thromboembolic event. Previous studies and all our efforts to assess the validity of coding indicate that approximately 95% of the cases coded as having DVT or PE had objectively documented events. Among the hip arthroplasty cases, the dates of 82% of the thromboembolic events were assigned using either the date of a diagnostic test or the date of a readmission for DVT or PE; in the remaining 18%, we had to use statistical methods to estimate the date of the thromboembolic event. Excluding all cases that could not be assigned an exact date, we observed a similar difference in the temporal pattern of thromboembolic complications. Although 30% of the thromboembolic events after total knee arthroplasty could not be assigned an exact date, most of these were diagnosed during the patient’s initial hospitalization for surgery.

Because hospital discharge abstracts are collected only from California hospitals, it is possible that we underestimated the number of postdischarge thromboembolic events because some patients moved or returned to a different state, were admitted to federal or military hospitals, or were treated as outpatients. However, migration is not common within 3 months of major surgery, and there are very few major population centers in states adjacent to California, minimizing the number of out-of-state residents treated in California hospitals. Until approval and release of low-molecular-weight heparin in 1995, outpatient treatment of thromboembolism was rare. None of these potential reasons for underestimating the number of events could have produced the observed difference in the temporal pattern of thromboembolism between the 2 surgical procedures.

It is very unlikely that we overestimated the incidence of thromboembolic complications. In our local chart review study of patients treated with an inferior vena cava filter, objectively confirmed or clinically diagnosed disease was present in 98% of cases coded as having DVT or PE. In previous audits, we found that cases were often coded with a secondary diagnosis of venous thrombosis if they had a recent history of venous thrombosis and were taking warfarin at the time of admission. By excluding cases with a recent history of thromboembolism, we minimized this potential problem. We also avoided overestimating the incidence of symptomatic thromboembolism by excluding hospitals that appeared to screen cases using venography or ultrasound testing.

The results of 2 recently published clinical trials also support the validity of our findings. In a study comparing the use of warfarin with that of low-molecular-weight heparin after hip and knee arthroplasty, Hull et al reported that 1.1% of 795 patients who underwent hip arthroplasty developed symptomatic DVT or PE within 3 months of hospital discharge, compared with 0.5% of 641 patients who underwent knee arthroplasty. These findings are similar to the incidences of 1.7% and 0.7% that we noted after hospital discharge among hip or knee arthroplasty cases, respectively. In the second comparison study, Kakkar et al published data concerning the incidence of clinically overt thromboembolism after abdominal surgery. We analyzed a similar cohort of cases using the discharge data set and compared the results. The rate of in-hospital DVT or PE from our analysis of abdominal surgery cases in California, 1.1%, was the same as the rate reported by Kakkar and colleagues, 1.1%. Also, the incidence of thromboembolism that they diagnosed within 45 days of discharge, 0.74%, was strikingly similar to our own finding of 0.67%.

The high proportion of cases diagnosed as having DVT and PE after hospital discharge, particularly after total hip arthroplasty, indicates that the period of risk for thromboembolism extends well beyond the initial hospital stay. The results of the present study, together with recent studies by Bergqvist et al and Planes et al, which documented the efficacy of extended prophylaxis in reducing the incidence of asymptomatic DVT, justify studying the effectiveness of extended (eg, 6-10 weeks) prophylaxis with heparin or warfarin after total hip arthroplasty. Our findings also provide a rationale for further studies of early preoperative or intraoperative prophylaxis to reduce the incidence of symptomatic thromboembolism after total knee arthroplasty.

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