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Calcanectomy in primary high-grade sarcomas: Foot salvage without the need for any reconstruction

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ABSTRACT

The calcaneum is a rare site for primary bone sarcomas. Calcanectomy is not considered for high-grade malignancies due to anticipated issues with obtaining negative margins, providing adequate soft-tissue coverage, and preserving satisfactory function. A below-knee amputation overcomes these difficulties and is very functional and, thus, the preferred local control option. The aim of this study is to evaluate the role of total calcanectomy, without any formal reconstruction, in high-grade calcaneal sarcomas. Over 14 years, three patients with highgrade calcaneal sarcomas underwent limb salvage surgery as opposed to amputation for their primary malignancy. Total calcanectomy was undertaken using a Cincinnati incision. No formal "calcaneal" reconstruction was undertaken after resection, essentially leaving the patient with an excision arthroplasty through the subtalar joint. The Achilles tendon was reattached to the posterior talus. Negative resection margins were achieved in all cases with the primary wound closure. Two patients are alive with no evidence of disease at 15 and 10 years. The third patient, at over 1 year postoperatively, has no evidence of local disease recurrence but has had metastasectomy for documented pulmonary metastases at the presentation. The average musculoskeletal tumor society score was 85.5%, and the average Toronto extremity salvage score was 88.5%. In our experience, even high-grade malignancies at this unusual site are potentially amenable to limb salvage. Our results show that perhaps ablative surgery should not be considered inevitable. Good functional outcomes can be achieved without reconstruction, thus minimizing potential "construct"-related morbidities.

Keywords: Calcaneus, Foot, Reconstruction, Salvage, Sarcoma

INTRODUCTION

High-grade sarcomas in the small bones of the foot are rare. The calcaneus bone is an even more rare site for a primary malignancy. The majority of these patients have an ablative procedure, as the modality of choice, for local surgical control.^[1] Limb salvage for calcaneal sarcomas is very demanding as it is difficult to get negative margins while retaining an adequate soft-tissue cover and preserving good function. A below-knee amputation has remained the standard surgical treatment of choice for these tumors as it achieves wide margins and a below-knee prosthesis is functionally excellent.^[2]

In selected cases, however, a total calcanectomy can be considered as a valid alternative to a below-knee amputation.^[3,4] It is a relatively infrequent treatment option. However, if opted for

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This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-Share Alike 4.0 License, which allows others to remix, transform, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms. ©2023 Published by Scientific Scholar on behalf of Journal of Musculoskeletal Surgery and Research these rare tumors, patient should meet a strict selection criteria. These include either an absence of or minimal softtissue component of the tumor and no significant associated underlying vasculopathy. In addition, the patient must be made fully aware of the fact that in the event of either unexpected positive margins or protracted wound healing complications, the salvage procedure would still be a belowknee amputation.

All patients were operated on in the prone position using an extended Cincinnati incision for surgical access.^[5] A proximal thigh tourniquet was used. Post-total calcanectomy, no formal reconstruction, was undertaken except for reattachment of the tendo-Achilles to the talus using Mitek sutures. The patients were immobilized in a cast for a minimum period of 8 weeks postoperatively. The cast was applied in full equinus, to begin with, and sequentially brought out to a neutral position. Unrestricted full weightbearing was commenced at 8 weeks postoperatively.

Major indications for calcanectomy include calcaneal osteomyelitis, intractable heel ulcers, severe calcaneal deformity, and primary bone tumors of the calcaneus.^[3,6,7]

Calcanectomy was first documented by Gaenslen in 1931. He treated 11 patients with hematogenous osteomyelitis of calcaneus.^[8] It mainly involved splitting the calcaneus and curettage of the medullary cavity, hollowing out the calcaneus, and leaving a healthy cortical bone shell.^[7] In the literature review, we could find a considerable amount of work done on calcanectomy for osteomyelitis of calcaneus.^[6-8] However, we could find a scant number of limb salvage procedures for high-grade calcaneal sarcomas in terms of total calcanectomy. The few cases which have been done are for relatively low-grade malignancies.^[3,4]

Post-calcanectomy, a variety of reconstruction options have been described. These include bone allograft, three-dimensional printed prosthesis, vascularized or pedicled autograft, composite allograft, and custom-made prosthesis.^[9-11] Some of these procedures may require longterm immobilization and an extended period of non-weightbearing ambulation. They are also prone to option-specific complications such as prosthetic infection, graft failure, graft collapse, graft non-union, and graft mal-union. These are in addition to generic wound healing complications of surgery at this site. Any of these complications could potentially result in a salvage below-knee amputation.

There are no reports in the literature of functional outcomes; however, when no reconstruction has been undertaken. While still prone to generic complications, it certainly avoids any option-specific complications. Two of our patients had high-grade sarcomas and underwent no reconstruction but still achieved good functional outcomes with a long-term follow-up. The third patient in our short series, however, has a short follow-up with a history of prior high-dose radiation therapy at the local site. Her outcomes will need to be seen from this perspective.

This report aimed to evaluate the role of total calcanectomy, without any formal reconstruction, in high-grade calcaneal sarcomas.

MATERIALS AND METHODS

Inclusion criteria

The following criteria were included in the study:

- 1. All patients with the primary high-grade calcaneal sarcoma
- 2. Tumors with minimal or no soft-tissue component.

Exclusion criteria

1. Tumors that are either encasing the posterior tibial neurovascular bundle or with imminent risk of fungation were excluded from the study.

It is a retrospective study. There were three patients who presented with a primary bone sarcoma of the calcaneus between 2005 and 2019. After taking informed consent, all patients were worked up before surgery according to the standard protocol. Local staging included plain radiographs and an magnetic resonance imaging (MRI) scan. Systemic staging included a chest radiograph, chest computed tomography (CT) scan, and a Technetium 99 m Bone scan. Two patients had an image-guided core needle biopsy for tissue confirmation of the diagnosis at our center. The third patient had a predetermined diagnosis from another tertiary health-care facility. The feasibility of performing limb salvage surgery was based both on MRI studies and an informed discussion with the patients. The option of a below-knee amputation was offered to all three patients, who were made fully aware of its potential advantages vis-à-vis attempts at limb salvage. All three elected to have limb salvage, being fully cognizant that any potential failure to either obtain negative margins or protracted wound healing complications would nevertheless still result in a transtibial amputation. None of the patients had any associated systemic vasculopathy though one had been previously locally irradiated.

The surgery was done under tourniquet control. Before starting, the subtalar joint was marked under C-arm control [Figure 1]. The Cincinnati approach was used with the patient in the prone position [Figure 2]. Dissection of the neurovascular bundle and peroneal tendons was done [Figure 3]. Subtalar disarticulation of the calcaneum was done after careful dissection around the tumor [Figure 4]. No reconstruction for the calcaneum was undertaken. The tendo-Achilles was sutured to the posterior talus using Mitek sutures and in Case #3, we needed to lengthen the



Figure 1: Marking for subtalar joint under C-arm guidance. (a) Metallic indicator, and (b) Confirmation under C-arm, and (c) marked foot.



Figure 2: Cincinnati incision. (a) Lateral side and (b) medial side.

tendo-Achilles with the use of a trevira tube [Figure 5]. Postoperatively, the patients were immobilized in full equinus in a protective below-knee cast for 4 weeks until the surgical wound healed. After that, the ankle was brought to a semi-equinus position, and the cast continued for a further 4 weeks. At 8 weeks postoperatively (if the wound healing was satisfactory), the cast was discontinued, the foot was brought out to neutral, and full weight-bearing physiotherapy commenced. In Case#3, cast immobilization was extended for a further 4 weeks due to the concern about delayed wound healing.



Figure 3: Dissection of neurovascular bundle and peroneal tendons. (a) Dissected peroneal tendons and (b) peroneal tendons and neurovascular bundle.



Figure 4: Subtalar disarticulation of calcaneus. (a) Articular surface of calcaneus and (b) plantar side of calcaneus.

Postoperatively, they were followed up at 3 months intervals for the first 2 years, every 4 months in year 3, and at 6 monthly intervals in years 4 and 5. Thereafter, they were followed up on an annual basis. Case #1, operated in 2005, discontinued his follow-up in 2013, whereas Case #2, operated in 2010, still attends for review on an annual basis. Case #3 was only operated on in 2019.

The patients were asked to complete the questionnaires to assess the functional outcome and quality of life. We used the Musculoskeletal Tumor Society scoring system (MSTS, 1993) and Toronto extremity salvage score (TESS) to provide both an objective and a subjective final functional outcome assessment.

In the MSTS system, numerical values (0–5) are assigned to each of the six categories of pain, function, emotional acceptance, support, walking, and gait. They give a total score of between 0 and 30.^[12] The TESS is a self-administered questionnaire that includes 30 items regarding activity limitations in daily life, such as restrictions in body movement, mobility, self-care, and performance of daily tasks and routines.^[13] The degree of physical disability is rated from 0 (not possible) to 5 (without any problem). The raw score is converted to a score ranging from 0 to 100 points, with higher scores indicating fewer functional limitations. Patients are able to answer questions concerning activities that they do not



Figure 5: Reattachment and reconstruction of Achilles tendon with trevira tube and Mitek sutures, forceps pointing toward Achilles tendon.

perform in daily life with "not applicable." These questions are deducted from the calculation of the total score.

RESULTS

Case #1

A 45-year-old male patient was referred in 2005 with an established diagnosis of osteosarcoma of the right calcaneus (non-metastatic). He had an image-guided biopsy undertaken elsewhere in April 2005, proofread in our institution. He, then, commenced neoadjuvant chemotherapy at our sister hospital – comprising three cycles of Adriamycin/Cisplatin. Unfortunately, the chemotherapy was complicated by cisplatin-induced neuropathy affecting cranial nerves VIII and XII, which, however, resolved. He was then referred back to us for local surgical control. The patient's medical history included maturity-onset diabetes managed by oral hypoglycemics. Plain radiographs showed an osteoblastic calcaneal lesion with lateral extraosseous extension, as shown in [Figure 6]. MRI imaging corroborated these findings and confirmed near-total calcaneal involvement with a small lateral extraosseous soft-tissue extension [Figure 7].



Figure 6: (a) Plain radiograph lateral view showing an osteoblastic calcaneal lesion and (b) axial view of calcaneus showing lateral extraosseous extension.



Figure 7: Magnetic resonance imaging showing involvement of almost the whole calcaneum (a) sagittal section and (b) axial sections with some lateral soft-tissue component.

The surgical option given to the patient was that of a belowknee amputation. Given the soft-tissue extension and his underlying history of diabetes, limb salvage was not considered. However, the patient declined ablative surgery. He insisted on having limb salvage being fully cognizant of the fact that the risks of failure would be high and, in that event, would still end up with an amputation. Under the circumstances, after a full and frank discussion, the patient was booked for a total calcanectomy. The surgery was undertaken in September 2005. A Cincinnati incision was used with the patient in the prone position. A thigh tourniquet was used. No formal reconstruction was undertaken for the calcaneum - in effect, this was an excisional arthroplasty through the subtalar joint. The Achilles tendon was reattached to the posterior talus using Mitek sutures. Negative resection margins were achieved, but the tumor necrosis rate was just 30%. The post-operative protocol envisaged 4 weeks in a cast in full equinus and then a further 4 weeks in a semi-equinus position before bringing the foot to neutral and commencing both full weight-bearing and physiotherapy. Immediate postoperative radiographs are shown in [Figure 8].

However, due to his diabetes, wound healing took longer than anticipated and he was in a cast for a total of 12 weeks. Our medical oncologist decided against giving the patient any adjuvant chemotherapy at this juncture. His reasoning was the very poor response rate, the inevitable delay incurred and compounded by the patient's previously documented neurotoxicity.

He continued to be followed up by us until November 2013, but after that, he could not come for a follow-up. Radiographs of his last visit after 8 years of surgery, as shown in [Figure 9], have good alignment. He remained in contact with us, and as of July 2019, the patient has remained disease free from an oncology viewpoint.

Functional evaluation was done after 14 years of surgery using the MSTS and TESS. He was given the questionnaires to fill out. His MSTS score was 28 out of 30 (93.3%), and his TESS score was 141 out of 150 (94%). [Figure 10] shows his recent pictures with acceptable cosmesis and good plantar flexion.

Case #2

A 21-year-old male patient was referred to us in March 2010 with an established diagnosis of Ewing sarcoma of the left calcaneus. He had been diagnosed in November 2009 at another institute. The patient had presented with 6 weeks history of increasing pain in the left heel. His primary workup, including



Figure 8: Post-operative radiographs showing absent calcaneum, Mitek sutures in talus for reconstruction of Achilles tendon and a back slab in equinus. (a) Lateral view and (b) Anteroposterior oblique view.



Figure 9: Radiographs at follow-up after 8 years (a) lateral view and (b) anteroposterior view.



Figure 10: Recent pictures of the foot (a) foot from medial side and (b) photograph showing heel lift off with patient on his toes.

a CT-guided core biopsy, had revealed a non-metastatic Ewing's sarcoma of the calcaneum. Induction chemotherapy had been commenced at the referring hospital (vincristine, adriamycin, and cyclophosphamide [VAC] alternating with ifosfamide/ etoposide) and after four cycles - he was, then, referred to us for consideration of local control. Plain radiographs [Figure 11] showed post-treatment sclerosis with trabecular thickening of the calcaneum. MRI [Figure 12] revealed an intramedullary space-occupying lesion involving almost all of the calcaneum, low in T1, and high in T2, with peripheral enhancement and a minimal lateral extraosseous soft-tissue component. The outside pathology was reviewed at our center and the diagnosis of Ewing's sarcoma was re-confirmed as "malignant small round cell tumor morphologically and immunohistochemically consistent with Ewing's, positive for CD99 and negative for CD45 staining." Fluorescence in situ hybridization was also positive. Surgical local control options were discussed with the patient. These included a below-knee amputation and a possible role for limb salvage by undertaking a calcanectomy. The risks/ benefits of both procedures were discussed with the patient. The patient also saw our radiation oncologist, who discussed the merits/demerits of radiation therapy as the means for "local control." The patient was not accepting a primary amputation and wanted us to proceed with limb salvage but was warned that the salvage option would still be an amputation in the event of any surgical failure.

The minimal soft-tissue component meant that limb salvage was still technically possible and in June 2010, he underwent a left total calcanectomy. A Cincinnati approach was used, with the surgical details being identical to those described with the previous patient. The tendo-Achilles was reattached to the posterior talus using Mitek sutures. The final pathology confirmed a 100% necrosis rate with no viable tumor cells and obviously, therefore, negative resection margins. Postoperatively [Figure 13], a below-knee front slab was applied for 4 weeks in full equinus and once the surgical wound had healed, splinting was continued for the next 4 weeks in a semi-equinus position. Thereafter, the patient was allowed to weight bear as tolerated without any splinting, and outpatient physiotherapy was commenced to regain range of motion at the ankle joint.



Figure 11: Radiographs of the calcaneum showing trabecular thickening with lytic lesions (a) lateral view and (b) anteroposterior oblique view.



Figure 12: Magnetic resonance imaging (a) axial view showing intramedullary space occupying lesion involving almost all of the calcaneus, with a small lateral extraosseous soft-tissue component. (b) Sagittal cuts showing intramedullary space occupying lesion involving almost all of the calcaneus, with a small lateral extraosseous soft-tissue component.

The patient completed his adjuvant chemotherapy at his parent hospital but has continued to follow-up with us from a surgical perspective. Radiographs taken after 8 years of surgery showed acceptable alignment [Figure 14]. In addition, his last positron emission tomography imaging from April 2018 and MR imaging from June 2019 [Figure 15] were negative for any local or systemic disease recurrence.

Functional evaluation was done 9 years postoperatively using the MSTS and TESS. His MSTS score was 27 out of 30 (90%), and his TESS score was 132 out of 140 (94%). [Figure 16] shows his foot with the surgical incision marked on it. [Figure 17] shows him standing and tip-toeing.

Case #3

A 29-year-old female had high-grade osteosarcoma of the calcaneus with pulmonary metastases. She was diagnosed with osteosarcoma of the calcaneus in some other country in December 2016. She had metastasis to the chest at presentation. The patient



Figure 13: Immediate post-operative radiographs showing absent calcaneus with Mitek sutures in talus for reattachment of Achilles tendon and a front slab in equinus (a) lateral view and (b) AP oblique view.



Figure 14: Radiographs at follow-up after 8 years (a) AP oblique view and (b) lateral view.

tolerated chemotherapy poorly. Neoadjuvant chemotherapy consisted of four cycles of Doxorubicin and Cisplatin with some evidence of local tumor regression. The patient was advised an amputation for local control, in which she declined. Therefore, she was treated by radiation therapy, 5000 cGy in five fractions. Adjuvant chemotherapy included doxorubicin and ifosfamide (also poorly tolerated), with both symptomatic and radiographic evidence of the progression of the disease in her left foot. Chemotherapy was then switched to gemcitabine and docetaxet and eventually to a reduced dose of pazopanib.

Subsequently, she returned home, saw her local oncologist, and was referred to us for revisiting the local control option. Before any surgical intervention, we got the thoracic surgeons to review her regarding the pulmonary metastases. Were these resectable? If pulmonary metastasis are resectable, only then local control would be justifiable as she had no local symptoms. Thoracic surgery opined that metastasectomy was feasible, provided, of course, we had first achieved local control.

In her case, especially with the history of radiation therapy, amputation was the preferred option for local control. However, this remained unacceptable to her. In the MRI





Figure 15: Magnetic resonance imaging at follow-up after 8 years (a) sagittal section showing Mitek sutures clearly visible in the talus with continuity of the Achilles tendon, (b) post-contrast sagittal view showing no evidence of disease recurrence, and (c) coronal section.



Figure 16: Pictures of the foot at follow-up after 8 years with acceptable cosmesis. Marking for the original surgical scar done showing Cincinnati incision. (a) medial view, (b) lateral view, and (c) posterior view.

study [Figure 18], there was a marrow-replacing lesion of the calcaneus with a soft-tissue extension on the posterior aspect in the region of the subtalar joint and enhancement of the distal Achilles tendon. We offered her the option of a calcanectomy but warned her of the considerably increased local risks of wound healing issues given her treatment history. If she had these wound concerns or local recurrence, she could still end up needing an amputation for salvage.



Figure 17: (a) Standing normally and (b) on tiptoes showing good function of tendo-Achilles.



Figure 18: (a) Pre-operative radiograph lateral view and (b) magnetic resonance imaging post contrast sagittal section showing involvement of calcaneus with posterior soft-tissue component of tumor.

She consented to proceed with calcanectomy, which was performed on March 2019. Unlike the previous two patients, in her case, the posteriorly located soft-tissue mass necessitated transecting the Achilles tendon well proximal to its insertion. A Trevira tube was wrapped around the shortened remnant Achilles tendon to gain length, with the tube, in turn, then being secured to the talus with Mitek sutures. Negative resection margins were achieved. The tumor was 5.5 cm in maximum diameter with 95% tumor necrosis. [Figure 19] shows her immediate post-operative radiograph. She, subsequently, underwent pulmonary metastasectomy with the removal of five lung lesions (all with negative margins).

The post-operative protocol was amended to a total of 12 weeks of cast immobilization as we anticipated potential wound healing issues, given her prior radiotherapy at this site. The primary wound healing was uneventful, but she developed a wound infection 4 months postoperatively. This needed a formal debridement and removal of the



Figure 19: Immediate post-operative radiograph showing Mitek sutures in Talus and a front slab in equines position.

Trevira tube, serial VAC dressings, and, subsequently, a secondary wound closure. The Achilles tendon remnant was left unattached to avoid the morbidity associated with its reconstruction. The patient remains disease free but under close monitoring, especially for her chest. [Figure 20] shows the final closure of the wound and subsequently after the removal of sutures and skin clips.

At 6 months follow-up appointment [Figure 21], functional evaluation was done using the MSTS and TESS. Her MSTS score was 14 out of 30 (46.66%) and her TESS score was 79 out of 135 (58.5%). At 1 year postoperatively, these scores were 22/30 (73.3%) and 105/135 (77.77%), respectively. Undoubtedly, the wound infection and need for debridement delayed her rehabilitation, but her scores subsequently improved. The question was put to her: Would she, in hindsight, knowing what she went through, have opted rather for a below-knee amputation? Her answer was an emphatic no!

Although she remained free of local recurrence, she developed progressive metastatic chest disease that did not respond to chemotherapy, and she succumbed to her illness in February 2021. Her systemic disease progression and palliative status made any meaningful MSTS or TESS documentation inappropriate, as the deterioration in her general condition became her primary limiting factor.

DISCUSSION

There has undoubtedly been significant improvement in survival post the initial introduction of chemotherapy for bone sarcomas due to optimized therapy. Regrettably, however, there have been no further dramatic breakthroughs over the last couple of decades, and overall, disease-free survival rates have remained unchanged.

The literature shows that "limb salvage is possible in up to 90% of all musculoskeletal malignancies, while the reconstruction modality that post-resection gives the best outcome remains debatable." Renard *et al.* and Rougraff *et al.* reported that



Figure 20: (a) Picture of the foot after infection being cured and secondary closure of the wound and (b) after removal of sutures and clips.



Figure 21: Radiographs of the foot at 6 months follow-up (a) lateral view and (b) anterior posterior oblique view.

patients after amputation have poor functional outcomes compared to patients after limb salvage procedures.^[4,14]

The foot is a rare site for both primary and secondary bone neoplasms (<1% of all tumors of the musculoskeletal system).^[15] Limb-salvage surgery remains a challenge, especially when it comes to calcaneal sarcomas and even benign aggressive lesions. According to Imanishi and Choong, only about 18 cases had been reported until 2015.^[11]

Limb-salvage surgery should be considered an option for calcaneal sarcomas, especially if the lesion is intracompartmental (Enneking I/IIA). However, in certain cases, providing the soft-tissue component of the tumor is limited. It may be feasible to perform limb-sparing surgery even for Enneking IIB lesions.^[16,17] Clinical judgment needs to be exercised provided that there is no disease progression, and the surgeon believes that the soft-tissue component can be safely excised with the tumor mass – then limb/foot salvage becomes an option.

As regards the reconstruction post-calcanectomy, various options have been utilized. These include the use of bone

allograft, vascularized or pedicled autograft, composite allograft, prosthetic replacement, and even threedimensional printed implants.^[9-11] Potential complications include infection, graft failure, graft collapse, non-union, malunion, skin flap necrosis, and the potential risk of subsequent amputation. In addition, the use of allografts, in particular, may entail a prolonged period of non-weightbearing postoperatively.

Calcanectomy without any reconstruction is an acceptable alternative option, in our opinion and one that has not been described in the literature post-tumor resections. Partial calcanectomy, if possible, would have an obvious advantage over total calcanectomy, but none of the patients in our limited series were in this category.^[18] The advantages of undertaking no reconstruction are an earlier return to full weight-bearing, a lower risk of infection as any implant/ foreign body insertion has been avoided, no associated "donor" site morbidity, shorter operating time and cheaper as there are no associated costs, incurred for "reconstruction."

Conversely, cosmetically speaking, the patient has to compromise. There is inevitably a degree of leg length discrepancy due to loss of heel height and a tendency to develop a "rocker-bottom" deformity of the foot. The limb length discrepancy tends to be around 2 cm and can be compensated for by either using insoles or a heel raise. The total contact inlay can be customized to provide a heel lift to compensate for the limb length discrepancy. The customized shoe must-have sufficient depth and height to accommodate this insole.

We made insoles for our patients, but they were not compliant with them. This could be a cultural factor as their preferred footwear was sandals rather than formal shoes. Even though they found the insoles comfortable, they did not continue using them. Cases # 1 and 2 could perform daily routines without difficulty, walk over a kilometer, and have desk jobs with no work-related issues.

Hind-foot surgery is inherently prone to relatively high complications, including wound healing issues, hypertrophic and tender scars, and sural nerve injury. The Cincinnati incision used in our surgical procedures has the advantage of preserving the neurovascular and lymphatic supply of the foot with good cosmesis in terms of scar formation. Our patients had acceptable foot cosmesis without any heel pad complications. Loss of sensation over the heel has not been a functional issue with any of our patients. Undoubtedly, heel sensation is diminished/altered. However, even our two longterm follow-up patients have not had any trophic issues as a result of it. The functional outcome was good in two patients with a long-term disease-free follow-up of 15 and 10 years, respectively. The last patient has just over a 1-year follow-up to date and accentuating circumstances, but even she remains very satisfied with the outcome to date.

CONCLUSION

Total calcanectomy can be considered a valid alternative option to amputation for selective patients with even high-grade calcaneal sarcomas. Formal reconstruction post-calcanectomy is not mandatory. Good functional outcomes with acceptable cosmesis can be achieved without reconstruction, thus minimizing potential "construct"related morbidities.

AUTHORS' CONTRIBUTIONS

IUK conceived and designed the study, conducted research, and wrote the article's initial and final drafts. MS and RP wrote the discussion. Finally, all authors have critically reviewed and approved the final draft and are responsible for the manuscript's content.

ETHICAL APPROVAL

Formal approval from the ethical committee of King Faisal Specialist Hospital and Research Center was obtained with reference number C380/167/39 on 21st December 2017.

DECLARATION OF PATIENT CONSENT

The authors certify that they have obtained all appropriate patient-informed consent. The patients have given their consent for their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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CONFLICTS OF INTEREST

There are no conflicting relationships or activities.

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