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Incidence of symptomatic venous thromboembolism in oncologic patients undergoing lower-extremity endoprosthetic arthroplasty

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Incidence of Symptomatic Venous Thromboembolism in Oncologic Patients Undergoing Lower-Extremity Endoprosthetic Arthroplasty

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Background: As both cancer and major orthopaedic surgery are risk factors for venous thromboembolism, patients undergoing lower-extremity oncologic endoprosthetic arthroplasty for neoplastic processes are at substantial risk of the development of symptomatic venous thromboembolism. Therefore, the primary purpose of this study was to determine the incidence of symptomatic venous thromboembolism in patients undergoing lower-extremity oncologic endoprosthetic arthroplasty. Secondary purposes were to assess whether chemoprophylaxis influenced the incidence of venous thromboembolism, surgical complications, or the incidence of local sarcoma recurrence. We also sought to determine whether any known risk factors for venous thromboembolism could be identified in this patient population.

Methods: We performed a retrospective comparative review of 423 patients who had undergone mega-endoprosthetic reconstruction following cancer resection. Univariate analysis was used to assess the association between chemoprophylaxis and the incidence of venous thromboembolism, to postulate the surgical complications associated with chemoprophylaxis, and to assess the rate of recurrence of local sarcoma as well the association between risk factors and venous thromboembolism.

Results: Seventeen patients (4.0%) (95% confidence interval: 2.5% to 6.3%) had a venous thromboembolic event, ten with deep venous thrombosis and seven with nonfatal pulmonary embolism. Risk factors and chemoprophylactic regimens were not statistically associated with the occurrence of venous thromboembolism.

Conclusions: The incidence of symptomatic venous thromboembolism in our group of cancer patients who underwent lower-extremity endoprosthetic arthroplasty was lower than anticipated. A significant difference was not identified between the use of any or no chemoprophylactic agent and the incidence of venous thromboembolism or complication rates. No risk factors were associated with the incidence of symptomatic venous thromboembolism.

Level of Evidence: Therapeutic Level III. See Instructions to Authors for a complete description of levels of evidence.

The role of anticoagulation in the management of patients undergoing lower-extremity total joint arthroplasty has become more defined; however, its role in limb-salvage surgery remains unclear[1-6]. Included in limb-salvage surgical procedures is the use of oncologic endoprostheses (Fig. 1), which are being employed with increasing frequency following massive bone resections for the treatment of cancer.

Cancer patients undergoing surgery have been shown to have a significantly higher risk of postoperative venous thromboembolism, deep venous thrombosis, and pulmonary embolism and as much as three times the likelihood of having a fatal pulmonary embolism as compared with the likelihood in patients who do not have cancer[4-6]. Cancer patients who have symptomatic venous thromboembolism have a higher mortality rate[7]. Major orthopaedic surgery is a significant risk factor and has an estimated odds ratio of ten to twenty with regard to venous thromboembolism[3,8-11]. Patients with an increased total number of risk factors may incur a greater indi-

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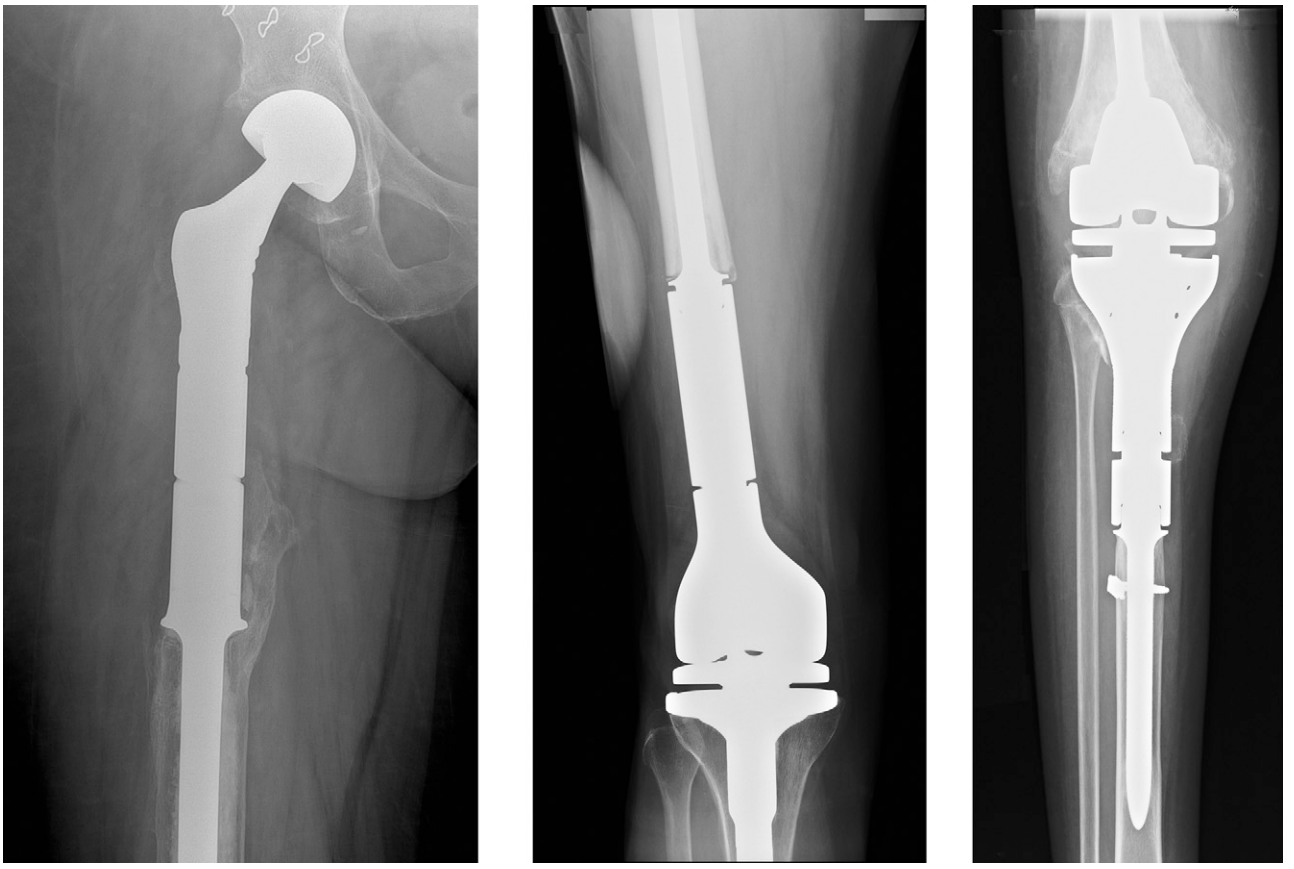

Fig. 1

Representative anteroposterior radiographs of endoprostheses that were implanted after tumor resection in the proximal part of the femur *(image at left),* distal part of the femur *(image in center),* and proximal part of the tibia *(image at right).*

vidual risk of venous thromboembolism[3,8-11]. It was therefore postulated that cancer patients who undergo oncologic endoprosthetic arthroplasty may be at a substantially higher risk of the development of symptomatic venous thromboembolism. Many patients undergoing limb salvage have historically not received routine chemoprophylaxis for fear of increased bleeding and subsequent wound complications[12]. Since sarcomas are highly implantable, hematomas as a result of aggressive anticoagulation may lead to increased rates of local recurrence[5]. Centers performing large volumes of lower-extremity bone-tumor resections have shown no higher incidences of symptomatic venous thromboembolism in patients who received no chemoprophylaxis than the incidence seen in other lower-extremity arthroplasty populations[13-15]. This knowledge leads one to question the routine use of chemoprophylaxis in this population at high risk of local recurrence, wound complications, and infection.

The purpose of this study was to determine the incidence of symptomatic venous thromboembolism for patients undergoing lower-extremity oncologic endoprosthetic arthroplasty. We compared this group with patients undergoing elective total hip and knee arthroplasty. As secondary goals, we sought to examine the effects that different chemoprophylactic agents had on the occurrence of symptomatic venous thromboembolism, on complication rates, and on local recurrence of sarcoma. Furthermore, we attempted to identify any risk factors for symptomatic venous thromboembolism that could potentially aid in establishing a protocol for the selective use of chemoprophylaxis.

Materials and Methods

Three tertiary referral centers for musculoskeletal oncology participated in this retrospective comparative study. Institutional review board approval was obtained at each institution. The study group consisted of all patients who were seventeen years of age or older and had a diagnosis of cancer that had been treated with primary or revision lower-extremity endoprosthetic joint arthroplasty sometime between 1989 and 2007. Indications for the surgical procedure were malignant tumors requiring wide resection of the proximal part of the femur, distal part of the femur, or proximal part of the tibia and resulting in inadequate remaining articulating bone for reconstruction without the use of a prosthesis. Age seventeen was chosen because this is a common age for musculoskeletal maturity and is the age at which patients are treated as adults at our institutions.

Historically, the rate of symptomatic venous thromboembolism in the population of patients undergoing elective total joint arthroplasty with chemoprophylaxis is estimated to be approximately 3%[9,16-21]. A doubling of this rate was chosen to represent a number that the authors believed would be a clinically significant difference between our population and the historical control. A power analysis indicated that a minimum sample size of 359 patients was needed to detect this clinically significant difference with 80% power with

use of a continuity-corrected chi-square statistic or Fisher exact test at a 5% significance level. Assumptions included (1) that all patients with symptomatic venous thromboembolism would be captured in retrospective review of the charts, and (2) that this represents the true rate of symptomatic venous thromboembolism.

Review of the databases from our three institutions yielded 561 consecutive patients who had undergone limb salvage with use of a lower-extremity oncologic endoprosthesis. One hundred and thirty-eight patients were excluded for reasons that included an age of less than seventeen years (forty-four patients), a noncancer diagnosis (seventy-six patients), and incomplete medical records or inadequate follow-up of less than six weeks (eighteen patients), yielding a final study number of 423 patients.

A review of the medical records for each patient was performed to extract pertinent demographic data, including diagnosis, age, sex, and body mass index. Our primary outcome variable was any symptomatic occurrence of venous thromboembolism within six weeks of the surgery. Our definition of venous thromboembolism was any deep venous thrombosis or pulmonary embolism confirmed by an imaging modality, including a positive result on a computed tomography scan of the chest, high-probability ventilation-perfusion scan, venographic study, or duplex ultrasound. Six weeks was used as the end point for time because we believe that any venous thromboembolism occurring after this point should not be attributed to the surgery.

We identified four postoperative anticoagulation regimens, which were the basis of our four groups: (1) no agent, (2) a low-molecular-weight heparin, (3) warfarin, and (4) an alternative regimen. We chose to combine different low-molecular-weight heparins (including enoxaparin and dalteparin) into a single group. In general, patients treated in the low-molecular-weight heparin and warfarin groups received ten to twenty-one days of anticoagulation. Group 4 consisted of several alternative prophylactic regimens, which included subcutaneous heparin used alone, aspirin used alone, and several drugs used in various combinations. For example, several patients received short-term anticoagulation with a low-molecular-weight heparin for three to five days while they were an inpatient, with conversion to aspirin or no agent at the time of discharge. Mechanical prophylaxis was routinely employed in all patients at all three institutions during the study period; hence, mechanical prophylaxis was not analyzed as a variable.

We identified any complications occurring in the early postoperative period that might be attributable to anticoagulation, including superficial infection; deep infection; superficial wound complications, such as a dehiscence; and deep wound complications, defined as hematoma or seroma requiring surgical intervention. Major bleeding was defined as transfusion of greater than five units of packed red blood cells postoperatively, a gastrointestinal bleed, or a retroperitoneal hematoma. We also identified local recurrences for all sarcomas with a minimum of two years of follow-up.

We identified and recorded known and potential risk factors for venous thromboembolism, including a history of venous thromboembolism, pathologic fracture, sex, obesity (body mass index >30 kg/m^2), anatomic location of procedure, residence in an institution, advanced age (greater than seventy years), history of cerebrovascular accident, history of a hypercoagulable state, tamoxifen use, oral contraceptive use, chronic renal insufficiency, or presence of a central venous catheter[7,22-25].

Descriptive statistics were used to explore all variables and to compute the incidence of symptomatic venous thromboembolism. The Wilcoxon rank-sum test for continuous variables and the Fisher exact test for dichotomous variables were used to examine the association between risk factors (age, sex, type of cancer, pathologic fracture, obesity, location of procedure [hip vs. knee]) and incidence of symptomatic venous thromboembolism. The Fisher exact test was used to examine the association between (1) prophylactic regimen and incidence of venous thromboembolism, (2) prophylactic regimen and specific complications (major bleeding, superficial and deep infections, or superficial and deep wound complications), and (3) prophylactic regimen and local recurrence (including only patients with sarcoma who had a minimum follow-up of two years). A multiple variable logistic regression analysis was used to examine the association between prophylactic regimen and the presence of one or more complications, controlling for age, body mass index, fracture, and location of surgery (hip vs. knee). All statistical tests were two-tailed, with a p value of 0.05 or less considered significant.

Source of Funding

There was no external source of funding for this study.

Results

Four hundred and twenty-three patients underwent reconstruction with an endoprosthesis following resection of a bone tumor and had greater than six weeks of follow-up. There were 341 sarcomas and eighty-two carcinomas (Table I). There

TABLE I Cancer Type

Type of Cancer	Number of Patients
Sarcoma	341
Osteosarcoma	158
Chondrosarcoma	69
Malignant fibrous histiosarcoma	27
Leiomyosarcoma	25
Ewing sarcoma	15
Fibrosarcoma	10
Angiosarcoma	7
Synovial sarcoma	5
Sarcoma not otherwise specified	5
Hemangiopericytoma	3
Malignant giant-cell tumor	3
Neurosarcoma	3
Spindle-cell sarcoma	2
Other*	9
Adenocarcinoma	58
Breast	17
Kidney	16
Prostate	6
Lung	4
Colon	3
Thyroid	2
Gastrointestinal tract (primary)	5
Uterus	1
Bladder	1
Unknown primary	3
Multiple myeloma	9
Lymphoma	6
Squamous-cell carcinoma	5
Melanoma	4
Total	423

*Sarcomas with ''other'' diagnoses include 1 each of liposarcoma, follicular dendritic-cell sarcoma, chondromatosis, malignant granular-cell tumor, peripheral-nerve-sheath tumor, postradiation sarcoma, alveolar soft-part sarcoma, telangiectatic sarcoma, and undifferentiated sarcoma.

TABLE II Distribution of Endoprostheses and Occurrence of Venous Thromboembolism by Location*

	Endoprosthetic Knee (N = 269)	Endoprosthetic Hip (N = 142)	Total Femur (N = 12)
Venous thromboembolisms	8 (3.0%; CI, 1.5 to 5.8)	8 (5.6%; CI, 2.9 to 10.7)	1 (8.3%; CI, 1.5 to 35.4)
Deep venous thrombosis†	3 (1.5%; CI, 0.6 to 3.8)	6 (4.2%; CI, 2.0 to 8.9)	1 (12.5%)
Pulmonary embolism†	5 (1.5%; CI, 0.6 to 3.8)	2 (1.4%; CI, 0.4 to 5.0)	0 (0%)

*CI = 95% confidence interval. †Two of the patients (one hip and one knee) with pulmonary embolism had concurrent evidence of deep venous thrombosis on Doppler examination but were included only in the pulmonary embolism group.

were 269 endoprosthetic procedures in the knee (distal part of the femur or proximal part of the tibia) and 142 in the proximal part of the femur, and there were twelve total femoral reconstructions (Table II).

Incidence of Symptomatic Venous Thromboembolism

Of the 423 cancer patients who underwent endoprosthetic arthroplasty, seventeen patients (4.0%) had a symptomatic venous thromboembolism (95% confidence interval, 2.5% to 6.3%). Of these, ten had a deep venous thrombosis (2.4%) (95% confidence interval, 1.3% to 4.3%) and seven had a pulmonary embolism (1.7%) (95% confidence interval, 0.8% to 3.4%). Two of the patients with a pulmonary embolism had concurrent evidence of deep venous thrombosis on Doppler examination and were included only in the pulmonary embolism group. There were no known occurrences of fatal pulmonary embolism. The characteristics of the seventeen patients with symptomatic venous thromboembolism are listed in Table III.

Symptomatic Venous Thromboembolism by Chemoprophylactic Regimen

Three hundred and twenty patients (76%) received some form of chemoprophylaxis, and 103 (24%) received none. Table IV

TABLE III Patients with Venous Thromboembolism*

Age *(yr)*	Sex	Diagnosis	Outcome	Location of Tumor	Hip or Knee	Prophylactic Regimen
58	M	Chondrosarcoma	DVT	PF	Hip	None
30	F	Chondrosarcoma	DVT	PF	Hip	Warfarin
36	M	Osteosarcoma	DVT	DF	Knee	Warfarin
67	M	Chondrosarcoma	PE	PF	Hip	None
80	F	Breast cancer; pathologic fracture	DVT	PF	Hip	Warfarin
70	M	Chondrosarcoma	DVT/PE	PF	Hip	Enoxaparin followed by warfarin
32	F	Osteosarcoma	DVT	DF	Knee	Aspirin
77	M	Osteosarcoma	DVT	PF	Hip	Warfarin
56	M	Melanoma, metastatic	PE	DF	Knee	Warfarin
62	M	SCC, metastatic	PE	PT	Knee	None
31	M	Chondrosarcoma	DVT	PF	Hip	Warfarin
33	M	Osteosarcoma	DVT	PF	Hip	Heparin
55	M	Chondrosarcoma	DVT/PE	PT	Knee	Dalteparin
18	M	Osteosarcoma	PE	PT	Knee	Dalteparin
31	M	Osteosarcoma	DVT	Femur	Total	Dalteparin
53	F	Malignant fibrous histiocytoma	PE	DF	Knee	Enoxaparin
59	F	Malignant fibrous histiocytoma	DVT	DF	Knee	Warfarin, heparin, IVC filter

*DVT = deep venous thrombosis, PF = proximal part of the femur, DF = distal part of the femur, PE = pulmonary embolism, SCC = squamous-cell carcinoma, PT = proximal part of the tibia, and IVC = inferior vena cava.

TABLE IV Incidence of Venous Thromboembolism by Chemoprophylactic Regimen*

	No Prophylaxis (N = 103)	Warfarin (N = 115)	Low-Molecular-Weight Heparin (N = 147)	Other (N = 58)	Total No. of Patients (N = 423)
Venous thromboemboli	3 (2.9%, CI: 1.0% to 8.2%)	6 (5.2%, CI: 2.4% to 10.9%)	4 (2.7%, CI: 1.1% to 6.8%)	4 (6.9%, CI: 2.7% to 16.4%)	17 (4.0%, CI: 2.5% to 6.3%)
Deep venous thrombosis	1 (1.0%, CI: 0.2% to 5.3%)	5 (4.3%, CI: 1.9% to 9.8%)	2 (1.4%, CI: 0.4% to 4.8%)	3 (5.2%, CI: 1.8% to 14.1%)	10 (2.4%, CI: 1.3% to 4.3%)
Pulmonary embolism	2 (1.9%, CI: 0.5% to 6.8%)	1 (0.9%, CI: 0.2% to 4.8%)	2 (1.4%, CI: 0.4% to 4.8%)	1 (1.7%, CI: 0.3% to 9.1%)	7 (1.6%, CI: 0.8% to 3.4%)

*CI = 95% confidence interval.

TABLE V Complications by Chemoprophylactic Regimen*

	No Prophylaxis (N = 103)	Warfarin (N = 115)	Low-Molecular-Weight Heparin (N = 147)	Other (N = 58)	Total Patients (N = 423)
Complications	13 (12.6%, CI: 7.5% to 20.4%)	16 (13.9%, CI: 8.7% to 21.4%)	28 (19.0%, CI: 13.5% to 26.2%)	13 (22.4%, CI: 13.6% to 34.7%)	70 (16.5%, CI: 13.3% to 20.4%)
Superficial wound problem	2 (1.9%, CI: 0.5% to 6.8%)	4 (3.5%, CI: 1.4% to 8.6%)	12 (8.2%, CI: 4.7% to 13.7%)	3 (5.2%, CI: 1.8% to 14.1%)	21 (5.0%, CI: 3.3% to 7.5%)
Deep wound problem	3 (2.9%, CI: 1.0% to 8.2%)	2 (1.7%, CI: 0.5% to 6.1%)	1 (0.7%, CI: 0.1% to 3.8%)	1 (1.7%, CI: 0.3% to 9.1%)	7 (1.6%, CI: 0.8% to 3.3%)
Superficial infection	1 (0.9%, CI: 0.2% to 5.3%)	1 (0.9%, CI: 0.2% to 4.8%)	2 (1.4%, CI: 0.4% to 4.8%)	2 (3.4%, CI: 1.0% to 11.7%)	6 (1.4%, CI: 0.7% to 3.1%)
Deep infection	6 (5.8%, CI: 2.7% to 12.1%)	8 (7.0%, CI: 3.6% to 13.1%)	11 (7.5%, CI: 4.2% to 12.9%)	4 (6.9%, CI: 2.7% to 16.4%)	29 (6.9%, CI: 4.8% to 9.7%)
Major bleeding	1 (0.9%, CI: 0.2% to 5.3%)	1 (0.9%, CI: 0.2% to 4.8%)	2 (1.4%, CI: 0.4% to 4.8%)	3 (5.2%, CI: 1.8% to 14.1%)	7 (1.6%, CI: 0.8% to 3.74%)

*CI = 95% confidence interval.

TABLE VI Sarcoma Local Recurrence Rates by Chemoprophylactic Regimen After a Minimum of Two Years of Follow-up*

	No Prophylaxis (N = 88)	Warfarin (N = 82)	Low-Molecular-Weight Heparin (N = 94)	Other (N = 32)	Total Patients (N = 296)
Local recurrence	11 (12.5%, CI: 7.1% to 21.0%)	5 (6.1%, CI: 2.6% to 13.5%)	2 (2.1%, CI: 0.6% to 7.4%)	6 (18.8%, CI: 8.9% to 35.3%)	24 (8.1%, CI: 5.5% to 11.8%)

*CI = 95% confidence interval.

demonstrates the number of symptomatic venous thromboembolism events by chemoprophylactic regimen. Three of 103 patients who received no prophylaxis had a venous thromboembolism event, whereas six of 115 patients who received Coumadin (warfarin), four of 147 patients who received low-molecular-weight heparin and four of fifty-eight patients who received an alternative regimen had venous thromboembolism events. These results did not achieve a significant difference ($p = 0.245$) on the basis of Fisher exact testing.

Complication Rates by Chemoprophylactic Regimen

There were no differences in specific complication rates by chemoprophylactic regimen on the basis of univariate analyses (Table V). Thirty-five patients (8.3%) had an infection, usually deep; twenty-eight patients (6.6%) had wound complications not attributable to infection; and seven patients (1.7%) had a major bleeding complication including a gastrointestinal bleed, cerebrovascular accident, or large hematoma requiring surgical debridement. The overall complication rate was 16.5% (seventy of 423 patients). Logistic regression analysis found no statistical association between chemoprophylactic regimen and presence of a complication; however, patients undergoing hip compared with knee arthroplasty were less likely to have a complication after surgery (odds ratio, 0.30; 95% confidence interval, 0.16 to 0.56).

Local Recurrence by Chemoprophylactic Regimen

Among sarcoma patients with at least two years of follow-up, statistical differences were noted in local recurrence on the basis of chemoprophylactic regimen (Fisher exact test $p = 0.0049$) (Table VI). The total number of local recurrences for 296 sarcoma patients was twenty-four, representing a local recurrence rate of 8.1%. Five (6.1%) of eighty-two sarcoma patients treated with Coumadin (warfarin) and two (2.1%) of ninety-four sarcoma patients treated with low-molecular-weight heparin had a local recurrence, in contrast to eleven (12.5%) of eighty-eight and six (18.8%) of thirty-two patients who were treated with no prophylaxis or a nontraditional form of prophylaxis, respectively, and had local recurrence.

Symptomatic Venous Thromboembolism and Risk Factors

The multiple risk factors for venous thromboembolism were evaluated with use of univariate analysis, and none were statistically associated with the incidence of symptomatic venous thromboembolism in our patient population.

Discussion

We found a low overall incidence of symptomatic venous thromboembolism (4%) with no fatal pulmonary emboli, which does not appear to be substantially different from rates seen in elective total hip and knee arthroplasty populations. We did not demonstrate that any one prophylactic regimen provided better protection than another against symptomatic venous thromboembolism, although we acknowledge an ostensible regimen selection bias between cohorts on the basis of tumor, resection, and reconstruction type. This finding is not surprising, given the lack of a definitive answer in the substantially larger patient population that has been reported in the elective arthroplasty literature, in which the overall risk of symptomatic venous thromboembolism is approximately 3%[9,16-21].

Studies addressing venous thromboembolism in orthopaedic oncology patients are rare. Lin et al. reported a prevalence of *asymptomatic* deep venous thrombosis of 14% and symptomatic pulmonary embolism of 0.6% in 169 cancer patients who were undergoing a variety of orthopaedic lower-extremity surgical procedures, but further analysis is difficult because of the heterogeneity of patients, diseases, and treatments, including multimodal anticoagulant regimens[4]. The same group later found an overall deep venous thrombosis rate of 4% in cancer patients who were undergoing hip arthroplasty for pathologic fractures or tumor resections along with low-molecular-weight heparin as chemoprophylaxis[6].

Mitchell et al. reported a venous thromboembolism rate of 5.2% and a fatal pulmonary embolism rate of 0.4% in a heterogeneous group of 252 patients with bone or soft-tissue sarcomas who were undergoing a variety of orthopaedic procedures[5]. All thirteen patients with venous thromboembolism had sarcoma of the hip or thigh, and two of thirty-one patients undergoing endoprosthesis arthroplasty had a venous thromboembolism. Further, they found that the majority of venous thromboembolism events actually occurred before definitive limb-salvage surgery, implying that the procedure itself may not be the main risk factor. The Royal Orthopaedic Hospital Oncology Service in Birmingham, United Kingdom, published the results of 661 endoprosthetic replacements after ten years of follow-up[14]. They noted a low (3.4% overall) incidence of venous thromboembolism, which was similar to that seen in our group. The incidence of deep venous thrombosis was 1.1%, whereas the incidence of pulmonary embolism accounted for a higher percentage and was 2.3%[14]. Another recent study of venous thromboembolism in arthroplasty patients, in which a total venous thromboembolism rate of 3.5% was demonstrated, showed via subgroup analysis that a history of malignancy conferred a 4.2% risk of the development of venous thromboembolism as compared with a prevalence of venous thromboembolism of 1.65% in patients without a history of malignancy[8].

There is little evidence-based guidance for the orthopaedic oncologist whose patients fall into the category of having a high risk of both bleeding and venous thromboembolism, according to the guidelines of both the American Academy of Orthopaedic Surgeons (AAOS) and the American College of Chest Physicians (ACCP). The ACCP Prevention of Venous Thromboembolism guidelines are inconclusive when applied to orthopaedic oncology patients[3]. The ACCP strongly considers most orthopaedic patients to be "high-risk," and they recommend the use of low-molecular-weight heparin, fondaparinux, or Coumadin (warfarin) for these patients. For cancer patients, the ACCP guidelines recommend "aggressive thromboprophylaxis" that is based on the type of surgery. There are several caveats to these recommendations, however. First, they note that patients with "high venous thromboembolism risk plus high bleeding risk" can be considered for mechanical prophylaxis alone. Second, there is a comment that descriptive terms, such as "high bleeding risk," are purposely left undefined to allow individual clinician interpretation. The AAOS Guidelines Oversight Committee conducted an evidence-based review of the literature and offered an alternative set of recommendations to the orthopaedic community in 2008[2]. Their recommendations with regard to patients undergoing limb salvage or endoprosthetic arthroplasty indicate that aspirin, Coumadin (warfarin), or no anticoagulant at all should be considered for patients who are at high risk for venous thromboembolism or bleeding.

We hypothesized that patients who received anticoagulants would demonstrate more complications that could be associated with anticoagulation, such as infections or wound dehiscences. We were unable to demonstrate that any prophylactic regimen was associated with higher complication rates, although we did note that complication rates were higher in patients who had undergone knee surgery than they were in patients who had undergone hip surgery. Our overall complication rates proved to be similar to those published in the largest comparable series, again emphasizing that this is a patient population already at high risk for complications that may be aggravated by aggressive anticoagulation[26]. We were unable to confirm these individual risk factors for deep venous thrombosis or pulmonary embolism in our patient population, al-

though such confirmation might have been useful in the creation of a selective-use protocol[3,8-11].

There were several limitations to our study. It was retrospective and observational, covering two decades of operative experience at multiple institutions. The use of chemoprophylactic agents was not randomized or standardized, and there may have been some differences between patients who did not receive prophylaxis and those who did. Further, multimodal chemoprophylaxis protocols were employed. These limitations reflect the current variability among orthopaedic surgeons in the use of different chemoprophylactic agents and also reflect the evolution in the use of these agents over the last few decades. The rarity of these limb-salvage surgical procedures, the low prevalence of symptomatic venous thromboembolism, and the availability of multimodal prophylaxis protocols make a prospective trial unachievable. In the absence of a large set of patients, we were forced to compare our findings to a historical control, acknowledging differences in technical aspects of the limb-salvage procedures, such as operative time, estimated blood loss, and the need for soft-tissue coverage. The authors acknowledge that the cancer ascertainment methods used for historical hip and knee arthroplasty controls may be different than the methods that we used in our patients.

In summary, the primary goal of this project was to provide a baseline incidence of symptomatic venous thromboembolism in oncologic patients undergoing lower-extremity endoprosthetic arthroplasty. In this study, patients undergoing endoprosthetic arthroplasty for the treatment of cancer did not have the extremely high incidence of symptomatic venous thromboembolism that we had anticipated, but our patients did have the high risks of wound complications and infections that are common to this population. The authors continue to be concerned about the widespread use of pan-prophylactic protocols for the avoidance of venous thromboembolism, particularly in this complex group of patients in whom multiple variables must be weighed regarding the potential benefits and risks of chemoprophylactic agents against venous thromboembolism. ■

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