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Morphomic analysis as an aid for preoperative risk stratification in patients undergoing major head and neck cancer surgery

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Abstract

Background—Patients undergoing major head and neck cancer surgery (MHNCS) may develop significant postoperative complications. To minimize the risk of complications, clinicians often assess multiple measures of preoperative health in terms of medical comorbidities. One emerging method to decrease surgical complications is preoperative assessment of patient frailty measured by specific tissue characteristics. We hypothesize that morphomic characteristics of the temporalis region serve as predictive markers for the development of complications after MHNCS.

Methods—We performed a retrospective review of 69 patients with available computed tomography (CT) imaging who underwent MHNCS from 2006–2012. To measure temporalis region characteristics, we used morphomic analysis of available preoperative CT scans to map out the region. All available CT scans had been performed as part of the patient's routine work-up and were not ordered for morphomic analysis. We describe the correlation among temporalis fat pad volume (TFPV), mean zygomatic arch thickness, and incidence of postoperative complications.

Results—We noted significant difference in the zygomatic bone thickness and TFPV between patients who had medical complications, surgical complications, or total major complications and those who did not. Furthermore, by use of binary logistic regression, our data suggest decreased TFPV and zygomatic arch thickness are stronger predictors of developing postoperative complications than previously studies preoperative characteristics.

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Conclusions—We describe morphomic analysis of the temporalis region in patients undergoing MHNCS to identify patients at risk for complications. Regional anatomic morphology may serve as a marker to objectively determine a patient's overall health. Use of the temporalis region is appropriate in patients undergoing MHNCS because of the availability of preoperative scans as part of routine work up for head and/or neck cancer.

Keywords

Head and neck cancer; Morphomics; Temporal fat pad; Zygomatic bone; Outcomes

1. Introduction

There is considerable debate as to whether surgical resection or nonsurgical management with chemotherapy and radiation therapy results in the best long-term quality of life for patients with advanced head and neck cancer. Major head and neck cancer surgery (MHNCS) exposes patients to a variety of postoperative complications. To optimize patient selection and postoperative management, patient characteristics such as age and medical comorbidities are considered before performing MHNCS. Recent studies have tried to elucidate the correlation between other patient characteristics such as American Society of Anesthesiologists (ASA) risk classification, smoking, preoperative hemoglobin, and perioperative crystalloid replacement and incidence of postoperative outcomes [1–12]. However, the correlation between patient frailty and postoperative outcomes after MHNCS remains unexplored.

Frailty is recognized as a syndromic condition due to the involvement of multiple organ systems [13]. By objectively measuring frailty, clinicians may form a robust portrait of the patient's overall health. Frailty can be measured in a variety of ways including loss of muscle and fat (sarcopenia) or diminished bone density [14]. Morphomic characteristics of the psoas muscle have also been shown to correlate with other measures of patient frailty and predict postsurgical outcomes [15–17]. Recently, we have shown that temporalis muscle dimensions may be used as a predictor of patient age and correlates well with psoas muscle characteristics [18]. Patients undergoing MHNCS often have preoperative computed tomography (CT) scans as part of their routine work up. We hypothesize that preoperative assessment of patient frailty using morphomic analysis of the temporalis region using available CT scans may aid in stratifying patients at risk for significant complications after MHNCS.

2. Methods

2.1. Patient data collection

This study was approved by the University of Michigan Institutional Review Board. We performed a retrospective review of 69 patients with head and neck cancer who underwent tumor resection with neck dissection from 2006–2012, and had available preoperative CT scans. Variables of interest included patient age, preoperative laboratory values, medical comorbidities, and surgical procedure. Postoperative medical and surgical complications were recorded. Surgical complications were defined as adverse events at the local site of

dissection or tumor excision, whereas medical complications were defined as any systemic adverse event distant from the surgical site. All data were acquired from a comprehensive review of patient charts with at least 1 y of follow up.

2.2. Image processing

All patients included in this study received preoperative CT scans as part of their routine work up for head and/or neck cancer. Archived CT scans were acquired using the Voxar 3D Workstation (Toshiba; Barco, Kortrijk, Belgium). Three landmarks were used to define the temporalis region—external meatus, mandibular coronoid process, and the anterior aspect of the medial orbital rim. These landmarks were placed by two individuals blinded to the outcome; and subsequently, the landmarks were verified by a surgeon who was also blinded to patient information. Temporalis fat pad and zygomatic arch were identified based on radiographic density using Hounsfield units. Temporalis fat pad volume (TFPV) and zygomatic arch thickness were both quantified using software designed in MATLAB version 13.0 (MathWorks, Natick, MA; Fig. 1). These values are relative values and would likely vary if different landmarks were chosen.

2.3. Statistical analysis

TFPV and zygomatic arch thickness were divided into quartiles. Univariate analysis was used to determine the correlation between TFPV or zygomatic arch thickness quartile and incidence of postoperative complications. Binary logistic regression was used to determine whether TFPV and zygomatic bone density were independent predictors of postoperative complications. Receiver operating characteristic (ROC) curves were developed using zygomatic arch thickness and TFPV as independent variables and complications (overall, medical, or surgical) as the dependent variable. Binary logistic regression was used to obtain predicted probabilities of complications using arch thickness and TFPV as independent variables; a separate ROC curve was developed using the predicted probabilities as the independent variable and complication as the dependent variable. All statistical analyses were performed using SPSS Statistics version 21 (SAS Institute, Inc, Cary, NC).

3. Results

3.1. Population description

A total of 69 patients who underwent MHNCS with an available preoperative CT scan were included in this retrospective study. The overall demographic, medical, and surgical characteristics of the population are indicated in Table 1. The mean standard deviation (SD) age of the HNC cohort was 60.8 y (11.4), and the mean SD weight was 79.7 kg (22.7). The gender makeup consisted of 28.0% females ($n = 19$) and 72.0% males ($n = 50$). The mean SD body mass index was 26.8 (7.0), and the mean ASA score was 3.00. Comorbidities included diabetes in 13.0% ($n = 9$), coronary artery disease in 17.0% ($n = 12$), chronic obstructive pulmonary disease in 4.0% ($n = 3$), and a history of smoking in 65.0% ($n = 45$) of patients. Breakdown by surgery type can be found in Table 2.

In total, 19 patients (27.5%) developed major postoperative complications (Table 3). Wound infection was the most common complication ($n = 8$, 11.6%) followed by respiratory illness

and/or pneumonia ($n = 4$, 5.0%). Flap-associated complications included failure or partial necrosis ($n = 3$, 4.35%) and wound breakdown ($n = 3$, 4.35%).

3.2. Association between complications and patient characteristics

We next examined the univariate odds of developing major postoperative complications (medical and surgical) based on various preoperative characteristics using binary logistic regression analysis. Data demonstrate that age, ASA score, tobacco use, and preoperative morbidities (diabetes, coronary artery disease, and chronic obstructive pulmonary disease) did not increase patients' odds of developing major postoperative complications in a statistically significant manner. Patients who underwent tumor excision with unilateral neck dissection were at significantly decreased odds of developing postoperative complication (odds ratio [OR] 0.12, 95% confidence interval [CI] [0.02–0.94], $P < 0.04$) (Results not shown). Moreover, when comparing albumin (OR 0.15, 95% CI [0.03–0.84], $P = 0.03$), preoperative chemotherapy (OR 4.15, 95% CI [1.09–15.83], $P = 0.04$), and preoperative radiation (OR 6.40, 95% CI [1.06–38.47] $P = 0.04$), there was a significant relationship with development of major postoperative complications. However, when comparing these preoperative markers with medical and surgical complications independently, results were not significant (Table 4).

3.3. Morphomic analysis of TFPV and zygomatic arch thickness

The mean zygomatic arch thickness was 2.69 mm (SD 0.54 mm) and mean TFPV was 1337 mm³ (SD 881 mm³). These two measurements were positively correlated ($r = 0.559$, $P < 0.001$). We further stratified the morphomic data by quartiles listed from smallest to largest for TFPV (mean, SD): (515.9, 203), (939.9, 114), (1358, 173), (2472, 909); and zygomatic arch thickness: (2.03, 0.21), (2.46, 0.09), (2.81, 0.13), (3.41, 0.26).

3.4. Correlation between morphomic parameters and frequency of major postoperative complications

Average zygomatic arch thickness was significantly smaller in patients who developed postoperative complications 2.40 mm (SD 0.47) compared with patients without complications 2.80 mm (SD 0.53; P value 0.0061). Similarly, patient who developed complications had significantly smaller TFPV compared with those who did not (991 mm³ versus 1469 mm³ P value 0.043).

3.5. Frequency of postoperative complication based on TFPV and zygomatic arch thickness quartile

Frequency of postoperative complication decreased with increases in zygomatic arch thickness by quartile (Fig. 2). A similar trend was observed with respect to TFPV (Fig. 3). Patients in the largest quartile of zygomatic arch thickness had a 36% reduction in major complication compared with patients in the smallest quartile. Patients in the largest TFPV quartile had a 42% reduction in major postoperative complication compared with patients in the smallest quartile.

3.6. Univariate analysis of zygomatic arch thickness and TFPV quartiles

Univariate analysis was performed to determine whether decreasing zygomatic arch thickness or TFPV quartile is associated with increasing odds of complications (Table 5). The odds of complications in the highest quartile of arch thickness (OR 0.07, 95% CI [0.01–0.66]) were significantly lower than the odds of complications in the lowest quartile (OR 1.00; $P < 0.05$). We noted a similar finding for the highest TFPV quartile (OR 0.06, 95% CI [0.01–0.52]) when compared with the lowest TFPV quartile (OR 1.00; $P < 0.05$). Analysis of variance confirmed no significant differences in the TFPV ($P = 0.15$) or zygomatic arch thickness ($P = 0.71$) among patients treated with different surgery types.

3.7. Zygomatic arch thickness or TFPV as independent tests for complications

Separate ROC curves were designed using zygomatic arch thickness or TFPV as tests for medical, surgical, or any major complication (Fig. 4). Area under the curves (AUC) for each variable was determined. TFPV was a better test for surgical complications in comparison with zygomatic arch thickness (AUC 0.719 and 0.684, respectively). The AUC for zygomatic arch thickness and TFPV with respect to medical complications were similar (AUC 0.642 and 0.637, respectively). When looking at overall major complications, zygomatic arch thickness served as a better test than TFPV (AUC 0.703 and 0.667, respectively). A binary logistic regression was performed using combination of zygomatic arch thickness and TFPV as covariates and complications as the outcome (Fig. 4). The AUC was 0.707, suggesting a combination of covariates provides a marginal improvement in testing for major postoperative complications.

4. Discussion

A reliable and accurate method that can identify patients at greatest risk for complications after MHNCS is important for patient selection and appropriate patient counseling. Previous studies have identified several potential predictors of postoperative mortality including patient age, comorbidities, smoking status, preoperative hemoglobin, and perioperative fluid management [11,12,19–22]. Up to this point, preoperative risk for individual patients has been estimated based on several categorical variables with little reduction in the postoperative complication rate. By using univariate analysis, we noted significant increase in odds of complications in patients within the lowest quartile of zygomatic arch thickness or TFPV. Furthermore, the trend between TFPV and complication rate follows previously published research using the temporalis as a predictor of postoperative complications after surgery for nonsyndromic craniosynostosis [23,24].

The use of CT imaging to identify morphologic characteristics, which portend a higher risk of postoperative complication remains in its infancy. This technique of morphologic study, known as morphomic analysis, allows clinicians to map out the three-dimensional anatomy of specific muscles, fat pads, and bone. By objectively quantifying the patient's tissue characteristics such as volume and thickness, surgeons may be able to produce a more complete picture of the patient's "morphologic age" and overall "fitness", a concept previously described in general and vascular abdominal surgery. Frailty, measured by core muscle size, has been shown to predict mortality after elective aortic aneurysm repair.

Furthermore, quantifying patient frailty has been shown to be useful in predicting outcome in patients with adrenocortical carcinoma by focusing on the psoas muscle and intra-abdominal fat characteristics [25]. Morphologic variations among patients have also been shown to predict liver transplant morbidity, surgical site infection, and length of stay and mortality in patients undergoing general and vascular surgery [26–28]. This method of morphomic analysis confers several advantages including the inter-institutional reproducibility of CT imaging, the ability to objectively assess these scans using programmed software, and the real-time nature of this data.

Our goal is to extend the use of morphomic analysis as an objective measure of patient frailty to assess the risk of patient complications after reconstruction for head and neck cancer patients. Our study specifically addresses the relationship between risk of complications and temporalis muscle and temporal fat pad characteristics and zygomatic arch thickness. The temporal fat pad size and zygomatic arch thickness have previously been shown to predict surgical complications and length of hospital stay in patients undergoing non-syndromic craniosynostosis and mandibular fractures [23,24]. Similar to these previous findings, we demonstrate patients in the largest quartile for TFPV and zygomatic arch thickness were significantly less likely to develop major postoperative complications compared with patients in the smallest quartiles. More specifically, the frequency of complication in the smallest quartiles of TFPV and arch thickness increased by 42 and 36%, respectively. Patients in the smallest morphomic quartiles may benefit from a nonsurgical approach to therapy (i.e., radiation and chemotherapy) due to increased likelihood of major postoperative complications although this deserves further attention with a larger cohort of patients.

In this analysis, we also use ROC curves to determine whether TFPV and/or zygomatic arch thickness may be used as tests for major complications. ROC curves are developed by plotting the sensitivity (y-axis) *versus* 1-specificity (x-axis). Increases in the 1-specificity term represent a lowering of the threshold “positive” reading. For example, the 1-specificity term would increase in our model by lowering the TFPV or zygomatic arch thickness cut-off value defined as “positive”; this positive value would signify a concern for major complication. The AUC represents the probability that our test using zygomatic arch thickness, TFPV, or both, will correctly classify a patient known to have a complication. We found that the AUC for using a zygomatic arch thickness and TFPV as a combined test for complications was 0.707 suggests that our test has a 70% probability of correctly classifying patients. This is a reasonable probability although refinements will be necessary to increase our AUC, including possibly other preoperative markers and greater cohort size.

This study has multiple limitations including a relatively small cohort size. In addition, this retrospective study represents multiple surgeons’ experiences at the University of Michigan. We hope to further expand on our results in the future and include a larger cohort of patients from multiple institutions. Next, this study examines patients who underwent various MHNC surgeries. Our analysis did examine the odds of developing postoperative complications with respect to surgery type; however, we did not perform multivariable logistic regression analysis because of limited cohort size and limited number of outcomes (complications). Additionally, we chose our three landmarks on which to analyze based on

ease of location and reliability among users. The position of the landmarks was validated by a single surgeon who ensured inter-rater reliability among users. It is possible that different landmarks may provide a more sensitive value of the temporalis region. We are currently working to enhance our landmarks to allow for easier automation.

The goal of this study was to assess the utility of analysis to predict postoperative complications and to compare this with other preoperative characteristics. In the future, we will apply morphomic parameters to generate an index that will help clinicians stratify patients into reliable and reproducible risk categories that will aid both the patient and the surgeon in assessing the hazards of surgery and in determining the most appropriate treatment plan for each individual afflicted with this devastating disease. By doing so, high-risk surgical patients may be guided to a more conservative management approach (i.e., chemotherapy and radiation). By having objective morphomic data, surgeons may have a more complete picture of patients' overall health before surgery. This may allow the surgeon to counsel and prepare the patient before surgery, assess risk for undertaking the operation, and potentially implement measures to reduce the incidence of major postoperative complications. Furthermore, future work should examine the utility of morphomics on assessing frailty in nonoperative HNC patients. This novel application has the potential to assist oncologists with selecting the best chemotherapy and/or radiation regimen and objectively tailoring therapy to reduce morbidity and mortality. Additional future studies in our laboratory are focused on developing bedside methodologies to assess prospective frailty using ultrasound assessment of the temporal region.

5. Conclusions

MHNCS represents a complex surgical procedure with multiple variables exposing patients to a variety of postoperative complications. Morphomic analysis may help stratify patients into high-risk categories. We demonstrate that decreased TFPV and zygomatic arch thickness are associated with increased odds of experiencing major postoperative complications. Therefore, patients with diminished morphomic parameters may benefit from undergoing shorter and less complex reconstructions or alternative treatment strategies.

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Fig. 1. Cross-section computed tomographic analysis displaying isolated TFPV (yellow) and zygomatic arch thickness (arrow) using morphomic analysis. (Color version of the figure is available online.)

Fig. 2.

Frequency of postoperative complication with patients stratified into quartiles of zygomatic arch thickness. Surgical, medical, and overall major complication frequencies are demonstrated. (Color version of the figure is available online.)

Fig. 3.

Frequency of postoperative complication with patients stratified into quartiles of TFPV. Surgical, medical, and overall major complication frequencies are demonstrated. (Color version of the figure is available online.)

Fig. 4.

ROC curve showing TFPV (green) and zygomatic arch thickness (blue) as independent tests for medical (A), surgical (B), and overall major complication (C), and combination of TFPV and zygomatic arch thickness for major medical complication (D). AUC is displayed in each separate ROC plot. (Color version of the figure is available online.)

Table 1General patient demographics ($n = 69$).

Characteristics	Data
Age at treatment (y), mean $\pm$ SD	60.8 $\pm$ 11.4
Weight (kg), mean $\pm$ SD	79.7 $\pm$ 22.7
Gender, n (%)	
Female	19 (28.0)
Male	50 (72.0)
BMI, mean $\pm$ SD	26.8 $\pm$ 7.0
ASA, mean	3.0
Diabetes, n (%)	9 (13.0)
CAD, n (%)	12 (17.0)
COPD, n (%)	3 (4.0)
Smoke within last 5 y, n (%)	45 (65.0)
Preoperative hgb, mean $\pm$ SD	13.4 $\pm$ 1.8
Preoperative creatinine, mean $\pm$ SD	0.90 $\pm$ 0.41

BMI = body mass index; CAD = coronary artery disease; COPD = chronic obstructive pulmonary disease; hgb = hemoglobin.

Table 2

Description and frequency of MHNCS performed.

Type of surgery	<i>n</i> (%)
Excision of tumor with local closure	6 (8.5)
Excision of tumor + unilateral neck dissection	19 (26.8)
Excision of tumor + bilateral neck dissection	18 (25.4)
Excision of tumor + flap closure (no neck dissection)	2 (2.8)
Excision of tumor + unilateral neck dissection + flap closure	18 (25.4)
Excision of tumor + bilateral neck dissection + flap closure	6 (11.3)

Table 3

Summary of major medical and surgical complications.

Major complication	<i>n</i> (%)
Medical	
Myocardial infarction	0 (0.00)
Congestive heart failure	0 (0.00)
Atrial fibrillation	0 (0.00)
Stroke	0 (0.00)
Thromboembolism	3 (4.35)
Pneumonia/respiratory	4 (5.80)
Multiorgan failure	0 (0.00)
Infection (non-wound site)	3 (4.34)
Deep vein thrombosis	1 (1.44)
Other	1 (1.44)
Total major medical	12 (16.9)
Surgical	
Flap	3 (4.35)
Wound breakdown	3 (4.35)
Wound infection	8 (11.6)
Hematoma	1 (1.45)
Donor site	0 (0.00)
Return to operating room	0 (0.00)
Total major surgical	15 (21.7)

Table 4

Univariate odds of complications based on significant preoperative patient characteristics.

Characteristic	OR	95% CI	P value
Major complication			
Preoperative chemotherapy	4.15	1.09–15.83	0.04
Preoperative radiation	6.40	1.06–38.47	0.04
Albumin *	0.15	0.03–0.84	0.03
Medical complication			
Preoperative chemotherapy	3.57	0.85–15.03	0.08
Preoperative radiation	6.00	1.04–34.49	0.05
Albumin *	0.12	0.02–0.81	0.30
Surgical complication			
Preoperative chemotherapy	2.44	0.60–9.83	0.21
Preoperative radiation	1.92	0.32–11.68	0.48
Albumin *	0.59	0.18–1.92	0.39

* 50 of the patients had albumin measurement recorded in their preoperative chart.

Table 5

Binary logistic regression comparing TFPV and zygomatic bone thickness with development of medical and surgical postoperative complications split up into quartiles.

Characteristic	OR	95% CI	P value
Major complication			
TFPV quartile			
1	1.00	—	—
2 *	0.190	0.04–0.92	<0.05
3	0.44	0.11–1.74	0.24
4 *	0.06	0.01–0.52	<0.05
Arch thickness quartile			
1	1.00	—	—
2	0.47	0.11–1.93	0.29
3	0.43	0.11–1.76	0.24
4 *	0.07	0.01–0.66	<0.05
Medical complication			
TFPV quartile			
1	1.00	—	—
2	0.51	0.10–2.61	>0.05
3	0.48	0.10–2.43	>0.05
4	0.15	0.02–1.46	>0.05
Arch thickness quartile			
1	1.00	—	—
2	0.59	0.11–3.07	>0.05
3	0.54	0.11–3.17	>0.05
4	0.25	0.02–3.14	>0.05
Surgical complication			
TFPV quartile			
1	1.00	—	—
2	0.15	0.03–0.87	<0.05
3	0.43	0.11–1.76	>0.05
4 **	0.00	—	<0.001
Arch thickness quartile			
1	1.00	—	—
2	0.56	0.13–2.52	>0.05
3	0.52	0.12–2.33	>0.05
4	0.12	0.01–1.09	>0.05

TFPV = Temporalis fat pad volume,

* $P < 0.05$,

** $P < 0.01$.