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Review

A systematic review of the role of hepatectomy in the management of metastatic renal cell carcinoma

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Abstract

Aim: This review sought to systematically appraise the literature to establish the role of hepatectomy in treating renal cell carcinoma hepatic metastases.
Method: Medline and EMBASE were systematically searched for papers reporting survival of patients who underwent hepatectomy for metastatic renal cell carcinoma.
Results: Six studies containing 140 patients were included. There were no randomised controlled trials. Perioperative mortality was 4.3%, with reported morbidity between 13 and 30%. Patients with metachronous presentation, and a greater time interval between resection of primary tumour and development of metachronous metastases, appeared to have better survival. There was no difference in survival between patients with solitary and multiple metastases.
Conclusion: Few patients with hepatic metastases from renal cell carcinoma are suitable for hepatectomy as metastatic disease is usually widespread. Selected patients may experience a survival benefit, but identifying these patients remains difficult.

Keywords: Renal cell carcinoma; Metastatic renal cell carcinoma; Hepatectomy

Introduction

While hepatectomy has been shown to provide a survival benefit in the treatment of metastatic disease from a variety of malignancies,[1,2] its role in the treatment of metastatic renal cell carcinoma is not clear. Renal cancer is the tenth commonest cancer worldwide and accounts for approximately 2% of all cancers diagnosed.[3] It is more common in developed countries and the incidence is rising.[3] Renal cell carcinoma accounts for approximately 90% of all renal malignancies.[4] At time of diagnosis, 25–30% of patients will have metastatic disease[5] and of those with localised disease, a further third will develop metastases after resection of the primary tumour.[6]

Treatment options for metastatic renal cancer are limited, with the British Association of Urological Surgeons guidelines recognising that there is currently no consensus on the optimal treatment strategy.[7] Renal cell carcinoma is generally resistant to chemotherapy.[8] There are a number of newer agents including immunotherapy agents and angiogenesis inhibitors which may have a role in the treatment of metastatic disease[7] although these agents generally have a low response rate.[9] The limited treatment options mean that prognosis in metastatic renal cell carcinoma is poor, with 5-year survival typically less than 10%.[10] The lungs are the commonest site of metastatic spread, accounting for 75% of cases of metastatic disease.[11] There is some evidence

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that resection of pulmonary metastases provides a survival benefit[12–14] and consideration of pulmonary resection for limited lung disease is currently recommended in British Association of Urological Surgeons guidelines. Guidelines issued by the European Association of Urology in 2014 concluded that "retrospective comparative studies consistently point towards a benefit of complete metastasectomy in metastatic renal cell carcinoma patients in terms of overall survival, cancer-specific survival and delay of systemic therapy" however they then stated that no general recommendations could be made due to the sparcity of strong evidence and that the decision to resect metastatic disease should be made on a case-by-case basis.[15]

The liver is involved in 20–40% of cases of metastatic renal cancer[11,16] usually as part of widespread dissemination. However, in 2–4% cases metastases are liver limited, and therefore may be amenable to surgical resection.[17] The evidence base supporting hepatectomy for metastatic renal cell carcinoma is limited. This study therefore sought to systematically evaluate the literature to offer guidance on the role of hepatectomy in patients with metastatic renal cell carcinoma.

Methods

Medline and EMBASE databases were searched on 01/07/13 and all reference from 1993 to this date were potentially eligible for inclusion. Searched terms used were "cancer OR malignant OR malignancy OR neoplasm OR neoplastic", "liver OR hepatic", "metastatic OR metastasis OR metastases OR secondary OR secondaries", "surgery OR resection OR hepatectomy OR hepatectomies OR segmentectomy OR segmentectomies OR metastasectomy OR metastasectomies" and "kidney OR renal".

Title search was conducted by a single author of all identified references, with those not relating to metastatic renal cell carcinoma excluded. Of the remaining references, abstracts were retrieved and independently assessed by two authors against inclusion/exclusion criteria. Of those abstracts considered eligible, full papers were obtained and underwent review by two authors independently against inclusion/exclusion criteria. Where discrepancies arose between two authors regarding inclusion, discussion between the authors was used to reach a consensus.

Inclusion criteria

- Paper presenting data on resected liver metastases from renal cell carcinoma
- Original data published (e.g. not review papers)
- Survival outcome available

Exclusion criteria

- Non-English language studies
- Full manuscript not available (e.g. abstracts presented at conference)
- Studies with less than ten patients
- Malignancy other than renal cell carcinoma
- Multiple papers published from same patient data set

Primary outcome was survival following hepatectomy; secondary outcomes included morbidity and mortality data and factors considered to be prognostic for survival, e.g. presentation of metastases (synchronous versus metachronous) or extent of metastases (solitary versus multiple metastases).

Results

The database searches returned 1729 citations. Fig. 1 shows how many of these were included/excluded at each stage of the search process. After inclusion and exclusion criteria were applied to identified abstracts, nine studies remained. Full papers of these were obtained. Two papers[11,18] contained data on the same series of patients. Alves et al.[18] was published in 2003 and included 14 patients with metastatic renal tumours (10 of which were renal cell carcinoma). Aloia et al.[11] was published in 2006 included 19 patients, 16 of whom had renal cell carcinoma. Despite Aloia et al.[11] being more recent and containing more patients, this was excluded as data on patients with renal cell carcinoma and patients whose tumours were of embryonal origin were included together in outcome data, which may have skewed results. Alves et al.[18] presented data for each of the fourteen patients individually, allowing data on only those patients with metastatic renal cell to be extracted and included in this review and so was included, despite being older and including fewer patients. Two further papers were excluded as they did not contain sufficient data; one reported on only two patients with hepatic metastases[19] and the other did not contain specific survival data on hepatic metastases of renal cell carcinoma origin.[20] Six studies[18,21–25] met the criteria for inclusion in this review and are summarised in Table 1. There were no randomised controlled trials. Two studies[22,25] presented data which were retrospectively collected from a prospectively maintained database, three studies[18,21,23] presented data which were retrospectively collected and one study[24] did not state the method of data collection.

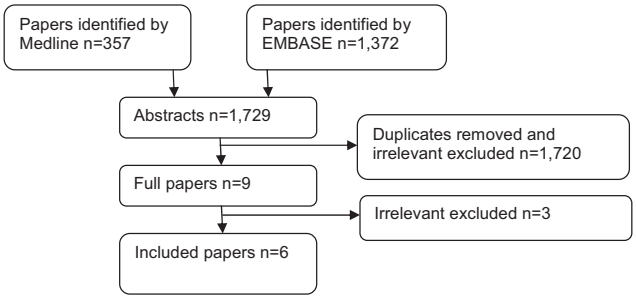

Figure 1. Diagram showing how many citations were included/excluded at each stage.