



HAL
open science

Surgical treatment of bone metastasis from osteophilic cancer. Results in 401 peripheral and spinal locations

Charlie Bouthors, Pierre Laumonerie, Vincent Crenn, Solène Prost, Benjamin Blondel, Stéphane Fuentes, Charles Court, Christian Mazel, Yann-Philippe Charles, Frédéric Sailhan, et al.

► To cite this version:

Charlie Bouthors, Pierre Laumonerie, Vincent Crenn, Solène Prost, Benjamin Blondel, et al.. Surgical treatment of bone metastasis from osteophilic cancer. Results in 401 peripheral and spinal locations. Orthopaedics & Traumatology: Surgery & Research, 2021, pp.103193. 10.1016/j.otsr.2021.103193 . hal-03574849

HAL Id: hal-03574849

<https://amu.hal.science/hal-03574849>

Submitted on 22 Jul 2024

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Distributed under a Creative Commons Attribution - NonCommercial 4.0 International License

Surgical treatment of bone metastasis from osteophilic cancer. Results in 401 peripheral and spinal locations.¹

Charlie **Bouthors**^a, Pierre **Laumonerie**^b, Vincent **Crenn**^c, Solène **Prost**^d, Benjamin
Blondel^d, Stéphane **Fuentes**^d, Charles **Court**^a, Christian **Mazel**^e, Yann-Philippe **Charles**^f,
Frédéric **Sailhan**^g, Paul **Bonnevialle**^h and the members of the SoFCOTⁱ¹

^a Université Paris-Saclay, Assistance Publique Hôpitaux de Paris, Hôpital Bicêtre, Service de
Chirurgie Orthopédique et Traumatologique, 78 Rue du Général Leclerc, 94270 Le Kremlin
Bicêtre, France

^b Département de Chirurgie Orthopédique, Hôpital Pellegrin, Place Amélie Raba Léon, 33000
Bordeaux, France

^c Clinique Chirurgicale Orthopédique et Traumatologique, CHU de Nantes, Hôtel-Dieu, Place
A. Ricordeau, 44093 Nantes Cedex, France.

^d Service de Neurochirurgie, Hôpital de la Timone, 264 Rue Saint Pierre, 13005 Marseille,
France.

^e Département de Chirurgie Orthopédique, Institut Montsouris, 42 Boulevard Jourdan, 75014
Paris, France

^f Service de Chirurgie du Rachis. Hôpital de Hautepierre, Avenue Molière, 67200 Strasbourg,
France

^g Service d'Orthopédie, Hôpital Cochin, 27 Rue du Faubourg Saint-Jacques, 75014 Paris,
France

¹ Article issued from a SOFCOT symposium

^h Département Universitaire d'Orthopédie Traumatologie, Hôpital Pierre Paul Riquet, Place Baylac, 31052 Toulouse Cedex, France

ⁱ Société Française de Chirurgie Orthopédique et Traumatologique, SOFCOT, 56 Rue Boissonade, 75014 Paris, France

* **Corresponding author:** Charlie Bouthors, Service de Chirurgie Orthopédique et Traumatologique et du Rachis, Hôpital Kremlin-Bicêtre, 78 Rue du Général Leclerc, 94270 Le Kremlin-Bicêtre, France
E-mail: charlie.bouthors@hotmail.fr

Abstract

Introduction

Peripheral and spinal bone metastases arise mainly from 5 osteophilic cancers: lung, prostate, kidney, breast and thyroid. Few studies combined results for the two types metastatic location (peripheral and spinal). Therefore we performed a multicenter retrospective study of surgically managed peripheral and spinal bone metastases to assess 1) global function at a minimum 1 year's follow-up and 2) factors affecting survival.

Hypothesis

Global function is improved by surgery, with acceptable survival.

Material and method

Between 2015 and 2016, 386 patients were operated on in 11 centers for 401 metastases: 231 peripheral, and 170 spinal. Mean age was 62.6 ± 12.5 years in the 212 female patients (54%) versus 66.4 ± 11.5 years in the 174 males (46%) ($p=0.001$). Pre- to postoperative comparison was made on pain on VAS (visual analog scale), WHO (World Health Organization) score, Karnofsky score, walking and global upper-limb function. Survival was estimated at 4 years' follow-up.

Results

The most frequent locations were in the femur ($n=146$, 36%) and thoracic spine ($n=107$, 27%). The primary cancer was revealed by the metastasis in 82 patients (21%). There were 55 general complications (14%) and 48 local complications (12%). Twenty-one patients (5.4%) died during the first month. VAS and Karnofsky scores improved: respectively, 6.6 ± 2.3 vs. 3.4 ± 2.1 ($p < 0.001$) and 65 ± 14 vs. 72 ± 20 ($p=0.01$). Walking, upper-limb function and Frankel grade improved in respectively 49/86 (57%), 19/29 (66%) and 31/84 (37%) patients. Median survival was 13.3 months (95% CI: 10.8-17.1), and was related to the primary (log-rank, $p < 0.001$): lung 6.5 months (95% CI: 5.2-8.9), prostate 11.1 months (95% CI: 5.3-43.6),

kidney 12.9 months (95% CI: 8.4-22.6), breast 26.5 months (95% CI: 19.0-34.0), and thyroid 49.0 months (95% CI: 12.2-NA). On multivariate analysis, independent factors for death comprised internal fixation rather than prosthesis (OR=2.20; 95% CI: 1.59-3.04 (p<0.001)), high preoperative ASA score (OR=1.78; 95% CI: 1.40-2.28 (p<0.001)), preoperative chemotherapy (OR=1.26; 95% CI: 1.13-1.41 (p<0.001)) and major visceral metastasis (lung, brain, liver) (OR=11.80; 95% CI: 5.21-26.71 (p<0.001)).

Conclusion.

Although function improved only slightly, pain relief and maintained autonomy suggest enhanced comfort in life, confirming the study hypothesis only partially. Factors affecting survival and clinical results argue for preventive surgery when possible, before general health status deteriorates.

Level of evidence: IV; retrospective observational

Key-words: Bone metastasis; Pathological fracture; Survival; Surgery; Osteophilic cancer

1. Introduction

Bone metastases often arise from osteophilic cancers, of the breast, kidney, lung, prostate or thyroid. Locations are commonly classified as peripheral (PBM) for the appendicular skeleton and spinal (SBM) for the axial skeleton. Bone metastasis, whether asymptomatic or inducing clinical events, is a stage of progression requiring multidisciplinary management [1–3].

With the exception of Bauer and Wedin [4] and Nathan et al. [5], overall postoperative function has not been studied in both locations together, due to surgical specialization. Few studies focused on factors for survival after bone metastasis surgery in the two locations. Oncologically, however, recruitment in both is identical, and the final objective in both cases is to improve quality of life [6–10]. We therefore performed a large-scale retrospective multicenter study of patients undergoing surgery for peripheral and spinal bone metastasis, to assess 1) global function at 1 year's follow-up, and 2) factors affecting survival. The study hypothesis was that global function is improved by surgery, with acceptable survival.

2. Material and Method

2.1. Data collection and inclusion criteria

Between December 2015 and December 2016, 11 university hospitals consecutively included 231 cases of PBM and 170 of SBM arising exclusively from the five osteophilic cancers and treated by first-line surgery. Seven centers (63%) had dedicated bone metastasis multidisciplinary team meetings. Revision surgeries were excluded. Data input was on-line (Calimed Santé, Marseille, France). Clinical assessments were performed successively for at

least 1 year. Survival was estimated between October 2020 and May 2021. Fourteen patients lost to follow-up were considered deceased at last follow-up.

2.2 Series data

The series included 386 patients (212 female (55%) and 174 male (45%)) with 401 operated sites (231 PBM, 170 SBM). Fourteen patients underwent surgery at several sites in the same year: 10 for 2 PBMs, 3 for 1 PBM and 1 SBM, and 1 for 3 PBMs. Mean age was 62.6 ± 12.5 years (range, 34-94 years) in females, versus 66.4 ± 11.6 years (range, 34-92 years) in males ($p=0.001$). Table 1 shows epidemiological characteristics according to primary.

The most frequent sites were the femur and thoracic vertebrae (Table 2). The metastasis revealed the primary in 82 patients (21%): 42 SBM and 40 PBM. Surgery was indicated for pathologic fracture in 177 sites (44%) for 172 patients (45%). There was synchronous visceral metastasis in 185 patients (48%), including 39 (10%) with at least 2 major visceral metastases (lung, liver, brain) and 167 (43%) with other bone metastases; 97 patients (25%) had visceral and multi-bone metastatic disease. Table 3 shows metastatic disease according to primary tumor.

2.3 Assessment criteria and results

Global assessment on American Society of Anesthesiologists (ASA) score [11], visual analog scale (VAS) [12], World Health Organization (WHO) score [13] and Karnofsky score [14] was performed preoperatively, at discharge, at 6 months and at a minimum 1 year's final follow-up. Specific assessment according to type of metastasis was performed preoperatively and at a minimum 1 year's follow-up. In cases of lower-limb metastasis, walking was categorized in 5 levels as impossible, possible with 2 crutches or a frame, possible with 1 crutch, unassisted but impaired, and normal. SBM patients were classified on neurologic grade Frankel [15]. Upper-limb outcomes were classified by limb use as impossible, possible with the help of the contralateral limb, limited by fatigue, or normal.

2.4. Surgical techniques

Preoperative radiotherapy was implemented in 48 sites (16 SBM, 32 PBM), and first-line cementoplasty in 14 (9 SBM, 5 PBM). Preoperative systemic treatment was administered in 224 patients (58%): standard chemotherapy in 105 cases (27%), hormone therapy in 74 (19%), immune or targeted therapy in 42 (11%), and radioactive iodine in 3 (0.8%). Surgery was indicated in a multidisciplinary team meeting for 250 patients (65%). Twelve PBM and 3 SBM sites underwent preventive embolization. Oncologic resection was performed in 18 sites (5%): 9 SBM and 9 PBM.

2.4.1 Spinal locations

Twenty-five SBMs (15%) were treated by stabilization by cementoplasty and/or internal fixation without decompression, 10 (11%) by laminectomy without internal fixation, 84 (49%) by laminectomy with internal fixation, and 42 (25%) by circumferential decompression (spondylectomy, laminectomy and anterior corpectomy, partial vertebrectomy).

2.4.2 Peripheral locations

Surgery comprised 88 arthroplasties (77 hip, 6 knee, 4 shoulder, 1 elbow), 115 intramedullary nailings (78 femur, 32 humerus, 1 tibia), 23 screw plates with cementoplasty (9 femur, 6 humerus, 5 tibia, 2 forearm) and 3 multiple pinnings (2 humerus, 1 radius). Resection without reconstruction was performed in two femoral necks, 2 scapulae and 1 iliac wing.

2.5. Statistics

Descriptive analysis used R software, version 3.3.2 (R Core Team, Vienna, Austria): mean and standard deviation for continuous variables, number and percentage for categorical variables. The Student or Wilcoxon rank sum test and χ^2 or Fisher exact test were used to compare continuous and categorical variables, respectively. Survival was analyzed on Kaplan-Meier estimation and compared according to etiology on log-rank test. The individual effects of epidemiological variables and initial WHO, ASA, Frankel, Karnofsky and VAS scores on

final scores, loss of walking autonomy and early death were analyzed on multivariate logistic regression and odds ratio (OR) with 95% confidence intervals (95% CI). Loss to follow-up counted as death at last follow-up. Missing data were imputed by combined additive regression, bootstrap and mean values predicted by matching. The significance threshold was set at $p < 0.05$.

3. Results

3.1. Clinical results

3.1.1 Global results

Pain on VAS (rated out of 10) decreased significantly between preoperative and final values, from 6.6 ± 2.3 to 3.4 ± 2.1 ($p < 0.001$) (Table 4), and at discharge (4.2 ± 2.1 ; $p = 0.001$) and at 6 months (3.6 ± 2.1 ($p = 0.01$)). Independent factors for worsened final pain comprised other bone metastases (OR=1.53; 95% CI: 1.02-2.30 ($p = 0.04$)), poor preoperative Frankel neurologic grade (OR=1.24; 95% CI: 1.02-1.50 ($p = 0.03$)), and internal fixation rather than arthroplasty (OR=3.65; 95% CI: 2.22-6.00 ($p < 0.001$)).

Karnofsky score increased from 65 ± 14 to 72 ± 15 ($p = 0.01$) at 6 months and 72 ± 20 ($p = 0.01$) at last follow-up (Table 4). Independent factors for worsened final Karnofsky score comprised poor preoperative WHO score (OR=1.38; 95% CI: 1.06-1.78 ($p = 0.014$)) and poor preoperative Frankel neurologic grade (OR=1.36; 95% CI: 1.10-1.68 ($p = 0.004$)).

Final WHO score did not differ from the preoperative value (Table 4). Independent factors for deterioration, however, comprised high preoperative ASA score (OR=1.32; 95% CI: 1.23-1.94 ($p < 0.001$)), visceral metastasis (OR=2.83; 95% CI: 1.82-4.40 ($p < 0.001$)) or other bone metastasis (OR=1.36; 95% CI: 1.00-1.84 ($p = 0.048$)), and poor preoperative Frankel neurologic grade (OR=1.27; 95% CI: 1.06-1.53 ($p = 0.01$)).

3.1.2. Specific clinical results

Preoperatively, in patients with lower-limb involvement (n=171), walking was impossible for 44 (26%), possible with 2 crutches or a frame for 47 (28%), possible with 1 crutch for 35 (24%), possible without assistance but impaired for 31 (18%), and normal for 14 (8%). In upper-limb involvement (n=46), limb use was impossible in 30 (65%) sites, possible with contralateral help in 7 (15%), limited by fatigue in 6 (13%), and normal in 3 (7%). Frankel grade in SBM (n=169) was A in 18 cases (11%), B in 62 (37%), C in 89 (53%), D in 8 (5%) and E in 10 (6%).

In patients with >1 year's survival, walking, upper-limb function and Frankel grade improved in respectively 49/86 (57%), 19/29 (66%) and 31/84 (37%) of cases (Table 5). Independent factors for deterioration in walking comprised oncologic resection (OR=5.74; 95% CI: 3.02-10.90 (p<0.001)), internal fixation rather than arthroplasty (OR=3.65; 95% CI: 2.49-5.34 (p<0.001)), high preoperative ASA score (OR=1.33; 95% CI: 1.05-1.69 (p=0.018)), and visceral metastasis (OR=1.57; 95% CI: 1.12-2.21 (p=0.008)). Independent factors for deterioration in Frankel grade comprised radiotherapy (OR=2.98; 95% CI: 1.4-6.3 (p<0.001)), and poor preoperative Frankel neurologic grade (OR=3.95; 95% CI: 2.7-5.7 (p<0.001)).

3. 2. Postoperative complications

The 48 local complications (12%) comprised 20 surgery site infections (12 SBM, 8 PBM), 8 epidural hematomas, 8 hardware failures (3 femoral with 1 nail, 1 prosthesis and 1 screw plate; 1 humeral with nail; and 4 spinal), and 12 other. They required 37 revision surgeries: 20 for hardware, 12 for lavage, and 5 for hematoma. Factors for surgical site infection comprised high preoperative ASA score (OR=1.66; 95% CI: 1.11-2.50 (p=0.014)), preoperative radiotherapy (OR=2.39; 95% CI: 1.12-5.07 (p=0.02)), major visceral metastasis (OR=3.57; 95% CI: 1.68-7.59 (p<0.001)), and poor preoperative Frankel neurologic grade (OR=1.96; 95% CI: 1.51-2.55 (p<0.001)).

There were 55 general complications (14%): 21 hemorrhages requiring transfusion, 9 deep venous thromboses, 9 cases of pneumonia, 8 urinary infections, and 8 other.

3.3. Early death

Twenty-one patients (5.4%) died within a month: 11 with lung cancer (10% of cases with this etiology), 3 with prostate cancer (8%), 4 with breast cancer (3%), 2 with kidney cancer (3%) and 1 with thyroid cancer (8%). On multivariate analysis (Table 6) independent factors for early death comprised high preoperative WHO score (OR=1.50; 95% CI: 1.25-1.80 (p<0.001)), high preoperative ASA score (OR=1.40; 95% CI: 1.11-1.77 (p=0.004)), low preoperative Karnofsky score (OR=0.98; 95% CI: 0.97-0.99 (p=0.02)), preoperative chemotherapy (OR=1.13; 95% CI: 1.02-1.24 (p=0.02)), and visceral metastasis (OR=2.95; 95% CI: 2.08-4.18 (p<0.001)).

3.4. Survival

One-year survival was 52% overall (201/386): 55% (93/170) in SBM, 47% (108/231) in PBM, 63% (82/131) in case of single bone metastasis without visceral metastasis, 44% (39/88) with visceral metastasis, and 61% (43/70) in multiple bone metastasis without visceral metastasis and 38% (37/97) with. An update at 4 years postoperatively found 63 patients (16.3%) still alive: 4 thyroid cancers (33% of this etiology), 33 breast cancers (23%), 13 kidney cancers (15%), 6 prostate cancers (15%) and 8 lung cancers (8%).

Median overall survival was 13.3 months (95% CI: 10.8-17.1), with significant differences according to primary (log-rank, p<0.001): lung 6.5 months (95% CI: 5.2-8.9), prostate 11.1 months (95% CI: 5.3-43.6), kidney 12.9 months (95% CI: 8.4-22.6), breast 26.5 months (95% CI: 19.1-34.0), thyroid 49.0 months (95% CI: 12.2-non-applicable) (Figure 1). There was no significant difference between SBM and PBM: respectively 13.3 months (95% CI: 10.8-18.1) and 12.7 months (95% CI: 7.9-17.1) (log-rank, p=0.41). Median survival was 26.4

months (95% CI: 18.3-35.7) in single bone metastasis versus 11.0 months (95% CI: 8.43-14.5) in multiple bone metastasis (log-rank, $p<0.001$), and 18.0 months (95% CI: 14.7-24.0) without visceral metastasis versus 7.9 months (95% CI: 6.1-11.0) with (log-rank, $p=0.003$). Patients discussed in a multidisciplinary team meeting showed median survival of 15.0 months (95% CI: 11.1-18.1) versus 11.5 months (95% CI: 7.4-17.4) otherwise (log-rank, $p=0.6$). On multivariate analysis, independent factors for death comprised internal fixation rather than arthroplasty (OR=2.20; 95% CI: 1.59-3.04 ($p<0.001$)), high preoperative ASA score (OR=1.78; 95% CI: 1.40-2.28 ($p<0.001$)), preoperative chemotherapy (OR=1.26; 95% CI: 1.13-1.41 ($p<0.001$)), and major visceral metastasis (lung, brain, liver) (OR=11.80; 95% CI: 5.21-26.71 ($p<0.001$)). Pathologic fracture was protective (OR=0.52; 95% CI: 0.37-0.72 ($p<0.001$)) and metastases revealing the primary showed a trend toward protection (OR=0.65; 95% CI: 0.41-1.05 ($p=0.07$)).

4. Discussion

The present retrospective study reports results in a multicenter cohort of 386 patients operated on in 2015 and 2016 for bone metastasis of osteophilic cancer. Its originality lies in reporting both peripheral ($n=231$) and spinal ($n=170$) bone metastases, which are usually dealt with separately, at long follow-up. The main findings were: a postoperative analgesic effect, conserving acceptable function, with relatively short survival depending on the type of primary and preoperative clinical status, independently of the metastasis site. Quantitatively, survival after metastasis of osteophilic cancer ranged between 1 and 4 years, except for lung cancer, where it was 6 months.

Most studies [4–10] reported peri-operative complications, with 6-12 months' survival, but failed to report precise clinical results, hindering comparison with the present study. The present study focused on objective clinical results, with global scores and specific

assessment: walking, upper-limb function, and Frankel score. In patients surviving beyond 1 year, general clinical status mostly stabilized or improved, in 69% according to WHO score and in 78% according to Karnofsky score. Analgesic effect was even more satisfactory, with improved VAS ratings in 79% of patients. Improvement in functional indices was less marked: walking improved in 57% of cases beyond 1 year and upper-limb function in 66%. Neurologic recovery was the least satisfactory criterion, with improvement in Frankel score in only 37% of patients. In many cases, clinical assessment was performed near the limit of the survival expected for the type of cancer, and general health status may have ineluctably deteriorated under the effect of metastatic spread, impairing scores without really expressing the clinical benefit of surgery [4,5].

Functional outcome on ASA and WHO scores depended on general preoperative status, as seen in the analysis of factors for deteriorated Karnofsky score. Poor ASA score was also associated with impairment in walking on final assessment (OR=1.33 (p=0.02)). The fact that oncologic resection was a factor for impairment of walking (OR=5.74 (p<0.001)) may be partly explained by the 50% of SBM cases treated by en-bloc vertebrectomy in this subgroup. The rates of initial neurologic disorder and of improvement agreed with the literature [2,16,17]. As also shown in many studies [17–19], poor preoperative neurologic status was of poor prognosis for neurological recovery (OR=3.95 (p<0.001)). These results indicate the importance of preventive treatment by stabilization and/or decompression before general and functional status is jeopardized by the progression of the cancer.

The main postoperative complication was surgery-site infection (5%). The literature reports rates of 5.8-12.9% for bone metastasis in the limbs [20–22] and of 5.1-25% in the spine [2,19,23,24]. Preoperative radiotherapy in the site increased infection risk 2.39-fold (p=0.023). Frail patients or those with visceral metastases also showed higher risk. Other

possible factors, such as body-mass index, smoking or blood loss, were not studied here, but have been implicated in other reports [24].

Median survival in the cohort was 13.3 months, and closely bound to primary type, in agreement with the literature [22], lung cancer showing by far the poorest prognosis (median, 6.5 months). Whether the metastasis was peripheral or spinal did not affect survival. It was however significantly impaired by multiple bone metastasis (median, 11.0 months) or visceral metastasis (18.0 months). Prognosis was also poorer in case of internal fixation rather than arthroplasty, although there may have been selection bias here as less invasive treatment was probably preferred in frailer patients.

Surprisingly, pathologic fracture was not associated with poorer prognosis, despite being reputed to having adverse impact on overall survival [1,4,6,8,10,17,18]. Although fracture risk is difficult to estimate [25], indications for preventive surgery need to be discussed in the multidisciplinary team meeting [26].

Death within 1 month suggests the surgical indication might not have been appropriate (wrong indication, major surgery in a frail patient,...). The rate is little studied in the literature, but in the present series was 5.4%, particularly concerning prostate and lung primaries. Tsuda et al. [27] reported 2.6% mortality at 30 days in 1,496 patients operated on for pathologic femoral fracture in a context of bone metastasis. In the present series, early death was significantly related to general preoperative health status on ASA, WHO and Karnofsky scores and to visceral metastasis. These factors related to the patient and the disease led to proposals in the multidisciplinary team meeting that improved survival in the present series. However, improvement was just a matter of a few months, and only slightly more than half the present centers had multidisciplinary team meetings.

The present study had several limitations. 1) It was an observational study, and surgical results were not compared versus non-operative treatment. Surgery may have been

indicated for patients with better prognosis, introducing a selection bias. 2) Analysis of surgical results was limited by not assessing self-reported quality of life. On the other hand, pain, function and autonomy were assessed on scores recognized in medical and surgical oncology. 3) The multicenter design introduced variations in indications and systemic treatment, and a large number of surgeons were involved. 4) In interpreting the results, it should be borne in mind that the alpha risk was increased by the multiple statistical tests used for subgroup analysis. There may also have been an estimation bias due to missing data and loss to follow-up; patients lost to follow-up were treated as deceased at last follow-up so as not to overestimate survival. However, despite these limitations, the study gives a good picture of the surgical management of bone metastases in France.

5. Conclusion

Surgical treatment of bone metastasis procured slight clinical improvement at a minimum 1 year's follow-up. The factors identified for early death, survival and satisfactory clinical results argue for early preventive surgery well before cancer progression undermines general health status. The choice and heaviness of the surgical technique should be discussed with the anesthesia and medical and surgical oncology teams in a comprehensive care project. It is also the role of the dedicated multidisciplinary team meeting to determine optimal surgical indications, notably preventive and oncologic.

Disclosure of interest

C Bouthors received training and transport subsidies from Johnson & Johnson, LDR Medical and Depuy Synthes, outside of the present study.

P Laumonerie received training and transport subsidies from Adler Ortho France, Arthrex SAS and Omnis Medica, outside of the present study.

V Crenn received subsidies from Ostium group and Iceram and non-financial support from Stryker, outside of the present study.

S Prost received training and transport subsidies from Zimmer and Stryker, outside of the present study.

P Bonneville is an associate editor for Orthopaedics & Traumatology: Surgery & Research. Outside of the present study, he is an education and clinical research consultant for Stryker and Zimmer-Biomet.

F Sailhan is a training consultant for Sanofi, Médacta and Branchet, outside of the present study.

C Courtis a shareholder in NeuroFrance (Spine) and teaching consultant for AO Spine

S Fuentes is a consultant for Medicea, Medtronic, Stryker, Eurospine and Safe Orthopedic

S Blondel is an associate editor for Orthopaedics & Traumatology: Surgery & Research and a research and teaching consultant for Medicea, Vexim-Stryker and 3M, research consultant for Implanet, and teaching consultant for Spineart, Depuys-Synthes and Johnson & Johnson.

Y-P Charles is a consultant for Ceraver, Stryker and Clariance.

C Mazel receives fees from Clariance, Medtronic, Zimmer Biomet and Johnson & Johnson; he is a member of AO Spine (Trustee), Chairman of the Fracture Tumor Deformity Technical Committee of AO Spine, and he undertakes research with AO Spine and ICOTEC, for which he receives per diem compensation.

Funding

The SoFCOT undertook online data entry on the software provided by Calimed.

Author contributions

C Bouthors and P Bonneville collated files and wrote the article.

P Laumonerie performed the statistical analyses and re-edited the article. F Sailhan collated files and re-edited the article. V Crenn, S Prost, B Blondel, S Fuentes, C Court, C Mazel, and Y-P Charles collated files

References

- [1] Errani C, Mavrogenis AF, Cevolani L, Spinelli S, Piccioli A, Maccauro G, et al. Treatment for long bone metastases based on a systematic literature review. *Eur J Orthop Surg Traumatol Orthop Traumatol* 2017;27:205–11. <https://doi.org/10.1007/s00590-016-1857-9>.
- [2] Sailhan F, Prost S, Zairi F, Gille O, Pascal-Mousselard H, Bennis S, et al. Retrospective multicenter study by the French Spine Society of surgical treatment for spinal metastasis in France. *Orthop Traumatol Surg Res* 2018;104:589–95. <https://doi.org/10.1016/j.otsr.2018.06.006>.
- [3] Bonneville P, Baron-Trocellier T, Niglis L, Ghazi A, Descamps J, Lebaron M, et al. Functional results and survival after surgery for peripheral skeletal metastasis: A 434-case multicenter retrospective series. *Orthop Traumatol Surg Res* 2020;106:997–1003. <https://doi.org/10.1016/j.otsr.2019.10.024>.
- [4] Bauer HC, Wedin R. Survival after surgery for spinal and extremity metastases. Prognostication in 241 patients. *Acta Orthop Scand* 1995;66:143–6. <https://doi.org/10.3109/17453679508995508>.
- [5] Nathan SS, Healey JH, Mellano D, Hoang B, Lewis I, Morris CD, et al. Survival in patients operated on for pathologic fracture: implications for end-of-life orthopedic care. *J Clin Oncol* 2005;23:6072–82. <https://doi.org/10.1200/JCO.2005.08.104>.
- [6] Weiss RJ, Tullberg E, Forsberg JA, Bauer HC, Wedin R. Skeletal metastases in 301 breast cancer patients: patient survival and complications after surgery. *Breast Edinb Scotl* 2014;23:286–90. <https://doi.org/10.1016/j.breast.2014.02.012>.
- [7] Weiss RJ, Forsberg JA, Wedin R. Surgery of skeletal metastases in 306 patients with prostate cancer. *Acta Orthop* 2012;83:74–9. <https://doi.org/10.3109/17453674.2011.645197>.
- [8] Weiss RJ, Wedin R. Surgery for skeletal metastases in lung cancer. *Acta Orthop*

2011;82:96–101. <https://doi.org/10.3109/17453674.2011.552779>.

[9] Higuchi T, Yamamoto N, Hayashi K, Takeuchi A, Abe K, Taniguchi Y, et al. Long-term patient survival after the surgical treatment of bone and soft-tissue metastases from renal cell carcinoma. *Bone Joint J* 2018;100:1241–8. <https://doi.org/10.1302/0301-620X.100B9.BJJ-2017-1163.R3>.

[10] Nakayama R, Horiuchi K, Susa M, Watanabe I, Watanabe K, Tsuji T, et al. Clinical outcome after bone metastasis (BM) surgery in patients with differentiated thyroid carcinoma (DTC): a retrospective study of 40 cases. *Jpn J Clin Oncol* 2014;44:918–25. <https://doi.org/10.1093/jjco/hyu099>.

[11] Doyle DJ, Garmon EH. American Society of Anesthesiologists Classification (ASA Class). StatPearls, Treasure Island (FL): StatPearls Publishing; 2018.

[12] Collins SL, Moore RA, McQuay HJ. The visual analogue pain intensity scale: what is moderate pain in millimetres? *Pain* 1997;72:95–7.

[13] Conill C, Verger E, Salamero M. Performance status assessment in cancer patients. *Cancer* 1990;65:1864–6. [https://doi.org/10.1002/1097-0142\(19900415\)65:8<1864::aid-cncr2820650832>3.0.co;2-u](https://doi.org/10.1002/1097-0142(19900415)65:8<1864::aid-cncr2820650832>3.0.co;2-u).

[14] Yates JW, Chalmer B, McKegney FP. Evaluation of patients with advanced cancer using the Karnofsky performance status. *Cancer* 1980;45:2220–4.

[15] Frankel HL. Ascending cord lesion in the early stages following spinal injury. *Paraplegia* 1969;7:111–8. <https://doi.org/10.1038/sc.1969.21>.

[16] Jansson KA, Bauer HCF. Survival, complications and outcome in 282 patients operated for neurological deficit due to thoracic or lumbar spinal metastases. *Eur Spine J Off* 2006;15:196–202. <https://doi.org/10.1007/s00586-004-0870-6>.

[17] Moon KY, Chung CK, Jahng TA, Kim HJ, Kim CH. Postoperative survival and ambulatory outcome in metastatic spinal tumors : prognostic factor analysis. *J Korean*

Neurosurg Soc 2011;50:216–23. <https://doi.org/10.3340/jkns.2011.50.3.216>.

[18] Quraishi NA, Rajagopal TS, Manoharan SR, Elsayed S, Edwards KL, Boszczyk BM. Effect of timing of surgery on neurological outcome and survival in metastatic spinal cord compression. *Eur Spine J* 2013;22:1383–8. <https://doi.org/10.1007/s00586-012-2635-y>.

[19] Fehlings MG, Nater A, Tetreault L, Kopjar B, Arnold P, Dekutoski M, et al. Survival and Clinical Outcomes in Surgically Treated Patients With Metastatic Epidural Spinal Cord Compression: Results of the Prospective Multicenter AOSpine Study. *J Clin Oncol* 2016;34:268–76. <https://doi.org/10.1200/JCO.2015.61.9338>.

[20] Ratasvuori M, Wedin R, Keller J, Nottrott M, Zaikova O, Bergh P, et al. Insight opinion to surgically treated metastatic bone disease: Scandinavian Sarcoma Group Skeletal Metastasis Registry report of 1195 operated skeletal metastasis. *Surg Oncol* 2013;22:132–8. <https://doi.org/10.1016/j.suronc.2013.02.008>.

[21] Mavrogenis AF, Pala E, Romagnoli C, Romantini M, Calabro T, Ruggieri P. Survival analysis of patients with femoral metastases. *J Surg Oncol* 2012;105:135–41. <https://doi.org/10.1002/jso.22061>.

[22] Hara H, Sakai Y, Kawamoto T, Fukase N, Kawakami Y, Takemori T, et al. Surgical outcomes of metastatic bone tumors in the extremities (Surgical outcomes of bone metastases). *J Bone Oncol* 2021;27:100352. <https://doi.org/10.1016/j.jbo.2021.100352>.

[23] Vanek P, Bradac O, Trebicky F, Saur K, de Lacy P, Benes V. Influence of the Preoperative Neurological Status on Survival After the Surgical Treatment of Symptomatic Spinal Metastases With Spinal Cord Compression. *Spine* 2015;40:1824–30. <https://doi.org/10.1097/BRS.0000000000001141>.

[24] Sebaaly A, Shedid D, Boubez G, Zairi F, Kanhonou M, Yuh S-J, et al. Surgical site infection in spinal metastasis: incidence and risk factors. *Spine* 2018;18:1382–7. <https://doi.org/10.1016/j.spinee.2018.01.002>.

[25] Crenn V, Carlier C, Gouin F, Sailhan F, Bonneville P, members of the So.F.C.O.T.

High rate of fracture in long-bone metastasis: Proposal for an improved Mirels predictive score. *Orthop Traumatol Surg Res* 2020;106:1005–11.

<https://doi.org/10.1016/j.otsr.2020.03.034>.

[26] Anract P, Biau D, Boudou-Rouquette P. Metastatic fractures of long limb bones.

Orthop Traumatol Surg Res 2017;103:S41–51. <https://doi.org/10.1016/j.otsr.2016.11.001>.

[27] Tsuda Y, Yasunaga H, Horiguchi H, Fushimi K, Kawano H, Tanaka S. Complications and Postoperative Mortality Rate After Surgery for Pathological Femur Fracture Related to Bone Metastasis: Analysis of a Nationwide Database. *Ann Surg Oncol* 2016;23:801–10.

<https://doi.org/10.1245/s10434-015-4881-9>.

Table 1. Epidemiological data for the 386 patients operated on at 401 sites of bone metastasis from the 5 osteophilic forms of cancer

Primary N (%)	Sex ratio N (%)	Age (mean±standard deviation)	Number of sites N (%)	Peripheral/spinal location N (%)
Breast 141 (37)	F= 136 (96) M= 5 (4)	61.2 ±12.6 (34-88)	145 (36)	P=88 (61) S=57 (39)
Lung 114 (30)	F= 39 (35) M= 75 (66)	64.8 ±11.1 (38-92)	120 (30)	P=71 (59) S=49 (41)
Kidney 80 (21)	F= 28 (35) M= 52 (65)	65.1 ±12 (34-86)	84 (21)	P=49 (58) S=35 (42)
Prostate 39 (10)	F= N-A M =39 (100)	70.8 ±10.9 (45-87)	40 (10)	P=19 (48) S=21 (52)
Thyroid 12 (3)	F= 9 (75) M= 3 (25)	69.9 ±14 (47-94)	12 (3)	P= 4 (33) S= 8 (77)
F: female; M: male; P: peripheral; S: spinal N-A: non-applicable				

Table 2. Distribution of the 401 bone metastases: peripheral (n=231) and spinal (n=170)

Bone metastases (N=401)			
Peripheral		Spinal	
n=231 (%)		n=170 (%)	
Femur	146 (36)	Thoracic	107 (27)
Humerus	45 (11)	Lumbar	37 (9)
Acetabulum	27 (7)	Cervical	22 (5)
Tibia	6 (1.5)	Sacral	4 (1)
Forearm	3 (0.7)		
Scapula	2 (0.5)		
Pelvis	2 (0.5)		

Table 3. Preoperative clinical data in 386 patients operated on for 401 locations of bone metastasis from the 5 osteophilic cancers.

Type Of cancer N (%) (patients)	Single bone metastasis		Multiple bone metastasis		Pathologic fracture N (%)	Revelatory metastasis N (%)	ASA score [11]	VAS [12]	WH O score [13]	Karnofsk y score [14]
	With visceral metastasis N (%)	Without visceral metastasis N (%)	With visceral metastasis N (%)	Without visceral metastasis N (%)						
Cohort N=386	88 (23)	131 (34)	97 (25)	70 (18)	172 (45)	82 (21)	2.5 ±0.7	7.0 ±2.3	2.0 ±1.0	60 ±15
Breast 141 (37)	25 (18)	53 (36)	32 (23)	31 (22)	64 (45)	19 (13)	2.4 ±0.7	7.1 ±2	1.9 ±0.9	60 ±16
Lung 114 (30)	25 (22)	46 (40)	36 (32)	7 (6)	47 (41)	41 (36)	2.6 ±0.7	6.9 ±2.3	2.2 ±1.1	59 ±16
Kidney 80 (21)	29 (36)	19 (24)	19 (24)	13 (16)	36 (45)	10 (13)	2.5 ±0.7	7.0 ±2.4	2.0 ±1.0	61 ±14
Prostate 39 (10)	4 (10)	9 (23)	9 (23)	17 (44)	21 (54)	7 (18)	2.6 ±0.6	7.1 ±2.7	2.4 ±0.9	53 ±16
Thyroid 12 (3)	5 (42)	4 (33)	1 (8)	2 (17)	4 (33)	5 (42)	2.6 ±0.5	6.4 ±2.8	1.8 ±1.0	67 ±16

Qualitative variables reported as number (percentage); continuous variables reported as mean ± standard deviation
 ASA: American Society of Anesthesiologists; VAS: visual analog scale; WHO: World Health Organization

Table 4. Progression of general scores from preoperative assessment to last follow-up in

		VAS [12]				WHO score [13]			Karnofsky	
		Initial	6 months	Final	p	Initial	Final	p	Initial	6 months
		6.6 ±2.4	3.6 ±2.1	3.4 ±2.1	<0.001	1.8 ±0.9	1.9 ±1.1	0.5	65 ±14	72 ±15
Metastasis		6.9 ±2	3.9 ±2.6	3.7 ±2.1	<0.001	2.2 ±1.1	1.9 ±0.8	0.27	65 ±15	71 ±17
Metastasis		6.4 ±2.6	3.9 ±2.6	3.1 ±2.1	<0.001	1.8 ±1	1.6 ±0.8	0.3	66 ±13	71 ±16
Metastasis	Without visceral metastasis	6.6 ±2.3	3.5 ±2.1	3.4 ±2.2	<0.001	1.8 ±1.0	1.9 ±1.1	0.58	65 ±14	72 ±15
	With visceral metastasis	6.6 ±2.3	3.5 ±2.1	3.4 ±2.2	<0.001	1.7 ±1.0	1.9 ±1.0	0.89	64 ±14	72 ±15
Metastasis	Without visceral metastasis	6.6 ±2.3	3.6 ±2.1	3.4 ±2.2	<0.001	2.0 ±1.0	1.9 ±1.1	0.88	65 ±14	72 ±15
	With visceral metastasis	6.6 ±2.4	3.5 ±2.1	3.4 ±2.2	<0.001	2.0 ±1.0	1.9 ±1.1	0.08	64 ±14	72 ±15

n ± standard deviation. P value between initial and final values.

of Anesthesiologists, VAS: visual analog scale, WHO: World Health Organization. P-values in bold: significant difference

patients with ≥ 1 year's survival.

Table 5. Final progression of general scores and function in patients with ≥ 1 year's survival; Improvement, aggravation or stability are indicated as 1 point on VAS, 1 grade on WHO score, 10 points on Karnofsky score, 1 grade for walking and for upper-limb function, and 1 Frankel grade.

Evolution	VAS [12] n=208 (%)	WHO [13] n=189 (%)	Karnofsky [14] n=197 (%)	Walking n=86 (%)	Upper-limb function n=29 (%)	Frankel [15] n=84 (%)
Aggravation	26 (13)	59 (31)	43 (22)	23 (27)	1 (3)	12 (14)

Stability	17 (8)	77 (41)	59 (30)	14 (16)	9 (31)	41 (49)
Improvement	165 (79)	53 (28)	95 (48)	49 (57)	19 (66)	31 (37)
Data reported as number (percentage). ASA: American Society of Anesthesiologists; VAS: visual analog scale; WHO: World Health Organization.						

Table 6. Multivariate analysis of general risk factors for early death (<30 days).

Parameter	Odds Ratio (95% CI)	p
WHO score [13]	1.50 (1.25-1.80)	<0.001
ASA score [11]	1.40 (1.11-1.77)	0.004
Karnofsky score [14]	0.98 (0.97-0.99)	0.02
Discussion in MDT meeting	1.03 (0.74-1.44)	0.84
Preoperative chemotherapy	1.13 (1.02-1.24)	0.01
Multiple bone metastases	1.33 (0.97-1.83)	0.07
Visceral metastasis	2.95 (2.08-4.18)	<0.001

MDT: multidisciplinary team; ASA: American Society of Anesthesiologists; VAS: visual analog scale; WHO: World Health Organization. P-values in bold indicate significant difference

Figure legend

Figure 1. Survival curves (months) following Kaplan-Meier for patients operated on for bone metastasis from the 5 osteophilic cancers.

Survival probability

- Lung cancer
- Prostate cancer
- Thyroid cancer
- Kidney cancer
- Breast cancer

