Systematic Review and Meta-Analysis

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Risk factors of the postoperative 30-day readmission of gastric cancer surgery after discharge

A PRISMA-compliant systematic review and meta-analysis

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Abstract

Background: Readmission is a common postoperative adverse event. This study aimed to analyze potential risk factors for the incidence of postoperative 30-day readmission after discharge for gastric cancer patients with surgical treatment.

Methods: Those studies that reported the risk factors of gastric cancer patients who have a postoperative 30-day readmission were identified systematically from the PubMed, Cochrane, and Embase databases through July 2018. A systematic review and meta-analysis was performed to estimate the risk factors of postoperative 30-day readmission after gastric cancer surgery.

Results: Ultimately, 6 studies with 12,586 gastric cancer patients were included in the present study. There were 1473 (11.7%) patients who had postoperative 30-day readmission and 12,586 (88.3%) patients without 30-day postoperative readmission. A greater proportion of the readmission group had cardiovascular comorbidity ($P<.001$), pulmonary comorbidity ($P<.001$), and diabetes mellitus ($P=.020$) than the nonreadmission group. Furthermore, more patients in the readmission group had total gastrectomy ($P<.001$), combined organ resection ($P<.001$) and postoperative complications ($P<.001$) than did patients in the nonreadmission group. Nonhome discharge (odds ratio [OR] 1.580, $P=.002$), diabetes mellitus (OR 1.181, $P=.044$), postoperative complications (OR 2.656, $P=.006$), total gastrectomy (OR 2.242, $P<.001$), and combined organ resection (OR 1.534, $P<.001$) were independent risk factors for postoperative readmission.

Conclusion: Postoperative readmission is influenced by the synthetic action of preparative, intraoperative, and postoperative factors, such as diabetes mellitus, total gastrectomy, combined organ resection, nonhome discharge, and postoperative complications. Extra attention should be paid to those patients with high risk factors during the postoperative follow-up and recovery periods.

Abbreviations: CI = confidence intervals, MD = mean difference, OR = odds ratio, SD = standard deviation.

Keywords: gastric cancer, operation, readmission, risk factors

1. Introduction

Gastric cancer is one of the most common malignant diseases of the digestive systems and has an extremely high incidence rate in East Asian countries.[1,2] In China, gastric cancer is the third leading cause of tumor-related deaths.[3–5] Readmission to the hospital is a common postoperative adverse event for patients who have undergone surgical treatment. Unplanned readmission can significantly increase the cost of Medicare Insurance.[6,7] The reported postoperative 30-day readmission rate of patients who underwent surgical treatment has ranged from 6.8% to 18.2%.[7–10] Different types of operations have different readmission rates; Sivsammye and Kailasam[11] reported that the 30-day readmission rates were 28.0% for esophageal cancer and 27.9% for pancreatic cancer after surgical treatment. The reported 30-day readmission rate of gastric cancer surgery has ranged from 2.7% to 16.5%.[12–17] Additionally, the readmission rate has varied in different time frames; it can rise from 14.4% at 30 days to 45% at 1 year postoperation for gastric cancer patients.[18] Kim et al[19] even reported that the readmission rate of gastric cancer surgery very high in the 30-day (7.5%) period during the 5-year postoperative follow up (13.0%). Therefore, in order to prevent unplanned readmission and its negative consequence, it is necessary to identify risk factors for postoperative readmission.[20–23]

We thus conducted this meta-analysis and systematic review with the intent to explore the potential risk factors for postoperative 30-day readmission of gastric cancer patients after surgical treatment.

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W-WW and WHZ have contributed equally to this work.

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2. Methods

2.1. Search strategy

We searched the Web of Knowledge, PubMed, Embase, and the Cochrane Collaborative Center Register of Controlled Trials database on the 2nd of January 2019 by using the terms "gastric cancer," "gastric carcinoma," "gastric neoplasm," "Thirty Day," "30 day," and "readmission" and strictly restricted search results to titles, abstracts, and keywords. We also searched previously published meta-analyses and systematic reviews. All of those articles were independently screened by 2 authors (W-WW and WHZ) based on the inclusion and exclusion criteria of the study. Because those studies included in this meta-analysis have been published, ethical approval was not needed from ethics committees.

2.2. Study selection

Those studies that reported the risk factors of postoperative 30-day readmission of gastric cancer patients after discharge were included in the present study. There was no limitation regarding open surgery, laparoscopic surgery or robotic surgery, total gastrectomy or subtotal gastrectomy or regarding whether or not patients had received preoperative chemotherapy. Exclusion criteria included following: mixed benign disease of the stomach; patients without gastrectomy; articles in languages other than English; and incomplete data or included duplicated data. For studies with >1 article and with duplicated data, only the article with the most complete data was included for analysis in this study.

2.3. Data extraction and quality assessment

Data from the included studies were independently extracted by 2 authors (WHZ and W-WW). For each study, we recorded the following information: name of the first author, year of publication, country of the study, study design, time period of the study, preoperative treatment strategy, and tumor stage. Further, the following clinicopathological characteristics were also extracted and included in the present study: age, sex, preoperative comorbidity, resection patterns (total gastrectomy or subtotal gastrectomy), resection type (laparoscopic surgery or open surgery), postoperative complications, and length of hospital stay. Patients were divided into a readmission group and a nonreadmission group according to the status of 30-day readmission after discharge.

Quality assessment of the included studies was evaluated by 2 authors (W-WW and WHZ) independently. Retrospective studies were assessed by the Newcastle-Ottawa Scale (NOS).[24] Studies were evaluated with 9 point grades by the Newcastle-Ottawa Scale. Studies with scores <6 were deemed moderate or low-quality studies. Disagreement of quality assessment was resolved by discussion with supervisors (WYZ and TZ).

2.4. Statistical analysis

This study was performed according to the Cochrane guidelines.[25] For studies that only reported the medians and ranges for continuous variables, data were converted to means and standard deviation (SD) by the method reported by Hozo et al.[26] Categorical variables were presented as ratios and analyzed by the Mantel–Haenszel method, and continuous variables were presented mean ± SD and analyzed by the Inverse Variance method. The odds ratio (OR) and mean difference (MD) were used to evaluate dichotomous and continuous data, respectively. Both the OR and MD were reported with 95% confidence intervals (CI). Heterogeneity among studies was assessment by the value of I^2. According to the value of the I^2, studies were assigned to low ($I^2 < 30\%$), moderate (30% to <50%), and considerable heterogeneity ($I^2 \geq 50\%$). A funnel plot was used to present publication bias. A P value <.05 was considered statistically significant in the present study. All of the statistical analysis was performed by STATA software, version 15.0 and Review Manager software, version 5.3 (Cochrane, London, UK).

3. Results

3.1. Characteristics of studies

According to the inclusion and exclusion criteria, there are 6 studies,[12–17] with 12,586 gastric cancer patients included in this meta-analysis. Specifically, 1473 (11.7%) patients had postoperative 30-day readmission (readmission group) and 12,586 (88.3%) patients did not have postoperative 30-day readmission (nonreadmission group). The selection procedures were presented according to the PRISMA flowchart in Fig. 1. General clinicopathological characteristics of those included studies were summarized in Table 1. All of those 6 studies were from 3 countries (United States, Japan, and China) from 2015 to 2018 and included patients who underwent surgical treatment from 1995 to 2017. All of these studies included patients who underwent total gastrectomy or subtotal gastrectomy. The quality of each study was assessed by the Newcastle-Ottawa Scale[24] and ranged from 6 to 8.

3.2. Comorbidity

Status of comorbidity was significantly different between the readmission and nonreadmission groups. A higher proportion of patients accompanied by cardiovascular comorbidity (OR: 2.11; 95% CI 1.44–3.09; $P < .001$), pulmonary comorbidity (OR: 1.34; 95% CI 1.15–1.58; $P < .001$), and diabetes mellitus (OR: 1.30; 95% CI 1.05–1.60; $P = .020$) were found in the readmission group compared with the nonreadmission group (Table 2).

3.3. Intraoperative characteristics

For the intraoperative variables, we analyzed the resection patterns (total gastrectomy or subtotal gastrectomy), resection types (laparoscopic surgery or open surgery), and combined organ resection (with or without) between the readmission and nonreadmission groups. More patients had total gastrectomy (OR 1.26; 95% CI 1.11–1.43, $P < .001$) and combined organ resection (OR 1.72, 95% CI 1.25–2.38; $P < .001$) in the readmission group than in the nonreadmission group. The proportions of laparoscopic surgery and open surgery were comparable between the 2 groups (OR 1.34, 95 CI 0.89–2.01; $P = .160$). Patients with postoperative 30-day readmission had a higher rate of postoperative complication (OR: 2.68; 95% CI: 1.54–4.65; $P < .001$).

3.4. Risk factors of 30-day readmission

Several conditions resulted in the incidence of postoperative readmission. We only included the independent risk factors in the

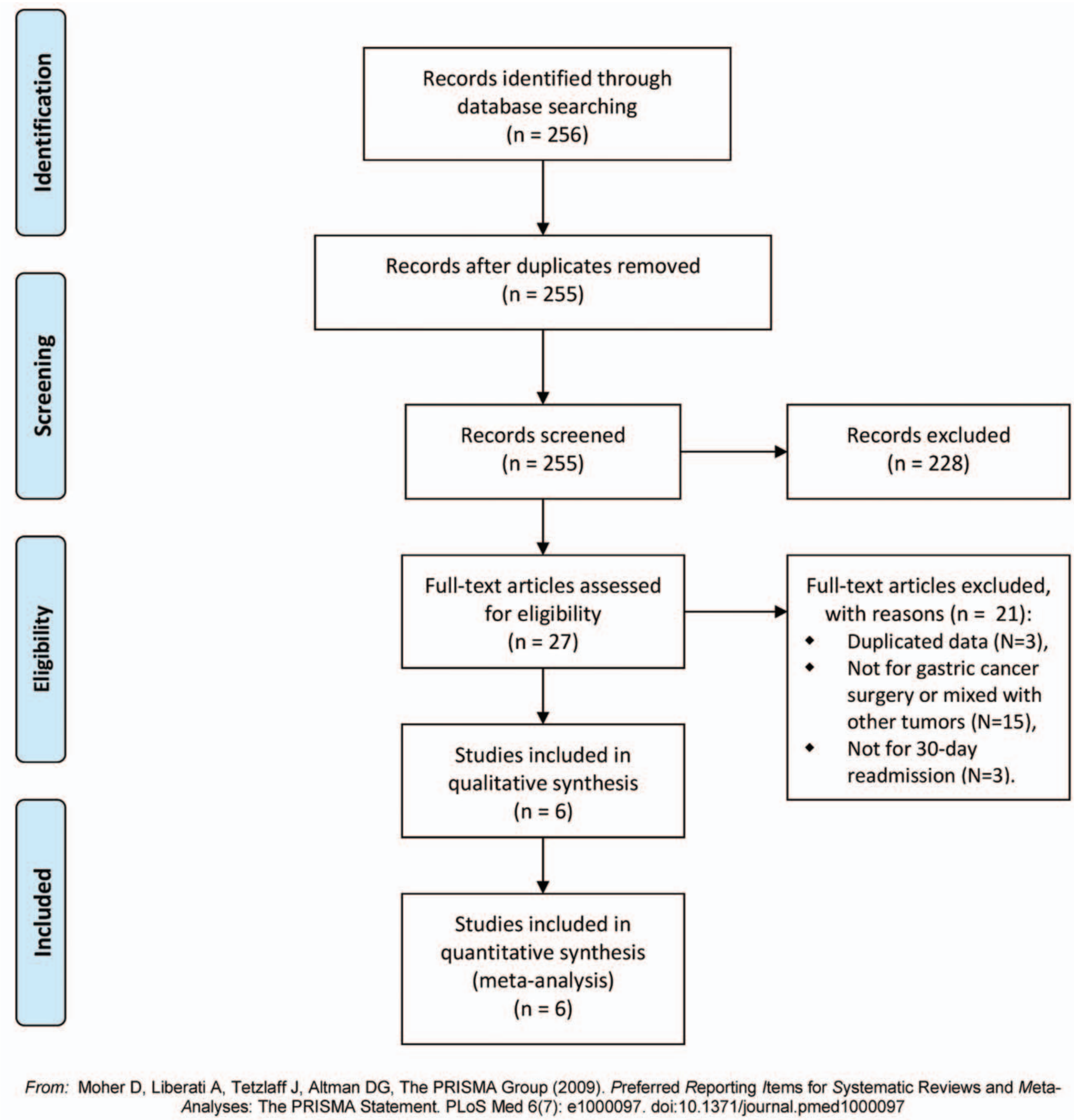

Figure 1. Prisma flow chart of study selection.

pooled analyses. We found that discharge status (OR 1.580, 95% CI 1.069–2.335; $P=.002$), diabetes mellitus (OR 1.181, 95% CI 1.004–1.389, $P=.044$), postoperative complications (OR 2.656, 95% CI 1.331–5.300, $P=.006$), resection pattern (total gastrectomy) (OR 2.242, 1.458–3.446, $P<.001$), and combined organ resection (OR 1.534, 95% 1.231–1.912, $P<.001$) were independent risk factors for postoperative readmission (Table 3). Upon analyzing the relationship between postoperative complications and discharge, there were 5 studies included,[12–14,16,17] and the merged results had high heterogeneity ($I^2=88.2$, $P<.001$). However, we found that the incidence of postoperative complications was positively correlated with readmission in all 5 of the studies,[12–14,16,17] and the results were presented in Fig. 2.

Additionally, it is notable that only 2 studies reported a relationship between the resection type and 30-day readmission. Asaoka et al[15] reported that laparoscopic surgery (OR 2.25; 95% CI: 1.17–4.31; $P=.015$) was an independent risk factor for postoperative readmission, whereas no significant difference (OR 2.039; 95% CI: 0.727–5.722; $P=.168$) was detected in the study performed by Zhuang et al.[17]

3.5. Outcomes of 30-day readmission

However, the total length of hospital stay (days) was comparable between the readmission and nonreadmission patients (MD 3.77; 95% CI –1.41 to 8.96; $P=.150$). We also collected the types of

Table 1

Characteristics of included studies.

Author	Year	Period	Country	Study design	Nonreadmission N= (%)	Readmission N= (%)	Tumor stage	Preoperative chemotherapy	NOS[24]
Acher[12]	2015	2000–2012	United States	Retro-M	734 (85.8)	121 (14.2)	All stage	NM	8
Ahamd[13]	2014	1995–2011	United States	Retro-S	357 (85.4)	61 (14.6)	All stage	Yes	7
Ammori[14]	2018	2005–2011	United States	Retro-S	5833 (83.5)	1152 (16.5)	NM	NM	6
Asaoka[15]	2018	2010–2016	Japan	Retro-S	1877 (97.3)	52 (2.7)	All stage	Yes	6
Xiao[16]	2018	2010–2017	China	Retro-S	1963 (97.0)	60 (2.9)	All stage	Yes	7
Zhuang[17]	2015	2013–2014	China	Prospective	349 (92.8)	27 (7.2)	All stage	NM	7

M=multicenter, NM=no mention, NOS=Newcastle-Ottawa scale[24], S=single.

Table 2

The meta-analysis of clinicopathological characteristics between patients with postoperative 30-day readmission or not.

				Test of heterogeneity			Meta-analysis		
Characteristics	No. of study	Readmission N=	Nonreadmission N=	I^2 (%)	*P* value	Model	OR or MD	(95% CI)	*P* value
Age, y*	3[12,15,16]	1334	6924	52	0.13	Random	2.02	0.73–3.32	.002
Gender (male)	5[12,14–17]	1412	10756	0	0.70	Random	1.15	1.02–1.29	.020
BMI level*	3[12,15,16]	233	4574	75	0.02	Random	0.33	−0.63–1.30	.500
Cardiovascular comorbidity (yes)	3[12,14,15]	1325	8444	68	0.04	Random	2.11	1.44–3.09	<.001
Pulmonary comorbidity (yes)	2[14,15]	1204	7710	0	0.34	Random	1.34	1.15–1.58	<.001
Diabetes mellitus (yes)	2[14,15]	1204	7710	10	0.29	Random	1.30	1.05–1.60	.020
Resection pattern (TG)	4[12,14–16]	1385	10407	0	0.39	Random	1.26	1.11–1.43	<.001
Operation type (laparoscopic)	3[14,15,16]	139	4189	0	0.86	Random	1.34	0.89–2.01	.160
Combined organ resection	4[12,14–16]	1385	10407	40	0.17	Random	1.72	1.25–2.38	.001
Discharge status (non-home)	3[12,14,17]	1300	6916	0	0.76	Random	1.70	1.50–1.92	<.001
Postoperative complications (yes)	4[12,14,16,17]	1360	8879	86	<0.01	Random	2.68	1.54–4.65	<.001
Length of hospital stay, d*	2[12,16]	181	2697	92	<0.01	Random	3.77	−1.41–8.96	.150

95% CI=95% confidence interval, BMI=body mass index, MD=mean difference, OR=odds ratio, TG=total gastrectomy.
* Mean difference (MD) was used to evaluate.

postoperative complications and found that infection-related complications, gastric cancer surgery-specific complications (obstruction and bleeding) and intolerability of oral intake during the recovery period were the major subtypes of postoperative complications (Table 4). Only 2 studies reported long-term survival outcomes,[12,13] and the pooled analysis found that patients in the readmission group had poorer survival outcomes than those in the nonreadmission group (OR: 1.41; 95% CI: 1.12–1.77; $P=.003$) (Fig. 3).

3.6. Publication bias

Because there were only 6 studies included, publication bias was only evaluated by Funnel plots and Begg test. The results demonstrated that there was no publication bias according to Begg test with continuity corrected ($P=.707$). The funnel plot presented by Begg test is shown in Fig. 4.

4. Discussion

Postoperative readmission is a common postoperative adverse event that is closely related with patients' long-term quality of life.[19] The reported postoperative readmission rate is nearly 20% at 30 days postoperation and can rise to 45% at 1-year postoperation.[7–10,18] Due to the different characteristics of different diseases and surgeries, the incidence rate and risk factors for postoperative readmission are various. Generally, physical condition was closely related to the incidence of postoperative readmission. A previous study reported that Eastern Cooperative Oncology Group performance status score and frailty were useful

Table 3

Meta-analysis of risk factors for postoperative 30-day readmission after discharge.

Characteristics	Included study	Heterogeneity chi-squared	I^2	*P* value	OR	95% CI	*P* value
Discharge status (non-home)	3[14,15,17]	3.62	44.8	.163	1.580	1.069–2.335	.022
Diabetes mellitus (yes)	2[14,17]	0.68	0	.409	1.181	1.004–1.389	.044
Cardiovascular comorbidity (yes)	3[12–14]	22.47	91.1	<.001	1.934	0.931–4.016	.077
Postoperative complications (yes)	5[12–14,16,17]	33.9	88.2	<.001	2.656	1.331–5.300	.006
Resection pattern (TG)	3[13,15,17]	0.69	0	.710	2.242	1.458–3.446	<.001
Combined organ resection	3[12,14,16]	1.49	0	.475	1.534	1.231–1.912	<.001

95% CI=confidence interval, OR=odds ratio, TG=total gastrectomy.

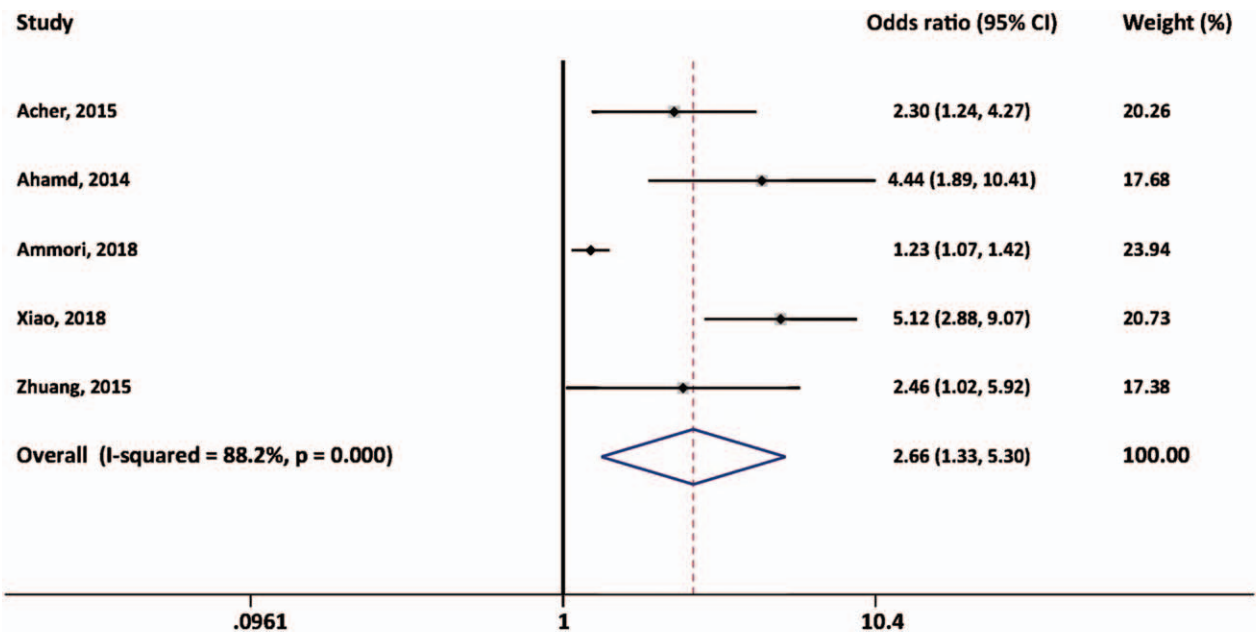

Figure 2. Forest plots showing the postoperative complications as the risk factors for the incidence of readmission.

predictive factors for readmission within 1 year after gastrectomy in older (over 65 years) gastric cancer patients.[27] We performed this study and found that the incidence rate of postoperative 30-day readmission was 11.7% for gastric cancer patients with surgical treatment. This study identified several risk factors for 30-day readmission after gastric cancer surgery. Nonhome discharge, diabetes mellitus, postoperative complications, resection pattern (total gastrectomy), and combined organ resection were independent risk factors for postoperative readmission. We also found that patients with postoperative 30-day readmission had significantly poorer survival outcomes than patients without readmission.

The incidence rate of postoperative readmission for gastric cancer patients was various in a different time frames. The results from the California Cancer Registry database showed that 28.8% patients had postoperative readmission, and the readmission rates were 53.6% in the first 30 days, 30.2% in the second 30 days, and 16.2% in the third 30 days.[28] Readmission in different time periods was caused by different reasons; the postoperative 30-day readmission rate reflected the short-term postoperative recovery process. However, the 90-day readmission rate reflected long-term postoperative complications, adverse events caused by adjuvant chemotherapy or radiotherapy, and some other factors. Therefore, the present study only explores the risk factors of postoperative 30-day readmission.

The incidence rate of postoperative readmission was closely related to the complexity of the operations. In the presented study, the readmission rate at 30 days postgastrectomy was 11.7%. The reported readmission rate was diverse among included studies; the incidence rate was 2.7%, 2.9%, and 7.2% in the 3 studies from East Asia[15–17] but was 14.2%, 14.6%, and 16.5% in the other 3 studies from the United States.[12–14] Reasons for the different readmission rates between these studies are unclear. We believe that the characteristics of patients and postoperative management strategies may be the cause. Different readmission criteria are another important factor that may result in the different readmission rates between the East and the West.

Table 4

Reasons for the postoperative 30-day readmission after discharge.

	Acher, 2015[12]	Ahamd, 2014[13]	Ammori, 2018[14]	Asaoka, 2018[15]	Xiao, 2018[16]	Zhuang, 2015[17]
No. of readmission patients	139	61	1152	52	60	27
Reasons, N= (%)						
Sepsis	1 (0.7)	1 (1.6)	72 (6.3)			
Fever	2 (1.4)	2 (3.3)				2 (7.4)
Intra-abdominal fluid collection		11 (18)			9 (15.0)	3 (11.1)
Leakage or fistula	7 (5)	3 (4.9)		1 (1.9)	4 (6.7)	2 (7.4)
Intra-abdominal abscess	19 (13.7)			15 (28.8)	3 (5)	
Thromboembolic	2 (1.4)	1 (1.6)				
PPCs	7 (5)	2 (3.3)	40 (3.5)		2 (3.3)	2 (7.4)
Obstruction	11 (7.9)	6 (9.8)	52 (4.5)	7 (13.5)	10 (16.7)	1 (3.7)
Intolerable of oral intake	30 (21.6)	13 (21.3)		16 (30.8)	4 (6.7)	5 (18.5)
GI bleed	6 (4.3)	2 (3.3)	36 (3.1)		3 (5)	2 (7.4)

GI = gastrointestinal, PPCs = postoperative pulmonary complications.

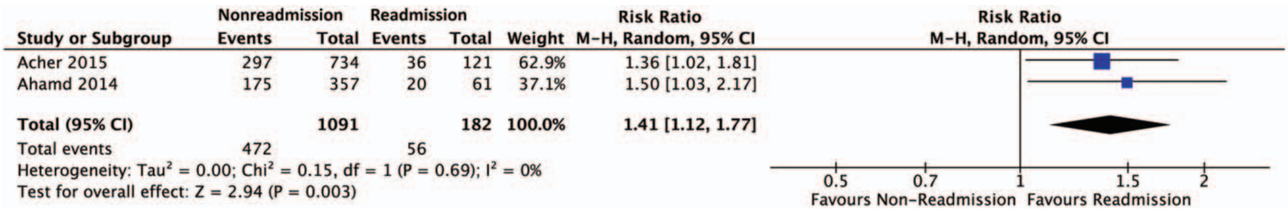

Figure 3. Forest plots showing the overall survival outcomes of meta-analysis compared between readmission and nonreadmission patients.

It is clear that the incidence of postoperative complications is closely related with postoperative readmission after discharge.[10,29,30] Additionally, in the present studies, we found that patients in the readmission group have a higher complications rate than those in the nonreadmission group (OR 2.68, 95% CI 1.54–4.65, $P<.01$), and postoperative complication is an independent risk factor for postoperative readmission after discharge (OR 2.656, 95% 1.331–5.300, $P=.006$). Although the results suggested that postoperative complication was a significant risk factor for the incidence of postoperative 30-day readmission, we also observed that these results had high heterogeneity in the meta-analysis. The high heterogeneity may be because the classifications of complications may be different among studies. Even so, these results have clinical implications for the postoperative management and follow-up period. On one hand, for those patients who have postoperative complications, extra attention should be given during the duration of the follow-up. On the other hand, for patients without postoperative complications during the hospital stay, attention should be paid to those patients who have high risk factors for either postoperative complications or postoperative readmission.

Nevertheless, different diseases have different reasons for postoperative readmission. The study based on the data of the American College of Surgeons National Surgery Quality Improvement Program reported that wound complications (55%) were the major reason for postoperative readmission after lower extremity bypass surgery.[31] In the present study, we found that the intolerability of oral intake was the most common reason for postoperative readmission (up to 30.8%).[12,13,15–17] Postoperative abdominal pain, eating disorders due to fear, gastrointestinal functional disorders, and incomplete obstruction are likely to result from the intolerability of oral intake, which is specific for operations of the esophagus and stomach. We also observed that the diversity of readmission causes was different among studies.

In addition, the general conditions of patients are another risk factor closely related to postoperative 30-day readmission. Comorbid conditions, such as diabetes, cardiovascular, and chronic pulmonary disease, can increase the risk of postoperative discharge.[32–34] These comorbidities increase the incidence risk of postoperative complications, which can result in the incidence of postoperative discharge. Moreover, acute exacerbation of these comorbidities during the postoperative rehabilitation period can also result in postoperative readmission.

Furthermore, whether laparoscopic surgery will increase the likelihood of postoperative 30-day readmission for gastric cancer surgery is unclear. There were several studies that reported that laparoscopic surgery was equally as safe as open surgery.[35,36] The study by Ammori et al[14] reported that laparoscopic surgery is an independent risk factor for 30-day readmission, and they concluded that pancreatic damage and, correspondingly, pancreatic fistula caused by laparoscopic surgery were the major

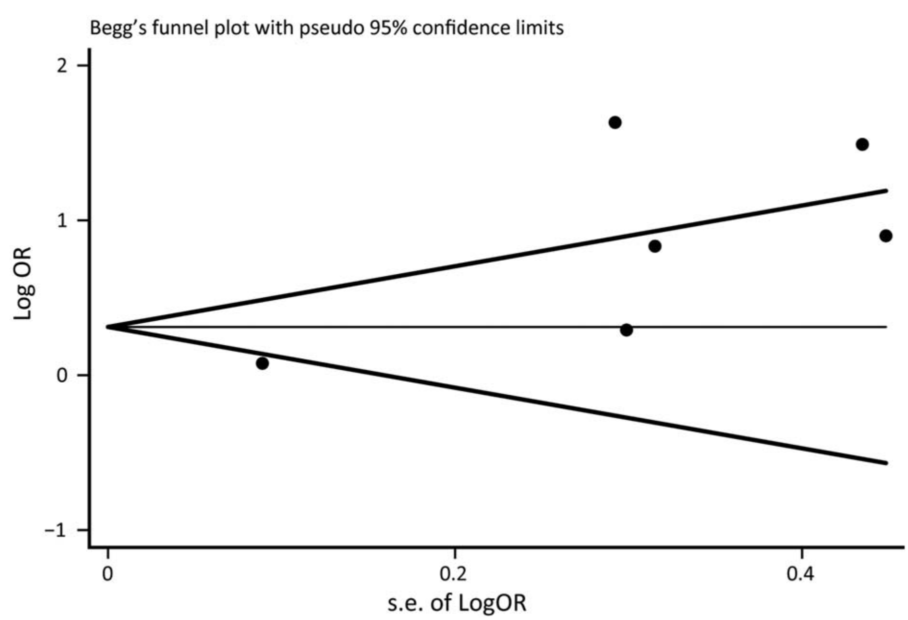

Figure 4. Begg funnel plots of the postoperative readmissions.

reasons for readmission. Additionally, we noticed that the readmission rate presented by a Japanese study was higher in the laparoscopic group than in the open surgery group.[37] Therefore, limited evidence explores the relationship between laparoscopic surgery and 30-day readmission; whether laparoscopic surgery increases the risk of postoperative 30-day readmission requires further investigation. Besides, robotic surgery is being employed with increasing frequency in recent years and it can be performed as safely as laparoscopic and open surgery.[38,39] However, there is no analysis about the relationship between robotic surgery and postoperative readmission of those 6 included studies. Asaoka et al[15] mentioned that they excluded the robotic surgery and the other 5 studies did not mention whether included robotic surgery in the analysis.[12–14,16,17] Besides, there is limited studies compared the postoperative readmission after robotic gastric cancer surgery with laparoscopic or open surgery. A Korean retrospective study reported that there is no difference of postoperative 30-day readmission among open, laparoscopic and total gastrectomy.[40] Therefore, further studies are expected to examine whether robotic surgery has specific risk factors of postoperative readmission.

We also observed that nonhome discharge is an independent risk factor for postoperative readmission in the pooled analysis. Discharge to a nonhome facility appeared to nearly double the risk of readmission, even when adjusting for confounding factors. Patients who are older, who have poor health status or who have postoperative complications were more likely have been discharged to such facilities.[32] Additionally, those facilities have a professional background and have a communication channel with hospital, which may increase the likelihood of readmission. However, those patients discharged to the local hospital or nursing facility may have reduced readmission due to some nonserious complications, such as superficial site infection. Therefore, the relationship between nonhome discharge and readmission may be underestimated and requires further exploration.

We also analyzed the survival outcomes between the readmission patients and nonreadmission patients and found poor survival outcomes for readmission patients. Although only 2 studies reported the overall survival outcomes in the present study,[12,13] the results coincided, and the pooled results lacked significant heterogeneity. We also noticed that there was another study, which was not included in the meta-analysis, that found that readmission (postoperative 90-day) was also closely correlated with poor long-term survival outcomes.[28] We hypothesize that poor survival outcomes of readmission patients may be due to the synthetic action of the poor characteristics of these patients and the delay of postoperative adjuvant therapy.

The present study also has some limitations. First, this study only included 6 studies, most of which were retrospective studies. Therefore, selection bias and quality deviation is likely among these studies, which may have an influence on the results of the meta-analysis. Second, the standard of the postoperative complications was different among included studies. Third, who makes the decision of postoperative readmission and the judgment standard of readmission was also different in the studies. Therefore, it is difficult to determine which complication is the major reason for postoperative readmission.

5. Conclusions

Postoperative readmission is a common postoperative adverse event after discharge and can be influenced by the synthetic action of preparative, intraoperative, and postoperative factors. Although postoperative complications are the major reason for readmission, the comorbidities and operative wounds also affect the incidence of postoperative 30-day readmission. Extra attention should be paid to those patients with high risk factors during the postoperative follow-up and recovery periods.

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