



Comparing Minimally Invasive and Open Pancreaticoduodenectomy for the Treatment of Pancreatic Cancer: a Win Ratio Analysis

Eliza W. Beal¹ · Djhenne Dalmacy¹ · Alessandro Paro¹ · J. Madison Hyer¹ · Jordan Cloyd¹ · Mary Dillhoff¹ · Aslam Ejaz¹ · Timothy M. Pawlik¹

Received: 17 December 2021 / Accepted: 3 June 2022 / Published online: 15 June 2022
© The Society for Surgery of the Alimentary Tract 2022

Abstract

Introduction Despite its rising adoption, the use of minimally invasive (MIS) pancreaticoduodenectomy (PD) in the treatment of pancreatic cancer remains controversial. We sought to compare MIS and open PD for pancreatic cancer resection in terms of short-term, long-term, and oncologic outcomes using the win ratio, a novel statistical approach.

Methods Patients undergoing PD for pancreatic adenocarcinoma 2010–2016 were identified from the National Cancer Database (NCDB). Patients were paired based on age, sex, race, tumor size, Charlson-Deyo score, and receipt of neoadjuvant chemotherapy. The win ratio was calculated based on 30-day and 3-year mortality, receipt of adjuvant chemotherapy, surgical margin status, examination of at least 11 lymph nodes, extended length of stay, and 30-day readmission.

Results Among 18,936 patients, median age was 67 (IQR: 60–74); most patients had stage II disease at diagnosis ($n = 16,530$, 87.3%) and tumor size ≥ 2 cm ($n = 15,880$, 83.9%). The majority of patients underwent open PD ($n = 16,409$, 86.7%) versus MIS PD ($n = 2527$, 13.3%). For every matched patient-patient pair, the odds of the patient undergoing MIS PD “winning” were 1.14 (95%CI 1.13–1.15) higher versus open PD. The benefits of MIS PD were most pronounced among patients with tumor size < 2 cm (WR 1.21, 95%CI 1.13–1.30 *versus* ≥ 2 cm, WR 1.13, 95%CI 1.12–1.14) and patients who received neoadjuvant chemotherapy prior to resection (WR 1.28, 95%CI 1.23–1.32 *versus* no neoadjuvant chemotherapy, WR 1.13, 95%CI 1.11–1.14).

Conclusions MIS PD may be preferable to open PD based on a hierarchical composite outcome that considered short-term, long-term, and oncologic outcomes.

Keywords Win ratio · Pancreaticoduodenectomy · Minimally invasive surgery (MIS)

Introduction

Pancreatic cancer is the 4th leading cause of cancer death among both men and women in the USA with a 5-year overall survival of approximately 8% [1]. While treatment for early-stage pancreatic cancer includes neoadjuvant and/or adjuvant chemotherapy, and sometimes radiation, surgical resection is the best potentially curative treatment option [2]. Only 10–15% of patients present, however, with surgically

resectable disease, and 5-year overall survival for this population approaches 25% [1]. Resectability may be limited by abutment or involvement of major vascular structures, distant disease, or severe patient comorbidities. [3]

Pancreaticoduodenectomy (PD) or the Whipple procedure is the surgical procedure of choice for resection of pancreatic adenocarcinoma of the head of the pancreas and was classically performed in an open fashion using a generous midline, subcostal, or L-shaped incision [4]. However, minimally invasive surgical (MIS) techniques are increasingly used for the performance of PD [5, 6]. MIS techniques for PD include both laparoscopic and robotic approaches. Randomized controlled trials (RCTs) comparing laparoscopic and open PD have reported variable outcomes [7–10]. Patients undergoing laparoscopic PD tend, however, to have shorter LOS, less blood loss, and longer operative time yet similar rates of major complications, number of lymph nodes

✉ Timothy M. Pawlik
tim.pawlik@osumc.edu

¹ Department of Surgery, The Ohio State University, Wexner Medical Center and James Cancer Hospital and Solove Research Institute, 395 W. 12th Ave., Suite 670, Columbus, OH, USA

retrieved, resection margins, and pancreatic-specific complications (delayed gastric emptying, pancreatic fistula, post-pancreatectomy hemorrhage) [7–10]. While no RCTs comparing robotic and open PD are currently available, an early prospective matched study demonstrated shorter LOS, less blood loss, better nutritional recovery, earlier return to activity, and faster resumption of bowel function, with comparable morbidity and mortality, margin status, and number of lymph nodes retrieved [11]. Despite these data, the use of MIS PD remains controversial due to the absence of high-quality long-term data on oncologic outcomes. The recent Miami International Evidence-Based Guideline on Minimally Invasive Pancreatic Resection concluded that there is insufficient data to recommend MIS PD over open PD. [12]

The win ratio, which was originally applied to cardiovascular clinical trials, is a novel composite outcome calculated by considering all potential pairs of patients undergoing two different treatments in a given data set [13]. Patients in each pair are compared based on hierarchically ordered component outcomes. Patient pairs are compared based on the first outcome, and if either patient fares better than the other, that pair is considered a “win” for the respective treatment. If neither patient fares better on the first outcome, then the patient pair is considered a tie and is then compared based on the second outcome and so forth. The win ratio is calculated as the total number of wins for the treatment of interest divided by the total number of losses [14]. Therefore, the win ratio accounts for both the proportion of the patients who achieve each component outcome and also the order of relative importance of the selected outcomes. Additionally, the win ratio can include information on both short- and long-term outcomes following surgery and allows for an overall comparison of MIS and open PD for pancreatic cancer. The objective of the current study was to compare MIS and open PD for pancreatic cancer resection in terms of short-term, long-term, and oncologic outcomes using the win ratio. In addition, we sought to stratify patients based on demographic and clinical characteristics to identify which patients may benefit most from MIS versus open PD.

Methods

Patient Population

Patients diagnosed with pancreatic adenocarcinoma were identified from the National Cancer Database (NCDB) using the relevant International Classification of Diseases for Oncology, third edition (ICD-O-3) histology codes (Supplemental Table 1). The NCDB 2017 PUF was utilized to identify patients who underwent PD as surgical treatment of their primary tumor between 2010 and 2016 with the corresponding values for the Surgical Procedure of Primary Site

NCDB variable (i.e., 35, 36, 37, 70); this ensured that every patient had at least 1 year of follow-up. NCDB is a nationwide clinical oncology database containing deidentified hospital registry data from more than 1500 Commission on Cancer (CoC)-accredited facilities. Data on approximately 70% of all newly diagnosed cancers in the USA are captured at the institutional level and reported to the NCDB, adding to the more than 34 million historical records [15]. In the current study, patients with metastatic disease were excluded. Additionally, patients for whom information on mortality, resection margins, and length of stay (LOS) was not available were also excluded.

Variables, Definitions, and Outcomes

Patients were split into two separate cohorts based on whether the patient underwent MIS (i.e., laparoscopic or robotic) or open PD. Other variables of interest included patient age, sex, race, and Charlson-Deyo comorbidity score. The Charlson-Deyo comorbidity score (CDCC) is a weighted score that predicts 1-year mortality following hospitalization for patients with specific comorbid conditions [16, 17]. Additionally, information on tumor size, American Joint Committee on Cancer (AJCC) stage, and receipt of neoadjuvant therapy was obtained. Receipt of neoadjuvant therapy was defined as receipt of any chemotherapy or radiotherapy prior to surgical resection.

The main outcome of interest was the win ratio, a composite outcome used to compare two alternative treatment or management options [13, 14]. In order to calculate the win ratio, each patient from one treatment group was paired with each patient from the other treatment group, after which the two patients were compared based on each component outcome, starting from the first in hierarchical order. If the patient receiving the treatment of interest had a better outcome, it was considered a “win”; if the patient receiving the alternative treatment had a better outcome, it was considered a “loss.” Otherwise, it is considered a “tie,” and the two patients were compared based on the next component outcome. The win ratio was then calculated by dividing the total number of wins by the total number of losses (Fig. 1). As such, the win ratio not only accounted for the achievement of each of its component outcomes but also for their relative priority. Additionally, the win ratio was not restricted to component outcomes of a single variable type, but included time-to-event, continuous, and/or categorical outcomes [18, 19]. A more thorough explanation of the win ratio approach is provided by Redfors et al. [13]

Component outcomes included in the win ratio calculation were, in hierarchical order, 30-day mortality, 3-year mortality, receipt of adjuvant therapy, negative surgical margins, examination of < 11 lymph nodes, extended LOS, and readmission at 30 days following surgery. Receipt of

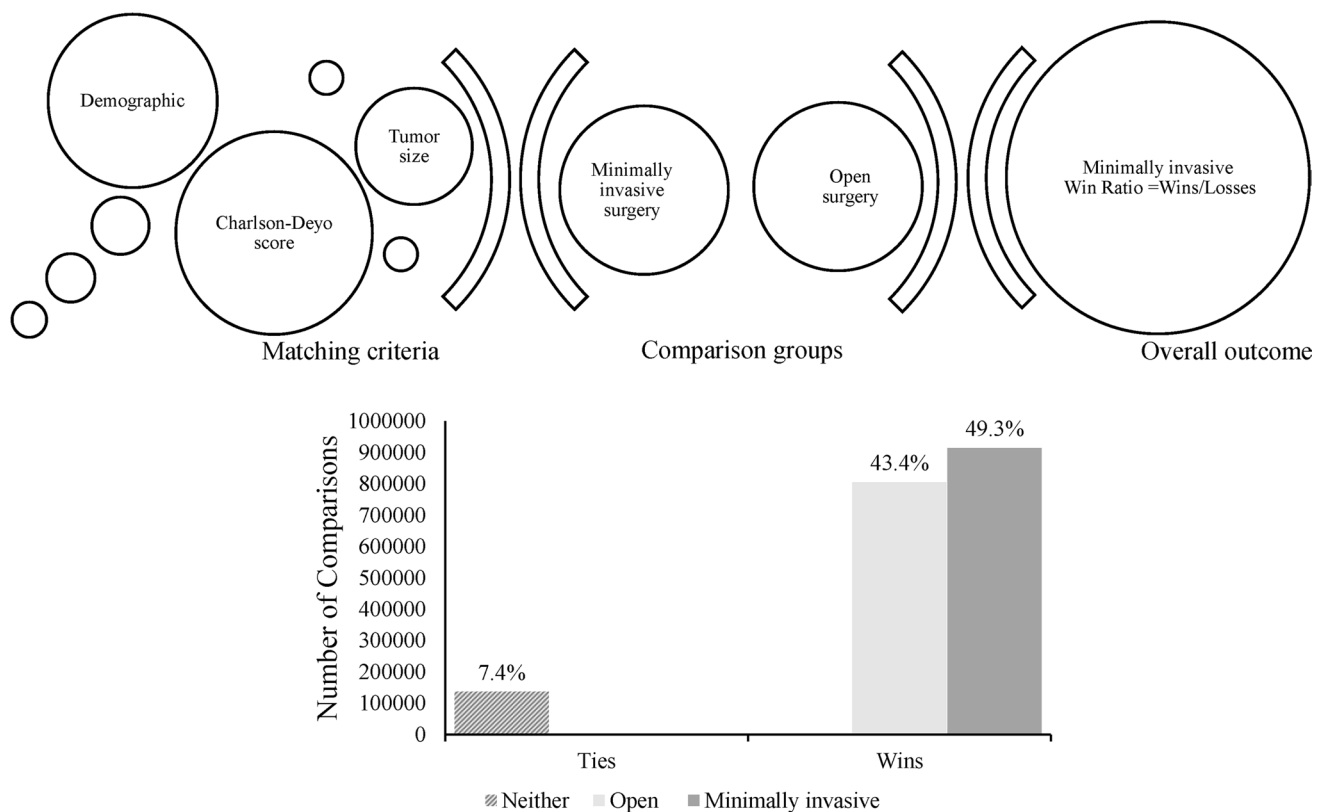


Fig. 1 At the top, the overall process for calculating the win ratio is illustrated. Patients who underwent minimally invasive versus open surgery were matched based on the variables shown on the left. Then, they were compared based on the component outcomes to obtain the

overall number of wins and losses. Lastly, the win ratio was calculated by dividing the total number of wins by the total number of losses, as shown on the right. At the bottom, a bar chart shows the relative number of wins for minimally invasive and open surgery

adjuvant therapy was defined as receipt of any radiotherapy or chemotherapy after surgical resection of the primary tumor. A cutoff of 11 examined lymph nodes was used as the threshold as it was the minimum number of lymph nodes to provide optimal staging according to the most recent NCCN guidelines [20, 21]. An extended LOS was defined as LOS exceeding the 75th percentile, as previously reported [22]. Of note, not all unmatched patient-patient pairs were considered when calculating the win ratio. Instead, only pairs in which the two patients were matched based on age, sex, race, CDCC, tumor size, and receipt of neoadjuvant therapy were included. For continuous variables, members of a pair were not allowed to differ by more than one standard deviation. For categorical variables, members of a pair were required to have the same value. Thus, the matching process avoided comparisons between patients in a pair with drastically different underlying risk profiles.

Statistical Analysis

Descriptive statistics were presented as median (interquartile range, IQR) for continuous variables and frequency (relative frequency, %) for categorical variables. Bivariate

associations between surgical approach (open or MIS PD) and patient characteristics or postoperative outcomes were assessed using Kruskal–Wallis one-way analysis of variance for continuous variables and Chi-square tests for categorical variables. All analyses were performed using SAS v9.4. Statistical significance was assessed at $\alpha = 0.05$.

Results

Patient Characteristics

Among 18,936 patients diagnosed with pancreatic adenocarcinoma who underwent PD between 2010 and 2016, median age was 67 (IQR: 60–74) and slightly more than one-half of the cohort was male ($n = 9786$, 51.7%) (Table 1). The overwhelming majority of patients were White ($n = 15,441$, 81.5%), with only a minority of patients being Black ($n = 1852$, 9.8%) or not identifying themselves as either White or Black ($n = 1643$, 8.7%). Most patients had relatively few preoperative comorbidities, with more than 9 in 10 patients having a CDCC of either 0 ($n = 11,732$, 62.0%) or 1 ($n = 5340$, 28.2%) and only approximately 1 in 10

Table 1 Patient demographic and clinical characteristics by treatment group (open surgery or minimally invasive surgery, MIS)

	Overall <i>n</i> = 18,936	Open surgery <i>n</i> = 16,409 (86.7%)	MIS <i>n</i> = 2527 (13.3%)	<i>P</i> value
Preoperative characteristics				
Age, median (IQR)	67 (60–74)	67 (60–74)	67 (60–74)	0.11
Male sex, <i>n</i> (%)	9786 (51.7)	8507 (51.8)	1279 (50.6)	0.25
Race, <i>n</i> (%)				0.02
White	15,441 (81.5)	13,333 (81.3)	2108 (83.4)	
Black	1852 (9.8)	1640 (10.0)	212 (8.4)	
Other	1643 (8.7)	1436 (8.8)	207 (8.2)	
CDCC total best, <i>n</i> (%)				0.58
0	11,732 (62.0)	10,150 (61.9)	1582 (62.6)	
1	5340 (28.2)	4653 (28.4)	687 (27.2)	
2	1302 (6.9)	1118 (6.8)	184 (7.3)	
3	562 (3.0)	488 (3.0)	74 (2.9)	
Tumor size ≤ 2 cm, <i>n</i> (%)	3056 (16.1)	2646 (16.1)	410 (16.2)	0.90
AJCC stage, <i>n</i> (%)				0.008
I	1947 (10.3)	1671 (10.2)	276 (10.9)	
II	16,530 (87.3)	14,319 (87.3)	2211 (87.5)	
III	459 (2.4)	419 (2.6)	40 (1.6)	
Neoadjuvant therapy, <i>n</i> (%)	3704 (19.6)	3177 (19.4)	527 (20.9)	0.08

MIS minimally invasive surgery, CDCC Charlson-Deyo comorbidity score

patients having a CDCC of either 2 (*n* = 1302, 6.9%) or 3 (*n* = 562, 3.0%). The vast majority of patients had a cancer larger than 2 cm in size (*n* = 15,880, 83.9%). Patients presented most frequently with stage II disease (*n* = 16,530, 87.3%), followed by stage I (*n* = 1947, 10.3%) and stage III disease (*n* = 459, 2.4%). Only about 1 in 5 patients received neoadjuvant therapy prior to resection (*n* = 3704, 19.6%).

The majority of patients underwent open surgery for resection of their primary tumor (*n* = 16,409, 86.7%), while the remaining subset underwent MIS PD (*n* = 2527, 13.3%) (Table 1). There were no major differences in age or sex between the two groups (median age, 67 years vs 67 years and male sex, 51.8% vs 50.6%, for open and MIS PD, respectively) (both *p* > 0.05). However, patients who underwent open PD were more often Black (10.0% vs 8.4%) or

more often self-identified as neither White nor Black (8.8% vs 8.2%) compared with patients who underwent MIS PD (*p* = 0.02). Additionally, patients who underwent open resection presented more often with disease at a later stage (stage III, 2.6% vs 1.6%) versus patients who underwent MIS PD (*p* = 0.008).

Component Outcomes

Table 2 lists the component outcomes in the order in which each was factored into the win ratio calculation. Only 3.1% of patients (*n* = 583) died within 30 days of resection; however, two-thirds of patients (*n* = 12,034, 63.6%) eventually died within 3 years of surgery. In terms of oncologic outcomes, more than 3 in 4 patients had negative surgical

Table 2 Component outcomes included in the win ratio, by treatment group (open surgery or minimally invasive surgery, MIS)

	Overall <i>n</i> = 18,936	Open surgery <i>n</i> = 16,409 (86.7%)	MIS <i>n</i> = 2527 (13.3%)	<i>P</i> value
Postoperative outcomes				
No mortality—30 days, <i>n</i> (%)	18,353 (96.9)	15,886 (96.8)	2467 (97.6)	0.028
No mortality—3 years, <i>n</i> (%)	6902 (36.4)	5895 (35.9)	1007 (39.8)	<0.001
Adjuvant therapy, <i>n</i> (%)	11,508 (60.8)	9919 (60.4)	1589 (62.9)	0.02
R0 margins, <i>n</i> (%)	14,662 (77.4)	12,646 (77.1)	2016 (79.8)	0.002
Lymph nodes examined ≥ 11, <i>n</i> (%)	14,825 (78.3)	12,754 (77.7)	2071 (82.0)	<0.001
No extended length of stay, <i>n</i> (%)	13,849 (73.1)	11,883 (72.4)	1966 (77.8)	<0.001
No readmission—30 days, <i>n</i> (%)	17,025 (89.9)	14,733 (89.8)	2292 (90.7)	0.16

MIS minimally invasive surgery, R0 microscopically negative margins

margins ($n = 14,662, 77.4\%$) or had at least 11 lymph nodes examined at the time of surgery ($n = 14,825, 78.3\%$). Approximately 6 in 10 patients received adjuvant therapy following resection ($n = 11,508, 60.8\%$). Additionally, 26.9% of patients ($n = 5087$) had a prolonged LOS during the index hospitalization, while 1 in 10 patients ($n = 1911, 10.1\%$) had at least one readmission within 30 days of surgery.

Of note, patients who underwent MIS PD had lower mortality at 30 days (2.4% vs 3.2%; $p = 0.028$) and 3 years (60.2% vs 64.1%; $p < 0.001$) following resection compared with patients who underwent open surgery. Additionally, patients who had MIS PD more often had negative surgical margins (79.8% vs 77.1%), had at least 11 lymph nodes examined (82.0% vs 77.7%), and received adjuvant therapy (62.9% vs 60.4%) versus patients who had open surgery (all $p < 0.05$). Patients who had MIS PD were also less likely to have an extended LOS than patients who had open resection (22.2% vs 27.6%; $p < 0.001$).

Win Ratio

The process for calculating the win ratio in the overall patient population is illustrated in Fig. 2. The overall win ratio was 1.14 (95% CI 1.13–1.15), which means that for every matched patient-patient pair, the odds of the patient undergoing MIS PD “winning” were 1.14. In effect, the probability that a patient undergoing MIS PD ended up “winning” was $1.14 / (1 + 1.14) = 53.3\%$. Notably, the win ratio was also calculated for relevant subsets of the

population (Table 3). In particular, the win ratio favored MIS PD regardless of age group (age < 65 , WR 1.18, 95% CI 1.15–1.20; age ≥ 65 , WR 1.11, 95% CI 1.10–1.13) or sex (female 1.10, 95% CI 1.08–1.11; male, WR 1.17, 95% CI 1.16–1.19). While the win ratio favored MIS PD regardless of race, the benefits of MIS PD appeared to be most pronounced among non-White patients (White, WR 1.13, 95% CI 1.12–1.14; Black, WR 1.34, 95% CI 1.23–1.46; Other, WR 1.30, 95% CI 1.18–1.42). Additionally, the win ratio increased stepwise with increasing CDCC, suggesting that patients with more preoperative comorbidities may benefit more from MIS PD than patients with few preoperative comorbidities (CDCC=0, WR 1.12, 95% CI 1.11–1.13; CDCC=1, WR 1.22, 95% CI 1.19–1.25; CDCC=2, WR 1.25, 95% CI 1.14–1.37; CDCC=3, WR 1.38, 95% CI 1.08–1.81). The benefits of MIS PD also appeared to be most pronounced among patients with a tumor < 2 cm in size (WR 1.21, 95% CI 1.13–1.30 vs WR 1.13, 95% CI 1.12–1.14 if tumor size ≥ 2 cm), as well as among patients who received neoadjuvant therapy prior to resection (WR 1.28, 95% CI 1.23–1.32 versus WR 1.13, 95% CI 1.11–1.14 if no neoadjuvant therapy).

Discussion

While gaining in popularity, MIS PD remains controversial due to the paucity of long-term data on oncologic outcomes and the absence of randomized controlled trials comparing

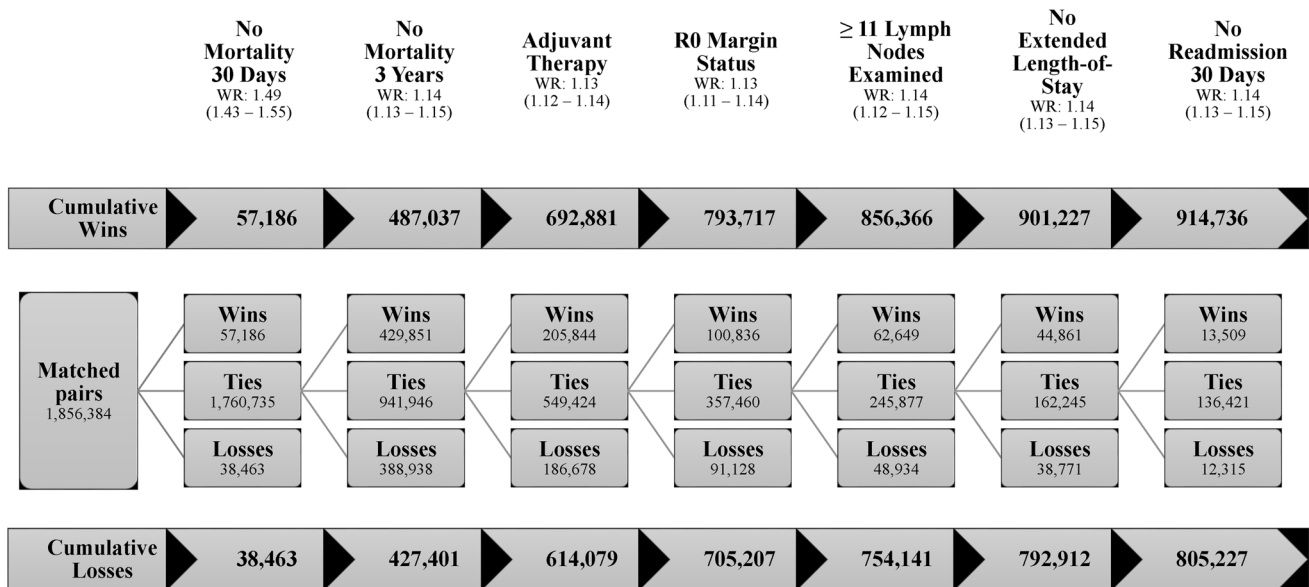


Fig. 2 Illustration of the step-by-step process for calculating the win ratio. The number of wins, losses, and ties relative to each component outcome is shown inside the boxes in the middle of the figure. On each side of these boxes, the number of cumulative wins and losses

up to that point is recorded. The number of cumulative wins and losses is then used to calculate the win ratio, as seen at the top of the figure

Table 3 Win ratio in the overall population, as well as stratified by relevant demographic and clinical characteristics

Group	Win ratio	95% CI
Overall population	1.14	1.13–1.15
Age		
< 65	1.18	1.15–1.20
≥ 65	1.11	1.10–1.13
Sex		
Male	1.17	1.16–1.19
Female	1.10	1.08–1.11
Race, n (%)		
White	1.13	1.12–1.14
Black	1.34	1.23–1.46
Other	1.30	1.18–1.42
CDCC total best		
0	1.12	1.11–1.13
1	1.22	1.19–1.25
2	1.25	1.14–1.37
3	1.38	1.08–1.81
Tumor size		
< 2 cm	1.21	1.13–1.30
≥ 2 cm	1.13	1.12–1.14
Neoadjuvant therapy, n (%)		
No	1.13	1.11–1.14
Yes	1.28	1.23–1.32

CDCC Charlson-Deyo comorbidity score

MIS versus open PD. There have been several RCTs comparing laparoscopic versus open PD [7–10]. The PADU-LAP trial, a single-center RCT, demonstrated shorter hospital stay (LOS), longer operative time, and a reduction in major complications (Clavien-Dindo ≥ 3) with laparoscopic PD versus open PD yet no difference in pancreatic-specific complications, number of lymph nodes retrieved, or resection margin status [7]. The PLOT trial, a single-center RCT, similarly reported shorter LOS and longer operative time for laparoscopic PD, with increased blood loss in the open group and no difference in overall complications, number of lymph nodes retrieved, resection margins, or risk of delayed gastric emptying, pancreatic fistula, or post-pancreatectomy hemorrhage [8]. In contrast, the multicenter LEOPARD-2 RCT was stopped early due to a difference in 90-day complication-related mortality favoring the open PD group and also an increased LOS in the laparoscopic PD group [9]. Given these disparate results, the current study was important because we utilized a novel methodological approach called the win ratio—a means to compare hierarchical outcomes into a composite metric—to define the benefits of MIS versus open PD for pancreatic cancer. Of note, among any given pair of matched patients, individuals who underwent MIS PD had 14% increased odds of “winning” versus

patients who had an open PD. Interestingly, the benefit of PD “winning” persisted even after accounting for 30-day mortality, receipt of adjuvant therapy, margin status, number of lymph nodes evaluated, extended hospital LOS and 30-day readmission, and 3-year mortality. Furthermore, the MIS PD approach won out over the open approach among patients regardless of age, sex, race, CDCC, tumor size, or receipt of neoadjuvant chemotherapy.

A recent systematic review and meta-analysis that incorporated data from previous MIS versus open PD trials reported no difference in most primary (90-day mortality, Clavien-Dindo complications, LOS) or secondary (postoperative pancreatic fistula, delayed gastric emptying, post-pancreatectomy hemorrhage, bile leak, reoperation, readmission, and oncologic outcomes including R0-resection, lymph nodes harvested) outcomes [23]. Operative time was, however, longer, and blood loss was higher among patients undergoing laparoscopic PD. In a more recent multicenter RCT including high volume PD centers, Wang et al. reported shorter LOS among patients who underwent laparoscopic PD; however 90-day mortality, serious postoperative morbidity (Clavien-Dindo ≥ 3), and the comprehensive complication index score were similar to patients who underwent open PD [10]. Although several cohort studies have reported outcomes following robotic PD, there are currently no RCTs comparing robotic and open PD [24–26]. Data from other systematic reviews had demonstrated similar outcomes following MIS versus open PD [27, 28]. Rather than aggregating previously published data into a systemic analysis, we sought to use a novel approach based on a composite endpoint to investigate the relative benefits of MIS versus open PD. The use of a composite metrics allows for a more holistic assessment of the therapeutic benefit of any given therapy, rather than assessing individual elements of quality. While increasingly embraced, the use of “simple” composite primary endpoints can, however, be problematic. Specifically, the conventional practice of analyzing component elements of any composite outcome as equally contributing to a “win” can be misleading. “Less” serious events such as extended LOS can dominate and be “counted” as equivalent as other “more serious” events such as morbidity and mortality. In particular, the use of such composite metrics as textbook outcome may allow “lesser” events to dominate when more “serious” events should be weighted more. By using the win ratio, we were able to utilize this new approach to analyze composite endpoints with varying severity and to account for the relative priority of the different components [14, 18, 19, 29, 30]. In this way, component outcomes were weighted and assessed in an incremental hierarchical manner to arrive at a “win” (Figs. 1 and 2). This novel approach represented an improvement in how to assess postoperative outcomes relative to composite quality metrics compared with other tools such as optimal or textbook outcome. [31–33]

Of note, patients who underwent MIS PD had higher odds of “winning” versus patients who underwent an open resection independent of age, sex, race, Charlson Deyo score, tumor size or receipt of neoadjuvant chemotherapy. Interestingly, although the win ratio favored patients regardless of race, the benefits did appear to be more pronounced among non-White patients. The win ratio also increased incrementally with increasing CDCC. Specifically, the data suggested that patients with a higher number of comorbidities benefited more from MIS PD than individuals with fewer comorbidities. Furthermore, the benefits of MIS PD appeared to be most pronounced among patients with a tumor < 2 cm in size and among patients who received neoadjuvant therapy. Patients with smaller tumors may facilitate a less technically challenging MIS operation. Furthermore, given that neoadjuvant therapy is more commonly administered at high-volume centers, the improved results among patients undergoing MIS PD may have been a surrogate for a volume-center effect. In particular, selection criteria for MIS PD remain not well defined, yet have expanded at high-volume centers to include some patients with borderline resectable or locally advanced tumors requiring vascular resection and reconstruction. [26, 34–39]

There are several limitations that should be considered when interpreting results of the current study. Given that patients were treated at a variety of centers across the USA, there was likely heterogeneity relative to patient selection for MIS versus open PD. The use of a large, national database did allow, however, for a population-based comparison of MIS versus open PD across a wide range of institutions and providers. In order to calculate the win ratio, patients were matched based on age, sex, race, CDCC, tumor size, and receipt of neoadjuvant therapy. Despite this matching process, residual selection bias may have persisted as some confounders may have been unknown and therefore could not be accounted for in the analysis. Additionally, the NCDB did not contain data on pancreas-specific post-PD complications such as delayed gastric emptying, post-pancreatectomy hemorrhage, or postoperative pancreatic fistula. Therefore, results from the current study should be validated in other databases (i.e., NSQIP, Medicare, institutional series). Additionally, center volume is not included in the NCDB; as such, center volume could not be controlled for in the WR analyses. In turn, center volume may have impacted difference in outcomes among patients independent of the MIS versus open PD approach.

In conclusion, using a novel statistical approach, the win ratio was used to assess a range of outcomes (e.g., 30-day mortality, 3-year mortality, receipt of adjuvant therapy, margin status, number of lymph nodes retrieved, extended hospital LOS and 30-day readmission) in a hierarchical manner to arrive at a win versus loss for patients undergoing PD. Unlike conventional methods for comparing composite

endpoints, the hierarchical win ratio approach accounted for the differing clinical importance of individual endpoint components. Of note, the win ratio demonstrated an overall head-to-head benefit of MIS versus open PD for pancreatic cancer, with MIS PD being associated with a 14% increased odds of winning independent of patient age, sex, race, CDCC, tumor size or receipt of neoadjuvant therapy. Data from the current study, as well as prospective trials, suggest that MIS PD could increasingly be considered in the surgical approach for patients with pancreas cancer.

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.1007/s11605-022-05380-3>.

Author Contribution EWB, DD, AP, JMH, JC, MD, AE, and TMP conceptualized the study design. DD, EWB, and AP performed the data analysis and drafted the work. EWB, DD, AP, JMH, JC, MD, AE, and TMP revised the work critically for important intellectual content. All authors approved the final version to be submitted and agree to be accountable for all aspects of the work.

Declarations

Conflict of Interest The authors declare no competing interests.

References

1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2018. *CA Cancer J Clin*. 2018;68(1):7-30. <https://doi.org/10.3322/caac.21442>
2. Tempero MA, Malafa MP, Al-Hawary M, et al. Pancreatic Adenocarcinoma, Version 2.2021, NCCN Clinical Practice Guidelines in Oncology. *J Natl Compr Canc Netw*. 2021;19(4):439–457. <https://doi.org/10.6004/jnccn.2021.0017>
3. Pawlik TM. Pancreatic Cancer. *Surg Oncol Clin N Am*. 2021;30(4):xiii-xv.
4. Gaitonde SG, Ahmad SA. Chapter 141: Pancreatic Cancer: Principles of Pancreaticoduodenectomy and Distal Pancreatectomy. In: Morita S, Balch C, Klimberg V, Pawlik T, Posner M, Tanabe K, eds. *Textbook of Complex General Surgical Oncology*. McGraw Hill; 2018.
5. Nassour I, Paniccia A, Moser AJ, Zureikat AH. Minimally Invasive Techniques for Pancreatic Resection. *Surg Oncol Clin N Am*. 2021;30(4):747-758. <https://doi.org/10.1016/j.soc.2021.06.007>
6. van Hilst J, de Graaf N, Abu Hilal M, Besselink MG. The Landmark Series: Minimally Invasive Pancreatic Resection. *Ann Surg Oncol*. 2021;28(3):1447-1456. <https://doi.org/10.1245/s10434-020-09335-3>
7. Poves I, Burdío F, Morató O, et al. Comparison of perioperative outcomes between laparoscopic and open approach for pancreatoduodenectomy: The Padulap randomized controlled trial. *Ann Surg*. 2018;268(5):731-739. <https://doi.org/10.1097/SLA.0000000000002893>
8. Palanivelu C, Senthilnathan P, Sabnis SC, et al. Randomized clinical trial of laparoscopic versus open pancreatoduodenectomy for periampullary tumours. *Br J Surg*. 2017;104(11):1443-1450. <https://doi.org/10.1002/bjs.10662>
9. van Hilst J, De Rooij T, Bosscha K, et al. Laparoscopic versus open pancreatoduodenectomy for pancreatic or periampullary tumours (LEOPARD-2): a multicentre, patient-blinded, randomised controlled phase 2/3 trial. *Lancet Gastroenterol Hepatol*.

- 2019;4(3):199-207. [https://doi.org/10.1016/S2468-1253\(19\)30004-4](https://doi.org/10.1016/S2468-1253(19)30004-4)
10. Wang M, Li D, Chen R, et al. Laparoscopic versus open pancreaticoduodenectomy for pancreatic or periampullary tumours: a multicentre, open-label, randomised controlled trial. *Lancet Gastroenterol Hepatol*. 2021;6(6):438-447. [https://doi.org/10.1016/S2468-1253\(21\)00054-6](https://doi.org/10.1016/S2468-1253(21)00054-6)
 11. Chen S, Chen JZ, Zhan Q, et al. Robot-assisted laparoscopic versus open pancreaticoduodenectomy: a prospective, matched, mid-term follow-up study. *Surg Endosc*. 2015;29(12):3698-3711. <https://doi.org/10.1007/s00464-015-4140-y>
 12. Asbun HJ, Moekotte AL, Vissers FL, et al. The Miami International Evidence-based Guidelines on Minimally Invasive Pancreas Resection. *Ann Surg*. 2020;271(1):1-14. <https://doi.org/10.1097/SLA.0000000000003590>
 13. Redfors B, Gregson J, Crowley A, et al. The win ratio approach for composite endpoints: Practical guidance based on previous experience. *Eur Heart J*. 2020;41(46):4391-4399. <https://doi.org/10.1093/eurheartj/ehaa665>
 14. Pocock SJ, Ariti CA, Collier TJ, Wang D. The win ratio: A new approach to the analysis of composite endpoints in clinical trials based on clinical priorities. *Eur Heart J*. 2012;33(2):176-182. <https://doi.org/10.1093/eurheartj/ehr352>
 15. American College of Surgeons National Cancer Database. <https://www.facs.org/quality-programs/cancer/ncdb>.
 16. Charlson M, Pompei P, Ales K, MacKenzie C. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis*. 1987;40(5):373-383.
 17. Deyo RA, Cherkin DC, Ciol MA. Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases. *J Clin Epidemiol*. 1992. [https://doi.org/10.1016/0895-4356\(92\)90133-8](https://doi.org/10.1016/0895-4356(92)90133-8)
 18. Finkelstein D, Schoenfeld D. Graphing the Win Ratio and its components over time. *Stat Med*. 2019;15(28):53-61.
 19. Oakes D. On the win-ratio statistic in clinical trials with multiple types of event. *Biometrika*. 2016;103(3):742-745.
 20. Huebner M, Kendrick M, Reid-Lombardo. Number of lymph nodes evaluated: prognostic value in pancreatic adenocarcinoma. *J Gastrointest Surg*. 2012;16(5):920-926.
 21. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology. Pancreatic Adenocarcinoma. Version 2.2021. <https://www.nccn.org/guidelines/guidelines-detail?category=1&id=1455>. Published 2021.
 22. Mehta R, Tsilimigras D, Paredes A. Dedicated Cancer Centers are More Likely to Achieve a Textbook Outcome Following Hepatopancreatic Surgery. *Ann Surg Oncol*. 2020;27(6):1889-1897.
 23. Nickel F, Haney CM, Kowalewski KF, et al. Laparoscopic Versus Open Pancreaticoduodenectomy: A Systematic Review and Meta-analysis of Randomized Controlled Trials. *Ann Surg*. 2020;271(1):54-66. <https://doi.org/10.1097/SLA.0000000000003309>
 24. Zureikat AH, Moser AJ, Boone BA, Bartlett DL, Zenati M, Zeh HJ. 250 Robotic Pancreatic Resections. *Ann Surg*. 2013;258(4):554-562. <https://doi.org/10.1097/sla.0b013e3182a4e87c>
 25. Zeh HJ, Zureikat AH, Secrest A, Dauoudi M, Bartlett D, Moser AJ. Outcomes after robot-assisted pancreaticoduodenectomy for periampullary lesions. *Ann Surg Oncol*. 2012;19(3):864-870. <https://doi.org/10.1245/s10434-011-2045-0>
 26. Boggi U, Signori S, De Lio N, et al. Feasibility of robotic pancreaticoduodenectomy. *Br J Surg*. 2013;100(7):917-925. <https://doi.org/10.1002/bjs.9135>
 27. Ricci C, Casadei R, Taffurelli G, Pacilio CA, Ricciardiello M, Minni F. Minimally Invasive Pancreaticoduodenectomy: What is the Best “Choice”? A Systematic Review and Network Meta-analysis of Non-randomized Comparative Studies. *World J Surg*. 2018;42(3):788-805. <https://doi.org/10.1007/s00268-017-4180-7>
 28. Wright GP, Zureikat AH. Development of Minimally Invasive Pancreatic Surgery: an Evidence-Based Systematic Review of Laparoscopic Versus Robotic Approaches. *J Gastrointest Surg*. 2016;20(9):1658-1665. <https://doi.org/10.1007/s11605-016-3204-1>
 29. Finkelstein D, Schoenfeld D. Combining mortality and longitudinal measures in clinical trials. *Stat Med*. 1999;18(11):1341-1354.
 30. Dong G, Hoaglin DC, Qiu J, et al. The Win Ratio: On Interpretation and Handling of Ties. *Stat Biopharm Res*. 2020;12(1):99-106. <https://doi.org/10.1080/19466315.2019.1575279>
 31. Wiseman JT, Abdel-Misih S, Beal EW, et al. A multi-institutional analysis of Textbook Outcomes among patients undergoing cytoreductive surgery for peritoneal surface malignancies. *Surg Oncol*. 2021;37:101492. <https://doi.org/10.1016/j.suronc.2020.11.006>
 32. Merath K, Chen Q, Bagante F, et al. Textbook Outcomes Among Medicare Patients Undergoing Hepatopancreatic Surgery. *Ann Surg*. 2020;271(6):1116-1123. <https://doi.org/10.1097/SLA.0000000000003105>
 33. Hyer JM, Beane JD, Spolverato G, et al. Trends in Textbook Outcomes over Time: Are Optimal Outcomes Following Complex Gastrointestinal Surgery for Cancer Increasing? *J Gastrointest Surg*. 2021;(0123456789). <https://doi.org/10.1007/s11605-021-05129-4>
 34. Allan BJ, Novak SM, Hogg ME, Zeh HJ. Robotic vascular resections during Whipple procedure. *J Vis Surg*. 2018;4(I):13-13. <https://doi.org/10.21037/jovs.2017.12.15>
 35. Correa-Gallego C, Dinkelspiel HE, Sulimanoff I, et al. Minimally-invasive vs open pancreaticoduodenectomy: Systematic review and meta-analysis. *J Am Coll Surg*. 2014;218(1):129-139. <https://doi.org/10.1016/j.jamcollsurg.2013.09.005>
 36. Croome KP, Farnell MB, Que FG, et al. Pancreaticoduodenectomy with Major Vascular Resection: a Comparison of Laparoscopic Versus Open Approaches. *J Gastrointest Surg*. 2015;19(1):189-194. <https://doi.org/10.1007/s11605-014-2644-8>
 37. Kendrick ML, Sclabas GM. Major venous resection during total laparoscopic pancreaticoduodenectomy. *Hpb*. 2011;13(7):454-458. <https://doi.org/10.1111/j.1477-2574.2011.00323.x>
 38. Müller SA, Hartel M, Mehrabi A, et al. Vascular resection in pancreatic cancer surgery: Survival determinants. *J Gastrointest Surg*. 2009;13(4):784-792. <https://doi.org/10.1007/s11605-008-0791-5>
 39. Giulianotti PC, Addeo P, Buchs NC, Ayloo SM, Bianco FM. Robotic extended pancreatectomy with vascular resection for locally advanced pancreatic tumors. *Pancreas*. 2011;40(8):1264-1270. <https://doi.org/10.1097/MPA.0b013e318220e3a4>

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.