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Morbid obesity but not obesity is associated with increased mortality in patients undergoing endoscopic retrograde cholangiopancreatography: A national cohort study

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Abstract

Background: The relationship between body weight and outcomes of endoscopic retrograde cholangiopancreatography (ERCP) is unclear.

Objectives: This study aimed to investigate the impact of obesity and morbid obesity on mortality and ERCP-related complications in patients who underwent ERCP.

Methods: We conducted a US population-based retrospective cohort study using the Nationwide Readmissions Databases (2013–2014). A total of 159,264 eligible patients who underwent ERCP were identified, of which 137,158 (86.12%) were normal weight, 12,522 (7.86%) were obese, and 9584 (6.02%) were morbidly obese. The primary outcome was in-hospital mortality. The secondary outcomes were the length of stay, total cost, and ERCP-related complications. Multivariate analysis and propensity score (PS) matching analysis were performed. The analysis was repeated in a restricted cohort to eliminate confounders.

Results: Patients with morbid obesity, as compared to normal-weight patients, were associated with a significantly higher in-hospital mortality (hazard ratio [HR]: 5.54; 95% confidence interval [CI]: 1.23–25.04). Obese patients were not associated with significantly different mortality comparing to normal weight (HR: 1.00; 95% CI: 0.14–7.12). Patients with morbid obesity were also found to have an increased length of hospital stay and total cost. The rate of ERCP-related complications was comparable among the three groups except for a higher cholecystitis rate after ERCP in obese patients.

Conclusions: Morbid obesity but not obesity was associated with increased mortality, length of stay, and total cost in patients undergoing ERCP.

KEYWORDS
ERCP, ERCP-related complications, morbid obesity, mortality, obesity

Key summary

Established knowledge on this subject

1. Obesity is a prevalent phenomenon.
2. The impact of obesity and morbid obesity on mortality in patients undergoing ERCP remains unclear.

Significant and/or new findings of this study?

1. Morbid obesity but not obesity was associated with increased mortality in patients undergoing ERCP.

INTRODUCTION

Endoscopic retrograde cholangiopancreatography (ERCP) has become a fundamental tool in diagnosing and treating pancreatic and biliary disease since its introduction in 1968. There were approximately 169,510 ERCPs performed in the United States in 2013.[1] It is a complex and technically demanding procedure with potential complications, including post-ERCP pancreatitis (PEP), ERCP-associated hemorrhage, perforation, and cholecystitis after ERCP.

Obesity is a contemporary phenomenon. In 2016, the World Health Organization (WHO) reported that 39% of adults aged 18 years and over were overweight, and 13% were obese. Both the WHO and CDC population obesity estimates are on the rise. This trend could potentially impact public health and the economy, given that obesity raises the risk of debilitating morbidity and mortality.[2] In 1999, the observation of an "obesity paradox" began appearing in the medical literature. Some investigators noticed that those with higher BMIs appeared to have lower mortality rates than leaner individuals across various acute and chronic diseases, including heart failure, chronic kidney disease (CKD), type 2 diabetes, and sepsis. Critics of the obesity paradox argue that the association with survival is due to a combination of intractable confounding by smoking and reverse causation since many of the patients included in these studies have chronic wasting conditions such as CKD in which patients tend to lose weight as their disease progresses.[3,4]

Although the obesity paradox has been debunked in some chronic illnesses and all-cause mortality, the relationship between BMI and mortality or ERCP-related complications of patients undergoing ERCP remains unclear and contradictory. There are some potential hypotheses about how obesity affects patients undergoing ERCP. Adiponectin, one kind of adipokine secreted by adipose tissue, has an anti-inflammatory effect by inhibiting proinflammatory signaling and NF-κB.[5,6] Adiponectin plays a protective role in experimental acute pancreatitis; however, its plasma concentrations in obese subjects were lower than those in nonobese subjects.[7,8] This may lead to a higher rate or a more severe form of PEP in obesity.

One retrospective study by Cotton et al.[9] suggested that obesity was associated with a higher rate of severe and fatal ERCP outcomes; however, this conclusion was limited by its unclear definition of obesity and the small number of fatal cases. Coelho-Prabhu et al.[10] found that BMI ≥35 is a risk factor for post-ERCP complications. A retrospective study, including 583 patients, revealed a significantly higher PEP rate in obesity and a lower rate in normal weight.[11] However, another study, including 2235 patients, indicated that neither obesity nor low body weight increased PEP's incidence or severity.[12]

This study aimed to investigate the effect of obesity and morbid obesity in patients undergoing ERCP by performing a three-way PS-matching analysis on both the full cohort and again on a restricted cohort that excluded smokers, alcoholics, and patients with chronic illness to avoid reverse causation.

MATERIAL AND METHODS

Population

Data for this analysis were obtained from the Nationwide Readmissions Databases (NRD) over 2 years (2013–2014). It is a nationally representative database developed and validated through a federal–state–industry partnership sponsored by the Agency for Healthcare Research and Quality (AHRQ). The NRD (2013–2014) includes approximately 14–15 million discharges each year, containing admission data from hospitals in 21–22 states and accounting for 49.1%–49.3% of all US hospitalizations.[13,14] This database allows a national assessment of hospital inpatient stays and readmissions among patients with all types of payers.[15] This study was considered an institutional review board exempt as it involved analysis of deidentified, publicly available datasets.

Study cohort and identification of patients undergoing ERCP

Patients who underwent ERCP were identified by using ICD-9 CM procedure codes for either diagnostic or therapeutic ERCP. Exclusion criteria included missing value for death or sex, uncertain disposition (e.g., left against medical advice, transfer to a short-term hospital), age less than 20, and underweight. Patients were further excluded if they had previous liver or pancreas transplant, pancreatobiliary and liver neoplasms, hepatobiliary or pancreatic surgery during the same admission, or altered anatomy.

Classifying BMI

Using ICD-9 codes of BMI to identify patients in different weight groups from NRD or National inpatient samples were validated in the previous studies.[4,16] The NRD includes specific International Classification of Diseases—9th Revision (ICD-9) codes (V85.XX) for BMI in cases where such measures were obtained during hospital admission. The National Institute of Health's classification of underweight (<18.5 kg/m^2), normal weight ($18.5 \leq 25.0$ kg/m^2), overweight ($25.0 \leq 30.0$ kg/m^2), and obese (>30.0 kg/m^2) was adopted. Morbid obesity was identified if BMI >40.0 kg/m^2 or with an ICD 9 code of morbid obesity.

Outcome measures

The associations between BMI categories and in-hospital all-cause mortality, hospital length of stay, and total cost among patients who underwent ERCP were examined. The rate of ERCP-related complications, including PEP, ERCP-associated hemorrhage, perforation, and cholecystitis after ERCP in different BMI categories, were calculated and compared. This study adopted previously defined definitions for these complications that have been validated before[17,18] (Appendix 1). Cardiopulmonary events and a few high-mortality complications, including septic shock, myocardial infarction, cardiac arrest, aspiration pneumonia, and mechanical ventilation requirement, which occurred during the same admission, were also compared in three groups.

Other covariates

To account for comorbidities that may contribute to the risk of mortality, the comorbidities defined by the Charlson Comorbidity Index were used as covariates. Other covariates used in the analysis included: age, gender, and residential income. Residential income was categorized into quartiles ranging from the lowest income to the highest income based on median household income at the zip code level.

Statistical analysis

Analysis of survey data was conducted following recommendations from the AHRQ. For example, we obtained descriptive statistics by using survey-specific statements, SURVEYMEANS. Continuous variables with normal distribution were presented as mean (standard error [SE]), and nonnormal variables were reported as median (interquartile range [IQR]). Categorical variables were reported as the percentage (%).

Given the variations in clinical characteristics among the three groups, we created a propensity score for adjustment and matching. The PS was defined as the conditional probability of morbid obesity or obesity compared to normal weight for patients undergoing ERCP. The PS was created from a multinomial logistic regression model, which included 20 potential predictors. We then performed a three-way (1:1:1) PS matching using the triad optimized nearest-neighbor matching algorithm developed by Rassen et al.[19] Each triad was selected using a distance function defined by the perimeter of a triangle with the maximum allowable propensity-score distance between patients set at 0.05. The success of matching was shown by a standardized difference graph (Figure 1). A standardized difference of less than 10% was viewed as matching success. We compared the in-hospital mortality, length of hospital stay, hospitalization cost, and ERCP-related complications in the three groups of patients before and after PS matching. Three group univariate comparisons were made with the Kruskal–Wallis test for continuous variables and the χ^2 test for categorical variables. Post-hoc tests were conducted using the Mann–Whitney *U* test for continuous variables and χ^2 test for categorical variables. To calculate the relative risk of mortality between obesity versus normal weight and morbidity obesity versus normal weight, we performed an unconditional logistic regression adjusting for PS in the full cohort and conditional logistic regression stratified by matching pairs in the PS-matched cohort.

The analysis mentioned above was repeated in a restricted cohort to avoid the potential bias of reverse causation and confounding. Therefore, the restricted cohort was created by excluding smokers, alcoholics, or patients with any of the chronic disease defined by the Charlson Comorbidity Index. All analyses and plots were conducted using SAS 9.4 for Windows (SAS Institute, Inc.). A *p* value of less than 0.05 was considered statistically significant.

RESULTS

Cohort assembly and baseline characteristics

During the study period, 159,264 eligible patients who underwent ERCP were identified, of which 137,158 (86.12%) were normal weight, 12,522 (7.86%) were obese, and 9584 (6.02%) were morbidly obese. The flow of the cohort assembling process is shown in Figure 2 Compared to normal-weight patients, patients with obesity or morbid obesity were more likely to be younger, females, in low-income quartile, hospitalized in rural or urban nonteaching hospitals, and to have hypertension, chronic pulmonary disease, congestive heart failure, diabetes, liver disease, pulmonary circulation disease, psychoses, depression, higher Charlson Comorbidity Index, and a higher transfer rate (Table 1). However, patients with obesity or morbid obesity were less likely to have malignancy. Patients with normal weight had a higher percentage of purely diagnostic ERCP (12.44% vs. 10.37% vs. 10.90%, $p < 0.001$).

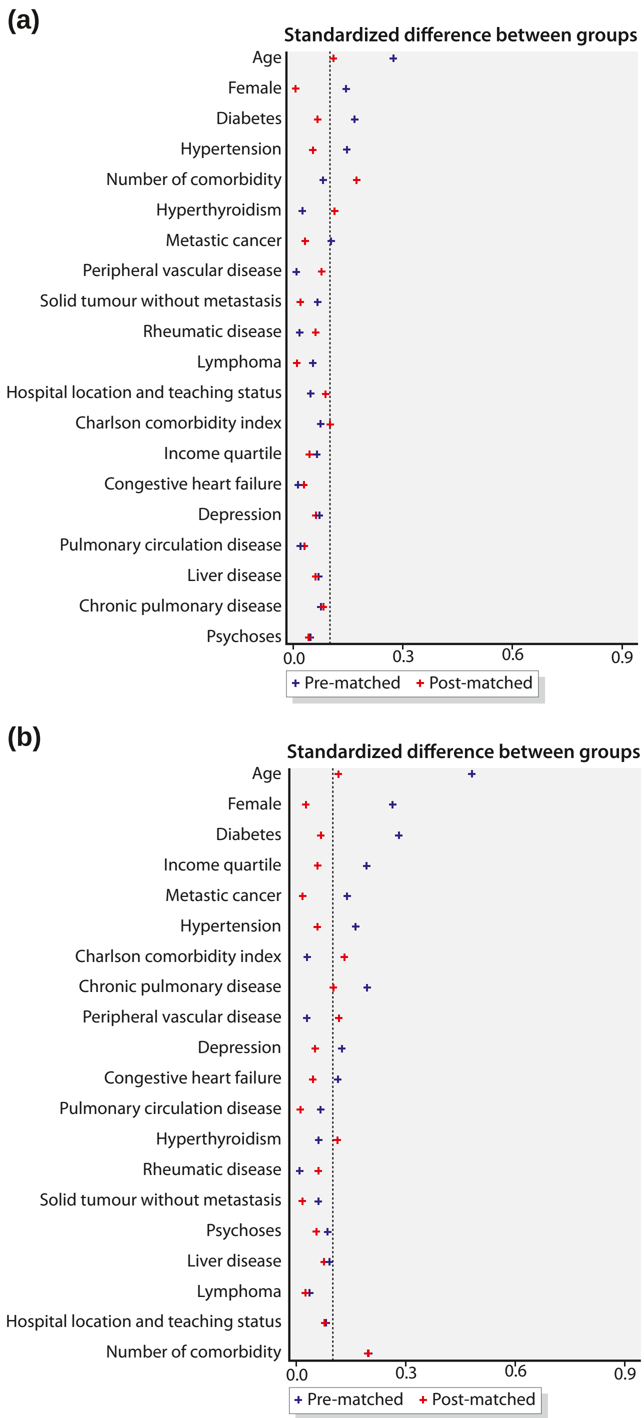

FIGURE 1 Standardized difference graph before and after PS-matching. (A) Obesity versus normal weight. (B) Morbid obesity versus normal weight

In-hospital all-cause mortality

In the full cohort, in comparison to the normal-weight group, in-hospital mortality was lower in the obese group with a hazard ratio of 0.67 (95% confidence interval [CI]: 0.48–0.93) and higher in the morbidly obese group with a hazard ratio of 1.54 (95% CI: 1.16–2.06) (Tables 2 and 3). When PS matching was applied to the full cohort, 3836 patients were matched among the three groups (Table 2). The obese group did not show significantly different mortality than normal weight (0.94% vs. 1.09%) with a hazard ratio of 0.86 (95%CI: 0.55-1.34). Morbid obesity was still associated with significantly higher mortality than normal weight (2.01% vs. 1.09%) with a hazard ratio of 1.83 (95% CI: 1.26-2.71).

When a restricted analysis was applied to the full cohort, in-hospital mortality dropped consistently among all three groups (Table 4). Compared with normal weight, morbid obesity was associated with higher mortality, while obesity did not significantly affect mortality. This finding was confirmed by applying PS matching. Morbid obesity was associated with significantly higher mortality in comparison to normal weight (0.86% vs. 0.16%) (Table 4) with a hazard ratio of 5.54 (95% CI: 1.23–25.04) (Table 3). No survival benefit was observed in the obese group (0.16% vs. 0.16%) with a hazard ratio of 1.00 (95% CI: 0.14–7.12).

Length of stay and total cost

In the full cohort, by conducting PS-matching analysis, a significantly increased length of hospital stay ($p < 0.001$) and total cost ($p < 0.001$) in patients with morbid obesity were observed (Table 2). In the restricted PS-matching cohort (Table 4), the difference in length of hospital stay ($p = 0.001$) and total cost ($p < 0.001$) in morbid obesity remained significant. Obesity was not found to have an impact on the length of stay in both cohorts. It was associated with a higher total cost in the PS-matching full cohort, which was not significant in the restricted cohort.

ERCP-related complications

The rates of post-ERCP pancreatitis, ERCP-associated hemorrhage, perforation, and cholecystitis after ERCP were not significantly different among the three groups in the full cohort (Table 5). After applying PS matching, the above findings remained similar, except for a considerably higher cholecystitis rate after ERCP in patients with obesity ($p = 0.018$). However, patients who were morbidly obese showed an increased rate of developing cardiopulmonary events during the same admission in both full cohorts (2.43% vs. 1.24%, $p < 0.001$) and PS-matched cohort (2.40% vs. 1.07, $p < 0.001$).

Common high-mortality complications

In the PS-matched full cohort, patients with morbid obesity had a significantly higher prevalence of septic shock (5.21% vs. 2.50%, $p < 0.001$), cardiac arrest (0.50% vs. 0.29%, $p = 0.080$), aspiration

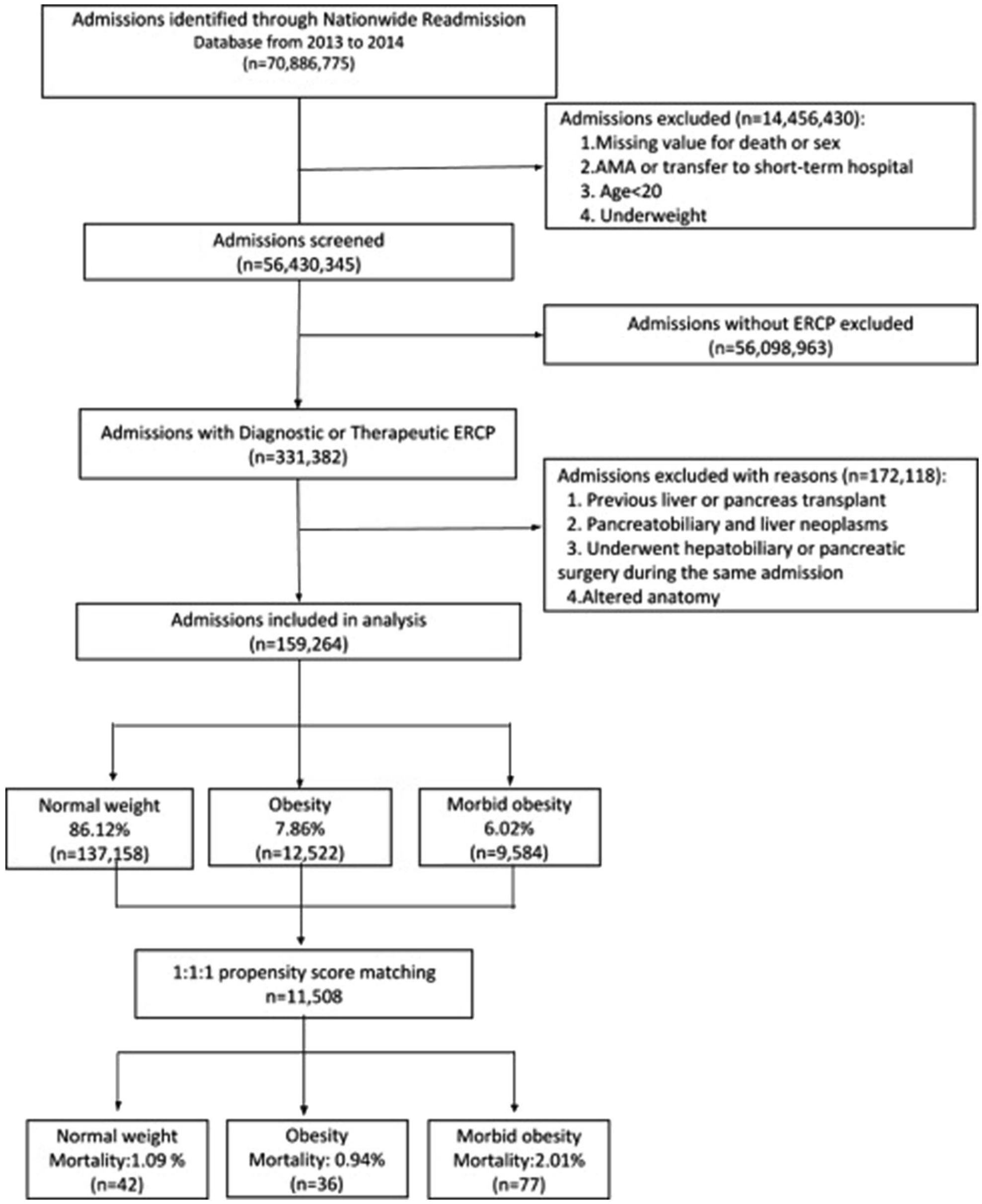

FIGURE 2 Flowchart of patient inclusion

pneumonia (1.28% vs. 0.78%, $p = 0.043$), and mechanical ventilation needs (5.76% vs. 2.29%, $p < 0.001$) (Table 6).

Mortality in patients without ERCP

Additional analysis to compare patients undergoing ERCP versus those who did not undergo ERCP was performed to understand ERCP's role in obesity and morbid obesity. Patients with a diagnosis of common indications for ERCP were selected from NRD, including choledocholithiasis, cholangitis, obstruction or stricture of the bile duct, acute biliary pancreatitis, and jaundice. ERCP was found to be associated with significantly lower mortality in patients with obesity [0.57% versus 4.21%, crude OR 0.13 (0.10–0.18)] and morbid obesity [1.25% versus 4.21%, crude OR 0.13 (0.10–0.18)].

DISCUSSION

This study is the first nationwide study regarding the impact of BMI on hospitalized patients undergoing ERCP. We found that patients with morbid obesity were associated with an increased risk of mortality, a longer length of stay, and higher medical costs. Obesity showed a survival benefit compared to normal weight in the full cohort. However, this phenomenon was not significant after applying the restricted analysis and PS matching, which supports the critics of

TABLE 1 Comparison of hospitalization for ERCP across patients with normal weight, obesity, and morbid obesity

	Normal weight $N = 137,158$	Obesity $N = 12,522$	Morbid obesity $N = 9584$	p
Demographics				
Gender male (%)	57,397 (41.85%)	4495 (35.90%)	2882 (30.07%)	<0.001
Age (mean ± SE)	62.89 ± 0.19	57.94 ± 0.29	53.86 ± 0.35	<0.001
Hospital location and teaching status				
Rural	6031 (4.40%)	642 (5.12%)	581 (6.07%)	<0.001
Urban non-teaching	39,864 (29.06%)	3750 (29.95%)	2880 (30.05%)	
Urban teaching	91,262 (66.54%)	8131 (64.93%)	6122 (63.88%)	
Income quartile, USD				
Quartile 1 (poorest)	33,068 (24.48%)	3119 (25.33%)	2720 (28.86%)	<0.001
Quartile 2	36,903 (27.32%)	3583 (29.10%)	3025 (32.10%)	
Quartile 3	33,968 (25.15%)	3115 (25.30%)	2182 (23.15%)	
Quartile 4 (wealthiest)	31,143 (23.05%)	2495 (20.26%)	1497 (15.88%)	
Comorbidity				
Hypertension	74,563 (54.36%)	7788 (62.19%)	6017 (62.78%)	<0.001
Chronic pulmonary disease	21,362 (15.57%)	2363 (18.87%)	2225 (23.22%)	<0.001
Congestive heart failure	11,538 (8.41%)	995.76 (7.95%)	1140 (11.89%)	<0.001
Hypothyroidism	17,511 (12.77%)	1725 (13.78%)	1406 (14.67%)	0.001
Peripheral vascular disease	7747 (5.65%)	656.94 (5.25%)	448.37 (4.68%)	0.029
Diabetes	26,109 (19.04%)	3416 (27.28%)	3052 (31.84%)	<0.001
Liver disease	6099 (4.45%)	732.92 (5.85%)	664.28 (6.93%)	<0.001
Pulmonary circulation disease	3057 (2.23%)	310.52 (2.48%)	349.93 (3.65%)	<0.001
Metastatic cancer	4513 (3.29%)	206.72 (1.65%)	126.08 (1.32%)	<0.001
Solid tumor without metastasis	2098 (1.53%)	94.08 (0.75%)	77.92 (0.81%)	<0.001
Lymphoma	1185 (0.86%)	53.56 (0.43%)	43.31 (0.45%)	<0.001
Rheumatic disease	3646 (2.66%)	312.44 (2.50%)	257.36 (2.69%)	0.836
Psychoses	4773 (3.48%)	509.8 (4.07%)	496.29 (5.18%)	<0.001
Depression	15,537 (11.33%)	1729 (13.81%)	1519 (15.85%)	<0.001
Number of comorbidity (median, IQR)	1.70 (0.50, 3.07)	1.86 (0.68,3.25)	2.10 (0.78,3.62)	<0.001
Charlson Comorbidity Index	1.49 ± 0.02	1.34 ± 0.03	1.55 ± 0.04	<0.001
Transfer	7411 (5.40%)	898 (7.17%)	818 (8.53%)	<0.001
ERCP interventions				
Purely diagnostic ERCP only	17,062 (12.44%)	1299 (10.37%)	1045 (10.90%)	<0.001
Therapeutic ERCP	120,098 (87.56%)	11224 (89.63%)	8539 (89.10%)	0.001

Abbreviation: IQR, interquartile range.

the obesity paradox that the survival benefit in obese patients is due to confounding factors and reverse causation.

The mortality in the PS-matched full cohort was 1.09% and 0.94% in normal weight and obesity groups respectively, which was comparable to the 1% mortality rate in a prospective study done by Christensen et al.[20] There was significantly higher mortality in patients with morbid obesity in our study. This finding was consistent with a retrospective study with 11,497 procedures, which showed obesity was associated with a higher rate of severe and fatal outcomes.[9]

The overall rates of ERCP-related complications for PEP, hemorrhage, perforation, and cholecystitis in our study were similar

TABLE 2 Comparison of in-hospital outcomes of patients underwent ERCP among three groups of patients in the full cohort

Full cohort	(A) Normal weight N = 137,158	(B) Obesity N = 12,522	(C) Morbid obesity N = 9584	*p*	Significant comparison
In-hospital mortality, no. (%)	2490 (1.82%)	113.77 (0.91%)	199.51 (2.08%)	<0.001	B Versus A
Length of hospital stay, days (mean ± SE)	6.20 ± 0.06	5.83 ± 0.10	6.95 ± 0.16	<0.001	B Versus A, C versus A
Total cost, median (IQR), USD	10,890.00 (7640.8, 16537.0)	10,786.00 (7602.1, 16176.0)	11538.00 (7978.8, 18188.0)	<0.001	C Versus A
Cost per day, median (IQR), USD	2597.08 (1960.7, 3538.6)	2577.52 (1953.9, 3488.7)	2561.87 (1961.5, 3451.9)	0.112	None
PS-matched cohort	Normal weight *N* = 3836	Obesity *N* = 3836	Morbid obesity *N* = 3836	*p*-value	Significant comparison
In-hospital mortality, no. (%)	42 (1.09%)	36 (0.94%)	77 (2.01%)	<0.001	C Versus A
Length of hospital stay, days (mean ± SE)	6.00 ± 0.11	5.86 ± 0.10	6.87 ± 0.14	<0.001	C Versus A
Total cost, median (IQR), USD	10522.64 (7420.3, 15903.7)	10786.59 (7666.3, 16321.0)	11646.15 (8057.3, 18615.2)	<0.001	B Versus A, C versus A
Cost per day, median (IQR), USD	2577.27 (1941.1, 3577.0)	2582.48 (1979.4, 3511.4)	2597.35 (1953.8, 3515.8)	0.996	None

Abbreviations: IQR, interquartile range; PS, propensity score; USD, United States Dollar.

TABLE 3 The association between weight and in-hospital mortality in patients underwent ERCP using normal weight as reference

Mortality	Crude OR (95% confidence interval)	Confounder adjusted OR (95% confidence interval)	PS-matched OR (95% confidence interval)
Full cohort			
Obesity	0.5 (0.36–0.69)***	0.67 (0.48, 0.93)*	0.86 (0.55, 1.34)
Morbid obesity	1.15 (0.88–1.51)	1.54 (1.16, 2.06)**	1.85 (1.26, 2.71)***
Restricted cohort			
Obesity	0.32 (0.11–0.93)*	0.56 (0.19, 1.63)	1.00 (0.14, 7.12)
Morbid obesity	2.00 (1.03–3.88)*	5.18 (2.72, 9.84)***	5.54 (1.23, 25.04)**

Note: Patients with normal weight as the reference group.
Abbreviations: HR, hazard ratio; PS, propensity score.
*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$.

compared to previously reported complications of ERCP rate of 1.6%–15.7%, 1.2%–1.5%, 0.1%–0.6%, and 0.2%–0.5%.[21] There is no significant difference between each complication among the three BMI categories except for a higher cholecystitis rate after ERCP in patients with obesity. While a study by Fujisawa et al.,[11] which retrospectively reviewed 583 patients undergoing therapeutic ERCP with 31 cases of PEP, found that there was a 30% PEP rate in obesity, and the rate was lower in normal weight (3%, $p < 0.001$). However, their study was limited by the small patient population, and the ERCPs they included were all therapeutic, which was different from our study. In a retrospective study by Deenadayalu et al.[22] with 964 patients undergoing diagnostic or therapeutic ERCP, obesity did not seem to confer an increased risk for PEP. There was no significant association between obesity and the severity of PEP.

Our results indicated that patients with morbid obesity undergoing ERCP had increased mortality while the four ERCP-related complications were comparable with normal-weight patients. However, a significantly higher rate of cardiopulmonary events during the same admission was found in morbidly obese patients, explaining the higher mortality in this group. This study was not able to be used to infer the association of the cardiopulmonary events and ERCP, but it is known that they are related. A systematic survey, including 16,855 patients undergoing ERCP, reported that 1.33% of the patients developed cardiopulmonary complications from ERCP, leading to a 0.07% mortality rate directly.[23] Higher BMI was associated with an increased frequency of sedation-related complications, mainly pulmonary events, including apnea, oxygen desaturation, and airway obstructions in advanced endoscopic procedures.[24] To further clarify

TABLE 4 Comparison of in-hospital outcomes in the patients underwent ERCP before and after three-way propensity score matching in the restricted cohort excluding patients with tobacco smoking, alcoholism, or Charlson score ≥ 1

Restrictive cohort[a]	Normal weight N = 52,105	Obesity N = 4486	Morbid obesity N = 3098	p	Significant comparison
In-hospital mortality y, no. (%)	265.75 (0.51%)	7.39 (0.16%)	31.39 (1.01%)	0.007	B Versus A, C versus A
Length of hospital stay, days (mean ± SE)	4.89 ± 0.06	5.00 ± 0.15	5.57 ± 0.23	0.007	C Versus A
Total cost, median (IQR), USD	9387.33 (6814.1, 13459.0)	9706.93 (7061.0, 14116.0)	10049.00 (7213.5, 14129.0)	0.005	C Versus A
Cost per day, median (IQR), USD	2665.5 (2000.3, 3663.9)	2654.05 (1989.5, 3560.0)	2600.65 (1970.9, 3458.7)	0.061	None
PS-matched cohort	Normal weight N = 1273	Obesity N = 1273	Morbid obesity N = 1273	p	Significant comparison
In-hospital mortality y, no. (%)	2 (0.16%)	2 (0.16%)	11 (0.86%)	0.004	C Versus A
Length of hospital stay, days (mean ± SE)	4.57 ± 0.15	4.78 ± 0.19	5.44 ± 0.18	0.001	C Versus A
Total cost, median (IQR), USD	9146.09 (6685.1, 12,801.6)	9391.16 (6855.2, 13,610.4)	10149.50 (7265.5, 14,412.7)	<0.001	C Versus A
Cost per day, median (IQR), USD	2663.48 (2003.8, 3759.3)	2709.11 (2054.9, 3576.1)	2632.33 (1963.8, 3485.4)	0.202	None

Abbreviations: IQR, interquartile range; PS, propensity score; USD, United States Dollar.

[a]Excluding patients with tobacco smoking, alcoholism, or Charlson score ≥ 1.

TABLE 5 Comparison of ERCP related outcomes among three groups of patients in the full cohort

Full Cohort	(A) Normal weight, N = 137,158	(B) Obese, N = 12,522	(C) Morbid obese, N = 9584	p	Significant comparison
Post-ERCP pancreatitis	3604 (2.63%)	389 (3.11%)	227 (2.37%)	0.118	None
ERCP-associated hemorrhage	1711 (1.25%)	134 (1.07%)	87 (0.91%)	0.166	None
Perforation	361.39 (0.26%)	27 (0.22%)	23 (0.24%)	0.812	None
Cholecystitis after ERCP	1080 (0.79%)	127 (1.02%)	88 (0.91%)	0.283	None
Pulmonary or cardiovascular	1701 (1.24%)	191.17 (1.53%)	233.36 (2.43%)	<0.001	C Versus A
PS-matched cohort	Normal weight, N = 3836	Obese, N = 3836	Morbid obese, N = 3836	p	Significant comparison
Post-ERCP pancreatitis	112 (2.92%)	120 (3.13%)	88 (2.29%)	0.069	None
ERCP-associated hemorrhage	41 (1.07%)	38 (0.99%)	33 (0.86%)	0.643	None
Perforation	5 (0.13%)	9 (0.23%)	10 (0.26%)	0.416	None
Cholecystitis after ERCP	22(0.57%)	44 (1.15%)	29 (0.76%)	0.018	B Versus A
Pulmonary or cardiovascular	41 (1.07%)	55 (1.43%)	92 (2.40%)	<0.001	C Versus A

Abbreviations: PS, propensity score.

the causes of death, some common high-mortality complications were compared among the three groups. Patients with morbid obesity were found to have a significantly higher prevalence of septic shock, cardiac arrest, aspiration pneumonia, and mechanical ventilation needs. Though they might not be directly associated with ERCP, those complications are likely to cause high mortality in the morbid obesity group.

ERCP was associated with significantly lower mortality in both obese and morbid obesity patients admitted with ERCP indications, as shown in our study. But the increased risk of ERCP in morbid obesity urges providers to consider the use of ERCP in this population carefully. Magnetic resonance cholangiopancreatography or endoscopic ultrasound should be considered first if the ERCP is not a definitive option. The risk should be discussed with the patient or family before

TABLE 6 Comparison of common high-mortality complications among three groups of patients in the full cohort

Full cohort	Normal weight N = 137,158	Obesity N = 12,522	Morbid obesity N = 9584	p	Significant comparison
Septic shock	4794 (3.50%)	325 (2.59%)	501 (5.23%)	<0.001	All
Myocardial infarction	1662 (1.21%)	114 (0.91%)	117 (1.22%)	0.244	None
Cardiac arrest	554 (0.40%)	17 (0.14%)	67 (0.70%)	<0.001	All
Aspiration pneumonia	1598 (1.17%)	89 (0.71%)	116 (1.21%)	0.015	C Versus B, B versus A
Required mechanical ventilation	3825 (2.79%)	349 (2.79%)	583 (6.08%)	<0.001	C Versus B, C versus A
PS-matched cohort	Normal Weight N = 3836	Obesity N = 3836	Morbid obesity N = 3836	p-value	Significant comparison
Septic shock	96 (2.50%)	91 (2.37%)	200 (5.21%)	<0.001	C Versus B, C versus A
Myocardial infarction	35 (0.91%)	36 (0.94%)	48 (1.25%)	0.268	None
Cardiac arrest	11 (0.29%)	8 (0.21%)	19 (0.50%)	0.080	C Versus B
Aspiration pneumonia	30 (0.78%)	31 (0.81%)	49 (1.28%)	0.043	C Versus B, C versus A
Required mechanical ventilation	88 (2.29%)	98 (2.55%)	221 (5.76%)	<0.001	C Versus B, C versus A

the procedure. Periprocedural management needs to be optimized, such as using a better strategy for sedation and airway management. Hasanein et al.[25] reported ketamine/propofol provided better sedation quality than fentanyl/propofol with less sedation-related side effects such as hypotension, bradycardia, and apnea and reduction of SpO_2 for sedating obese patients undergoing ERCP.[25] A randomized controlled trial including 200 patients with risk factors for sedation-related adverse events (SRAEs), of those some with BMI $\geq$ 35, showed that sedation with general endotracheal anesthesia is associated with a significantly lower incidence of SRAEs, without impacting procedure duration, success, recovery, or in-room time.[26]

This study has several notable strengths. First, a highly restricted cohort was adopted to decrease the potential confounding bias and reverse causation. The Global BMI Mortality Collaboration pointed out that mortality can be confounded by smoking and chronic diseases due to their effects on baseline BMI.[27] Using the restricted cohort to never smokers and excluding patients with pre-existing chronic diseases, the possible confounding factors and reverse causation could be eliminated in our study. Second, this study used the three-way PS-matching approach, which minimizes other unmeasured confounders by including patients paired with similar conditions except for their BMI categories.

However, some limitations to this analysis do exist. First, our study is limited by its retrospective nature. Second, the NRD data are purely an inpatient database. Thus, it may not be generalizable to outpatient ERCP despite that a large proportion of ERCP is performed as an outpatient in the United States. Third, the NRD database is dependent on correct coding by providers. There was potential misclassification. However, assuming the misclassification is random, results would be biased toward the null. Fourth, the laboratory and imaging data were not available in this database, making the rate of ERCP-related complications less accurate even though we used the ICD-9 codes validated in previous studies. However, we found the complication rates in our study were similar to those reported in the literature. Finally, long-term data were not available for this study. The outcomes were restricted in that particular admission—the information about death and other complications that occurred after discharge could not be captured.

CONCLUSIONS

In summary, we found that morbid obesity but not obesity was associated with increased mortality, length of stay, and total cost in patients undergoing ERCP by using the largest nationwide database in the United States. This will help providers to better risk-stratify patients with obesity or morbid obesity while considering this procedure.

CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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