Published in final edited form as:

Ann Surg. 2015 December ; 262(6): 1071–1078. doi:10.1097/SLA.0000000000001048.

90-day postoperative mortality is a legitimate measure of hepatopancreatobiliary surgical quality

Yoshihiro Mise, MD, PhD, Jean-Nicolas Vauthey, MD, Giuseppe Zimmitti, MD, Nathan H. Parker, MPH, Claudius Conrad, MD, PhD, Thomas A. Aloia, MD, Jeffery E. Lee, MD, Jason B. Fleming, MD, and Matthew H. G. Katz, MD

Department of Surgical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX

Abstract

Objective—To investigate the legitimacy of 90-day mortality as a measure of hepatopancreatobiliary quality.

Summary Background Data—The 90-day mortality rate has been increasingly but not universally reported after hepatopancreatobiliary surgery. The legitimacy of this definition as a measure of surgical quality has not been evaluated.

Methods—We retrospectively reviewed the causes of all deaths that occurred within 365 postoperative days in patients undergoing hepatectomy ($n = 2811$) and/or pancreatectomy ($n = 1092$) from January 1997 through December 2012. The rates of surgery-related, disease-related, and overall mortality within 30 days, within 30 days or during the index hospitalization, within 90 days, and within 180 days following surgery were calculated.

Results—Seventy-nine (3%) surgery-related deaths and 92 (3%) disease-related deaths occurred within 365 days after hepatectomy. Twenty (2%) surgery-related deaths and 112 (10%) disease-related deaths occurred within 365 days after pancreatectomy. The overall mortality rates at 99 day and 118 days optimally reflected surgery-related mortality following hepatobiliary and pancreatic operations, respectively. The 90-day overall mortality rate was a less sensitive but equivalently specific measure of surgery-related death.

Conclusions and Relevance—The 99-day and 118-day definitions of postoperative mortality optimally reflected surgery-related mortality following hepatobiliary and pancreatic operations, respectively. However, among commonly reported metrics, the 90-day overall mortality rate represents a legitimate measure of surgical quality.

Keywords

Mortality; Hepatectomy; Pancreatectomy; Root cause analysis

Introduction

A number of different outcome metrics have been used as measures of surgical quality. Among them, length of hospital stay and rates of readmission and morbidity may be influenced by differences in discharge practices, complication grading and reporting algorithms, and reimbursement systems. In contrast, postoperative mortality is a comparatively objective indicator of surgical quality. Postoperative mortality is therefore routinely measured and reported by surgeons, hospitals, payers, and policy makers^{1,2}. It is used to assess and to communicate risk, to evaluate surgeons' performance and competence, to compare hospital quality, and to provide a benchmark for quality improvement initiatives³.

However, the accuracy of postoperative mortality in terms of capturing surgery-related deaths and excluding deaths due to underlying disease depends on the follow-up time over which deaths are tracked^{4,5}. Historically, the 30-day mortality rate has been used to measure performance across a wide range of surgical disciplines. Indeed, the American College of Surgeons National Surgical Quality Improvement Program database, widely considered the gold standard database for surgical quality-improvement and future pay-for-performance programs, records 30-day complication and mortality outcomes after surgery⁶. However, because surgery-related deaths may occur later than 30 days following surgery, this deaths-within-30-days definition is limited. Alternate definitions of postoperative mortality are therefore frequently used, including in-hospital mortality, 90-day mortality, and 100-day mortality, but extending the duration of monitoring of primary patient sources is costly and resource intensive^{5,7}. Further, in many administrative databases, the mortality events recorded are those from any cause, and discrimination between surgery-related deaths and deaths from other causes can be problematic. Significant prolongation of the follow-up period during which all deaths are included in calculations of postoperative mortality may falsely attribute a substantial number of unrelated deaths to lapses in the quality of surgical care⁷. The legitimacy of postoperative mortality as a surgical quality indicator is therefore contingent upon the definition of postoperative mortality that is used.

The optimal definition of postoperative mortality depends on multiple factors, including the type of operation performed and the tumor type for which it is employed⁴. For hepatopancreatobiliary (HPB) surgical procedures, the importance of extending follow-up to identify surgery-related deaths beyond 30 days has long been emphasized because complications specific to this group of operations, such as hepatic insufficiency and pancreatic fistula, may lead to death late in the postoperative course. Monitoring durations as long as 180 days have been proposed⁸. Recently, there has been a trend toward the use of 90-day mortality to measure the quality of hepatopancreatobiliary surgical operations⁹⁻¹⁹. However, the use of 90-day mortality is still not universal^{20,21}. Furthermore, the concordance of this definition with surgery-related mortality has not been validated—a significant limitation among this population of patients in whom early cancer recurrence represents a common alternate cause of death. An optimal definition of postoperative mortality as a measure of the quality of HPB surgery has therefore not been established.

In this study, we sought to evaluate the legitimacy of 90-day mortality as a measure of surgical quality. We performed a root cause analysis of all deaths that occurred within 1 year following almost 4000 hepatopancreatobiliary operations to determine the extent to which this metric, and others commonly reported, accurately captured surgery-related deaths and excluded disease-related deaths.

Patients and Methods

The Institutional Review Board of The University of Texas MD Anderson Cancer Center approved this study protocol. Through review of a clinical database prospectively maintained by the Department of Surgical Oncology, we identified 2811 consecutive patients who underwent hepatectomy between December 1997 and December 2012 and 1133 patients who underwent pancreatectomy between January 2000 and December 2012 for any diagnosis.²² Patients who underwent concomitant hepatectomy and pancreatectomy were included in the hepatectomy group.

Definitions of Major Complications

We identified all patients who developed a major complication after HPB surgery according to the following definitions. Hepatic insufficiency was defined according to the definitions of the International Surgical Group of Liver Surgery (ISGLS).²³ Postoperative hemorrhage was defined according to the grading system of the ISGLS for patients undergoing hepatectomy and according to the grading system of the International Surgical Group of Pancreatic Surgery (ISGPS) for patients undergoing pancreatectomy because the 2 grading systems are different.^{24,25} Each of these adverse events was assigned a severity grade of A, B, or C, with A indicating least severe and C indicating most severe complication. Events graded B or C were considered major.

The abdomen was not always drained, and the levels of bilirubin or amylase in effluent were not always measured, so data were not always available to conclusively differentiate bile leaks or pancreatic fistulas from abscesses or sterile collections. As a result, use of the ISGLS and ISGPS definitions alone might underestimate the number of bile leaks and pancreatic fistulas. Therefore, drained fluid collections were also categorized as “fluid collection” and were graded according to the Clavien-Dindo classification. Adverse events other than hepatic insufficiency, fluid collection, and hemorrhage (e.g., cardiac, respiratory, gastrointestinal, neurological, and renal) were categorized as “other complications”. Any complication graded III, IV, or V on the Clavien-Dindo scale was considered major.²

For patients who suffered more than one major complication, the most severe complication was reported unless an alternate complication was clearly the proximal cause of a death. A notable exception was hemorrhage of a pseudoaneurysm associated with pancreatic fistula, in which case fluid collection was reported as the major complication. In rare cases, the most severe complication grade of a patient who did not die a surgery-related death was shared by more than 1 complication. In such cases, the complication that appeared upon complete re-review of the case to have the most clinical significance was reported.

Attribution of Cause of Death

We performed a root cause analysis of all deaths that occurred within 365 days from the date of surgery by thorough re-review of all clinical data contained within the electronic medical record. Death was classified as surgery-related when it was judged to have occurred as a direct result of an active major complication or Clavien-Dindo-graded event, regardless of its temporal relationship to the index operation, in the absence of disease progression. Death was defined as disease-related when it occurred in the presence of persistent or recurrent disease without active sequelae of a surgical complication. If the root cause of death (ie, active complication or disease) could not be determined, the cause of death was reported as unknown.

Definitions of Mortality Rates

We calculated rates of overall mortality (all deaths), surgery-related mortality (surgery-related deaths), and disease-related mortality (disease-related deaths) according to the following 4 definitions^{8-19,26-31}:

30-day mortality: Deaths within 30 days after surgery, as either an inpatient or outpatient

30-day and in-hospital mortality: Deaths within 30 days after surgery or during the index hospitalization (if the patient was hospitalized longer than 30 days)

90-day mortality: Death within 90 days after surgery, as either an inpatient or outpatient

180-day mortality: Death within 180 days after surgery, as either an inpatient or outpatient

Statistical Analysis

Continuous variables were expressed as median (range). Time to death was calculated using the Kaplan-Meier method from the date of hepatectomy or pancreatectomy. The optimal duration of follow-up for overall postoperative mortality as an indicator of surgical quality was defined as that which would simultaneously maximize capture of surgery-related deaths and minimize capture of disease-related deaths. A receiver operating characteristics analysis was used to assess the correlation between time to death and surgery-related death in all patients who died within 1 year after surgery. The optimal duration was defined using the Youden index³²⁻³⁴. Optimal duration of follow-up was calculated separately for hepatectomy and pancreatectomy. Statistical analyses were performed using JMP software (version 10.0.2; SAS Institute Inc., Cary, NC) and IBM SPSS Statistics (version 19; IBM, Armonk, NY).

Results

Patient Demographics

The 1-year postoperative courses of all patients included in this study are summarized in Figure 1.

Among the 2811 consecutive patients who underwent hepatectomy, 183 (6.5%) died within 1 year of hepatectomy. A total of 425 patients (15.1%) developed at least 1 major

postoperative complication, and of these patients, 79 (18.6%) died of surgery-related causes within 1 year, at a median of 41 days (range, 0-362 days) after hepatectomy, and 22 (5.1%) died of disease-related causes within 1 year, at a median of 207 days (range, 111-329 days) after hepatectomy. The causes of death could not be determined for 3 patients who suffered a major complication, were discharged without sequelae, and subsequently died within 1 year (at 89, 138, and 281 days after hepatectomy, respectively).

Of the 2386 patients (84.9%) who did not develop a major postoperative complication, 70 (2.9%) died of disease-related causes within 1 year of hepatectomy, at a median of 255 days (range, 111-365 days). The causes of death could not be determined for 9 patients who did not develop a postoperative complication but died within 1 year (at a median of 257 days [range, 89-338 days]).

Of the 1133 consecutive patients who underwent pancreatectomy, 41 patients (3.6%) underwent simultaneous hepatectomy. Among the 1092 remaining patients, 139 (12.7%) died within 1 year of pancreatectomy. A total of 262 patients (23.9%) developed at least 1 major postoperative complication, and of these patients, 20 (7.6%) died of surgery-related causes within 1 year, at a median of 43 days (range, 0-155 days) after pancreatectomy, and 35 (13.4%) died of disease-related causes within 1 year, at a median of 236 days (range, 71-354 days) after pancreatectomy. The causes of death could not be determined for 2 patients who suffered a major complication, were discharged without sequelae, and subsequently died within 1 year of pancreatectomy (at 220 and 227 days after pancreatectomy, respectively).

Of the 830 patients (76.0%) who did not develop a major postoperative complication, 77 (9.2%) died of disease-related causes within 1 year of pancreatectomy, at a median of 278 days (range, 90-359 days). The causes of death could not be determined for 5 patients who did not develop a postoperative complication but died within 1 year (at a median of 213 days [range, 142-338 days]).

The demographic and clinical profiles of all patients who suffered at least 1 major complication are reported in Table 1 and Table 2 for patients who underwent hepatectomy and pancreatectomy, respectively. The clinicopathologic profiles of patients who died a surgery related death after hepatectomy and pancreatectomy are reported in supplemental tables (see Supplemental Table 1 and 2, respectively).

Time to Death and Rates of Mortality

Mortality curves for outcomes after hepatectomy and pancreatectomy are shown in Figure 2. The overall mortality rate ranged from 0.9% at 30 days to 6.5% at 365 days for hepatectomy and from 0.7% at 30 days to 12.7% at 365 days for pancreatectomy (Figure 2A). The surgery-related mortality rate ranged from 0.9% at 30 days to 2.8% at 365 days for hepatectomy and from 0.7% at 30 days to 1.8% at 365 days for pancreatectomy (Figure 2B). The disease-related mortality rate ranged from 0% at 30 days to 3.2% at 365 days for hepatectomy and from 0% at 30 days to 10.3% at 365 days for pancreatectomy (Figure 2C).

Mortality curves for patients who developed a major complication following hepatectomy or pancreatectomy are shown in Figure 2D and Figure 2E, respectively. The 30-day, 90-day, and 180-day surgery-related mortality rates following hepatectomy were 16.9%, 57.3%, and 61.3% among patients who developed hepatic insufficiency; 1.6%, 2.6%, and 3.2% among patients who developed a fluid collection; and 13.8%, 13.8%, and 13.8% among patients who had a hemorrhage postoperatively. The 30-day, 90-day, and 180-day surgery-related mortality rates following pancreatectomy were 1.9%, 2.6%, and 4.5% among patients who developed a fluid collection and 18.2%, 18.2%, and 28.4% among patients who hemorrhaged postoperatively. Figure 3 shows the distributions of time to death in patients who died of major complications and patients who died of disease after hepatectomy or pancreatectomy.

Figure 4 shows the numbers of surgery-related and disease-related deaths within 1 year captured and not captured by each of the 4 overall mortality definitions. The true-positive (sensitivity) and false-positive (1-specificity) rates for capturing surgery-related deaths that were associated with each of the metrics considered are summarized in Table 3. The optimal duration of follow-up for calculation of overall mortality was estimated as 99 days for hepatectomy (sensitivity, 86%; specificity, 99%; area under the curve, 0.94 [95% confidence interval, 0.90-0.98]) and 118 days for pancreatectomy (sensitivity, 95%; specificity, 97%; area under the curve, 0.99 [95% confidence interval, 0.98-1.00]). The 90-day mortality definition was associated with a sensitivity of 82% and 85% for hepatectomy and pancreatectomy, respectively, and a specificity of 99% and 98% for hepatectomy and pancreatectomy, respectively.

Discussion

In this series of almost 4000 hepatopancreatobiliary operations, the overall mortality rate increased from 0.9% at 30 days to 6.5% at 365 days for hepatectomy and from 0.7% at 30 days to 12.7% at 365 days for pancreatectomy. Surgery-related deaths accounted for essentially all early deaths, but late deaths directly attributed to surgery were also common, particularly following hepatectomy. In contrast, disease-related deaths were uncommon prior to 90 days; thereafter, an increase in their number contributed to significant disparity between surgery-related and overall mortality that was more pronounced following pancreatectomy. A receiver operating characteristics analysis showed that the 99-day and 118-day mortality definitions optimally distinguished between surgery-related and disease-related death following hepatobiliary and pancreatic operations, respectively. The overall mortality rate at 90 days was a somewhat less sensitive but an almost equivalently specific measure of surgery-related death for both groups of operations. Extension of follow-up to durations of 99 and 118 days could be advocated based on these findings. These data also suggest that the oft-reported 90-day overall mortality rate represents a legitimate measure of HPB surgical quality.

Judgments regarding the quality of surgical performance are contingent upon the definition and application of the outcome metrics that are used to measure it. To evaluate the effect of varying the definition of postoperative mortality on the quality assessment of cardiac procedures performed at Veterans Administration hospitals, Johnson et al varied the

definition from 30-days all-cause mortality to 30-days all-cause mortality plus any death judged to be directly related to surgery that occurred 30 days to 6 months following surgery⁷. The ranking of 86% of hospitals was different for the 2 different definitions, and 21% of hospitals had a change in their quartile of rank. A standard definition of postoperative mortality that both accurately measures quality and is universally applied and reported is critical to process-improvement initiatives and to cross-study comparisons⁵.

A recent survey of operations for 8 different cancers other than those of the liver or pancreas led to the recommendation that 30-day postoperative mortality be used as an international reporting standard⁴. For HPB procedures, 30-day and in-hospital mortality rates are reported frequently, particularly in the context of single-institution case series²⁶⁻³¹. In this study, however, we demonstrate that these metrics are inappropriate measures of surgical quality because they underestimate the number of deaths directly related to surgery by approximately 50%. Among patients who undergo HPB operations, late surgery-related death is relatively common from complications associated with a protracted course of morbidity, including the development of fluid collections and, following hepatectomy, hepatic insufficiency^{8,9,35,36}. Hepatic failure is particularly significant: although it was observed following only 2.7% of hepatectomies in this series, 68% of patients who developed hepatic failure died within 1 year as a direct result. Indeed, hepatic failure represented the most common cause of post-hepatectomy death, and it routinely occurred late in the postoperative course—60% of all deaths from hepatic insufficiency occurred between 31 and 90 days after surgery, and 10% of deaths occurred later than 180 days after hepatectomy.

Use of longer follow-up durations to calculate postoperative morbidity may capture greater numbers of surgery-related deaths but may simultaneously capture greater numbers of disease-related deaths not immediately related to the technical aspects of surgery. To the extent that cause of death may not be reported in large registries and is difficult and expensive to monitor using prospective surveillance systems, use of longer durations may inappropriately overestimate surgery-related mortality among patients with cancer. In our present study, disease-related death accounted for 0% and 11% of overall mortality at 90 days after hepatectomy and pancreatectomy, respectively, but accounted for 12% and 46% at 180 days. Early disease-related death represents a particularly significant problem following pancreatectomy; indeed, over 10% of patients who underwent pancreatectomy for any cause died of a disease-related cause within 1 year. Furthermore, patients who suffered a major complication following pancreatectomy were more likely to die of disease-related causes than of surgery-related causes within 1 year, an observation that could be linked to either the long-term sequelae of inflammation or immunosuppression or an inability of patients with cancer to receive necessary adjuvant therapies³⁷. Although the early disease-related deaths observed following both hepatectomy and pancreatectomy are in large part related to the relatively aggressive tumor biology associated with the cancers typically resected by these operations, early disease-related mortality may serve as an additional indicator of the quality of cancer staging, patient selection for surgery, and preoperative therapies^{4,38,39}.

The overall 90-day mortality rates of 2.3% after hepatectomy and 1.7% after pancreatectomy reported here are consistent with those reported by other high-volume tertiary care centers for liver and pancreatic disease^{10,12-14,16,38,40}. However, the mortality rates in our current series are much lower than those for patients who underwent hepatectomy (10.1%)⁴¹ or pancreatectomy (60-day mortality rate, 11.9%) reported on the basis of analysis of large administrative datasets⁴². This discordance may, to some degree, relate to differences in the definitions used to calculate postoperative mortality. However, this discordance also attests to the difficulties associated with comparing single-institution data, which are often confounded by reporting biases, with data from large administrative datasets, which better represent mortality at the national level but include data from both high- and low-volume centers. Given that outcomes following major surgical operations are more favorable in high-volume centers and given the trend toward centralization of high-risk procedures, perioperative mortality should be both defined and benchmarked by centers with significant experience^{27,42-50}.

The data reported herein should be evaluated in the context of their limitations. First, this study represents a retrospective analysis of patients treated at a single institution. Although we maintain close follow-up of all patients (for pancreatectomy, for example, 92% of patients have complete followup⁵¹), it is possible that some patients treated for complications at an outside facility were missed. However, the databases we use are prospectively maintained and managed by trained, full-time personnel using abstracted data and standardized algorithms similar to those used in the management of large, national datasets. Furthermore, these datasets offer the broad scope of national datasets but also the granularity required to precisely differentiate disease-related from surgery-related deaths as required in this study. It is also possible that our retrospective root cause analysis mischaracterized the cause of death of some patients. However, thorough re-review of all clinical data contained within the medical record minimized this possibility. Finally, we considered all tumor pathologic subtypes in this series, even benign subtypes, but most patients treated at our high-volume cancer center have a cancer diagnosis. Thus, the number of disease-related deaths in this series may be somewhat high relative to the numbers of disease-related deaths at centers that perform a greater number of operations for benign disease. Although disease-specific analyses may yield more accurate metrics to define surgical quality according to the disease resected, our objective was to define a standard for general HPB procedures.

In conclusion, we report that the 99-day and 118-day definitions of postoperative mortality optimally distinguished between surgery-related and disease-related deaths that occurred following hepatobiliary and pancreatic operations, respectively. Among metrics that are commonly reported, the 90-day overall mortality rate captured most surgery-related deaths and excluded most disease-related deaths. It therefore also represents a legitimate measure of surgical quality.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Sources of Support: Supported by the Khalifa Bin Zayed Al Nahyan Foundation and by the Various Donor Pancreatic Research Fund at the University of Texas MD Anderson Cancer Center.

References

1. Strasberg SM, Linehan DC, Hawkins WG. The accordion severity grading system of surgical complications. *Ann Surg.* 2009; 250:177–186. [PubMed: 19638919]
2. 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; 240:205–213. [PubMed: 15273542]
3. Bilimoria KY, Bentrem DJ, Lillemoe KD, et al. Assessment of pancreatic cancer care in the United States based on formally developed quality indicators. *J Natl Cancer Inst.* 2009; 101:848–859. [PubMed: 19509366]
4. Damhuis RA, Wijnhoven BP, Plaisier PW, et al. Comparison of 30-day, 90-day and in-hospital postoperative mortality for eight different cancer types. *Br J Surg.* 2012; 99:1149–1154. [PubMed: 22718521]
5. Russell EM, Bruce J, Krukowski ZH. Systematic review of the quality of surgical mortality monitoring. *Br J Surg.* 2003; 90:527–532. [PubMed: 12734856]
6. Khuri SF, Daley J, Henderson W, et al. The Department of Veterans Affairs' NSQIP: the first national, validated, outcome-based, risk-adjusted, and peer-controlled program for the measurement and enhancement of the quality of surgical care. National VA Surgical Quality Improvement Program. *Ann Surg.* 1998; 228:491–507. [PubMed: 9790339]
7. Johnson ML, Gordon HS, Petersen NJ, et al. Effect of definition of mortality on hospital profiles. *Med Care.* 2002; 40:7–16. [PubMed: 11748422]
8. Shirabe K, Shimada M, Gion T, et al. Postoperative liver failure after major hepatic resection for hepatocellular carcinoma in the modern era with special reference to remnant liver volume. *J Am Coll Surg.* 1999; 188:304–309. [PubMed: 10065820]
9. Tanabe G, Sakamoto M, Akazawa K, et al. Intraoperative risk factors associated with hepatic resection. *Br J Surg.* 1995; 82:1262–1265. [PubMed: 7552014]
10. Adham M, Chopin-Laly X, Lepilliez V, et al. Pancreatic resection: drain or no drain? *Surgery.* 2013; 154:1069–1077. [PubMed: 23876363]
11. Brouquet A, Abdalla EK, Kopetz S, et al. High survival rate after two-stage resection of advanced colorectal liver metastases: response-based selection and complete resection define outcome. *J Clin Oncol.* 2011; 29:1083–1090. [PubMed: 21263087]
12. Dokmak S, Fteriche FS, Borscheid R, et al. 2012 Liver resections in the 21st century: we are far from zero mortality. *HPB (Oxford).* 2013
13. Gold JS, Are C, Kornprat P, et al. Increased use of parenchymal-sparing surgery for bilateral liver metastases from colorectal cancer is associated with improved mortality without change in oncologic outcome: trends in treatment over time in 440 patients. *Ann Surg.* 2008; 247:109–117. [PubMed: 18156930]
14. Lewis R, Drebin JA, Callery MP, et al. A contemporary analysis of survival for resected pancreatic ductal adenocarcinoma. *HPB (Oxford).* 2013; 15:49–60. [PubMed: 23216779]
15. Mullen JT, Ribero D, Reddy SK, et al. Hepatic insufficiency and mortality in 1,059 noncirrhotic patients undergoing major hepatectomy. *J Am Coll Surg.* 2007; 204:854–862. discussion 862–854. [PubMed: 17481498]
16. Reddy SK, Barbas AS, Turley RS, et al. A standard definition of major hepatectomy: resection of four or more liver segments. *HPB (Oxford).* 2011; 13:494–502. [PubMed: 21689233]
17. Shindoh J, Vauthey JN, Zimmitti G, et al. Analysis of the efficacy of portal vein embolization for patients with extensive liver malignancy and very low future liver remnant volume, including a comparison with the associating liver partition with portal vein ligation for staged hepatectomy approach. *J Am Coll Surg.* 2013; 217:126–133. discussion 133–124. [PubMed: 23632095]

18. Torzilli G, Belghiti J, Kokudo N, et al. A snapshot of the effective indications and results of surgery for hepatocellular carcinoma in tertiary referral centers: is it adherent to the EASL/AASLD recommendations?: an observational study of the HCC East-West study group. *Ann Surg.* 2013; 257:929–937. [PubMed: 23426336]
19. Vauthey JN, Pawlik TM, Ribero D, et al. Chemotherapy regimen predicts steatohepatitis and an increase in 90-day mortality after surgery for hepatic colorectal metastases. *J Clin Oncol.* 2006; 24:2065–2072. [PubMed: 16648507]
20. Hartwig W, Gluth A, Hinz U, et al. Total Pancreatectomy for Primary Pancreatic Neoplasms: Renaissance of an Unpopular Operation. *Ann Surg.* 2014
21. Voron T, Tselikas L, Pietrasz D, et al. Sarcopenia Impacts on Short- and Long-term Results of Hepatectomy for Hepatocellular Carcinoma. *Ann Surg.* 2014
22. Hwang RF, Wang H, Lara A, et al. Development of an integrated biospecimen bank and multidisciplinary clinical database for pancreatic cancer. *Ann Surg Oncol.* 2008; 15:1356–1366. [PubMed: 18256882]
23. Rahbari NN, Garden OJ, Padbury R, et al. Posthepatectomy liver failure: a definition and grading by the International Study Group of Liver Surgery (ISGLS). *Surgery.* 2011; 149:713–724. [PubMed: 21236455]
24. Koch M, Garden OJ, Padbury R, et al. Bile leakage after hepatobiliary and pancreatic surgery: a definition and grading of severity by the International Study Group of Liver Surgery. *Surgery.* 2011; 149:680–688. [PubMed: 21316725]
25. Wente MN, Veit JA, Bassi C, et al. Postpancreatectomy hemorrhage (PPH): an International Study Group of Pancreatic Surgery (ISGPS) definition. *Surgery.* 2007; 142:20–25. [PubMed: 17629996]
26. Belghiti J, Hiramatsu K, Benoist S, et al. Seven hundred forty-seven hepatectomies in the 1990s: an update to evaluate the actual risk of liver resection. *J Am Coll Surg.* 2000; 191:38–46. [PubMed: 10898182]
27. 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. [PubMed: 21631325]
28. Fong Y, Fortner J, Sun RL, et al. Clinical score for predicting recurrence after hepatic resection for metastatic colorectal cancer: analysis of 1001 consecutive cases. *Ann Surg.* 1999; 230:309–318. discussion 318–321. [PubMed: 10493478]
29. Imamura H, Seyama Y, Kokudo N, et al. One thousand fifty-six hepatectomies without mortality in 8 years. *Arch Surg.* 2003; 138:1198–1206. discussion 1206. [PubMed: 14609867]
30. Sosa JA, Bowman HM, Gordon TA, et al. Importance of hospital volume in the overall management of pancreatic cancer. *Ann Surg.* 1998; 228:429–438. [PubMed: 9742926]
31. Torzilli G, Makuuchi M, Inoue K, et al. No-mortality liver resection for hepatocellular carcinoma in cirrhotic and noncirrhotic patients: is there a way? A prospective analysis of our approach. *Arch Surg.* 1999; 134:984–992. [PubMed: 10487594]
32. Perkins NJ, Schisterman EF. The inconsistency of “optimal” cutpoints obtained using two criteria based on the receiver operating characteristic curve. *Am J Epidemiol.* 2006; 163:670–675. [PubMed: 16410346]
33. Niro GA, Casey JL, Gravinese E, et al. Intrafamilial transmission of hepatitis delta virus: molecular evidence. *J Hepatol.* 1999; 30:564–569. [PubMed: 10207796]
34. Youden WJ. Index for rating diagnostic tests. *Cancer.* 1950; 3:32–35. [PubMed: 15405679]
35. Nagino M, Kamiya J, Uesaka K, et al. Complications of hepatectomy for hilar cholangiocarcinoma. *World J Surg.* 2001; 25:1277–1283. [PubMed: 11596890]
36. Takeda K, Togo S, Kunihiro O, et al. Clinicohistological features of liver failure after excessive hepatectomy. *Hepatogastroenterology.* 2002; 49:354–358. [PubMed: 11995449]
37. Tzeng CW, Tran Cao HS, Lee JE, et al. Treatment sequencing for resectable pancreatic cancer: influence of early metastases and surgical complications on multimodality therapy completion and survival. *J Gastrointest Surg.* 2014; 18:16–25. [PubMed: 24241967]
38. Vollmer CM Jr, Sanchez N, Gondek S, et al. A root-cause analysis of mortality following major pancreatectomy. *J Gastrointest Surg.* 2012; 16:89–102. discussion 102–103. [PubMed: 22065319]

39. Hsu CC, Wolfgang CL, Laheru DA, et al. Early mortality risk score: identification of poor outcomes following upfront surgery for resectable pancreatic cancer. *J Gastrointest Surg.* 2012; 16:753–761. [PubMed: 22311282]
40. Baumgartner JM, Krasinskas A, Daouadi M, et al. Distal pancreatectomy with en bloc celiac axis resection for locally advanced pancreatic adenocarcinoma following neoadjuvant therapy. *J Gastrointest Surg.* 2012; 16:1152–1159. [PubMed: 22399269]
41. Mayo SC, Shore AD, Nathan H, et al. Refining the definition of perioperative mortality following hepatectomy using death within 90 days as the standard criterion. *HPB (Oxford).* 2011; 13:473–482. [PubMed: 21689231]
42. Carroll JE, Smith JK, Simons JP, et al. Redefining mortality after pancreatic cancer resection. *J Gastrointest Surg.* 2010; 14:1701–1708. [PubMed: 20844977]
43. Choti MA, Bowman HM, Pitt HA, et al. Should hepatic resections be performed at high-volume referral centers? *J Gastrointest Surg.* 1998; 2:11–20. [PubMed: 9841963]
44. Birkmeyer JD, Siewers AE, Finlayson EV, et al. Hospital volume and surgical mortality in the United States. *N Engl J Med.* 2002; 346:1128–1137. [PubMed: 11948273]
45. Fong Y, Gonen M, Rubin D, et al. Long-term survival is superior after resection for cancer in high-volume centers. *Ann Surg.* 2005; 242:540–544. discussion 544–547. [PubMed: 16192814]
46. Csiksz NG, Simons JP, Tseng JF, Shah SA. Surgical specialization and operative mortality in hepato-pancreatico-biliary (HPB) surgery. *J Gastrointest Surg.* 2008; 12:1534–1539. [PubMed: 18612710]
47. McKay A, You I, Bigam D, et al. Impact of surgeon training on outcomes after resective hepatic surgery. *Ann Surg Oncol.* 2008; 15:1348–1355. [PubMed: 18306973]
48. Katz MH, Wang H, Fleming JB, et al. Long-term survival after multidisciplinary management of resected pancreatic adenocarcinoma. *Ann Surg Oncol.* 2009; 16:836–847. [PubMed: 19194760]
49. de Wilde RF, Besselink MG, van der Tweel I, et al. Impact of nationwide centralization of pancreaticoduodenectomy on hospital mortality. *Br J Surg.* 2012; 99:404–410. [PubMed: 22237731]
50. McPhee JT, Hill JS, Whalen GF, et al. Perioperative mortality for pancreatectomy: a national perspective. *Ann Surg.* 2007; 246:246–253. [PubMed: 17667503]
51. Tzeng CW, Fleming JB, Lee JE, et al. Yield of clinical and radiographic surveillance in patients with resected pancreatic adenocarcinoma following multimodal therapy. *HPB (Oxford).* 2012; 14:365–372. [PubMed: 22568412]

Figure 1. Patient selection

Figure 2. Mortality Curves after Hepatectomy and Pancreatectomy Curves are shown for (A) Overall mortality. (B) surgery-related deaths, (C) disease-related deaths, (D) surgery-related deaths in patients with major complications after hepatectomy, stratified by hepatic insufficiency (blue), hemorrhage (red), fluid collection (yellow), and other complications (gray) and (E) surgery-related deaths in patients with major complications after pancreatectomy stratified by hemorrhage (red), fluid collection (yellow), and other complications (gray).

Figure 3.
Distribution of Time to Death from Major Complications and Disease Progression after Hepatectomy (A) and Pancreatectomy (B)

Figure 4.
Overall Mortality after Hepatectomy (A) and Pancreatectomy (B) according to Different Definitions
A total of 183 deaths within 1 year after hepatectomy and 139 deaths within 1 year after pancreatectomy were stratified by cause.

Table 1

Clinicopathologic profile of 425 patients who developed a major postoperative complication following hepatectomy.

	Total n = 425	Hepatic insufficiency n = 77	Fluid collection* n = 208	Hemorrhage n = 30	Others n = 110
Age (year)	58 (5-87)	63 (29-82)	57 (5-87)	55 (21-77)	59 (26-83)
Male (%)	257 (60)	55 (71)	116 (56)	19 (63)	67 (61)
ASA score >2 (%)	283 (67)	55 (71)	135 (66)	20 (67)	73 (67)
BMI >30 (%)	91 (21)	19 (25)	39 (19)	6 (20)	27 (25)
Comorbidity					
Diabetes (%)	52 (12)	18 (23)	18 (9)	1 (3)	15 (14)
Hypertension (%)	179 (42)	45 (58)	78 (38)	11 (37)	45 (41)
Others (%)	42 (10)	9 (12)	16 (8)	4 (13)	13 (12)
Diagnosis					
CLM (%)	244 (57)	44 (57)	105 (50)	18 (60)	77 (70)
HCC (%)	33 (8)	14 (18)	10 (5)	1 (3)	8 (7)
Biliary tumors (%)	47 (11)	9 (12)	32 (15)	0 (0)	6 (5)
Other malignancies (%)	56 (13)	7 (9)	29 (14)	5 (17)	15 (14)
NET (%)	39 (9)	3 (4)	26 (13)	6 (20)	4 (1)
Benign (%)	6 (1)	0 (0)	6 (3)	0 (0)	0 (0)
Surgery					
Major hepatectomy (%)	315 (74)	66 (86)	152 (73)	22 (73)	75 (68)
Bile duct resection (%)	50 (12)	8 (10)	39 (19)	0 (0)	3 (3)
Other abdominal procedures (%)	141 (33)	24 (31)	106 (51)	10 (33)	49 (45)
Operation time (min)	220 (25-929)	200 (33-851)	244 (45-929)	198 (65-490)	192 (25-665)
Blood loss (mL)	350 (0-12500)	600 (50-12500)	350 (0-4150)	625 (50-6000)	300 (0-6800)
Length of hospital stay (day)	12 (3-73)	15 (5-73)	10 (3-69)	8 (3-26)	10 (4-57)

* Bile leakage (grade B and C) and fluid collection requiring interventional treatment.

ASA, American Society of Anesthesiologists; BMI, body mass index; CLM, colorectal liver metastases; HCC, hepatocellular carcinoma; NET, neuroendocrine tumor. Continuous data were expressed as median (range).

Table 2

Clinicopathologic profile of 262 patients who developed a major postoperative complication following pancreatotomy.

	Total n = 262	Fluid collection* n = 172	Hemorrhage n = 14	Others n = 76
Age (year)	64 (28-82)	65 (28-82)	65 (36-76)	62 (33-80)
Male (%)	147 (56)	103 (60)	6 (43)	38 (50)
ASA score >2 (%)	177 (68)	114 (66)	11 (79)	52 (68)
BMI >30 (%)	73 (28)	50 (29)	5 (36)	18 (24)
Comorbidity				
Diabetes (%)	56 (22)	33 (19)	4 (29)	19 (25)
Hypertension (%)	116 (44)	65 (38)	9 (64)	42 (55)
Others (%)	35 (13)	25 (15)	2 (14)	8 (11)
Diagnosis				
PDAC (%)	153 (58)	93 (54)	10 (71)	50 (66)
NET (%)	49 (19)	34 (20)	3 (21)	12 (16)
IPMN (%)	17 (6)	14 (8)	0 (0)	3 (4)
Metastasis (%)	3 (1)	1 (1)	0 (0)	2 (3)
Other malignancies (%)	24 (9)	20 (12)	0 (0)	4 (5)
Benign (%)	16 (6)	10 (6)	1 (7)	5 (7)
Surgery				
Pancreaticoduodenectomy (%)	197 (75)	128 (74)	12 (86)	57 (75)
Distal pancreatectomy (%)	57 (22)	40 (23)	1 (7)	16 (21)
Total pancreatectomy (%)	4 (2)	2 (1)	0 (0)	2 (3)
Central pancreatectomy (%)	4 (2)	2 (1)	1 (7)	1 (1)
Vascular reconstruction (%)	58 (22)	33 (19)	6 (43)	19 (25)
Other abdominal procedures (%)	23 (9)	11 (6)	1 (7)	11 (14)
Operation time (min)	433 (102-1044)	430 (133-880)	465 (294-666)	430 (102-1044)
Blood loss (mL)	675 (50-8000)	600 (50-6000)	700 (200-2100)	750 (50-8000)
Length of hospital stay (day)	14 (5-108)	15 (6-89)	16 (7-88)	14 (5-108)

* Pancreatic fistula (grade B and C) and fluid collection requiring interventional treatment.

ASA, American Society of Anesthesiologists; BMI, body mass index; PDAC, pancreatic ductal adenocarcinoma; IPMN, intraductal papillary mucinous neoplasm; NET, neuroendocrine tumor.

Continuous data were expressed as median (range).

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Table 3

Rates of Overall Mortality and Surgery-Related Mortality

Definition	Overall mortality % (deaths/N)	Surgery-related mortality % (deaths/N)	Sensitivity ^a	1-Specificity ^a
Hepatectomy				
30-day	0.9 (25/2811)	0.9 (25/2811)	0.32	0.00
30-day and in-hospital	1.3 (37/2811)	1.3 (37/2811)	0.47	0.00
90-day	2.3 (66/2811)	2.3 (65/2811)	0.82	0.01
90-day ^b	2.4 (69/2811)	2.4 (68/2811)	0.86	0.01
180-day	3.0 (83/2811)	2.5 (71/2811)	0.90	0.12
365-day	6.5 (183/2811)	2.8 (79/2811)	1.00	1.00
Pancreatectomy				
30-day	0.7 (8/1092)	0.7 (8/1092)	0.40	0.00
30-day and in-hospital	1.0 (11/1092)	0.9 (10/1092)	0.50	0.01
90-day	1.7 (19/1092)	1.5 (17/1092)	0.85	0.02
118-day ^b	2.1 (23/1092)	1.7 (19/1092)	0.95	0.03
180-day	3.7 (41/1092)	1.8 (20/1092)	1.00	0.19
365-day	12.7 (139/1092)	1.8 (20/1092)	1.00	1.00

^aFor capturing surgery-related deaths.

^bReceiver operating characteristics analysis revealed that 99 days and 118 days were the best durations for identifying surgery-related deaths after hepatectomy (area under the curve [AUC], 0.94) and pancreatectomy (AUC, 0.99), respectively.