JOURNAL OF SURGICAL RESEARCH 196 (2015) 294–301

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.JournalofSurgicalResearch.com

# Diabetes and risk of anastomotic leakage after gastrointestinal surgery

Xiaoti Lin, MD, PhD,[a,b,c,1] Jingjing Li, MD, PhD,[d,e,1] Weiyu Chen, MD,[f] Fengqin Wei, MD,[g] Mingang Ying, MD, PhD,[c] Weidong Wei, MD, PhD,[a,b] and Xiaoming Xie, MD, PhD[a,b,*]

[a] *Department of Breast Oncology, Sun Yat-Sen University Cancer Center, Guangzhou, China*
[b] *State Key Laboratory of Oncology in South China, Sun Yat-Sen University Cancer Center, Collaborative Innovation Center for Cancer Medicine, Guangzhou, China*
[c] *Department of Surgery, Fujian Provincial Tumor Hospital, Teaching Hospital of Fujian Medical University, Fuzhou, China*
[d] *State Key Laboratory of Ophthalmology, Zhongshan Ophthalmic Center, Sun Yat-Sen University, Guangzhou, China*
[e] *Department of Ophthalmology, Xiangyang Central Hospital, Teaching Hospital of Medical College of Hubei University of Arts and Science, Hubei, China*
[f] *Department of Physiology, Zhongshan School of Medicine, Sun Yat-Sen University, Guangzhou, China*
[g] *Department of Emergency, Fujian Provincial 2nd People's Hospital, Affiliated Hospital of Fujian University of Traditional Chinese Medicine, Fuzhou, China*

ARTICLE INFO

*Article history:*
Received 22 October 2014
Received in revised form
22 February 2015
Accepted 11 March 2015
Available online 19 March 2015

*Keywords:*
Anastomotic leak
Peptic disease
Surgery
Diabetes
Meta-analysis

ABSTRACT

*Background:* Anastomotic leakage (AL) is one of the most common and lethal complications in gastrointestinal surgery. However, the relationship between AL risk and diabetes mellitus (DM) remains ambiguous. This meta-analysis was to evaluate the association between DM and AL risk in patients after gastrointestinal resection.

*Methods:* Odds ratios (OR) estimate with their corresponding 95% confidence intervals (CIs) were combined and weighted to produce pooled OR using the fixed-effects model. Relative risks were calculated in subgroup analysis of prospective studies. We calculated publication bias by Begg rank correlation test and Egger linear regression test.

*Results:* DM was significantly and independently associated with an increased risk of AL morbidity in colorectal patients, 1.661 times in total patients (95% CIs = 1.266–2.178), 1.995 times in a subgroup of case-control studies, 1.581 times in cohort investigations, 1.688 times in retrospective trials, and 1.562 times in prospective designs. After adjusting for the factor of obesity and/or body mass index in the subgroup analyses of colorectal surgery, DM patients without obesity experienced a significantly increased risk of AL (OR = 1.572, 95% CIs = 1.112–2.222). Furthermore, when obesity had not been adjusted, DM patients endured a dramatical increase of AL incidence (OR = 1.812, 95% CIs = 1.171–2.804). Perforation incidence after gastric resection showed borderline association with DM (OR = 2.170, 95% CIs = 0.956–4.926).

* *Corresponding author*. Department of Breast Oncology, Sun Yat-Sen University Cancer Center, 651 East Dong Feng Road, Guangzhou 510060, People's Republic of China. Tel./fax: +86 2061639540.
E-mail address: xiexiaoming001@gmail.com (X. Xie).

[1] X.L. and J.L. contributed equally.

0022-4804/$ – see front matter 
http://dx.doi.org/10.1016/j.jss.2015.03.017

*Conclusions:* The present meta-analysis provides strong evidence for the first time that DM is significantly and independently associated with an increased risk of AL mortality in colorectal surgery.



## 1. Introduction

Anastomotic leakage (AL) is one of the most common and lethal complications after gastrointestinal surgery [1–5]. Morbidity and mortality of AL varied from location to location. The occurrence rate of AL in patients with colorectal resection accounted for 1.2%–14.9% [6–12], and the ensuing mortality amounted to 8.2%–9.3% [7,8]. Reports demonstrated that prevalence rate of AL in stomach surgery occurred from 2.1%–5.6% [13–16]. Fatality rate after gastric leakage accounted for 18.2% [13]. Diabetes mellitus (DM) becomes a global health problem because worldwide prevalence has more than doubled in the past 30 y. Researches had reported that 347 million people suffered from diabetes in 2010, and diabetic patients amounted to 1.3 million deaths in 2008 [17,18]. It has been reported that DM damaged the heart, blood vessels, kidneys, eyes, and nerves [18–21]. However, there have been conflicting reports about the association between DM and AL risk in patients suffering from gastrointestinal surgery. Some investigations showed that DM was not found to be related with AL morbidity after colorectal surgery [3,22–25]. But other trials reported DM increased the incidence of AL [26–28]. Additionally, obesity resulted in a significantly decreased health status and increased technical difficulty and operative time in surgery procedure [10,29]. Several studies reported that morbid obesity enhanced the risk of AL after gastrointestinal operation [22,30–37]. Kayani *et al.* [38] found that obesity did not increase risk of postoperative complications on esophagectomy, but DM patients in conjunction with obesity might lead to increased risk of AL after esophagectomy. Therefore, obesity should be an important confounding factor for this study. Given the controversy of the published articles and the insufficient statistical power of primary studies, our aim was to explore the associations among DM, obesity, and AL risk in patients with gastrointestinal resection.

## 2. Materials and methods

### 2.1. Search strategy

We attempted to follow the meta-analysis of observational studies in epidemiology guidelines to report the present meta-analysis [39]. Two investigators (X.L. and J.L.) independently searched MEDLINE via PubMed, Ovid Online, ISI Web of Science, Scopus, Cochrane Controlled Trials Register database, Wiley, Clinical Evidence, and Clinical Key databases from inception to August 2014. We used the combined terms as follows: either MeSH or title/abstract relating to ("diabetes" or "DM") and ("leak" or "fistula" or "perforation" or "break"), restricting to English. In addition, the authors performed a manual search of the reference lists of retrieved articles and review articles.

### 2.2. Eligibility criteria and exclusion criteria

Studies were considered included if they met the following criteria: (a) they evaluated the association between DM (either type 1 or type 2) and AL risk after gastrointestinal surgery; (b) they were of cross-sectional, cohort, or case-control design; (c) they included healthy subjects without diabetes as controls; (d) reported odds ratio (OR) in case-control/cross-sectional studies or relative risk (RR) in prospective cohort studies and their 95% confidence intervals (CIs) (or data to calculate them); and (e) length of follow-up lasted for at least 2 y (mean or median). Studies all regarded as ineligible are as follows: (a) nonhuman populations, review articles, experimental studies, case reports or studies that lacked controls; (b) to avoid being influenced by unusually high levels of blood sugar, studies of pancreatic diseases, and diseases related to pancreatic resection were excluded; (c) perforation caused by nonsurgical procedures, such as anal fistula, biliary fistula, and so forth.

### 2.3. Data extraction

Data extraction was completed in duplicate and independently by two authors (J.L. and W.C.). A third reviewer (X.L.) independently assessed the study for consensus in the case of disagreement. If there were multiple publications from the same study, we selected the most recent one. A standard data collection form was used when we carried out data extraction. These are the following information extracted from the included studies: journal title, author name, status of obesity or body mass index (BMI), publication year, study design, geographical region of the study, time of follow up, number of participants, mean age, gender, matched or adjusted factors, OR/RR, and their 95% CIs.

### 2.4. Statistical analysis

All statistical analyses were performed with STATA version 12.0 (StataCorp LP, College Station, TX). OR estimated with their corresponding 95% CIs were combined and weighted to produce pooled OR in the fixed-effects model. We assessed heterogeneity using the Q and $I^2$ statistics. For the Q statistic, a $P$ value of $<0.10$ was considered representative of statistically significant heterogeneity; for $I^2$, a value $>50\%$ was considered a measure of severe heterogeneity. Potential publication bias were calculated by Begg rank correlation test and Egger linear regression test. A two-tailed $P$ value of $<0.05$ was considered representative of statistically significant publication bias. Subgroup analysis was further performed. If there was heterogeneity within studies statistically, random-effects model was performed. Otherwise, the fixed-effects model was evaluated for pooling the data. In the present study, all subgroup