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## Scientific letter

## Surgery of pancreatic metastasis from renal cell carcinoma<sup>☆</sup>



## Cirugía en las metástasis pancreáticas por carcinoma renal

Renal cell carcinoma is responsible for 2%–3% of all malignant tumors in adults, with a higher incidence in men. The 5-year survival rate is 95% in tumors limited to the kidney, while the survival rate in disseminated tumors is 20%<sup>1</sup>. Some 20%–30% of patients have metastasis at diagnosis, and 50% will develop metastasis after nephrectomy. The most common locations are the lung, liver, bone, and brain, but it is also relatively common to find lesions in unusual places, such as the thyroid, skeletal muscle, and pancreas<sup>2</sup>.

The reported incidence of pancreatic metastases from renal cell carcinoma is 2%. They typically appear long after nephrectomy, with intervals even longer than 30 years. Preoperatively, they can be difficult to differentiate from other types of pancreatic lesions. The typical CT image is a hypervascular nodule with defined margins, whose main differential diagnosis includes pancreatic neuroendocrine tumors. Endoscopic ultrasound and biopsy of the lesion may be necessary. In some cases, its nature is only determined after immunohistochemical analysis of the surgical specimen. Therefore, with a history of renal cell carcinoma, it is important to have a high rate of suspicion when evaluating this type of lesion<sup>2,3</sup>.

Metastases in the pancreas are associated with a better prognosis than other locations. Patients with resectable metastases should be candidates for surgery, as this increases survival<sup>4</sup>.

We conducted a retrospective analysis of 7 patients who were treated surgically at our hospital between 2000 and 2019 for pancreatic metastases of renal carcinoma. The variables studied are summarized in Table 1.

Mean age was 63 years (IQR 59–75). The patients were 4 men and 3 women. The primary tumor was located in the left kidney in 5 patients and in the right kidney in 2 (Table 1).

None of the patients presented symptoms at diagnosis. The median latency between surgery of the primary tumor and the development of pancreatic metastases was 125 months (IQR 15–228) with a minimum of 4 months and a maximum of 332 months. Two patients (28.6%) had previously presented

metastases in other organs (lung and oral cavity), and both cases were treated with R0 resection.

Regarding the surgical technique, we performed 4 distal pancreatectomies, 2 pancreaticoduodenectomies (PD) and one resection of the uncinate process, achieving R0 resection in all cases. Morbidity was 70% (40% Clavien Dindo II and another 40% grade IIIa). Regarding mortality, one of the 7 patients died 83 days after surgery due to heart failure.

Median survival was 5.9 years (IQR 2.25–8.1). Two of the 7 patients are still alive after follow-up periods of 20 and 12 months. The latency time to metastasis and the percentage of involvement of other organs were similar reports in the literature<sup>5</sup>.

No relationship has been demonstrated between the location of the primary tumor and the location of the metastasis; therefore, local venous or lymphatic spread seems unlikely. The dissemination mechanism appears to be hematogenous, with a certain affinity for the pancreatic parenchyma<sup>6</sup>.

Tanis et al. estimated that after resection of the pancreatic metastasis, the local recurrence rate was 4%, and the extrapancreatic recurrence rate was 17.1%<sup>3</sup>. In our experience, we found one case of recurrence in the pancreas that required completion of the pancreatectomy and two cases of distant recurrence (lung and retroperitoneal).

Most publications are short series and case reports, but a systematic review published in 2009 compared the survival of 321 patients who underwent pancreatic resection and another 73 in whom resection was not performed. The study showed an increase in 2-year and 5-year survival rates (80.6 and 72.6%) in the surgery group compared to the group without resection (41% and 14%)<sup>3,7</sup> (Table 2).

These metastases usually appear as metachronous isolated metastases, although cases of two or more pancreatic metastases have been reported. The type of surgical treatment remains controversial. Some authors advocate atypical resections with the selective excision of the lesion to preserve the pancreatic endocrine and exocrine function, whereas other

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**Table 1 – Clinical and demographic characteristics.**

	1	2	3	4	5	6	7
Age/sex	75/F	68/M	59/M	63/M	82/F	62/F	47/M
ASA	2	3	3	2	3	3	1
Nephrectomy type	Partial	Radical	Partial	Radical	Radical	Radical	Radical
Resection type	R0	R0	R0	R0	R0	R0	R0
Kidney	Right	Left	Left	Left	Left	Right	Left
TNM primary tumor	T2N0	–	T3N0	T1N0	T2N0	T1bN0	T3N0
Months since nephrectomy	94	228	125	191	332	15	4
MTS location	Head	Body	Head	Body	Tail	Body	Uncinate
Pancreas surgery	PD	TP	PD	Distal	Distal	Distal	Uncinectomy
Type of resection	R0	R0	R0	R0	R0	R0	R0
MTS size in cm	2,2	2	3	1,1	3	2	1,5
Peripancreatic involvement	No	No	No	No	No	No	No
Pathologic lymphadenopathies	No	No	No	No	No	No	No
Morbidity (Clavien Dindo)	5	2	3 A	3 A	No	No	2
Evolution	Exitus	Exitus	Exitus	Exitus	Exitus	Living	Living
	Post-op						
Recurrence and disease-free time	No	Pancreas 16 months	Lung 4 months	Retroperitoneum 6 months	No	No	No
Months SV*	2	106	89	52	71	20	12

The categorical variables are expressed as percentage and quantitative variables with non-normal distribution as median and interquartile range.

PD: pancreaticoduodenectomy; F: female; M: male; MTS: metastasis; Post-op: postoperative; TP: total pancreatectomy.

\* Months of survival since surgery of the pancreatic metastasis.

**Table 2 – Latency and survival times in the main series published.**

	n	Nephrectomy-to-metastasis latency time (months)	SV in months	% SV 2–3 years	% SV 5 years
Chatzizacharias et al. <sup>8</sup>	7	86	98	71%	71%
Tanis et al. <sup>3</sup>	321	117	69	80.6%	72.6%
Grassi et al. <sup>4</sup>	77	91	106-	–	75%
Zerbi et al. <sup>9</sup>	23	–	–	88%	88%
Schwarz et al. <sup>10</sup>	62	120	52.6	72%	63%
Eidt et al. <sup>11</sup>	7	169	65	85.7%	85.7%

SV: survival.

surgeons prefer standard pancreatectomies (PD, distal pancreatectomies and TP) in order to reduce pancreatic recurrences<sup>8,9</sup>.

In recent years, studies have been published with tyrosine kinase inhibitors, showing no statistically significant differences in survival versus surgery, but with lower survival curves<sup>10</sup>. Chemotherapy may be an option in patients who are not candidates for surgery due to either unresectable disease or comorbidities<sup>4</sup>.

In conclusion, pancreatic metastases of renal carcinomas are rare and can occur many years after the primary tumor, so this should be considered as a possible differential diagnosis. Pancreatic surgery should be considered in these patients as it increases survival.

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## Step-up approach in severe necrotizing pancreatitis: Combination of video-assisted retroperitoneal debridement and endoscopic necrosectomy<sup>☆</sup>



## Step-up approach en pancreatitis necrosante grave: combinación de desbridamiento retroperitoneal videoasistido y necrosectomía endoscópica

Walled-off pancreatic necrosis is one of the most feared complications of severe acute pancreatitis. Although most cases evolve favorably with conservative management, up to one-quarter of patients will require interventional techniques<sup>1,2</sup>. The management of peripancreatic collections has evolved in recent years, and the benefits of the step-up approach have been widely demonstrated<sup>3-5</sup>. The current debate in this field focuses on demonstrating the superiority of endoscopic necrosectomy (EN) over video-assisted retroperitoneal debridement (VARD), or vice versa<sup>6</sup>. We present the case of a patient with severe acute pancreatitis and large walled-off necrosis that required the combined use of EN and VARD for its resolution.

The patient is a 69-year-old man with arterial hypertension and hyperuricemia, who came to the emergency room due to sudden and intense abdominal pain in the epigastrium. We observed notable impairment of his general condition and signs of peripheral hypoperfusion. Blood pressure was 153/95 mmHg; heart rate 86 bpm. He maintained an oxygen saturation of 89%-92%, with an inspired oxygen fraction of 21%. Intra-abdominal

pressure was 27 mmHg, measured indirectly. His abdomen was very distended, with generalized tenderness and muscle guarding. Lab work-up showed normal renal function and ions, alanine aminotransferase 256 U/L, aspartate aminotransferase 518 U/L, total bilirubin 1.63 mg/dL (direct 0.96 mg/dL), amylase 6.396 U/L, lipase 21 200 U/L, C-reactive protein 51 mg/dL, leukocytes 262 900  $\mu$ L (80% neutrophils) and coagulation in normal ranges. Abdominal computed tomography (CT) scan was performed 48 h after admission, showing images compatible with pancreatitis, with focal areas of necrosis and gallstones (Fig. 1A). During the first month of hospitalization in the Intensive Care Unit, he presented multiple organ failure and required non-invasive mechanical ventilation, hemofiltration, and high doses of vasoactive drugs. Due to suspected superinfection of the collection, empirical antibiotic therapy was started with piperacillin/tazobactam 4/0.5 every 8 h. The patient then presented an episode of upper gastrointestinal bleeding and endoscopy was performed, during which a large clot was observed with no other observable findings. An

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