JBUON 2018; 23(6): 1648-1654
ISSN: 1107-0625, online ISSN: 2241-6293 • www.jbuon.com
E-mail: editorial_office@jbuon.com

ORIGINAL ARTICLE

Metastasectomy of pancreatic and periampullary adenocarcinoma to solid organ: The current evidence

Mahmud Saedon[1], Ioannis Maroulis[2], Adam Brooks[1], Evangelos Alexiou[3], Konstantinos Bouliaris[3], Theofilos Amanatidis[2], Stylianos Germanos[2,3]

[1]Nottingham University Hospitals NHS Trust, United Kingdom; [2]General University Hospital of Patras, Greece; [3]General Hospital of Larissa, Greece

Summary

Purpose: *Pancreatic and periampullary adenocarcinoma have not generally been included in the tumour types considered for metastasectomy. However, there is an increasing interest that metastasectomy in well-selected patients can prolong survival. This review aims to establish the recent evidence on the surgical management of oligometastatic disease and survival outcome in patients who underwent metastasectomy focusing on isolated hepatic and pulmonary metastases.*

Methods: *A systematic search was performed in the PubMed database to identify all original articles on the role of metastasectomy for oligometastasis of pancreatic and periampullary adenocarcinoma. Data on methodologies used, 1,3,5 – year survival and median overall survival were summarized, and used to address relevant clinical questions related to the survival outcome in patients who underwent metastasectomy.*

Results: *Sixteen studies were included in this review. All the studies included were retrospective and heterogenous in nature and did not have a uniform reporting on survival outcomes.*

Conclusion: *There is insufficient evidence to support a change of current practice in managing metastatic pancreatic and periampullary cancer. However, patients with ampullary cancer as the primary and any patients with first recurrence as isolated pulmonary metastases had better prognosis than patients with synchronous metastasis or metastases to the liver. This need to be explored in future studies.*

Key words: *metastasectomy, pancreatic adenocarcinoma, periampullary adenocarcinoma*

Introduction

Approximately, 50% of new pancreatic and periampullary adenocarcinoma cases are found to have distant metastases at diagnosis [1]. Owing to the difficulties in early detection, patients often present with locally advanced and unresectable or metastatic disease. Even with surgical therapy actual 5-year survival is only 15% for pancreatic cancer, 27% for distal cholangiocarcinomas and 39% for ampullary cancers [2]. Metastatic or recurrent cancer is notoriously difficult to manage surgically, as it is characterised by aggressive growth, a multifocal recurrence pattern, and technical unresectability [3]. Even with intensive treatment regimens, median overall survival for metastatic pancreatic cancer patients with good performance status has been reported to be less than one year [4,5].

Currently, the most effective treatment for the tumours is surgical resection, but patients with metastases are considered unresectable based upon National Comprehensive Cancer Network (NCCN) and National Cancer Institute (NCI) treatment guidelines [6,7]. Palliative chemotherapy remains the mainstay of metastatic pancreatic carcinoma [8].

Correspondence to: Stylianos Germanos, MD. Surgical Department General University Hospital of Patras, Rio 265 04, Patras, Greece
Tel: +30 2613603825, Fax: +30 2613603299, E-mail: stylianos.germanos@yahoo.co.uk
Received: 23/05/2018; Accepted: 25/06/2018

More recent evidence suggests that a complete resection of metastasis can potentially be curative and prolong survival [9]. An improvement in systemic therapy combined with metastasectomy has improved survival in other advance disease such as colorectal cancer where 5-year overall survival is upward of 50% [10]. Whether this translates to metastatic pancreatic cancer in the current era is unknown due to the paucity of data.

The aim of this systematic review is to investigate the survival outcomes of metastasectomy for oligometastasis of pancreatic and periampullary adenocarcinoma.

Methods

Inclusion criteria

Only published studies that reported 5 or more patients of oligometastases of primary pancreatic cancer were included with an intention for statistical analysis. We excluded studies without original patient data such as case reports or case series which included less than 5

Table 1. Patient perioperative characteristics

Author	*Year*	*Study design*	*Number of patients*	*Organ Metastasectomy*	*Synchronous (S) vs Metachronous (M)*	*1- Year OS (%)*	*3- Year OS (%)*	*5- Year OS (%)*	*Median OS (months)*
Wright GP et al [21]	2016	Retrospective	n=23: Liver=16, Lung=6, Peritoneum=2	Liver = 9, lung = 2	S	N/A	N/A	37.1	N/A
Claire D et al [22]	2016	Retrospective-Case Control*	n=74: Liver=37, Lung=37	Lung = 3	M	N/A	N/A	N/A	31.8
Tachezy et al [19]	2016	Retrospective-Case Control**	n=69: Liver=69	Liver = 69	S	N/A	N/A	N/A	14
Robinson LA et al [23]	2016	Retrospective – Case Control***	n=16	Lung = 16	M	N/A	N/A	37.1	28
Downs-Canner S et al [26]	2015	Retrospective	n=8	Lung = 8	M	N/A	N/A	50	67.5
Yamashita K et al [9]	2015	Retrospective	n=14	Lung = 2	M	N/A	N/A		N/A
Klein F et al [11]	2012	Retrospective– Case Control****	n=22	Liver = 22	S	N/A	5		7.1
Thomas RM et a l[40]	2012	Retrospective	n=7	Lung = 7	M	N/A	N/A	N/A	N/A
Arnaoutakis et al [27]	2011	Retrospective	n=9	Lung = 10	M	N/A	N/A	N/A	51
Singh A et al [12]	2010	Case Series	n=7	Liver = 7	S	N/A	N/A	N/A	N/A
De Jong et al [13]	2010	Retrospective	n=20	Liver = 20	S & M	N/A	8	N/A	13
Seelig SK et al [14]	2010	Retrospective	n=14	Liver = 14	S	43	17	N/A	11
Shrikhande SV et al [15]	2007	Retrospective	n=11	Liver = 11	S	58.9	N/A	N/A	11.4
Gleisner AL et al [16]	2007	Retrospective	n=17	Liver = 17	S	N/A	6.7	N/A	5.9
Adam R et al [20]	2006	Retrospective	n=40	Liver = 40	S & M	N/A	N/A	25	20
Takada T et al [17]	1997	Retrospective	n=11	Liver = 11	S	N/A	N/A		6
Klempnauer J et al [18]	1996	Retrospective	n=20	Liver = 20	S & M	41			8.3

OS overall survival; * Metastatic lung vs liver; ** Resected primary pancreatic cancer vs Bypass pancreatic cancer; *** Metastatic lung vs Non metastatic lung; **** Metastatic liver vs Non metastatic liver; N/A: not available

patients, review articles, 'grey literature' (non-refereed journals and conference proceedings), commentaries, letters, and editorials.

Search strategy

The MEDLINE database was searched via the PubMed interface using keywords: '(pancreatic cancer OR periampullary adenocarcinoma) AND (metastases OR recurrence) AND surgical management'. We concentrated on reports published for the last 5 years.

Titles and abstracts, where available, were screened initially and articles not meeting the inclusion criteria were excluded at this stage. The full-text versions of the remaining studies were obtained for further detailed evaluation. Studies without original patient data such as reviews and letters, and those for which an English translation could not be obtained, were excluded.

Study selection and data extraction

After the initial electronic search, we identified all relevant abstracts and excluded articles not meeting the inclusion criteria. Two reviewers screened the full-text versions of the remaining studies for detailed evaluation for eligibility. To avoid double-counting patient data, we evaluated multiple articles from the same authors and institutions for possible duplication and overlap. We extracted all relevant data into Microsoft@Excel (Microsoft, Redmond, Washington, USA), and cross-checked them for accuracy. We resolved disagreements about the inclusion of the studies through discussion between the reviewers.

Results

1035 abstracts were identified following the systematic search of the MEDLINE database. 16 studies were included in this review. All the studies included were retrospective, had small numbers of patients, were heterogeneous in nature and did not have a uniform reporting on survival outcomes. Therefore, we were not able to perform meta-analysis and the results were presented as narrative review focussing on lung and hepatic metastases. The results were summarised in the Table 1 focussing on 1-, 3- and 5- year survival and median overall survival.

Liver

Liver is the most common site of pancreatic tumor and ampullary metastasis. Early publications on hepatic resection for hepatic metastasised pancreatic carcinoma focussed on the safety and feasibility of hepatic resection. However, the median survival remains poor where most studies demonstrated less than 12 months of median overall survival (Table 1).

Klein et al. [11] reported on 22 patients who underwent pancreatic resection and synchronous liver resection for metastasized pancreatic adenocarcinoma. All liver metastases were detected during operative exploration as an incidental finding. All patients had standard lymphadenectomy and 7 of them underwent liver segmentectomy while the other 15 had an enucleation of the metastasis. R0 (complete resection) resection was achieved in 7 patients (32%) with a median survival of 13 months. Patients with removal of all macroscopic disease but positive tumor margin (R1 resection, 68%) had a median survival of 6.5 months. There were no difference of postoperative mortality and morbidity between hepatic metastasised pancreatic carcinoma who underwent simultaneous pancreatic/hepatic resection and nonmetastasised pancreatic carcinoma only resection.

Singh et al. [12] reported their experience of seven patients with pancreatic head cancer or periampullary cancer who underwent synchronous resection of an isolated liver metastasis with a pancreaticoduodenectomy. Three out of four patients with periampullary cancer were disease free at follow-up after 16, 48 and 60 months. All three patients with pancreatic head cancer died at 7, 14 and 18 months. Despite the too small number of patients this could be an indication that periampullary cancers with a traditionally better prognosis as compared to pancreatic cancer might be candidates for synchronous resection of liver oligometastasis.

De Jong et al. [13] reported on 40 patients with hepatic metastasis from peri-ampullary carcinomas. 85% of the patients presented with a solitary tumour with a size of 0.2 to 5.9 cm. Pancreatic head adenocarcinoma was the most common primary tumour (n=20) followed by ampullary cancer (n=10), distal common bile duct (n=5) and duodenum (n=5). Median survival following hepatic metastasectomy from intestinal tumours (ampulla and duodenum) was 23 months with 3 years survival of 33% compared with 13 months and 3 years survival of 8% for patients with pancreaticobiliary tumours (p=0.05). The conclusion of this study was that patients with solitary or oligo-centic hepatic metastasis from intestinal type primary tumours should be considered for resection.

Seelig et al. [14] reported 43% 1- year overall survival and 11 months of median overall survival which was not significantly different from a matched-pair group of patients who underwent pancreatic resection for adenocarcinoma of the pancreas and had a median survival of 15.6 months. They concluded that the decision for metastasectomy should be set on individual basis and only when R0 resection seems possible. Radical resection of M1 (the cancer has spread to distant or-

gans/lymph nodes) pancreatic carcinoma may be justified in young patients with strong desire to undergo surgery in specialized centres with low morbidity and mortality.

Shrikhande et al. [15] included in their study patients who were in good health with high probability of complete pancreatic resection with small number of isolated liver metastases. They reported 58.9% of 1-year overall survival and 11.4 months of median overall survival which is similar to other published data.

In Gleisner et al. [16] 1563 patients with periampullary carcinoma or pancreatic adenocarcinoma, only 22 patients underwent simultaneous hepatic resection for synchronous liver metastasis. They reported 6.7% 3–year overall survival and 5.9 months of median overall survival in their study. They concluded that synchronous resection of pancreatic cancer and liver metastasis did not result in long term survival in the majority of patients.

Takada et al. [17] reported a similar finding as Gleisner et al. [16] series which showed no improvement in overall survival in addition to high surgical morbidity and mortality.

Klempnauer et al. [18] reported a median survival of 8.3 months after synchronous hepatic and pancreatic resection an 5.8% after metachronous hepatic resection.

In a retrospective multicentre study from Europe which included 69 patients in a 20-year period, Tachezy et al. [19] reported significant survival benefit for patients receiving a combined liver and pancreas resection compared with patients with liver metastases who did not undergo resection (14.5 vs 7.5 months, p<0.001). The 5-year survival was 5.8% after combined resection and 0% in the non-resection group. Stratification regarding the location of the tumour showed that tumours located to the body/tail of the pancreas did not show differences in median overall survival and there was significant survival benefit only for tumours located in the head.

Adam et al. [20] data demonstrated improved long term survival with 5-year survival rate of 25% and a median overall survival of 20 months for those who underwent metastatic hepatic resection from pancreatic tumour and a favourable 5-year survival of 46% in those patients with primary ampullary tumours.

A bi-institutional retrospective review [21] of 23 patients who were diagnosed with stage IV pancreatic cancer and underwent surgery following chemotherapy with favourable imaging and CA 19-9 response reported median overall survival for all patients who underwent liver and lung metastasectomy was 18.2 months relatively comparable to the survival seen in patients who have undergone curative resection in the absence of known distant metastasis. No separate data on overall median survival available for those who underwent hepatic metastasectomy or pulmonary metastasectomy.

Pulmonary

Isolated Pulmonary metastasis as a first site of dissemination is very rare. Early publications on pulmonary resection for pulmonary metastasised pancreatic carcinoma focussed on the safety and feasibility of pulmonary resection. Unlike hepatic resection, patients who underwent pulmonary resection seem to have a longer median overall survival up to 67.5 months (Table 1).

Claire et al. [22] noted delayed appearances of metastasise were observed in the lung - metastasised group in comparison to the liver-metastasised group (59 vs 11%; p<0.0001). Overall, the lung-metastasised group has longer median survival in comparison to the liver-metastasised group (31.8 months vs 9.1, HR = 0.24 (0.14-0.42), p<0.001). Key observations noted in this study were late development, less nodules and lower tumour marker expression associated with lung metastasised correlated with higher survival than the liver-metastasised group.

Robinson et al. [23] in a retrospective cohort study of primary pancreatic and biliary carcinoma patients (n=16) who, after a pacreaticoduodenectomy of their primary underwent a pulmonary resection reported a median overall survival of 28 months corresponding to an estimated 5-year survival rate of 37.1%. They pointed out the general criteria for pulmonary metastasectomy for potential therapeutic benefit based on the previous published studies [24,25]: 1: the primary cancer was completely resected or controlled; 2: limited number of pulmonary metastasis (<6); 3: all pulmonary metastasises can be removed; 4: the patient can tolerate the necessary lung resection; 5: no other metastasises apart from the pulmonary metastases; 6: no better alternative treatments are available.

Yamashita K et al. [9] identified 99 recurrence out of 142 resected pancreatic cancer between 2003 and 2012. Patients with isolated pulmonary recurrence (n=14) had longer median overall survival than other metastases (40.3 vs 20.9 months). Resected pulmonary recurrence (n=2) survived for ~70 months after the primary resection.

Downs-Canner S et al. [26] study included 78 patients who underwent resection of the primary cancer tumour. The median survival from time of diagnosis for those patients with lungs as a first recurrence following pancreatic resection was 35.6

months (95% CI 31.4-6.1) compared to 23.8 months (95% CI 18.97-31.2) for those with abdominal organ metastasised first. 8 patients who underwent pulmonary metastasised resected was found to have significantly better overall median survival and 5-year survival rate in comparison to those who underwent metastases-directed chemotherapy or observation (67.5 vs. 33.8 months, 50 vs 8.7%, p=0.0006).

Arnaoutakis et al. [27] study included 9 patients who underwent pulmonary resection for their metastatic pancreatic cancer over a 10 years period. These patients had had overall median survival of 51 months compared to 23 months in matched controls.

Discussion

Pancreatic cancer is estimated to become the second leading cause of death in the US by the year 2020. It is believed to be a systemic disease on diagnosis and even patients with T1 tumors (<20mm) metastasized in 45% of cases [28]. Liver is the most common site of metastasis followed by lung, brain and bone. Our review shows an increasing evidence that metastatic disease heterogenous and that patients with pulmonary metastasis represent a different biologic phenotype than patients who develop liver metastasis.

Surgery for pancreatic cancer continues to evolve. During the mid-80s pancreatic surgery resection rates were less than 3% with 30 days mortality more than 27% [29]. Nowadays improvements in perioperative management in combination with vascular resections in pancreatic surgery have increase resectability rates up to 20% with 30 days mortality rates less than 4% in specialized centres [29].

Periampullary tumors are rare and determining the precise origin of cancer can be challenging due to the anatomic complexity of the region which is enclosed by the distal bile duct, ampulla of Vater and duodenum. All periampullary tumors are divided histopathologically into intestinal type or pancreatobiliary type, irrespectively of their anatomic origin with the intestinal type having more favorable prognosis [30].

There is some evidence that pancreatic adenocarcinoma patients with isolated lung metastasis have better outcome compared to patients with isolated liver metastasis. Surgery to the primary tumour and surgery to the metastatic disease were associated with better overall survival and pancreatic cancer specific survival in a multivariate analysis which included 13233 patients with stage IV pancreatic cancer [31].

Current evidence has demonstrated a similar natural history of metastatic pancreatic cancer and metastatic colorectal cancer. In advanced colorectal cancer, hepatic metastasis is more common in patients with synchronous metastasis, while pulmonary metastasis is more common in those with metachronous metastasis [32]. The pulmonary metastasis group showed a better prognosis [32].

Series of studies have demonstrated a similar finding associated the prolonged time to lung metastases development to favourable outcomes of pulmonary metastasectomy. This is also reflected in the trend of metastasectomy for oligometastasis of pancreatic cancer. More data is currently required regarding the feasibility and outcomes of pulmonary resection of the pancreatic cancer.

The outcomes of metastasectomy for oligometastasis of pancreatic cancer in recent years especially with modern chemotherapeutic regimens are unknown and restricted to case series. Approximately up to 80% of pancreatic carcinoma resected patients will develop disease recurrence within 2 years of surgery [33,34], and die of their recurrence at a median 14-20 months [35]. The potential benefit of offering resection is to provide an extended time period for the patient to be off systemic chemotherapy treatment and potentially enhancing quality of life.

Previous studies reported liver as the most common metastatic site in part because it is the first major organ reached by portal venous blood draining from the pancreas, followed by the peritoneum and lung, pleura, bones and adrenal gland [9,36,37]. Current published data has shown that synchronous and metachronous pancreatectomy and hepatic metastasectomy can be performed safely without a significant increase in morbidity and mortality [11,13,14,38,39]. However, the median overall survival remains poor.

Patients who developed lung metastases appear to have a prolonged time to development of metastases [9,27,40]. Among those who do achieve 5-year survival following resected primary pancreatic cancer, recurrence is most commonly observed in the lungs [36]. Yamashita et al. [9] reported patients with isolated pulmonary recurrence has longer median overall survival than other type of metastases with 5-year overall survival rate was 14.9% among patients with pulmonary metastases, and was 4.9% among patients with other kinds of recurrences. More recent report by Downs-Canner et al. [26] demonstrated longer median survival from time of diagnosis for those patients with lungs as a first recurrence following pancreatic resection compared to those with abdominal organ

metastasised first. They also reported that patients who underwent pulmonary metastasised resected was also found to have significantly better overall median survival and 5-year survival rate in comparison to those who underwent metastases-directed chemotherapy or observation.

Should metastasectomy for periampullary cancers be the next step for increasing resectability and improving survival? There is some evidence that patients with metachronous metastasis particularly isolated to the lung may benefit from surgery and also patients with periampullary cancer which per se has more indolent course may benefit from metastasectomy.

Limitations

The review suffers from the inherent limitations to any retrospective series that has a small sample size and potential for selection and lead-time bias.

Due the heterogeneous nature of the studies, we cannot draw conclusions confounding factors such as role of chemotherapy, synchronous or metachronous disease and anatomical location of the metastasis within the organs. It is also difficult to compare the outcome of metastasectomy between organs as evidence suggested that each metastatic organ has different biologic phenotype.

Owing to the limited number of patients who qualify for the metastasectomy in pancreatic adenocarcinoma, clinical registry may be more appropriate than prospective randomised trial. Further analysis however is required.

Conflict of interests

The authors declare no conflict of interests.

References

1. Louvet C, Philip PA. Accomplishments in 2007 in the treatment of metastatic pancreatic cancer. Gastrointest Cancer Res 2008;2:37-41.
2. Ammori JB, Choong K, Hardacre JM. Surgical Therapy for Pancreatic and Periampullary Cancer. Surg Clin North Am 2016;96:1271-86.
3. Sperti C, Pasquali C, Piccoli A, Pedrazzoli S. Recurrence after resection for ductal adenocarcinoma of the pancreas. World J Surg 1997;21:195-200.
4. Kruger S, Haas M, Burger PJ et al. Isolated pulmonary metastases define a favorable subgroup in metastatic pancreatic cancer. Pancreatology 2016;16:593-8. doi: 10.1016/j.pan.2016.03.016.
5. Von Hoff DD, Ervin T, Arena FP et al. Increased survival in pancreatic cancer with nab-paclitaxel plus gemcitabine. N Engl J Med 2013;369:1691-703.
6. Mayo SC, Nathan H, Cameron JL et al. Conditional survival in patients with pancreatic ductal adenocarcinoma resected with curative intent. Cancer 2012;118:2674-81.
7. Sohn TA, Yeo CJ, Cameron JL et al. Resected adenocarcinoma of the pancreas-616 patients: results, outcomes, and prognostic indicators. J Gastrointest Surg. 2000;4:567-579.
8. Conroy T, Desseigne F, Ychou M et al. FOLFIRINOX versus gemcitabine for metastatic pancreatic cancer. N Engl J Med 2011;364:1817-25.
9. Yamashita K, Miyamoto A, Hama N et al. Survival Impact of Pulmonary Metastasis as Recurrence of Pancreatic Ductal Adenocarcinoma. Dig Surg 2015;32:464-71.
10. Leal JN, Bressan AK, Vachharajani N et al. Time-to-Surgery and Survival Outcomes in Resectable Colorectal Liver Metastases: A Multi-Institutional Evaluation. J Am Coll Surg 2016;222:766-79.
11. Klein F, Puhl G, Guckelberger O et al. The impact of simultaneous liver resection for occult liver metastases of pancreatic adenocarcinoma. Gastroenterol Res Pract 2012;2012:939350.
12. Singh A, Singh T, Chaudhary A. Synchronous resection of solitary liver metastases with pancreaticoduodenectomy. JOP 2010;11:434-8.
13. de Jong MC, Tsai S, Cameron JL et al. Safety and efficacy of curative intent surgery for peri-ampullary liver metastasis. J Surg Oncol 2010;102:256-63.
14. Seelig SK, Burkert B, Chromik AM, Tannapfel A, Uhl W, Seelig MH. Pancreatic resections for advanced M1-pancreatic carcinoma: the value of synchronous metastasectomy. HPB Surg 2010;2010:579672.
15. Shrikhande SV, Kleeff J, Reiser C et al. Pancreatic resection for M1 pancreatic ductal adenocarcinoma. Ann Surg Oncol 2007;14:118-27.
16. Gleisner AL, Assumpcao L, Cameron JL et al. Is resection of periampullary or pancreatic adenocarcinoma with synchronous hepatic metastasis justified? Cancer 2007;110:2484-92.
17. Takada T, Yasuda H, Amano H, Yoshida M, Uchida T. Simultaneous hepatic resection with pancreato-duodenectomy for metastatic pancreatic head carcinoma: does it improve survival? Hepatogastroenterology 1997;44:567-73.
18. Klempnauer J, Grothues F, Bektas H, Pichlmayr R. Long-term results after surgery for acute mesenteric ischemia. Surgery 1997;121:239-43.
19. Tachezy M, Gebauer F, Janot M et al. Synchronous resections of hepatic oligometastatic pancreatic cancer: Disputing a principle in a time of safe pancreatic operations in a retrospective multicenter analysis. Surgery 2016;160:136-44.

20. Adam R, Chiche L, Aloia T et al. Hepatic resection for noncolorectal nonendocrine liver metastases: analysis of 1,452 patients and development of a prognostic model. Ann Surg 2006;244:524-35.
21. Wright GP, Poruk KE, Zenati MS et al. Primary Tumor Resection Following Favorable Response to Systemic Chemotherapy in Stage IV Pancreatic Adenocarcinoma with Synchronous Metastases: a Bi-institutional Analysis. J Gastrointest Surg 2016;20:1830-5.
22. Docoster Claire GM, Autret Aurelie, Turrini Oliver et al. Heterogeneity of metastatic pancreatic adenocarcinoma: Lung metastasis show better prognosis than liver metastasis - a case control study. Oncotarget 2016;7:45549-655.
23. Robinson LA, Tanvetyanon T, Springett G et al. Pulmonary metastasectomy for suspected pancreaticobiliary cancer. J Thorac Cardiovasc Surg 2016;152:75-82.
24. Ripley RT, Downey RJ. Pulmonary metastasectomy. J Surg Oncol 2014;109:42-6.
25. Thomford NR, Woolner LB, Clagett OT. The Surgical Treatment of Metastatic Tumors in the Lungs. J Thorac Cardiovasc Surg 1965;49:357-63.
26. Downs-Canner S, Zenati M, Boone BA et al. The indolent nature of pulmonary metastases from ductal adenocarcinoma of the pancreas. J Surg Oncol 2015;112:80-5.
27. Arnaoutakis GJ, Rangachari D, Laheru DA et al. Pulmonary resection for isolated pancreatic adenocarcinoma metastasis: an analysis of outcomes and survival. J Gastrointest Surg 2011;15:1611-7.
28. Chari ST, Kelly K, Hollingsworth MA et al. Early detection of sporadic pancreatic cancer: summative review. Pancreas 2015;44:693-712.
29. Bramhall SR, Allum WH, Jones AG, Allwood A, Cummins C, Neoptolemos JP. Treatment and survival in 13,560 patients with pancreatic cancer, and incidence of the disease, in the West Midlands: an epidemiological study. Br J Surg 1995;82:111-5.
30. Williams JL, Chan CK, Toste PA et al. Association of Histopathologic Phenotype of Periampullary Adenocarcinomas With Survival. JAMA Surg 2017;152:82-8.
31. Oweira H, Petrausch U, Helbling D et al. Prognostic value of site-specific metastases in pancreatic adenocarcinoma: A Surveillance Epidemiology and End Results database analysis. World J Gastroenterol 2017;23:1872-80.
32. Oh SY, Kim DY, Suh KW. Oncologic outcomes following metastasectomy in colorectal cancer patients developing distant metastases after initial treatment. Ann Surg Treat Res 2015;88:253-9.
33. Hattangadi JA, Hong TS, Yeap BY, Mamon HJ. Results and patterns of failure in patients treated with adjuvant combined chemoradiation therapy for resected pancreatic adenocarcinoma. Cancer 2009;115:3640-50.
34. Hernandez JM, Morton CA, Al-Saadi S et al. The natural history of resected pancreatic cancer without adjuvant chemotherapy. Am Surg 2010;76:480-5.
35. Conlon KC, Klimstra DS, Brennan MF. Long-term survival after curative resection for pancreatic ductal adenocarcinoma. Clinicopathologic analysis of 5-year survivors. Ann Surg 1996;223:273-9.
36. Katz MH, Wang H, Fleming JB et al. Long-term survival after multidisciplinary management of resected pancreatic adenocarcinoma. Ann Surg Oncol 2009;16:836-47.
37. Deeb A, Haque SU, Olowokure O. Pulmonary metastases in pancreatic cancer, is there a survival influence? J Gastrointest Oncol 2015;6:E48-51.
38. Nikfarjam M, Sehmbey M, Kimchi ET et al. Additional organ resection combined with pancreaticoduodenectomy does not increase postoperative morbidity and mortality. J Gastrointest Surg 2009;13:915-21.
39. McKay A, Sutherland FR, Bathe OF, Dixon E. Morbidity and mortality following multivisceral resections in complex hepatic and pancreatic surgery. J Gastrointest Surg 2008;12:86-90
40. Thomas RM, Truty MJ, Nogueras-Gonzalez GM et al. Selective reoperation for locally recurrent or metastatic pancreatic ductal adenocarcinoma following primary pancreatic resection. J Gastrointest Surg 2012;16:1696-704.