Clinical effect of surgical resection on primary malignant and invasive bone tumours of the proximal fibula

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Abstract. There is no unified surgical plan for fibular proximal malignant tumours; therefore, the present study retrospectively analysed the medical records of 19 patients with primary malignant and invasive tumours in the proximal fibula and discussed the postoperative oncological results, complications and postoperative functions of limb salvage surgery. According to pathological classification, there were 10 osteosarcoma cases, 3 chondrosarcoma cases, 2 invasive giant cell osteosarcoma tumour cases, 1 epithelioid sarcoma case, 1 leiomyosarcoma case, 1 fibrosarcoma case and 1 lymphoma case. According to the Enneking instalment, IB stage was found in 2 cases, IIA in 2 cases and IIB in 15 cases. A total of 3 patients underwent Malawer I resection, and 16 patients underwent Malawer II resection. The follow-up period was 11-174 months, with an average of 76.58 months. Local recurrence occurred in three patients and distant metastasis in seven patients; 4 patients succumbed and 15 survived. After biceps femoris tendon reconstruction and lateral collateral ligament insertion, 18 patients had good knee stability. The Musculoskeletal Tumour Society scale ranged between 23 and 29 points, with an average of 27.26 points; the Lysholm Knee Score was 65-84 points, with an average of 83 points. After the resection of proximal fibula primary and invasive tumours, the biceps femoris tendon and lateral collateral ligament insertion point was reconstructed. The data show that this technique can effectively reconstruct stability and restore knee function.

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Introduction

The fibula is a rare site of primary bone tumour; the most common location for both benign (58.3%) and malignant (71.4%) tumours is the proximal fibula (1). Approximately half of all tumours are malignant, with osteosarcoma, Ewing sarcoma and giant cell bone tumour being the most common, the incidence of osteosarcoma and giant cell tumour in the proximal fibula was 2.3 and 2.8-8% respectively (2). The incidences of osteosarcoma and giant cell tumour in the proximal fibula are 2.3 and 2.8-8%, respectively. The main clinical manifestations are pain, common peroneal nerve palsy and swelling (3,4). The proximal fibular cortex is thinner and has more muscles and ligaments attached; these anatomical features lead to a higher probability of proximal fibular malignancy invading the surrounding soft tissue and developing into an extraosseous compartment tumour (5).

The bone cortex at the proximal end of the fibula is relatively thin, and the tumour can easily break through the bone cortex and invade the muscle. Most patients have been found in Enneking stage IIB; therefore, when selecting limb salvage surgery, sufficient surgical boundaries should be identified to obtain good oncological results (4,6). There is no unified surgical plan for fibular proximal malignant tumours, and proximal fibula tumours are usually treated with limb salvage surgery for extensive or radical resection (2). However, the proximal fibula is adjacent to the common peroneal nerve, the anterior tibial artery and ligaments of the knee joint; therefore, complications such as knee instability, tumour recurrence, peroneal nerve paralysis and arterial dysfunction may occur after tumour resection (6).

The present study retrospectively analysed the data of patients with primary malignant and invasive tumours in the proximal fibula and discussed the postoperative oncological results, complications and postoperative functions of resection operation.

Materials and methods

Patients. Between October 2005 and October 2019, 19 patients (12 male, 7 female; age range, 8-62 years; average age 25.58) with primary malignant or invasive tumours of the proximal fibula received limb salvage treatment at Union Hospital, Tongji Medical College, Huazhong University of Science and Technology (Wuhan, China). The inclusion criteria were as follows: i) Fibular proximal tumour, ii) pathological diagnosis of primary malignant or invasive tumour, iii) complete resection adopted, iv) a follow-up time >6 months, and v) complete imaging data. The exclusion criteria were as follows: i) Benign or metastatic tumours, ii) amputation or intracapsular curettage as the first surgical procedure, iii) patients lost to follow-up, and iv) follow-up time <6 months.

According to the pathological classification, there were 10 cases of osteosarcoma, 3 cases of chondrosarcoma, 2 cases of invasive giant cell tumour of osteosarcoma, 1 case of epithelioid sarcoma, 1 case of leiomyosarcoma, 1 case of fibrosarcoma and 1 case of lymphoma. All patients were initially diagnosed and treated in our hospital, and pre-operative puncture biopsy confirmed the pathological diagnosis. All patients were eligible for limb salvage surgery, and 10 patients received 2 cycles of pre-operative and 4 cycles of postoperative neoadjuvant chemotherapy.

Detailed medical history was collected. Physical examination was conducted carefully, and imaging examinations, including X-ray, CT, MRI, computed tomography angiography and emission computed tomography, were performed; positron emission tomography-CT) examination was performed when necessary. Enneking staging was performed for fibular tumours to assess the degree of malignancy and whether there was a breakthrough in the compartment (7). Attention was also paid to the relationship between the tumour and the surrounding tissue structures (e.g., nerves, blood vessels and tibia). For pre-operative C-arm guided puncture biopsy, the biopsy channel was the shortest distance from the lesion to the skin and avoided major nerve or blood vessel damage, particularly the common peroneal nerve.

All excised tumour specimens were fixed in 10% buffered-formalin for 24 h at 25˚C, embedded in paraffin and cut into 4-μm-thick sections. Haematoxylin and eosin (H&E) staining was performed for 20 min at 37˚C and the sections were observed using an Olympus BX51 light microscope (magnification, x100; Olympus Corporation).

Treatment. According to the Enneking stage, stage IB was found in 2 cases, stage IIA in 2 cases and stage IIB in 15 cases. Malawer I and II resection operations were performed in 3 and 16 cases, respectively. After successful general anaesthesia, the patients were placed in a semi-supine position with the affected limb elevated by 45˚. According to the Malawer I excision method (8), a longitudinal incision was made, and the proximal fibula along with 2-3 cm of normal diaphysis were removed. Simultaneously, a complete excision of the thin muscle sleeve around the perimeter, including the insertion of the lateral collateral ligament, was conducted. The common peroneal nerve and its motor nerve branches were preserved. Finally, the upper tibiofibular joint was excised through the capsular joint. Using the ditto incision for Malawer II excision, the resected proximal fibular tumour and its distal 2-3 cm normal diaphysis, the lateral muscle septum, common peroneal nerve and anterior tibial artery were excised (8). The superior tibiofibular joint was excised laterally through the knee joint. Gastrocnemius muscle flap transposition was required to repair the defect after tumour resection. The incision included the previous biopsy channel and 2-3 cm of the tissue at the edge. During surgical excision, the continuity of the biceps femoris tendon and lateral collateral ligament, as well as the continuity of the lateral deep fascia and the iliotibial band, were retained as much as possible. Using the rivet and non-absorbable nylon thread, the biceps femoris tendon and the insertion point of the lateral collateral ligament were closely sutured through the perforation of the lateral tibial condylar cortex. Small holes were made in the lateral cortex of the tibial condyle, the rivet and non-absorbable nylon suture were used to reconstruct the insertion point of the biceps femoris and lateral collateral ligament.

Patients with Malawer I resection underwent rehabilitation exercises of knee flexion and extension at 3 weeks post-surgery, whereas patients with Malawer II resection had to delay exercise for 2-3 weeks. Foot sagging was caused by common peroneal nerve resection. Ankle braces were used to assist walking exercise at 6 weeks post-surgery.

Postoperative follow-up. Postoperative re-examination was conducted to determine tumour recurrence, metastasis, complications and postoperative limb function. The Musculoskeletal Tumour Society (MSTS) functional score was used to evaluate lower limb extremity function, with a total score of 30 and a high score indicating good affected limb function (9). The Chinese version of the Lysholm knee score (LKS) was used to assess the knee function of patients, with a total score of 100 and a high score indicating good function of the affected knee (10). The evaluation of knee stability was mainly based on patient self-assessment and the medial stress test. X-ray examination was performed under the medial stress of knee flexion at 30˚; compared with the healthy side, an increase of >5 mm in the affected side knee joint was considered unstable (11).

This study was designed as a single-centre retrospective study in Union Hospital, Tongji Medical College, Huazhong University of Science and Technology and conducted in line with The Declaration of Helsinki. The surgical procedure and data collection were approved by the Huazhong University of Science and Technology Committee on Human Research (2019-IEC-S274).

Results

The basic information of the patients is listed in Table I; according to pathological classification, there were 10 osteosarcoma cases, 3 chondrosarcoma cases, 2 invasive giant cell osteosarcoma tumour cases, 1 epithelioid sarcoma case, 1 leiomyosarcoma case, 1 fibrosarcoma case and 1 lymphoma case. According to the Enneking classification, IB stage was found in 2 cases, IIA in 2 cases and IIB in 15 cases. The indicators of treatment modalities and prognostic follow-up are listed in Table II; a total of 3 patients underwent Malawer I resection, and 16 patients underwent Malawer II resection. The follow-up time was 11-174 months, with an average of 76.58 months. None of the patients had incision infection or skin necrosis;

Table I. Patient clinicopathological characteristics.

Case no.	Sex	Age, years	Initial symptom(s)	Follow-up time, months	Pathological classification	Enneking stage
1	Male	14	Pain, nerve palsy, mass	92	Osteosarcoma	IIB
2	Male	23	Pain, nerve palsy	36	Invasive giant cell tumour of bone	IB
3	Female	17	Pain	62	Osteosarcoma	IIB
4	Female	8	Pain	117	Osteosarcoma	IIB
5	Male	38	Pain, nerve palsy	54	Chondrosarcoma	IIB
6	Male	15	Pain, mass	11	Osteosarcoma	IIB
7	Male	12	Pain	132	Osteosarcoma	IIB
8	Female	31	Pain, nerve palsy	174	Epithelioid sarcoma	IIB
9	Male	43	Pain	63	Chondrosarcoma	IIA
10	Male	51	Pain, nerve palsy	113	Fibrosarcoma	IIB
11	Male	13	Pain	36	Osteosarcoma	IIB
12	Male	42	Pain, nerve palsy, mass	52	Chondrosarcoma	IIB
13	Female	27	Pain, nerve palsy	39	Invasive giant cell tumour of bone	IB
14	Male	10	Pain	70	Osteosarcoma	IIB
15	Male	62	Pain, mass	63	Lymphoma	IIB
16	Female	12	Pain, nerve palsy	29	Osteosarcoma	IIB
17	Male	37	Pain, nerve palsy	124	Leiomyosarcoma	IIA
18	Female	14	Pain	82	Osteosarcoma	IIB
19	Female	17	Pain, nerve palsy, mass	106	Osteosarcoma	IIB

however, there were two patients with common peroneal nerve injury. Local recurrence occurred in three patients (two with osteosarcoma and one with leiomyosarcoma); all three patients underwent Malawer I resection. In addition, one patient underwent amputation, one patient underwent extensive resection and one patient underwent local radiotherapy. Seven patients developed pulmonary metastasis, of which four of these patients succumbed. After the resection of proximal fibula primary and invasive tumours, the biceps femoris tendon and lateral collateral ligament insertion point was reconstructed. After the reconstruction of the biceps femoris tendon and lateral collateral ligament, knee joint function was stable in all but one patient who reported self-perceived instability of the knee joint. The MSTS score at the last postoperative follow-up was 23-29 points, with an average of 27.26 points (90.87%; postoperative MSTS score divided by total MSTS score). The LKS was 65-84 points, with an average of 83 points. Most patients experienced pain relief and their daily life was not affected. Patients with permanent common peroneal nerve palsy needed to wear braces to walk after surgery. Two typical cases are presented in the figures, including an invasive giant cell tumour of the proximal right fibula treated with Malawer I resection (Fig. 1), and a chondrosarcoma of the proximal left fibula treated with Malawer II resection (Fig. 2).

Discussion

A rare primary malignant tumour of the proximal peroneal bone presents a challenge for orthopaedic surgeons owing to its proximity to the biceps femoris tendon, lateral collateral ligament, common peroneal nerve and anterior tibial artery (12,13). The classic surgical modalities for the treatment of proximal fibular tumours were first reported by Malawer in 1984 (8). In the Malawer I resection for marginal excision, the common peroneal nerve is preserved, the tibial blood vessels are rarely ligated and cut off, and the superior tibiofibular joint is excised intragastrically (8). In the Malawer II method for extensive resection, the common peroneal nerve and the anterior tibial vessels are excised, and the tibiofibular joint is excised outside the joint (8). The avoidance of postoperative recurrence and metastasis are considered as the main reference indicators in limb salvage surgery; amputation should be performed in some cases, particularly in the following (14,15): i) A large range of malignant tumours that invade the tibia, ii) multiple invaded fascia compartments, especially the posterior deep compartment, and iii) previous biopsies and surgeries causing the contamination of multiple fascia compartments.

Results from the present study are consistent with those reported in the literature. For example, a previous study comprising 112 cases of proximal fibula malignant tumours, including 50 cases of amputation (45%), 29 cases of Malawer I resection (26%), and 24 cases of Malawer II resection (21%), reported that 56 (50%) patients had distant metastasis and 12 (11%) had local recurrence (3). In addition, local recurrence was found in six patients receiving Malawer I and in three patients with Malawer II resection. Takahashi *et al* (16) examined 13 cases of proximal fibular osteosarcoma; according to Enneking staging, there was 1 case of IA, 1 case of IIA

Table II. Indicators of treatment modalities and prognostic follow-up.

Case no.	Surgery method	Recurrence	Distant metastases	Prognosis	Joint stability	Increase of joint space, mm	MSTS score	LNS
1	Malawer I	No	Yes	Death	Yes	2	28	82
2	Malawer I	No	No	Survival	Yes	2	28	81
3	Malawer I	Yes	No	Survival	Yes	2	29	84
4	Malawer I	No	No	Survival	Yes	1	28	82
5	Malawer I	No	No	Survival	Yes	2	29	82
6	Malawer I	No	No	Survival	Yes	2	27	79
7	Malawer I	No	Yes	Survival	Yes	3	28	80
8	Malawer II	No	Yes	Death	Yes	2	26	78
9	Malawer I	No	No	Survival	Yes	3	29	82
10	Malawer I	No	No	Survival	Yes	3	25	76
11	Malawer I	No	Yes	Death	Yes	2	28	80
12	Malawer II	No	No	Survival	No	4	23	65
13	Malawer I	No	No	Survival	Yes	2	26	70
14	Malawer I	No	No	Survival	Yes	2	28	78
15	Malawer I	No	Yes	Survival	Yes	2	29	84
16	Malawer I	Yes	Yes	Death	Yes	2	27	80
17	Malawer I	Yes	No	Survival	Yes	3	26	79
18	Malawer II	No	Yes	Survival	Yes	2	29	82
19	Malawer I	No	No	Survival	Yes	2	25	70

LKS, Lysholm knee score; MSTS, Musculoskeletal Tumor Society.

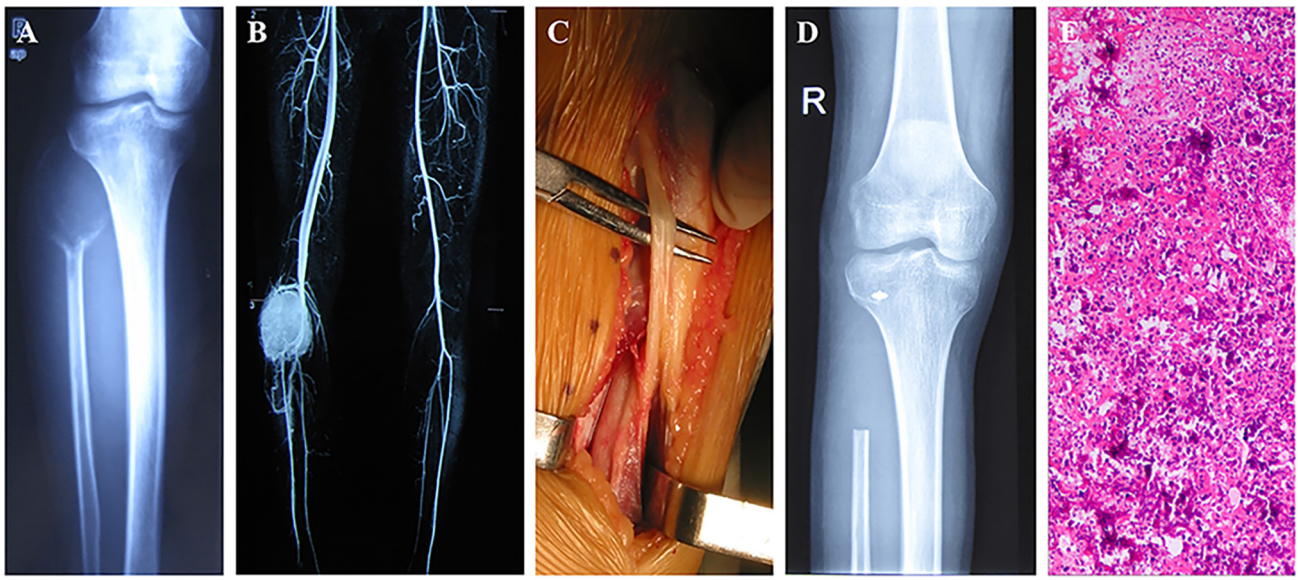

Figure 1. An invasive giant cell tumour of the proximal right fibula treated with Malawer I resection. (A) Pre-operative X-ray imaging showing that the proximal fibular cortex expanded and thinned as a bony shell. (B) CTA showing patency of the anterior tibial artery, posterior tibial artery, and peroneal artery. (C) The common peroneal nerve and its motor branches were carefully separated and protected during the operation. (D) Postoperative X-ray examination showing good stability of the knee joint. (E) Pathological examination of H&E-stained tissues revealed that the tumour consisted of osteoclast-like giant cells and spindle stromal cells (magnification, x200). CTA, computed tomography angiography.

and 11 cases of IIB. Limb salvage treatment was selected for all patients at the first operative treatment, seven cases were extensively resected, four cases were marginal resected, two cases were curettage, and six cases had local recurrence post-operatively. In the present study, 3 cases were treated with Malawer I resection and 16 cases with Malawer II resection. Postoperative local recurrence occurred in three patients, all of whom were treated with Malawer I, and pulmonary metastasis occurred in seven patients which treated with Malawer II.

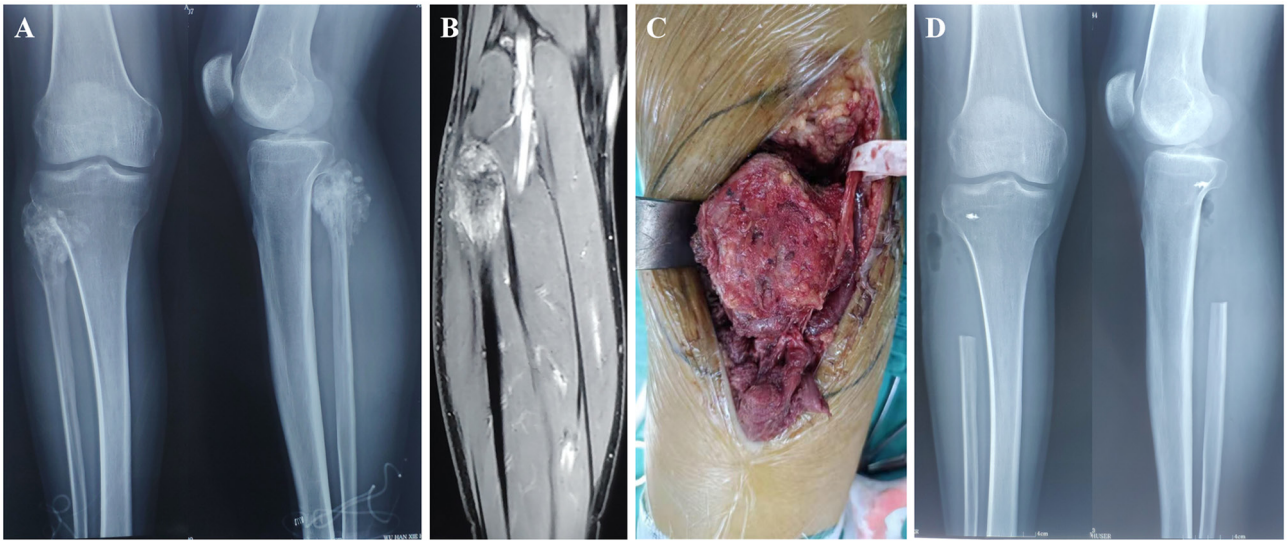

Figure 2. A chondrosarcoma of the proximal left fibula treated with Malawer II resection. (A) Pre-operative X-ray imaging showing the irregular bone destruction with calcification of proximal fibula. (B) MRI showing inhomogeneous high signals in intramedullary lesions and soft tissue masses. (C) The tumour invaded the common peroneal nerve. (D) Postoperative X-ray examination showing good stability of the knee joint.

During Malawer I and II resection, the lateral collateral ligament, the biceps femoris tendon and other structures that maintain the lateral stability of the knee must be removed to obtain a safe range of excision (17). For stability and good function of the knee joint postoperatively, the lateral stable structure of the knee joint should be reconstructed (18,19). Currently, the reconstruction of the biceps femoris tendon and the lateral collateral ligament after removing the proximal fibula tumour remains controversial. One study reported that the lateral collateral ligaments and free tendons should be fixed on the proximal tibia to restore knee stability (18). Malawer *et al* (8) and Faezypour *et al* (20) also been reported that the biceps femoris tendon and the lateral collateral ligament should be sutured to the surrounding tissues and the anterolateral joint capsule using non-absorbable suture, which is a simple reconstruction method. These studies found that none of the patients complained of instability of the knee joint, no arthrovarus was found on physical examination, and the medial stress test was negative (8,20). However, different opinions have been put forward in the relevant literature. In the study by Einoder *et al* (21), no reconstruction of the lateral stable structure of the knee was performed intraoperatively, and the average follow-up period was 33 months. Although there was clinical evidence of lateral knee instability in three patients, there was no dysfunction, and all six patients could return to their level of activity before disease diagnosis. It has also been suggested that even if the lateral collateral ligament and the tendon insertion of the biceps femoris are reconstructed during proximal peroneal excision and the knee is still unstable, the gait is not affected because once the ligament and tendon insertion are damaged, it is impossible to restore the original position (22). After reconstruction of the biceps femoris tendon and lateral collateral ligament in all patients in the present study, one patient reported self-perceived instability of the knee joint in, whereas knee joint function in all other patients was stable. Abdel *et al* (3) reviewed 112 cases of aggressive proximal fibular tumours and found no long-term knee instability in the 53 patients who underwent resection with lateral collateral ligament reconstruction at a mean follow-up period of 7.4 years, suggesting that ligament reconstruction is important for functional knee recovery following operation. Most of these previous studies have reinforced that, after the resection of proximal fibula primary and invasive tumours, the biceps femoris tendon and lateral collateral ligament insertion point was reconstructed. In our opinion, continuity of the biceps femoris tendon, lateral collateral ligament, lateral deep fascia and iliotibial band should be retained as much as possible, and the insertion of the biceps femoris and lateral collateral ligament should be reconstructed through the hole in the lateral cortex of the tibial condyle; these techniques can effectively reconstruct stability and restore knee function.

There are a number of complications after resecting proximal fibular tumours; in addition to common peroneal nerve injury or knee instability, complications may include synovial leakage, skin necrosis, wound infection and posterior tibial artery thrombosis (23). Of the 112 cases reported by Abdel *et al* (3), 14 (12.5%) had postoperative complications after resection of proximal fibula tumours; Malawer II resection was performed in these 14 patients, including 6 cases of wound infection, 2 cases of posterior tibial artery thrombosis and 2 cases of common peroneal nerve injury. There were two patients with common peroneal nerve injury, and none of the patients in the present study experienced complications, such as wound infection or arterial thrombosis, which may be related to the Malawer I resection used in most patients. Results from the present study are consistent with those of the literature.

There are some limitations to the present study. First, this was a retrospective study with a limited number of patients; therefore, studies with larger sample sizes are necessary. Second, this study lacked an appropriate control group; therefore, appropriate control groups are necessary. And last, the follow-up time was relatively short, and longer follow-up period are necessary.

In summary, for patients with aggressive tumours such as proximal fibular giant cell tumours or with osteosarcoma with good pre-operative chemotherapy efficacy, marginal

resection can achieve safety and good postoperative function. For large tumours with high degree of malignancy and sensitivity to chemotherapy, extensive resection is necessary and feasible to reduce recurrence and metastasis. At the same time, reconstruction of the biceps femoris tendon and lateral collateral ligament after removing the proximal fibula tumour can achieve knee stability.

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Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

FP and YY gathered the records of the treated patients and documented the details of tumour, surgery and final follow up. ZZ and JL analysed the follow-up data. JF, FC and ZS made substantial contributions to conception and design. JF and FC confirm the authenticity of all the raw data. All authors have read and approved the final version of the manuscript.

Ethics approval and consent to participate

This article contains a study with human participants, and the study protocol was approved by the Huazhong University of Science and Technology Committee on Human Research (Wuhan, China; reference no. 2019-IEC-S274). Written informed consent to use the patient data for this study was obtained from all patients.

Patient consent for publication

Consent for publication of images was obtained from all patients.

Competing interests

The authors declare that they have no competing interests.

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