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Massive endoprosthetic replacement for bone metastases resulting from renal cell carcinoma: Factors influencing patient survival

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Abstract

Background: Surgery remains the main treatment of bone metastases due to renal cell carcinoma (RCC). We reviewed 135 patients treated with resection and endoprosthetic replacement (EPR) and examined clinico-pathological factors predicting survival.
Methods: Surgical and oncological outcomes were examined using a prospectively maintained database between 1976 and 2012. Survival rates were calculated by Kaplan–Meier method. Multivariate analyses were performed to investigate factors predictive of increased survival.
Results: At diagnosis, 81 patients had synchronous RCC and bone metastases and the remaining developed metachronous metastases after primary treatment for RCC. The majority were solitary tumours (75%) and 77% had ≥ one concurrent visceral metastases. The median age at surgery was 61 years old (IQR 53–69). The median follow-up was 20 months (IQR 10–43) and the overall survival was 72% at one-year. This declined to 45% and 28% at three and five-years, respectively. After adjustments for prognostic factors, there was an increased risk of death in patients with multiple skeletal metastases (HR = 2), ≥one visceral metastases (HR = 3) and local recurrence (HR = 3) (all $p \leq 0.01$). Ten patients required revision (7%) and the risk of revision was 4% at one-year and remained low at 8% from two years postoperatively.
Conclusion: Patients with solitary bone lesions and no visceral metastases should be considered for bone resection and EPR. As survival beyond one-year can be expected in a majority of patients and the risk of further surgery after EPR is low, patients with multiple skeletal metastases and visceral metastases should also be considered.

Keywords: Renal cell carcinoma; Bone metastasis; Endoprosthetic replacement; Survival rate

Introduction

Bone metastases from renal cell carcinoma (RCC) are relatively resistant to radiotherapy and chemotherapy. Currently, surgery remains the preferred treatment to control these metastastic lesions. Surgical options include curettage and cementation, internal fixation or resection with reconstruction. In patients with osseous renal metastases, there is a particularly high failure rate after intralesional surgery due to local tumour progression. Despite adjuvant radiotherapy, it carries a high implant failure rate (23%) that necessitates further surgery.[1]

The resection of bone metastases and reconstruction with an endoprosthetic replacement (EPR) minimises these skeletal complications and the need for reoperation.[2] Studies have shown that the reoperation rate after resection and EPR (2–3%) is considerably lower than intra-lesional surgery (14–41%).[2,13] In particular with solitary lesions, resection and EPR achieves local tumour control that prolongs patient survival (median survival 35–45 months) in comparison to intra-lesional procedures (20–22 months).[1,3,13] Stabilisation of pathological fractures with an EPR furthermore allows immediate weight bearing, facilitates early resumption to mobility and improves the patient's quality of life.[4]

Several studies have evaluated the clinico-pathological factors predictive of patient survival after EPR for bone metastases due to RCC. In these studies, the median survival

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of patients with bone metastases from RCC has been reported between 20 and 45 months after surgery.[1,8,13] There is a consensus that the best prognostic factors are solitary bone lesions, the absence of visceral metastases and clear surgical margins. Some of these results, however, are unadjusted for other important prognostic variables and limit the clinical interpretation of their observed effects on survival.[1,5] Furthermore, the existing prognostic data is either only applicable to patients diagnosed with solitary bone lesions[6,7] or includes all patients treated by a variety of methods (e.g. curettage or nailing).[1,5,8,9]

In the present study, we reviewed our surgical experience exclusively on the use of massive EPR as the primary treatment for RCC bone metastases. Our purpose was to identify prognostic factors that affect patient survival.

Methods

Patients

Between August 1, 1976 and July 31, 2012, all patients treated with an EPR for metastatic bone tumours secondary to RCC were identified using an institutional prospectively maintained database. The study population was limited to patients who underwent an EPR as a primary procedure for treatment of their skeletal metastasis. Patients who had previously undergone previous internal fixation for pathological fracture were excluded ($n = 34$). One patient was excluded because of no follow-up data after the time of surgery.

After exclusion, the study therefore included 135 patients who were treated by an EPR. Patient demographics, tumour characteristics, operative details, radiographs, postoperative complications, additional procedures, and oncological outcomes were gathered for analysis. Research and ethics approval was obtained through the institution's review board.

Patients were followed up until July 31, 2012. The duration of follow-up was calculated from the date of their primary operation to the date of death or last known follow-up on our database. Deaths attributed to RCC were checked and confirmed through the United Kingdom Cancer Registry.

Preoperative investigations & diagnosis

All patients were investigated with CT, MRI and a bone scan to define the extent of the tumour and whether the metastasis was solitary or multiple. Staging CT studies were done to detect concurrent visceral involvement. All patients had blood tests including serum calcium to detect hypercalcaemia.

For the purposes of this study, multiple bone metastases were defined as the presence of at least two lesions in one or more skeletal sites. Bone metastases were furthermore classified as a synchronous onset when the diagnosis of RCC and bone metastases was made simultaneously. A metachronous onset was recorded in cases when the bone metastasis developed after treatment of the primary RCC. The definition of visceral metastases included lung, lymph nodes, any intra-abdominal organ, and brain.

In cases of a synchronous presentation, a biopsy was obtained to confirm the histological diagnosis. For those with an untreated primary tumour, referral to the urological multidisciplinary team was made for consideration of nephrectomy after EPR. All patients in this study who presented with a metachronous onset of bone metastases had a previous nephrectomy.

Surgery

Patients were offered bone resection and EPR following assessment by a multidisciplinary team. The indication for resection and EPR was for patients diagnosed with a solitary metastasis, or in patients with multiple metastases who had such extensive bone destruction that an EPR would likely give a better functional outcome than any other form of fixation.

In patients with a large soft tissue component, preoperative embolisation was used to diminish the vascularity of the procedure. All surgical procedures were conducted by one of the five senior authors and surgery was performed following oncological principles. An en-bloc resection was carried out, where possible, aiming to achieve a wide surgical margin including a layer of healthy tissue covering the tumour. The resected segment of bone was then replaced by either a cemented custom-made or modular endoprosthesis (Stanmore Implants, United Kingdom). At six weeks postoperatively, all patients underwent a standardised one-week regime of intensive inpatient physiotherapy.

Adjuvant therapies

Patients were referred to their local radiation oncologist for consideration of adjuvant radiotherapy to improve local control if there were contaminated margins on the final pathological specimen and no history of previous surgical or radiation treatment to the operated limb.

The use of adjuvant chemotherapy regimes, biological and multi-kinase inhibitor therapies for metastatic disease were in accordance to local protocols and best current practice at the time of treatment between 1976 and 2012.

Statistical analyses

Survival rates were calculated using the Kaplan–Meier method. The difference between groups with respect to death was assessed in a univariate manner using a log-rank test. A multivariate Cox proportional hazard model was employed to detect factors that increase the risk of death when adjusted for the joint effect of patient,