



Original research

Retrospective analysis of survival after resection of pancreatic renal cell carcinoma metastases



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HIGHLIGHTS

- Pancreatic renal cell carcinoma metastasis is rare and the best treatment is uncertain.
- We analysed outcome after resection of those metastasis in two German centers.
- Due to selection of patients we found no risk factor.
- Due to lymph node metastases in some patients we advice to perform lymphadenectomy.

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ABSTRACT

Introduction: Previous reports showed an excellent survival for patients after resection of pancreatic metastases from renal cell cancer (pRCC) and reported several predictive factors. This study aims to give more evidence to reported risk factors by analyzing a large cohort of patients with pancreatic resection due to pRCC. **Patients and methods:** We retrospectively analyzed all pancreatic resections due to pRCC between January 1993 and October 2014 in two German pancreatic surgery centers. Predictive factors were analyzed using the chi square test.

Results: Surgery was performed in 40 patients. Mean survival after resection was 147.9 months (SD 25.6 months). No predictive factors for survival were identified. Pathological examination showed that five out of 21 patients with examined peripancreatic lymph nodes had lymph node metastases.

Conclusions: Although our analysis comprised the biggest cohort of patients with pRCC it rendered no significant predictor for survival. This might be due to the overall excellent prognosis of study patients and the relatively rare condition with a limited number of patients. Several patients had lymph node metastases. Therefore lymphadenectomy should be considered in pRCC resection if the health condition of the patient permits this. By this more aggressive approach to pRCC, a better prognosis after resection might be achieved.

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1. Introduction

Renal cell carcinoma (RCC) is a cancer with a high incidence; for example, there were an estimated 64,000 new cases in the US alone

in 2014 [1]. Metastases may occur a long time after resection of the primary tumor [2]. Although RCC is one of only few tumors that spreads to the pancreas, pancreatic metastases are rare. Only 4% of all pancreatic resections account for metastases of RCC (pRCC) and less than 300 cases were reported in the last 60 years [2]. Consequently, there is limited data in the literature concerning the prognosis after resection of pRCC. The European Society for Medical Oncology (ESMO) guidelines for the treatment of metastatic renal cell carcinoma state that metastasectomy may provide a possible survival benefit for a selected group of patients with lung

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metastases only (i.e., those a long metachronous disease-free interval and a positive response to immunotherapy/targeted therapy) [3]. Recently it was also shown that targeted therapy might be an option for metastatic RCC [4,5]. However, several retrospective and nonrandomized studies with a limited number of pRCC patients suggested that resection of metastases might also lead to a prolonged median survival [6]. After operation, three- and five-year survival rates were 78% and 72%, respectively [2].

RCC is highly resistant to chemotherapy, thus surgery seems to be a better option than chemotherapy in the opinion of the authors [7]. Data from a randomized controlled clinical trial for the treatment of metastatic renal cell carcinoma only showed a survival of up to 11 months under first line chemotherapy [8]. Therefore chemotherapy must be regarded as relatively ineffective and surgery still must be considered as an alternative. Although mortality after pancreatic surgery has recently decreased, it nonetheless has a high morbidity rate and not all patients may benefit from resection of pRCC [9,10]. Predictive factors could facilitate the decision of when to operate. Recent retrospective studies revealed different predictive factors for patient survival after resection of pRCC. These include lymph node involvement [11], multifocal metastases, synchronous metastases, symptomatic metastases [12,13], size of the metastasis [13], and recurrent metastases [2]. The aim of this study was twofold: to evaluate the prognosis after resection of pRCC, and to both analyse predictive factors and identify new predictive factors, in a large cohort of patients with pRCC.

2. Patients and methods

2.1. Patients

A retrospective search for patients with a diagnosis of metastases from RCC (pRCC) was performed at the Department of General, Thoracic, and Vascular Surgery of the Carl Gustav Carus University Hospital, Dresden, and the Surgical Department of the University Hospital, Mannheim. The patients were selected from the prospective pancreas databases. Between October 1993 and March 2014 we identified 40 consecutive patients that were resected for pRCC. The final pathological diagnosis confirmed metastases from RCC in all patients. The demographic characteristics of the patients are summarized in Table 1.

2.2. Data collection

Patients who had undergone pancreas resection for pRCC were identified from our databases and their medical records were analyzed retrospectively. In accordance with the guidelines for human subject research, approval was obtained from the Ethics Committee at the University Hospital, Mannheim. The data were complemented with clinical notes from the patients' physicians and surgeons. The information regarding deceased patients was obtained from family members or from the respective general practitioner. Patient characteristics and parameters used for statistical analysis are listed in Supplementary information 1. The postoperative events and clinical outcomes were also recorded prospectively and analyzed retrospectively. Tumor stage designation was categorized according to the TNM system of the Union Internationale Contre le Cancer (UICC) 2007 guidelines. Literature search was performed using Pubmed (www.pubmed.com) and the keywords "pancreatic metastases" and "renal cell carcinoma".

2.3. Definitions

Perioperative mortality was defined as in-hospital mortality.

Table 1

Characteristics of our patient cohort. (SD = standard deviation; BMI = Body-Mass-Index; x = missing data). * Values are mean with standard deviation.

	Patients n = 40 n (%)
Age (years)	65.5 (SD 9.0)*
Male sex	24 (60)
BMI	28.0 (SD 4.5)*
Time after primary tumor (months)	125.4 (SD 77.4)*
Age at initial diagnosis (years)	55.7 (SD 9.6)*
Classification of primary tumor	
T	
1	11 (27.5)
2	11 (27.5)
3	7 (17.5)
4	–
x	11 (27.5)
N	
0	21 (52.5)
1	–
x	19 (47.5)
G	
1	1 (2.5)
2	8 (20)
3	–
x	31 (77.5)
R	
0	3 (7.5)
x	37 (92.5)
Metachronous metastases (>6 months)	39 (97.5)
History of other metachronous metastases	13 (32.5)

Postoperative pancreatic hemorrhage (PPH) was categorized according to the International Study Group on Pancreatic Surgery (ISGPS) consensus definition [14]. Delayed gastric emptying (DGE) was classified according to the suggested definition by the ISGPS [15]. Postoperative pancreatic fistula (POPF) was defined analogous to the ISGPF criteria [16]. Synchronous metastasis was defined as metastasis within 6 month of initial diagnosis.

2.4. Statistical analysis

Statistical analyses were performed using the Statistical Package for the Social Sciences for Windows, version 15.0 (SPSS, Inc., Chicago, IL, USA). All clinical and pathological characteristics were stratified to build categorical or nominal variables. The thresholds used for categorization were based on previously described thresholds in the literature and/or recursive partitioning as previously described [18]. Laboratory values were defined as elevated if values were higher than the normal cut-off value. Continuous data are presented as mean with standard deviation (SD). The univariate examination of the relationship between the assessed criteria and survival was performed with a Chi-square test. For the assessment of the impact of different parameters on survival, we utilized a three-year survival rate. The estimates of patient survival were generated using the Kaplan–Meier method. Factors significant (at $p < 0.10$) at the univariate level were entered into the multivariate model. A Cox regression analysis with stepwise backwards elimination based on likelihood ratios was employed to test for independent predictors of survival (at $p < 0.05$).

3. Results

3.1. Study cohort

Analysis of the pancreatic databases showed that 2% of all operations at the two centers were performed for pRCC. A total of 40

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