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Hospital readmission after pancreaticoduodenectomy: A systematic review and meta-analysis

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ABSTRACT

Background: Appropriate postoperative readmission rates and modifiable risk factors for readmission have yet to be defined for many operations. This systematic review and meta-analysis attempt to define these parameters for pancreaticoduodenectomy.

Materials and methods: The main outcomes were readmission rate, risk factors, and reasons for readmission. Meta-analyses were performed when data was homogeneous, otherwise, a qualitative review was performed.

Results: The 30-day, 90-day, and overall readmission rates were 17.63%, 26.14%, and 27.18%, respectively. In the meta-analysis, chronic pancreatitis (OR, 1.44, $p = 0.04$), operative length (MD, 26.1; $p < 0.01$), wound infection (OR, 1.9, $p < 0.01$), intra-abdominal abscess (OR, 3.79, $p < 0.01$), VTE (OR, 2.27, $p = 0.01$), and LOS (MD, 1.66, $p < 0.01$) where associated with readmission.

Conclusion: Hospital readmission will continue to be a quality metric and will influence reimbursement models. Thirty and 60-day readmission data underestimate the true readmission rate. Chronic pancreatitis, operative length, and several post-operative complications were associated with greater readmission. More uniform reporting is necessary to identify modifiable risk factors associated with readmission.

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Introduction

Hospital readmission is a frequent occurrence in both medical and surgical patients and is estimated to cost the healthcare system billions of dollars annually.[1,2] The role of readmission as a healthcare quality metric is currently the topic of fervent debate. Policymakers, administrators, and some physicians ardently promote readmission as an accurate indicator of inferior care and poorer outcomes,[2] while others contest the validity of those claims.[3,4] Even without agreement, provisions in recent legislation have allowed for reductions in reimbursement for those with readmission rates higher than an assigned observed-to-expected ratio.[1,3,5,6] Therefore, it is prudent that the surgical community work to establish operation-specific readmission rates.

Pancreaticoduodencectomy (PD) has historically been associated with high mortality and morbidity.[7] Despite improvements in operative technique, perioperative care, and regionalization to high volume centers, complications continue to occur in 30–60% of patients undergoing PD.[2,8] A small number of studies, mostly from single institutions, have reported readmission rates and contributing factors. It is currently unclear if data from these studies can be applied to populations outside of their respective institutions. The aim of the current study is two-fold: (1) to establish an expected readmission rate for PD, and (2) to identify risk factors associated with readmission after PD.

Methods

Search strategy and study selection

This systematic review was conducted in accordance with the PRISMA guidelines.[9] An electronic search of the Medline and PubMed databases was conducted using combinations of the terms 'readmission,' 'pancreaticoduodenectomy,' 'pancreatoduodenectomy,' and 'whipple.' The search was limited to

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studies published between January 1, 2005 and August 31, 2016. Inclusion criteria included studies focusing on readmission after pancreaticoduodenectomy, with a concentration on PD for oncologic purposes. Studies evaluating PD for non-oncologic purposes were reviewed for possible inclusion. Exclusion criteria included non-English language publications and meta-analyses. Studies not including data for readmissions or rates, factors associated with readmission, and reasons for readmission were excluded. Case reports were also excluded.

Inclusion and exclusion criteria

Two examiners reviewed all abstracts for potential inclusion. Additional studies were identified from the references of studies identified in the database search. Reviewers then compiled study characteristics and outcomes of interest, including study type (single center, multi-institutional or administrative database), patient demographics, disease type, complications, readmission interval (30 days, 90 days, or greater), and the time-period of data collection. Outcomes of interest included: number of readmissions, time frame of readmission, number and type of complications, risk factors for readmission, reasons for readmission, and preventive measures for readmission. Complications were considered defined if the explicit type of complications were reported and were considered graded if reported on an ordinal scale. Studies were then compared along the lines of readmission rates and risk factors for readmission. The quality of each study included was evaluated using the Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomized cohort studies.[10] Studies were considered high-quality if they scored $\geq$7 and moderate-quality if they score $\geq$5.

Data extraction

Relevant data was extracted from the included studies by two reviewers independently. Extracted data included: number of readmissions, time frame of readmission, patient demographics, patient comorbidities, number and type of complications, risk factors for readmission, reasons for readmission, and preventive measures for readmission.

Statistical analysis

For the chosen outcomes of interest, the random effects meta-analysis was performed with Review Manager ("RevMan", Version 5.3. Copenhagen: The Nordic Cochrane Center, the Cochrane Collaboration, 2014). Odds ratios (OR) with the Mantel-Haenszel method was utilized for analysis of dichotomous variables. Mean difference (MD) with the inverse variance method was utilized for analysis of continuous variables. A 95% confidence interval (CI) was reported for both measures. For studies providing medians and ranges instead of means and standard deviations or not providing standard deviation when mean data was supplied, the means and/or standard deviations were determined using the formula described by Hozo et al.[11] Forest plots were constructed for each outcome.

Results

Literature selection

Fig. 1 displays the results of the review process, which initially identified 152 records of which 119 remained after removing duplicates. Additional screening resulted in 11 articles being suitable for inclusion and a cohort of 19,976 patients with 4936 being readmitted. There was heterogeneity amongst the included articles, however, when homogenous reporting amongst the studies was present, meta-analyses were performed. The findings of all the meta-analyses are described in the paragraphs immediately following. Only meta-analyses in which a statistically significant association was discovered are represented in figure form.

Characteristics of the selected studies

The quality of each study was assessed using the NOS. The results of this evaluation are shown in Table 1. All included studies were considered high-quality. Study design measures and the time-period for readmission is shown in Table 2. Two (18%) studies utilized administrative databases, 2 (18%) utilized multi-institutional data, and 7 (64%) studies utilized single-center data. The reported time-periods for readmission data were 30-day (n = 2,18%), 60-day (n = 1,9%), 90-day (n = 3,27%), and greater than 90-days (n = 5,45%).

Readmission rate

All studies included in this analysis reported readmission rates, which are summarized in Table 3. The mean 30-day readmission rate was 17.63%, the mean 90-day readmission rate was 26.14%, and the overall mean readmission rate was 27.18%.

Patient demographics and comorbidities

Ten studies reported data regarding patient age.[2,12–20] Schneider et al. Emick et al., Rosemurgy et al. and Yermilov et al. demonstrated a significant relationship between age and readmission ($p = 0.028$, $p < 0.0001$, $p < 0.001$, $p < 0.02$, respectively). Seven studies reported patient age data suitable for meta-analysis.[12–16,18,20] For the combined data, the mean age of readmitted patients was 63.7 (SD = 2.9) and mean age of non-readmitted patients was 63.2 (SD = 4.1). There was no significant difference in mean age between the two groups (MD, −0.84; 95% CI, −2.23-0.56; $p = 0.56$). A random effects model was used for significant heterogeneity between the two groups ($p = 0.24$, $I^2 = 89\%$).

Ten studies reported data regarding patient sex.[2,12–20] Emick et al. and Zhu et al. both found a significant relationship between male sex and readmission after PD ($p = 0.05$ and $p = 0.019$, respectively). All 10 studies reported data suitable for meta-analysis, which failed to demonstrate a significant relationship (Female: OR, 0.92; 95% CI, 0.77–1.11, $p = 0.40$; Male: OR, 1; 95% CI, 0.84–1.13, $p = 0.99$). For both meta-analyses a random effects model was used (Female: $p < 0.00001$, $I^2 = 82\%$; Male: $p < 0.00001$, $I^2 = 80\%$).

Meta-analyses were performed for diabetes, hypertension, coronary artery disease, chronic obstructive pulmonary disease, and tobacco usage. None of the meta-analyses demonstrated a significant relationship with readmission after PD. Qualitative review for these comorbidities are summarized in Table 3.

Diagnosis

Six studies reported chronic pancreatitis diagnosis data.[2,12–14,16,17] Grewal et al. Ahmad et al., Sutton et al. Rosemurgy et al., and Yermilov et al. reported a significant relationship ($p = 0.002$, $p = 0.007$, $p < 0.001$, $p < 0.001$, and $p = 0.01$ respectively). Chronic pancreatitis was significantly associated with readmission on meta-analysis (OR, 1.44; 95% CI, 1.02–2.04, $p = 0.04$). A random effects model was used as there was significant heterogeneity between the two groups ($p = 0.07$, $I^2 = 51\%$) (Fig. 2).

Five studies reported malignant neoplasm diagnosis data.[2,14–16] In the meta-analysis, the diagnosis of a malignant

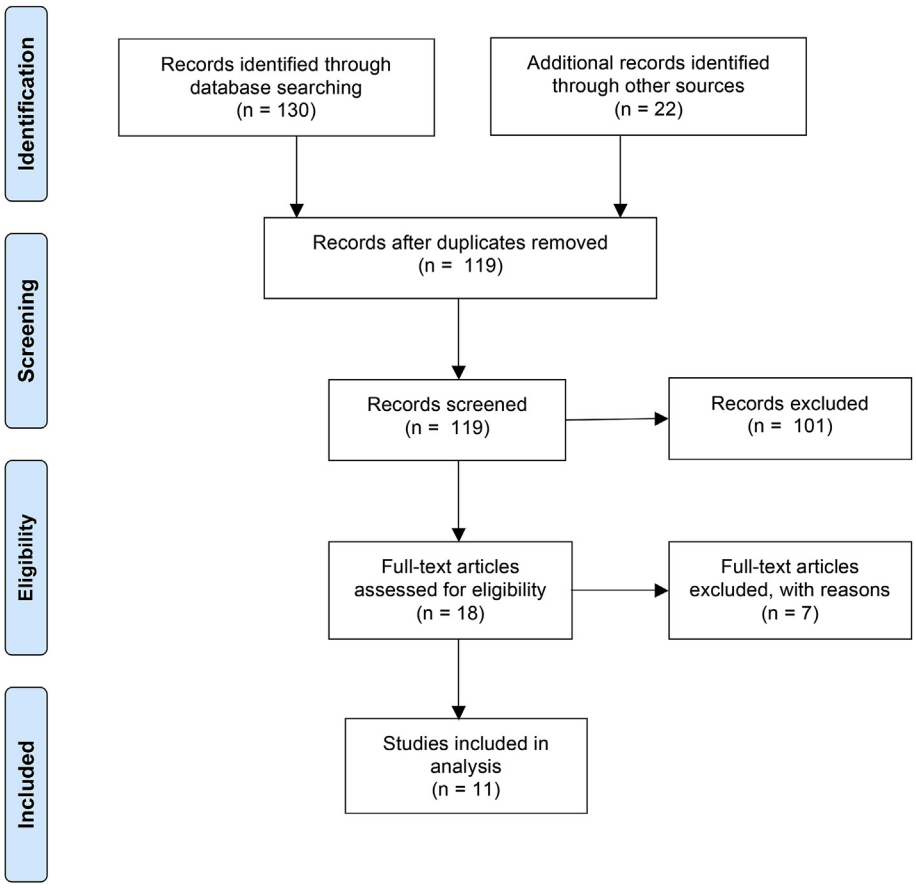

Fig. 1. Flow diagram illustrating the selection of studies in the review process.[9]

neoplasm as the reason for PD was not significantly associated with readmission (OR, 0.74; 95% CI, 0.33–1.67, $p = 0.47$). A random effects model was used for significant heterogeneity between the two groups ($p < 0.01$, $I^2 = 95\%$).

Operative variables

Five studies provided data regarding operative length.[2,12–14,16] Emick et al. and Fong et al. both found operative length to be positively related to readmission after PD ($p < 0.01$ and $p = 0.01$, respectively). The meta-analysis also demonstrated a positive relationship between operative length and readmission (MD, 26.1; 95% CI, 18.72–33.47, $p < 0.01$). A random effects model was used for significant heterogeneity between the two groups ($p = 0.3$, $I^2 = 17\%$) (Fig. 3).

Table 1
Newcastle-Ottawa scale for quality assessment of the included studies.[2,3,10,12–20]

Author	Selection	Comparability	Outcome
Schneider et al.	****	*	***
Grewal et al.	****		***
Ahmad et al.	****		***
Kastenberg et al.	****	*	***
Emick et al.	****	*	***
Zhu et al.	****	*	***
Brown et al.	****	*	**
Sutton et al.	****	*	**
Rosemurgy et al.	****		**
Yermilov et al.	****	*	***
Fong et al.	****	*	***

Six studies provided data regarding estimated blood loss.[2,12–16] Only Emick et al., found a significant correlation between estimated blood loss and readmission after PD ($p < 0.01$). The meta-analysis did not demonstrate a significant relationship between estimated blood loss and readmission after PD (MD, 102.7; 95% CI, 143.93–349.32, $p = 0.41$). A random effects model was used as there was significant heterogeneity between the two groups ($p < 0.01$, $I^2 = 95\%$).

Complications and other postoperative findings

Meta-analyses were performed for any postoperative complication, wound infection, intra-abdominal abscess, pneumonia, pancreatic fistula, delated gastric emptying, venous thromboembolism (VTE), and length of stay (LOS). A significant relationship with readmission was found for wound infection (OR, 1.9; 95% CI, 1.31–2.76, $p < 0.01$; $p = 0.05$, $I^2 = 54\%$), intra-abdominal abscess (OR, 3.79; 95% CI, 1.84–7.77, $p < 0.01$; $p = 0.03$, $I^2 = 66\%$), VTE (OR, 2.27; 95% CI, 1.17–4.38, $p = 0.01$; $p = 0.15$, $I^2 = 48\%$), and LOS (MD, 1.66; 95% CI, 0.97–2.34, $p < 0.01$; $p < 0.01$, $I^2 = 92$) (Figs. 3–7).

Other factors, outcomes, and complications

For data that was isolated or incompatible for meta-analysis, qualitative review was performed. Exposures in this category included transfusion, vessel resection, R1 resection, positive lymph nodes, stent placement, and disposition other than home. Four authors (Grewal et al. Ahmad et al., Emick et al. and Fong et al.) found the need for blood transfusion to be significantly related to

Table 2
Summary of study design parameters for studies reporting readmission.[2,3,12–20]

Data Source	
Administrative Database	2/11 (18%)
Multi-institutional	2/11 (18%)
Single-center	7/11 (64%)
Time-Period for Readmission	
30 day	2/11 (18%)
60 day	1/11 (9%)
90 day	3/11 (27%)
> 90 day	5/11 (45%)

readmission after PD ($p < 0.01$, $p = 0.01$, $p = 0.04$, and $p = 0.03$ respectively). Emick et al. found vessel resection to be associated with readmission after PD ($p = 0.05$). None of the studies found R1 resection to associated with readmission after PD. Kastenberg et al. found stent placement to be associated with readmission after PD ($p = 0.03$). Schneider et al. Kastenberg et al., and Sutton et al. found disposition other than home to be associated with readmission after PD ($p < 0.01$, $p = 0.02$, and $p < 0.01$ respectively). The published literature is summarized in Table 3.

Reasons for readmission

The consistency of reporting reasons for readmission amongst the included studies was poor and did not allow for meta-analysis. For this reason, a qualitative review was performed. For most studies, malnutrition, dehydration, and electrolyte disturbances were considered in the same category as a cause for readmission.

Table 3
Cohort data, readmission data, and reasons for readmission after pancreaticoduodenectomy, a summary of published literature.[2,3,12–20]

	Schneider et al., 2015	Grewal et al., 2011	Ahmad et al., 2012	Kastenberg et al., 2012	Emick et al., 2006	Zhu et al., 2011	Brown et al., 2014	Sutton et al., 2015	Rosemurgy et al., 2012	Yermilov et al., 2009	Fong et al., 2014
Cohort (n)	2209	124	1302	257	1643	438	89	9805	913	2023	1173
Patient demographics and comorbidities											
Gender	NS	NS	NS	NS	$p = 0.05$, male	$p = 0.019$, male	–	NS	NS	NS	NS
Race	–	NS	NS	–	$p = 0.01$, white	–	–	NS	–	NS	–
Age	$p = 0.028$, 55-64yo	NS	NS	NS	$p < 0.0001$	NS	–	NS	$p < 0.001$, younger	$p < 0.02$, ≥73yo	NS
BMI	–	NS	–	–	–	–	–	–	NS	–	NS
Illness severity score	NS	NS	NS	–	–	–	–	$p < 0.001$	$p < 0.001$	$p = 0.01$	–
Chronic pancreatitis	NS	$p = 0.002$	$p = 0.007$	–	–	–	–	–	–	–	NS
Cancer stage	–	–	NS	–	–	$p = 0.023$	–	–	NS	$p = 0.003$, T4	NS
Diabetes	NS	NS	NS	NS	–	–	–	–	–	–	NS
Coronary artery disease	$p = 0.02$	NS	NS	NS	–	–	–	–	–	–	–
Hypertension	–	NS	NS	NS	–	–	–	–	–	–	–
COPD	NS	NS	NS	–	–	–	–	–	–	–	–
Tobacco use	–	–	NS	NS	–	–	–	–	–	–	NS
Operative factors											
Operative time	–	NS	NS	–	$p < 0.0001$	–	–	–	NS	–	$p = 0.001$
Estimated blood loss	–	NS	NS	NS	$p = 0.0002$	–	–	–	NS	–	NS
Transfusion	–	$p = 0.001$	$p = 0.007$	–	$p = 0.04$	–	–	–	–	–	$p = 0.025$
Vessel resection	–	–	–	NS	$p = 0.05$	–	–	–	–	–	NS
R1 resection	–	–	NS	–	–	–	–	–	NS	–	–
Positive lymph nodes	–	–	NS	–	–	$p = 0.007$	–	–	NS	NS	–
Stent placement	–	NS	NS	$p = 0.03$	–	–	–	–	–	–	–
Postoperative findings											
Any postoperative complication	$p = 0.001$	–	–	$p = 0.0049$	$p = 0.003$	–	–	–	–	–	$p < 0.001$
SSI	NS	–	$p < 0.0001$	NS	$p = 0.01$	–	–	–	–	–	$p = 0.025$
Intra-abdominal abscess	–	–	$p < 0.02$	–	$p < 0.0001$	–	–	–	–	–	$p = 0.022$
PNA	$p = 0.042$	–	NS	–	NS	–	–	–	–	–	–
Pancreatic fistula	–	–	$p = 0.02$	NS	$p = 0.0003$	–	–	–	–	–	$p = 0.004$
DGE	–	–	$p = 0.04$	NS	NS	–	–	–	–	–	NS
VTE	NS	–	$p = 0.0007$	–	–	–	–	–	–	–	NS
LOS (index hospitalization)	$p = 0.019$	$p = 0.02$	NS	NS	$p = 0.02$	NS	–	$p < 0.001$	NS	$p < 0.0001$	$p = 0.01$
Disposition other than home	$p = 0.004$	–	–	$p = 0.018$	–	–	–	$p < 0.001$	–	–	–
Postoperative findings											
Wound infection	–	3	72	4	22	–	4	–	5	–	40
Intra-abdominal abscess	–	–	56	13	65	–	–	–	–	–	–
Pancreatic fistula	–	–	–	13	–	–	2	–	–	–	10
Pneumonia	–	–	3	–	4	–	0	–	–	–	6
Fever	–	–	7	4	–	–	–	–	10	–	–
DGE	–	–	51	–	52	–	4	–	–	–	9
SBO	–	–	17	–	34	9	–	–	–	–	5
Malnutrition/dehydration/ Electrolyte disturbances	–	15	58	–	4	9	–	–	–	74	23
GI bleed	–	–	6	–	17	4	–	–	14	–	5
Pain	–	5	25	–	–	–	–	–	31	18	6
VTE	–	–	5	1	–	–	–	–	1	36	–

COPD: chronic obstruction pulmonary disease; SSI: surgical site infection; PNA: pneumonia; DGE: delayed gastric emptying; VTE: venous thromboembolism; LOS: length of stay; SBO: small bowel obstruction; GI: gastrointestinal.

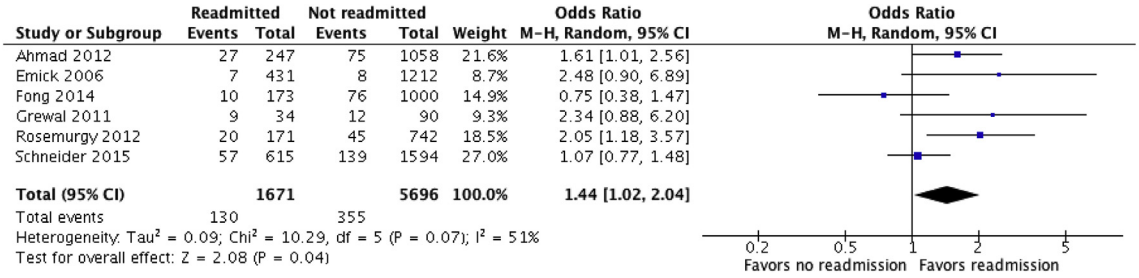

Fig. 2. Meta-analysis of chronic pancreatitis.[2,12–14,16,17]

The most common explicitly defined causes for readmission were intra-abdominal abscess and malnutrition, dehydration, and electrolyte disturbances. These were followed closely by wound infection and delayed gastric emptying. The reported causes for readmission are summarized in Table 3.

Discussion

Recent healthcare legislation has focused on improving healthcare efficiency by minimizing hospital readmissions.[1,2] The role and necessity of readmission as a quality metric is unclear. Moreover, the ability to define its expected occurrence rate after major surgery is difficult and often inaccurate. Nonetheless, some promote readmission rates as a potential modifier in reimbursement models.[1,3,5,6] As such, it is imperative that the surgical community accurately determine the readmission rates for use as reasonable quality metrics, and effectively identify modifiable risk factors to reduce health care costs.

Pancreaticoduodectomy has traditionally been associated with high mortality and morbidity. This has improved in recent years owing to better operative technique, improved postoperative care, and transition to centers of excellence. Despite such improvements the complication rate after PD remains high.[2,8] As such, PD is a potential target operation for improving readmission rates.

A great deal of heterogeneity was identified in the studies reporting readmission rates, factors associated with readmission, and reasons for readmission after PD. A measure as straightforward as readmission rate varied considerably in its time frame (i.e. 30, 60, 90, >90 days).

In this analysis, readmission rates (mean ± stdev) at 30-days, 90-days, and overall were 17.63 ± 2.63%, 26.14 ± 8.11%, and 27.18 ± 12.64%, respectively. Wise et al. previously demonstrated that 90-day reporting of readmission data was superior to 30-day reporting.[7] Findings of this study were consistent with this conclusion. The 30-day readmission rate underestimated the 90-day readmission rate by approximately 9% and the overall readmission rate by approximately 10%.

In the meta-analysis, chronic pancreatitis, wound infection, intra-abdominal abscess, VTE, and LOS were associated with readmission after PD. No patient demographics or comorbidities were associated with readmission in the meta-analysis.

Heterogeneous reporting of transfusions, vessel resection, R1 resection, positive lymph nodes, stent placement, and disposition other than home produced data that was not amenable to meta-analysis. It is should be noted that transfusion, vessel resection, positive lymph nodes, stent placement, and disposition other than home were significantly related to readmission in individual studies. It is unfortunate that these parameters where inconsistently reportedly as they may represent modifiable outcomes that can be targeted to decrease readmission rates.

Significant inconsistencies were discovered in the reporting of the reasons for readmission in the studies included in this review. As a result, meta-analyses could not be accomplished. The most common explicitly defined causes for readmission were intra-abdominal abscess and malnutrition, dehydration, and electrolyte disturbances. These were followed closely by wound infection and delayed gastric emptying. For most studies a large portion of readmissions were attributed to 'other.' In future studies, we recommend clear and homogenous reporting of reasons for admission. We suggest that this include the following data points: wound infection, intra-abdominal abscess, pancreatic fistula, pneumonia, fever, delayed gastric emptying, ileus, small bowel obstruction, malnutrition/diabetes/electrolyte perturbations, gastrointestinal bleeding, pain, and venous thromboembolism. Efforts should be made to avoid catchall categories such as *other*.

Several limitations of this study should be taken into consideration. First, variation amongst the various centers certainly exists. Sixty-four percent of the included studies were performed from single-center data. The characteristics of these patients, surgical technique, and pathology may not be applicable to other populations. Second, there was limited and inconsistent reporting amongst the included studies. For example, regarding illness severity scores, there were 4 different reporting structures utilized amongst the 11 studies. As a result, illness severity evaluation was not useful for this analysis. Third, the causes of readmission were poorly reported in terms of consistency, explicitness, and uniformity. The goal of studying readmission data is to identify preventable causes of readmission. This cannot be accomplished if the common causes of readmission cannot be delineated. Fourth, two of the studies utilized administrative data, which could possible result in duplication of participant involvement. Finally, it is expected that most studies, especially those from single centers, do

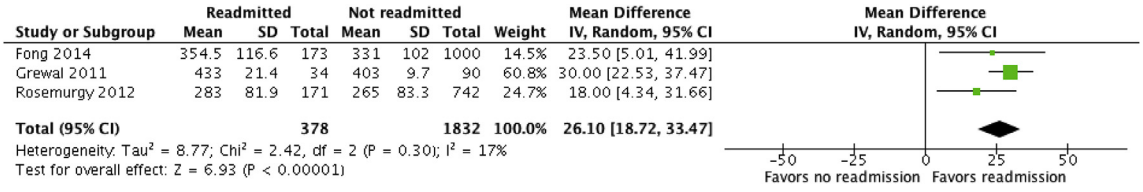

Fig. 3. Meta-analysis of operative time.[13,14,16]

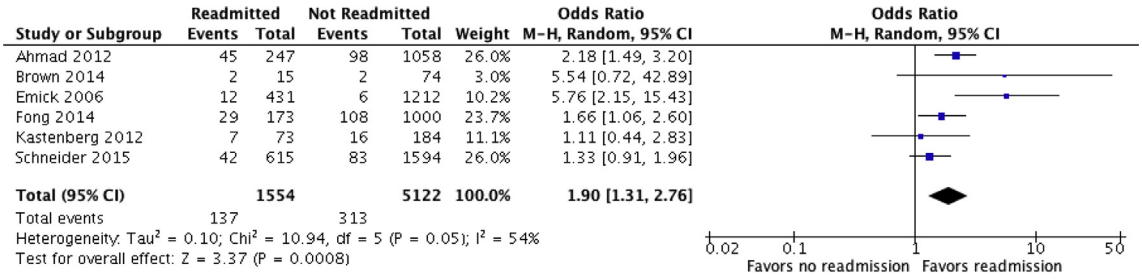

Fig. 4. Meta-analysis of wound infection.[2,12,13,15,17]

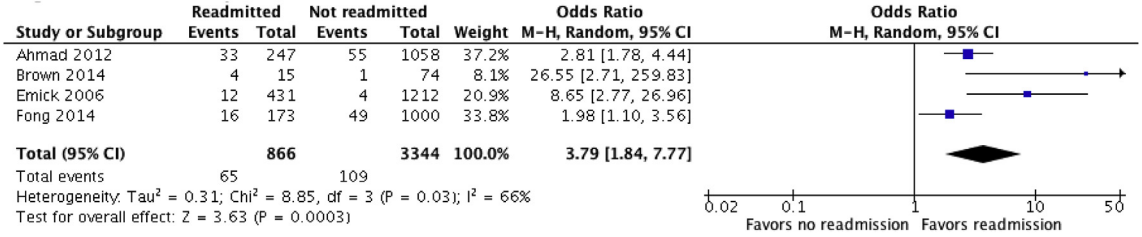

Fig. 5. Meta-analysis of intra-abdominal abscess.[2,3,12,13]

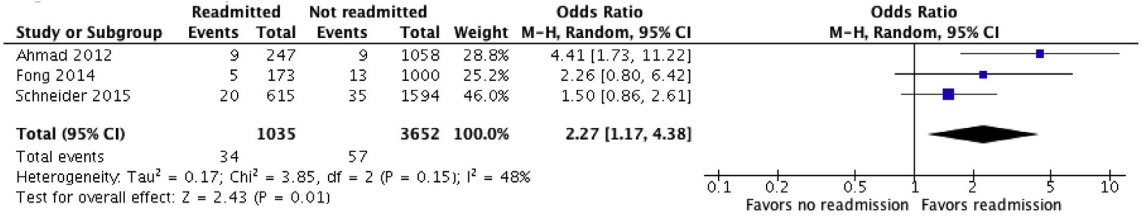

Fig. 6. Meta-analysis of postoperative venous thromboembolism.[2,13,17]

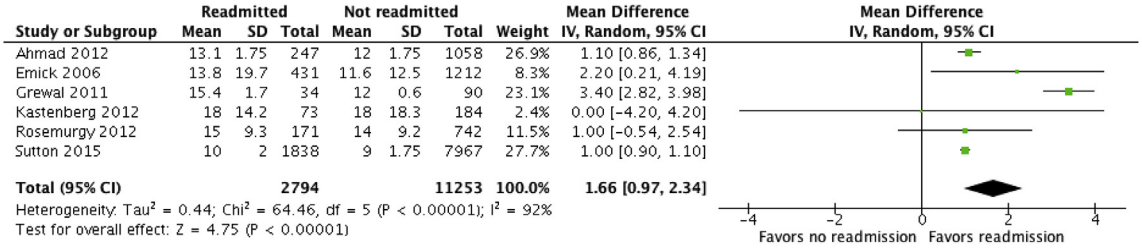

Fig. 7. Meta-analysis of length of stay.[2,12,14–16,18]

not capture readmission to outlying facilities. As a result, the true readmission rate after PD may be underestimated.

Healthcare policy is an ever-evolving entity, which is multifaceted and overwhelming for most physicians. Nonetheless, physicians must remain actively involved in healthcare policy discussion and negotiation. Readmission rates as a measure of healthcare quality have become a fundamental issue and are currently being used to modify reimbursement for certain diagnoses and procedures. Complex surgeries, such as PD, likely necessitate a certain rate of readmission for optimal patient care. Efforts should be focused on identifying modifiable factors that increase the likelihood of readmission. Appropriate patient education is paramount in this process. This is especially true for patients traveling long distances to centers of excellence and do not have easy access to the operating surgeon. Kastenberg et al. pointed out that surgeons must consciously avoid stigmatization of readmission after PD, as some are necessary. This is precisely why surgeons must assume a front-line position regarding these discussions.

Conclusion

Hospital readmission bears the unfortunate and incorrect connotation of poor quality medical care in the view of many policymakers, administrators, and physicians. Despite this incorrect stigmatization, we submit that readmission after major surgery is a necessary component of responsible patient care and thus should occur at some reasonable rate. Neither the appropriate rates of readmission for most surgical procedures nor the modifiable factors associated with readmission have yet to be defined. Despite the lack of data supporting appropriate readmission rates, readmission is being utilized to modify reimbursements for specific diagnoses and procedures. Therefore, it is imperative that surgeons work to

identify appropriate rates of readmission as well as modifiable factors associated with readmission after major surgery. In this meta-analysis, PD for chronic pancreatitis, prolonged operative time, wound infection, intra-abdominal abscess, VTE, and LOS were associated with readmission after PD. However, further evaluation of modifiable factors was limited secondary to inconsistencies in reporting, which must be addressed for future improvements in readmission and accurately defining expected readmission rates.

Conflicts of interest

The authors have no conflicts of interest to disclose.

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