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# Pancreatic metastasectomy of renal cell carcinoma: a single institution experience

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**Introduction:** Renal cell carcinoma (RCC) is the most common primary neoplasia that metastasizes to the pancreas. Pancreatic metastasis (PM) occur in asymptomatic older patients and are identified during follow up. If resectable, surgery is the treatment of choice for long term survival. Our goal is to analyze outcomes of patients with RCC-PM.

**Material and methods:** We reviewed all patients with metastatic RCC (mRCC) who underwent resection, from known primary RCC and RCC-PM.

**Results:** There were 16 patients (mean age of  $67 \pm 8$  years, male 8 (50%), mean BMI  $29 \pm 5.36$  kg/m<sup>2</sup>). Half of them were asymptomatic. Diagnosis was incidental in 56.25% with a median lesion size of 25 mm (12-80). Pancreatic

resections performed were: pancreatoduodenectomy (31.25%), distal pancreatectomy (56.25%) and total pancreatectomy (12.5%). Median estimated blood loss was 225 mL (15-2,200), median operative time was 242 min (63-420). Median length of stay was 6 days (2-30). New-onset diabetes was 6.25%. The minor complication and reoperation rates, were 37.5% and 6.25%, respectively. The median number of harvested lymph nodes was 17 (4-31), all were negative. All had a R0 resection. Recurrence of disease was 18.75% with a median time after surgery of 3 years (2-6). The median follow up was 9 years (0-15). Thirteen (81.25%) patients are still alive, eight are disease free. Three (18.75%) died.

**Conclusions:** Long term survival can be achieved with surgical resection of PM from RCC in selected patients in whom complete resection is possible.

**Key Words:** renal cell carcinoma, metastasis, pancreas

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## Introduction

Pancreatic metastasis (PM) accounts for 1%-2% of all pancreatic tumors, and are considered very rare.<sup>1-4</sup> Renal cell cancer (RCC) is the most common primary neoplasia that can metastasize to the pancreas, and is followed by lung (adenocarcinoma and non-small cell lung carcinoma) and lobular breast cancer.<sup>5-7</sup> Approximately 22% of the cases of pancreatic metastasis are identified during the diagnosis of the primary tumor.<sup>6,8,9</sup>

PM from other organ sites is generally associated with diffuse metastatic disease. However, RCC is unique in that it presents with isolated PM in approximated half of the cases.<sup>8-11</sup> Isolated PM from RCC generally occurs in asymptomatic patients who are older than 70-years old<sup>8</sup> and identified during follow up after management for the primary neoplasia.<sup>12</sup> Distinguishing PM from primary pancreatic ductal adenocarcinoma or pancreatic neuroendocrine tumor on cross-sectional imaging modalities, such as computed tomography (CT), magnetic resonance imaging (MRI), and 18F-fluorodeoxyglucose position emission tomography (PET-CT) is challenging. Primary exocrine tumors of the pancreas usually appear as

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hypovascular masses while neuroendocrine tumors, similar to metastatic RCC (mRCC), are frequently hypervascular.<sup>13</sup> They account for 90% and 5% of all pancreatic tumors, respectively.<sup>14-16</sup>

Prognostic models have been developed to predict the behavior of disease in patients with mRCC. Motzer et al<sup>17</sup> proposed to categorize patients with mRCC into good, intermediate, and poor risk groups by using five prognostic factors: performance status, lactate dehydrogenase level, hemoglobin level, corrected serum calcium level, and disease-free survival from nephrectomy. This prognostic score was recently validated and modified by adding prior radiotherapy and number of metastatic sites instead of performance status.<sup>11,18</sup>

In patients with resectable PM, surgery is accepted as the treatment of choice for long term survival.<sup>12,19,20</sup> This study examines our outcomes of PM from mRCC at a single institution in a 17-year time period.

## Materials and methods

After institutional review board approval we conducted a retrospective evaluation of patients who were diagnosed with mRCC at our institution between 2001 and 2018. Patients aged  $\geq 18$  years with mRCC, who underwent surgical resection were included. Cases without pancreatic resection were excluded from the study. Institutional electronic medical records were used to extract information. The variables studied in this case series include patient demographics, clinical presentation, tumor characteristics, surgical management, and outcome. All patients had a known primary RCC and a pathology report consistent with PM from RCC. Follow up information was obtained by office visit, by reviewing records or by contacting the patient directly.

**TABLE 1. Clinical presentation at the time of diagnosis. Results reported as n (%)**

None (asymptomatic)	8 (50)
Fatigue	5 (31.25)
Abdominal pain	3 (18.75)
Weight loss	2 (12.5)
Vomiting	2 (12.5)
Diarrhea	2 (12.5)
Nausea	1 (6.25)
Early satiety	1 (6.25)
Jaundice	1 (6.25)

## Results

A total of 16 patients with mRCC were included half of patients, of which, 8 (50%) were male, with an average age of  $67 \pm 8$  years, body mass index of  $29 \pm 5.36$  kg/m<sup>2</sup>. Of these, 9 (56%) were incidentally found. Eight (50%) were asymptomatic, symptoms are described in Table 1. Five (31.25%) patients had multiple pancreatic metastasis, and 11 (68.75%) had a single anatomic site metastasis. Procedures performed are described in Table 2.

Operative and postoperative results are given in Table 3. Eight patients (50%) underwent a minimally invasive approach.

Reoperation was necessary in one patient (6.25%) who had undergone a pancreaticoduodenectomy, subsequently required partial colectomy with end ileostomy for ischemic colon. The patient recovered uneventfully.

Pathologic variables and long term follow up are summarized in Table 4. Three (18.75%) patients had recurrence of disease, one in the lung (79 months after

**TABLE 2. Pancreatic metastasis anatomical site and surgical procedure. Results reported as n (%)**

Site	Procedure (n)
Head, 5 (31.25)	Pancreatoduodenectomy (3) Pylorus preserving pancreatoduodenectomy (2)
Body, 1 (6.25)	Distal pancreatectomy (1)
Tail, 5 (31.25)	Distal pancreatectomy (5)
Multiple, 5 (31.25)	Partial pancreatectomy (1) Total pancreatectomy (1) Pylorus preserving total pancreatectomy (1) Distal pancreatectomy (2)

TABLE 3. Operative and postoperative data. Results reported as n (%) or median (range)

Estimated blood loss (mL)	225 (15-2200)
Operative time (min)	242 (63-420)
Length of stay (days)	6 (2-30)
Wound infection	2 (12.5)
Abdominal abscess	4 (25)
Diabetes after surgery	1 (6.25)
Pancreatic fistula	3 (18.75)
Reoperation	1 (6.25)
Time from surgery to discharge (days)	6 (2-30)

disease onset), one had local recurrence (35 months after disease onset), and one on the right adrenal (27 months after disease onset). The median time from surgery to recurrence was 3 years (2-6). Three (18.75%) patients died: one due to a gastric ulcer, and subsequent gastrointestinal bleeding (17 months after the surgery); one of an unknown cause or period after surgery; and one due widespread metastasis. Thirteen (81.25%) patients are still alive. The median follow up from surgery was 9 years (0-15).

TABLE 4. Pathological variables and long term follow up. Results reported as n (%) or median (range)

Size (mm)	25 (12-80)
Analyzed lymph nodes	17 (4-31)
Positive lymph nodes	0 (0)
R0 resection	16 (100)
Lymphovascular invasion	0 (0)
Perineural invasion	0 (0)
Recurrence	3 (18.75)
Recurrence site, months after disease onset	
Lung, 79	
Local, 35	
Right adrenal, 27	
Dead	3 (18.25)
Cause of death, months after surgery	
GI bleeding, 17	
Unknown	
Widespread metastasis, 2	
Patients alive	13 (81.25)
Years from surgery	9 (0-15)

## Discussion

RCC is a unique and unpredictable tumor that can metastasize to the pancreas. Some authors<sup>21</sup> failed to find any predilection of metastasis for a specific pancreatic anatomical site irrespective of the primary site of RCC. No known mechanism explains the occurrence of isolated mRCC.

Patients with a history of RCC should be monitored for at least 10 years in order to detect recurrence, and the evidence at imaging studies of a hypervascular pancreatic lesion may correspond to a metastasis. In these clinical situations, preoperative biopsy may not be necessary.<sup>11</sup> High index of suspicion should arise when finding a pancreatic mass in a patient with a previously treated extra-pancreatic primary tumor.<sup>20,22,23</sup> Preoperative adequate localization using endoscopic ultrasound or MRI are important to determine the location, number and relation to main pancreatic duct. Operative localization measures include: mobilization of the pancreas, manual palpation, and intraoperative ultrasonography.<sup>11</sup> Although isolated PM from RCC are rare, their behavior is often unusual because some patients have an indolent natural history, with presentation of mRCC many years after treatment of the primary tumor.<sup>13</sup>

Timing of metastasis, lymph node status of the primary tumor, and size and number of metastasis in the pancreas do not play a role in predicting the survival outcome after pancreatic resection for RCC metastasis.<sup>24</sup> Multifocality of pancreatic metastasis from RCC is not an unusual finding, ranging from 20% to 45%, and does not correlate with a worse outcome and is not a contraindication to surgery.<sup>11</sup> Furthermore, peripancreatic lymph node involvement with pancreatic metastasis was uncommon.<sup>25</sup> Most previously published studies indicate that lymph node involvement in metastatic pancreatic malignancy is

very rare, and patients with positive lymph nodes did not survive as long as patients without lymph node involvement.<sup>19,25</sup>

Moreover, literature reported a 43% to 88% five-year survival rate on patients who underwent pancreatic resection for RCC metastasis that were limited to the pancreas.<sup>19</sup> Studies show that complete surgical resection, even for multiple PM from RCC, is the most effective treatment option.<sup>23</sup> Surgical resection of RCC metastasis to the pancreas should be considered in all patients in whom complete resection of disease is possible.<sup>13</sup> The prognosis of RCC metastatic to the pancreas is more favorable than that of primary pancreatic carcinoma.<sup>22</sup> Major resections are no longer a contraindication for secondary malignancy of the pancreas in selected patients in terms of surgical risk.<sup>24</sup> Pancreatic resections were for many years associated with high rates of morbidity and mortality, but recent data show that pancreatic surgery in high-volume centers is safe.<sup>26</sup> Nevertheless, management of secondary malignancy to the pancreas must be individualized with an emphasis on the medical comorbidities and surgical risk of the patient and the extent of disease,<sup>24</sup> and an optimal resection strategy that provides adequate disease-free resection margins and maximal tissue preservation of the pancreas.<sup>11</sup>

## Conclusions

PM should be considered when a patient with a pancreatic mass has a history of other malignancy, even if diagnosed and treated years before. In the absence of widely metastatic disease, surgical approach may offer long term survival. Whenever possible, resection of pancreatic and simultaneous extrapancreatic metastasis should be considered.<sup>24</sup>

In long term survival can be achieved with surgical resection of PM from RCC in selected patients in whom complete resection is possible. □

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