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ORIGINAL ARTICLE – HEALTHCARE POLICY AND OUTCOMES

Readmissions Following Pancreaticoduodenectomy for Pancreas Cancer: A Population-Based Appraisal

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ABSTRACT Procedure complexity and volume–outcome relationships have led to increased regionalization of pancreaticoduodenectomy (PD) for pancreas cancer. Knowledge regarding outcomes after PD comes from single-institutional series, which may be limited if a significant number of patients follow up at other hospitals. Thus, readmission data may be underreported. This study utilizes a population-based data set to examine readmission data following PD. California Cancer Registry (1994–2003) was linked to the California's Office of Statewide Health Planning and Development (OSHPD) database; patients with pancreatic adenocarcinoma who had undergone PD, excluding perioperative (30-day) mortality, were identified. All hospital readmissions within 1 year following PD were analyzed with respect to timing, location, and reason for readmission. Our cohort included 2,023 patients who underwent PD for pancreas cancer. Fifty-nine percent were readmitted within 1 year following PD and 47% were readmitted to a secondary hospital. Readmission was associated with worse median survival compared with those not readmitted (10.5 versus 22 months, $p < 0.0001$). Multivariate analysis revealed that increasing T-stage, age, and comorbidities were associated with increased likelihood of readmission. Diagnoses associated with high rates of readmission included progression of disease (24%), surgery-related complications (14%), and infection (13%). Diabetes (1.4%) and pain (1.5%) were associated with low rates of readmission. We found a readmission rate of 59%, which is much higher than previously reported by single institutional series. Concordantly, nearly half of patients readmitted were readmitted to a secondary hospital. Common reasons for readmission included progression of disease, surgical complications, and infection. These findings should assist in both anticipating and facilitating postoperative care as well as managing patient expectations. This study utilizes a novel population-based database to evaluate incidence, timing, location, and reasons for readmission within 1 year following pancreaticoduodenectomy. Fifty-nine percent of patients were readmitted within 1 year after pancreaticoduodenectomy and 47% were readmitted to a secondary hospital.

With mortality approximating incidence, pancreas cancer remains the fourth leading cause of cancer death in the USA accounting for 35,000 deaths annually.[1] As both chemotherapy and radiation remain minimally effective, surgical resection remains the only chance for cure, with high-volume centers reporting 5-year survival rates of up to 20%.[2–9] Pancreaticoduodenectomy (PD), a complex procedure with high morbidity, is the most common operation performed for adenocarcinoma of the pancreas. Although mortality rates following PD at high-volume centers have declined considerably, morbidity remains as high as 48%, and the curative intent of the operation is achieved in a minority of patients.[2,6,7,10–14] Given the combination of high morbidity and low cure rate following PD, it is important to investigate the long-term impact of this complex surgical procedure on pancreas cancer survivorship. Examination of readmission data after PD would provide valuable insight into the impact on cancer survivorship with the goal of uncovering mutable factors to improve care after PD.

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Considering the volume–outcome relationship and the inherent complexity of the procedure, PD for pancreas cancer has naturally undergone regionalization in which the majority of resections are performed in tertiary referral centers.[15–17] Thus, much of our knowledge regarding PD comes from robust large single-institutional databases.[5–7] Previous studies utilizing such databases of high-volume centers have attempted to evaluate readmissions following PD; however, these studies admittedly were not able to capture all readmissions that occurred at secondary hospitals and reported overall readmission rates ranging from 26% to 38%.[18,19] We hypothesized that evaluating postoperative readmissions following PD using a statewide administrative database will more effectively capture all hospital admissions within the state and provide more complete data regarding incidence and timing of readmissions relative to the surgery.

Given the regionalization of the surgical treatment of pancreas cancer, we believe single-institution series underreport readmissions following PD. Although single-institution series data are more robust regarding clinical detail, population-based administrative data can complement the single-institution series, especially in diseases in which regionalization of only a portion of the care occurs. Therefore, through the use of a novel statewide database, our study aims to characterize the (1) number, (2) timing, (3) location, and (4) reasons for readmission within 1 year following PD. We feel that this type of analysis will complement high-volume single-institution series data by providing more complete data to facilitate postoperative resource strategies and assist in communications with other health care providers. Finally, this knowledge may be important in setting realistic postoperative expectations for both the patient and physician.

PATIENTS AND METHODS

Creation of Novel Database

All patients with a diagnosis of pancreatic cancer recorded between the years of 1994 and 2003 in the California Cancer Registry Database were linked to the California's Office of Statewide Health Planning and Development (OSHPD) database as well as to the State Death File. The California Cancer Registry is a statewide population-based cancer surveillance system that records demographics, cancer type, extent of disease, and treatment data along with survival information.[20] The OSHPD database collects semi-annual data from all inpatients discharged from nonfederal hospitals licensed by the state of California. Each record includes patient demographics, hospital identification code, dates of admission and discharge, and codes for inpatient procedures and diagnoses. All procedures and diagnoses are categorized by the International Classification of Disease, 9th Clinical Modification (ICD-9, CM) coding scheme.[21] The State Death File provided accurate mortality data. The final linked database consisted of 52,222 hospital admissions for 23,803 patients diagnosed with adenocarcinoma of the pancreas.

Patient Selection

The cohort was identified based on primary tumor site location (i.e., pancreas) and ICD-9 procedure code for pancreaticoduodenectomy (52.51, 52.53, and 52.7). Only patients with adenocarcinoma were included; adenocarcinoma cases were selected using histopathology codes for adenocarcinomas, as defined by the International Classification of Diseases for Oncology, 3rd edition: 8000, 8001, 8003, 8010, 8012, 8020, 8021, 8022, 8030, 8031, 8033, 8035, 8041, 8045, 8046, 8050, 8070, 8140, 8141, 8144, 8154, 8201, 8210, 8230, 8260, 8290, 8310, 8440, 8441, 8450, 8452, 8453, 8460, 8470, 8471, 8472, 8473, 8480, 8481, 8482, 8490, 8500, 8501, 8503, 8550, 8560. Patients with perioperative mortality, defined as death within 30 days from date of PD, were excluded from the analysis. Finally, nine patients were excluded from the analysis due to miscoding.

Analysis was performed for two groups of patients who had undergone PD for adenocarcinoma. The first cohort, referred to as the readmission group, had $\geq$1 readmission within the year following PD. The second cohort, defined as the no readmission group, did not have a readmission within the first year following the procedure and included patients who were never readmitted and those that had their first readmission more than 1 year following PD.

Patient-Level Factors

Demographics recorded for each patient included: age at diagnosis, sex, race/ethnicity, node status, and T-stage. The Charlson comorbidity index (CCI) was utilized to risk adjust patients in the groups according to their comorbidities. The CCI consists of 19 disease conditions with different weights based on risk of mortality within 1 year. For example, myocardial infarction carries a score of 1, whereas severe liver disease carries a score of 3 and thus the risk of mortality within 1 year is higher for a patient with severe liver disease than for a patient with a history of myocardial infarction. These scores are summed for each patient, indicating higher burden of comorbid disease.[22] In this study, a revised CCI was recorded as 0, 1, 2 or 3 or more, excluding scoring for a cancer diagnoses since all patients in this study have pancreatic cancer. If patients underwent radiation and/or chemotherapy, they were considered to have had adjuvant

therapy. Median length of stay was calculated for the initial surgical admission. Overall survival in months was calculated from date of operation to date of death or last follow-up, as was median follow-up of survivors.

Readmission Analyses

All readmissions that occurred within the year following PD were identified and tallied. Analysis of these readmissions included timing, location, and reasons for readmissions. Location of readmission was recorded as a dichotomous variable: either the patient was readmitted at the hospital where the PD was performed, referred to as the primary hospital, or the patient was readmitted to a hospital other than the primary hospital referred to as the secondary hospital.

To determine the reasons for readmission, ICD-9 diagnosis codes for each readmission were compiled and sorted into categories. The first step of this process was to collect all principal diagnosis codes for each readmission within the first year. Ideally, the principal diagnosis code, of which there is only one per admission, provides the main reason for the inpatient admission. These codes were then sorted and grouped into clinically appropriate categories, i.e., progression of disease, pain, infection, etc. (see Supplementary Table). The number of readmissions represented by each category was then divided by the total number of readmissions to determine the percentage of readmissions associated within each category.

Statistical Analyses

Histograms were constructed to determine distribution of readmissions over time. *t*-Test analyses of both means and proportions were completed, comparing the readmission group with the no readmission group. The Mann–Whitney test was utilized for the comparison of median values. *p*-values <0.05 were considered to be statistically significant. Survival analysis was performed using the Kaplan–Meier method and comparison was carried out using log-rank analysis. Multivariate logistic regression was performed to identify perioperative predictors of readmission, controlling for age by quartiles, sex, race/ethnicity, node status, T-stage, and CCI score. All statistical analyses were completed using Stata version 9.0 (Stata Corporation, College Station, TX, USA). This study was approved by our institutional review boards.

RESULTS

Patient-Level Factors

Utilizing our novel database we identified 2,158 patients who underwent PD for adenocarcinoma of the pancreas in the state of California from 1994 to 2003. Patients experiencing 30-day perioperative mortality were excluded from the analysis, which decreased the cohort by 6% to 2,023. Median follow-up of survivors was 43 months, and 82% of patients were followed until death. Overall, the cohort consisted of 51% males and had median age of 66 years. Administrative data for each admission was analyzed and demonstrated that 1,194 (59%) of patients had $\geq$1 readmission within 1 year following PD. The remainder of the demographics can be seen in Table 1. There were several differences between the readmission group and the no readmission group, including that a patient with a CCI score of 0 was less likely to be in the readmission group (61.6% versus 54.4%, $p < 0.001$), and that low T-stage was associated with the no readmission group (23.6% versus 20.0%, $p < 0.05$), whereas stage T4 was more likely to be associated with the readmission group (15.8% versus 11.1%, $p < 0.003$). Interestingly, there was no significant difference in readmission within 1 year in patients who received adjuvant therapy. However, as expected, patients who were found to have had longer surgical lengths of stay were more likely to be in the readmission group (15 versus 13 days, $p < 0.0001$). Survival curves were generated by the Kaplan–Meier method for both the readmission group and the no readmission group and can be seen in Fig. 1. Median survival was much lower for the readmission group compared with the no readmission group (12.3 versus 22.0 months, $p < 0.0001$) which was significant on log-rank analysis.

Predictors of Readmission

Given the significantly decreased survival associated with readmission, we performed multivariate logistic regression, controlling for age at diagnosis, sex, race/ethnicity, node status, T-stage, and comorbidities (CCI score) in an attempt to determine if there are any perioperative factors that will predict readmission following PD. Increasing age, comorbidities, and advanced T-stage were all associated with an increased likelihood of readmission. Specifically, patients who are greater than 73 years old have a greater odds of readmission within the first year [odds ratio (OR) $= 1.37, p < 0.02$]. Additionally, when compared with patients with a CCI score of 0, patients with a CCI score of 1 or 3 have a 1.31 ($p < 0.01$) and 1.62 ($p < 0.01$) odds of being in the readmission cohort, respectively. Lastly, a patient with a T4 tumor has a 1.69 ($p < 0.001$) odds of being in the readmission group (Table 2).

Readmission Analyses

There were a total of 2,435 readmissions within 1 year following PD for pancreas cancer which took place in 1,194 patients or 59% of the total cohort. The mean number

TABLE 1 Demographics

All adeno	Overall $n = 2,023$	Readmission cohort $n = 1,194$ (59.0%)	No readmission cohort $n = 829$ (41.0%)	p value
Sex				
Males	50.8%	51.6%	49.6%	NS
Median age (years)	66	66	65	NS
Race				
White	73.2%	72.5%	74.0%	NS
Black	5.5%	5.7%	5.3%	NS
Hispanic	13.3%	13.3%	13.2%	NS
Asian	7.6%	8.1%	6.8%	NS
Other	0.2%	0.0%	0.4%	0.03
Unknown	0.4%	0.3%	0.4%	NS
Charlson				
0	57.3%	54.4%	61.6%	0.001
1	27.1%	29.1%	24.4%	0.02
2	8.8%	8.9%	8.6%	NS
3+	6.8%	7.7%	5.4%	NS
T-Stage				
1	21.5%	20.0%	23.6%	0.05
2	5.3%	5.7%	4.8%	NS
3	56.8%	56.1%	57.7%	NS
4	13.8%	15.8%	11.1%	0.003
Unknown	2.6%	2.4%	2.8%	NS
Node status				
Positive	51.5%	53.1%	49.1%	NS
Unknown	8.4%	8.3%	8.4%	NS
Adjuvant therapy	49.2%	49.9%	48.3%	NS
Median postoperative length of stay (days)	14	15	13	<0.0001
Median survival (months)	16.9	12.5	22.0	<0.0001

NS nonsignificant

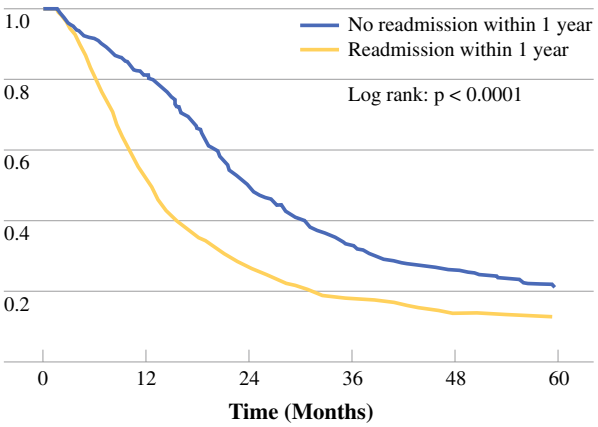

FIG. 1 Kaplan–Meier curve comparing the readmission group with the no readmission group

of readmissions for the readmission cohort was 2.0, ranging from 1 to 10. The distribution of readmissions over the first year following surgery can be seen in Fig. 2. When evaluating the number of readmissions over time, 19% occurred within 30 days, and 42% occurred within 90 days of the PD. When evaluating location of readmission, we found that 47% of patients were readmitted to a secondary hospital at least once (Fig. 3).

Upon categorizing and analyzing the reasons for readmission within 1 year following PD, we found certain categories to be higher than expected, and others to be lower than expected (Fig. 4). The largest number of readmissions was associated with progression of disease (24.3%), which is to be expected given the aggressive biology of pancreas cancer and low cure rate after resection. Other larger categories included surgery-related complications (14.0%), infection (12.3%), dehydration, malnutrition, and electrolyte disorders (6.2%). Approximately 5% of readmissions are planned admissions for either adjuvant therapy or rehabilitation. Readmissions for deep venous thrombosis (DVT) and pulmonary embolism (PE) were significant, accounting for 3% of all readmissions. However, readmissions for both pain (1.5%) and diabetes (1.4%) were lower than expected.

TABLE 2 Multivariate logistic regression predicting readmission

	Odds ratio	*p* value	95% Confidence interval
Age < 57 years	1.00	–	–
57 ≥ age < 66 years	1.26	0.08	0.97, 1.63
66 ≥ age < 73 years	1.22	0.14	0.94, 1.58
≥73 years	1.37	0.02	1.06, 1.77
Male	1.00	–	–
Female	0.92	0.36	0.77, 1.10
Charlson 0	1.00	–	–
Charlson 1	1.31	0.01	1.06, 1.63
Charlson 2	1.13	0.44	0.82, 1.58
Charlson ≥ 3	1.62	0.01	1.11, 2.37
White	1.00	–	–
Black	1.14	0.51	0.77, 1.70
Hispanic	1.04	0.78	0.79, 1.36
Asian	1.24	0.23	0.87, 1.75
Unknown	0.96	0.96	0.21, 4.38
T1	1.00	–	–
T2	1.37	0.16	0.88, 2.12
T3	1.14	0.26	0.91, 1.42
T4	1.69	0.001	1.23, 2.32
Unknown T-stage	0.96	0.90	0.53, 1.75
Node negative	1.00	–	–
Node positive	0.99	0.89	0.96, 1.03

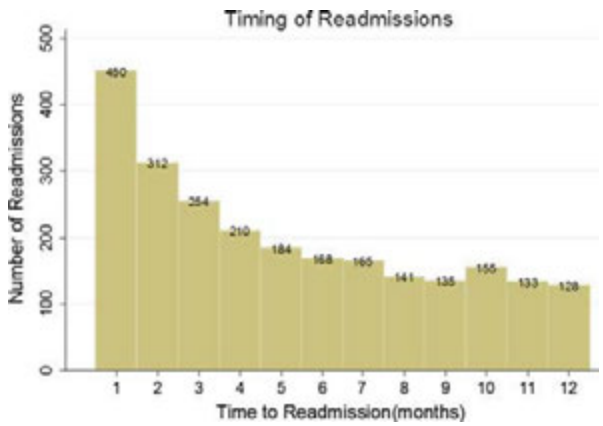

FIG. 2 Timing of Readmissions one year following PD. Total number of readmissions was 2435; 19% of readmissions occurred within 30 days and 42% occurred within 90 days of PD

Next, we evaluated whether the reasons for readmission were different between the primary versus secondary hospital. We found that the readmission rates for most diagnoses were statistically similar between primary and secondary hospitals (data not shown) with one exception. The majority (72%) of patients readmitted for pancreaticobiliary disorders returned to the primary hospital, versus 28% being readmitted to a secondary hospital.

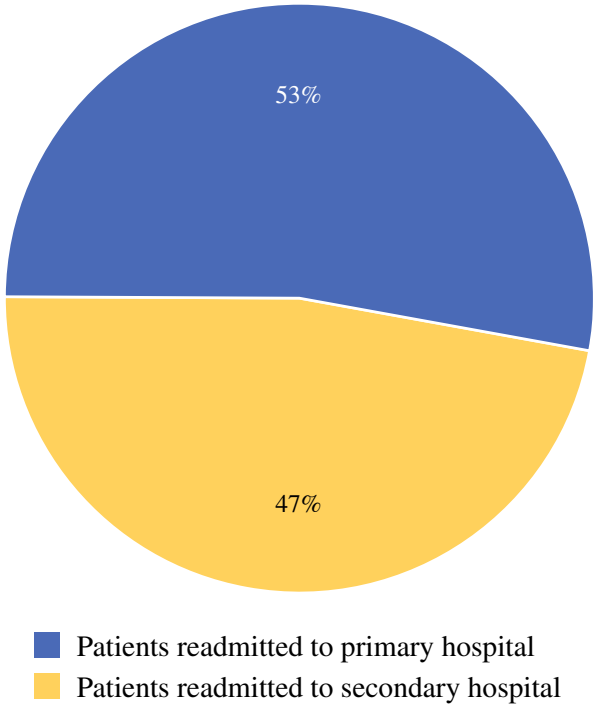

FIG. 3 Location of readmissions 1 year following PD: primary hospital versus secondary hospital

DISCUSSION

Despite improvements in perioperative care, PD for pancreas cancer remains a complex procedure with associated high morbidity and recurrence rates. With resection yielding such a low cure rate of this biologically aggressive cancer, we must thoroughly investigate the impact of PD on pancreatic cancer survivorship. In this study we have chosen to evaluate postoperative readmissions of pancreas cancer survivors following PD. Given the regionalization of the PD procedure, we created a novel population-based data set which would yield accurate readmission data for the entire state of California. This database was created by merging the California Cancer Registry with the California's Office of Statewide Health Planning and Development (OSHPD) database as well as the State Death File.

Our study evaluated more than 2,000 patients diagnosed with adenocarcinoma of the pancreas in the State of California between the years of 1994 to 2003 and determined that 59% were readmitted to a hospital at least once within 1 year following PD. Older age at diagnosis, increasing presence of comorbidities (CCI > 0), and higher T-stage were all predictors of readmission within 1 year in a multivariate model. Nearly half of patients readmitted to the hospital after surgery were readmitted to a secondary hospital at least once during the first year. Readmission following PD was associated with a significantly worse survival as demonstrated by a median survival decrease of

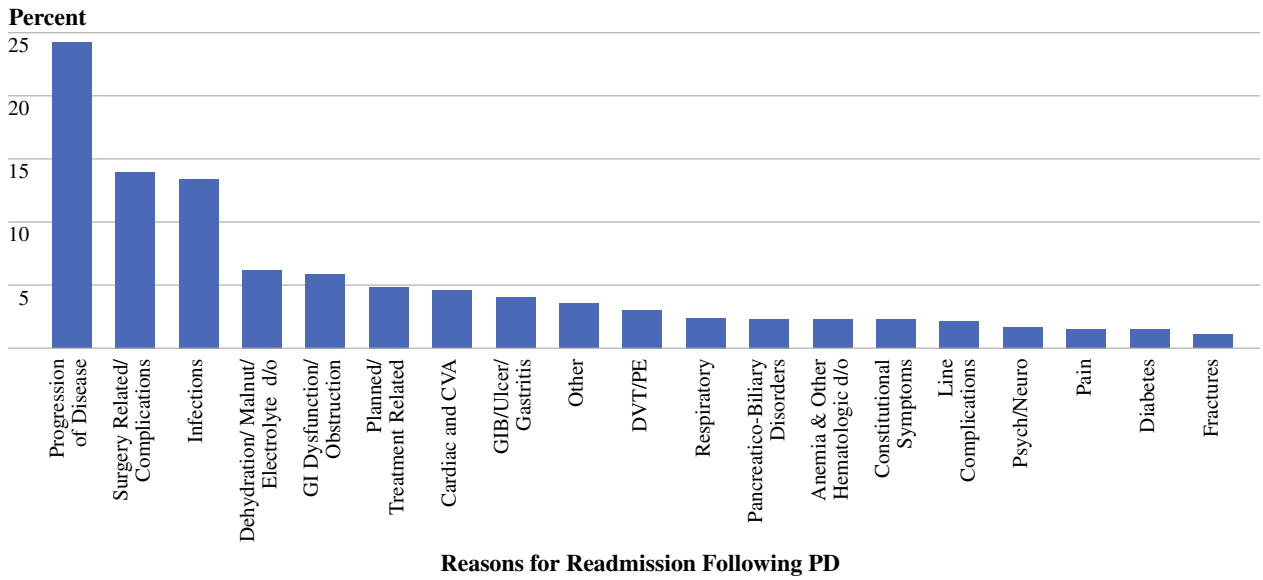

FIG. 4 Reasons for readmission within 1 year following PD

approximately 12 months compared with patients that were not readmitted. As expected from this survival association, the most common reason for readmission was progression of disease. Other common reasons for readmission included surgery-related complications, and infection. Readmissions for pain and diabetes were uncommon.

Previous studies have examined readmissions after PD; however, these studies were performed utilizing single-institution data and reported overall readmission rates of 26–38%.[18,19] We found that many more patients in our sample had been readmitted following PD than reported in these previous studies. This discrepancy is likely explained by the fact that, in our study, 47% were readmitted to a secondary hospital at least once within the first year.

Regionalization of the PD procedure has been spurred by studies demonstrating not only decreased operative mortality but also better long-term cancer outcomes when complex surgical procedures are performed at high- versus low-volume hospitals. Thus, many patients travel to high-volume centers to undergo surgical procedures like PD.[16,17] These patients, however, often go to the closest hospital for unscheduled readmissions following PD and do not travel back to the high-volume center. This phenomenon can lead to significant underreporting of readmission rates in high-volume center databases, and therefore some would argue that accurate readmission rates and reasons for readmission following PD remain largely unknown. By utilizing California's OSHPD database, we were able to capture all readmissions in the state of California following PD, thereby accounting for patients who were operated on at a high-volume center and readmitted at a community hospital.

The greatest percentage of readmissions occurred due to progression of disease (24.3%). There were also relatively high rates of readmissions for mutable causes such as dehydration, malnutrition, and electrolyte disorders (12.3%). This high rate highlights an area where increased awareness and utilization of home health care services may decrease inpatient admissions, which can be both less disruptive and less expensive to the patient and their family than unscheduled inpatient admission. Furthermore, there should be an effort to treat diagnoses such as anemia and dehydration in an outpatient or hospice setting. Another diagnosis that maybe decreased through further prevention is the rate of readmissions for DVT and PE (3.0%). Improved compliance with DVT prevention policies may decrease the number of these readmissions. Likewise, 4% of readmissions were due to gastritis/ulcer/gastrointestinal (GI) bleeding and may be decreased with offering routine long-term anti-acid prophylaxis. Notably, only 1.5% of readmissions were due to pain. Taking into consideration that 44% of patients admitted to a palliative care setting have severe pain, the number of readmission associated with pain is relatively low and this may point to a palliative benefit of primary tumor resection.[23]

One could argue that, by capturing all statewide readmissions, readmissions to secondary hospitals are for different diagnoses when compared with the primary hospital. In fact, we found that the readmission rates for most pancreas cancer-related diagnoses were similar, when comparing reasons for readmission at a primary versus secondary hospital (data not shown). There was one exception: 72% readmissions due to pancreaticobiliary dysfunction/obstruction took place at the primary hospital, leaving 28% of these readmissions to a secondary hospital. The complexity of care necessary to deal with recurrent biliary or pancreatic dysfunction following PD is one

explanation for increased referral back to the primary hospital in which the PD was performed.

With respect to timing of admissions, 19% or 450 admissions occurred within 30 days of the operative date. Considering that a median length of stay of 15 days was associated with the surgical admission for the patients that were eventually readmitted, some of these readmissions occurred within 2 weeks from the discharge date. These early postoperative readmissions represent an area in need of improvement. Perhaps, earlier and more frequent follow-up visits or something as radical as baseline discharge imaging in the form of abdominal ultrasound or computed tomography exam may identify the subclinical problems that appear to manifest very early in the postdischarge period. Obviously, further study along with increased vigilance for subclinical postoperative problems are needed in order to reduce these early readmissions.

Limitations to this study include those associated with utilizing an administrative database; the use of ICD-9 coding, rather than the medical record itself, can lead to miscoding of reasons for readmission.[24] Additionally, by utilizing administrative data, the wealth of clinical data in the medical record is not available. Although there will always be inherent limitations to utilizing administrative data, a statewide chart review for this high number of patients would have been financially prohibitive. These data, although not as accurate as a formal chart review, are able to determine trends in pancreas cancer care for our most populous state.

This is a unique study that investigated the incidence, timing, and reasons for readmission for all patients in the State of California who underwent PD for adenocarcinoma of the pancreas over a 9-year period. Given that 59% of patients experienced at least one readmission during the year following PD, our study demonstrates that readmission rates are significantly higher than previously reported. This fact can likely be explained by nearly half of readmitted patients being readmitted at a secondary hospital at least once. Many readmissions are due to progression of disease, surgery-related issues, and infection, whereas few are associated with pain and diabetes. Additionally, there appear to be readmissions that could be prevented, such as those for dehydration, malnutrition/electrolyte disorders, DVT/PE, and gastritis/ulcer disease with improved awareness, better prevention strategies, and utilization of home health services.

Finally, our study provides a comprehensive denominator for the incidence, timing, and reasons for readmission following PD in the setting of pancreas cancer. These findings should assist clinicians in both anticipating and facilitating postoperative care as well as managing patient expectations. We hope these data will serve as an impetus for further study as we strive to improve the impact of PD on pancreas cancer survivorship.

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