# ORIGINAL ARTICLE



# High Performing Whipple Patients: Factors Associated with Short Length of Stay after Open Pancreaticoduodenectomy

Grace C. Lee • Zhi Ven Fong • Cristina R. Ferrone • Sarah P. Thayer • Andrew L. Warshaw • Keith D. Lillemoe • Carlos Fernández-del Castillo

Received: 22 May 2014/Accepted: 21 July 2014/Published online: 5 August 2014 © 2014 The Society for Surgery of the Alimentary Tract

## Abstract

*Introduction* Despite the decreasing mortality of pancreaticoduodenectomy (PD), it continues to be associated with prolonged length of postoperative hospital stay (LOS). This study aimed to determine factors that could predict short LOS after PD. Additionally, as preliminary data of minimally invasive PD emerges, we sought to determine the average LOS after open PD at a high-volume center to set a standard to which minimally invasive PD can be compared.

*Methods* A total of 634 consecutive patients who underwent open PD between January 2007 and December 2012 at the Massachusetts General Hospital comprised the study cohort. "High performers" were defined as patients with postoperative LOS  $\leq 5$  days.

*Results* Median LOS was 7 days. A total of 61 patients (9.6 %) had LOS  $\leq$ 5 days and were deemed "high performing." In multivariate logistic regression analysis, male gender (p=0.032), neoadjuvant chemoradiation (p=0.001), epidural success (p= 0.019), epidural duration  $\leq$ 3 days (p=0.001), lack of complications (p<0.001), surgery on Thursday or Friday (p=0.001), and discharge on Monday through Wednesday (p<0.001) were independently associated with LOS  $\leq$ 5 days. Readmission rate, time to readmission, and mortality were not different between the two groups. The proportion of patients with pancreatic ductal adenocarcinoma who went on to receive adjuvant therapy was no different if LOS was  $\leq$ 5 or >5 days, but high performance was predictive of beginning therapy <8 weeks after surgery (p=0.010).

*Conclusion* In our experience, median LOS was 7 days, and early discharge ( $\leq$ 5 days) after open PD is safe and feasible in about 10 % of patients. These high performers are more likely to be male, have received neoadjuvant therapy, and had successful epidural analgesia. High performers with cancer are more likely to start chemotherapy <8 weeks after surgery. Minimally invasive PD should be compared to this high standard for median LOS, among other quality metrics, to justify its increased cost, operative duration, and learning curve.

**Keywords** Length of stay · Pancreaticoduodenectomy · Cost · Epidural analgesia · Weekday

# Introduction

In this era of health care reform, there has been tremendous political and institutional pressure to slow the rise in health care costs. Since 2002, health care has been growing at a rate of 3 % per year, faster than any other industry or the gross domestic product.<sup>1</sup> Among the main contributors to this growth are hospital charges, which have been increasing at a rate of 4.2 % per year.<sup>1</sup> Therefore, much emphasis has been placed on reducing length of hospital stay (LOS) and readmission rates, particularly after surgical procedures.<sup>2</sup>

One major abdominal procedure that continues to be associated with significant LOS and readmission rates is pancreaticoduodenectomy (PD). In recent times, a number of advances in imaging and neoadjuvant therapies have led

Prior presentations: Presented at the Pancreas Club Annual Meeting (May 2014, Chicago, IL), Digestive Disease Week (May 2014, Chicago, IL), and the New England Surgical Society Resident and Fellow Research Day (May 2014, Worcester, MA)

G. C. Lee  $\cdot$  Z. V. Fong  $\cdot$  C. R. Ferrone  $\cdot$  S. P. Thayer  $\cdot$ 

A. L. Warshaw · K. D. Lillemoe · C. Fernández-del Castillo (⊠) Department of Surgery, Massachusetts General Hospital, Harvard Medical School, 15 Parkman Street, Boston, MA 02114-3117, USA e-mail: cfernandez@partners.org

to the increased utilization of PD for diagnoses ranging from benign entities to borderline resectable cancers.<sup>3</sup> Although the mortality of PD has been decreasing, with most high-volume tertiary care centers reporting 30-day mortality rates of less than 2 %, LOS continues to plateau at a median of 7 to 11 days even at high-volume hospitals.<sup>2, 4–9</sup> This prolonged LOS may not only delay the start of adjuvant therapy in patients with malignancy but also increases the risk of patients developing hospital-associated complications, such as infections, venous thromboembolisms, and pressure ulcers.

Minimizing LOS after PD holds particular importance for cost reduction given the especially high expenses associated with admissions for elective PD. Several studies estimate the cost of the surgery and postoperative hospital stay to range from \$30,000 to \$50,000,<sup>10, 11</sup> while another study demonstrated that the postoperative hospital stay, not the surgery itself, contributes the majority of the total cost of the admission.<sup>12</sup> Furthermore, two institutions that implemented critical pathways for postoperative management of PD patients have shown decreased costs associated with shorter LOS.<sup>8, 11</sup> Therefore, decreasing LOS has the potential to improve hospital profitability, particularly as Medicare and private insurance companies implement more diagnosis-related group-based and episode-based bundled payment methods.<sup>13</sup>

Amidst this pressure for cost containment, the debate surrounding minimally invasive pancreatic surgery has intensified. First introduced in 1994, laparoscopic PD has not been widely adopted, likely due to the technical difficulties and lack of demonstrated improvement in outcomes.<sup>14, 15</sup> Alternatively, robotic PD has been touted as the next trend in minimally invasive pancreatic surgery because of the dexterity of the robotic arms and three-dimensional visualization offered by improved optics, with an increasing number of cases being reported annually over the last 10 years.<sup>16</sup> Yet, robotic PD continues to be associated with significantly longer operative times and higher costs, with one study estimating that the surgical costs of robotic PD exceed that of open PD by €6,193, approximately \$8,500.<sup>17</sup> As more hospitals purchase robotic systems and more surgeons begin performing robotic procedures, it is critical to first prove that minimally invasive pancreatic surgery offers improved outcomes that justify the high cost, longer operative times, and steep learning curve.

Several studies have previously investigated variables associated with LOS after PD, mostly examining hospital and surgeon volume.<sup>4, 18–21</sup> However, there is limited data on patient-related variables as predictors of LOS at a highvolume tertiary care center, which is particularly relevant given the increased centralization of complex pancreatic surgery at high-volume centers.<sup>21, 22</sup> This study aims to determine factors predictive of "high performance" after PD, defined as LOS  $\leq$ 5 days. It also seeks to establish a standard for LOS after open PD to which minimally invasive PD must be compared before consideration for widespread adoption.

# Methods

We performed a retrospective, cross-sectional study of patients who underwent PD between January 2007 and December 2012 using a prospectively maintained database of pancreatic surgery patients at the Massachusetts General Hospital (MGH). This study was approved by the Institutional Review Board (Protocol #2013P000897). All patients underwent open PD using standard techniques and postoperative clinical pathways as previously described.<sup>6, 23</sup> Briefly, nearly all cases were classic pancreaticoduodenectomies (of the 570 cases for which technique was recorded, only 5 were pylorus preserving) with creation of duct-to-mucosa pancreaticojejunostomies. One surgeon creates antecolic gastrojejunostomies while three surgeons prefer retrocolic gastrojejunostomies. The practice at our institution is to leave an external pancreatic ductal stent and two intraperitoneal closed suction drains. There was no difference in technique between the high performing and non-high performing patients.

Our institution's postoperative pathway includes transfer from the postanesthesia care unit to a normal surgical unit floor, with no routine postoperative intensive care unit stays. Nasogastric tubes were removed on postoperative day (POD) 1, with advancement to a clear liquid diet by POD 2. It is routine practice at our institution to use epidural catheters for perioperative analgesia; in rare instances where epidural placement is unsuccessful or a patient prefers not to have an epidural, then intravenous therapies are utilized. Pain control was assessed daily by a pain management team; most patients received patient-controlled epidural analgesia until they were tolerating a diet and could be transitioned to oral medications. Epidural catheters were used for no longer than 4-5 days postoperatively. Foley catheters were discontinued at the time of epidural removal. Drain amylases were checked daily and removed on PODs 3 and 4 if fluid amylase levels were low. Patients with International Study Group on Pancreatic Fistula (ISGPF) grade A fistulas were discharged home with visiting nurse services, and drains were removed in the outpatient setting.<sup>24</sup> The postdischarge protocol included a phone call from a nurse practitioner to the patient usually 2-4 days after discharge as well as a follow-up appointment in 3-4 weeks. No alterations to this protocol were made for high performers.

The patient database was supplemented with additional demographic, clinicopathologic, and perioperative data collected by independent review of medical records by a designated author (GCL). The social security death index was used to confirm survival data. Additional readmission and adjuvant

therapy data were collected by a dedicated research nurse through phone calls to patients' local physicians and patients.

Length of stay was defined as the postoperative duration of hospitalization, not including the day of surgery. The ageadjusted Charlson comorbidity index was calculated for each patient as previously described and validated.<sup>25, 26</sup> Pancreatic fistula was defined as any measurable drain output on or after POD 3 with drain amylase levels greater than three times the serum amylase levels, as proposed by the ISGPF.<sup>24</sup> Delayed gastric emptying was defined as inability to tolerate solid oral intake by POD 7, inability to remove nasogastric suction before POD 4, or replacement of nasogastric suction after POD 3, as established by the International Study Group of Pancreatic Surgery (ISGPS).<sup>27</sup> Epidural success was defined as lack of need to alter the planned postoperative epidural regimen due to patients' reporting of pain. Low-volume surgeons performed 1 to 4 cases per year, medium-volume surgeons 5 to 15 cases per year, and high-volume surgeons  $\geq 16$ cases per year. Surgeon volume was determined on a year-byyear basis.

The distribution of LOS among the cohort was determined, and "high performers" were defined as patients with a LOS  $\leq$ 5 days after PD. Demographic and clinical factors were compared between the high performing and non-high performing groups.

Statistical analyses were performed using Stata software, version SE 13.0 (StataCorp, College Station, TX, USA). Univariate analysis was performed using the Chi-squared test for categorical variables and dichotomized continuous variables and the Kruskal-Wallis test for continuous variables. Thresholds used for dichotomized continuous variables were age >70 years, ASA class  $\geq$ 3, Charlson comorbidity index  $\geq$ 5, operative time >330 min, estimated blood loss >600 cc, amount of transfusion  $\geq 2$  units of packed red blood cells, and epidural duration  $\leq 3$  days. Multivariate analysis was performed using logistic regression. Criteria for inclusion into the multivariate model was p < 0.07 in the univariate analysis. Statistical significance was accepted at the p < 0.05 level.

# Results

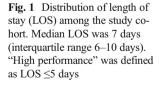
A total of 634 consecutive patients underwent open PD between January 2007 and December 2012 at the MGH. The median LOS was 7 days (interguartile range 6-10 days). which remained stable between the first and second halves of the study period (Fig. 1). Of the entire cohort, 61 patients (9.6%) had a LOS  $\leq$ 5 days and were deemed high performers.

Patient Demographics and Diagnosis

High performing patients were more likely to be young (p=0.008), a past or current smoker (p=0.037), and have a Charlson comorbidity index <5 (p=0.001) (Table 1). Of the overall cohort, 12.6 % of patients were current smokers, all of whom received routine tobacco cessation education while inpatients. High performers with pancreatic ductal adenocarcinoma (PDAC) were also more likely to have received neoadjuvant chemoradiation (p=0.058), although this difference was not statistically significant on univariate analysis.

Race, BMI, ASA class  $\geq$ 3, diabetes diagnosis, and patient's home address being out-of-state did not differ significantly between the two cohorts. History of endoscopic retrograde cholangiopancreatography (ERCP), common bile duct stent placement, and prior abdominal surgery were also not correlated with LOS  $\leq 5$  days. Of the high performing patients, 49.2 % had PDAC on final pathology, not different from that of the non-high performing cohort (p=0.880).

160 140 120 100 Frequency 80 60 40 20 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 34 35 36 37 40 41 46 47 52



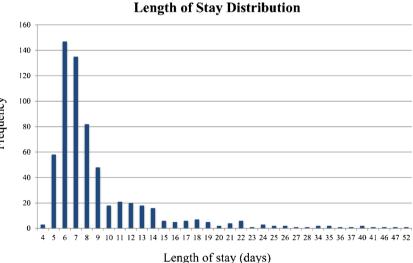


Table 1 Univariate analysis of patient demographics and pathologic diagnosis between the length of stay  $\leq$ 5-day ("high performers") and >5-day cohorts

	All patients, % ( <i>n</i> =634)	LOS $\leq 5$ days, % (n=61)	LOS >5 days, % ( <i>n</i> =573)	p Value
Demographics				
Age >70 years	35.0	19.7	36.7	0.008
Gender (male)	49.4	60.7	48.2	0.064
Race (white)	91.9	95.1	91.6	0.338
BMI (kg/m <sup>2</sup> )	25.7	25.3	25.8	0.211
ASA class ≥3	38.4	31.7	39.1	0.263
CCI≥5	50.6	29.5	52.9	0.001
Diabetes <sup>a</sup>	23.1	23.0	23.1	0.982
Smoker <sup>b</sup>	56.2	68.9	54.9	0.037
Prior abdominal surgery	65.4	60.7	65.9	0.412
Prior ERCP	63.8	65.6	63.6	0.765
Prior CBD stent	57.0	57.4	57.0	0.954
Neoadjuvant chemoradiation <sup>c</sup>	16.4	25.0	15.5	0.058
Home address out-of- state	35.6	39.3	35.2	0.521
Pathology				
Any malignancy	81.9	84.9	81.6	0.556
PDAC	48.3	49.2	48.2	0.880
PDAC arising from IPMN	3.9	3.3	4.0	0.861

<sup>a</sup> Includes diabetes types I and II

<sup>b</sup> Includes past and current smokers

<sup>c</sup> Only calculated in patients with PDAC

LOS length of stay, BMI body mass index, ASA American Society of Anesthesiologists, CCI Charlson comorbidity index, ERCP endoscopic retrograde cholangiopancreatography, CBD common bile duct, PDAC pancreatic ductal adenocarcinoma, IPMN intraductal papillary mucinous neoplasm

## Perioperative Factors

High performing patients tended to have less estimated intraoperative blood loss (p=0.037) and no intraoperative blood transfusion (p=0.038) (Table 2). Major visceral vessel resection, multivisceral organ resection, and amount of intraoperative blood transfusion, if a patient was transfused, were not associated with LOS  $\leq 5$  days. High performers tended to have shorter operative times; however, the trend did not reach statistical significance (p=0.055).

In terms of postoperative factors, delayed gastric emptying (p=0.001), transfer to an intensive care unit due to clinical instability (p=0.027), and discharge to a rehabilitation facility (p<0.001) predicted LOS >5 days (Table 2). Thirteen patients (2.1 %) required reoperation during the initial admission, none of whom were high performers (p=0.235). A functioning

epidural was accomplished in 92.9 % of high performers and 85.1 % of patients with LOS >5 days (p=0.114), and epidural duration of ≤3 days was predictive of LOS ≤5 days (p=0.001). The overall morbidity rate was 58.2 %, with high performers being less likely to have at least one complication (26.2 vs 61.6 % in non-high performers, p<0.001). In particular, the incidence of pancreatic fistulae was markedly lower in high performers (1.6 vs 18.3 %, p=0.001) even with our practice of discharging all patients with pancreatic fistulae but who are otherwise well (ISGPF class A), leaving intraabdominal drains in place for gradual removal as an outpatient. Among the high performing cohort, the most common complications were wound infection (9.8 %), intra-abdominal abscess (6.6 %), Clostridium difficile infection (4.9 %), and fever (3.3 %).

Surgeon Volume and "the Weekend Effect"

High-volume surgeons performed 68.1 % of the total cases included in this study. High surgeon volume was associated with LOS  $\leq 5$  days (p=0.021); 83.6 % of high performing patients had been operated on and cared for by high-volume surgeons (Table 2). The day of the week on which surgery was performed also correlated with LOS  $\leq 5$  days. High performers were more likely to be operated on at the end of the week on a Thursday or Friday, although the difference did not reach statistical significance (p=0.053). The weekday of discharge also predicted LOS  $\leq 5$  days, as high performers tended to be discharged early in the week, on a Monday, Tuesday, or Wednesday, versus later in the week or on the weekends (p<0.001) (Table 2).

#### Multivariate Analysis

In order to identify independent predictors of LOS  $\leq$ 5 days, a multivariate logistic regression model was created that included all variables with p values <0.07 in the univariate analyses (Table 3). Epidural success was included in the model because epidural duration  $\leq 3$  days was only analyzed if the epidural analgesia was effective. The factors that remained independently associated with LOS  $\leq 5$  days were male gender (OR 2.16, p=0.032), neoadjuvant chemoradiation (OR 3.84, p=0.001), epidural success (OR 4.47, p=0.019), epidural duration  $\leq 3$  days (OR 3.42, p=0.001), lack of any complications (OR 3.79, p < 0.001), surgery on Thursday or Friday (OR 3.25, p=0.001), and discharge on Monday through Wednesday (OR 5.34, p < 0.001). Age, Charlson comorbidity index  $\geq 5$ , smoking status, surgeon volume, operative time, estimated blood loss, transfusion, and pancreatic fistula did not maintain statistical significance in the multivariate model.

Table 2 Univariate analysis of intraoperative and postoperative factors between the length of stay		All patients, $\%$ ( <i>n</i> =634)	LOS $\leq 5$ days, % ( $n=61$ )	LOS >5 days, % ( <i>n</i> =573)	p Value
≤5-day ("high performers") and >5-day cohorts	Surgeon volume by year				0.021
	Low (1–4 cases/year)	6.2	1.6	6.6	
	Medium (5–15 cases/year)	25.7	14.8	26.9	
	High (≥16 cases/year)	68.1	83.6	66.5	
	Intraoperative factors				
	Surgery on Thursday/Friday <sup>a</sup>	47.4	59.3	46.1	0.053
	Vessel resection	10.6	6.6	11.0	0.284
	Multivisceral resection	2.1	1.6	2.1	0.812
	Operative time >330 min	49.4	37.7	50.6	0.055
	Estimated blood loss >600 mL	45.4	32.8	46.8	0.037
	Transfused intraoperatively	21.9	11.5	23.0	0.038
	Transfused $\geq 2$ units of PRBC <sup>b</sup>	71.2	42.9	72.7	0.089
	Postoperative factors				
	Epidural success	85.9	92.9	85.1	0.114
<sup>a</sup> Omitted operations performed on Saturday and Sunday from the	Epidural duration $\leq 3$ days <sup>c</sup>	21.8	40.4	19.5	0.001
	Any complication	58.2	26.2	61.6	< 0.001
	Urinary retention	4.1	1.6	4.4	0.305
analysis	Pancreatic fistula	16.7	1.6	18.3	0.001
<sup>b</sup> Analysis performed only in pa- tients who were intraoperatively transfused <sup>c</sup> Analysis performed only in pa- tients for whom the epidural was successful	Delayed gastric emptying	15.0	0.0	16.6	0.001
	ICU transfer	6.8	0.0	7.5	0.027
	Reoperation	2.1	0.0	2.3	0.235
	Discharged to rehabilitation center	17.0	0.0	18.9	< 0.001
	Discharged on Mon/Tues/Wed	53.6	80.3	50.7	< 0.001
<sup>d</sup> Analysis performed only in pa-	30-day mortality	0.5	0.0	0.5	0.571
tients who were readmitted	90-day mortality	2.5	0.0	2.8	0.186
LOS length of stay, PRBC packed	Readmission	21.6	16.4	22.2	0.298
red blood cells, <i>ICU</i> intensive care unit	Time to readmission (days) <sup>d</sup>	11 days	5.5 days	12 days	0.661

Readmission and Length of Stay

Readmission rates did not differ significantly between the high performing and non-high performing patients (16.4 vs 22.2 %, p=0.298) (Table 2). Likewise, time to readmission was not associated with LOS  $\leq$ 5 days; among the readmitted high performers, median time to readmission was 5.5 days, while that of readmitted non-high performers was 12 days (p=0.661). Among the high performers, reasons for readmission included intra-abdominal abscess (n=4), wound infection (n=4)1), sepsis (n=1), Clostridium difficile infection (n=1), abdominal wall abscess (n=1), retained common bile duct stent (n=1)1), and abdominal pain of unclear origin (n=1).

# Receipt and Timing of Adjuvant Therapy

In the entire cohort, 306 patients (48.3 %) had PDAC on final pathology. Of these patients with PDAC, 76.1 % went on to receive adjuvant chemotherapy (Table 4). Reasons for not receiving adjuvant therapy included patient preference (n=

25, 35.7 %), oncologist recommendation (n=15, 21.4 %), and postoperative performance status (n=27, 38.6 %). Common reasons for oncologists not recommending adjuvant therapy were the patients' receipt of a full course of neoadjuvant chemoradiation, advanced age, or inability to tolerate neoadjuvant therapy. Among the patients who received adjuvant therapy, the median time to beginning therapy was 51 days (interquartile range 41-68 days), with 57.8 % of patients starting <8 weeks after surgery. A total of 91.2 % of the patients who received therapy were able to tolerate it for at least 4 months.

The proportion of high performers who went on to receive adjuvant therapy was not significantly different from that of those with LOS >5 days (69.0 and 76.9 %, respectively, p=0.343); however, 25.0 % of high performers had received neoadjuvant treatment, compared to 15.5 % of non-high performers, and therefore, further treatment may not have been indicated in all of those patients. High performance was predictive of beginning adjuvant therapy <8 weeks after surgery on univariate analysis (p=0.010). All high performers

**Table 3** Multivariate logistic regression model for length of stay  $\leq 5$  days ("high performance") after pancreaticoduodenectomy

Factor	Odds ratio	95 % Confidence interval	p Value
Age >70 years	0.64	0.22-1.80	0.396
Male gender	2.16	1.07-4.36	0.032*
Charlson comorbidity index $\geq 5$	0.52	0.22-1.24	0.142
Past or current smoker	1.72	0.86–3.46	0.126
Neoadjuvant chemoradiation	3.84	1.68-8.82	0.001*
Surgeon volume by year	1.16	0.59-2.31	0.662
Surgery performed on Thursday/ Friday	3.25	1.60-6.58	0.001*
Operative time >330 min	0.65	0.31-1.38	0.262
Estimated blood loss >600 mL	0.79	0.35-1.78	0.562
Transfused intraoperatively	0.88	0.30-2.59	0.810
Epidural success <sup>a</sup>	4.47	1.27-15.66	0.019*
Epidural duration $\leq 3$ days	3.42	1.68-6.97	0.001*
Lack of any complication	3.79	1.80-8.00	< 0.001*
Lack of pancreatic fistula	3.45	0.42-28.24	0.249
Discharged on Mon/Tues/Wed	5.34	2.40-11.85	< 0.001*

Criteria for entry of factor into the multivariate model was p < 0.07 in univariate analyses

<sup>a</sup> Epidural success was entered into the multivariate model because univariate analysis of epidural duration was only performed in patients for whom the epidural successfully worked

\*Denotes statistical significance (p < 0.05)

with PDAC who received adjuvant therapy were able to tolerate it for at least 4 months (100 vs 90.4 % in non-high performers), although LOS <5 days was not significantly associated with tolerance of 4 months of therapy (p=0.146).

#### Mortality and Overall Survival

Only three patients in the overall cohort (0.5 %) died within 30 days of surgery, none of whom were high performers (Table 2). A total of 16 patients (2.5 % of the overall cohort)

<b>Table 4</b> Univariate analysis of adjuvant therapy outcomes be- tween the length of stay ≤5-day ("high performers") and >5-day cohorts, only in patients with		All PDAC patients, $\%$ ( <i>n</i> =306)	LOS ≤5 days, % ( <i>n</i> =30)	LOS >5 days, % ( <i>n</i> =276)
	Adjuvant therapy receipt	76.1	69.0	76.9
pancreatic ductal adenocarcinoma	Reason for not receiving therapy	( <i>n</i> =71)	( <i>n</i> =9)	( <i>n</i> =62)
	Patient preference	35.7	33.3	36.1
	Not recommended by oncologist	21.4	44.4	18.0
	Postoperative performance status	38.6	22.2	41.0
	Time to beginning therapy			
	Median time to therapy (days)	51 days	42 days	52 days
	<8 weeks after surgery	57.8	85.0	55.1
<i>PDAC</i> pancreatic ductal adeno- carcinoma, <i>LOS</i> length of stay	Tolerated >4 months of therapy	91.2	100.0	90.4

died within 90 days of surgery; again, none of these patients were high performers. LOS  $\leq 5$  days was not significantly associated with 30- or 90-day mortality.

Among the PDAC patients, 1-, 2-, and 5-year overall survival was 70.6, 46.9, and 11.1 %, respectively (Table 5). Among patients with PDAC who died during the follow-up period, median survival was 412.5 days after resection. In univariate analysis, high performance did not correlate with prolonged overall survival at any time point among the entire cohort or among only PDAC patients. After adjusting for factors predictive of overall survival among PDAC patients using multivariate logistic regression analysis, LOS ≤5 days remained unassociated with overall survival.

#### Discussion

In this contemporary cohort of patients who underwent open PD at a high-volume tertiary care center, the median length of stay was 7 days, with a 9.6 % rate of "high performance," defined as LOS  $\leq 5$  days. This is similar to LOS at other centers of excellence<sup>8, 9</sup> and compares favorably to previously published data on high-volume hospitals in the USA (defined as >32 cases/year), in which the median LOS was 11 days.<sup>4</sup> Despite the high performers' early discharges, there was no significant difference in readmission rate, time to readmission, or 30-day mortality rate. While several institutions that implemented clinical pathways in which discharge is targeted for PODs 6-7 have demonstrated decreased LOS without increased readmission or mortality rates,8, 28-30 our data suggests that it may be safe and feasible to aim for even more aggressive discharge goals in patients meeting specific criteria. Additionally, the fact that high performance was not associated with lower readmission rates suggests that many readmissions after PD may not be predictable or preventable, an idea proposed by multiple groups that further brings into question the validity of readmission rate as a quality measure.<sup>2, 31–35</sup>

p Value

0.343

0.292

0.008

0.010

0.146

**Table 5** Univariate analysis of overall survival between the length of stay  $\leq$ 5-day ("high performers") and >5-day cohorts, in the overall cohort and in patients with pancreatic ductal adenocarcinoma

	All patients, $\%$ ( <i>n</i> =634)	p Value (LOS $\leq 5$ vs >5 days)	All PDAC patients, % ( <i>n</i> =306)	<i>p</i> Value (LOS ≤5 vs >5 days)
Overall su	urvival			
1 year	82.2	0.857	70.6	0.736
2 years	67.3	0.917	46.9	0.466
3 years	54.7	0.852	30.2	0.980
4 years	42.2	0.408	20.4	0.471
5 years	28.5	0.891	11.1	0.560

LOS length of stay, PDAC pancreatic ductal adenocarcinoma

This study determined several demographic and perioperative factors associated with LOS  $\leq$ 5 days, which hold predictive value as to which patients have a tendency to be high performers and have clinical implications in accelerating postoperative recovery and expediting discharge without risking readmission and/or mortality.

The finding that administration of neoadjuvant chemoradiation for PDAC predicted LOS  $\leq 5$  days is consistent with prior national database analysis that found an association between neoadjuvant radiation and shorter LOS.34 This finding is interesting given the common belief that fibrosis induced by neoadjuvant radiation complicates technical aspects of the surgery and possibly leads to increased morbidity. However, prior studies demonstrate no relationship between preoperative chemotherapy or radiation and post-PD morbidity and show mixed results about a possible association between preoperative radiation and post-PD mortality.34-36 Our findings could be attributed to decreased pancreatic fistulae in patients who received neoadjuvant therapy due to hard gland texture from radiation-induced fibrosis and/or delay in surgery, although we did not analyze gland texture in this cohort. Our study is limited by the fact that type of neoadjuvant therapy was not recorded, as some of these patients were enrolled in a preoperative proton beam and capecitabine trial whereas others received more traditional chemoradiation.

Epidural success and epidural duration  $\leq 3$  days also independently predicted high performance after PD. On review of the literature, a large retrospective study also found decreased postoperative complications and shorter LOS in PD patients who received epidural analgesia.<sup>37</sup> Our study was not designed to compare epidural with intravenous analgesia, as most of our patients received epidural catheters. Nevertheless, our findings suggest that effective postoperative pain control enables early discharge, even with a large abdominal incision. Thus, epidural placement, monitoring by an acute pain service, and early removal should be considered for inclusion in critical pathways after PD.

An interesting finding of our study was that having surgery on Thursday or Friday and being discharged on Monday through Wednesday were both significantly correlated with LOS  $\leq$ 5 days. This is likely the case because, for patients who have surgery late in the week, the weekend coverage is only responsible for small steps early in our institution's postoperative pathway, primarily advancing their diet and early postoperative mobilization. When the primary team, who is more familiar with the patient, returns on Monday, they can be more aggressive with the later steps in the pathway toward discharge. Furthermore, the weekend coverage team's lack of familiarity with the patients may make them more inclined to keep patients ready for discharge until the primary team's return. This effect may be particularly pronounced at our institution, where most attending surgeons do not round on their patients over the weekend if they are not on call. The correlation between weekday of surgery and LOS may also be related to the expected LOS of 7 days after PD; one study found that, because the target LOS after colectomy is 4 days, colectomies performed on Mondays were significantly more likely to have a shorter LOS than those performed on any other day of the week.<sup>38</sup> The authors of this study note that optimizing the timing of surgery based on the expected LOS may enable improved utilization of health care resources. Empowering weekend coverage teams to discharge patients ready to leave the hospital would also shorten LOS without compromising patient safety.

Another important outcome after PD for PDAC is whether and when patients are able to begin adjuvant therapy after surgery, as well as their ability to tolerate a full course of therapy. Our data compares favorably to previously published studies; more of our patients (76.1 vs 57.7 %) received adjuvant therapy and fewer began treatment >70 days after surgery (19.7 vs 24.1 %) when compared to a large retrospective study that utilized national databases,<sup>39</sup> and more of our patients began therapy < 8 weeks after surgery (57.8 vs 46.4 %) when compared to recent results published from the ESPAC-3 trial.<sup>40</sup> Even among our patients who did not receive adjuvant therapy, a relatively small percentage did not undergo treatment because of postoperative recovery and performance status (38.6 %); the majority either chose or was not recommended to have further therapy. Furthermore, an encouraging 91.2 % of our patients who began adjuvant therapy were able to tolerate at least 4 months of treatment.

High performers were significantly more likely to start adjuvant therapy <8 weeks after surgery, although emerging data suggests that completing the full course of therapy may be more important for survival than early timing of therapy.<sup>40</sup> All PDAC patients who received adjuvant therapy and who had LOS  $\leq$ 5 days tolerated at least 4 months of therapy. It is not surprising that overall survival in PDAC patients was not associated with LOS  $\leq$ 5 days, as recovery from surgery is

unrelated to the biology of the patient's tumor, likely the major determinant of survival.

Multiple single-institution studies, systematic reviews, and meta-analyses have been published comparing the outcomes of laparoscopic and robotic PD with those of open PD. Thus far, minimally invasive PD has not been shown to improve overall morbidity, mortality, or rates of pancreatic fistula and delayed gastric emptying, although it has been shown to decrease intraoperative blood loss and transfusions while significantly increasing operative time.<sup>16, 41–43</sup> Interestingly, data in press by a single institution demonstrates that significantly fewer laparoscopic PD patients than open PD patients began adjuvant therapy >8 weeks after surgery (27 vs 41 %, p=0.01), although again, there was no difference in overall survival.<sup>44</sup> While the importance of adjuvant therapy timing for overall survival is under debate,<sup>40</sup> it will be very informative to see if other institutions and larger trials corroborate these results. In terms of length of stay, several singleinstitution studies describe a significantly decreased LOS after laparoscopic or robotic PD when compared to their open PD outcomes; nevertheless, their mean LOS after minimally invasive PD ranges from 6.2 to 38 days, comparable to or considerably longer than our median LOS of 7 days after open PD.<sup>16, 41, 43, 45, 46</sup> Although this comparison of our singleinstitution, retrospective data with other previously published studies is somewhat artificial, particularly due to differences in institutional practices, patient characteristics, and surgeon experience with minimally invasive technology, we believe that our median LOS may still be a useful benchmark as surgeons, hospitals, and insurance providers assess the utility of minimally invasive techniques.

Potential limitations of this study include its retrospective nature as well as the fact that it was conducted at a single institution. Our institution-specific postoperative management could have influenced our patients' LOS, such as our use of an epidural catheter for postoperative analgesia.<sup>23</sup> Our recently implemented postdischarge protocols designed to decrease readmission rates, including phone calls to patients by a nurse practitioner soon after discharge, may have also had a positive impact. Our institution's multidisciplinary approach to oncology patients may have contributed to the short time to adjuvant therapy and high rates of therapy receipt among this cohort. Also, as a tertiary referral center, many of our patients are not local, which may have affected discharge planning. Although a dedicated research nurse called patients and their physicians for routine follow-up to ascertain readmission and receipt of adjuvant therapy information, it is possible that some care received at unaffiliated institutions was missed. Another limitation is that this study does not include patient satisfaction scores; however, we hope that our results will help to establish appropriate LOS expectations with patients and thus improve satisfaction.

Of note, while this study demonstrates expedited discharge to be safe in our cohort of patients, generalization of these results to low-volume hospitals would require further investigation before such a practice is widely implemented. Nevertheless, the increasing centralization of pancreatic surgery at centers of excellence makes our results increasingly applicable and a fair benchmark from which to compare minimally invasive pancreatic surgery.<sup>22</sup>

## Conclusion

In this contemporary cohort of patients who underwent open PD at a high-volume tertiary care hospital, the median length of stay was 7 days, with a 9.6 % rate of high performance, defined as LOS  $\leq$ 5 days. High performers demonstrated no increase in readmission rates or mortality after their early discharges. Factors independently predictive of LOS  $\leq$ 5 days include receipt of neoadjuvant therapy, epidural success, epidural duration  $\leq 3$  days, and surgery at the end of the week. Inclusion of epidural analgesia and short epidural duration in clinical postoperative pathways may lead to decreased LOS. and it may be appropriate for pathways to begin targeting discharge for POD 5 in certain patients. High performance was predictive of beginning adjuvant therapy < 8 weeks after surgery. Minimally invasive PD must be held to this high standard for LOS in order to justify their increased operative times, steep learning curve, and significantly increased operative costs.<sup>12, 17</sup> the latter of which will be closely scrutinized in this era of health care cost containment.

## References

- Moses H, 3rd, Matheson DH, Dorsey ER, George BP, Sadoff D, Yoshimura S. The anatomy of health care in the United States. JAMA 2013;310:1947-63.
- 2. Fong ZV, Ferrone CR, Thayer SP, Wargo JA, Sahora K, Seefeld KJ, Warshaw AL, Lillemoe KD, Hutter MM, Fernandez-Del Castillo C. Understanding hospital readmissions after pancreaticoduodenectomy: can we prevent them?: a 10-year contemporary experience with 1,173 patients at the Massachusetts General Hospital. J Gastrointest Surg 2014;18:137-44.
- Teh SH, Diggs BS, Deveney CW, Sheppard BC. Patient and hospital characteristics on the variance of perioperative outcomes for pancreatic resection in the United States: a plea for outcome-based and not volume-based referral guidelines. Arch Surg 2009;144:713-21.
- Schneider EB, Hyder O, Wolfgang CL, Dodson RM, Haider AH, Herman JM, Pawlik TM. Provider versus patient factors impacting hospital length of stay after pancreaticoduodenectomy. Surgery 2013;154:152-61.
- Balcom JH, Rattner DW, Warshaw AL, Chang Y, Fernandez-del Castillo C. Ten-year experience with 733 pancreatic resections: changing indications, older patients, and decreasing length of hospitalization. Arch Surg 2001;136:391-8.

- Fernandez-del Castillo C, Morales-Oyarvide V, McGrath D, Wargo JA, Ferrone CR, Thayer SP, Lillemoe KD, Warshaw AL. Evolution of the Whipple procedure at the Massachusetts General Hospital. Surgery 2012;152:S56-63.
- He J, Ahuja N, Makary MA, Cameron JL, Eckhauser FE, Choti MA, Hruban RH, Pawlik TM, Wolfgang CL. 2564 resected periampullary adenocarcinomas at a single institution: trends over three decades. HPB (Oxford) 2014;16:83-90.
- Kennedy EP, Rosato EL, Sauter PK, Rosenberg LM, Doria C, Marino IR, Chojnacki KA, Berger AC, Yeo CJ. Initiation of a critical pathway for pancreaticoduodenectomy at an academic institution the first step in multidisciplinary team building. J Am Coll Surg 2007;204:917-23.
- Winter JM, Cameron JL, Campbell KA, Arnold MA, Chang DC, Coleman J, Hodgin MB, Sauter PK, Hruban RH, Riall TS, Schulick RD, Choti MA, Lillemoe KD, Yeo CJ. 1423 pancreaticoduodenectomies for pancreatic cancer: A singleinstitution experience. J Gastrointest Surg 2006;10:1199-210.
- Ho V, Aloia T. Hospital volume, surgeon volume, and patient costs for cancer surgery. Med Care 2008;46:718-25.
- Porter GA, Pisters PW, Mansyur C, Bisanz A, Reyna K, Stanford P, Lee JE, Evans DB. Cost and utilization impact of a clinical pathway for patients undergoing pancreaticoduodenectomy. Ann Surg Oncol 2000;7:484-9.
- Mesleh MG, Stauffer JA, Bowers SP, Asbun HJ. Cost analysis of open and laparoscopic pancreaticoduodenectomy: a single institution comparison. Surg Endosc 2013;27:4518-23.
- Mechanic R, Tompkins C. Lessons learned preparing for Medicare bundled payments. N Engl J Med 2012;367:1873-5.
- Gagner M, Palermo M. Laparoscopic Whipple procedure: review of the literature. J Hepatobiliary Pancreat Surg 2009;16:726-30.
- Zenoni SA, Arnoletti JP, de la Fuente SG. Recent developments in surgery: minimally invasive approaches for patients requiring pancreaticoduodenectomy. JAMA Surg 2013;148:1154-7.
- Cirocchi R, Partelli S, Trastulli S, Coratti A, Parisi A, Falconi M. A systematic review on robotic pancreaticoduodenectomy. Surg Oncol 2013;22:238-46.
- Boggi U, Signori S, De Lio N, Perrone VG, Vistoli F, Belluomini M, Cappelli C, Amorese G, Mosca F. Feasibility of robotic pancreaticoduodenectomy. Br J Surg 2013;100:917-25.
- Enomoto LM, Gusani NJ, Dillon PW, Hollenbeak CS. Impact of Surgeon and Hospital Volume on Mortality, Length of Stay, and Cost of Pancreaticoduodenectomy. J Gastrointest Surg 2013;18:690-700.
- Shi HY, Wang SN, Lee KT. Temporal trends and volume-outcome associations in periampullary cancer patients: a propensity scoreadjusted nationwide population-based study. Am J Surg 2013;207: 512-9.
- 20. Xie YB, Wang CF, Zhao DB, Shan Y, Bai XF, Sun YM, Chen YT, Zhao P, Tian YT. Risk factors associated with postoperative hospital stay after pancreaticoduodenectomy: a retrospective study. Chin Med J (Engl) 2013;126:3685-9.
- Yoshioka R, Yasunaga H, Hasegawa K, Horiguchi H, Fushimi K, Aoki T, Sakamoto Y, Sugawara Y, Kokudo N. Impact of hospital volume on hospital mortality, length of stay and total costs after pancreaticoduodenectomy. Br J Surg 2014;101:523-9.
- Mohammed S, Fisher WE. Quality metrics in pancreatic surgery. Surg Clin North Am 2013;93:693-709.
- Veillette G, Dominguez I, Ferrone C, Thayer SP, McGrath D, Warshaw AL, Fernandez-del Castillo C. Implications and management of pancreatic fistulas following pancreaticoduodenectomy: the Massachusetts General Hospital experience. Arch Surg 2008;143: 476-81.
- Bassi C, Dervenis C, Butturini G, Fingerhut A, Yeo C, Izbicki J, Neoptolemos J, Sarr M, Traverso W, Buchler M, International Study Group on Pancreatic Fistula D. Postoperative pancreatic fistula: an

🖄 Springer

international study group (ISGPF) definition. Surgery 2005;138:8-13.

- Charlson M, Szatrowski TP, Peterson J, Gold J. Validation of a combined comorbidity index. J Clin Epidemiol 1994;47:1245-51.
- Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987;40:373-83.
- 27. Wente MN, Bassi C, Dervenis C, Fingerhut A, Gouma DJ, Izbicki JR, Neoptolemos JP, Padbury RT, Sarr MG, Traverso LW, Yeo CJ, Buchler MW. Delayed gastric emptying (DGE) after pancreatic surgery: a suggested definition by the International Study Group of Pancreatic Surgery (ISGPS). Surgery 2007;142:761-8.
- Nikfarjam M, Weinberg L, Low N, Fink MA, Muralidharan V, Houli N, Starkey G, Jones R, Christophi C. A fast track recovery program significantly reduces hospital length of stay following uncomplicated pancreaticoduodenectomy. JOP 2013;14:63-70.
- Robertson N, Gallacher PJ, Peel N, Garden OJ, Duxbury M, Lassen K, Parks RW. Implementation of an enhanced recovery programme following pancreaticoduodenectomy. HPB (Oxford) 2012;14:700-8.
- 30. Walters DM, McGarey P, LaPar DJ, Strong A, Good E, Adams RB, B a u er TW. A 6-day clinical pathway after a pancreaticoduodenectomy is feasible, safe and efficient. HPB (Oxford) 2013;15:668-73.
- Gawlas I, Sethi M, Winner M, Epelboym I, Lee J, Schrope B, Chabot J, Allendorf J. Readmission after pancreatic resection is not an appropriate measure of quality. Ann Surg Oncol 2013;20:1781-7.
- Kent T, Sachs T, Callery M, Vollmer CJ. Readmission after major pancreatic resection: a necessary evil? J Am Coll Surg 2011;213:515-23.
- 33. Ahmad SA, Edwards MJ, Sutton JM, Grewal SS, Hanseman DJ, Maithel SK, Patel SH, Bentram DJ, Weber SM, Cho CS, Winslow ER, Scoggins CR, Martin RC, Kim HJ, Baker JJ, Merchant NB, Parikh AA, Kooby DA. Factors influencing readmission after pancreaticoduodenectomy: a multi-institutional study of 1302 patients. Ann Surg 2012;256:529-37.
- 34. Cho SW, Tzeng CW, Johnston WC, Cassera MA, Newell PH, Hammill CW, Wolf RF, Aloia TA, Hansen PD. Neoadjuvant radiation therapy and its impact on complications after pancreaticoduodenectomy for pancreatic cancer: analysis of the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP). HPB (Oxford) 2013;16:350-6.
- 35. Greenblatt DY, Kelly KJ, Rajamanickam V, Wan Y, Hanson T, Rettammel R, Winslow ER, Cho CS, Weber SM. Preoperative factors predict perioperative morbidity and mortality after pancreaticoduodenectomy. Ann Surg Oncol 2011;18:2126-35.
- 36. Pecorelli N, Braga M, Doglioni C, Balzano G, Reni M, Cereda S, Albarello L, Castoldi R, Capretti G, Di Carlo V. Preoperative chemotherapy does not adversely affect pancreatic structure and short-term outcome after pancreatectomy. J Gastrointest Surg 2013;17:488-93.
- Amini A, Patanwala AE, Maegawa FB, Skrepnek GH, Jie T, Gruessner RW, Ong ES. Effect of epidural analgesia on postoperative complications following pancreaticoduodenectomy. Am J Surg 2012;204:1000-4.
- Gilmore DM, Curran T, Gautam S, Nagle D, Poylin V. Timing is everything-colectomy performed on Monday decreases length of stay. Am J Surg 2013;206:340-5.
- 39. Merkow RP, Bilimoria KY, Tomlinson JS, Paruch JL, Fleming JB, Talamonti MS, Ko CY, Bentrem DJ. Postoperative Complications Reduce Adjuvant Chemotherapy Use in Resectable Pancreatic Cancer. Ann Surg 2013:Epub ahead of print.
- 40. Valle JW, Palmer D, Jackson R, Cox T, Neoptolemos JP, Ghaneh P, Rawcliffe CL, Bassi C, Stocken DD, Cunningham D, O'Reilly D, Goldstein D, Robinson BA, Karapetis C, Scarfe A, Lacaine F, Sand J, Izbicki JR, Mayerle J, Dervenis C, Olah A, Butturini G, Lind PA, Middleton MR, Anthoney A, Sumpter K, Carter R, Buchler MW.

Optimal Duration and Timing of Adjuvant Chemotherapy After Definitive Surgery for Ductal Adenocarcinoma of the Pancreas: Ongoing Lessons From the ESPAC-3 Study. J Clin Oncol 2014;32: 504-12.

- 41. Asbun HJ, Stauffer JA. Laparoscopic vs open pancreaticoduodenectomy: overall outcomes and severity of complications using the Accordion Severity Grading System. J Am Coll Surg 2012;215:810-9.
- 42. Bao PQ, Mazirka PO, Watkins KT. Retrospective Comparison of Robot-Assisted Minimally Invasive Versus Open Pancreaticoduodenectomy for Periampullary Neoplasms. J Gastrointest Surg 2013;18:682-9.
- Correa-Gallego C, Dinkelspiel HE, Sulimanoff I, Fisher S, Vinuela EF, Kingham TP, Fong Y, DeMatteo RP, D'Angelica MI, Jarnagin

W R, Allen PJ. Minimally-invasive vs open pancreaticoduodenectomy: systematic review and meta-analysis. J Am Coll Surg 2014;218:129-39.

- 44. Croome KP, Farnell M, Que FG, Reid-Lombardo K, Truty M, Nagorney D, Kendrick ML. Total laparoscopic pancreaticoduodenectomy for pancreatic ductal adenocarcinoma: Oncologic advantages over open approaches? Ann Surg 2014;In press.
- 45. Mesleh MG, Stauffer JA, Asbun HJ. Minimally invasive surgical techniques for pancreatic cancer: ready for prime time? J Hepatobiliary Pancreat Sci 2013:Epub ahead of print.
- 46. Zureikat AH, Moser AJ, Boone BA, Bartlett DL, Zenati M, Zeh HJ, 3rd. 250 robotic pancreatic resections: safety and feasibility. Ann Surg 2013;258:554'9.