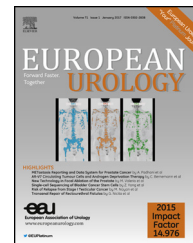


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Platinum Priority – Brief Correspondence

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Complications After Metastasectomy for Renal Cell Carcinoma—A Population-based Assessment

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Abstract

Metastasectomy has long been considered a valid treatment option for patients with oligometastatic renal cell carcinoma (oligo-mRCC). However, the literature on complications in this setting is scarce. Our objective was to describe in-hospital complications after metastasectomy in a contemporary cohort of patients with mRCC. Using the National Inpatient Sample database (2000–2011), 45 279 mRCC patients were identified. Of those, 1102 underwent metastasectomies. The metastatic sites were the lungs, bone, liver, lymph nodes, adrenal glands, and brain in, respectively, 52%, 29%, 19%, 14%, 11%, and 3.4% of patients. The overall complication rate was 45.7%. Major complications (Clavien III–V) constituted 27.5%. Resections of hepatic lesions were significantly associated with higher odds of overall complications compared with any other site (odds ratio 2.59, 95% confidence interval 1.84–3.62, $p < 0.001$). While metastasectomy remains a potential treatment option in RCC with oligometastatic disease, the associated complication rates are non-negligible; therefore, careful patient selection is warranted. **Patient summary:** We studied outcomes of patients with metastatic kidney cancer treated with metastasectomy. While metastasectomy is a treatment option for metastatic renal cell carcinoma, complications are not insignificant and our results may guide preoperative counseling.

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Patients with metastatic renal cell carcinoma (mRCC) can be treated with medical, ablative, or surgical therapy. Surgical management of metastases may be offered with curative intent in selected patients. Most studies to date on metastasectomies in mRCC focused on cancer control. In contrast, perioperative morbidity in patients treated with

metastasectomy has scarcely been evaluated [1]. Therefore, we sought to comprehensively assess in-hospital complications following metastasectomy for mRCC patients treated in the pre-targeted and targeted therapy era.

Using the National Inpatient Sample, patients with a primary diagnosis of mRCC between 2000 and 2011 were

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abstracted ($n = 45\,279$). Patients who underwent a metastasectomy were identified using concomitant codes of the site of metastases, as well as the code for the procedure corresponding to organ-specific resection, as described previously [2]. The main outcomes of interest were overall and major complications (Clavien grade III–IV). Covariates consisted of metastatic sites (lung, liver, bone, adrenal gland, and lymph node), time of surgery (target vs non-target therapy era [≥ 2006 vs < 2006]) patient age, sex, race/ethnicity, insurance status, Charlson Comorbidity Index (CCI), as well as hospital location, academic status, hospital size, and annual caseload. Univariable logistic regression models assessed the association of covariates with overall and major complications. All results were weighted to reflect national estimates. A two-sided p value of < 0.05 was considered to be statistically significant. This study was reviewed and deemed exempt from approval by the Brigham and Women's Institutional Review Board.

Overall, 1102 metastasectomies were identified (Supplementary Table 1). Most common metastatic sites were the lungs (51.8%), bone (29%), and liver (18.6%, Supplementary Fig. 1). Metastasectomy was predominantly performed for lung (43.5%), bone (27.1%), and liver (16.1%) lesions. Intraoperative complications occurred in 7.9% of patients. The overall complication rate was 45.7%. The most frequent complication types were of respiratory (12.0%) nature. Major complications (Clavien III–IV) occurred in 25.1%. In-hospital mortality rate (Clavien V) was 2.4% (Fig. 1).

Univariable logistic regression analysis identified increasing age (odds ratio [OR]: 1.02, 95% confidence interval [CI]: 1.01–1.03, $p = 0.001$), and hepatic (OR 2.59, 95% CI 1.84–3.62, $p < 0.001$) and pulmonary metastasis (OR 0.63, 95% CI 0.50–0.81, $p < 0.001$), both compared with any other site, as independent predictors of overall complications (Table 1). Predictors of major complications were a high comorbidity burden (CCI ≥ 2 ; OR: 2.41, 95% CI: 1.60–3.62, $p < 0.001$) and private insurance (OR: 0.68, 95% CI: 0.51–0.92, $p = 0.01$).

Our study provides several important findings regarding short-term outcomes following metastasectomy for mRCC. Consistent with previous reports [1,3], major complications (Clavien III–IV) were recorded in one-fourth of metastasectomy patients. Overall, in-hospital mortality

after a metastasectomy was 2.4% ($n = 27$), of which the majority underwent lung ($n = 11$) or bone ($n = 9$) resections. The rate of perioperative mortality following metastasectomy was comparable with that in previous reports (0.9–2.3%) [4,5].

In the current study, patients in the target therapy era (> 2006) did not experience a higher likelihood of in-hospital complications after metastasectomy. While it has previously been observed in the context of cytoreductive nephrectomy that presurgical systemic therapy is associated with higher rates of 90-d complications, > 1 complication, and wound complications [6], the association with systemic therapies could not be ascertained for metastasectomies with the data at hand.

Unsurprisingly, a higher comorbidity score was significantly associated with major complications, similar to previous findings [7]. We also established a significantly higher likelihood of overall complications among liver resections. This is likely due to the fact that visceral metastases have more detrimental effects on survival and are most difficult to make amenable to successful therapy. Contrary to synchronous hepatic resection for direct invasion or metastatic disease during nephrectomy, we could not establish a higher likelihood for Clavien grade III–IV complications in hepatic resections [8]. It is possible that the significantly lower association of covariates with overall complications in pulmonary resections compared with any other site is a consequence of a more routine surgical approach in this most common metastatic location.

Several limitations are applicable. First, the validity of the Clavien classification using International Classification of Diseases, ninth revision, diagnostic codes has not been assessed, despite its use in other population-based reports [7]. Although the bias of procedural misclassifications cannot be ruled out entirely, we relied on the previous methodology, which demonstrated robust outcomes [9]. Second, since the data capture only in-hospital events, 90-d morbidity could not be assessed. Third, the retrospective nature of the study is associated with a selection bias; unmeasured confounders such as the number of metastases operated, type of surgery, synchronous or metachronous metastasis, performance status at surgery, or risk group classification; and other residual errors that are mostly

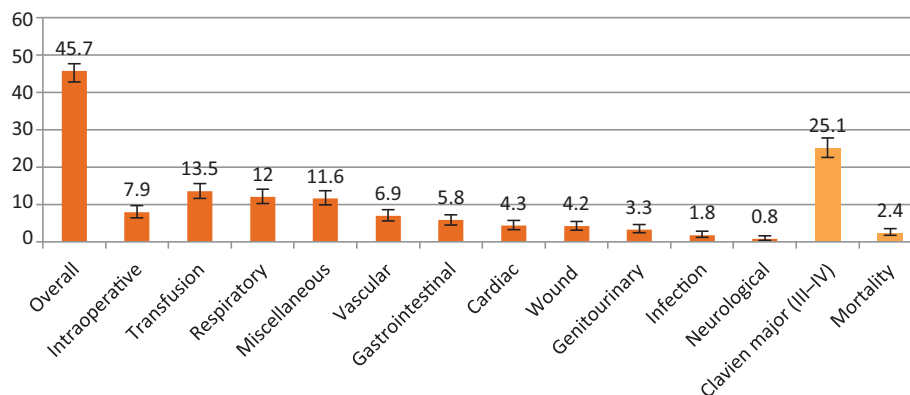


Fig. 1 – National estimated overall complications/outcomes of metastasectomies for RCC (in %), NIS 2000–2011. Bars represent 95% confidence intervals. NIS = National Inpatient Sample; RCC = renal cell carcinoma.

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