Review

# Surgical management of tibial metastases: a systematic review

*Tommaso Greco[1,2], Camillo Fulchignoni[1,2], Luigi Cianni[1,2], Giulio Maccauro[1,2], Carlo Perisano[1,2]*
[1]Policlinico Universitario A. Gemelli Foundation IRCCS, Rome, Italy; [2]Catholic University of Sacro Cuore, Rome, Italy

**Abstract.** *Background:* Tibia is a rare location among all skeletal metastases. Those lesions are often discovered in an advanced stage of disease and are mainly reported to the orthopedic surgeon to reduce pain, to improve the patient quality of life and his functional status. Current literature on the surgical management of metastases and/or pathological tibial fractures shows mostly few case reports, case series or at most retrospective studies on very small and heterogeneous groups of patients. The purpose of this study is to analyze those articles highlighting epidemiology and discussing surgical options and relative outcomes. *Methods:* Studies were searched on PubMed, Google Scholar and Web of Knowledge from inception to September 2020 and 30 articles discussing tibial metastasis surgical treatment were included. *Results:* Results discuss age and sex of patients, location of tibial metastases, origin of metastases, type of lesion and spread of disease, surgical treatment, outcomes in terms of pain evolution, gain of function and general status, complication and relapse, and survival of patients. *Conclusions:* Despite the lack of randomized trials and the absence of high-level studies, guidelines suggest different types of treatments depending on location and stage of disease. The analysis of the articles included in this review confirms the heterogeneity of possible treatments, assuring, independently of the chosen techniques, good and similar results, leading to the conclusion that the choice of the surgical technique must take in consideration each patient's characteristics and the surgeon's experience. (www.actabiomedica.it)

**Key words:** Tibia, Surgical treatment, Palliative treatment, Bone metastasis, Cancer staging

## Introduction

Bone is the third site for incidence rates of secondary metastatic lesions, after lung and liver(1). The management of metastatic bone disease and typical skeletal-related events (SRE) is complex and requires a comprehensive approach with the coordination of a multidisciplinary team(2).

Prostate, breast, lung, kidney and thyroid cancers represent approximately 80% of all skeletal metastasis.

In 85% of cases, the axial skeleton is concerned with involvement of the vertebral column, ribs, pelvis, humerus and proximal femur(3); whereas "below-the-knee metastases" involving the tibia, fibula and bones of the foot are rarer(4–6).

Although rare, tibial metastases with actual or impending pathological fracture have a significant impact on patients' quality of life, in terms of function and mobility, compared to other sites of metastasis in the axial skeleton.

Goals in treating pathological fractures or tibial metastases are pain control, improvement of patients' quality of life, preservation of joint function and segmental stability(7).

The treatment choice depends on a number of prognostic factors: patient's general condition, type, stage and grade of cancer, survival time expectancy, affected tibial segment (proximal, diaphyseal or distal), size and type of lesion (lytic or osteoblastic), and sensitivity to non-surgical therapies(8).

Various methods, such as narcotic analgesics, bisphosphonate, chemotherapy, radiation therapy, radiopharmaceutical agents, and surgeries have been developed for palliative pain improvement(9).

Surgical techniques for tibial metastases treatment include curettage, open or closed reduction and internal fixation, allograft reconstruction, prosthetic replacement or even amputation(10).

Current literature on the surgical management of metastases and/or pathological tibial fractures shows mostly few case reports, case series or at most retrospective studies on very small and heterogeneous groups of patients. Often the few cases of tibial metastases are included in larger series including other primary bone tumors of the tibia or other bone metastases in more frequent locations, resulting in the impossibility of extracting specific data on surgical treatments and post-operative outcomes. This is all due to the low incidence of these metastases, to the high complexity and wide heterogeneity of affected patients and to their poor clinical prognosis that does not allow a long and accurate follow-up.

Therefore, the purpose of this descriptive review is to analyze the available literature highlighting incidence, epidemiology and which primary tumors most metastasize to the tibia. Moreover, our interest was focused on the various surgical options proposed for treatment, evaluating the post-operative results in terms of quality-of-life improvement, pain relief, functional recovery and ability to walk, relapse of disease and survival.

## Materials and Methods

### *Literature search and study selection*

A literature search was performed on MEDLINE through PubMed, Google Scholar and Web of Knowledge to identify scientific publications concerning metastases or pathological fractures of the tibia. Literature search was performed on September 30, 2020, without applying any restriction on date of publication. To avoid missing studies, no filters were applied to the search strategies (Appendix 1). Using titles and abstracts, three authors independently selected studies for inclusion. Studies with levels of evidence from I to V that recruited people of any age with tibial metastasis or tibial pathological fracture from any known or unknown primary tumor were included. Only papers published in English and with full-text available were considered for inclusion.

Exclusion criteria were studies with non-surgical treatment of tibial metastases, studies with unspecified surgical treatment and studies on animal models. Literature reviews and editorial pieces were also excluded.

In cases of disagreement about paper inclusion/exclusion at any stage of the selection process, a consensus was reached through discussion or, when not possible, by arbitration from the senior author.

Titles of journals, names of authors or supporting institutions were not masked at any stage.

Moreover, when we had doubt on possible overlapping of patients, authors of concerned articles have been contacted to exclude any possibility of overlapping.

### *Data extraction and analysis*

Two authors independently extracted available data from the full text of all eligible studies using a pilot form. Collected information included: authors and year of publication, type of study, level of evidence, number of patients with tibial metastases, location of metastases in the tibia, sex and age of patients, primary tumor if known, type of surgical treatment, and survival of patient or duration of follow-up. For each study, always when available, the incidence of disease recurrence, patient survival and any scores used for pain assessment, functional recovery, walking ability were collected and reported.

Due to the heterogeneity of analyzed publications in terms of patient samples and study designs, many of these values were often not reported or impossible to extrapolate and were considered missing and not applicable in the presentation of the results. A third author checked the extracted data.

Level of evidence was assessed using the Clinical Orthopaedics and Related Research level of evidence chart, which is an adaptation from published information from the Centre for Evidence-Based Medicine (Oxford, UK)(11).

Descriptive statistics was used to summarize findings across all included studies.

## Results

The electronic search resulted in 2566 articles. After exclusion of duplicates, of non-English articles, of articles on animal models and of articles without full text available, 1169 studies remained. Titles and abstract were screened, resulting in 146 remaining articles. After full-text review, 116 articles were excluded. Thus 30 studies were finally included in this review, following the PRISMA flow chart(12) (5,7,13–40).

Of 30 selected articles two were level III of evidence (6.7%), sixteen were level IV (53.3%) and twelve were level V (40.0%) (Tab. 1).

*Age and sex*

Among the 30 selected studies, 108 patients (for 109 tibias) were included in this review (Tab.2). In 9 studies (20,27–29,32,34,38–40) the age of participants (44 of 108) was not declared; average age calculated on the remaining 64 patients (5,7,13–19,21–26,30,31,33,35–37) was of 64.4 years old, with a range between 29 and 86 years old.

Furthermore, in 42 out of 108 patients, gender was not declared either (20, 27–29, 31, 32, 34, 38, 39). The remaining 66 patients (5, 7, 13–17, 19, 21–26, 30, 33, 33, 35–37, 40) were 35 males (57.0%) and 31 females (47.0%).

*Tibial location*

Tibial metastases were located in 48 cases at proximal tibia (5, 14, 18, 26, 27, 29, 32, 40) (44.1%), in 38 cases at tibial shaft (7, 16, 22, 24–26, 30, 31, 33, 34, 36–39) (34.9%) and 13 of them were located at distal tibia (5, 7, 13, 15, 23, 26, 27, 35) (11.9%). One patient had a synchronal proximal and diaphyseal location(7), and another had multiple skip lesions(17). For 8 patients surgically treated for tibial metastasis, the exact location was not specified (19–21, 28).

*Primary tumor*

Primary tumors were reported in 91 (84.3%) patients examined out of 108 in this review. In 4 studies (20,28,29,38) that involved the remaining 17 patients (15.7%), the primary tumor was not reported. Renal cell carcinoma involved 26 patients (24.1%) and was the tumor that most frequently metastasized on the tibia (5, 7, 19, 22, 26, 27, 31, 34, 36). For 14 patients (13.0%) the metastasis came from lung cancer (7, 24, 30, 31, 34, 35, 37, 40), and in 9 patients from colorectal cancer (8.3%) (7, 13, 23, 26, 40). Seven patients had lymphoma (6.5%) (7, 25, 26) among which none was primary lymphoma of the bone and 4 had a myeloma (3.7%) (7, 21, 26, 34). Eight females patients had breast cancer (7.4%) (7, 26, 30, 40) and 6 endometrial cancer (5.6%) (33, 34, 37, 40). Skin cancer was involved in 4 cases (3.7%): 2 melanomas (14,17), 1 tricholemmal carcinoma (16) and 1 squamous cell carcinoma (7). Three patients had a prostatic cancer (2.8%) (7) and 3 had a urothelial cancer (2.8%) (5,26). The metastasis came from other tumor location in 5 patients: bladder in two cases (18,26), stomach (13), duodenum (15) and thyroid (26) in one case each. One patient had an undifferenced carcinoma (34), and in one patient primary tumor was declared unknown (39).

*Clinical presentation*

In 75 cases it was specified if the author treated an impending or a pathological fracture. In 47 cases patients presented an impending fracture (62.7%) (7, 13, 16, 17, 19, 21–23, 26, 28–31, 33, 33, 36, 37,40), whereas in the remaining 28 cases patients had a fracture on the location of the metastasis (37.3%)(5, 7, 14, 15, 20, 25, 26, 35, 39, 40).

*Number of metastasis*

Only for 32 patients authors defined whether the metastases were solitary (11 cases) (5, 17, 22, 26, 30, 33, 36) or in multiple locations (21 cases) (5, 13–16, 19, 21, 25, 26, 30, 35) either visceral or bony.

*Surgical treatment*

In the articles included in this review, most commonly described surgical treatment for tibial metastasis was intramedullary nailing (IMN) either with or without cementation, that was used in 45 tibias (41.3%) (7, 20, 21, 26, 30, 33, 34, 36–38). The second most used

**Table 1.** Studies included in the review and main features.

| Author | Year | Level of evidence | N°of patients | Location - Treatment | Used score | N° of dead patients (survival in months) / n° of patients alive (follow-up in months) |
|---|---|---|---|---|---|---|
| **Tadross**[13] | 2000 | V | 2 | 2 Distal – 2 Ankle arthrodesis with IMN | none | 2 (5,5) / none |
| **Schaefer**[14] | 2002 | V | 1 | 1 Proximal – 1 RF and cementoplasty | none | 1 (6) / none |
| **Futani**[15] | 2002 | V | 1 | 1 Distal – 1 Ankle arthrodesis with IMN | MSTS | 1 (4) / none |
| **Kelly**[7] | 2003 | IV | 25 | 16 Proximal – 8 ORIF + cementation, 2 cementoplasty, 3 IMN, 2 prosthesis + flap, 1 curettage<br>6 Diaphyseal – 6 IMN (4 with cement, 2 without cement)<br>2 Distal – 2 IMN (with cement)<br>1 Synchronous proximal and diaphyseal – 1 IMN (with cement) | none | 14 (15) / 11 (21) |
| **Knoeller**[16] | 2004 | V | 1 | 1 Diaphyseal – 1 ORIF + cementation | none | none / 1 (12) |
| **Takahashi**[17] | 2006 | V | 1 | 1 Multiple skip lesion – 1 Extracorporal irradiation and reimplantation | ROM | 1 (16) / none |
| **Ali**[18] | 2007 | V | 1 | 1 Proximal – 1 Knee arthrodesis with IMN | none | 1 (3) / none |
| **Hoffmann**[19] | 2008 | IV | 1 | Not specified – 1 RF and cementoplasty | VAS | Not specified |
| **Siegel**[20] | 2008 | IV | 3 | Not specified – 3 IMN | none | Not specified |
| **Moon**[21] | 2011 | IV | 1 | Not specified – 1 IMN | none | 1 (11) / none |
| **Sewell**[22] | 2011 | IV | 1 | 1 Diaphyseal – 1 Custom-made intercalary endoprosthesis | MSTS, TESS | Not specified |
| **Hamada**[23] | 2011 | V | 1 | 1 Distal – 1 Prosthesis | MSTS, ROM | none / 1 (36) |
| **Ruggieri**[24] | 2011 | IV | 1 | 1 Diaphyseal – 1 Intercalary prosthesis with proximal and distal cementation | MSTS | 1 (36) / none |
| **Chang**[25] | 2013 | V | 1 | 1 Diaphyseal – 1 ORIF | none | 1 (1,5) / none |
| **Piccioli**[26] | 2013 | IV | 13 (14 tibias) | 5 Proximal – 3 Cementoplasty, 2 endoprosthesis<br>5 Diaphyseal – 5 IMN<br>4 Distal – 4 IMN or cementatoplasty+pinning | ECOG, QLQ-C30 | 13 (17) / none |
| **Hwang**[27] | 2014 | IV | 15 | 14 Proximal – 14 Endoprosthesis<br>1 Diaphyseal – 1 Endoprosthesis | none | Not specified |
| **Sun**[28] | 2014 | IV | 3 | Not specified – 3 Cementoplasty | VAS | Not specified |
| **Tian**[29] | 2014 | IV | 1 | 1 Proximal – 1 RF and cementoplasty | VAS, Karnofsky | Not specified |
| **Kim**[30] | 2014 | IV | 4 | 4 Diaphyseal – 4 IMN (flexible nails) + cementation | VAS, SUV (on PET) | 3 (5) / 1 (32) |
| **Benevenia**[31] | 2016 | III | 2 | 2 Diaphyseal – 2 Intercalary prosthesis (with/without cementation) | MSTS | 2 (7,5) / none |
| **Guzik**[32] | 2016 | IV | 5 | 5 Proximal – 5 Modular proximal tibia prosthesis with cement | VAS, Karnofsky | Not specified |
| **Choi**[5] | 2017 | V | 2 | 1 Proximal – Total knee arthroplasty + ORIF<br>1 Distal – ORIF + cementation | none | Not specified |

**Table 1.** Studies included in the review and main features.

| Author | Year | Level of evidence | N°of patients | Location - Treatment | Used score | N° of dead patients (survival in months) / n ° of patients alive (follow-up in months) |
|---|---|---|---|---|---|---|
| **Soylemez**[23] | 2017 | V | 1 | 1 Diaphyseal – 1 IMN (with intercalary allograft and fixation with plate) | none | none / 1 (17) |
| **Piccioli**[34] | 2017 | IV | 7 | 7 Diaphyseal – 7 IMN | none | Not specified |
| **Hsu**[35] | 2018 | V | 1 | 1 Distal – Ankle arthrodesis with IMN (with fibula autograft and cement) | MSTS | 1 (12) / none |
| **Panagopoulos**[36] | 2018 | V | 1 | 1 Diaphyseal – 1 IMN (with intercalary allograft and soleus flap coverage) | MSTS | none / 1 (60) |
| **Park**[37] | 2019 | IV | 2 | 2 Diaphyseal – 2 IMN (with cement) | MSTS, VAS | 1 (5) / 1 (6) |
| **Kask**[38] | 2019 | III | 5 | 5 Diaphyseal – 5 IMN (2 without cement, 3 with cement) | none | Not specified |
| **Zheng**[39] | 2019 | IV | 1 | 1 Diaphyseal – 1 Modular intercalary prosthesis + plate | MSTS | Not specified |
| **Johnson**[40] | 2020 | IV | 4 | 4 Proximal – 4 Prosthesis (1 proximal tibia replacement, 3 rotating hinge) | MSTS, KSS-f, ROM | 3 (23) / 1 (36) |

*IMN: intramedullary nailing; RF: radio frequency; ORIF: open reduction internal fixation (with plate); MSTS: Musculoskeletal Tumor Society Score; TESS: Toronto Extremity Salvage Score ; ROM: range of motion; ECOG score: Eastern Cooperative Oncology Group score; QLQ-C30 score: Quality of life questionnaire score; VAS: Visual Analog Scale; SUV: Standardized Uptake Value; PET: Positron Emission Tomography; KSS-f: Knee Society Score functional.*

**Tabel 2.** Patients demographic characteristics

| | | |
|---|---|---|
| **Total cases - n° of tibias** | | 108 – 109 |
| **Average age (range)** | Not specified | 64.4 yo (29-86) 44 |
| **Sex** | M | 35/66 (53.0%) |
| | F | 31/66 (47.0%) |
| | Not specified | 42 |
| **Tibial location** | Proximal | 48 (44.1%) |
| | Diaphysis | 38 (34.9%) |
| | Distal | 13 (11.9%) |
| | Synchronous | 1 (0.9%) |
| | Multiple skip lesion | 1 (0.9%) |
| | Not specified | 8 (7.3%) |
| **Primary tumor origin** | Renal | 26 (24.1%) |
| | Lung | 14 (13.0%) |
| | Blood | 11 (10.2%) |
| | Colorectal | 9 (8.3%) |
| | Breast | 8 (7.4%) |
| | Endometrial | 6 (5.6%) |
| | Skin | 4 (3.7%) |
| | Prostate | 3 (2.8%) |
| | Urothelial | 3 (2.8%) |
| | Other | 5 (4.6%) |
| | Unknown | 2 (1.8%) |
| | Not specified | 17 (15.7%) |
| **Clinical presentation** | Impending fracture | 47/75 (62.7%) |
| | Pathological fracture | 28/75 (37.3%) |
| | Not specified | 34 |
| **Number of metastases** | Solitary metastasis | 11/32 (34.4%) |
| | Plurimetastatic | 21/32 (65.6%) |
| | Not specified | 76 |

treatment was prosthesis implant that was described in 35 cases (32.1%) (5, 7, 22–24, 26, 27, 31, 32, 39, 40). Both IMN and prosthesis have been used at least once in all location (proximal, diaphyseal and distal). Open reduction internal fixation (ORIF) with plate (5, 7, 16, 25), and cementoplasty (7, 14, 19, 26, 28, 29) have been used each in 11 patients (10.1% for each). Knee or ankle arthrodesis with either retrograde or anterograde nailing was proposed in 5 patients (4.6%) (13, 15, 18, 35). Finally, curettage alone (0.9%) (7) and extracorporeal irradiation and reimplantation of the tibia (0.9%)(17) were used each in one specific case.

*Pain*

Out of the 30 selected articles, outcomes in term of pain reduction was not specified in 10 cases (15, 16, 18, 22, 25, 27, 33, 34, 38, 39). Among the 20 other articles, pain evolution was evaluated using visual analog scale (VAS) in 5 cases (19, 28–30, 37) (Tab. 1) whereas it was simply described without using any scale in the remaining 15 cases. Where specific data were available (30, 37) mean VAS score before surgery was 8.0 and decreased to 2.8 after surgery. Overall, pain reduction was achieved in 69 patients out of 70 (98.6%) (Tab. 3). The only patient who did not improve his pain symptomatology was a patient with a metastasis located at the diaphyseal tibia treated with an intercalary prosthesis (31).

*Functional outcome and general status*

In 8 articles(19–22, 27–29, 38) included in this review, it was not possible to extrapolate functional outcomes of patients surgically treated for tibial metastases as in those articles patients with primary bone tumors or other metastases location were included and results were not detailed for each patient. In two other cases authors do not describe the functional status of their patients(18,33). Among the 20 other articles, Musculoskeletal Tumor Society Score (MSTS) was used in 9 cases (15, 23, 24, 31, 35–37, 39, 40), range of motion (ROM) in 4 cases (17, 23, 32, 40) and functional Knee Society Score (KSS-f) in 1 case (40). Overall, 43 out of 44 patients (97.7%) improved their functional outcomes. The only patient who did not improve his functional outcome is the same patient that did not had pain resolution in Benevenia et al. article (31).

Ability (or absence of ability) to go back to ambulation was described in 20 articles (5, 7, 13–18, 22–24, 26, 30–36, 40) and 48 out of 50 patients (96.0%) were able to go back to walking after surgery. The two patients who didn't go back to walking after surgery are the patient who had intercalary prosthesis implant from Benevania et al. article (31) and one patient who underwent IMN with flexible nail for a diaphyseal metastasis(30).

General status was evaluated with Karnosfky score in only 2 articles(29,32) but only in Guzik(32) study we could extrapolate results for patients treated for tibial metastases: 5 out 5 had an improvement of Karnofsky score. General status of patients was also evaluated by Piccioli et al.(26): in 13 patients (14 tibias) general condition was improved with a mean ECOG (Eastern Cooperative Oncology Group) index score evolving from 3.75 before surgery to 1.80 at 3 months follow-up, and an average QLQ-C30 (Quality of life questionnaire) score improving from 17% to 66%.

*Specific results sorted by location and surgical treatment*

*Proximal tibia*

Forty-eight patients had proximal metastasis. The most commonly used treatment – in 28 cases - was prosthesis implant (5, 7, 26, 27, 32, 40) (Tab. 3). The results indicate, when described, that all patients improved their functional status, reduced their pain and went back to walking. Other techniques have been used for proximal metastasis treatment: ORIF in 8 cases (7), cementoplasty in 7 cases (7, 14, 26, 29), IMN in 3 cases (7), knee arthrodesis with IMN in 1 case(18) and curettage in one other case (7). As for prosthesis, reported outcomes indicate that all patients had pain reduction and improvement of functional status. Regarding their ability to ambulate, only Schaeffer et al. (14), Ali and Harrington (18). and Piccioli et al.(26) stated that all their patients went back to walking.

*Tibial diaphysis*

Regarding diaphyseal metastasis, 38 patients were included in this review, having either IMN, prosthesis or ORIF. Among the 31 patients who had IMN (7, 26, 30, 33, 34, 36–38) different techniques were described such as use or not of cement(38), use of intercalary allograft (33, 36), use of flexible(30) or standard nail. Among those, in 18 cases pain was discussed and, in all cases, there was a reduction. In 9 cases, functional outcomes were analyzed and all of them showed improvement. In 17 out of 18 cases patients went back to walking. Use of intercalary diaphyseal prosthesis was described by Sewell et al. (22) for 1 patient, by Ruggieri et al. (24) for another patient, Benevenia et al. (31) for 2 patients, and by Zheng et al. (39) for 1 patient

**Table 3:** Specific results sorted by location and surgical treatment

| Location | | Treatment | | Pain Reduction | Improvement of functional status | Back to walking | Relapse |
|---|---|---|---|---|---|---|---|
| **Proximal tibia** | 48 | Prosthesis | 28 (58.3%) | 13/13 | 11/11 | 11/11 | 1/6 |
| | | ORIF | 8 (16.7%) | 8/8 | 8/8 | Not specified | Not specified |
| | | Cementoplasty | 7 (14.6%) | 7/7 | 2/2 | 4/4 | 0/4 |
| | | IMN | 3 (6.2%) | 3/3 | 3/3 | Not specified | Not specified |
| | | Curettage | 1 (2.1%) | 1/1 | 1/1 | Not specified | Not specified |
| | | Arthrodesis | 1 (2.1%) | Not Specified | Not specified | 1/1 | 0/1 |
| **Diaphyseal tibia** | 38 | IMN | 31 (81.6%) | 18/18 | 9/9 | 17/18 | 2/12 |
| | | Prosthesis | 5 (13.2%) | 2/3 | 2/3 | 3/4 | 1/4 |
| | | ORIF | 2 (5.2%) | Not specified | Not specified | 1/1 | 1/1 |
| **Distal tibia** | 13 | IMN | 6 (46,2%) | 6/6 | 2/2 | 4/4 | 0/4 |
| | | Arthrodesis | 4 (30,8%) | 3/3 | 2/2 | 4/4 | 1/3 |
| | | Prosthesis | 2 (15,3%) | 1/1 | 1/1 | 1/1 | 0/1 |
| | | ORIF | 1 (7,7%) | 1/1 | 1/1 | 1/1 | Not specified |
| **Synchronous metastasis** | 1 | IMN | 1 | 1/1 | 1/1 | Not specified | Not specified |
| **Multiple Skip lesion** | 1 | Extracorporeal irradiation and reimplantation | 1 | 1/1 | Not specified | 1/1 | 0/1 |
| **Not specified** | 8 | IMN | 4 | Not specified | Not specified | Not specified | Not specified |
| | | Cementoplasty | 4 | 4/4 | Not specified | Not specified | Not specified |

*IMN: intramedullary nailing; ORIF: open reduction internal fixation (with plate).*

using an assistant plate in association to the prosthesis. Available data shows that 2 out of 3 patients had an improvement of pain and functional status, and 3 out of 4 went back to ambulate. Two patients had ORIF (16, 25) and available data indicates that Knoeller's et al. (16) patient went back to walking.

*Distal tibia*

Thirteen patients had distal metastasis. Six underwent IMN (7,26) and all of them had pain reduction. Moreover, reported results show that 2 out of 2 had an improvement of functional status and 4 out of 4 were able to ambulate after surgery. Four patients underwent tibio-calcaneal arthrodesis (13, 15, 35), all achieving full weight-bearing; for those whose outcomes have been reported, all had pain reduction and functional improvement. In two cases patients were treated with prosthesis (23, 27), but only Hamada et al. (23) stated that their patient had pain reduction, improvement of function and went back to walking. Choi et al. (5) describe one case of distal metastasis treated with ORIF. Their patient, as the precedent one, achieved improvement in the three parameters taken in consideration.

*Others*

Kelly et al. (7) described one case of synchronous proximal and diaphyseal metastasis of the same tibia treated with IMN, achieving pain reduction and gain of function. Takahashi et al. (17) had one patient with multiple skip lesions treated with en-bloc tibia resection, extracorporeal irradiation and reimplantation. This patient was able to ambulate and experienced pain reduction.

In 8 cases metastasis location was not specified. Four of these patients had IMN and four had cementoplasty. Among those last 4 all experienced pain reduction.

These data show that all the described techniques seem useful in achieving outcomes requested by terminal patients, and none of them has shown superior or inferior to the others. There does not seem to be any difference when comparing outcomes of proximal, diaphyseal and distal tibia treatments.

*Complications*

The number of patients recruited for whom the presence or absence of complications was mentioned was 46. In between those, in 34 cases no complication was described (14, 15, 17, 20, 23, 27, 31, 34, 37–40). The remaining 12 patients (26.1%) had complications (13, 16, 22, 24, 26, 27, 31, 36, 38, 40). Two patients had deep venous thrombosis (DVT), and both came from Johnson et al. (40) case series and were treated for proximal tibia metastases with a prosthesis implant. Two other patients treated by Hwang et al. (27) have presented fever and pain shortly after surgery (prosthesis implant to treat proximal lesion). One patient treated with IMN and intercalary allograft (36) had a nonunion, and was treated with nailing exchange, fibular osteotomy and bone graft. Two patients treated with intercalary prosthesis for diaphyseal metastasis were reported to have mechanical loosening. Sewell et al. (22) patient had adequate bone stock to allow a re-cementation of proximal component associated with bone graft, whereas Ruggieri et al. (24) patient had his prosthesis replaced with a similar implant.

Moreover, 6 patients had recurrence. One of them was one of Johnson et al. (40) patient with DVT, and in that case the recurrence was so important that it led to above-knee amputation (AKA). Among the five remaining patients, in only one case (31) the local recurrence needed AKA. The two patients with local recurrence who underwent AKA had both renal cell carcinoma and were both treated with prosthesis. The other patients had IMN in two cases (26, 38), arthrodesis with IMN in 1 case (13) and plate fixation in another case (16).

*Survival and follow-up*

In 64 cases, it was specified if patients were still alive or dead when the study was published. 18 patients were still alive with a mean follow-up of 23.9 months and 46 were dead with a mean interval from surgery of 13.9 months and a median of 15 months (Tab. 1).

## Discussion

Tibial metastases are a rare clinical finding compared to other bone metastasis(5) making it more challenging to find a consensus on surgical treatment. As introduced above, what appears at first glance when reviewing the literature is the small number of cases of tibial metastasis treatment described, the low level of

evidence of the published studies, the vast non-uniformity of both patients and evaluation methods.

Despite the lack of randomized trials and the absence of high-level studies, international and nationals guidelines (8, 41, 42) discussing the treatment of long bone metastases have been published. They firstly discuss the importance of analyzing prognostic factors such as type of primary tumor and supposed sensibility to non-surgical treatments, spread of disease, location, and presence of pathological fracture or impending fracture using Mirels score (43). Regarding surgical treatment of tibial metastasis, based on "very low evidence", those guidelines would "highly suggest":

- To treat patients with a solitary metastasis, with a good prognosis primary tumor (some of breast and prostate tumors, renal tumors and differenced thyroid tumors), free of illness during at least 3 years, with a radical asportation of metastatic lesion followed by a stable reconstruction (without specifying which type of reconstruction).
- To treat pathological or impending fractures of proximal tibia with curettage, cement and osteosynthesis with plate, or with intra-articular resection and prosthesis implant.
- To treat pathological or impending fractures of tibial diaphysis with osteosynthesis (ORIF or IMN), or with resection of lesion and implant of intercalary prosthesis, or with cementoplasty.
- To treat pathological or impending fractures of distal tibia with curettage, cement and osteosynthesis with plate, or with intra-articular resection and tibio-tarsal arthrodesis.

The "low evidence" on which those guidelines are based, and the multiple options offered in certain cases - go along with the vast heterogeneity of treatments found in the patients included in this review. Moreover, the good results in terms of pain reduction, improvement of functional status and capacity to walk again after surgery (Tab. 3), similar for all the different techniques might also explain these different choices for surgical treatment of tibial metastasis.

This variability of treatment is not surprising as even in other location in which bone metastasis are more frequent, such as proximal femur, no real consensus is present among orthopedic oncology surgeons(44).

Regarding complications, available data are even less significant as presence or absence of complication is reported for less than half of the patients included in this review. Nevertheless, among the reported complications (relapse, non-union, post-operative fever and mechanical loosening) most of them seem to occur in patients treated with prosthesis, confirming what has already been cited in other studies relative to other location (45, 46). Moreover, the two only amputations described occurred in patient who underwent prosthesis implant. This should lead surgeons to weight carefully the use of prosthesis in metastasis treatment, certainly offering a better mobility to the patient(40), but with what seems to be a higher risk of complications.

## Conclusions

In spite of the limitations of this review such as the lack of scientific evidence in the literature, what seems to be the most common scenario is for surgeons treating tibial metastasis to use prothesis for proximal metastasis, IMN for diaphyseal metastasis, and IMN or arthrodesis for distal metastasis. Whatever the technique, even if some complications have been described, it is important to surgically treat the patients to fit with their needs: reduction of pain, ability to ambulate and improving functional status.

We understand the vulnerability of the treated patients in this field, and the difficulties that can be encountered by the surgeons to produce high quality studies, we nonetheless believe that in future comparative prospective studies regarding the treatment of tibial metastasis would be useful to help surgeons make their decisions.

Meanwhile the choice of the technique must take in consideration the patient's characteristics and the surgeon's experience.

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**APPENDIX 1: Search strategies**

**Medline (PubMed)**
(tibial metastases) OR (tibial pathological fracture) OR (tibial metastatic disease)

**Web of knowledge**
TOPIC: (tibial metastases) OR TOPIC: (tibial pathological fracture) OR TOPIC: (tibial metastatic disease)

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Correspondence:
Camillo Fulchignoni, MD
UOC Ortopedia e Traumatologia
Fondazione Policlinico Universitario A. Gemelli IRCCS, Roma, Italia
Università Cattolica del Sacro Cuore,
Largo A. Gemelli, 8 - Rome, 00168 Italy
Phone: +393317880630
Email: camillo.fulchignoni@gmail.com