IVC Filters May Prevent Fatal Pulmonary Embolism in Musculoskeletal Tumor Surgery

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Abstract To determine whether inferior vena cava (IVC) filter placement protects patients with musculoskeletal tumors from fatal pulmonary embolisms (PE), we retrospectively analyzed the records of 81 patients who underwent surgery for pelvic and lower extremity malignancies. All 81 patients received an IVC filter and mechanical compression for deep venous thrombosis (DVT) prophylaxis, but no pharmacologic anticoagulation. Duplex imaging was performed before hospital discharge and when clinical suspicion of DVT arose. Seventy-six of the 81 (94%) patients were followed at least 3 months (mean, 21.3 months; range, 3–77 months) postoperatively. We reviewed the perioperative medical records and office visit notes to determine the rate of clinically evident DVT, symptomatic PE, wound complications, and IVC filter-related complications. DVT and PE incidences in the early postoperative period (< 30 days) were 21% (17 of 81) and 2% (two of 81), respectively. There were no known deaths from PE. Patients undergoing reconstruction surgery ($n = 41$) were more likely to have early DVT develop after definitive tumor surgery. Patient age, tumor type or histology, anatomic location, presence of pathologic fracture,

or development of wound complications did not correlate with an increased DVT rate. Two (3%) patients had late DVT, and none had a late PE. Combining an IVC filter with mechanical limb compression prevented fatal PE in patients undergoing orthopaedic surgery for malignancies of the pelvis and lower extremity and is a reasonable form of thromboembolic prophylaxis specific for this patient population.

Level of Evidence: Level IV, therapeutic study. See the Guidelines for Authors for a complete description of levels of evidence.

Introduction

Patients with malignant disease undergoing major orthopaedic procedures possess two major risk factors for venous thrombosis or embolism [2, 3, 19]. Cancer carries a fourfold increase in the risk of thrombosis; the baseline DVT rate in patients with malignancy can be as much as 35.2% [11, 20]. PE can occur in as many as 17% of patients with cancer, with 14% being fatal [34]. However, major orthopaedic surgery is a strong risk factor for venous thrombosis or embolism [10]. Most patients undergoing resections and/or reconstructions for pelvic and lower extremity malignancies will have long postoperative recovery periods and will require extensive dissections around blood vessels of various calibers [3], with the risk of endothelial injury that can lead to thrombus formation and subsequent DVT. Although prophylaxis for DVT and PE have been described extensively for patients undergoing major orthopaedic procedures, such as hip fracture surgery and total joint arthroplasties [10, 24, 26, 37, 38], few have been described specifically for patients with musculoskeletal tumors [3, 22, 27, 30].

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Although pharmacologic anticoagulation may be effective in reducing the risk of venous thrombosis or embolism in patients undergoing major orthopaedic procedures [10, 26], its use in patients with cancer should be viewed cautiously. Patients with cancer who are treated with standard or low-molecular-weight heparin have a higher risk of bleeding compared with patients without cancer [12, 29, 31]. In addition, patients with cancer are at increased risk of recurrent thrombosis despite anticoagulant therapy [21]. IVC filters are safe and effective in preventing PE and PE-related deaths in patients with cancer [3, 6, 32, 33, 36]. In a previous study from our institution, IVC filter insertion combined with mechanical prophylaxis was a low-risk procedure that prevented fatal PE in patients with metastatic pathologic fractures of the lower extremities [3]. We have since adopted this protocol for patients with pelvic and lower extremity malignancies undergoing definitive surgery.

After implementing this protocol specifically for this patient group, we determined the rate of early and long-term detectable DVT and symptomatic PE. We then determined the DVT rate associated with the following variables: the type of tumor, its anatomic site, presence of pathologic fracture, type of surgery performed, performance of skeletal reconstruction, and occurrence of wound complications. Finally, we identified complications associated with IVC filter placement.

Materials and Methods

We identified, through a musculoskeletal tumor database, all patients who had IVC filter insertion from 2001 to 2006. For inclusion in the study, the patients must have (1) had a pelvic or lower extremity malignancy, including sarcomas, lymphomas, myelomas, and metastatic cancer; (2) undergone definitive surgical treatment, with or without reconstruction; (3) and had placement of an IVC filter before the definitive surgery. We identified 103 patients and excluded 22 patients for the following reasons. Six patients had benign tumors, six had resection of upper extremity malignancies, seven had metastatic lesions that required biopsy only, without definitive surgical treatment, and three were diagnosed with PE before placement of an IVC filter. This left 81 patients, 35 males and 46 females with a mean age of 57 years (range, 16–88 years). Perioperative medical records, office visit notes, and duplex ultrasound reports were reviewed. Clinical reports of acute DVT or PE and associated emergency visits or hospital admission were recorded, and the patient's primary care doctors or oncologists were contacted as needed for confirmation. Only the 76 patients with a minimum followup of 3 months (mean, 21.3 months; range, 3–77 months)

postoperatively were included in the description of late episodes of venous thrombosis or embolism. We obtained prior approval by our Institutional Review Board.

We stratified patients based on eight variables, including age, histologic diagnosis, tumor origin (bone or soft tissue), anatomic location, pathologic fracture, type of surgery, skeletal reconstruction, and postoperative wound complications (Table 1), to determine if these were associated with a higher rate of DVT. Eleven patients were 40 years or younger and 70 were older than 40 years. Forty-six patients were diagnosed with a sarcoma and 35 with either a metastatic cancer or hematologic malignancy, including lymphoma and myeloma. Seventeen patients had soft tissue tumors and 64 had bone tumors. In 37 patients, the lesions were localized to the pelvic bones, acetabulum, and proximal portion of the femur. Lesions of the thigh, including the body of the femur and its distal articulation, occurred in 37 patients. Seven patients had malignancies distal to the knee. Pathologic fractures were present preoperatively in 31 patients. The surgeries performed consisted of 53 en bloc or wide resections, 16 curettage procedures with or without prophylactic internal fixation, and seven amputations, including hemipelvectomy or hip disarticulation. Major reconstructive surgery was defined as any procedure requiring an arthroplasty, structural allograft transplantation, or an allograft prosthetic composite. Surgeries involving internal fixation for impending or completed pathologic fractures in 11 patients were not considered reconstruction in this study. Thirty-eight patients underwent reconstructive surgery. Seventeen patients had postoperative wound-healing complications. These patients had wound-site infection or wound necrosis, with four requiring reoperations. Two of these patients required revision surgery and two required amputation of the affected limb for inability to eradicate infections.

IVC filters were inserted by the vascular service in 69 cases and by interventional radiology in 12 cases. The vascular service's preference was for titanium Greenfield filters (Boston Scientific, Watertown, MA), which were inserted in the operating room after induction of anesthesia and before commencement of the surgical resection. The filters were placed percutaneously through the common femoral vein in 66 cases and through the right internal jugular vein in three cases. The interventional radiologists preferentially used Vena TechTM LGM[®] filters (B. Braun, Evanston, IL), which were inserted 24 hours before surgery at the radiology suite; six were placed percutaneously through the right common femoral vein, five through the right internal jugular vein, and one through the right external jugular vein. All patients received permanent filters except for two who received recoverable Greenfield filters because of their relatively young age. One was an 18-year-old woman with a distal femur osteosarcoma and

Table 1. Demographics within variable categories

Category	Number of patients	DVT	No DVT	p Value	PE
Total	81	17	64		2
Age				0.443	
≤ 40 years	11	1	10		0
> 40 years	70	16	54		2
Tumor type				0.273	
Sarcoma	46	12	34		2
Metastatic/myeloma/lymphoma	35	5	30		0
Tissue type of origin				0.503	
Soft tissue	17	2	15		0
Bone	64	15	49		2
Anatomic location of lesion				0.470	
Pelvis/hip	37	10	27		1
Thigh/femur	37	6	31		1
Leg/tibia-fibula	7	1	6		0
Pathologic fracture				0.786	
Yes	31	7	24		0
No	50	10	40		2
Type of surgery				0.408	
Resection	56	14	42		2
Curettage	18	2	16		0
Amputation	7	1	6		0
Skeletal reconstruction				0.027	
Yes	41	13	28		2
No	40	4	36		0
Wound complications				0.176	
Yes	17	6	11		2
No	64	11	53		0

DVT = deep venous thrombosis; PE = pulmonary embolism.

the other was a 16-year-old boy with a proximal femur Ewing's sarcoma.

All patients were fitted with antiembolism stockings (T.E.D.TM; Tyco Healthcare, Mansfield, MA) and sequential compression devices (SCD Response[®]; Kendall, Mansfield, MA) with thigh-length sleeves before, during, and after surgery, until the time of discharge. These were placed on both lower limbs whenever the site of surgery allowed for it; if not, only the nonoperative limb was fitted with the devices. Preoperative venous duplex scanning was not performed routinely; however, all patients were screened for DVT within 24 hours before discharge or earlier if clinical suspicion of DVT arose. Spiral chest CT scans were performed only on patients clinically suspected to have PE.

To analyze the associated DVT rate, we used Fisher's (two-sided) exact test for categorical variables when a 2 × 2 contingency table could be constructed (age, tumor type, pathologic fracture, wound complication, skeletal reconstruction). We used Pearson's chi square test to assess the

association of DVT with categorical variables that required 2 × 3 tables (type of surgery, tumor location).

Results

Seventeen of 81 patients (21%) had clinically detectable DVT and two (3%) had symptomatic PE confirmed by spiral chest CT during the early postoperative period (Table 1). The average time to detection of a DVT was 10 days (range, 2–21 days). Treatment of DVT was determined on an individual basis, with input from the vascular service, based on the extent of the thrombus and the patient's symptoms. Nine of the DVTs involved short segments located in the common femoral vein, saphenofemoral junction, or popliteal veins; these generally were not treated, except for two patients who concurrently had symptomatic, CT-proven PE. They then were treated with warfarin bridged with unfractionated heparin (Coumadin[®]; Cerner Multum, Denver, CO). Two patients had painful,

swollen calves with isolated DVT of the calf veins; they were treated with aspirin. Extensive thrombi extending from the calf veins up to the common femoral veins or external veins occurred in six patients, who were treated with warfarin and bridged with low-molecular-weight heparin or unfractionated heparin.

Concomitant performance of skeletal reconstruction correlated with a higher rate of DVT (Table 1). Age, histologic type and tissue origin of cancer, tumor location, pathologic fracture, type of reconstruction procedure, or wound-healing complications did not correlate with an increased rate of DVT.

Insertion site thrombosis is defined as thrombosis occurring within 24 hours in the vein accessed for IVC filter placement [25]. In seven patients (9%), insertion-site thrombosis could not be excluded because the DVT occurred on the limb through which the filter was inserted when it was not the side of the tumor excision. In seven of 81 patients (9%), a DVT occurred in the limb of tumor excision, which was also the limb accessed for filter insertion. In these cases, traction from surgical manipulation of the limb and filter placement may have contributed to the thrombus, and insertion site thrombosis was less certain. In six of the 17 patients (7%), early postoperative DVT occurred bilaterally.

There were two technical difficulties during filter placement. In one instance, the filter deployed prematurely in the carrier sheath; however, a second attempt was successful in the same sitting. In another instance, there was a mass in the IVC discovered during routine venacavagram before filter placement. Filter placement in this patient was performed successfully via a suprarenal (jugular) approach rather than via a femoral approach. No complications relating to filter malposition, migration, or insertion-site hematoma occurred. At last followup, no long-term complication related to the IVC filters had been identified. Two of 76 (3%) patients with a followup of at least 3 months had DVT, and none was known to have had a PE.

Discussion

We have adopted a protocol of IVC filter placement combined with mechanical compression for prophylaxis of venous thrombosis or embolism in patients with pelvic and lower extremity malignancies before definitive surgical treatment after an initial study on patients with metastatic pathologic fractures showed this protocol was safe and effective in preventing PE-related deaths [3]. In the current study, we evaluated this protocol of IVC filter placement in conjunction with perioperative mechanical compression to protect against fatal PE.

Some limitations of our study include a relatively small sample size, variability in the patient population, absence of a control group, and lack of routine screening for silent DVT and PE. The patients in this study may have been in different stages of their disease and may have had other comorbidities. We did not look back at records of patients we treated before adopting this protocol for comparison. However, a previous study showed a reduced rate of DVT and PE-related fatality between a group of 24 patients who followed this protocol and a group of 23 who received only mechanical prophylaxis. The DVT rate in the first group was 8.3% with no PE; there were five patients with PE in the second group, including two fatalities. In addition, our data included only Doppler-proven DVT and we may have missed some early DVTs because we did not routinely perform duplex scans at specific intervals during the patients' hospital stay, including preoperatively. Patients had only lower extremity ultrasound scans at followup if there was clinical suspicion of DVT, and therefore we also may have missed some late-developing asymptomatic DVT. Likewise, we can report only on symptomatic PE because we did not routinely perform spiral chest CT scans on our patients unless clinically indicated. Even so, the absence of symptomatic PE in this late period is encouraging, and to our knowledge, this series has the longest followup surveillance. We segregated the rate of thromboembolic events occurring during the early postoperative period from those occurring later, in contrast to previous studies that reported one DVT or PE rate encompassing a variable followup period. This is important because anticoagulants for thromboembolic prophylaxis usually are given during the early postoperative period and thus protect patients only during that period. The low rate of clinically evident DVT and PE during late followup in our patients (> 3 months) provides partial evidence that IVC filter placement effectively protects patients from fatal PE beyond the early postoperative period, at a time when these patients may still be at risk for various reasons, such as disease progression, adjuvant chemotherapy or radiation therapy, or even unexpectedly slow mobilization during rehabilitation or complications requiring additional surgery.

The main goal of this protocol is to prevent fatal PE, while avoiding the use of pharmacologic coagulation and its inherent risk of bleeding complications. Fatal PE may be the first manifestation of a DVT and is the foremost goal of thromboembolic prophylaxis [39]. The use of IVC filters safely and effectively reduces the risk of PE-related deaths in patients with cancer [9, 13, 32, 36]. Wallace et al. [36] reported a PE rate of 1.3% in 308 patients with cancer who had thromboembolic disease. Schwarz et al. [33] reported a 2.2% PE rate after IVC filter placement in 182 patients with cancer, and Jarrett et al. [13] reported a rate of 2.6% in 116 patients.

Orthopaedic oncologists sometimes are reluctant to give pharmacologic anticoagulation and are selective when doing so [3, 27, 30], mainly for fear of the patient experiencing bleeding into large potential dead spaces with raw surfaces left by tumor resections. This sentiment has been voiced in scientific meetings but is undocumented. Among patients with venous thrombosis or embolism in general (not specifically patients with cancer), the risk of major bleeding with vitamin K antagonists ranged from 0% to 16.7% according to one review [7] and may be modulated by other factors, such as patient age, simultaneous use of drugs interfering with hemostasis, and length of therapy. However, anticoagulation in patients with cancer may be hazardous. Patients with cancer who are treated with standard or low-molecular-weight heparin have a 12% to 50% risk of bleeding compared with patients without cancer [12, 29, 31]. In addition, recurrent thrombosis occurs in 20% to 27% of patients with cancer despite anticoagulant therapy [12, 21, 29, 31].

Our results suggest a higher rate of early postoperative DVT (21%) compared with results in other studies (Table 2). Nathan et al. [30] reported a 4% proximal DVT rate in 87 patients undergoing hip arthroplasties for tumors. The majority of the patients received anticoagulation and mechanical prophylaxis; however, some patients were not given anticoagulants because of the individual surgeon's concern for bleeding potential. Likewise, Mitchell et al. [27] reported a 4% DVT rate among patients with primary bone and soft tissue sarcomas undergoing surgery, including trunk and upper extremity locations. Our higher DVT rate also may have been accounted for by the large number of patients in our study who had metastatic disease or hematologic malignancies, both of which are risk factors for thrombosis and embolism [4, 15, 35]. Another difference from the other studies is that mechanical compression was our primary form of DVT prophylaxis and we did not use pharmacologic anticoagulation. IVC filters are not meant to prevent or treat DVT [14]. Nevertheless, the use of intermittent pneumatic compression devices for DVT prophylaxis without anticoagulation is not without merit. In one meta-analysis [37], pneumatic compression effected the lowest rates of DVT after TKA compared with low-molecular-weight heparin, aspirin, and warfarin, resulting in a 17.5% rate of DVT and 6.3% rate of asymptomatic PE [38]. Our DVT rate is closer to that of Lin et al. [22], who reported a 14.2% rate of proximal DVT in 169 patients with cancer undergoing major orthopaedic surgery and receiving mechanical prophylaxis. When they analyzed a subgroup of 54 patients who also received anticoagulation, the DVT rate was not substantially reduced. Benevenia et al. [3] reported a DVT rate of 23% in a group of 23 patients with

Table 2. Summary of data on DVT and PE in musculoskeletal tumor surgery

Study	Study sample	Type of DVT prophylaxis	DVT rate	PE rate	Factors associated with higher DVT rate
Mitchell et al. [27]	Bone and soft tissue sarcoma of the trunk or lower extremity	Diverse; 141/252 (57%) received LMWH; 33/252 received LMWH and mechanical prophylaxis	10/252 (4%)	3/252 (1.2%)	Tumors in the hip and thigh
Benevenia et al. [3]	Lower extremity pathologic fractures from metastasis	IVC filter and mechanical prophylaxis	2/24 (8%)	0/24 (0%)	Not studied
Nathan et al. [30]	Hip arthroplasty for malignant tumor resection or pathologic fracture	Mechanical prophylaxis only	6/23 (26%)	5/23 (22%)	
		Mechanical prophylaxis and LMWH (dalteparin)	3/78 (4%)	0/78 (0%)	Tumors in the pelvis; sarcomas
		Mechanical only	1/9 (11%)	1/9 (11%)	
Lin et al. [21]	Major pelvic or lower extremity surgery for cancer	Mechanical prophylaxis only	24/169 (4%)	1/169 (0.6%)	No difference by location, surgery performed, pathologic diagnosis, or lesion type
		Mechanical prophylaxis and anticoagulation (a subgroup of the entire sample)	7/54 (13%)		
Current study	Major pelvic and lower extremity surgery for cancer	Mechanical prophylaxis and IVC filter	17/81 (21%)	2/81 (2%)	Concomitant performance of skeletal reconstruction

DVT = deep venous thrombosis; PE = pulmonary embolism; LMWH = low-molecular-weight heparin; IVC = inferior vena cava.

metastatic pathologic fractures of the lower extremity who received only mechanical prophylaxis because of contraindications to anticoagulation.

We included not only proximal DVT but also distal or calf vein DVT in our accounting because as much as $\frac{1}{3}$ of thrombi in the calf veins are known to migrate proximally in 1 week to 3 months without treatment [8, 18, 23]. This also may explain our higher DVT rate compared with rates in prior studies, which reported only proximal DVT. Our patients diagnosed with DVT did not always receive anticoagulants because an IVC filter was in place to protect against PE. This avoided exposing the patients with fresh operative wounds from therapeutic doses of anticoagulants and the bleeding risk associated with them. Our PE rate of 2% is slightly higher than rates of 0.6% to 1% reported for patients with orthopaedic tumors who received mechanical prophylaxis and anticoagulation [22, 27, 30], but this may be related to our smaller sample size. We found only skeletal reconstruction as a substantial risk factor for DVT. This may be related to the presumably greater amount of limb manipulation with potential for vascular injury and the longer operative time required for reconstructive procedures. In contrast to previous studies [27, 30], we did not find a specific anatomic location, whether pelvis, hip, or thigh, to result in a higher incidence of DVT (Table 2).

The rate of potential insertion-site thrombosis in our patients ranged from 9% to 18%, which concurs with the reported variable rates of 4% to 41% [25, 28]. We cannot categorically state these were true insertion-site thromboses because we did not routinely perform a duplex scan before and within 24 hours after IVC filter placement. There were only two instances of minor technical difficulties in filter placement. There were no cases of malposition, migration, insertion-site hematoma, or IVC perforation, all potential but infrequent complications of filter placement [14]. Athanasoulis et al. [1] highlighted the rarity of major complications during IVC filter insertion, citing a rate of 0.3%. Others have reported rates ranging from 3% to 7% [6, 13, 32, 36] and included maldeployed filters, new caval thrombosis, retroperitoneal hemorrhage, wound infection, and arrhythmia [33, 36].

Few studies have focused on the risk factors and specific prophylaxis of thromboembolic disease in patients with orthopaedic tumors, and it seems thromboembolic prophylaxis is patterned after those used for other major orthopaedic procedures [22, 27, 30]. However, patients undergoing musculoskeletal cancer resection have important differences from the usual patients having total joint arthroplasties. Often, large segments of bone and soft tissue are resected in tumor surgery, more than the periarticular cuts in routine hip and knee arthroplasties. Dissection around blood vessels of various calibers is also common, carrying the risk of vascular endothelial injury [3]. Finally,

these patients often will have several patient-, cancer-, and treatment-related risk factors [24] for venous thrombosis or embolism that are not often seen in other patients with orthopaedic diagnoses. These include older age [15], elevated prechemotherapy platelet counts [16], current metastatic disease [4, 5, 15], active chemotherapy or hormonal therapy [5, 17], and use of erythropoietic drugs [16]. Certain tumors that commonly metastasize to bone, such as renal, lung, and hematologic cancers, are high risk for venous thrombosis or embolism [4, 5, 15, 35]. The initial 3 to 6 months from cancer diagnosis is also a known high-risk period [4]. Therefore, the risk in patients with orthopaedic tumors may be much different from that in the usual patient having a total joint arthroplasty, and prophylaxis may need to be tailored accordingly.

We propose mechanical compression and IVC filter placement should be considered for patients with cancer undergoing definitive surgery for pelvic or lower limb malignancy. Such a protocol carries a low morbidity and may be effective in reducing the incidence of fatal PE during the early and late postoperative periods while avoiding the risk of hemorrhagic consequences associated with pharmacologic anticoagulation.

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