Letters

RESEARCH LETTER

Association of Long-term Anastomotic Ulceration After Roux-en-Y Gastric Bypass With Tobacco Smoking

Bariatric surgery is the most effective treatment for obesity, leading to long-term weight loss, improvements in quality of life, and reduction of obesity-associated comorbidities.[1] However, long-term complications are reported. Importantly, concerns about such complications represent a considerable barrier for eligible patients considering surgery.[2] A common long-term postoperative complication for the Roux-en-Y gastric bypass (RYGB) procedure is anastomotic ulceration (AU). Although AU after RYGB is a well-recognized adverse event, its documented incidence varies widely.[3] Additionally, tobacco-smoking has been implicated in the pathogenesis of AU.[4] The aim of this study was to describe the epidemiology of AU after RYGB and measure the association of tobacco smoking with long-term AU incidence.

Methods | The Statewide Planning and Research Cooperative System database of the Department of Health of New York State was used to identify adult patients who underwent laparoscopic or open RYGB for obesity in the state of New York in 2005 through 2010. Patients were followed up for a subsequent hospital-based diagnosis of AU, using *International Classification of Diseases, Ninth Revision* classification codes for gastrojejunal ulcer.

This study was approved by the Stony Brook University institutional review board. Informed consent was not obtained because of the unidentified nature of the data.

Patients who developed AU were compared with patients without AU on measures of demographics and comorbidities present at the time of the initial RYGB procedure. Possible prognostic factors were selected according to the variable importance ranking from 5 cross-validation processes that were repeated 10-fold using logistic regression models to prospectively identify odds of AU. The cumulative incidence is reported with corresponding 95% CIs. The association of tobacco smoking and AU diagnosis was examined through a multivariable Cox proportion hazard model after adjusting for age, sex, and the remaining associated factors (**Table**). Analysis was performed using SAS, version 9.4 (SAS Institute Inc). We regarded a $P < .05$ as indicating statistical significance.

Results | There were 35 075 patients who underwent an RYGB procedure. Their mean (SD) age at the time of surgery was 42.5 (10.9) years; 28 439 (81.1%) were women. The overall cumulative incidence of AU was 3.2% (95% CI, 3.0%-3.4%) after 1 year, 4.7% (95% CI, 4.5%-5.0%) after 2 years, 7.9% (95% CI, 7.6%-8.3%) after 5 years, and 11.4% (95% CI, 10.9%-11.9%) at 8 years after RYGB. Risk factors that were independently associated with AU development were identified (Table); these included history of tobacco use. The observed 5-year incidence ranged from 5.2% (95% CI, 4.4%-5.9%) for patients with 0 or 1 risk factors to 15.9% (95% CI, 13.5%-18.4%) for patients with 5 or more risk factors.

Table. Estimated Hazard Ratios of Risk Factors Associated With Anastomotic Ulceration[a]

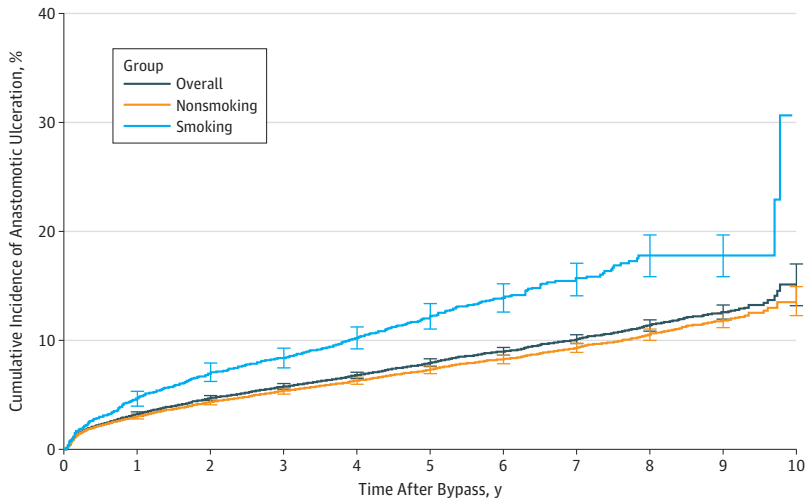
Variable	No. (%) (N = 35 075)	Hazard Ratio (95% CI)	*P* Value
Sex			
Female	28 439 (81.1)	1 [Reference]	.01
Male	6636 (18.9)	1.14 (1.03-1.26)	
Race/ethnicity			
All other race/ethnicities	14 207 (40.5)	1 [Reference]	<.001
White	20 868 (59.5)	0.70 (0.64-0.77)	
Insurance			
Commercial	30 410 (86.7)	1 [Reference]	<.001
Medicaid/Medicare	4276 (12.2)	1.31 (1.17-1.46)	
Other	389 (1.1)	1.44 (1.00-2.07)	
Chronic pulmonary disease			
No	27 734 (79.1)	1 [Reference]	<.001
Yes	7341 (20.9)	1.22 (1.11-1.34)	
Liver disease			
No	31 455 (89.7)	1 [Reference]	.005
Yes	3620 (10.3)	0.82 (0.71-0.94	
Fluid and electrolyte disorders			
No	34 096 (97.2)	1 [Reference]	<.001
Yes	979 (2.8)	1.49 (1.23-1.82)	
Renal failure			
No	34 881 (99.5)	1 [Reference]	<.001
Yes	194 (0.6)	1.87 (1.29-2.71)	
Psychosis			
No	34 509 (98.4)	1 [Reference]	.02
Yes	566 (1.6)	1.35 (1.05-1.74)	
Hypertension			
No	16 848 (48.0)	1 [Reference]	.03
Yes	18 227 (52.0)	1.10 (1.01-1.20)	
Tobacco use			
No	30 606 (87.3)	1 [Reference]	<.001
Yes	4468 (14.6)	1.56 (1.41-1.73)	

[a] *P* values were based on multivariable Cox proportional hazard models.

History of tobacco use was significantly associated with the development of AU (adjusted hazard ratio, 1.56; 95% CI, 1.41-1.73; $P < .001$), with significantly higher cumulative incidence at all points examined (**Figure**). Notably, the estimated 8-year cumulative incidence of AU in patients who used tobacco at the time of surgery was 17.8% (95% CI, 15.9%-19.7%).

Discussion | This study illustrates the significant long-term risk of AU after an RYGB procedure. Although there is a wide

Figure. Estimated Cumulative Incidence of Anastomotic Ulceration After Roux-en-Y Gastric Bypass



No. of patients at risk

Overall	35074	27008	24775	22446	19190	14778	10734	7202	4085	1494	1
Nonsmoking	30606	23559	21652	19644	16869	13102	9648	6568	3786	1413	1
Smoking	4468	3449	3123	2802	2321	1676	1086	634	299	81	0

variation in the previously reported rate of AU,[3] the present study suggests that this complication is commonly identified on longer follow-up. Importantly, longitudinal assessment demonstrates a progressive increase in the cumulative incidence of AU throughout the period examined. This dose-response effect of time on AU incidence is in accordance with previous studies that show lower rate of AU with prolonged preventive therapy.[5]

The effect of tobacco use on AU has been suggested by previous studies, although the exact impact size has been unclear.[4] In this study, 17.8% of patients with a history of tobacco use at the time of RYGB surgery developed AU within 8 years. Given the postbariatric surgery recidivism of substance use, including tobacco, despite perioperative cessation,[6] these findings emphasize the need for proper patient and bariatric procedure selection.

The findings of this study underline that the incidence of AU after RYGB is more common than previously reported and that it progressively increases over time. Despite the limitations of the retrospective design, the lack of bariatric-specific granular data, and the possibility of missing patients with AU who were diagnosed and managed exclusively outside the hospital setting, the long-term effect of tobacco use on this complication is profound. Such information can potentially aid in procedure selection at the time of initial bariatric surgery or guide patient selection for targeted AU preventive and surveillance strategies.

Konstantinos Spaniolas, MD
Jie Yang, PhD
Shelby Crowley, BS
Donglei Yin, MS
Salvatore Docimo, DO
Andrew T. Bates, MD
Aurora D. Pryor, MD

Author Affiliations: Division of Bariatric, Foregut, and Advanced Gastrointestinal Surgery, Department of Surgery, Stony Brook University, Stony Brook, New York (Spaniolas, Crowley, Docimo, Bates, Pryor); Division of Epidemiology and Biostatistics, Department of Family, Population and Preventive Medicine, Stony Brook University, Stony Brook, New York (Yang); Department of Applied Mathematics and Statistics, Stony Brook University, Stony Brook, New York (Yin).

Corresponding Author: Konstantinos Spaniolas, MD, Stony Brook University, HST T19, Room 053, Stony Brook, NY 11794-8191 (konstantinos.spaniolas@stonybrookmedicine.edu).

Accepted for Publication: March 25, 2018.

Published Online: June 20, 2018. doi:10.1001/jamasurg.2018.1616

Author Contributions: Dr Spaniolas had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: Spaniolas, Bates, Pryor.
Acquisition, analysis, or interpretation of data: Spaniolas, Yang, Crowley, Yin, Docimo, Pryor.
Drafting of the manuscript: Spaniolas, Crowley.
Critical revision of the manuscript for important intellectual content: Spaniolas, Yang, Yin, Docimo, Bates, Pryor.
Statistical analysis: Yang, Yin.
Obtained funding: Pryor.
Administrative, technical, or material support: Spaniolas, Crowley, Pryor.
Study supervision: Spaniolas, Yang, Pryor.

Conflict of Interest Disclosures: Dr Pryor reports acting as a speaker for Ethicon, Gore, Medtronic, and Stryker and as a consultant for Merck. Dr Spaniolas reports acting as a consultant for Mallinckrodt and has receiving research support from Merck. Dr Docimo reports acting as a consultant for Boston Scientific. No other disclosures are reported.

Funding/Support: This research was supported internally by the Stony Brook Medicine Department of Surgery.

Role of the Funder/Sponsor: Drs Spaniolas, Docimo, Bates, and Pryor and Ms Crowley are employees of the Stony Brook Medicine Department of Surgery. The funder had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Additional Contributions: We acknowledge the biostatistical consultation and support provided by the Biostatistical Consulting Core and Lizhou Nie, MS, School of Medicine, Stony Brook University, for assistance with some of the statistical analysis for this study. No compensation was provided directly to this individual from the funding source.

1. Maciejewski ML, Arterburn DE, Van Scoyoc L, et al. Bariatric surgery and long-term durability of weight loss. *JAMA Surg*. 2016;151(11):1046-1055.

2. Fung M, Wharton S, Macpherson A, Kuk JL. Receptivity to bariatric surgery in qualified patients. *J Obes*. 2016;2016:5372190.

3. Coblijn UK, Goucham AB, Lagarde SM, Kuiken SD, van Wagensveld BA. Development of ulcer disease after Roux-en-Y gastric bypass, incidence, risk factors, and patient presentation: a systematic review. *Obes Surg*. 2014;24(2):299-309.

4. Coblijn UK, Lagarde SM, de Castro SM, Kuiken SD, van Wagensveld BA. Symptomatic marginal ulcer disease after Roux-en-Y gastric bypass: incidence, risk factors and management. *Obes Surg*. 2015;25(5):805-811.

5. Kang X, Zurita-Macias L, Hong D, Cadeddu M, Anvari M, Gmora S. A comparison of 30-day versus 90-day proton pump inhibitor therapy in prevention of marginal ulcers after laparoscopic Roux-en-Y gastric bypass. *Surg Obes Relat Dis*. 2016;12(5):1003-1007.

6. Conason A, Teixeira J, Hsu CH, Puma L, Knafo D, Geliebter A. Substance use following bariatric weight loss surgery. *JAMA Surg*. 2013;148(2):145-150.