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Risk of Advanced Papillary Thyroid Cancer in Obese Patients

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Risk of Advanced Papillary Thyroid Cancer in Obese Patients

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Master of Science in Clinical Research

By Avital Harari

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ABSTRACT

Risk of Advanced Papillary Thyroid Cancer in Obese Patients

By

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Master of Science in Clinical Research

University of California, Los Angeles, 2013

Professor Robert Elashoff, Chair

Objective: To determine if increasing body mass index (BMI) is associated with more aggressive disease and adverse surgical outcomes in patients with papillary thyroid cancer (PTC).

Design: Retrospective review of a prospective database.

Setting: Single academic tertiary care center.

Patients: A total of 443 patients over age 18 who underwent total thyroidectomy for PTC from January 1, 2004 to March 31, 2011 were included in the analysis. Patients were organized into four BMI groups: normal (18.5-24.9 kg/m2), overweight (25-29.9 kg/m2), obese (30-39.9 kg/m2), and morbidly obese (≥40 kg/m2).

Main Outcome Measures: Disease stage at presentation; histological subtype; duration of anesthetic induction and extubation; duration of surgery; surgical complications; length of hospital stay, and American Society of Anesthesiology Classification (ASA).

Results: Ages ranged from 18-89. Greater BMI was associated with more advanced disease stage at presentation ($p<0.0001$) and with more aggressive PTC histopathology ($p=0.027$).

Morbidly obese patients presented more frequently with stage III or stage IV disease (OR 3.67, $p<0.0001$). Greater BMI was also associated with longer duration of anesthetic induction ($p<0.01$), increased length of stay ($p<0.001$), and higher ASA classification ($p<0.001$). Duration of surgery was not associated with BMI. There was a trend towards larger tumors with increasing BMI ($p=0.06$). Obese BMI was associated with more preoperative vocal cord paralysis due to local invasion (OR 9.21, $p=0.001$).

Conclusions: Obese patients present with more advanced stage and more aggressive forms of papillary thyroid cancer. This suggests that obese patients should be screened for thyroid cancer.

The Master's Thesis of Avital Harari is approved.

Katrina Dipple

Michael Yeh

Ning Li

Robert Elashoff, committee chair

University of California, Los Angeles
2013

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    - **c.** Stacie Nishimoto, BS: acquisition of data, drafting article, final approval for publishing
    - **d.** Philip H.G. Ituarte, PhD: interpretation of data, statistical support, drafting of the article, final approval for publishing
    - **e.** Michael W. Yeh, MD: design, interpretation of data, article revision, final approval for publishing
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Risk of Advanced Papillary Thyroid Cancer in Obese Patients

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Introduction/Background:

The rising prevalence of obesity in the United States has been a concerning issue in recent decades. There is increasing interest in understanding the debilitating effects and disease risks associated with increased body fat percentage. Elevated body mass index (BMI) is associated with a number of medical co-morbidities, including hypertension, diabetes, cardiovascular disease, and cancer[1].

The incidence and prevalence of thyroid cancer is also on the rise in the United States.[2, 3] Most of this increase is due to papillary thyroid cancer[2]. It is still debatable whether the cause of this increase is a result of enhanced risk for the development of cancer or a result of an increase in detection capabilities in light of the new and more sensitive technology[4]. Regardless, thyroid cancer remains the most common endocrine cancer and is responsible for more deaths every year than all other endocrine malignancies combined[4].

Obesity is now recognized as a risk factor for a variety of cancers in patient populations around the world. BMI has been associated with esophageal adenocarcinoma, colon cancer, endometrial cancer, and renal cancer[5]. In addition, some studies have linked a higher BMI to an increased incidence of thyroid cancer in the USA, Korea, Norway, and French Polynesia. [5-10].

Furthermore, increased BMI has also been linked to a more severe presentation and a higher risk of death from other types of cancers. Presentation of more advanced stages of breast - cancer has been attributed to certain racial groups, explained by obesity differences between the groups, among other factors[11]. Higher grade prostate cancer and a higher risk of recurrence of these patients after treatment have also been associated with obesity[12]. It has also been shown that excess body weight is associated with a higher mortality risk from all cancers combined[13].

An association between higher BMI and more aggressive or later stage cancer has never been shown with papillary thyroid cancer. We conducted this study to address the association of increasing BMI with papillary thyroid cancer stage at presentation, with the presence of aggressive malignant features, and with adverse surgical outcomes.

Methods:

We reviewed the records of all patients over the age of 18 who underwent total thyroidectomy as an initial procedure for papillary thyroid cancer (PTC) or its variants from January 1, 2004 to March 31, 2011 at a single tertiary referral center. These patients were identified using the UCLA Cancer Registry and UCLA Financial Services databases. We excluded patients who had missing data, had less than a total thyroidectomy at initial procedure, had concomitant parathyroid disease or parathyroid operations, and/or had other types of thyroid cancer pathology. Patients with missing data were evenly spread throughout BMI groups.

ICD-9-CM codes were used to identify all patients with papillary thyroid cancer as well as their subtype and variants. For inpatient cases only (n=363), the ICD-9 codes were also used to define surgical complications, according to coding previously applied in other papers as well as adding codes that are specific to thyroid surgery.[14] A complete list of ICD-9 coding for diagnoses complications is located in Table 1. The number of complications were tallied to create summary scores. For some analyses, complications were dichotomized into absent (0) or present (1) categories. Medical complications and comorbidities were grossly undercoded and therefore not used in this study. Of note, our surgeons do not routinely perform pre-operative and/or post-operative laryngoscopy. ASA class was taken from anesthesia records. Staging was

performed by applying AJCC criteria. This information was supplied by the UCLA Cancer Registry.

We set power at 80% with a two-sided alpha of 0.05 to estimate the sample size needed for a logistic regression with an expected odds ratio range of 1.52 to 2.23.[5] The effect size was based on the expected association between BMI and thyroid cancer. With these parameters, a minimum sample size of 196 patients would be required. With the same power and two sided alpha values, we also calculated a sample size of 434 patients would be needed to detect a 3% complication rate if 5 predictors or less were used in multivariable analyses. Power analyses were calculated using GPower 3.1.0 software.[15]

BMI was calculated as weight (in kilograms) divided by height (in meters) squared. Patients were organized into four BMI groups: normal (18.5-24.9 kg/m2), overweight (25-29.9 kg/m2), obese (30-39.9 kg/m2), and morbidly obese (≥40 kg/m2). Histopathology was separated into four groups: papillary, papillary with follicular variant, papillary microcarcinoma, or other (hyalinizing, tall cell, or sclerosing). Surgical time was defined as the time from incision to closure. Anesthesia induction time was defined as anesthesia start time to surgical incision time.

Univariate analyses, including chi-square or oneway ANOVA, were conducted to study differences in BMI by demographic or clinical factors. Multivariable regression analyses were applied to control for the influence of co-factors affecting outcomes such as surgical time, or length of stay. BMI was the main predictor in all analyses. The main outcome measures studied were: disease stage at presentation; histological subtype; duration of anesthetic induction and extubation; duration of surgery; surgical complications; length of hospital stay (LOS), and American Society of Anesthesiology Classification (ASA). All analyses were conducted using

Stata/SE v.11 (StataCorp, College Station, TX). The research protocol was approved by the UCLA institutional review board.

Results:

Of 551 patients, 443 patients were included in the final analysis. See Table 2 for demographic information. Average age was 48.2 (range 18-93). Normal weight patients were slightly younger than the other BMI categories ($p<0.05$). Although women represent the majority of cases overall, men were more overweight and obese than females in this cohort ($p<0.001$). African Americans were more obese and morbidly obese than other races ($p<0.05$). A higher frequency of ASA class 3 was represented in the obese and morbidly obese categories ($p<0.001$).

Greater BMI was associated with more advanced disease stage at presentation ($p=0.035$, see Table 3). Specifically, the obese and morbidly obese categories presented more as stage III or IV disease. There was no difference in overall subtype of papillary cancer histology amongst BMI groups as defined in the methods section. However, in a sub-group analysis, there was a significant increase in the percentage of the more aggressive subtype of tall cell variant of papillary thyroid cancer in the obese and morbidly obese categories as compared to the normal weight and overweight categories ($p=0.027$). There was no association between those with tall cell variant and age in this cohort ($p=0.617$). There was also a trend towards greater tumor size in patients with increasing BMI.

Patients did not demonstrate any association between total surgical complication rates and BMI groups (See Table 4). However, those in the obese BMI group had significantly more recurrent laryngeal nerve dysfunction (n=10, 12.2%) than those in the normal weight (n=2, 2%) and overweight (n=3, 2.6%) categories, (χ^2, $p=0.001$). Most of this was due to presentation with

preoperative vocal cord dysfunction with more advanced local disease. Obese BMI (n=9) was associated with more preoperative vocal cord paralysis due to local invasion, with an odds ratio (OR) of 9.21 (95% CI: 1.9-43.9; p=0.001) when compared to normal weight individuals (n=2). These preoperative paralyses were not included in the number of surgical complications in Table 4. There was no difference between BMI groups in complications related to wound infection, bleeding (n=5), hypocalcemia (n=16), respiratory issues, and/or re-intubation rates. However, the amount of patients was underpowered to detect a less than 3% complication rate.

Increasing BMI was a significant predictor of longer LOS on both univariate and multivariable analyses, controlling for surgeon and ASA class (see Tables 4 and 5, $p<0.05$). In univariate analysis, morbidly obese patients had a significantly longer anesthesia induction time (mean = 43.1; $p < 0.001$) compared with other groups. There was also a trend toward longer extubation times with increasing BMI. In both univariate and multivariable analyses (controlling for surgeon and AJCC stage), there was a trend towards longer total surgical times associated with increasing BMI (see Table 4).

In the entire cohort, higher BMI was a significant predictor of presenting with either stage III or IV disease as compared to normal weight (see Table 5): overweight OR=1.94 (95% CI 1.07-3.5); obese OR=2.11 (95% CI 1.2-3.99): and morbidly obese OR=3.67 (95% CI 1.51-8.93). When excluding microcarcinomas, this association was strengthened in all three BMI groups, noted especially in the morbidly obese group's OR of 5.22 (95% CI 1.90-14.39). Likewise, when excluding tall cell variants from the group, the morbidly obese group remained significantly associated with later stage disease (OR=2.9, 95% CI 1.13-7.43). When analyzing only the microcarcinoma group, there was no significant association between BMI and late stage presentation.

When analyzing only those greater than 45 years of age (n=256), the morbidly obese group remained significantly associated with later stage disease (OR=3.66, 95% CI 1.24-10.24). When analyzing only those under age 45 (n=187) in their presentation of either stage I or stage II disease, there were no patients who presented with stage II disease. In addition, in this younger cohort, there were significantly more patients with lymph node involvement than in the older cohort (19.8%-vs-9.7%, p=0.003). However, in the younger cohort, there was no significant association between BMI and lymph node status or T3/T4 status.

When analyzing only women, the morbidly obese group remained significantly associated with later stage disease (OR=3.09, 95% CI 1.11-8.57). There was also a similar trend in men (morbid obese OR=6.5, p=0.055), however the group was underpowered to detect a difference (n=120).

Discussion:

Our study shows that those patients with increasing BMI have a progressively increasing risk in presenting with late stage papillary thyroid cancer (PTC) (see Table 5). This is especially seen in the obese and morbidly obese populations.

Recently, it has been shown that thyroid cancer has an increased incidence in the obese population. [8, 9, 16] Our study is novel in that it assesses the risk of presenting with both aggressive and disseminated disease. In addition, this study was performed in a multiethnic population with a large sample size. Paes et al. performed a study in a predominately Caucasian population to assess the relationship between obesity and thyroid cancer pathology and stage. Their study was unable to show any significant trends or associations[17]. However, this study, we believe, was most likely underpowered (n=250).

We believe that the cause of this increase in aggressive PTC behavior in the overweight and obese population could be multifactorial. It may be explained by both delayed detection as well as a possible biological/physiologic cause, as has been postulated in other cancers. As noted in the introduction, increased BMI has been linked to a more severe presentation and a higher risk of death from other types of cancers. Presentation of more advanced stages of breast cancer has been partially explained by obesity differences between the groups, among other factors[11]. Higher grade prostate cancer and a higher risk of recurrence of these patients after treatment have also been associated with obesity[12]. It has also been shown that excess body weight is associated with a higher mortality risk from all cancers combined[13].

To investigate the possible biological etiologies of more aggressive PTC tumor types in the obese population, we measured the prevalence of PTC tumors with more aggressive tall cell variant within the four groups. We found that the obese and morbidly obese groups both presented with a higher prevalence of PTC tall cell variant (See Table 3), suggesting that these groups have a higher risk of more aggressive tumor types. This association was seen regardless of age. Other studies have suggested there was no difference in histologic PTC subtype associated with obesity. [8, 17] However, one of these studies did not assess specifically the tall cell variant. [8] The other study was also likely underpowered to detect a difference.[17] In addition, we showed that obese patients were more likely to present with pre-operative vocal cord paralysis due to locally advanced disease. One limitation to this finding, however, is that our surgeons do not routinely perform pre-operative and/or post-operative laryngoscopy. Thus the denominator for the number of post-operative vocal cord paralyses is not truly know.

Other groups have also noted an increase in certain obesity biomarkers that are linked with cancer. For example, leptin, an adipocyte-derived cytokine, has been shown to be involved

in cancer development and progression.[16] Hedayati et al. recently showed that there are higher leptin levels in papillary thyroid cancer patients compared with healthy individuals. [18] Cheng et al. also previously demonstrated that papillary thyroid cancers expressing leptin receptors and/or leptin have a higher incidence of lymph node metastasis.[16]

Another plausible biological link between obesity and thyroid cancer may be through diabetes. It is well known that obesity is linked to diabetes. Recently, a study of 500,000 patients from the NIH-AARP Diet and Heath study showed an increased risk of PTC in women with diabetes (HR of 1.25).[19] Since medical comorbidities, especially the prevalence of diabetes, were undercoded in our cohort, we could not assess this relationship.

Exclusion of microcarcinomas from our analysis led to an accentuated association between advanced stage and obesity. This is likely due to the omission of a subset of patients with stage I disease who were overrepresented among the obese. Excluding tall cell variants from our analysis showed a persistent increased risk in the morbidly obese category but eliminated the risk in the other categories. This suggests that factors other than cancer subtype may also explain the link between obesity and presenting with later stage thyroid cancer.

One factor to consider in this population, other than a potential physiologic link between obesity and disease aggressiveness, is a delay in diagnosis which may arise from difficulty in detecting thyroid nodules when examining the obese neck. To investigate this in the obese population, we measured the primary tumor size amongst the groups (see Table 3). Although there was a trend towards greater tumor size with increasing BMI, the variance was too great and no statistical difference was observed.

Studies have shown an increase in incidence of thyroid cancer in obese women.[8, 10] Our study also showed that morbidly obese women have a significantly higher presentation of late

stage disease compared with normal weight individuals. This finding was not corroborated in men, although this group was likely underpowered to detect a difference (n=120).

The rarity of adverse events following total thyroidectomy for cancer limited our ability to assess the full range of potential complications with adequate statistical power. However, we did find a significant increase in preoperative recurrent laryngeal nerve dysfunction associated with obesity. This was due mostly to more locally aggressive and invasive disease. A recent NSQIP study of 26,000 thyroidectomy patients also suggested an increase in morbidity due to obesity. [20]

We found that increasing BMI was a significant predictor of increased LOS and anesthesia induction times. This suggests that obese patients consume additional hospital resources during thyroid cancer treatment.

Given our findings, we believe that obese patients are at a higher risk of developing aggressive thyroid cancers and thus should be screened for thyroid cancer by sonography, which has been shown to be more sensitive in detecting thyroid cancer than by physical examination alone. [21] Patients more likely to benefit from screening are those who are overweight, obese, or morbidly obese and those over the age of 45, who, by AJCC stage definition, have a higher risk of stage III or IV disease. Our recommendation mirrors a similar proposal for breast cancer screening, where studies have suggested that a more vigilant mammogram screening regimen should be instituted for obese patients.[22]

Conclusion:

Obese patients present with more advanced stage and more aggressive forms of papillary thyroid cancer. This suggests that obese patients should be screened for thyroid cancer.

STATISTICAL ANALYSIS:

In the data analysis we evaluated the association between body mass index (BMI) and the outcome measures including disease stage at presentation, histologic subtype, duration of anesthetic induction and extubation, duration of surgery, surgical complications, length of hospital stay, and American Society of Anesthesiologists (ASA) class. The analysis was done with and without adjustment for other covariates that may confound the association between BMI and the outcome measures.

Some of the main variables were coded as follows. BMI was calculated as weight in kilograms divided by height in meters squared. This variable was categories into four groups: normal (18.5 – 24.9), overweight (25-29.9), obese (30-39.9), and morbidly obese (>=40). Histopathologic subtype was separated into four groups: papillary, papillary with follicular variant, papillary microcarcinoma, or other (hyalinizing, tall cell, or sclerosing). Surgical time was defined as the time from incision to closure. Anesthesia induction time was defined as anesthesia start time to surgical incision time.

The analysis included 443 patients. We compared these patients in terms of their demographics, clinical characteristics, and the main outcome measures across the four BMI categories. Data were summarized using sample means (SDs) and frequencies (percentages) for continuous and categorical variables, respectively. Comparisons across the BMI groups in univariate analyses were carried out using the Chi-squared test (for categorical variables) and one-way ANOVA (for continuous variables).

In particular, prior to fitting ANOVA models, we examined if the continuous variables followed normal distributions using Q-Q plot and Kolmogorov-Smirnov test. None of the

variables showed significant deviations from normality, so they were analyzed using ANOVA models without data transformation. Since ANOVA assumes equal variance across the groups (here defined by BMI), we tested equality of the variances and the results indicated that the data variation was about the same between the BMI groups. We also screened for potential outliers and influential data points pre- and post-model fitting. None of the data points exerted undue influence and the results were almost unchanged by running the analyses with and without outliers and influential points.

The association between BMI and the outcome measures were further evaluated in multivariable regression analyses, adjusting for covariates that may confound the association between the main predictor BMI and the outcomes. Linear regression models were applied to continuous outcome measures. The model included three dummy variables for BMI, representing overweight, obese, and morbidly obese and treating the normal level as reference. Similar procedures as described previously were used to check normality of outcome variables. Scatter plots of residuals versus the predicted values were used to examine the constant variance assumption and scatter plots of residuals versus predictors (continuous) were used to check whether the linearity assumption holds. No serious departures from these assumptions were found.

Logistic regression was also used to study the association between BMI and the categorical outcome variables (dichotomized) while adjusting for other covariates. In particular, the AJCC stage was classified as being III or IV versus I or II, and we predicted the risk of advanced stages (III or IV) in our logistic regression models. BMI was entered the model as a categorical variable with the normal level as the reference group, similar to the linear regression analyses outlines above. We evaluated the odds ratio of stages III or IV associated with each level of BMI as

compared to the reference level (normal) and calculated the 95% confidence intervals for the odds ratios. Such analysis was conducted in the whole cohort (N = 443), as well as in sub-samples including: (1) those >= 45 years old (N = 256); (2) the whole cohort excluding tall cell variant (N = 429); (3) the whole cohort excluding microcarcinomas (N = 120); (4) men only (N = 120); (5) women only (N = 323). We used standardized Pearson residuals and DFBETAs to screen for possible outliers and influential data points. No data points exerted undue impact on the parameter estimates. Note that logistic regression assumes that the log odds of the outcome is linear in continuous predictors. We compared the empirical logit of the outcome with the model-based logit and concluded that the linearity assumption was approximately held. Further, the Hosmer- Lemeshow test confirmed an overall adequate fit of the model.

All tests were two-sided. A p-value < 0.05 was considered statistically significant. Analyses were conducted using STATA/SE v.11 statistical software (StataCorp).

APPENDIX :

Table 1 : **Surgical Complications ICD-9-CM index codes**

SURGICAL COMPLICATIONS

	Code	Number	Description
Hemorrhagic Complications	ICD-9D	998.1	Hemorrhage, hematoma, or seroma complicating a procedure
	ICD-9D	998.11	Hemorrhage complicating a procedure
	ICD-9D	998.12	Hematoma complicating a procedure
	ICD-9D	998.13	Seroma complicating a procedure
	ICD-9D	998.2	Accidental puncture or laceration during a procedure
	ICD-9D	E870.0	Surgical operation
	ICD-9P	6.01	Aspiration of thyroid field
	ICD-	6.02	Reopening of wound of thyroid field

	9P		
	ICD-9P	39.98	Control of hemorrhage, not otherwise specified
	ICD-9P	99.04	Transfusion of packed cells
Respiratory Complications	ICD-9D	465	Acute upper respiratory infections of multiple or unspecified sites
	ICD-9D	465.9	Acute upper respiratory infections of multiple or unspecified sites - Unspecified site
	ICD-9D	482	Other bacterial pneumonia
	ICD-9D	482.0	Pneumonia due to Klebsiella pneumoniae
	ICD-9D	482.1	Pneumonia due to Pseudomonas
	ICD-9D	482.2	Pneumonia due to Hemophilus influenzae

ICD-9D	482.41	Methicillin susceptible pneumonia due to Staphylococcus aureus
ICD-9D	482.82	Pneumonia due to other specified bacteria - Escherichia coli
ICD-9D	482.83	Pneumonia due to other specified bacteria - Other gram-negative bacteria
ICD-9D	486	Pneumonia, organism unspecified
ICD-9D	511.9	Pleurisy - Unspecified pleural effusion
ICD-9D	518	Other diseases of lung
ICD-9D	518.0	Pulmonary collapse
ICD-9D	518.4	Acute edema of lung, unspecified
ICD-9D	518.5	Pulmonary insufficiency following trauma and surgery
ICD-	518.81	Acute respiratory failure

	9D		
	ICD-9D	518.82	Other pulmonary insufficiency, not elsewhere classified
	ICD-9D	518.84	Acute and chronic respiratory failure
	ICD-9D	799.1	Other ill-defined and unknown causes of morbidity and mortality - Respiratory arrest
	ICD-9D	997.3	Complications affecting specified body systems, not elsewhere classified - Respiratory complications
Neurologic complications and issues related to recurrent laryngeal nerve dysfunction	ICD-9D	478.3	Paralysis of vocal cords or larynx
	ICD-9D	478.31	Paralysis of vocal cords or larynx - Unilateral, partial

	ICD-9D	478.32	Paralysis of vocal cords or larynx - Unilateral, complete
	ICD-9D	478.33	Paralysis of vocal cords or larynx - Bilateral, partial
	ICD-9D	478.34	Paralysis of vocal cords or larynx - Bilateral, complete
	ICD-9D	784.49	Voice disturbance- Other (Change in voice, dysphonia, hoarseness, hypernasality, hyponasality)
Wound-related complicaitons	ICD-9D	682.1	Other cellulitis and abscess - Neck
	ICD-9D	998.3	Disruption of wound
	ICD-9D	998.31	Disruption of internal operation (surgical) wound
	ICD-9D	998.32	Disruption of external operation (surgical) wound
	ICD-	998.5	Postoperative infection

	9D		
	ICD-9D	998.51	Infected postoperative seroma
	ICD-9D	998.59	Other postoperative infection
	ICD-9D	998.83	Non-healing surgical wound
	ICD-9P	86.04	Other incision with drainage of skin and subcutaneous tissue
	ICD-9P	86.22	Excisional debridement of wound, infection, or burn
Hypocalcemia	ICD-9D	252.1	Hypoparathyroidism - tetany
	ICD-9D	275.4	Disorders of calcium metabolism
	ICD-9D	275.41	Hypocalcemia

	ICD-9D	781.7	Tetany (carpopedal spasm)
Complications from Re-intubation	ICD-9P	31.1	Temporary tracheostomy
	ICD-9P	31.21	Permanent tracheostomy- Mediastinal tracheostomy
	ICD-9P	31.29	Permanent tracheostomy- Other permanent tracheostomy
	ICD-9P	96.04	Insertion of endotracheal tube
	ICD-9P	96.70	Invasive mechanical ventilation NOS
	ICD-9P	96.71	Continuous invasive mechanical ventilation for less than 96 consecutive hours
	ICD-9P	96.72	Continuous invasive mechanical ventilation for 96 consecutive hours or more

Cerebrovascular accidents	ICD-9D	997.0	Complications affecting specified body systems, not elsewhere classified - Nervous system complications
	ICD-9D	997.01	Central nervous system complication (Anoxic brain damage; Cerebral hypoxia)
	ICD-9D	997.02	Iatrogenic cerebrovascular infarction or hemorrhage
	ICD-9D	997.09	Other nervous system complications

ICD9-D : Diagnosis codes

ICD-9P : Procedure codes

Table 2

Patient demographics and clinical characteristics (n = 443)

	Body Mass Index				
Predictors	**Normal 18.5-24.9 kg/m^2**	**Overweight 25-29.9 kg/m^2**	**Obese 30-39.9 kg/m^2**	**Morbidly Obese ≥40 kg/m^2**	***p* value**
Age, years[b]					
Mean (s.d.)	44.9 (15.4)	51.5 (15.2)	50.3 (12.9)	48.3 (10.4)	0.0006*
Sex[a] [row %]					
Male	30 (25.0)	52 (43.3)	32 (26.7)	6 (5.0)	0.001*
Female	145 (44.9)	89 (27.6)	67 (20.7)	22 (6.8)	
Race[a] [row %]					
Caucasian	117 (36.6)	103 (32.2)	77 (24.0)	23 (7.2)	0.0005*
African-American	0 (0)	7 (38.9)	8 (44.4)	3 (16.7)	
Asian/Pacific Islander	45 (59.2)	19 (25.0)	10 (13.2)	2 (2.6)	
Other/Undetermined	13 (44.8)	12 (41.4)	4 (13.8)	0 (0)	
ASA Class[a] [row %]					

1	21 (63.6)	9 (27.3)	3 (9.1)	0 (0)	0.0005*
2	139 (44.8)	97 (31.3)	61 (19.7)	13 (4.2)	
3	13 (13.7)	33 (34.7)	34 (35.8)	15 (15.8)	
4	0 (0)	0 (0)	1 (100.0)	0 (0)	
Admission type [row %]					
Inpatient	148 (40.7)	113 (31.1)	82 (22.6)	20 (5.5)	0.352
Ambulatory (<23 hours)	27 (33.8)	28 (35)	17 (21.3)	8 (10)	

Cells sum horizontally.

[a]Chi Square

[b]Oneway ANOVA

*p<0.05

Table 3

Association of BMI with Stage and Histology

	Body Mass Index				
Predictors	**Normal 18.5-24.9 kg/m^2**	**Overweight 25-29.9 kg/m^2**	**Obese 30-39.9 kg/m^2**	**Morbidly Obese ≥40 kg/m^2**	***p* value**
AJCC Stage[a] [column %]					
I	144 (82.3)	99 (70.2)	69 (69.7)	18 (64.3)	0.035*
II	8 (4.5)	10 (7.1)	6 (6.1)	0 (0)	
III	15 (8.6)	15 (10.6)	9 (9.1)	6 (21.4)	
IV	8 (4.6)	17 (12.1)	15 (15.1)	4 (14.3)	
Papillary subtype Cancer Histology[a] [column %]					
Papillary	92 (52.6)	73 (51.8)	46 (46.5)	11 (39.3)	0.16
Papillary w/ follicular variant	43 (24.5)	44 (31.2)	24	6 (21.5)	

			(24.2)		
Papillary microcarcinoma	32 (4.6)	21 (14.9)	20 (20.2)	9 (32.1)	
Other	8 (18.3)	3 (2.1)	9 (9.1)	2 (7.1)	
Tumor size, cm[b]					
Mean (s.d.)	1.53 (1.11)	1.71 (1.50)	2.03 (1.99)	2.12 (2.90)	0.06†
Tall Cell Variant PTC[a] [column %]					
Absent	173 (98.9)	138 (97.9)	92 (92.9)	26 (92.9)	0.027*
Present	2 (1.1)	3 (2.1)	7 (7.1)	2 (7.1)	

Cells sum vertically.

[a]Chi Square

[b]Oneway ANOVA

*p<0.05

†trend

Table 4

Univariate analyses

	Body Mass Index				
Predictors	**Normal 18.5-24.9 kg/m^2**	**Overweight 25-29.9 kg/m^2**	**Obese 30-39.9 kg/m^2**	**Morbidly Obese ≥40 kg/m^2**	***p* value**
No. Surgical Complications[a]					
0	141	104	75	19	0.62
≥1	7	9	7	1	
Anesthesia Induction Time, min.[b]					
Mean (s.d.)	34.0 (16.6)	33.8 (17.8)	41.4 (21.0)	43.1 (21.3)	0.0009*
Extubation Time, min.[b]					
Mean (s.d.)	11.7 (7.4)	13.5 (12.4)	15.6 (16.4)	13.1 (8.0)	0.06†
Surgical Time, min.[b]					
Mean (s.d.)	148 (64)	156 (77)	171 (92)	171 (93)	0.10†

Length of stay, days[b]					
Mean (s.d.)	1.8 (1.1)	2.3 (1.9)	2.7 (1.9)	2.4 (1.9)	0.0004*

[a]Chi Square

[b]Oneway ANOVA

*$p < 0.05$

†trend

Table 5

Multivariable analyses

	Body Mass Index			
Predictors	**Normal 18.5-24.9 kg/m^2**	**Overweight 25-29.9 kg/m^2**	**Obese 30-39.9 kg/m^2**	**Morbidly Obese ≥40 kg/m^2**
Presenting with AJCC Stage III or IV (whole cohort)[a]				
Odds ratio	ref	1.94*	2.11*	3.67**
(95% C. I.)		(1.07 -3.50)	(1.20-3.99)	(1.51-8.93)
Presenting with AJCC Stage III or IV (For those ≥ 45 y.o. only, n=256)[a]				
Odds ratio	ref	1.32	1.57	3.66*
(95% C. I.)		0.70-2.52	0.78-3.18	1.24-10.24
Presenting with AJCC Stage III or IV (excluding tall cell variant, n=429)[a]				

Odds ratio	ref	1.81†	1.70	2.90*
(95% C. I.)		0.997-3.29	0.87-3.31	1.13-7.43
Presenting with AJCC Stage III or IV (excluding microcarcinomas, n=361)[a]				
Odds ratio	ref	2.02*	2.24*	5.22*
(95% C. I.)		1.09-3.75	1.14-4.41	1.90-14.39
Presenting with AJCC Stage III or IV (for men only, n=120)[a]				
Odds ratio	ref	2.89	3.40	6.35†
(95% C. I.)		0.86-9.65	0.94-12.2	0.94-44.1
Presenting with AJCC Stage III or IV (for women only, n=323)[a]				
Odds ratio	ref	1.45	1.59	3.09*
(95% C. I.)		0.70-3.00	0.74-3.46	1.11-8.57

[a] Logistic regression

*$p < 0.05$

**p < 0.01

†trend

Ref=reference category

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