Association between underweight status and chylothorax after esophagectomy for esophageal cancer: A propensity score–matched analysis

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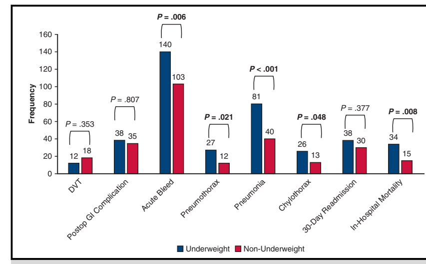
ABSTRACT

Objective: To use a nationwide database of hospitalizations to investigate underweight status as a risk factor for postesophagectomy complications.

Methods: We identified all patients who underwent esophagectomy with a diagnosis of esophageal cancer and known body mass index in the 2018-2020 Nationwide Readmissions Database. All hospital visits for esophagectomy and within 30 days of initial discharge were analyzed for postoperative complications, including chylothorax. Patients who were underweight were propensity score matched with patients who were not. Multivariable logistic regression was performed to identify complications that were significantly associated with underweight status.

Results: There were 1877 patients with esophageal cancer meeting inclusion criteria. Following propensity score matching, 433 patients who were underweight were matched to 433 patients who were not. In the multivariable model of the matched sample, which adjusted for age, sex, Charlson Comorbidity Index, history of chemotherapy or radiation therapy, and preoperative surgical feeding access, patients who were underweight were estimated to have 2.06 times the odds for chylothorax (95% confidence interval [CI], 1.07-4.25, $P = .035$). Underweight status was also significantly associated with acute bleed (odds ratio [OR], 1.52; 95% CI, 1.12-2.05, $P = .007$), pneumothorax (OR, 2.33; 95% CI, 1.19-4.85; $P = .017$), pneumonia (OR, 2.30; 95% CI, 1.53-3.50, $P < .001$), and in-hospital mortality (OR, 2.42; 95% CI, 1.31-4.69, $P = .006$).

Conclusions: Underweight status was found to be a risk factor for chylothorax after esophagectomy, which may have implications for perioperative care of esophageal cancer patients. Future studies should assess whether using feeding tubes or total parenteral nutrition preoperatively or thoracic duct ligation intraoperatively decreases risk of chylothorax among patients who were underweight. (JTCVS Open 2024;17:322-35)



Frequency of postoperative complications in propensity score–matched cohorts.

CENTRAL MESSAGE

Underweight status was a significant risk factor for chylothorax after esophagectomy, which may have important implications for perioperative care of patients with esophageal cancer.

PERSPECTIVE

As patients who were underweight were identified to be at increased risk of postoperative chylothorax in this study, future studies should assess whether intervening on nutrition preoperatively or intervening on the thoracic duct perioperatively decreases risk of chylothorax in this subgroup.

Esophageal cancer may cause weight loss and impaired oral intake, especially in aggressive disease, possibly leading to underweight status. Patients with low body mass index (BMI) who undergo esophagectomy may have increased risk for pulmonary complications and longer hospital length of stay.[1-3] Underweight status is an important risk factor to investigate, as it can possibly be intervened upon with additional nutritional support or surgical feeding access to strengthen patients before esophagectomy.

Chylothorax after esophagectomy is a rare complication, with an estimated incidence of approximately 2.6% among patients who undergo esophagectomy.[4] This complication can result in significant morbidity, such as infection, malnutrition, or thrombosis, and increased risk of mortality.[4,5] Owing to the nature of the dissection, patients undergoing esophagectomy for esophageal cancer may be especially at risk for chylothorax. Patients with esophageal cancer often require neoadjuvant chemotherapy or radiation, which can

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Abbreviations and Acronyms

BMI	= body mass index
CI	= confidence interval
ICD-10	= *International Classification of Diseases, Tenth Revision*
NRD	= Nationwide Readmissions Database
OR	= odds ratio

render this dissection more challenging and increase the risk of thoracic duct injury during esophagectomy.

Given its rarity, risk factors for chylothorax after esophagectomy are not well understood. Previous studies of relatively small sample size have proposed surgeon experience, history of chemotherapy, low BMI, radicality of dissection, and high intraoperative fluid balance as potential risk factors for chylothorax.[6-8] The goal of this study was to use a large nationwide all-payer database of hospitalizations to investigate underweight BMI as a risk factor for postoperative complications, such as chylothorax, after esophagectomy through a propensity score–matched analysis of patients who are underweight and not underweight.

METHODS

Patients who underwent total esophagectomy or lower esophageal resection with a diagnosis of esophageal cancer were identified in the 2018-2020 Healthcare Cost and Utilization Project Nationwide Readmissions Database (NRD). This large database contains information on all-payer hospital inpatient stays in the United States and tracks patients across hospitals within the calendar year using a unique patient linkage number.[9] Inclusion criteria and *International Classification of Diseases*, *Tenth Revision* (ICD-10) codes used are reported in Figure 1 and Table E1. All patients with BMI recorded during their hospitalization for esophagectomy were included for the analysis.

Data on hospital stays for esophagectomy and all hospital stays within 30 days of initial discharge were analyzed for the outcomes of interest: deep-vein thrombosis, pulmonary embolism, postoperative gastrointestinal complication (which includes esophageal anastomotic leak), mediastinitis, acute bleed, pneumothorax, pneumonia, chylothorax, 30-day readmission, and in-hospital mortality. The exposure of interest was underweight status, which was defined based on BMI (with the lowest possible BMI being <19.9 due to ICD-10 coding) and age (Figure 1 and Table E1).[10] Propensity score matching was used to match patients who were underweight with patients who were not in a 1:1 ratio, using a caliper of 0.1 and the nearest neighbor matching algorithm.[11,12] Patients who were not underweight were chosen as the control group so that there was sufficient sample to create a balanced matched cohort to the underweight group and because the non-underweight group was largely composed of patients who were overweight, which would be more generalizable to the adult population in the United States. The propensity score was constructed using logistic regression to match patients based on preoperative characteristics: age, sex, Charlson Comorbidity Index, history of chemotherapy or radiation therapy (to any part of the body), and preoperative surgical feeding access. The chosen covariates were proposed risk factors for postoperative complications, including chylothorax, in previous studies.[6-8] Charlson Comorbidity Index was included as a covariate to represent patient morbidity which could confound the association between underweight status and postoperative outcomes. Balance of the covariates in the propensity score–matched groups was evaluated using absolute standardized mean differences. Patient characteristics of those excluded from the propensity score matched analysis are reported in Table E2.

The χ^2 test, Fisher exact test, or Student t test was used to investigate associations between underweight status and the outcomes of interest in the sample cohort prior to matching. The paired t test or Fisher exact test was used in the matched cohort to examine bivariate associations. Unadjusted odds ratios (ORs) and Wald 95% confidence intervals (CIs) were constructed, with patients who were not underweight as the reference group. Multivariable logistic regression for the outcomes of interest, which adjusted for the covariates chosen a priori (age, sex, Charlson Comorbidity Index, history of chemotherapy and/or radiation therapy, preoperative surgical feeding access, and underweight status) was performed to calculate adjusted ORs and 95% CIs for matched cohorts. Multivariable logistic regression models were used to provide adjustment for any remaining covariate imbalances following matching.[11] Two-sided P values <.05 were considered statistically significant. This study followed STROBE reporting guidelines (Table E3). The University of Southern California Institutional Review Board approved of this study protocol and publication of data (HS-16-00906) on December 19, 2016. Patient written consent for the publication of the study data was waived by the institutional review board because this study is not considered human subjects research. Analyses were conducted using R, version 4.2.1 (The R Project for Statistical Computing; The R Foundation). Data were analyzed from March to September 2023.

RESULTS

There were 1877 patients with esophageal cancer who underwent esophagectomy from 2018 to 2020 with BMI captured in the Healthcare Cost and Utilization Project NRD (Figure 1). There were 433 patients with an underweight BMI and 1444 patients with a not-underweight BMI. The average age was 63.9 ± 9.5 years, and female patients comprised 21% (390/1877) of the sample (Table 1). Before matching, there were statistically significant differences between patients who were underweight and patients who were not underweight with regards to age (65.3 vs 63.4 years, P < .001), female sex (31% vs 18%, P < .001), presence of preoperative surgical feeding access (14% vs 6%, P < .001), and resection of thoracic lymphatics during esophagectomy (52% vs 59%, P = .007) (Table 1). A 1:1 propensity score matching based on age, sex, Charlson Comorbidity Index, history of chemotherapy and/or radiation therapy, preoperative surgical feeding access, and underweight status resulted in 433 patients who were underweight matched to 433 patients who were not. Absolute standardized mean difference of the covariates were all less than 0.1, indicating sufficient balance in the covariates between matched cohorts. Following matching, only resection of thoracic lymphatics (52% vs 61%, P = .006) remained statistically significantly different between groups.

Postoperative complications were examined in Table 2 for all patients and by underweight status, for the study sample before and after propensity score matching. Before matching, underweight status was associated with increased risk for acute bleed (OR, 1.42; 95% CI, 1.12-1.79, P = .004), pneumothorax (OR, 1.89; 95% CI, 1.17-3.07, P = .012), pneumonia (OR, 2.31; 95% CI, 1.71-3.12,

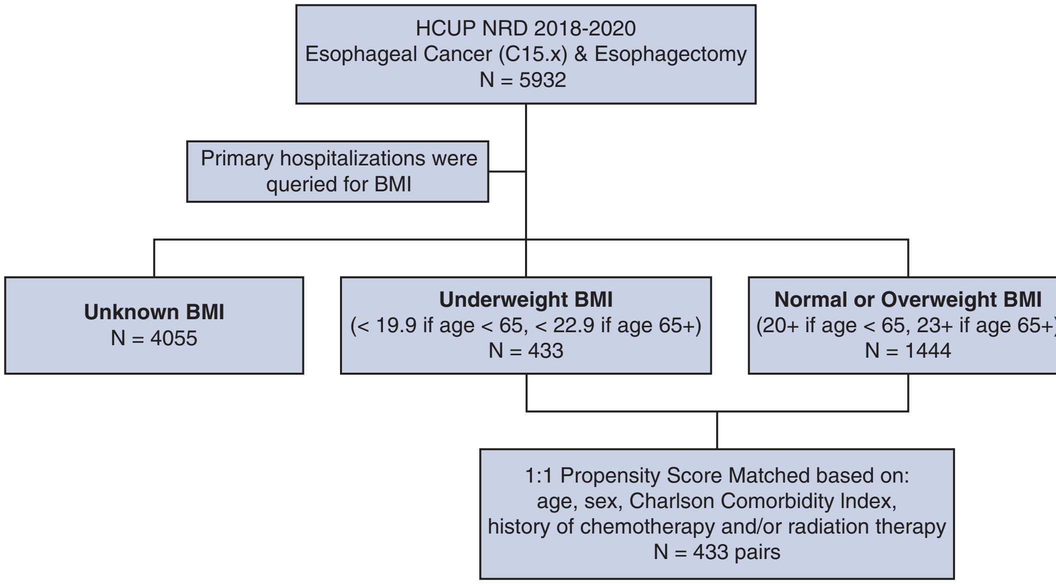

FIGURE 1. Sample generation flowchart diagram. *HCUP NRD*, Healthcare Cost and Utilization Project Nationwide Readmissions Database; *BMI*, body mass index.

$P < .001$), chylothorax (OR, 1.90; 95% CI; 1.16-3.10, $P = .015$), and in-hospital mortality (OR, 2.24; 95% CI, 1.43-3.49, $P < .001$). There was insufficient evidence to show that underweight status was associated with chylothorax requiring surgical intervention.

Following propensity score matching, multivariable logistic regression models adjusted for covariates chosen a priori to control for patient morbidity and proposed risk factors of chylothorax following esophagectomy from prior studies.[6-8] In the matched cohort, the association of underweight status with chylothorax or other postoperative complications, after adjusting for Charlson Comorbidity Index, history of chemotherapy or radiation therapy, minimally invasive approach, and resection of thoracic lymphatics was assessed (Table 2). Patients who were underweight were estimated to have 2.06 times the odds for chylothorax (95% CI, 1.07-4.25, $P = .035$) in the multivariable analysis. Following propensity score matching and multivariable logistic regression, underweight status was also significantly associated with acute bleed (OR, 1.52; 95% CI; 1.12-2.05, $P = .007$), pneumothorax (OR, 2.33; 95% CI, 1.19-4.85, $P = .017$), pneumonia (OR, 2.30; 95% CI; 1.53-3.50, $P < .001$), and in-hospital mortality (OR, 2.42; 95% CI, 1.31-4.69, $P = .006$). The frequencies of the postoperative complications in propensity score matched cohorts are shown in Figure 2, with unadjusted *P*-values for the association between underweight status and the outcome variables. Acute bleed was the most common postoperative complication in the matched sample, followed by pneumonia. Although chylothorax and in-hospital mortality were rare complications, they were experienced approximately twice as frequently for the underweight group.

Lastly, a subgroup analysis of only patients who were underweight was performed (Figures E1 and E2). The presence of surgical feeding access before esophagectomy was examined for its association with postoperative complications among patients who were underweight, as this may intervene on perioperative nutrition for patients who were underweight and decrease risk of postoperative complications. There was insufficient evidence to show that patients with surgical feeding access before surgery had significantly different risks for postoperative complications. In Figure E2, the outcome of chylothorax was further investigated. Among patients who were underweight, there were not statistically significant differences in percentage of patients experiencing chylothorax with feeding tube ($P > .999$) or with a thoracic duct intervention during the principal esophagectomy ($P = .611$). Among patients who were underweight, although nonsignificant, thoracic duct intervention performed with esophagectomy was associated with greater prevalence of chylothorax (11% vs 3%, $P = .097$).

DISCUSSION

In this study, the association between underweight BMI and risk of complications such as chylothorax after esophagectomy using the 2018-2020 NRD was investigated through a propensity score–matched analysis (Figure 3). Before matching, patients who were underweight were more likely to be older, female, have surgical feeding access preoperatively, and less likely to have had resection of thoracic lymphatics compared with patients who were not underweight. In the matched cohorts, patients who were underweight were found to have greater risk of postoperative

TABLE 1. Characteristics of patients with esophageal cancer undergoing esophagectomy, for sample cohorts before and after propensity score matching

Characteristic, n (%)	Before matching Total N = 1877	Underweight BMI n = 433	Nonunderweight BMI n = 1444	*P* value	After matching Total N = 866	Underweight BMI n = 433	Nonunderweight BMI n = 433	*P* value	ASMD
Age, y, mean (SD)	63.9 (9.5)	65.3 (9.4)	63.4 (9.5)	**<.001**	65.6 (9.3)	65.3 (9.4)	65.9 (9.3)	.328	0.062
Female	390 (21%)	135 (31%)	255 (18%)	**<.001**	263 (30%)	135 (31%)	128 (30%)	.658	0.035
Charlson Comorbidity Index				.775				.785	
0-1	329 (18%)	72 (17%)	257 (18%)		138 (16%)	72 (17%)	66 (15%)		0.037
2-3	928 (49%)	220 (51%)	708 (49%)		449 (52%)	220 (51%)	229 (53%)		0.042
4+	620 (33%)	149 (34%)	479 (33%)		279 (32%)	149 (34%)	138 (32%)		0.015
History of chemotherapy and/or radiation				.185				.922	
Neither	858 (46%)	183 (42%)	675 (47%)		371 (43%)	183 (42%)	188 (43%)		0.023
Chemotherapy only	175 (9%)	38 (9%)	137 (9%)		72 (8%)	38 (9%)	34 (8%)		0.033
Radiation only*	80 (4%)	24 (6%)	56 (4%)		45 (5%)	24 (6%)	21 (5%)		0.030
Both	764 (41%)	188 (43%)	576 (40%)		378 (44%)	188 (43%)	190 (44%)		0.009
Preoperative surgical feeding access (jejunostomy or gastrostomy)	146 (8%)	60 (14%)	86 (6%)	**<.001**	114 (13%)	60 (14%)	54 (12%)	.615	0.040
Metastases				.501				.138	
None	1494 (80%)	336 (78%)	1158 (80%)		694 (80%)	336 (78%)	358 (83%)		
Lymph nodes only	284 (15%)	72 (17%)	212 (15%)		124 (14%)	72 (17%)	52 (12%)		
Solid organ or disseminated	99 (5%)	25 (6%)	74 (5%)		48 (6%)	25 (6%)	23 (5%)		
Resection of thoracic lymphatics (lymph node dissection)	1078 (57%)	224 (52%)	854 (59%)	**.007**	489 (56%)	224 (52%)	265 (61%)	**.006**	
Minimally invasive esophagectomy	824 (44%)	180 (42%)	644 (45%)	.290	360 (42%)	180 (42%)	180 (42%)	>.999	
Thoracic duct intervention				.094				.055	
With principal esophagectomy	73 (4%)	15 (3%)	58 (5%)		33 (4%)	15 (3%)	18 (4%)		
After esophagectomy*	28 (1%)	11 (3%)	17 (1%)		14 (2%)	*	*		

P value less than .05 indicated in bold. *BMI*, Body mass index; *ASMD*, absolute standardized mean difference; *SD*, standard deviation. *Absolute cell counts are not reported in compliance with Centers for Medicare & Medicaid Services Cell Suppression Policy.

complications, including approximately 2-fold greater risk of chylothorax, pneumonia, pneumothorax, and in-hospital mortality while controlling for age, sex, Charlson Comorbidity Index, history of chemotherapy and/or radiation therapy, and preoperative surgical feeding access.

One of the most important findings from this study was that underweight status was associated with almost 2 times the odds for chylothorax, a rare but significant postesophagectomy complication. Although the strength of the association between chylothorax and underweight status was not the largest of the complications shown in Table 2, this study used the cumulative experience of a large database to focus on chylothorax, given the rarity of its occurrence and the difficulty that many single institutions or any modest consortium of institutions would encounter in accumulating this same experience. Patients who were underweight represent a high-risk subgroup for patients with esophageal cancer undergoing esophagectomy. A previous study of a Dutch cancer registry similarly found a significant association between underweight status and chyle leakage, with a much greater prevalence of chylothorax in their comparatively smaller sample (21%, 15 of 70 patients who were underweight).[3] Low BMI can be related to cachexia and frailty, which increases surgical risk and may present anatomical challenges during surgery.[1] In addition, malnutrition may increase risk of certain clinical outcomes due to compromised immune function, including increased risk of sepsis, heart failure, or poor wound healing.[13,14] In this

TABLE 2. Postesophagectomy complications among sample cohort before and after matching

	Before matching					After matching						
Characteristic, n (%)	**Total N = 1877**	**Underweight BMI n = 433**	**Nonunderweight BMI n = 1444**	**Odds ratio (95% CI)**	***P* value**	**Total N = 866**	**Underweight BMI n = 433**	**Nonunderweight BMI n = 433**	**Odds ratio (95% CI)**	***P* value**	**Adjusted odds ratio† (95% CI)**	***P* value**
Deep vein thrombosis	61 (3%)	12 (3%)	49 (3%)	0.81 (0.43-1.54)	.643	30 (3%)	12 (3%)	18 (4%)	0.66 (0.31-1.38)	.353	0.67 (0.31-1.39)	.286
Pulmonary embolism*	50 (3%)	*	*	0.73 (0.35-1.51)	.497	25 (3%)	*	*	0.55 (0.24-1.27)	.222	0.56 (0.23-1.25)	.166
Postoperative gastrointestinal complication (includes esophageal leak)	183 (10%)	38 (9%)	145 (10%)	0.86 (0.59-1.25)	.461	73 (8%)	38 (9%)	35 (8%)	1.09 (0.67-1.77)	.807	1.07 (0.66-1.74)	.787
Mediastinitis*	32 (2%)	*	*	1.11 (0.43-2.59)	.832	13 (2%)	*	*	1.61 (0.52-4.97)	.578	1.49 (0.48-5.06)	.494
Acute bleed	504 (27%)	140 (32%)	364 (25%)	**1.42 (1.12-1.79)**	**.004**	243 (28%)	140 (32%)	103 (24%)	**1.53 (1.14-2.06)**	**.006**	**1.52 (1.12-2.05)**	**.007**
Pneumothorax	76 (4%)	27 (6%)	49 (3%)	**1.89 (1.17-3.07)**	**.012**	39 (5%)	27 (6%)	12 (3%)	**2.33 (1.17-4.67)**	**.021**	**2.33 (1.19-4.85)**	**.017**
Pneumonia	212 (11%)	81 (19%)	131 (9%)	**2.31 (1.71-3.12)**	**<.001**	121 (14%)	81 (19%)	40 (9%)	**2.26 (1.51-3.39)**	**<.001**	**2.30 (1.53-3.50)**	**<.001**
Chylothorax	73 (4%)	26 (6%)	47 (3%)	**1.90 (1.16-3.10)**	**.015**	39 (5%)	26 (6%)	13 (3%)	**2.06 (1.05-4.07)**	**.048**	**2.08 (1.07-4.25)**	**.035**
Chylothorax requiring surgical intervention*	32 (2%)	*	*	1.53 (0.64-3.39)	.290	15 (2%)	*	*	2.02 (0.69-5.97)	.297	2.02 (0.71-6.55)	.207
30-d readmission	161 (9%)	38 (9%)	123 (9%)	1.03 (0.71-1.51)	.845	68 (8%)	38 (9%)	30 (7%)	1.29 (0.79-2.13)	.377	1.28 (0.78-2.14)	.333
In-hospital mortality	87 (5%)	34 (8%)	53 (4%)	**2.24 (1.43-3.49)**	**<.001**	49 (6%)	34 (8%)	15 (3%)	**2.37 (1.27-4.43)**	**.008**	**2.42 (1.31-4.69)**	**.006**

P value less than .05 indicated in bold. *BMI*, Body mass index; *CI*, confidence interval. *Absolute cell counts are not reported in compliance with Centers for Medicare & Medicaid Services Cell Suppression Policy. †Multivariable models adjusted for Charlson Comorbidity Index, history of chemotherapy or radiation therapy, minimally invasive approach, and resection of thoracic lymphatics.

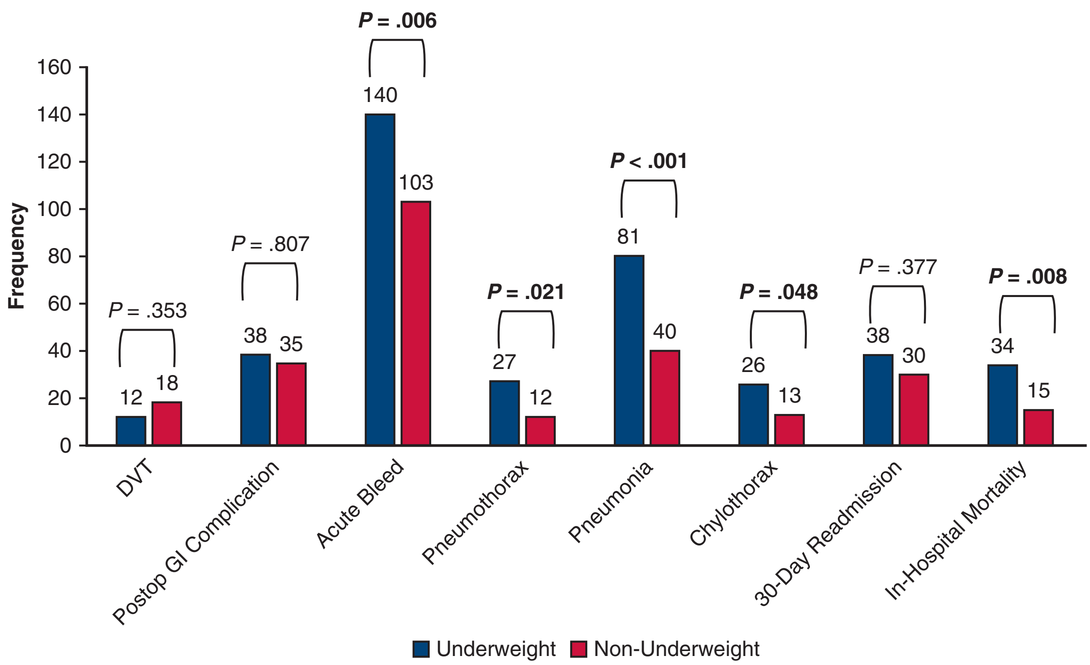

FIGURE 2. Frequency of postoperative complications in propensity score–matched cohorts. *DVT*, Deep-vein thrombosis; *GI*, gastrointestinal.

study, the ICD-10 diagnosis of malnutrition was excluded from analyses as a potential risk factor following esophagectomy. This exclusion was due to significant collinearity between underweight status and malnutrition (data not shown), and because malnutrition could not be discerned as a preoperative comorbidity versus a postoperative complication in the NRD. Rather, presence of preoperative surgical feeding access (gastrostomy or jejunostomy) was used as a marker of severe preoperative malnutrition. To limit confounding, preoperative surgical feeding access was included as a covariate for matching and in the multivariable regression so that the association between patient

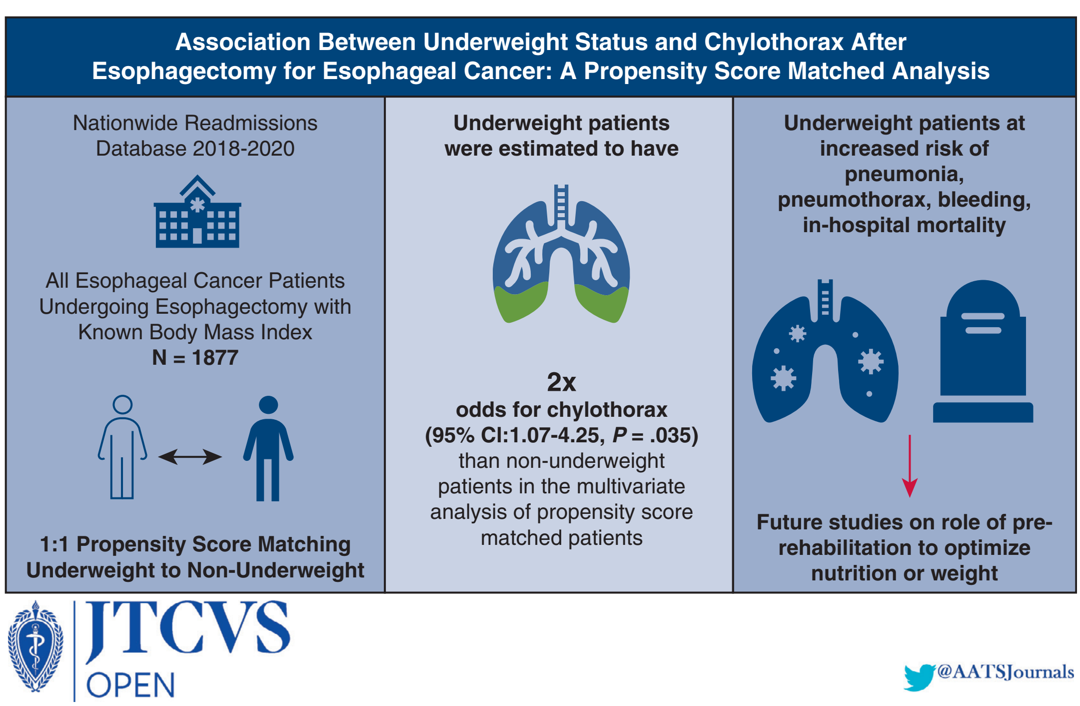

FIGURE 3. Graphical abstract. *CI*, Confidence interval.

BMI and chylothorax could be examined. Future studies should aim to adjust for more objective measures of nutrition, such as albumin or prealbumin, when examining the relationship between underweight BMI and postoperative complications. It is also important to note that underweight status was not found to be significantly associated with increased risk of chylothorax requiring surgical intervention. Future studies should assess the risk factors for surgical chylothorax.

This study adds to the growing body of literature demonstrating how low body mass index is associated with chylothorax risk.[3,4,7] Previous studies have shown mixed associations between chylothorax and preoperative chemotherapy or chemoradiation therapy.[4,6,8] Therefore, our study controlled for preoperative chemotherapy and/or radiation therapy in the matched analysis and multivariable logistic regression models. In the multivariable analysis, underweight status remained a significant risk factor for development of chylothorax. Surgeon experience was proposed as a risk factor for chylothorax as well, demonstrating how a human factor can also affect esophagectomy outcomes.[6] As a study showed that overweight status was protective of chylothorax likely due to easier visualization of the thoracic duct, the association between underweight patients and chylothorax may be related to poor surgeon visualization and unintentional injury to the duct during the operation.[6,15]

Underweight patients were examined as a subgroup as they were identified to be at highest risk of chylothorax following esophagectomy (Figures E1 and E2). Patients who were underweight who had a gastrostomy or jejunostomy (surgical feeding access) before esophagectomy were not found to have a significantly decreased risk for postoperative complications. Given the retrospective nature of this study, it is difficult to assess the presence of a feeding tube as an appropriate intervention on weight, and future studies should prospectively determine the benefit of optimizing weight in this manner or with total parenteral nutrition for pre-rehabilitation prior to esophagectomy. Patients who were underweight who had a thoracic duct intervention at time of esophagectomy were also examined; however, this group did not have significantly decreased risk of chylothorax. While not statistically significant, patients who were not underweight who had a thoracic duct intervention had a greater proportion experiencing chylothorax, whereas patients who were underweight with a thoracic duct intervention had much similar rates of chylothorax (11% vs 3% for nonunderweight, 7% vs 6% for underweight). Although the indications for thoracic duct intervention with esophagectomy are not captured by NRD, it is likely to represent patients who sustained an iatrogenic injury to the thoracic duct during the operation as well as surgeons who prophylactically ligate the duct.

The role of prophylactic thoracic duct ligation requires further investigation, as our study could not discern whether a thoracic duct intervention during the index esophagectomy was used prophylactically. A recent systematic review of 16 studies found that prophylactic thoracic duct ligation resulted in increased rate of chylothorax, which may be consistent with Figure E2.[16] In addition, routine thoracic duct resection was associated with increased risk of metastasis to distant organs and similar overall survival (compared with those with preserved thoracic duct) among patients receiving neoadjuvant chemoradiation therapy for esophageal squamous cell cancer, likely due to the immunosuppressive effect of thoracic duct resection.[17] However, several other studies advocate for prophylactic thoracic duct ligation, citing that the occurrence of chylothorax following a prophylactic thoracic duct ligation is rare.[18-20] This study grouped together all interventions on the thoracic duct, including mass ligation, excision, or resection. The varying efficacies of these interventions may confound the data in this study,[18] and future research on the best approach to intraoperative thoracic duct intervention is necessary, especially for patients who were underweight.

Numerous other postoperative complications were associated with underweight status. Patients who were underweight had increased risk of acute bleed, pneumothorax, pneumonia, and in-hospital mortality. Pulmonary complications in general have previously been associated with patients who were underweight undergoing esophagectomy; this study found that underweight status may be a risk factor for pneumothorax and pneumonia in particular.[1] In addition, patients who were underweight had greater risk of in-hospital mortality, which may be a consequence of being more likely to have aggressive disease or having poorer wound healing and immune function. Unfortunately, these processes could not be distinguished in this study, as information on BMI trends or nutrition markers are not captured in the database. Future studies should investigate the underlying processes by which patients who are underweight are at increased risk of these postoperative complications and death.

It is interesting to note that in this sample, 46% (858/1877) patients did not receive neoadjuvant chemoradiation therapy. Historically since the publication of landmark information, only patients with low-risk, node-negative T1b or T2 esophageal cancers would qualify for esophagectomy alone.[21] As most patients are diagnosed as having late-stage esophageal carcinoma (regional or distant disease), the finding that almost one half of the sample did not receive neoadjuvant chemotherapy is surprising.[22] However, there are also patients in this group who may have been postoperatively upstaged, warranting adjuvant therapy. In addition, a previous study of a cancer registry in Ontario, Canada, found similarly that only 61% (1849/3047) of patients who underwent esophagectomy had received neoadjuvant therapy.[23] These results may reflect the volume-outcome effect on management for esophagectomy patients, where hospitals with few esophagectomy cases might not have adopted evidence-based standards yet, and therefore may not provide neoadjuvant therapy to eligible patients.

Limitations of this study include the use of administrative data, which lacks more granular information. Given how cancer stage dictates management with chemotherapy and/or radiation therapy, and may influence the radicality of lymph node dissections, cancer stage may confound the effect of underweight status patients and chylothorax. This study's interpretation of ICD-10 coding for thoracic lymph node dissection may not accurately reflect the number of lymph nodes resected. As detailed operative reports and indications for interventions were not available, thoracic duct intervention on same day as esophagectomy was assumed to have been performed in the same surgery; however, it could represent same-day reoperation. There could also be potential for misclassification of patients who received radiation therapy. Although our study assumes that it was to the chest (therefore potentially altering the thoracic duct), given only patients with esophageal cancer were included in the sample, the ICD-10 code for personal history of radiation therapy was not specific to body part. In addition, much of the original sample was excluded from our analysis, given there was not information on BMI, the exposure of interest. With the propensity-matched sample and exclusion of patients who had unknown BMI, the generalizability of this study may be limited to samples which are similar to our matched cohorts. Use of a validation cohort, especially one composed of a contemporaneous, nationwide patient sample, is necessary to evaluate the generalizability of the results. Lastly, this study could not thoroughly investigate the efficacy of chylothorax treatments, as much of that data is not available in the NRD.

CONCLUSIONS

This study found underweight status to be a significant risk factor for numerous complications, including chylothorax, after esophagectomy, which may have important implications for perioperative care of patients with esophageal cancer. As these findings suggest that patients with esophageal cancer who are underweight are at increased risk for adverse outcomes, there may be benefit in prerehabilitation from a nutritional or weight standpoint before surgery. Future studies should assess whether intervening on nutrition preoperatively decreases postoperative morbidity and mortality or whether intervening on the thoracic duct perioperatively decreases risk of chylothorax.

Conflict of Interest Statement

The authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

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Key Words: esophagectomy, chylothorax, risk factors, underweight, body mass index

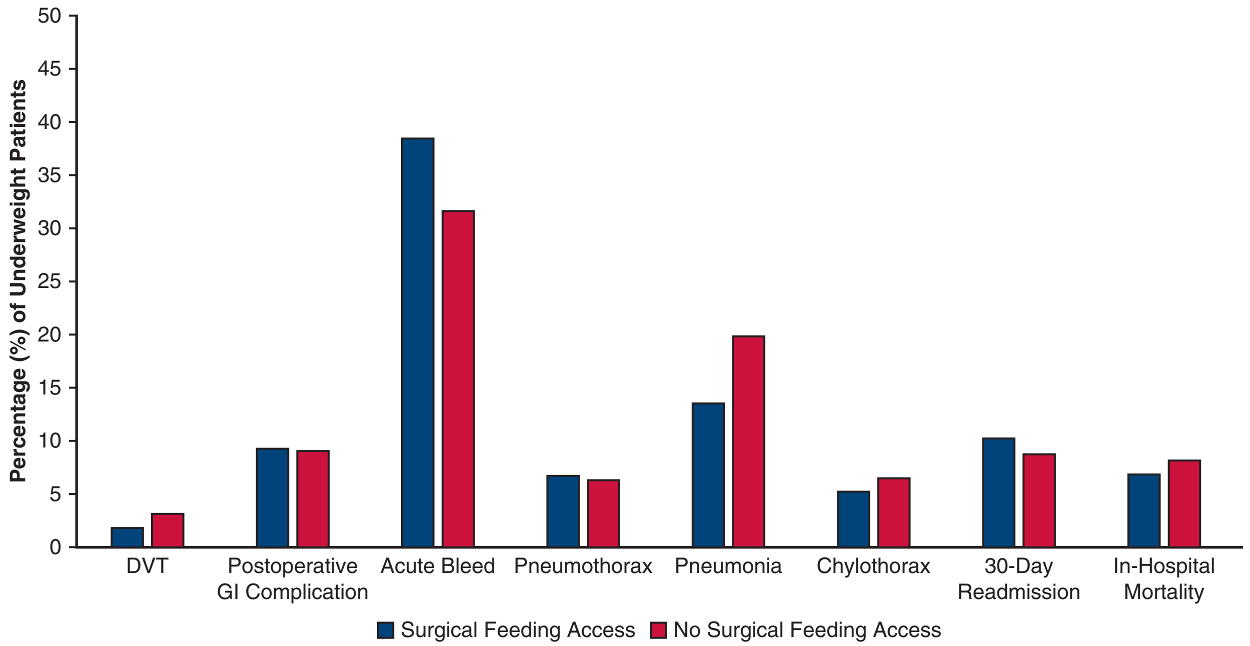

FIGURE E1. Percentage of patients with underweight body mass index with and without surgical feeding access (N = 60 and N = 373) who experienced postesophagectomy complications. *DVT*, Deep-vein thrombosis; *GI*, gastrointestinal.

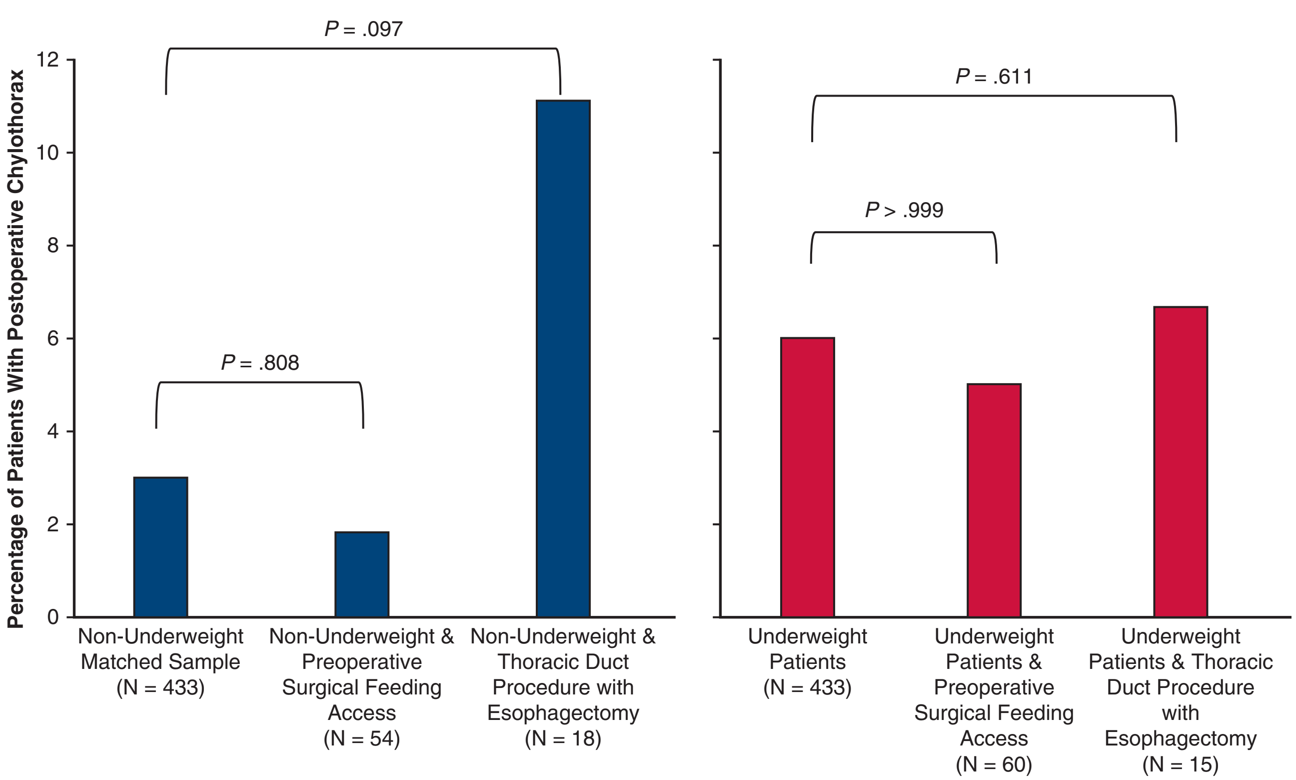

FIGURE E2. Percentage of patients who developed postoperative chylothorax among non-underweight and underweight matched samples.

TABLE E1. ICD-10 codes used to identify patient diagnoses and procedures

Diagnosis/procedure	ICD-10 diagnosis or procedure codes
Esophageal cancer	C15.x
Esophagectomy	0DB30ZZ, 0DB34ZZ, 0DB40ZZ, 0DB44ZZ, 0DB50ZZ, 0DB54ZZ, 0DT30ZZ, 0DT34ZZ, 0DT40ZZ, 0DT44ZZ, 0DT50ZZ, 0DT54ZZ
Thoracic lymph node dissection	0757xxx, 075Dxxx, 07B7xxx, 07BDxxx, 07T7xxx, 07TDxxx
Minimally invasive approach	0DB34ZZ, 0DB44ZZ, 0DB54ZZ, 0DT34ZZ, 0DT44ZZ, 0DT54ZZ
Preoperative surgical feeding access	0DH60UZ, 0DH63UZ, 0DH64UZ, 0DH68UZ, 0DHA3UZ, 0DHA0UZ, 0DHA4UZ, 0DHA7UZ, 0DHA8UZ during hospitalization prior to admission for esophagectomy or Z93.1 or Z93.4
Chylothorax	J94.0, I89.8
Thoracic duct intervention	07LKxxx, 07BKxxx, 07QKxxx, 07TKxxx, 07PKxxx, 07LLxxx, 07BLxxx, 07QLxxx, 07TLxxx, 07PLxxx, 07WKxxx, 07WLxxx A thoracic duct intervention dated for the same day as esophagectomy was assumed to have been performed with the esophagectomy.
History of chemotherapy	Z92.21
History of radiation therapy	Z92.3
Known BMI	Z68.x
Underweight BMI	For age <65: Z68.1 For age 65+: Z68.1, Z68.20, Z68.21, Z68.22
Metastases to organ	C78.x, C79.x, C80.x
Metastases to lymph nodes	C77.x
Obesity	Z68.3, Z68.4, E66.x
Deep vein thrombosis	I82.4, I82.6, I82.8, I82.9
Pulmonary embolism	I26.x
Postoperative gastrointestinal complication	K91.89
Mediastinitis	J98.51
Acute bleed	D62.x, I97.6, G97.5, T81.0
Postoperative pneumothorax	J95.811
Pneumonia	J12.x, J13.x, J14.x, J15.x, J16.x, J17.x, J18.x
Acute respiratory distress syndrome	J80.x

Charlson Comorbidity Index	Points	Code(s)
Age, y	<50: 0 50-59: +1 60-69: +2 70-79: +3 ≥80: +4	
History of myocardial infarction	+1	I25.2
Congestive heart failure	+1	I10.99, I11.0, I13.0, I13.2, I25.5, I42.0, I42.5, I42.6, I42.7, I42.8, I42.9, I43.x, I50.x, P29.0
Peripheral vascular disease	+1	I70.x, I71.x, I73.1, I73.8, I73.9, I77.1, I79.0, I79.2, K55.1, K55.8, K55.9, Z95.8, Z95.9
History of cerebrovascular accident or transient ischemic attack	+1	Z86.73
Dementia	+1	F01.x, F02.x, F03.x, I69.01, I69.11, I69.21, I69.31, I69.81, I69.91, G30.x, G31.x
Chronic obstructive pulmonary disease	+1	J41.x, J42.x, J43.x, J44.x

(Continued)

TABLE E1. Continued

Charlson Comorbidity Index	Points	Code(s)
Connective tissue disease	+1	L94.0, L94.1, L94.3, M05.x, M06.x, M08.x, M12.0, M12.3, M30.x, M31.0, M31.1, M31.2, M31.3, M32.x, M33.x, M34.x, M35.x, M45.x, M46.1, M46.8, M46.9
Peptic ulcer disease	+1	K25.7, K25.9, K26.9, K27.7, K27.9, K28.7, K28.9
Liver disease	Mild: +1	Mild: B18.x, I85.x, I86.4, I98.2, K70.x, K71.1, K71.3, K71.4, K71.5, K71.7, K72.x, K73.x, K74.x, K76.0, K76.2, K76.3, K76.4, K76.5, K76.6, K76.7, K76.8, K76.9, Z94.4
	Moderate/Severe: +3	Moderate/severe: K74.3, K74.4, K74.5, K74.6, K76.6, I85.01, I85.11
Diabetes mellitus	Uncomplicated: +1	Uncomplicated: E10.0, E10.1, E10.9, E11.0, E11.1, E11.9, E12.0, E12.1, E12.9, E13.0, E13.1, E13.9, E14.0, E14.1, E14.9
	Complicated: +2	Complicated: E10.2, E10.3, E10.4, E10.5, E10.6, E10.7, E10.8, E11.2, E11.3, E11.4, E11.5, E11.6, E11.7, E11.8, E12.2, E12.3, E12.4, E12.5, E12.6, E12.7, E12.8, E13.2, E13.3, E13.4, E13.5, E13.6, E13.7, E13.8, E14.2, E14.3, E14.4, E14.5, E14.6, E14.7, E14.8
Hemiplegia	+2	G81.x, I69.05, I69.15, I69.25, I69.35, I69.85, I69.95
Moderate-to-severe chronic kidney disease	+2	N18.3, N18.4, N18.5, N18.6, N19.x
Solid tumor	Omitted, due to inclusion criteria	
Leukemia	+2	C91.x, C92.x, C93.x, C94.x, C95.x
Lymphoma	+2	C81.x, C82.x, C83.x, C84.x, C85.x, C88.x, C96.x, C90.0, C90.2
AIDS	+6	B20.x, B21.x, B22.x, B24.x

ICD-10, *International Classification of Diseases, Tenth Revision*; *BMI*, body mass index; *AIDS*, acquired immunodeficiency syndrome.

TABLE E2. Sample characteristics of excluded patients from the propensity score matching analysis

Characteristic, N (%)	Matched patients N = 866	Excluded patients N = 1011	*P* value
Age, y, mean (SD)	65.6 (9.3)	62.4 (9.4)	**<.001**
Female	263 (30%)	127 (13%)	**<.001**
Charlson Comorbidity Index			.104
0-1	138 (16%)	191 (19%)	
2-3	449 (52%)	479 (47%)	
4+	279 (32%)	341 (34%)	
History of chemotherapy and/or radiation			**.009**
Neither	371 (43%)	487 (48%)	
Chemotherapy only	72 (8%)	103 (10%)	
Radiation only	45 (5%)	35 (3%)	
Both	378 (44%)	386 (38%)	
Preoperative surgical feeding access (jejunostomy or gastrostomy)	114 (13%)	32 (3%)	**<.001**
Metastases			.613
None	694 (80%)	800 (79%)	
Lymph nodes only	124 (14%)	160 (16%)	
Solid organ or disseminated	48 (6%)	51 (5%)	
Resection of thoracic lymphatics (lymph node dissection)	489 (56%)	589 (58%)	.462
Minimally invasive esophagectomy	360 (42%)	464 (46%)	.066
Thoracic duct intervention			.362
With principal esophagectomy	33 (4%)	40 (4%)	
After esophagectomy	14 (2%)	14 (1%)	
Deep vein thrombosis	30 (3%)	31 (3%)	.723
Pulmonary embolism	25 (3%)	25 (2%)	.681
Postoperative gastrointestinal complication (includes esophageal leak)	73 (8%)	110 (11%)	.088
Mediastinitis	13 (2%)	19 (2%)	.651
Acute bleed	243 (28%)	261 (26%)	.298
Pneumothorax	39 (5%)	37 (4%)	.420
Pneumonia	121 (14%)	91 (9%)	**<.001**
Chylothorax	39 (5%)	34 (3%)	.248
Chylothorax requiring surgical intervention	15 (2%)	17 (2%)	>.999
30-day readmission	68 (8%)	93 (9%)	.339
In-hospital mortality	49 (6%)	38 (4%)	.066

P values less than .05 indicated in bold. *SD*, Standard deviation.

TABLE E3. STROBE checklist for observational studies

	Item no.	Recommendation	Check
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found	Study type is indicated in title and abstract The abstract provides a summary of the study
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Background and rationale are reported
Objectives	3	State specific objectives, including any prespecified hypotheses	Objective is stated
Methods			
Study design	4	Present key elements of study design early in the paper	Key elements are reported
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Setting, locations, and dates are reported
Participants	6	(a) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case–control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants (b) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case–control study*—For matched studies, give matching criteria and the number of controls per case	Eligibility criteria and methods of selection are described.
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Outcomes, exposures, confounders are described.
Data sources/ measurement	8	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Data source and ICD-10 codes are reported for each variable of interest.
Bias	9	Describe any efforts to address potential sources of bias	Propensity score matching and multivariable logistic regression were used to address bias.
Study size	10	Explain how the study size was arrived at	Study size was determined based on inclusion criteria (see Figure 1)
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Method of handling quantitative variables is described. BMI was categorized based on Winter et al definitions.
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case–control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy (e) Describe any sensitivity analyses	Statistical methods were described in Methods Subgroup analysis of underweight patients was described Missing data were excluded Matching methods were described N/A

ICD-10, *International Classification of Diseases, Tenth Revision*; *N/A*, not applicable.