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Surgical management of proximal fibular tumors: risk factors for recurrence and complications

Changzhi Guo[1,*], Xiaoran Zhang[1,*], Feng Gao[2], Lingxiang Wang[3] and Tao Sun[1]

Abstract

Objectives: The aim of this study was to identify patient- and treatment-specific independent risk factors for the recurrence of proximal fibular tumors and complications of their surgical management.

Methods: Patients who underwent surgical treatment of proximal fibular tumors at our institution from 2004 to 2015 were retrospectively reviewed. All patients had a pathologically confirmed diagnosis and were followed up for at least 12 months for recurrence and complications. All patients were evaluated with respect to seven patient-, disease-, and treatment-specific variables.

Results: In the univariate analysis, peroneal nerve palsy at presentation and malignancy were associated with an increased risk of recurrence, iatrogenic peroneal nerve injury, and wound healing problems. The multivariate analysis showed that peroneal nerve palsy at presentation was an independent risk factor for recurrence and iatrogenic peroneal nerve injury and that malignancy was an independent risk factor for wound healing problems.

Conclusions: Peroneal nerve palsy and malignant potential are independent risk factors for complications of surgical treatment of proximal fibular tumors. The recognition of these factors may contribute to proper management and help to prevent recurrence and postoperative complications.

[1]Department of Orthopaedic Surgery, Third Hospital of Hebei Medical University, Shijiazhuang, Hebei Province, China
[2]Department of Pathology, Third Hospital of Hebei Medical University, Shijiazhuang, Hebei Province, China
[3]Department of Gynaecology, Fourth Hospital of Hebei Medical University, Shijiazhuang, Hebei Province, China

[*]These authors contributed equally to this work.

Corresponding author:
Tao Sun, Department of Orthopaedic Surgery, Third Hospital of Hebei Medical University, 139 Ziqiang Road, Shijiazhuang, Hebei Province 050051, China.
Email: doctorsun@139.com

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Introduction

Tumors in the proximal fibula are rare. Only 2.5% of all primary bone tumors are located in the fibula.[1] Patients with benign tumors in the proximal fibula require intralesional or marginal excision, while benign aggressive tumors, which are symptomatic, grow rapidly, and are tender on palpation, require marginal en bloc resection described by Malawer[1] (type I resection).[1–3] In addition, approximately half of malignant tumors require radical or wide en bloc resection (type II resection).[1,3] Especially for patients with osteosarcoma in the proximal fibula, the current treatment approach is neoadjuvant chemotherapy followed by radical resection (above-the-knee amputation) or wide (type II) resection and postoperative chemotherapy.[3,4]

The superficial and deep peroneal nerves, anterior tibial artery, and lateral collateral ligament are the most important structures in relation to bone tumors in the proximal fibula; therefore, it is important to avoid damaging these structures and to preserve maximal limb function while performing adequate resection of the tumor.[5,6] The main complications associated with proximal fibular resection are potential postoperative knee instability, peroneal nerve palsy, arterial insufficiency, incisional drainage, infection, skin necrosis, and local recurrence of the tumor. Malignant potential, more invasive surgical treatments, huge tumor volumes, and some other factors are considered associated with a poorer prognosis; however, these factors appear to be interactive with one another, and their association with recurrence and postoperative complications have not been fully explored in contemporary studies.[3,4,7,8]

The purpose of this retrospective study was to evaluate patients with surgically treated proximal fibular tumors over a contemporary time period to identify any patient-, disease-, or treatment-specific factors associated with a significant increase in tumor recurrence and postoperative complications.

Patients and methods

Patient selection

Data regarding patients with tumors in the proximal fibula that underwent surgical management were retrieved from our institution's pathologic and surgical databases from March 2004 to January 2015. In the preoperative period, patients were evaluated with bone and chest radiographs, bone scintigraphy, computed tomography (CT), and magnetic resonance imaging. Fine needle or incisional biopsy was performed with patient consent in those with a high suspicion of malignancy. Preoperative chemotherapy was administered for patients with osteosarcoma confirmed by biopsy. Histopathological diagnoses were obtained after the final surgeries. The inclusion criteria were as follows: proximal fibular tumor confirmed by histopathological examination; surgical treatment with/without biopsy;

available explicit imaging data including radiographs, CT, or magnetic resonance imaging for diagnosis; and complete records including diagnosis, therapy, follow-up, and recurrence. The exclusion criteria were as follows: recurrence of the tumor or non-tumor disease in the proximal fibula, tumor involving both the proximal fibula and tibia, and a follow-up period of <12 months.

Surgical management

All patients underwent operations in the supine position under general or spinal anesthesia. The incision started approximately 8 cm proximal to the fibular head and extended along the border of the biceps muscle to the fibula; it then straightened and further extended along the line of the fibular shaft approximately 5 cm below the planned level of osteotomy. First, the common peroneal nerve was explored and approached with the intent of mobilizing the common peroneal nerve and opening and exposing the common peroneal and deep peroneal nerve branches throughout the fibromuscular tunnel.[6] Second, intralesional or en bloc resection of the proximal fibular tumor was performed.

Type I resection was performed for benign aggressive lesions, and type I or II resection was performed for malignant lesions according to Malawer[1] with minor modifications. Type I marginal en bloc resection included resection of the proximal fibula with 1 to 2 cm of the normal diaphysis and a thin muscle cuff in all dimensions while preserving the peroneal nerve and all motor branches. Type II wide intracompartmental en bloc resection included resection of the proximal fibula with 3 to 5 cm of the normal diaphysis with the anterior and lateral muscle compartments, peroneal nerve, and anterior tibial artery if involved by the tumor. A knee immobilizer was used full-time for the first 4 weeks postoperatively. Reconstruction consisted of repairing the lateral collateral ligament and reinsertion of the biceps femoris tendon on the lateral condyle of the tibia to prevent knee instability. For the subsequent 2 weeks, patients were allowed to perform gentle knee motion exercises. After 6 weeks, the patients were allowed to gradually progress to full weight bearing.

Follow-up and functional outcome

Patients were followed through the tumor registry at our institution. Our follow-up routine included examinations of patients every 3 months for the first 2 years postoperatively. Thereafter, follow-up was dependent on the particular patient and the pathological results. Routine follow-ups included physical examination, radiographic examination, and chest CT for giant cell tumors and malignancy. Knee stability was evaluated by the patient's history, clinical examination findings, and valgus-varus stress radiographs. The patients were not recalled specifically for the study; all data were retrieved from the medical records.

Ethics

This study was approved by the ethics committee of our institute. The methods were conducted in accordance with the approved guidelines. Written informed consent was obtained from all patients.

Statistical analysis

The relationship of each variable with tumor recurrence and surgical complications was assessed with a significance level of 0.05. Due to the rarity of the events, univariate analysis was performed using Fisher's exact test for categorical variables. Multivariate regression was also performed for dichotomous variables to identify any independent associations.

Results

A total of 52 patients (26 male, 26 female) met our inclusion criteria. The mean age at diagnosis was 26.5 years (range, 4–72 years). There were 44 (84.6%) benign and 8 (15.4%) malignant tumors, the distribution of which is shown in Figure 1. Patients presented due to incidental discovery of a tumor (13.5%) or symptoms such as pain (46.2%), a palpable mass (52.0%), and peroneal nerve palsy (5.6%). Intralesional excision was performed for 26 benign tumors, type I resection for 18 benign and 4 malignant tumors, and type II resection for 4 malignant tumors. During a mean follow-up time of 2.7 years (range, 12 months to 6 years), 9 (17.3%) of 52 patients developed local recurrence or postoperative complications. No patients reported or were diagnosed with knee instability (Table 1).

Four (7.7%) patients developed local recurrence from 4 months to 2 years after the first surgery. Two of them developed the second local recurrence at 11 and 13 months after the second surgery, respectively, and they finally underwent above-the-knee amputation. In the univariate analysis (Table 2), peroneal nerve palsy at presentation was found to be a significant factor for recurrence and was noted in 3 of 4 patients with recurrence compared with 2 of 48 patients without recurrence ($P = 0.002$). A relative risk of 69.000 of developing recurrence was noted in patients with peroneal nerve palsy at presentation. Malignancy was also found to be a significant risk factor for recurrence and was noted in 3 of 4 patients with recurrence compared with 5 of 48 patients without recurrence ($P = 0.009$). A relative risk of 25.800 of developing recurrence was noted in patients with malignant tumors in the proximal fibula. No other factors, including age, sex, laterality, biopsy or not, and resection method, were associated with recurrence.

Seven (13.5%) patients had a postoperative peroneal nerve injury, three of which were newly developed and four of which had worsened compared with the preoperative status (Table 1). Three (5.8%) of the 52 patients recovered from 2 weeks to 12 months after surgery, and 4 (7.7%) sustained permanent postoperative peroneal nerve palsy. Peroneal nerve palsy at presentation ($P = 0.001$) and malignant tumors in the proximal fibula ($P = 0.007$) were found to be significant risk factors for postoperative peroneal nerve injury. Iatrogenic peroneal nerve injury was identified in 4 of

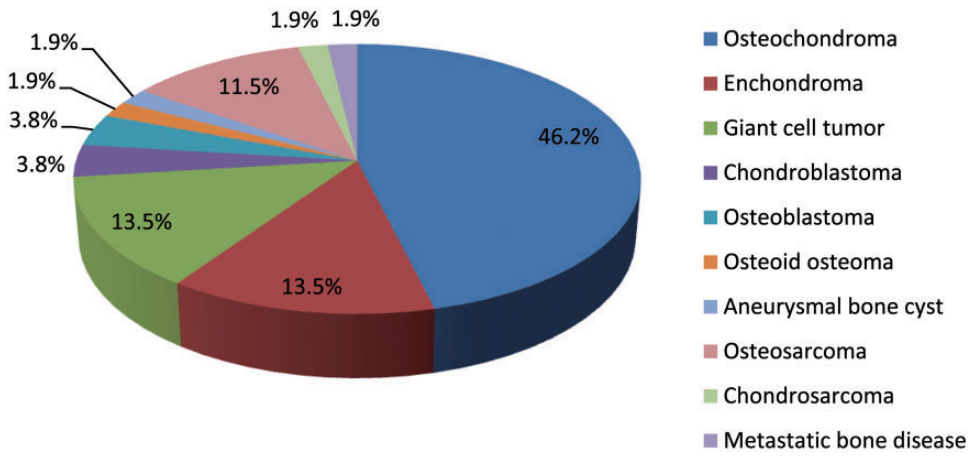

Figure 1. Distribution of benign and malignant tumors.

Table 1. Profile of patients with recurrence and postoperative complications

Case	Age at diagnosis (y)	Sex	Diagnosis	Treatment method	Local recurrences (n)	Peroneal nerve palsy (pre/post)	Wound healing problems
1	16	M	Osteosarcoma	Type I	2	+/−	+
2	22	M	Osteosarcoma	Type II	–	+/+	+
3	15	M	Osteochondroma	Intralesional excision	–	−/+	−
4	49	F	Osteosarcoma	Type II	1	+/+	+
5	45	F	Enchondroma	Type I	–	−/+	−
6	16	M	Chondroblastoma and aneurysmal bone cyst	Type I	–	−/+	−
7	18	M	Osteosarcoma	Type I	2	+/+	−
8	63	F	Osteosarcoma	Type II	–	+/+	−
9	18	M	Giant cell tumor	Type I	1	−/−	−
10	10	F	Osteosarcoma	Type II	0	−/−	+
11	72	F	Metastatic bone disease	Type I	0	−/−	+

M, male; F, female; pre, preoperative; post, postoperative.

Table 2. Univariate analysis of associations of factors with recurrence and complications

	Recurrence			Iatrogenic peroneal nerve injury			Wound healing problems		
Factors	Relative risk	95% Confidence interval	*P* value	Relative risk	95% Confidence interval	*P* value	Relative risk	95% confidence interval	*P* value
Age (>30 vs. <30 y)	0.667	0.064–6.930	0.604	1.661	0.327–8.430	0.670	1.422	0.215–9.427	1.000
Sex (male vs. female)	3.261	0.316–33.614	0.610	1.394	0.279–6.953	1.000	0.639	0.098–4.180	1.000
Laterality (right vs. left)	1.400	0.182–10.791	1.000	1.026	0.205–5.132	1.000	2.211	0.337–14.511	0.639
Peroneal nerve palsy	69.000	4.781–995.851	0.002*	58.667	4.894–703.271	0.001*	33.750	3.445–330.608	0.004*
Malignant vs. benign	25.800	2.237–297.582	0.009*	13.667	2.225–83.944	0.007*	N/A	N/A	0.001*
En bloc	0.458	0.337–0.623	0.110	7.500	0.833–67.494	0.099	N/A	N/A	0.051
Biopsy	2.867	0.249–33.065	0.397	4.100	0.592–28.380	0.180	7.167	0.912–56.329	0.096

N/A, not available. *$P<0.05$ was considered statistically significant.

5 patients with peroneal nerve injury at presentation compared with 3 of 47 patients without such injury at presentation. Malignancy was also identified as a significant risk factor for postoperative peroneal nerve injury ($P = 0.007$) and was identified in 4 of 8 patients with postoperative peroneal nerve injury compared with 3 of 44 patients without postoperative peroneal nerve injury. Relative risks of 58.667 and 13.667 for sustained postoperative peroneal nerve injury were noted in patients with

peroneal nerve palsy at presentation and malignancy, respectively. The other factors were not associated with recurrence.

Five (9.6%) of 52 patients had wound healing problems due to incision drainage, and 1 of them developed skin necrosis. One patient had a postoperative fever and elevated white blood cell count, and the others had normal temperatures and normal white blood cell counts. All five patients received longer antibiotic therapy, and none underwent a wound culture. The wounds healed after bedside dressing and debridement from 3 to 6 weeks after the surgeries, and none of them required further surgeries. Peroneal nerve palsy at presentation was found to be a significant risk factor for wound healing problems and was identified in 3 of 5 patients with peroneal nerve palsy at presentation compared with 2 of 47 patients without peroneal nerve palsy at presentation ($P = 0.004$). A relative risk of 33.750 for developing wound healing problems was noted in patients with peroneal nerve palsy at presentation. A malignant tumor in the proximal fibula was found to be a significant risk factor for wound healing issues ($P < 0.001$). The relative risk was not available. Type II resection was found to be a significant risk factor for wound healing problems and was noted in 3 of 4 patients after type II resection compared with 2 of 48 patients after surgeries other than type II resection ($P = 0.002$). A relative risk of 69.000 (95% confidence interval, 4.781–995.851) of developing wound healing problems was noted in patients who had undergone type II resection.

Multivariate analysis was performed to identify independent factors associated with recurrence, postoperative peroneal nerve injury, and wound healing problems (Table 3). Of the factors assessed, only peroneal nerve palsy at presentation was found to be independently associated with recurrence ($P = 0.001$) and postoperative peroneal nerve injury ($P < 0.001$). In addition, malignancy was found to be independently associated with wound healing problems ($P < 0.001$).

Discussion

Most proximal fibular tumors are benign. Although only a small proportion is malignant, such tumors may be life-threatening. In the present study, only 15.4% of proximal fibular tumors were malignant while the other 84.6% were benign. This percentage is much lower than in previous studies. One study showed that approximately half of these tumors were malignant.[9] Another two studies reported 112 patients with malignant tumors and 121 patients with benign tumors in the proximal fibula that were treated surgically from 1910 to 2007 in Mayo Clinic.[3,10] Because all malignant tumors in the proximal fibula must be

Table 3. Multivariate regression analysis of association of factors with recurrence and complications

Factors	Recurrence (multivariate *P*-value)	Iatrogenic peroneal nerve injury (multivariate *P*-value)	Wound healing Issue (multivariate *P*-value)
Age (>30 vs. <30 y)	0.444	0.626	0.473
Sex (male vs. female)	0.308	0.922	0.953
Side (right vs. left)	0.487	0.872	0.546
Peroneal nerve palsy	0.001*	<0.001*	0.642
Malignant vs. benign	0.945	0.490	<0.001*
En bloc	0.255	0.476	0.893
Biopsy	0.231	0.799	0.986

*$P<0.05$ was considered statistically significant.

surgically managed while only some benign tumors require surgical treatment, the proportion of malignant tumors in the proximal fibula might be overestimated. In the present study, osteochondromas were the most common benign tumors in the proximal fibula and osteosarcomas were the most common malignant tumors; these findings are similar to the results of the Mayo Clinic study.[3,10]

In the present study, the overall local recurrence rate was 7.7%. Other researchers have similarly reported an 8% recurrence rate for benign tumors and an 11% recurrence rate for malignant tumors.[3,10] The univariate analysis of this study showed that a malignant tumor in the proximal fibula was a significant risk factor for recurrence. However, malignancy was not an independent risk factor in the multivariate analysis. This indicates that the recurrence rates are the same between benign and malignant tumors in the proximal fibula if an appropriate surgical technique is applied. For benign aggressive tumors in the proximal fibula, intralesional curettage alone is considered to be a risk factor for local recurrence;[10] therefore, total en bloc resection of giant cell tumors and aneurysmal bone cysts in the proximal fibula is strongly recommended. The recurrence rate after curettage and bone grafting is reportedly higher (41%) than that after resection (7%).[10–12] For malignant tumors in the proximal fibula, neoadjuvant chemotherapy followed by radical resection (above-the-knee amputation) or wide (type II) resection and postoperative chemotherapy are recommended.[3,4] When a malignant bone tumor is suspected, preoperative biopsy should be performed. Biopsy should be performed in all bone tumors that are suspected to be malignant. However, the biopsy rate of malignant tumors in the proximal fibula is relatively low (6%–48%). This low biopsy rate is due to the fact that many orthopedic surgeons believe that biopsy of the proximal fibular tumor may increase the risk of injury to the peroneal nerve, and anterior tibial artery and vein.[3,4] Neoadjuvant chemotherapy and more extensive resection, especially amputation, are accepted by orthopedic oncologists and patients based only on a pathologic diagnosis of malignancy; this may decrease the recurrence rate.

The present study showed that peroneal nerve palsy developed in 13.5% of patients and was permanent in 5.8%. Despite protective measures, previous studies have revealed a higher iatrogenic peroneal nerve palsy rate of 7% to 57%, especially after en bloc resection,[1,2,7] and a lower rate of 3% in benign proximal fibular tumors.[10] In the present series, more than half of the peroneal nerve palsies resolved within the first postoperative year.

Many experts consider en bloc resection, especially type II resection, as a risk factor for postoperative peroneal nerve palsy.[1,3,13] Iatrogenic peroneal nerve palsies may be reversible because the peroneal nerve can be completely freed from the fibro-osseous tunnel at the fibular neck during intralesional excision and type I en bloc resection of proximal fibula tumors.[1,10] In contrast, iatrogenic permanent loss of peroneal nerve function is expected in type II en bloc resection of proximal fibula tumors.[8] In the present study, we found that malignancy rather than en bloc resection was a significant risk factor in the univariate analysis. In the multivariate analysis, neither malignancy nor en bloc resection was an independent risk factor for postoperative peroneal nerve palsy. We speculate that the above two factors are closely related or were significant due to the small sample size of this study. Type II resection undoubtedly leads to unrecoverable peroneal nerve injury, and type I resection may increase the risk of iatrogenic nerve injury.

We found that peroneal nerve symptoms and signs at presentation were an

independent risk factor for iatrogenic peroneal nerve injury and local tumor recurrence, which has not been noted previously. Benign aggressive or malignant proximal fibula tumors with a substantial soft tissue mass may elevate and stretch the peroneal nerve, which may result in spontaneous neurologic symptoms and signs. However, one study suggested that a slow process of nerve traction resulting from the gradual expansion of the soft tissue mass at the neck of the fibula may protect the nerve from operative dissection.[3] This may be possible before the onset of peroneal nerve dysfunction; when peroneal nerve palsy occurs, however, the risk of operative peroneal nerve stretching injury dramatically increases. This situation is quite different from dissection because the nerve function will recover within a year. This may explain why peroneal nerve palsy at presentation is a risk factor for iatrogenic peroneal nerve injury and why peroneal nerve palsy at presentation is a risk factor for local tumor recurrence. Peroneal nerve palsy at presentation is caused by compression by huge, expansive tumors or direct invasion of malignant tumors in the proximal fibula, and if the surgeon pays excessive attention to preservation of peroneal nerve function, the surgical margin is usually inadequate; this will lead to local recurrence.[3,4]

Wound healing problems, such as wound dehiscence, incision drainage, and skin necrosis, can be major after type II en bloc resection, requiring muscle flaps or above-the-knee amputation.[3] In one study, 8.9% of surgically treated malignant proximal fibular tumors developed this complication.[3] Similar to these results, 9.6% of patients in our series had wound healing problems. All of them were malignant, and most of them occurred after type II resection. Our results suggest that patients with malignant proximal fibula tumors treated by type II resection have a higher risk of wound healing problems. Preoperative chemotherapy and radiotherapy may have adverse effects on wound healing.[14,15] Given that only one patient in our series received chemotherapy before surgery, evaluation of this factor was outside scope of this study.

No long-term knee instability was observed in the present study. Other authors have reported similar results in patients who underwent resection and lateral collateral ligament and biceps femoris tendon reconstruction by staples or suture anchors.[3,4,8,10] Generally, patients who have undergone type II resection have a higher rate of knee instability than those who have undergone type I resection, and patients without reconstruction exhibit a higher rate of knee instability than those with reconstruction.[8] Other postoperative complications, such as thrombosis of the posterior tibial artery and deep venous thrombosis,[3,10] were not identified in the present study.

The present study is limited by its relatively small sample size and retrospective nature. Because proximal fibular tumors are relatively rare, large numbers of patients are not available in a single institute. A multicenter prospective study with standard treatment may overcome these limitations.

Conclusion

For patients undergoing surgical treatment of proximal fibular tumors, the risk factors for recurrence and iatrogenic peroneal nerve palsy are peroneal nerve palsy at presentation and malignancy. The risk factors for wound healing problems are malignancy, type II resection, and peroneal nerve palsy at presentation. The recognition of these factors may contribute to the proper management of patients with tumors in the proximal fibula, helping to prevent recurrence and postoperative complications.

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Declaration of conflicting interest

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ORCID iD

Tao Sun http://orcid.org/0000-0003-2676-7309

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