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Role of surgery in pancreatic cancer

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Abstract

Treatment of pancreatic cancer is multimodal and surgery is an essential part, mandatory for curative potential. Also chemotherapy is essential, and serious postoperative complications or rapid disease progression

may preclude completion of multimodal treatment. The sequence of treatment interventions has therefore become an important concern, and numerous ongoing randomized controlled trials compare clinical outcome after upfront surgery and neoadjuvant treatment with subsequent resection. In previous years, borderline resectable and locally advanced pancreatic cancer was most often considered unresectable. More effective chemotherapy together with the latest improvements in surgical expertise has resulted in extended operations, pushing the borders of resectability. Multivisceral resections with or without resection of major mesenteric vessels are now performed in numerous patients, resulting in better outcome, recorded as overall survival and/or patient reported outcome. But postoperative morbidity increases concurrently, and clinical benefit must be carefully evaluated against risk of potential harm, associated with new comprehensive multimodal treatment sequences. Even though cost/utility analyses are deficient, extended surgery has resulted in significantly longer and better life for many patients with no other treatment alternative. Improved selection of patients to surgery and/or chemotherapy will in the near future be possible, based on better tumor biology insight. Clinically available biomarkers enabling personalized treatment are forthcoming, but these options are still limited. The importance of surgical resection for each patient's prognosis is presently increasing, justifying sustained expansion of the surgical treatment modality.

Key words: Adjuvant chemotherapy; Neoadjuvant chemotherapy; Metastasis; Pancreatic cancer; Patient reported outcome; Survival

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Core tip: Both surgery and chemotherapy are mandatory in multimodal treatment of pancreatic cancer to obtain curative potential. The sequence of interventions is a core question: Upfront surgery or neoadjuvant chemotherapy with subsequent resection.

Also the role of extended operations incorporating reconstruction of major mesenteric vessels and multi-visceral resections is a matter of ongoing evaluation. The current direction of this development is increasing prognostic importance of surgical resection.

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INTRODUCTION

What should be the first treatment intervention in a patient with resectable pancreatic cancer (PC), surgery or chemotherapy? This is currently a core question for clinicians and patients, as standard of care is multimodal treatment, necessitating both^[1,2]. Increasing numbers of patients with borderline resectable or locally advanced tumors undergo resectional surgery, often after neoadjuvant chemotherapy^[3,4], but in metastatic disease palliative chemotherapy without resectional surgery is standard of care^[5]. Surgical expertise is rapidly improving due to technological development, reorganization of patient management and above all; better training of surgeons^[6,7], and the role of surgery in the multimodal treatment algorithm is revised continually^[8]. Available evidence and ongoing trials focusing the role of surgery, is summarized below, together with future topics of research and development.

CLARIFICATION OF CONCEPTS - SELECTION OF ENDPOINTS

Even though the purpose of resectional surgery is complete removal of the tumor (R0 resection), the distinction from R1 status (residual microscopic disease) is controversial. The first problem is two different R0 definitions, zero mm^[9] versus one mm^[10] tumor free margin. Second, divergence in pathology specimen examination is widespread even though a standardized protocol for examination of pancreaticoduodenectomy specimens was clearly described ten years ago^[10]. Also the dispersed tumor growth in PC^[11] and morphological heterogeneity in ductal adenocarcinoma of the pancreas^[12] contribute to incomparable data on R0 rates from different surgical centers. Rate of R0 resection is therefore an inappropriate endpoint in clinical studies, particularly after neoadjuvant chemotherapy. The tumor does not necessarily shrink from the periphery, but spot wise, and no clear definition of R0 status after neoadjuvant chemotherapy exists.

The rate of surgical resection after neoadjuvant treatment is another parameter, inappropriate as

endpoint in the evaluation of putative treatment benefit. In patients with a resectable tumor, the rate of resection decreases after neoadjuvant chemotherapy, as some patients become unresectable due to progressive disease. But in patients with borderline resectable or locally advanced tumors, resection rates are supposed to increase after neoadjuvant treatment, even though the resection rate does not yield core information on treatment significance.

The ultimate quality indicator of pancreatic surgery is clinical outcome in operated patients^[13], and only trials with overall survival (OS) and patient reported outcome (PRO)/quality of life (QoL) as endpoints can generate valid evidence, clarifying the role of surgery in the study population^[2,14].

PRIMARY RESECTABLE TUMORS

Neoadjuvant chemotherapy has been advocated in patients with resectable tumors to secure completion of systemic treatment^[15] which may be precluded by postoperative complications or early disease progression after upfront surgery^[16]. The net result of neoadjuvance is selection of patients with favorable tumor biology for subsequent resection. However, single center studies^[15,17] with median OS in the range 36-44.9 mo in this selected group, have left questions on the clinical consequences for the residual group mostly unanswered. Mokdad *et al*^[18] described median OS 26 mo in 2005 patients, operated after neoadjuvant chemotherapy compared to median 21 mo in 6015 patients after upfront surgery. However, this comprehensive report from the National Cancer Data Base for the years 2006-2012 is based on the same selection bias - still avoiding focus on outcome of conservative treatment. Metaanalysis, mainly based on retrospective studies, have not documented survival differences in patients operated upfront vs after neoadjuvant chemotherapy^[19], and randomized controlled trials (RCT) are mandatory. Currently accepted consensus is that patients with resectable tumors should undergo upfront surgery and subsequent adjuvant chemotherapy^[1]. However, numerous RCTs are running, one is the PEROPANC trial, opened April 2013 with endpoint OS^[20], and new evidence enabling improved clinical practice is foreseen within the near future.

At present, significant alterations of treatment sequences take place outside clinical trials. In the US, neoadjuvant chemotherapy is increasingly favored^[21], whereas the European preference tends to be upfront surgery^[22,23]. In line with the European strategy, different adjuvant regimens have been evaluated, and addition of Capecitabine to Gemcitabine was recently found to increase median survival to 27 mo in the ESPAC 4 trial^[24]. This is at present standard of care, but evaluation of even more effective antitumor regimens are under evaluation in ongoing trials, and

a scenario with second line treatment as an option in case of recurrent/progressive disease postoperatively seems to be in the pipeline. Adjuvant immunotherapy with RAS-peptides has been found to generate long term immunological memory, documented in a phase I/II study in 23 patients after resection of pancreatic ductal adenocarcinoma (PDAC)^[25] with no other adjuvant treatment. Five year survival was 22%, ten year 20%. In the ESPAC 1 study, including patients during approximately the same time interval, median survival without any adjuvant chemotherapy was median 8 mo, and adjuvant RAS vaccination seemingly increased survival. The clinical benefit of adjuvant immunotherapy it probably going to play an important role in the future^[26], even though it is not standard of care yet. But in this setting, removal of the primary tumor is crucial in order to avoid the effect of inhibitory regulatory T-cells^[27]. This perspective is favoring upfront surgery.

BORDERLINE RESECTABLE AND LOCALLY ADVANCED PANCRATIC CANCER

Borderline resectable tumors have been clearly defined radiologically^[28,29], and the possible benefit of neoadjuvant chemoradiation in this group was published by Katz *et al*^[30] 2008. Subsequently, the ability to stabilize metastatic PC has been demonstrated for FLFIRINOX in 2011^[31], then gemcitabine plus nab-paclitaxel in 2013^[32], both highly relevant regimens also for neoadjuvant evaluation. A meta-analysis including 13 studies on FOLFIRINOX-based neoadjuvant therapy in a total of 253 patients with borderline resectable (BRPC) or locally advanced pancreatic cancer (LAPC) tumors, described median survival in the range 13.7 to 24.2 mo^[3]. The Heidelberg group has recently published outcome in 575 LAPC patients all receiving neoadjuvant treatment and restaging between December 2001 and June 2015^[4]. In 125 patients, receiving neoadjuvant FOLFIRINOX, successful resection was possible in 76 (61%). Median OS in resected patients was 15.3 mo vs 8.5 mo after exploration alone. This information strongly support active multimodal treatment of BRPC and LAPC patients, as permanent cure seems achievable for some patients, also in these groups.

METASTATIC DISEASE

Metastatic PC (M1) is conceived a palliative condition in which surgical resection is contraindicated^[5,29]. Curative intent surgery (resection of primary tumor and metastases) has been evaluated in 29 M1 patients, published 2007. Median OS was 13.8 mo, one year survival 58.9%^[33], supporting the conservative guidelines. However, in a recent report 128 patients, undergoing resection of the primary

tumor and metastases, OS 12.3 mo and 10% five year survival was obtained^[34]. In another prospective study 11 patients obtained median OS 39 mo after resection of the pancreatic tumor and metastases^[35]. Recent evidence also suggest that patients with only pulmonary metastases is a subgroup with better prognosis^[36], and selected M1 patients seem to benefit from surgical resection.

When M1 disease can be stabilized with chemotherapy and local tumor growth does not preclude resection, reassessment of resectability should be offered, as shown from Heidelberg: In 575 LAPC patients, receiving neoadjuvant chemotherapy, M1 disease was the primary reason for unresectability in 135 patients (23.5%). Resectional surgery almost doubled OS in this cohort, compared with chemotherapy alone. A new window of opportunity seems to open for patients with metastatic PC, when stable disease can be achieved by neoadjuvant treatment.

SURGERY IN RECURRENT DISEASE

Also postoperative recurrence of PC has been conceived as a palliative condition with no indication for surgical intervention. New evidence suggests that a modification of current practice is required. In 57 patients with histologically proven local recurrence, surgical resection of the isolated local recurrence was possible in 41 (72%), resulting in median OS 16.4 mo, compared to median 9.4 mo in the 16 patients (28%) after exploration only^[37]. Increased survival after repeat pancreatectomy of local recurrence have also been reported from Japan^[38] and this procedure can be successfully performed laparoscopically^[39]. In pulmonary recurrence, long term survival after resection of metastases has recently been reported^[36]. New chemotherapeutic regimens with improved response rates^[31,32,40] seem to open new windows of opportunity for surgical interventions with curative intent, when recurrent disease can be stabilized.

SURGICAL DEVELOPMENT

After reorganization of care for PC patients into multidisciplinary centers with high patient volume for single surgeons and hospitals, postoperative morbidity and mortality has been significantly improved^[41-45]. But extended operations have concurrently been offered more patients, combining resection/reconstruction of major mesenteric vessels and multivisceral resections (MVR)^[46]. This development has increased postoperative morbidity but not mortality^[47]. Clinical benefit has been documented as a result of this expansion for the surgical part of PC treatment. Burdelski *et al*^[48] found median OS 16 mo after MVR in 55 patients vs 6 mo in 154 patients after palliative bypass ($P < 0.001$). Sahakyan *et al*^[49] reported median OS 20.3 mo and 3 year survival 26.3% after extended distal laparoscopic resection of advanced

PDAC. Selection of patients for these comprehensive procedures and prospective registration of survival and PRO is mandatory to guide future development.

CONCLUSION

The role of surgery is changing and altering resection rates result in better clinical outcome for some, worse for others. Improved patients section is therefore essential. In this matter, the general scarcity of biomarkers enabling prediction of treatment outcome is a major problem. Prospective clinical trials, based on available diagnostic tools are running, and will in the near future enable evidence based update of treatment guidelines. The current direction of this development is increasing prognostic importance of surgical resection.

REFERENCES

- 1 **Khorana AA**, Mangu PB, Berlin J, Engebretson A, Hong TS, Maitra A, Mohile SG, Mumber M, Schulick R, Shapiro M, Urba S, Zeh HJ, Katz MH. Potentially Curable Pancreatic Cancer: American Society of Clinical Oncology Clinical Practice Guideline. *J Clin Oncol* 2016; **34**: 2541-2556 [PMID: 27247221 DOI: 10.1200/jco.2016.67.5553]
- 2 **Kleeff J**, Korc M, Apte M, La Vecchia C, Johnson CD, Biankin AV, Neale RE, Tempero M, Tuvesson DA, Hruban RH, Neoptolemos JP. Pancreatic cancer. *Nat Rev Dis Primers* 2016; **2**: 16022 [PMID: 27158978 DOI: 10.1038/nrdp.2016.22]
- 3 **Petrelli F**, Coiru A, Borgonovo K, Cabiddu M, Ghilardi M, Lonati V, Aitini E, Barni S. FOLFIRINOX-based neoadjuvant therapy in borderline resectable or unresectable pancreatic cancer: a meta-analytical review of published studies. *Pancreas* 2015; **44**: 515-521 [PMID: 25872127 DOI: 10.1097/mpa.0000000000000314]
- 4 **Hackert T**, Sachsenmaier M, Hinz U, Schneider L, Michalski CW, Springfield C, Strobel O, Jäger D, Ulrich A, Büchler MW. Locally Advanced Pancreatic Cancer: Neoadjuvant Therapy With Folfirinox Results in Resectability in 60% of the Patients. *Ann Surg* 2016; **264**: 457-463 [PMID: 27355262 DOI: 10.1097/sla.0000000000001850]
- 5 **Sohal DP**, Mangu PB, Khorana AA, Shah MA, Philip PA, O'Reilly EM, Uronis HE, Ramanathan RK, Crane CH, Engebretson A, Ruggiero JT, Copur MS, Lau M, Urba S, Laheru D. Metastatic Pancreatic Cancer: American Society of Clinical Oncology Clinical Practice Guideline. *J Clin Oncol* 2016; **34**: 2784-2796 [PMID: 27247222 DOI: 10.1200/jco.2016.67.1412]
- 6 **Reames BN**, Ghaferi AA, Birkmeyer JD, Dimick JB. Hospital volume and operative mortality in the modern era. *Ann Surg* 2014; **260**: 244-251 [PMID: 24368634 DOI: 10.1097/sla.0000000000000375]
- 7 **Shrikhande SV**, Sivasanker M, Vollmer CM, Friess H, Besselink MG, Fingerhut A, Yeo CJ, Fernandez-delCastillo C, Dervenis C, Halloran C, Gouma DJ, Radenkovic D, Asbun HJ, Neoptolemos JP, Izbicki JR, Lillemoe KD, Conlon KC, Fernandez-Cruz L, Montorsi M, Bockhorn M, Adham M, Charnley R, Carter R, Hackert T, Hartwig W, Miao Y, Sarr M, Bassi C, Büchler MW. Pancreatic anastomosis after pancreatoduodenectomy: A position statement by the International Study Group of Pancreatic Surgery (ISGPS). *Surgery* 2017; **161**: 1221-1234 [PMID: 28027816 DOI: 10.1016/j.surg.2016.11.021]
- 8 **Strobel O**, Büchler MW. Pancreatic cancer: Clinical practice guidelines - what is the evidence? *Nat Rev Clin Oncol* 2016; **13**: 593-594 [PMID: 27531701 DOI: 10.1038/nrclinonc.2016.127]
- 9 **Chandrasegaram MD**, Goldstein D, Simes J, GebSKI V, Kench JG, Gill AJ, Samra JS, Merrett ND, Richardson AJ, Barbour AP.

- Meta-analysis of radical resection rates and margin assessment in pancreatic cancer. *Br J Surg* 2015; **102**: 1459-1472 [PMID: 26350029 DOI: 10.1002/bjs.9892]
- 10 **Verbeke CS**, Leitch D, Menon KV, McMahon MJ, Guillou PJ, Anthony A. Redefining the R1 resection in pancreatic cancer. *Br J Surg* 2006; **93**: 1232-1237 [PMID: 16804874 DOI: 10.1002/bjs.5397]
- 11 **Verbeke CS**, Knapp J, Gladhaug IP. Tumour growth is more dispersed in pancreatic head cancers than in rectal cancer: implications for resection margin assessment. *Histopathology* 2011; **59**: 1111-1121 [PMID: 22175891 DOI: 10.1111/j.1365-2559.2011.04056.x]
- 12 **Verbeke C**. Morphological heterogeneity in ductal adenocarcinoma of the pancreas - Does it matter? *Pancreatol* 2016; **16**: 295-301 [PMID: 26924665 DOI: 10.1016/j.pan.2016.02.004]
- 13 **Bilimoria KY**, Bentrem DJ, Lillemoe KD, Talamonti MS, Ko CY. Assessment of pancreatic cancer care in the United States based on formally developed quality indicators. *J Natl Cancer Inst* 2009; **101**: 848-859 [PMID: 19509366 DOI: 10.1093/jnci/djp107]
- 14 **Buanes TA**. Pancreatic cancer-improved care achievable. *World J Gastroenterol* 2014; **20**: 10405-10418 [PMID: 25132756 DOI: 10.3748/wjg.v20.i30.10405]
- 15 **Tzeng CW**, Tran Cao HS, Lee JE, Pisters PW, Varadhachary GR, Wolff RA, Abbruzzese JL, Crane CH, Evans DB, Wang H, Abbott DE, Vauthey JN, Aloia TA, Fleming JB, Katz MH. Treatment sequencing for resectable pancreatic cancer: influence of early metastases and surgical complications on multimodality therapy completion and survival. *J Gastrointest Surg* 2014; **18**: 16-24; discussion 24-25 [PMID: 24241967 DOI: 10.1007/s11605-013-2412-1]
- 16 **Labori KJ**, Katz MH, Tzeng CW, Bjørneth BA, Cvancarova M, Edwin B, Kure EH, Eide TJ, Dueland S, Buanes T, Gladhaug IP. Impact of early disease progression and surgical complications on adjuvant chemotherapy completion rates and survival in patients undergoing the surgery first approach for resectable pancreatic ductal adenocarcinoma - A population-based cohort study. *Acta Oncol* 2016; **55**: 265-277 [PMID: 26213211 DOI: 10.3109/0284186x.2015.1068445]
- 17 **Christians KK**, Heimler JW, George B, Ritch PS, Erickson BA, Johnston F, Tolat PP, Foley WD, Evans DB, Tsai S. Survival of patients with resectable pancreatic cancer who received neoadjuvant therapy. *Surgery* 2016; **159**: 893-900 [PMID: 26602840 DOI: 10.1016/j.surg.2015.09.018]
- 18 **Mokdad AA**, Minter RM, Zhu H, Augustine MM, Porembka MR, Wang SC, Yopp AC, Mansour JC, Choti MA, Polanco PM. Neoadjuvant Therapy Followed by Resection Versus Upfront Resection for Resectable Pancreatic Cancer: A Propensity Score Matched Analysis. *J Clin Oncol* 2016; Epub ahead of print [PMID: 27621388 DOI: 10.1200/jco.2016.68.5081]
- 19 **Gillen S**, Schuster T, Meyer Zum Büschenfelde C, Friess H, Kleeff J. Preoperative/neoadjuvant therapy in pancreatic cancer: a systematic review and meta-analysis of response and resection percentages. *PLoS Med* 2010; **7**: e1000267 [PMID: 20422030 DOI: 10.1371/journal.pmed.1000267]
- 20 **Versteijne E**, van Eijck CH, Punt CJ, Suker M, Zwinderman AH, Dohmen MA, Groothuis KB, Busch OR, Besselink MG, de Hingh IH, Ten Tije AJ, Patijn GA, Bonsing BA, de Vos-Geelen J, Klaase JM, Festen S, Boerma D, Erdmann JI, Molenaar IQ, van der Harst E, van der Kolk MB, Rasch CR, van Tienhoven G. Preoperative radiochemotherapy versus immediate surgery for resectable and borderline resectable pancreatic cancer (PREOPANC trial): study protocol for a multicentre randomized controlled trial. *Trials* 2016; **17**: 127 [PMID: 26955809 DOI: 10.1186/s13063-016-1262-z]
- 21 **Lutfi W**, Talamonti MS, Kantor O, Wang CH, Liederbach E, Stocker SJ, Bentrem DJ, Roggin KK, Winchester DJ, Marsh R, Prinz RA, Baker MS. Perioperative chemotherapy is associated with a survival advantage in early stage adenocarcinoma of the pancreatic head. *Surgery* 2016; **160**: 714-724 [PMID: 27422328 DOI: 10.1016/j.surg.2016.05.029]
- 22 **Hartwig W**, Werner J, Jäger D, Debus J, Büchler MW. Improvement of surgical results for pancreatic cancer. *Lancet*

- Oncol* 2013; **14**: e476-e485 [PMID: 24079875 DOI: 10.1016/s1470-2045(13)70172-4]
- 23 **Werner J**, Combs SE, Springfield C, Hartwig W, Hackert T, Büchler MW. Advanced-stage pancreatic cancer: therapy options. *Nat Rev Clin Oncol* 2013; **10**: 323-333 [PMID: 23629472 DOI: 10.1038/nrclinonc.2013.66]
- 24 **Neoptolemos J**, Palmer D, Ghaneh P, Valle JW, Cunningham D, Wadsley J, Meyer T, Anthony A, Glimelius B, Lind P, Falk S, Izbicki J, Middleton G, Ross P, Wasan H, McDonald A, Crosby T, Psarelli E, Hammel P, Büchler M. ESPAC-4: A multicenter, international, open label randomized controlled phase III trial of adjuvant combination chemotherapy of gemcitabine (GEM) and capecitabine (CAP), versus monotherapy gemcitabine in patients with resected pancreatic ductal adenocarcinoma. Proceedings of the ASCO Annual Meeting, Abstract No: LBA4006. Available from: URL: <http://meetinglibraryasco.org/content/122648?media=vm;201606.06.16;Chicago>
- 25 **Wedén S**, Klemp M, Gladhaug IP, Møller M, Eriksen JA, Gaudernack G, Buanes T. Long-term follow-up of patients with resected pancreatic cancer following vaccination against mutant K-ras. *Int J Cancer* 2011; **128**: 1120-1128 [PMID: 20473937 DOI: 10.1002/ijc.25449]
- 26 **Johansson H**, Andersson R, Bauden M, Hammes S, Holdenrieder S, Ansari D. Immune checkpoint therapy for pancreatic cancer. *World J Gastroenterol* 2016; **22**: 9457-9476 [PMID: 27920468 DOI: 10.3748/wjg.v22.i43.9457]
- 27 **Hwang HK**, Kim HI, Kim SH, Choi J, Kang CM, Kim KS, Lee WJ. Prognostic impact of the tumor-infiltrating regulatory T-cell (Foxp3(+))/activated cytotoxic T lymphocyte (granzyme B(+)) ratio on resected left-sided pancreatic cancer. *Oncol Lett* 2016; **12**: 4477-4484 [PMID: 28105157 DOI: 10.3892/ol.2016.5252]
- 28 **Al-Hawary MM**, Francis IR, Chari ST, Fishman EK, Hough DM, Lu DS, Macari M, Megibow AJ, Miller FH, Mortelet KJ, Merchant NB, Minter RM, Tamm EP, Sahani DV, Simeone DM. Pancreatic ductal adenocarcinoma radiology reporting template: consensus statement of the society of abdominal radiology and the american pancreatic association. *Gastroenterology* 2014; **146**: 291-304.e1 [PMID: 24355035 DOI: 10.1053/j.gastro.2013.11.004]
- 29 **Tempero MA**, Arnoletti JP, Behrman SW, Ben-Josef E, Benson AB, Casper ES, Cohen SJ, Czito B, Ellenhorn JD, Hawkins WG, Herman J, Hoffman JP, Ko A, Komanduri S, Koong A, Ma WW, Malafa MP, Merchant NB, Mulvihill SJ, Muscarella P, Nakakura EK, Obando J, Pitman MB, Sisson AR, Tally A, Thayer SP, Whiting S, Wolff RA, Wolpin BM, Freedman-Cass DA, Sheath DA. Pancreatic Adenocarcinoma, version 2.2012: featured updates to the NCCN Guidelines. *J Natl Compr Canc Netw* 2012; **10**: 703-713 [PMID: 22679115]
- 30 **Katz MH**, Pisters PW, Evans DB, Sun CC, Lee JE, Fleming JB, Vauthey JN, Abdalla EK, Crane CH, Wolff RA, Varadhachary GR, Hwang RF. Borderline resectable pancreatic cancer: the importance of this emerging stage of disease. *J Am Coll Surg* 2008; **206**: 833-846; discussion 846-848 [PMID: 18471707 DOI: 10.1016/j.jamcollsurg.2007.12.020]
- 31 **Conroy T**, Desseigne F, Ychou M, Bouché O, Guimbaud R, Bécouarn Y, Adenis A, Raoul JL, Gourgou-Bourgade S, de la Fouchardière C, Bannoun J, Bachet JB, Khemissa-Akouz F, Péré-Vergé D, Delbaldo C, Assenet E, Chauffert B, Michel P, Montoto-Grillot C, Ducreux M. FOLFIRINOX versus gemcitabine for metastatic pancreatic cancer. *N Engl J Med* 2011; **364**: 1817-1825 [PMID: 21561347 DOI: 10.1056/NEJMoa1011923]
- 32 **Von Hoff DD**, Ervin T, Arena FP, Chiorean EG, Infante J, Moore M, Seay T, Tjulandin SA, Ma WW, Saleh MN, Harris M, Reni M, Dowden S, Laheru D, Bahary N, Ramanathan RK, Tabernero J, Hidalgo M, Goldstein D, Van Cutsem E, Wei X, Iglesias J, Renschler MF. Increased survival in pancreatic cancer with nab-paclitaxel plus gemcitabine. *N Engl J Med* 2013; **369**: 1691-1703 [PMID: 24131140 DOI: 10.1056/NEJMoa1304369]
- 33 **Shrikhande SV**, Kleeff J, Reiser C, Weitz J, Hinz U, Esposito I, Schmidt J, Friess H, Büchler MW. Pancreatic resection for M1 pancreatic ductal adenocarcinoma. *Ann Surg Oncol* 2007; **14**: 118-127 [PMID: 17066229 DOI: 10.1245/s10434-006-9131-8]
- 34 **Hackert T**, Niesen W, Hinz U, Tjaden C, Strobel O, Ulrich A, Michalski CW, Büchler MW. Radical surgery of oligometastatic pancreatic cancer. *Eur J Surg Oncol* 2017; **43**: 358-363 [PMID: 27856064 DOI: 10.1016/j.ejso.2016.10.023]
- 35 **Crippa S**, Bittoni A, Sebastiani E, Partelli S, Zanon S, Lanese A, Andrikou K, Muffatti F, Balzano G, Reni M, Cascinu S, Falconi M. Is there a role for surgical resection in patients with pancreatic cancer with liver metastases responding to chemotherapy? *Eur J Surg Oncol* 2016; **42**: 1533-1539 [PMID: 27423449 DOI: 10.1016/j.ejso.2016.06.398]
- 36 **Deeb A**, Haque SU, Olowokure O. Pulmonary metastases in pancreatic cancer, is there a survival influence? *J Gastrointest Oncol* 2015; **6**: E48-E51 [PMID: 26029466 DOI: 10.3978/j.issn.2078-6891.2014.114]
- 37 **Strobel O**, Hartwig W, Hackert T, Hinz U, Berens V, Grenacher L, Bergmann F, Debus J, Jäger D, Büchler M, Werner J. Re-resection for isolated local recurrence of pancreatic cancer is feasible, safe, and associated with encouraging survival. *Ann Surg Oncol* 2013; **20**: 964-972 [PMID: 23233235 DOI: 10.1245/s10434-012-2762-z]
- 38 **Miyazaki M**, Yoshitomi H, Shimizu H, Ohtsuka M, Yoshidome H, Furukawa K, Takayasiki T, Kuboki S, Okamura D, Suzuki D, Nakajima M. Repeat pancreatotomy for pancreatic ductal cancer recurrence in the remnant pancreas after initial pancreatotomy: is it worthwhile? *Surgery* 2014; **155**: 58-66 [PMID: 24238124 DOI: 10.1016/j.surg.2013.06.050]
- 39 **Sahakyan MA**, Yaqub S, Kazaryan AM, Villanger O, Berstad AE, Labori KJ, Edwin B, Røsok BI. Laparoscopic Completion Pancreatotomy for Local Recurrence in the Pancreatic Remnant after Pancreaticoduodenectomy: Case Reports and Review of the Literature. *J Gastrointest Cancer* 2016; **47**: 509-513 [PMID: 26732389 DOI: 10.1007/s12029-015-9796-y]
- 40 **Chiorean EG**, Von Hoff DD, Tabernero J, El-Maraghi R, Ma WW, Reni M, Harris M, Whorf R, Liu H, Li JS, Manax V, Romano A, Lu B, Goldstein D. Second-line therapy after nab-paclitaxel plus gemcitabine or after gemcitabine for patients with metastatic pancreatic cancer. *Br J Cancer* 2016; **115**: 188-194 [PMID: 27351217 DOI: 10.1038/bjc.2016.185]
- 41 **Birkmeyer JD**, Sun Y, Wong SL, Stukel TA. Hospital volume and late survival after cancer surgery. *Ann Surg* 2007; **245**: 777-783 [PMID: 17457171 DOI: 10.1097/01.sla.0000252402.33814.dd]
- 42 **Ghaferi AA**, Osborne NH, Birkmeyer JD, Dimick JB. Hospital characteristics associated with failure to rescue from complications after pancreatotomy. *J Am Coll Surg* 2010; **211**: 325-330 [PMID: 20800188 DOI: 10.1016/j.jamcollsurg.2010.04.025]
- 43 **Finks JF**, Osborne NH, Birkmeyer JD. Trends in hospital volume and operative mortality for high-risk surgery. *N Engl J Med* 2011; **364**: 2128-2137 [PMID: 21631325 DOI: 10.1056/NEJMsa1010705]
- 44 **Gooiker GA**, Lemmens VE, Besselink MG, Busch OR, Bonsing BA, Molenaar IQ, Tollenaar RA, de Hingh IH, Wouters MW. Impact of centralization of pancreatic cancer surgery on resection rates and survival. *Br J Surg* 2014; **101**: 1000-1005 [PMID: 24844590 DOI: 10.1002/bjs.9468]
- 45 **Gooiker GA**, van Gijn W, Wouters MW, Post PN, van de Velde CJ, Tollenaar RA. Systematic review and meta-analysis of the volume-outcome relationship in pancreatic surgery. *Br J Surg* 2011; **98**: 485-494 [PMID: 21500187 DOI: 10.1002/bjs.7413]
- 46 **Hackert T**, Schneider L, Büchler MW. Current State of Vascular Resections in Pancreatic Cancer Surgery. *Gastroenterol Res Pract* 2015; **2015**: 120207 [PMID: 26609306 DOI: 10.1155/2015/120207]
- 47 **Hartwig W**, Hackert T, Hinz U, Hassenpflug M, Strobel O, Büchler MW, Werner J. Multivisceral resection for pancreatic malignancies: risk-analysis and long-term outcome. *Ann Surg* 2009; **250**: 81-87 [PMID: 19561478 DOI: 10.1097/SLA.0b013e3181ad657b]
- 48 **Burdelski CM**, Reeh M, Bogoevski D, Gebauer F, Tachezy M, Vashist YK, Cataldegirmen G, Yekebas E, Izbicki JR, Bockhorn M. Multivisceral resections in pancreatic cancer: identification of risk factors. *World J Surg* 2011; **35**: 2756-2763 [PMID: 21938586 DOI: 10.1007/s12029-011-9796-y]

Buanes TA. Increasing importance of surgical resection

10.1007/s00268-011-1263-8]

- 49 **Sahakyan MA**, Kazaryan AM, Rawashdeh M, Fuks D, Shmavonyan M, Haugvik SP, Labori KJ, Buanes T, Røsok BI, Ignjatovic D, Abu Hilal M, Gayet B, Kim SC, Edwin B.

Laparoscopic distal pancreatectomy for pancreatic ductal adenocarcinoma: results of a multicenter cohort study on 196 patients. *Surg Endosc* 2016; **30**: 3409-3418 [PMID: 26514135 DOI: 10.1007/s00464-015-4623-x]

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