

Journal of Surgery and Medicine
e-ISSN=2602-2079

The effect of hospital volume on mortality, morbidity and dissected lymph nodes in pancreaticoduodenectomy for periampullary region tumors

Veysel Barış Turhan [1], Kürşat Dikmen [2], Mustafa Kerem [2]

[1] Hitit University, Erol Olçok Training and Research Hospital, Department of General Surgery, Çorum, Turkey
[2] Gazi University, Department of General Surgery, Ankara, Turkey

ORCID ID of the author(s)
VBT: 0000-0001-5093-4993
KD: 0000-0002-9150-9499
MK: 0000-0002-1797-6291

Corresponding Author
Veysel Barış Turhan
Hitit University, Erol Olçok Training and Research Hospital, Department of General Surgery, Çorum, Turkey
E-mail: drbaristurhan@hotmail.com

Ethics Committee Approval
The study was approved by Gazi University Clinical Research Ethics Committee, Date: 23.06.2016, Decision no: 331.
All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

Conflict of Interest
No conflict of interest was declared by the authors.

Financial Disclosure
The authors declared that this study has received no financial support.

Previous Presentation
This article was previously presented as an oral presentation at the 21th National Surgery Congress (April 2018, Antalya, Turkey).

Published
2022 February 27

Abstract

Background/Aim: Since the first pancreaticoduodenectomy (PD) surgeries, mortality, morbidity and length of hospital stay decreased, in return, the number of uncomplicated cases and dissected lymph nodes increased over the years. The aim of our study was to determine the effect of hospital volume on survival, postoperative hospital stay, fistula rate, morbidity rate and the number of lymph nodes dissected.
Methods: In this retrospective cohort study, 213 patients who were operated with the diagnosis of periampullary tumor between January 2008 and January 2016 were included in the study. The patients were divided into four groups according to the years of surgery: Group A (n=31, 2008-2009), Group B (n=46, 2010-2011), Group C (n=50, 2012-2013) and Group D (n=86, 2014-2016). The groups were compared with each other in terms of the following factors; Pancreatic fistula rates, postoperative hospital stay, mortality rates, morbidity rates, number of dissected lymph nodes.
Results: It has been observed that there is a relation between pancreatic tissue quality and duct size with fistulas (P=0.0016 and P=0.017, respectively). It is seen that as the amount of number lymph nodules increases, the quality of staging improves (P=0.009). Rates of mortality and morbidity are decreased, as the hospital volume increased (P=0.037), The same effect of hospital volume is observed in length of hospital stay and fistula rates, both improved (P=0.017 and P<0.001, respectively).
Conclusion: It is easy to state that the increase in hospital volume and surgeon's experience is directly related with patient outcomes. As the understanding of anatomy increases, quality of the surgery is assumed to be increased as well as the reduction in length of hospital stay, mortality and morbidity rates, and the increase in quantity of dissected lymph nodules.

Keywords: Periampullary tumor, Hospital volume, Pancreaticoduodenectomy

How to cite: Turhan VB, Dikmen K, Kerem M. The effect of hospital volume on mortality, morbidity and dissected lymph nodes in pancreaticoduodenectomy for periampullary region tumors. J Surg Med. 2022;6(3):263-267.

Introduction

Periampullary region tumors (PRT) have a poor prognosis. Its incidence increases after the 5th decade. The female/male ratio is 1/2-3. Risk factors for periampullary cancers are age, gender, genetics, smoking, chronic pancreatitis, diabetes mellitus, previous small bowel surgery, and ulcer bleeding [1-3]. Pancreaticoduodenectomy (PD), which had a 20% mortality at the beginning, has become a more applicable surgery with modifications and surgical experience over time, and mortality rates have decreased to below 3% in experienced centers [4,5].

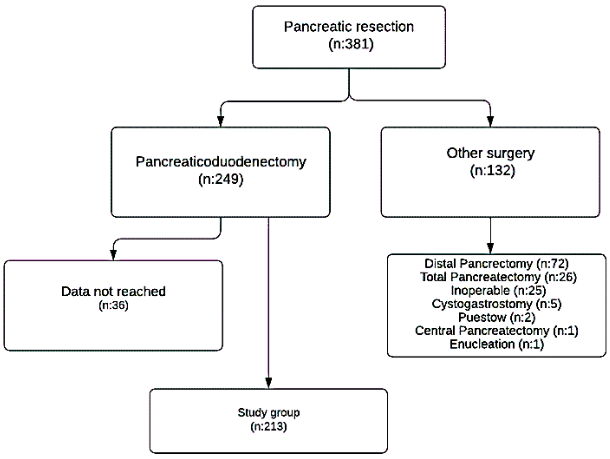
Lymph node dissection is one of the most important prognostic factors for gastrointestinal tumors. In addition, tumor size, locoregional invasion, and resection margin are also important prognostic factors [6,7]. In some studies, it has been reported that there is a positive correlation between the curability of lymph node dissection in stage I and II tumors [8]. Although up to 50% of paraaortic lymph node metastases have been observed in some previous autopsy series, dissections of these lymph nodes are not included in the standard Whipple procedure [9].

In this study, the results of PD operations performed with the preliminary diagnosis of PRT were examined. The relationship between gland texture of pancreatic tissue, pancreatic duct diameter and fistula rates was investigated in patients undergoing PD. It was aimed to determine the effect of hospital volume on survival, number of dissected lymph nodes, postoperative hospital stay and rate of fistula and morbidity.

Materials and methods

After the approval of Gazi University Clinical Research Ethics Committee (Date: 23.06.2016, Decision no: 331), 381 pancreatic surgeries performed between January 2008 and January 2016 were evaluated. PD was performed in 249 of these patients. Other surgeries were excluded from the study (Figure 1). 36 patients were excluded from the study because all data could not be accessed. Patients were staged according to the American Joint Committee on Cancer (AJCC) TNM staging system.

Figure 1: Flowchart of patients



Preoperatively with the help of CT, USG, and EUS, perioperative USG, and postoperative pathology results, pancreatic tissue was evaluated as hard and soft according to its density. The main pancreatic duct diameter was divided into 2 groups as ≤3mm and >3mm, for its relationship with rates of pancreatic fistula. The effect of dissected lymph node and metastatic lymph node numbers on survival of patients who underwent PD according to pathology results was evaluated. After that, patients were divided into 4 groups as 2008-2009 (Group A), 2010-2011 (Group B), 2012-2013 (Group C), 2014-2016 (Group D) according to the years of surgery. Pancreatic fistula rates, postoperative hospital stay, mortality and morbidity rates according to Dindo-Clavien [10], and the number of dissected lymph nodes were evaluated according to these groups.

As the definition of pancreatic fistula, the drain fluid amylase levels measured in the 3rd and 5th days after PD were accepted as being 3 times higher than the amylase levels in serum or levels determined as the upper limit by the hospital laboratory. Pancreatic fistula grading was classified according to the "International Study Group Postoperative Pancreatic Fistula" (ISGPF) [11]. The length of hospital stay was recorded as the number of days between the day of surgery and discharge.

Statistical analysis

Data analysis was evaluated with SPSS 15.0 for the Windows data analysis program. Kolmogorov-Smirnov test was performed to observe the distribution of the parameters. Descriptive statistics (frequency, percentage distribution) were used as statistical analysis. In the comparison of the two groups, Chi-Square test, one-way ANOVA, and Spearman's rho analysis methods were used. $P<0.05$ was considered statistically significant.

Results

The age distribution of patients was between 14 and 87, and the mean age was 59.71 (13.23). Of 213 patients, 87 (40.9%) were female and 126 (59.1%) were male. The mean follow-up period of the patients within the study was found 21.5 (35.5) months. The duration of hospital stay was seen as a minimum of 1 and a maximum of 85 months.

The pathological diagnosis distribution is shown in Table 1. According to the tumor stages, 107 (50.2%) were T3 tumors, whereas 53 (24.9%) were T2, 15 (7%) were T4, and 12 (5.6%) were T1. Pathological malignancy was not found in remaining 26 (12.2%) patients.

Table 1: Pathological diagnosis of patients.

Pathological diagnoses	n=213	%
Well Differentiated Adenocarcinoma	63	29.6
Moderately Differentiated Adenocarcinoma	52	24.4
Poorly Differentiated Adenocarcinoma	21	9.9
Well Differentiated Neuroendocrine Tumor	16	7.5
Chronic Pancreatitis	13	6.1
Serous Microcystic Adenoma	11	5.2
Solid Pseudo papillary Tumor	7	3.3
İntraductal Papillary Mucinous Adenoma	7	3.3
IPMN	7	3.3
Mucinous Adenocarcinoma	5	2.3
Pseudocyst	5	2.3
Signet-ring cell carcinoma	4	1.9
PAN-IN	2	0.9

IPMN: Intraductal papillary mucinous neoplasm, PAN-IN: Pancreatic intraepithelial neoplasia

The fistula was detected in 64 (30%) patients in the study. The fistula grades of the patients are given in Table 2.

Grade A fistula was not considered as a cause of morbidity. While 95 (44.6%) of the 213 patients included in the study had morbidity due to the reasons given in Table 3, 118 (55.4%) patients were considered uncomplicated.

The surgical margin was positive in 54 patients (25.4%) and negative in 159 patients (74.6%), in pathological examination.

Table 2: Percentage of patients with pancreatic fistula

Pancreatic fistula	n=64/213	%
Grade A	37	57.8
Grade B	18	28.1
Grade C	9	14.1

Table 3: Causes and percentages of morbidity

Causes and percentages of morbidity	n=95/213	%
Anastomotic leak	27	28.4
Wound Infection	18	18.9
Intraabdominal Abscess	14	14.7
Pleural Effusion	8	8.4
Kidney failure	4	4.2
Pulmonary Thromboembolism	4	4.2
Mesenteric Ischemia	3	3.1
Evisceration	3	3.1
Intraabdominal Bleeding	3	3.1
Gastrointestinal Bleeding	3	3.1
Aspiration Pneumonia	3	3.1
Biliary Obstruction	3	3.1
Intraoperative myocardial infarction	2	2.1

Pancreatic tissue was found to be hard in 71 (3.3%) patients, while the gland texture of pancreas was soft in 142 patients (66.7%). When the pancreatic fistula rates were compared, it was seen that the effect of hard or soft tissue on fistula formation was statistically significant (Table 4). The fistula was statistically less common in cases with hard pancreatic tissue (P<0.001).

The main pancreatic duct diameter widths were ≤3 mm in 118 (5.4%) patients and >3mm in 95 (44.6%) patients (Table 5). It was observed that fistula rates increased statistically in patients with a main pancreatic duct width less than 3 mm (P=0.016).

Table 4: Fistula rates by the gland texture of the pancreatic tissue

Pancreatic tissue's texture	Pancreatic fistula (+) (n=149)	Pancreatic fistula (–) (n=64)	*P*-value*
Hard (n=71)	60 (85.5%)	11 (15.5%)	0.05
Soft (n=142)	89 (62.6%)	53 (37.4%)	

*Chi-Square test

Table 5: Fistula rates by main pancreatic duct width

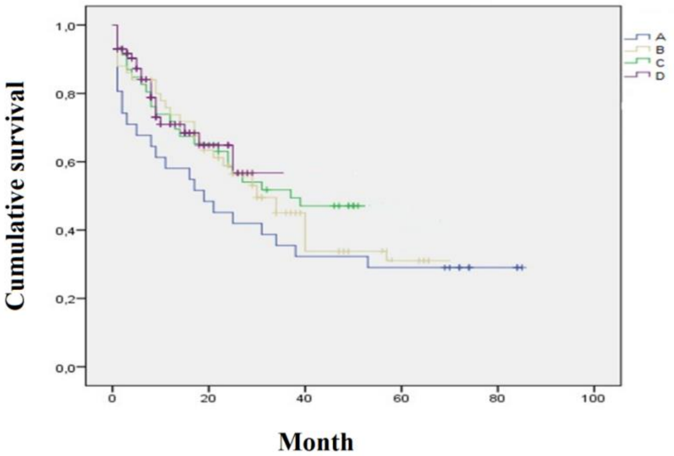
Pancreatic duct diameter	Pancreatic fistula (+) (n=149)	Pancreatic fistula (-) (n=64)	*P*-value
3mm and below (n=95)	58(61.1%)	37(38.9%)	0.016
Over 3mm (n=18)	91(77.1%)	27(22.9%)	

*Chi-Square test

213 patients were divided into 4 groups as 2008-2009 (Group A), 2010-2011 (Group B), 2012-2013 (Group C), 2014-2016 (Group D). When the groups were compared, no statistically significant difference was found according to age (P=0.789) and gender (P=0.460). The groups were homogeneously distributed.

The overall survival is shown to be increased as the number of surgeries performed and the experience are increased. This percentage increase was considered significant (Figure 2).

Figure 2: Cumulative survival by years (2008-2009 (Group A), 2010-2011 (Group B), 2012-2013 (Group C), 2014-2016 (Group D))



The 1, 3, and 5-year survivals of the patients included in the study were evaluated. The 1-year survival was calculated for all four groups. 1-year survival was 58%, 65%, 71%, and 73% in group A, B, C, and D, respectively. This increase was found to be significant. The 3-year survival was evaluated for groups A, B, and C. The survival rate was 29%, 47%, and 49% in group A, B, and D, respectively. 5-year survival was evaluated between groups A and B, which were 21% and 41% in group A and B, respectively. This increase in percentage was considered significant.

It was observed that the perioperative mortality rates decreased with the increase in hospital volume. As a result of this analysis between groups, this decrease in perioperative mortality was found to be statistically significant (P=0.037).

When the pancreatic fistula rates between the groups were compared, they were decreased as the hospital volume increased. This decrease was found to be statistically significant (P=0.017) (Table 6).

Table 6: Pancreatic fistula rates by years

Pancreatic fistula	A (n=31)	B (n=46)	C (n=50)	D (n=86)	Total (n=213)	*P*-value *
(-)	n=17	n=29	n=33	n=70	n=149	0.017
	54.8%	63%	66%	81.40%	70%	
(+)	n=14	n=17	n=17	n=16	n=64	
	45.2%	37%	34%	18.6%	30%	

*Chi-Square test

The mean length of hospital stay was found to be 15.46 (10.8) days. According to the comparison, the length of hospital stay was 18.85 (10.52), 18.48 (15.81), 14.86 (7) and 13 (8.6) days in group A, B, C and D, respectively. When these data were analyzed with one-way ANOVA test [12], it was shown that this decrease in group D was statistically significant (P=0.017).

It was clinically demonstrated that the number of dissected lymph nodes increased over the years (Table 7). The mean number of lymph nodes (LN) dissected was 13.12 (7.1). Patients were divided into three groups according to the number of dissected LNs; 0-5 LN removal (X group), 5-10 LN removal patients (Y group), 10 and more LN removal patients (Z group). When the survivals of the X, Y, and Z groups were evaluated, the cumulative survival rate of group Z was found to be statistically better (P=0.009).

Table 7: Distribution of dissected lymph node numbers by years

	A (n=31)	B (n=46)	C (n=50)	D (n=86)	Total (n=213)	*P*-value *
Mean	8.54	10.28	10.78	17.66	13.12	<0.001
SD	3.9	6.3	5.9	6.5	7.1	
Minimum	1	1	1	8	1	
Maximum	21	25	23	43	43	

SD: Standard deviation, * One-way ANOVA test

Patients with and without metastatic LN involvement were divided into 2 groups. One and three-year survivals of these patients were evaluated. 1-year survival rate of patients with LN negative was 83.9%, while it was 63% for patients with LN positive, which presents statistically significant (P=0.003). Considering the 5-year survival, it was found to be 60.8% in patients with negative LN and 24.5% in patients with positive LN. It was evaluated as statistically significant (P<0.001). 1 and 3-year survivals were statistically decreased in LN positive patients. Survival rates were decreased in patients with LN positive.

According to Dindo-Clavien classification (Table 8), they were divided into seven groups as grade I, II, IIIa, IIIb, IVa, IVb, and V. There was no statistically significant difference between the groups (P=0.101). Although there was no statistically significant difference between the patients, all of grade I patients and patients without complications were statistically evaluated as grade I. This result was statistically significant (P=0.002). As a result, uncomplicated discharge rates decreased significantly over the years.

Table 8: Distribution of patients, according to Dindo-Clavien classification

Dindo-Clavien	A (n=31)	B (n=46)	C (n=50)	D (n=86)	Total (n=213)
Grade I	11	25	26	56	118
Grade II	5	4	3	9	21
Grade IIIa	4	4	3	5	16
Grade IIIb	3	5	5	5	18
Grade 4a	2	4	4	4	14
Grade 4b	1	2	3	2	8
Grade 5	5	2	6	5	18

Discussion

The mortality of PD surgery is less than 5% in experienced centers, and the complication rate is between 25-40%. Morbidity rates have decreased to 5-10% with the improvement of surgical technique and postoperative care conditions [13, 14].

One of the factors responsible for mortality and morbidity during or after PD is the small number of pancreatic resections performed in low-volume centers. In many studies in the literature, positive effects of hospital volume on mortality, morbidity rates, number of dissected lymph nodes, and length of hospital stay have been reported. Firstly, Luft et al. [15] put two theories in their study in 1979, for the relationship between hospital volume and outcomes. Success increases with experience, and patients should be referred to centers where more operations are performed. Van Heek et al. [16] defined hospitals where fewer than five PDs per year were performed as low-volume hospitals. Although the mortality rate is 13% in centers with pancreatic resection, it is around 2% in centers with a high number of patients [17, 18].

Three different studies confirmed that increasing hospital volume reduces mortality and morbidity [19-21]. Birkmeyer et al. [19] showed that an increase in hospital volume reduces mortality and morbidity, independent from the surgeon's volume. Bahmann et al. [22] similarly evaluated that statistically significant better survival was achieved with an increase in hospital volume. Contrary to these views, Nathan et al. [23] concluded in a study conducted in 2009 that the effect of the surgeon's patient volume is not significant. Similar to our study, the common points of these studies are that better results are obtained as the patient volume of the hospital and the surgeon increases. Because in a center where a complex surgery like PD is performed, patient selection with experience, preoperative patient evaluation, technical skills, and postoperative patient care gain importance.

One of the reasons for the decrease in mortality and morbidity in high-volume hospitals in the 2 studies conducted by Ghaferi et al. [24, 25] is the more effective management of complications in these centers. It has been shown that co-morbidities have no effect on mortality in high-volume hospitals. In a meta-analysis of 17 studies conducted by Van Heek et al. [16], only one study reported that mortality and morbidity rates in high-volume hospitals were statistically insignificantly low. It was thought that this study was also due to the inclusion of low volume centers as 2 PD per year. Today, while mortality rates are below 5% in high-volume centers, morbidity rate is around 40% despite all developments.

The most important complication after PD is the development of the pancreatic fistula. Pancreatic fistula is thought to be the cause of other major complications. Activation of enzymes secreted from pancreatic leakage causes auto digestion, which results in peripancreatic collection, intra-abdominal abscess, delayed gastric emptying, and postoperative hemorrhage. The common point in pancreatic anastomosis leaks is to protect the patient from sepsis, peritonitis, hemorrhage, and organ failure. The rate of pancreatic fistula has been reported between 2-50%. The reason for this wide range is the absence of an internationally accepted definition of fistula [5].

In this study, it was statistically shown that the rate of fistula related to hospital volume decreased over the years. Fistula rates were found to be similar in studies [26, 27]. Pratt et al. [28] showed that postoperative fistula rates decreased in high-volume hospitals by mentioning the surgeon's experience and preoperative patient preparations in a large-scale study. However, Kollmar et al. [29] defended that hospital volume showed a minimal correlation with pancreatic fistula rates.

It is a known fact that the quality of pancreatic tissue and the width of the pancreatic duct may be associated with pancreatic fistula rates. Pancreatic anastomosis, which is a complex surgery as PD, is an issue that needs to be emphasized, both in terms of its neighborhood and in terms of the tissue it contains. Pancreatic tissue evaluated preoperatively, perioperatively, and postoperatively is an important risk factor for anastomotic leakage. In a study by Yeo et al. [5] the softness of the pancreatic tissue is shown as statistically increased risk for pancreatic anastomosis leakage. Similarly, in a study of 1891 patients, Lin et al. obtained similar results [30]. However, large-scale studies have found that the size of the pancreatic duct is effective in pancreatic leakage, and the risk increases in ducts with a diameter of ≤3mm [31-33]. One study showed that each 1mm reduction in the pancreatic duct increases the risk of an anastomotic leak by 68% [28]. These data are directly proportional to our study.

As it is known, in parallel with the number of surgeries performed in high-volume hospitals, the dominance of anatomy is increasing. With increasing experience, the duration of the operation shortens and the quality of the exploration increases. In this study, it was shown that as the volume increased, the number of lymph node dissections and the number of removed lymph nodes increased statistically. It is supported by various studies that the number of dissected lymph nodes has an effect on survival and that expanded lymph node dissection provides better prognosis [34–36]. The number of lymph nodes involved in standard lymphadenectomy has been the subject of debate. Pawlik et al. [37] determined this number as 12, but in some studies, this number was accepted as ≥15 [38]. 10-15 lymph nodes are generally considered optimal [39, 40]. In our study, a mean of 13.12 (7.1) lymph nodes were dissected. This number increased statistically depending on the year.

The decrease in mortality and morbidity rates and the increase in the number of dissected lymph nodes were observed with the increase in the number of cases and experiences over the years, designed in a high-volume center as a retrospective cohort study. However, it has been observed that the length of hospital stay of the patients has decreased over the years. It has also been found that the gland texture of pancreatic tissue and the width of the main pancreatic duct are associated with the possibility of pancreatic fistula. Fistula rates were found to statistically significantly increase in patients with soft pancreatic tissue and a main pancreatic duct smaller than 3mm. Although it has been shown that the number of dissected LNs has a percentage effect on survival, the most important point is that a better staging can be made with the increase in the number of lymph nodes resected in this complex region, which increased in every following year, with the increasing experience.

Limitations

The retrospective design of our study, and the inclusion of only PD cases can be considered as limitations. However, the number of patients is higher than most studies in terms of decision making. Future studies with larger series and more homogeneously paired groups are needed.

Conclusion

Our study showed that the quality of the surgery can be increased by increasing the volume. Accordingly, morbidity and morbidity rates decrease, the number of dissected lymph nodes increases, and the length of hospital stay decreases. It may be appropriate for low-volume centers, where preoperative diagnosis is difficult and postoperative care is difficult, to refer patients to a higher-volume hospital in hepatopancreatobiliary surgery.

Acknowledgements

The authors would like to thank Associate Professor Asiye Uğraş Dikmen from Gazi University Faculty of Medicine, Department of Public Health, who assisted in the statistical part of the study.

References

1. Perek S. İ.Ü. Cerrahpaşa Tıp Fakültesi Sürekli Tıp Eğitimi Etkinlikleri, Hepato-Bilier Sistem ve Pankreas Hastalıkları Sempozyum Dizisi. Pankreas kanseri. 2002;28:217-8.
2. Sakin A, Sahin S, Sakin A, Atci M, Geredeli Ç, Cihan Ş. Effect of type 2 diabetes mellitus on survival in metastatic pancreatic cancer. J Surg Med. 2021;5(1):17-21.
3. Cameron JL, Riall TS, Coleman J, Belcher KA. One thousand consecutive pancreaticoduodenectomies. Ann Surg. 2006;244(1):10-5.
4. Crist DW, Sitzmann JV, Cameron JL. Improved hospital morbidity, mortality, and survival after the Whipple procedure. Ann Surg. 1987;206(3):358-65.
5. Yeo CJ, Cameron JL, Sohn TA, Lillemoe KD, Pitt HA, Talamini MA, et al. Six hundred fifty consecutive pancreaticoduodenectomies in the 1990s: pathology, complications, and outcomes. Ann Surg. 1997;226(3):248-60.
6. Kuhlmann KFD, De Castro SMM, Wesseling, Ten Kate FJW, Offerhaus GJA, Busch ORC, et al. Surgical treatment of pancreatic adenocarcinoma: actual survival and prognostic factors in 343 patients. Eur j cancer, 2004;40(4):549-58.
7. Makary MA, Winter JM, Cameron JL, Campbell KA, Chang D, Cunningham SC, et al. Pancreaticoduodenectomy in the very elderly. J Gastrointest Surg. 2006;10:347–56.
8. Mukaiya M, Hirata K, Satoh T, Kimura M, Yamashiro K, Ura H, et al. Lack of Survival Benefit of Extended Lymph Node Dissection for Ductal Adenocarcinoma of the Head of the Pancreas: Retrospective Multi-institutional Analysis in Japan. World J Surg. 1998;22:248–53.
9. Nagai H, Kuroda A, Morioka Y. Lymphatic and local spread of T1 and T2 pancreatic cancer. A study of autopsy material. Ann Surg. 1986;204(1):65-71.
10. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg. 2004;240(2):205-13.
11. Bassi C. International Study Group on Pancreatic Fistula Definition; Postoperative parcreatic fistula; an international study group (ISGPF) definition. Surgery. 2005;138:8-13.
12. Tabachnick BG, Fidell LS. Using multivariate statistics. Boston: Allyn& Bacon; 2007.
13. Silen V SM. Pancreas. In : Schwartz SI, Shires GT, Spencer FC, eds. Principles of Surgery 5. ed. McGraw- Hill; 1998. pp. 1413-1440.
14. Jones L, Russell C, Mosca F, Boggi U, Sutton R, Slavin J, et al. Standard Kausch-Whipple Pancreatoduodenectomy. Dig Surg. 1999;16:297-304.
15. Luft HS, Bunker JP, Enthoven AC. Should operations be regionalized? The empirical relation between surgical volume and mortality. N Engl J Med. 1979;301(25):1364-69.
16. van Heek NT, Kuhlmann KF, Scholten RJ, de Castro SM, Busch OR, van Gulik TM, et al. Hospital volume and mortality after pancreatic resection: a systematic review and an evaluation of intervention in the Netherlands. Ann Surg. 2005;242(6):781-90.
17. Finlayson EVA, Goodney PP, Birkmeyer JD. Hospital Volume and Operative Mortality in Cancer Surgery: A National Study. Arch Surg. 2003;138(7):721–5.
18. Begg CB, Cramer LD, Hoskins WJ, Brennan MF. Impact of hospital volume on operative mortality for major cancer surgery. JAMA. 1998;280:1747-51.
19. Birkmeyer JD, Stukel TA, Siewers A, Goodney PP, Wennberg DE, Lucas FL. Surgeon volume and operative mortality in the United States. N Engl J Med. 2003;22:2117-27.
20. Eppsteiner RW, Csikesz NG, McPhee JT, Tseng JF, Shah SA. Surgeon volume impacts hospital mortality for pancreatic resection. Ann Surg. 2009;249:635–40.
21. Nordback I, Parviainen M, Raty S, Kuivanen H, Sand J. Resection of the head of the pancreas in Finland: effects of hospital and surgeon on short-term and long-term results. Scand J Gastroenterol. 2002;37:1454–60.
22. Bachmann MO, Alderson D, Peters TJ, Bedford C, Edwards D, Wotton S, et al. Influence of specialization on the management and outcome of patients with pancreatic cancer. Br J Surg. 2003;90:171–7.
23. Nathan H, Cameron JL, Choti MA, Schulick RD, Pawlik TM. The volume–outcomes effect in hepato-pancreato-biliary surgery: hospital versus surgeon contributions and specificity of the relationship. J Am Coll Surg. 2009;208:528–38.
24. Ghaferi AA, Birkmeyer JD, Dimick JB. Complications, failure to rescue, and mortality with major inpatient surgery in medicare patients. Ann Surg. 2009;250:1029–34.
25. Ghaferi AA, Birkmeyer JD, Dimick JB. Variation in hospital mortality associated with inpatient surgery. N Engl J Med. 2009;361:1368–75.
26. Tran K, Van Eijck C, Di Carlo V, Hop WC, Zerbi A, Balzano G, et al. Occlusion of the pancreatic duct versus pancreaticojejunostomy: a prospective randomized trial. Ann Surg. 2002;236:422–8.
27. Conlon KC, Labow D, Leung D, Smith A, Jarnagin W, Coit DG, et al. Prospective randomized clinical trial of the value of intraperitoneal drainage after pancreatic resection. Ann Surg. 2001;234:487–93.
28. Pratt WB, Mark P. Callery M. Risk prediction for development of pancreatic fistula using the ISGPF classification scheme. World J Surg. 2008;32(3)419-28.
29. Kollmar O, Moussavian MR, Bolli M, Richter S, Schilling MK. Pancreatojejunal leakage after pancreas head resection: anatomic and surgeon-related factors. J Gastrointest Surg. 2007;11:1699-703.
30. Lin JW, Cameron JL, Yeo CJ, Riall TS, Lillemoe K. Risk factors and outcomes in post pancreaticoduodenectomy pancreaticocutaneous fistula. J Gastrointest Surg . 2004;8:951–9.
31. Marcus SG, Cohen H, Ranson JH. Optimal management of the pancreatic remnant after pancreaticoduodenectomy. Ann Surg. 1995;221:635–48.
32. Van Berge Henegouwen MI, De Wit LT, Van Gulik TM, Obertop H, Gouma DJ. Incidence, risk factors, and treatment of pancreatic leakage after pancreaticoduodenectomy: drainage versus resection of the pancreatic remnant. J Am Coll Surg. 1997;185:18–24.
33. Yang YM, Tian XD, Zhuan Y, Wang WM, Wan YL, Huang YT. Risk factors of pancreatic leakage after pancreaticoduodenectomy. World J Gastroenterol. 2005;11:2456–61.
34. House MG, Gönen M, Jarnagin WR, D'Angelica M, DeMatteo RP, Fong Y et al. Prognostic significance of pathologic nodal status in patients with resected pancreatic cancer. J Gastrointest Surg. 2007;11:1549–55.
35. Pedrazzoli S, DiCarlo V, Dionigi R, Mosca F, Pederzoli P, Pasquali C et al. Standard versus extended lymphadenectomy associated with pancreatoduodenectomy in the surgical treatment of adenocarcinoma of the head of the pancreas: a multicenter, prospective, randomized study. Lymphadenectomy Study Group. Ann Surg. 1998;228:508–17.
36. Capussotti L, Massucco P, Ribero D, Vigano L, Muratore A, Calgaro M. Extended lymphadenectomy and vein resection for pancreatic head cancer: outcomes and implications for therapy. Arch Surg. 2003;138:1316–22.
37. Pawlik TM, Gleisner AL, Cameron JL, Winter JM, Assumpcao L, Lillemoe KD, et al. Prognostic relevance of lymph node ratio following pancreaticoduodenectomy for pancreatic cancer. Surgery 2007;141:610–618.
38. Tomlinson JS, Jain S, Bentrem DJ, Sekeris EG, Maggard MA, Hines OJ et al. Accuracy of staging node-negative pancreas cancer: a potential quality measure. Arch Surg. 2007;142:767–73.
39. Gutierrez JC, Franceschi D, Koniaris LG. How many lymph nodes properly stage a periampullary malignancy? J Gastrointest Surg. 2008;12:77– 85.
40. Schwarz RE, Smith DD. Extent of lymph node retrieval and pancreatic cancer survival: information from a large US population database. Ann Surg Oncol. 2006;13:1189–200.

This paper has been checked for language accuracy by JOSAM editors.
The National Library of Medicine (NLM) citation style guide has been used in this paper.