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Survival and complications of skeletal reconstructions after surgical treatment of bony metastatic renal cell carcinoma

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Abstract

Improvements in survival for patients with renal cell carcinoma have resulted in an increase in the burden of disease due to skeletal metastases, which are often solitary and resistant to radiotherapy. Surgical intervention remains a valid treatment to improve function and relieve pain, and replacement is able to achieve this and improve disease free implant survival. The aim of this study was identify prognostic factors for reconstruction survival of skeletal metastases in renal cell carcinoma and to characterise the nature of the reconstruction related complications.

A retrospective analysis of all patients treated for metastatic renal cell carcinoma in three international bone tumour units between 2000 and 2014 identified 268 surgical interventions suitable for inclusion. Reconstruction survivorship was calculated using the Kaplan–Meier method whilst factors affecting reconstruction survival were assessed using Cox-regression multivariate analysis. Differences in proportions were assessed using Fisher's exact test.

The overall rate of complications was 17%, which were classified as structural failure (7.1%), infection (4.9%) and tumour progression (3.7%). Endoprosthetic replacement when performed as the primary procedure demonstrate the best survivorship whilst factors associated with compromised reconstruction survival included previous surgical intervention and pre operative radiotherapy, and intralesional resection margins.

We conclude that endoprosthetic replacement be considered as the index surgical intervention for skeletal metastases from renal cell carcinoma in certain locations as this carries the lowest incidence of complications. Revision of previous skeletal stabilisation, especially when combined with radiotherapy carries a high risk of complication, including infection, which often necessitates amputation.

Keywords: Skeletal metastases; Implant survival; Reconstruction; Complication; Renal cell carcinoma

Introduction

Renal cell carcinoma (RCC)[1] accounts for 5% of cancers in males and 3% in females, with an estimated incidence of 65,150 cases accounting for 13,680 deaths in the USA 2013.[2] Despite improvements in diagnosis, particularly cross sectional imaging, approximately 30% of patients with RCC have evidence of metastatic disease at presentation.[3] Common sites of metastatic disease in RCC are the lung (45%), bone (30%), lymph nodes (22%) and the liver (20%).[4] Skeletal metastases in RCC can be extremely debilitating, secondary to pain and skeletaly related events, including pathological fracture, hypercalcaemia, spinal

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cord compression and the subsequent need for orthopaedic surgical intervention.[5]

Treatment options for patients with disseminated RCC have previously been limited to immunotherapy or supportive care with a typical survival of 12 months from the development of metastases.[6] The development of targeted therapies using tyrosine kinase inhibitors have demonstrated improved overall survival benefits compared to immunomodulation therapies,[7] though their effect on long term disease free survival in the presence of bone or lung metastases is less apparent.[8]

It is expected that improvements in disease free survival, earlier diagnosis of RCC and improved survival with metastatic disease in RCC will result in an increased burden of disease from RCC with metastases to bone.[9] Surgical resection and reconstruction has a role in the management of metastatic disease in RCC. The destructive nature of the metastases results in a reduced load bearing capability in affected bones, with microfracture, pain and eventual pathological fracture at the site of the metastasis[10] with surgical intervention indicated for impending or existing fracture, or intractable pain.[11,12] Aggressive surgical intervention for solitary or multiple skeletal metastases with en bloc resection and reconstruction, has demonstrated an improved survival at both short and medium term.[13,14]

Whilst a number of studies have investigated the prognostic factors influencing patient survival following surgical intervention for skeletal metastases,[5,13,15–17] little attention has been given to the survival of the reconstructions and especially to the implants used for reconstruction following resection of these metastases. The aim of this study, therefore, was identify prognostic factors for reconstruction survival of skeletal metastases in RCC and to characterise the nature of the reconstruction related complications.

Patients and methods

Institutional ethical review boards approvals for the study were completed. Patients were identified from prospectively maintained databases at three institutions acting as referral bone tumour centres (Royal Orthopaedic Hospital, Birmingham, UK, Tampere University Hospital, Finland and Karolinska University Hospital, Stockholm, Sweden). All patients treated for non-spinal skeletal metastases from a RCC primary malignancy were identified between 1st January, 2000 and 31st July 2014. Details of patient demographics, including age at presentation, sex, site of metastases, pre operative radiotherapy and embolization, where indicated, surgical resection including margin of resection and method of reconstruction where recorded. To allow analysis of survivorship of the reconstruction, details of time to reconstruction revision for any cause or death were also recorded. To identify prognostic factors affecting reconstruction survival, the incidence of pathological fracture prior to reconstruction, periprosthetic fracture following reconstruction, post operative radiotherapy, and the mode of failure, according to the Henderson classification[18,19] were recorded. The primary outcome of the study was reconstruction survival with revision for any reason as the final end point. Secondary outcomes included postoperative complications.

Reconstruction, implant and patient survival were assessed using the Kaplan–Meier method using a log-rank test whilst Cox regression analysis was used to identify independent factors affecting implant and patient survival. Differences in proportions were assessed using Fisher's exact test. All analyses were completed using SPSS Statistics 20.0 (IBM, New York, US).

Results

Demographics

A total of 268 procedures were performed in 253 patients. The study population comprised 173 (65%) males and 95 (35%) females with a mean age at primary reconstruction of 64.2 years (median age 64.0, IQR 57.0–64.0). The mean lag time between diagnosis of the primary malignancy and diagnosis of skeletal metastases was 2.4 years (median lag time 0, IQR 0–3.0) and the mean lag time between diagnosis of skeletal metastases and reconstruction was 5.8 months (median lag time 1.0, IQR 0–3.8). Pathological fracture was the mode of presentation of the primary malignancy in 137 (51.0%) and was the presenting feature of skeletal metastases in 128 patients (47.8%). In 131 patients (48.9%), reconstruction was undertaken for impending fracture indicated by significant bone destruction, intractable pain and loss of function.

Skeletal metastases without any lung or extrarenal metastases were present in 149 patients (55.6%), where 104 patients (38.8.%) had solitary skeletal metastases and 45 patients (21.3%) multiple skeletal metastases, whilst 92 patients (34.3%) had synchronous metastases to bone and lung. 27 patients (10.1%) had disseminated metastases with multiple skeletal, pulmonary and extra renal metastases. Skeletal metastases were distributed as follows: lower extremity in 161 (60.1%) patients, comprising 140 femoral and 21 tibial lesions, pelvis in 35 (13.1%), and upper extremity in 72 (26.8%) patients, comprising 60 humeral, 7 radial or ulnar, 2 scapula and 3 clavicular lesion.

In the majority of cases, 238 (88.6%), no previous surgical intervention at the site of the skeletal metastasis had been performed. 30 patients (11.4%) had undergone operative intervention and this intervention comprised one uncemented hemiarthroplasty, one open reduction and plate osteosynthesis, and 28 intramedullary nailing procedures (22 femoral, 3 tibial and 3 humeral).

Pre operative radiotherapy had been administered prior to reconstruction in 50 patients (19.0%) whilst 63 patients (23.5%) received pre operative embolization. Post operative