

**Title:** Pancreatectomy for Metastatic Disease: A Systematic Review

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## **Abstract**

**Aim:** Tumours rarely metastasise to the pancreas. While surgical resection of such metastases is believed to confer a survival benefit, there is limited data to support such management. We present a systematic review of case series of pancreatic metastasectomy and analysis of survival outcomes.

**Methods:** A literature search was performed using the PubMed and Cochrane databases and the reference lists of relevant articles, searching for sizeable case series of pancreatic metastasectomy with curative intent. Data extracted included basic demographics, histological primary tumour, presentation, operative management, complications and survival, while the MINORS index was used to assess study quality.

**Results:** 18 studies were found which met our inclusion criteria, involving 399 patients. Renal cell carcinoma (RCC) was the commonest malignancy metastasising to the pancreas, responsible for 62.6% of cases, followed by sarcoma (7.2%) and colorectal carcinoma (6.2%). While survival data was not uniformly reported, the median survival post-metastasectomy was 50.2 months, with a one-year survival of 86.81% and five-year survival of 50.02%. Median survival for RCC was 71.7 months with 70.4% five-year survival. Median survival was similar in patients with synchronous and metachronous pancreatic metastases, but patients with additional extrapancreatic metastases had a significantly shorter survival than patients with isolated pancreatic metastases (26 versus 45 months). Study quality was poor, with a median MINORS score of 10/16.

**Conclusions:** Within the limitations of a review of non-randomised case series, it would appear that pancreatic metastasectomy confers a survival benefit in selected patients. Better evidence is required, but may prove difficult to acquire.

## **Key words:**

pancreatic metastasis, metastasectomy, pancreatectomy, metastatic renal cell cancer,

**Introduction:**

Metastatic tumours of the pancreas are extremely rare, accounting for less than 5% of pancreatic malignancies diagnosed in living patients [1]. Pancreatic metastases are found more frequently at autopsy, being identified in up to 15% of patients with malignant disease [2]. While resection of metastatic lesions to liver and lung has been well described and is generally accepted to improve survival, the optimal management of pancreatic metastases is ill-defined. Surgical resection of these metastases is believed to confer a survival benefit, although evidence supporting this theory is weak and based solely on case reports and small retrospective case series. The aim of this study was to perform a systematic review of the literature to better define the outcomes after pancreatic metastasectomy.

**Methods:**

This review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [3].

***Search Strategy for Identification of Studies***

A systematic literature search of the Cochrane and PubMed databases was performed. For the PubMed database search, the keywords were used as both text words and Medical Search Headings (MeSH terms). The keywords were combined using Boolean operators as follows: (pancreas AND (metastasis OR metastases) AND (surgery OR surgical OR resection OR pancreatectomy OR metastasectomy)). There was no restriction on the date of publication. In addition to the primary electronic search we reviewed all 'related citations' linked to each relevant abstract in PubMed and manually reviewed the bibliographies of selected articles and relevant review papers to identify other studies for inclusion.

***Study selection***

Inclusion criteria for this systematic review were case series with at least ten patients, published in the English language before 24 October 2013, reporting survival data after pancreatic resection for secondary malignancies. Exclusion criteria were: case reports, review articles, studies reporting on surgical technique only and studies reporting resections for lymphoma or en-bloc resections involving the pancreas. Potentially relevant manuscripts were retrieved in full and assessed based on inclusion and exclusion criteria. When two publications were believed to involve potentially duplicated or overlapping patient populations (based on authors, institutions and study years), only

the larger cohort was included in this review to avoid double-counting of patients. Series focusing on the palliative management of pancreatic metastases were excluded. Series of secondary malignancies of the pancreas in which some were managed medically were included if the survival data for patients who underwent resection could be extracted separately.

#### ***Data collection and statistical analysis***

Data extracted from selected studies included (but was not limited to) the year of publication, authors' institution and country, number of patients and their demographics, histology of primary tumour, presentation (symptomatic or incidental finding), timing (synchronous or metachronous with the primary tumour), presence or absence of extrapancreatic metastases, operation performed, operative mortality and morbidity and survival data. Given the paucity of data on this topic, any measure of survival (median, one, two or five-year survival) was extracted. Statistical analyses were performed only on extracted summarised data from the selected studies. Basic descriptive statistics (percentages and weighted means) were used to summarize the patient, study, and outcomes data. Weighted means were calculated for oncological outcomes across all studies, with the unpaired t-test used to compare survival outcomes. Statistical analysis was performed using GraphPad software (GraphPad Software Inc, California, 2013).

We assessed the methodological quality of the selected studies using the Methodological Index for Non-Randomised Studies (MINORS) criteria [4]. This tool, validated by its original authors, assesses eight items (12 items in controlled studies), each of which is assigned a score of 0 (not reported), 1 (reported but inadequate) or 2 (reported and adequate).

## **Results**

### ***Search yields & data retrieval***

Our initial literature search yielded 3405 citations. After an initial screening of titles and abstracts, 34 articles were reviewed in full to determine whether they met the inclusion criteria. Of these, 4 featured patient populations that overlapped with subsequent, larger studies, and 12 were rejected because they did not fulfil the inclusion criteria. The remaining 18 studies met the above criteria to merit inclusion in the extractable and analysable dataset [5-23]. The search strategy and outcomes are summarised in Figure 1.

### ***Study characteristics***

The dataset consisted of 18 original studies, involving 399 patients who had undergone resection of pancreatic metastases. All studies were retrospective single-institution case series, although 7 relied on prospectively-maintained databases. Mean cohort size was 27, median 18 patients per study (range 10-70). The majority of studies were from Europe (n=12), followed by series from the USA (n=4), Canada (n=1) and Korea (n=1).

### ***Patient characteristics***

Of the 399 patients investigated in the 18 studies, 42% were female. At the time pancreatic metastases were discovered, the mean age of the patients was 61.7 years. Disease free interval (DFI, time from resection of primary tumour to diagnosis of pancreatic secondary lesions) was not consistently reported, however among studies which reported mean DFI the weighted mean was 65.9 months (data not shown). Demographic characteristics are summarised in Table 1.

RCC was the commonest malignancy metastasising to the pancreas, accounting for 62.6% of all primary tumours (n=250); six articles focused entirely on RCC. Sarcomas were the second commonest primary tumour (n=29, 7.2%), followed by colorectal carcinoma (n=25, 6.2%), ovarian carcinoma (n=19, 4.7%) and melanoma (n=16, 4%) (Figure 2).

Most centres performed standard procedures for resection of a pancreatic lesion —distal pancreatectomy (n=174, 43.6%), pancreaticoduodenectomy (n=144, 36.1%), and total pancreatectomy (n=52, 13.0%). Some units performed variants of the standard procedures such as simple enucleation (n=20, 5.0%), middle pancreatectomy (n=6, 1.5%) and duodenum-preserving pancreatic head resection (n=3, 0.7%).

### ***Morbidity and mortality***

Operative mortality was low, as would be expected following pancreatectomy in high-volume centres (weighted mean 2.21%, range 0—10%). Postoperative morbidity was similar to that reported after pancreatectomy for primary pancreatic tumours, at 39.85%, while the rate of fistula formation was 18.78% on average (Table 2).

### ***Survival data***

The average duration of follow-up was only reported in 9 studies, from which the weighted mean follow-up post pancreatic metastasectomy was 33.4 months (range 15.2 – 48 months). Pooled analysis of all studies determined the median survival to be 50.2 months (range 26—78 months) (Table 3).

One- and 5-year survival data were available for 4 and 11 studies respectively. The overall one-year survival was 86.81% and 5-year survival was 50.02%. Survival outcomes appeared better for RCC than for non-RCC related metastases (median survival 71.7 months vs. 24.7 months, respectively, although only three studies directly compared the outcomes for RCC versus non-RCC metastases). The 5-year survival after resection of RCC-related pancreatic metastases was 70.4%. Although it was only reported in one study, the 5-year survival from non-RCC related pancreatic metastases was 22%. Due to the paucity of data reported and heterogeneity in the reporting of survival data, more detailed meta-analysis of the included studies was not possible.

183 patients were reported to have presented with isolated pancreatic metastases, versus 33 with multiorgan metastases. This information was not recorded for the remainder of the patients in our dataset. The weighted mean survival of patients with extrapancreatic disease was 26 months, while that of patients without extrapancreatic disease was 45 months ( $p = 0.0016$  using the unpaired t-test). The weighted mean survival of the 28 patients whose pancreatic metastases were reportedly synchronous with their primary tumour was 36 months, while that of the 301 patients with metachronous metastases was 40 months ( $p = 0.315$ ).

### ***Methodological quality of studies***

No study in this review had a control group and no study was conducted prospectively. The 18 studies achieved a median MINORS score of 10/16 (range 7—11).

## Discussion

Metastasectomy is a well-established treatment modality for metastases to a range of organs, particularly liver and lung. However, this strategy has yet to be validated in the context of a prospective randomised controlled trial, and hence clinicians are guided by accumulated experience in the form of case series from high-volume centres [24-26]. Given the rarity of pancreatic metastases, it is understandably difficult to accrue sufficient data to justify any particular management approach. The results of our systematic review suggest that resection of cancers which have metastasised to the pancreas is feasible in selected patients and appears to confer a survival benefit. While the rate of complications after such procedures is not insignificant, the operative mortality is reassuringly low.

Renal cell carcinoma is the most commonly reported metastatic tumour to be resected from the pancreas, as evinced by the number of case series and reviews focusing solely on this clinical entity. This systematic review identified RCC to be the primary tumour in 62.6% of cases. 5-year survival after pancreatectomy for metastatic RCC was 70.4%. While extrapolating from small-volume case series is not ideal, the consensus from all articles included in this review is that patients with RCC metastasising to the pancreas benefit from resection.

Metastasectomy for metastatic RCC is a well-established treatment modality, particularly in the case of lung metastases [34]. The most recent guidelines from the European Organisation for Research and Treatment of Cancer's Genito-Urinary group on the management of metastatic RCC are in favour of metastasectomy, without reference to any particular metastatic site [35]. The management of RCC has recently been revolutionised with the advent of tyrosine kinase inhibitors, and it has been hypothesised that these may augment or even obviate the need for metastasectomy in the future. To our knowledge, only one study thus far has specifically looked at the effect of tyrosine kinase inhibitors in the setting of pancreatic metastases: Medioni et al performed a retrospective chart review at three sites involving 15 adult patients and concluded that sunitinib was effective in the treatment of RCC with pancreatic metastases [36]. However, median follow-up was only 20 months, and the authors themselves conceded that surgery remains the only potentially curative management option in this disease. Furthermore, given the heterogenous genetic makeup of RCC, with extreme genetic variability in different regions of the same tumour, there are obvious advantages in surgically removing the entire tumour mass [37].



Several groups have used the revised Memorial Sloan Kettering risk stratification tool to characterise their patients with RCC metastases; this risk calculator allocates a score based on the presence or absence of six adverse prognostic indicators in order to stratify patients with metastatic RCC into 'favourable', 'intermediate' and 'poor' risk groups [32, 33]. While Reddy and Zerbi found that those patients with pancreatic metastases from RCC, who were found retrospectively to have been in the "favourable" category, appeared to benefit most from resection [18, 23], Konstantinidis et al found no such correlation [12].

A thorough systematic review in 2009 examined all available case reports and patient series of RCC with pancreatic metastases available at that time, and concluded that patients with such metastases who are fit for surgery should be considered for curative resection [27]. The authors cautioned that patients with early multi-organ metastases might be better managed with observation and neoadjuvant therapy, as early recurrence seemed to predict a more aggressive clinical course. Our review yielded limited information regarding this scenario. Few papers have examined this issue of multi-organ metastases in any depth. Niess et al directly compared the outcome of patients with extrapancreatic metastases at the time of their resection, versus those with isolated pancreatic metastases. They reported a median survival of 11 months in their eight patients with multi-organ disease, while the 18 patients without extrapancreatic metastases had a median survival of 64 months ( $p = 0.05$ ) [17]. Strobel et al found an association between extrapancreatic disease and shorter median survival on univariate analysis ( $p = 0.0386$ ) but not on multivariate analysis. Interestingly, Zerbi et al excluded 11 patients with simultaneous lung and pancreatic metastases from their total patient cohort on the grounds of unresectability [23]. Based on data extracted from all the papers cited in this study, patients presenting with extrapancreatic metastases appeared to have a significantly shorter median survival than those with isolated pancreatic metastases. Therefore, despite the temptation to perform a multivisceral resection in such patients, it could be argued that these presentations represent aggressive, widespread disease, and that a poor oncological outcome is to be expected.

It was not possible to extract any meaningful data from our systematic review to compare outcomes in patients with short versus long DFIs, or to compare the DFIs of different primary tumours. Furthermore, no papers directly compared the survival of patients with synchronous versus metachronous metastases. It was possible to extract some data from the included studies to compare these outcomes, but no statistically significant difference could be demonstrated between the two groups. In general, metastasectomies for synchronous metastases are associated with

shorter median survival than resection of metachronous metastases; this has been shown in the case of hepatectomy for colorectal metastases [28, 29], pulmonary resection for RCC metastases [30] and adrenalectomy for metastatic non-small-cell lung cancer [31]. The previously-mentioned review of case reports and series of pancreatectomy for metastatic RCC suggest that the same principle applies [27]; our data are not consistent with this, but a dedicated study looking specifically at this question remains to be performed. The reason for this association between synchronous metastases and shorter overall survival following metastasectomy remains to be elucidated—it may indicate a more aggressive underlying biology in the primary tumour, or else reflect the increased morbidity following resection of both the primary and the metastasis either simultaneously or in quick succession.

There are fewer data supporting metastasectomy for non-RCC primaries. Three studies directly compared outcomes of resection for metastatic RCC versus all others; all showed a trend towards a shorter median survival for non-RCC metastasectomies [7, 11, 20]. However, given the aggressive nature of the other primaries in question, this is not to suggest that no survival benefit at all is gained from such resections. Given the well-established practice of metastasectomy in sarcoma [38], it is reasonable to attempt resection of pancreatic metastases in such patients if they may thus be rendered disease free. The only study to have exclusively evaluated colorectal metastases to the pancreas analysed data from nine patients, and hence did not meet the inclusion criteria for this review. The authors found a median survival of 17.4 months after pancreatic metastasectomy for colorectal carcinoma [39]. They concluded that, bearing in mind the minimal data available, resection of such metastases provides good palliation of symptoms, while not conferring any particular survival benefit over conventional chemotherapy. There are far too few examples of metastasectomy for other malignancies to make any recommendations.

Several papers have considered the various operative approaches to resection of secondary tumours of the pancreas, comparing “standard” resections (Whipple, distal or total pancreatectomy) to “atypical” resections (enucleation, middle pancreatectomy etc). Bassi et al found a higher rate of morbidity and local recurrence after atypical resections, and consequently advised standard resections for all pancreatic metastases [6]. However, other authors did not find any statistically significant difference in outcomes when comparing standard versus atypical resections [12, 21, 23]. Zerbi et al concluded that a thorough search for multifocal pancreatic metastases (including both manual palpation and intraoperative ultrasound) was a critical intra-operative step in deciding the type of resection to perform [23]. Reddy and Strobel both found peripancreatic lymph node

involvement in 20-30% of patients and hence advocated lymphadenectomy in all patients [18, 19]. Other case series and reviews did not find such a high rate of lymph node involvement. Ability to perform lymphadenectomy is one advantage in performing a standard resection; at this point, there is insufficient evidence to advocate whether or not a lymphadenectomy is required in this setting—all that is certain is that the overwhelming majority of surgeons have favoured “typical” resections up to this point. Meanwhile, surgical technique continues to evolve in new and exciting directions, with reports emerging of single-incision laparoscopic pancreatectomy for RCC metastases [40].

Pancreatic metastases are often assumed to represent primary pancreatic carcinoma, at least initially. Hyperenhancement on CT scan following the administration of intravenous contrast was found to be a distinguishing feature of metastatic RCC on one of the earliest case series we reviewed [10]. This has since been refined by reports from a number of other institutions—for example, metastatic lesions are best viewed during the early phases of three-phase helical CT [41], and more lesions are detected on arterial than on portal venous phase imaging [42]. However, the above reports only apply to metastatic RCC. More recently, several institutions have reported a high level of accuracy when using endoscopic ultrasound with fine-needle aspiration to diagnose pancreatic metastases from a wide range of different primary tumours [43, 44].

A degree of publication and selection bias is likely to be present in the studies we reviewed. The median MINORS score of 10/16 indicated a degree of methodological flaw in these papers, and is consistent with MINORS scores found in a recent systematic review of hepatic metastasectomy [24]. The criteria used in devising this score should act as a guide to future researchers designing studies examining outcomes following pancreatic metastasectomy. Nevertheless, it would be difficult to conceive of a study of metastasectomy that did not rely on a retrospective, non-randomised case series, and hence an element of methodological imperfection may be inevitable. However, this should not deter clinicians from striving to improve our methods of assessing outcomes following these procedures.

Our systematic review is therefore limited by the design of the studies available for inclusion, potential publication bias, heterogeneity of reported results and the lack of comparative studies whereby patients who undergo metastasectomy of pancreatic secondaries are compared to patients who undergo non-operative management of these lesions. However, it should be pointed out that there are no randomised studies of metastasectomy in any setting [24-26, 35]. A further limitation is the short duration of follow-up—11 of 18 studies reported 5-year survival data, but new data are

emerging to suggest that, in the case of liver metastases at least, 10-year survival may a more pertinent measure, as cancer-related death only appears to plateau after 10 years [45, 46].

In conclusion, radical resection of metastases to the pancreas is feasible and safe, and may confer a survival benefit for selected patients. We advocate such resections in patients for whom no contraindication to surgery exists; this recommendation is particularly strong in the case of metastatic renal cell carcinoma. However, presentation with multiorgan metastases may be an adverse prognostic indicator. Decisions regarding the choice of operative approach should be made on a case-by-case basis. The evidence base for the management of pancreatic metastases is quite poor at present, and a multicentre prospective trial comparing resection of secondary pancreatic tumours with conservative management would be required to provide a more definitive conclusion. Given the rarity of this clinical entity, our current practice when confronted by a patient with isolated pancreatic metastases can only be guided by clinical acumen and the best available evidence, all of which point in favour of resection.

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## References

1. Adsay NV, et al. Secondary tumors of the pancreas: an analysis of a surgical and autopsy database and review of the literature. *Virchows Archiv : an international journal of pathology* 2004;444:527-35.
2. Nakamura E, et al. Secondary tumors of the pancreas: clinicopathological study of 103 autopsy cases of Japanese patients. *Pathology international* 2001;51:686-90.
3. Moher D, et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Annals of internal medicine* 2009;151:264-9, w64.
4. Slim K, et al. Methodological index for non-randomized studies (minors): development and validation of a new instrument. *ANZ journal of surgery* 2003;73:712-6.
5. Alzahrani MA, et al. Metastases to the pancreas: the experience of a high volume center and a review of the literature. *Journal of surgical oncology* 2012;105:156-61.
6. Bassi C, et al. High recurrence rate after atypical resection for pancreatic metastases from renal cell carcinoma. *The British journal of surgery* 2003;90:555-9.
7. Crippa S, et al. Surgical treatment of metastatic tumors to the pancreas: a single center experience and review of the literature. *World journal of surgery* 2006;30:1536-42.
8. Eidt S, et al. Metastasis to the pancreas--an indication for pancreatic resection? *Langenbeck's archives of surgery / Deutsche Gesellschaft fur Chirurgie* 2007;392:539-42.
9. Facy O, et al. Interest of intraoperative ultrasonography during pancreatectomy for metastatic renal cell carcinoma. *Clinics and research in hepatology and gastroenterology* 2013.
10. Ghavamian R, et al. Renal cell carcinoma metastatic to the pancreas: clinical and radiological features. *Mayo Clinic proceedings Mayo Clinic* 2000;75:581-5.
11. Jarufe N, et al. Surgical treatment of metastases to the pancreas. *The surgeon : journal of the Royal Colleges of Surgeons of Edinburgh and Ireland* 2005;3:79-83.
12. Konstantinidis IT, et al. Metastatic tumors in the pancreas in the modern era. *Journal of the American College of Surgeons* 2010;211:749-53.
13. Law CH, et al. Pancreatic resection for metastatic renal cell carcinoma: presentation, treatment, and outcome. *Annals of surgical oncology* 2003;10:922-6.
14. Le Borgne J, et al. Pancreaticoduodenectomy for metastatic ampullary and pancreatic tumors. *Hepato-gastroenterology* 2000;47:540-4.
15. Mourra N, et al. Isolated metastatic tumors to the pancreas: Hopital St-Antoine experience. *Pancreas* 2010;39:577-80.
16. Moussa A, et al. Pancreatic metastases: a multicentric study of 22 patients. *Gastroenterologie clinique et biologique* 2004;28:872-6.
17. Niess H, et al. Surgery for metastasis to the pancreas: is it safe and effective? *Journal of surgical oncology* 2013;107:859-64.
18. Reddy S, et al. Pancreatic resection of isolated metastases from nonpancreatic primary cancers. *Annals of surgical oncology* 2008;15:3199-206.
19. Strobel O, et al. Survival data justifies resection for pancreatic metastases. *Annals of surgical oncology* 2009;16:3340-9.
20. Untch BR and Allen PJ. Pancreatic metastasectomy: The Memorial Sloan-Kettering experience and a review of the literature. *Journal of surgical oncology* 2013. Epub ahead of print Oct 7 2013. DOI 10.1002/jso.23460
21. Yazbek T and Gayet B. The place of enucleation and enucleo-resection in the treatment of pancreatic metastasis of renal cell carcinoma. *JOP : Journal of the pancreas* 2012;13:433-8.
22. You DD, et al. Surgical resection of metastasis to the pancreas. *Journal of the Korean Surgical Society* 2011;80:278-82.
23. Zerbi A, et al. Pancreatic metastasis from renal cell carcinoma: which patients benefit from surgical resection? *Annals of surgical oncology* 2008;15:1161-8.
24. Aubin JM, et al. Systematic review and meta-analysis of liver resection for metastatic melanoma. *The British journal of surgery* 2013;100:1138-47.

25. Primrose J, et al. Lung metastasectomy in colorectal cancer: is this surgery effective in prolonging life? *Respirology* (Carlton, Vic) 2010;15:742-6.
26. Simmonds PC, et al. Surgical resection of hepatic metastases from colorectal cancer: a systematic review of published studies. *British journal of cancer* 2006;94:982-99.
27. Tanis PJ, et al. Systematic review of pancreatic surgery for metastatic renal cell carcinoma. *The British journal of surgery* 2009;96:579-92.
28. Sugawara Y, et al. Estimating the prognosis of hepatic resection in patients with metastatic liver tumors from colorectal cancer with special concern for the timing of hepatectomy. *Surgery* 2001;129:408-13.
29. Miller G, et al. Outcomes after resection of synchronous or metachronous hepatic and pulmonary colorectal metastases. *Journal of the American College of Surgeons* 2007;205:231-8.
30. Hofmann HS, et al. Prognostic factors and survival after pulmonary resection of metastatic renal cell carcinoma. *European urology* 2005;48:77-81; discussion -2.
31. Tanvetyanon T, et al. Outcomes of adrenalectomy for isolated synchronous versus metachronous adrenal metastases in non-small-cell lung cancer: a systematic review and pooled analysis. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology* 2008;26:1142-7.
32. Mekhail TM, et al. Validation and extension of the Memorial Sloan-Kettering prognostic factors model for survival in patients with previously untreated metastatic renal cell carcinoma. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology* 2005;23:832-41.
33. Motzer RJ, et al. Survival and prognostic stratification of 670 patients with advanced renal cell carcinoma. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology* 1999;17:2530-40.
34. Murthy SC, et al. Can we predict long-term survival after pulmonary metastasectomy for renal cell carcinoma? *The Annals of thoracic surgery* 2005;79:996-1003.
35. de Reijke TM, et al. EORTC-GU group expert opinion on metastatic renal cell cancer. *European journal of cancer (Oxford, England : 1990)* 2009;45:765-73.
36. Medioni J, et al. Response of renal cell carcinoma pancreatic metastasis to sunitinib treatment: a retrospective analysis. *The Journal of urology* 2009;181:2470-5; discussion 5.
37. Gerlinger M, et al. Intratumor heterogeneity and branched evolution revealed by multiregion sequencing. *The New England journal of medicine* 2012;366:883-92.
38. Pawlik TM, et al. Results of a single-center experience with resection and ablation for sarcoma metastatic to the liver. *Archives of surgery (Chicago, Ill : 1960)* 2006;141:537-43; discussion 43-4.
39. Sperti C, et al. Metastasis to the pancreas from colorectal cancer: is there a place for pancreatic resection? *Diseases of the colon and rectum* 2009;52:1154-9.
40. Barbaros U, et al. Single incision laparoscopic pancreas resection for pancreatic metastasis of renal cell carcinoma. *JSLs : Journal of the Society of Laparoendoscopic Surgeons / Society of Laparoendoscopic Surgeons* 2010;14:566-70.
41. Ng CS, et al. Metastases to the pancreas from renal cell carcinoma: findings on three-phase contrast-enhanced helical CT. *AJR American journal of roentgenology* 1999;172:1555-9.
42. Corwin MT, et al. Renal cell carcinoma metastases to the pancreas: value of arterial phase imaging at MDCT. *Acta radiologica (Stockholm, Sweden : 1987)* 2013;54:349-54.
43. El H, II, et al. Endoscopic ultrasound-guided biopsy of pancreatic metastases: a large single-center experience. *Pancreas* 2013;42:524-30.
44. Atiq M, et al. Role of endoscopic ultrasonography in evaluation of metastatic lesions to the pancreas: a tertiary cancer center experience. *Pancreas* 2013;42:516-23.
45. Pulitano C, et al. What defines 'cure' after liver resection for colorectal metastases? Results after 10 years of follow-up. *HPB : the official journal of the International Hepato Pancreato Biliary Association* 2010;12:244-9.

46. Tomlinson JS, et al. Actual 10-year survival after resection of colorectal liver metastases defines cure. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology* 2007;25:4575-80.