Morphometric Age and Surgical Risk

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BACKGROUND: A cornerstone of a surgeon's clinical assessment of suitability for major surgery is best described as the "eyeball test." Preoperative imaging may provide objective measures of this subjective assessment by calculating a patient's morphometric age. Our hypothesis is that morphometric age is a surgical risk factor distinct from chronologic age and comorbidity and correlates with surgical mortality and length of stay.

STUDY DESIGN: This is a retrospective cohort study within a large academic medical center. Using novel analytic morphomic techniques on preoperative CT scans, a morphometric age was assigned to a random sample of patients having inpatient general and vascular abdominal surgery from 2006 to 2011. The primary outcomes for this study were postoperative mortality (1-year) and length of stay (LOS).

RESULTS: The study cohort (n = 1,370) was stratified into tertiles based on morphometric age. The postoperative risk of mortality was significantly higher in the morphometric old age group when compared with the morphometric middle age group (odds ratio 2.42, 95% CI 1.52 to 3.84, $p < 0.001$). Morphometric old age patients were predicted to have a LOS 4.6 days longer than the morphometric middle age tertile. Similar trends were appreciated when comparing morphometric middle and young age tertiles. Chronologic age correlated poorly with these outcomes. Furthermore, patients in the chronologic middle age tertile found to be of morphometric old age had significantly inferior outcomes (mortality 21.4% and mean LOS 13.8 days) compared with patients in the chronologic middle age tertile found to be of morphometric young age (mortality 4.5% and mean LOS 6.3 days, $p < 0.001$ for both).

CONCLUSIONS: Preoperative imaging can be used to assign a morphometric age to patients, which accurately predicts mortality and length of stay. (J Am Coll Surg 2013;216:976–985. © 2013 by the American College of Surgeons)

When considering a patient for major surgery, surgeons rely on clinical instinct to judge a patient's likelihood of a successful outcome. Patient age is often a central factor in this assessment, but may not accurately represent a patient's overall health, as reflected by often used phrases such as, "the patient looks older (younger) than his/her stated age." Although validated risk stratification tools exist to assist surgeons, these tools typically evaluate only 1 portion of the patient's operative risk (eg, cardiovascular health) and are helpful only when patients have advanced comorbid disease. Therefore, a surgeon's clinical decision-making is largely subjective and difficult to communicate to patients and other clinicians. Better objective measures of preoperative risk are needed.

Underlying a surgeon's subjective patient assessment, often referred to as the "eyeball test," is primarily a visual assessment of the patient's physical appearance relative to his or her stated age. Physical changes that occur with age have previously been well documented and are associated with functional and clinical health outcomes.[1-4] Furthermore, recent work has shown strong relationships between patient age, patient morphometric characteristics on preoperative imaging, and surgical outcomes after surgery.[5-13] Moreover, data in preoperative images may inform perioperative risk assessments and add objectivity to the "eyeball test."

With this work, we propose a new paradigm: using preoperative imaging studies to quantitatively assess whether patients are morphometrically younger or older

Disclosure Information: Nothing to disclose.

Financial support: Dr Englesbe is supported by NIH – NIDDK (K08 DK0827508) and the Blue Cross Blue Shield of Michigan Foundation.

Received September 6, 2012; Revised December 7, 2012; Accepted January 29, 2013.

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ISSN 1072-7515/13/$36.00
http://dx.doi.org/10.1016/j.jamcollsurg.2013.01.052

Abbreviations and Acronyms

AUROC = area under the receiver operating characteristic curve
HU = Hounsfield units
LOS = length of stay
OR = odds ratio
RVU = relative value units

than their stated age. This will provide an objective global assessment of the patient that is intuitive to clinicians and patients. Our previous work identified 3 morphometric measures that strongly correlate with surgical outcomes and advancing age (trunk muscle size, trunk muscle density, and vascular calcification).[5-10] In this study, we use a population of kidney donors and trauma patients to determine the baseline morphometric characteristics of aging. Then, for each study patient having major surgery, we use his or her morphometric characteristics to assign a morphometric age, as calibrated by our reference population. Our hypothesis was that morphometric age is a surgical risk factor distinct from chronologic age and comorbidity and correlates with surgical mortality and length of stay.

METHODS

Analytic morphomics

Our previous work has described these methods in detail.[5-10] In brief, individual vertebral levels were first identified on each patient's CT scan. The cross-sectional area and average density, in Hounsfield Units (HU), of the left and right psoas muscles at the level of the fourth lumbar vertebra (L4) were measured.

Abdominal aortic calcification was measured in the wall of the infrarenal aorta. The center of the aorta was manually located at the inferior aspect of the L1 vertebrae. The centerline and radius of the aorta were defined from this imaging slice to the inferior aspect of the L3 vertebrae. To adjust for differences in contrast, the density of the aortic lumen, in HU, was used to define the minimum window level. Calcification was selected in a semiautomatic fashion, as a group of pixels between 3 and 2,000 pixels contained in the aortic wall, with HU at least 25% greater than HU of the aortic lumen. Manual adjustments were made to capture all calcification. Given the limitations of this calcification algorithm, patients with aortic disease were excluded. Abdominal aortic calcification was expressed as percentage of the total wall area containing calcification.

All analytic morphomic procedures were completed using custom algorithms programmed in MATLAB v13.0 (MathWorks). All algorithm outputs were visually confirmed by an image processor.

Patient populations

Control population

The baseline morphometric characteristics of aging were determined using a pool of control patients. We selected 2 patient populations as controls: individuals approved as kidney donors at the University of Michigan Health System (UMHS) (n = 1,624) and a random sample of trauma patients treated at the University of Michigan Health System (n = 1,689). Kidney donors are deemed healthy by a surgeon and nephrologist before receiving a CT scan, and trauma patients likely represent a reasonable cross-section of the healthy general population. These groups were selected as controls because they were thought to best represent a patient and clinician's perception of "normal" aging. The inclusion period for the control patients was 2000 to 2010.

Study population

Our study population comprised patients in the Michigan Surgical Quality Collaborative database, who underwent major inpatient general and vascular surgery at the University of Michigan Health System and had a CT scan of the abdomen specifically for preoperative planning (within 90 days before the surgical event), from 2006 to 2011 (n = 1,370). The Michigan Surgical Quality Collaborative database represents a prospectively collected and random sample of surgical patients. The specific methods for patient selection, data collection, and data definitions have been well described previously by our group and others.[14-17] Data were collected on more than 30 preoperative risk factors, which are detailed in Table 1.

Outcomes

The primary outcomes measures for this study were mortality within 1 year of the index surgical event and length of stay (LOS). Mortality was ascertained by referencing the Social Security master death index. Length of stay was calculated from admission to discharge.

Determining morphometric age

Morphometric age was modeled within the control population using a multivariable linear regression model. For these models, the dependent variable was morphometric age, and the independent variables included previously validated morphometric characteristics (psoas area, psoas density, and percent wall aortic calcification). Separate models were created for men and women, as we described previously.[7,10]

Table 1. Patient Characteristics of the Study Population (n = 1,370) Stratified by Tertiles of Chronologic Age

Characteristic	Chronologic tertile		
	Youngest	Middle	Oldest
Demographic characteristics			
n	456	457	457
Age, y, mean ± SD	36.9 ± 8.8	55.7 ± 4.1	71.6 ± 6.6
Height, cm, mean ± SD	170.6 ± 10.6	171.7 ± 10.4	168.7 ± 11.0
Weight, kg, mean ± SD	83.1 ± 24.5	86.6 ± 24.2	80.7 ± 19.8
Body mass index, kg/m^2, mean ± SD	28.6 ± 8.3	29.3 ± 7.9	28.3 ± 6.4
Preoperative albumin, g/dL, mean ± SD	3.9 ± 0.8	4.0 ± 0.7	3.8 ± 0.7
Clinical characteristics, n (%)			
Male sex	213 (46.7)	255 (55.8)	252 (55.1)
Nonwhite race	89 (19.5)	74 (16.2)	59 (12.9)
Diabetes mellitus	44 (9.6)	76 (16.6)	128 (28.0)
Smoker	85 (18.6)	90 (19.7)	45 (9.8)
Nonindependent functional status	23 (5.0)	33 (7.2)	46 (10.1)
COPD	10 (2.2)	18 (3.9)	31 (6.8)
Recent transient ischemic attack	4 (0.9)	2 (0.4)	18 (3.9)
Cancer diagnosis	25 (5.5)	43 (9.4)	33 (7.2)
Currently receiving radiotherapy	2 (0.4)	17 (3.7)	23 (5.0)
Currently receiving chemotherapy	12 (2.6)	27 (5.9)	22 (4.8)
Taking preoperative steroids	46 (10.1)	40 (8.8)	36 (7.9)
Preoperative sepsis	51 (11.2)	30 (6.6)	29 (6.3)
Peripheral vascular disease	3 (0.7)	13 (2.8)	13 (2.8)
Ascites	8 (1.8)	4 (0.9)	6 (1.3)
Case mix characteristics, n (%)			
Emergent priority	74 (16.2)	49 (10.7)	45 (9.8)
Liver resection	15 (3.3)	22 (4.8)	23 (5.0)
Pancreatic resection	17 (3.7)	51 (11.2)	68 (14.9)
Major vascular	24 (5.3)	23 (5.0)	32 (7.0)
Other general surgery	400 (87.7)	361 (79.0)	334 (73.1)

There were some important differences between the control and study populations with respect to chronologic age and sex distribution. To address this issue, control patients were selected for inclusion using an SAS Greedy Matching algorithm (based on chronologic age and sex in a 1:1 fashion). The morphometric age models were then applied to each study population patient in order to determine morphometric age.

As a sensitivity analysis, morphometric age was also determined using an alternative method. Instead of using matching algorithms for the control and study populations, mean morphometric measures for control patients of the same chronologic age and sex were calculated. Morphometric age was then modeled using this control population (separate models for sexes) and the model was subsequently used for the study patients to determine their morphometric age. All analyses were repeated using this second method, with negligible differences in outcomes and no differences in conclusions. As a result, the initial method of determination of morphometric age is reported.

Outcomes analyses

Continuous variables were compared using a *t*-test, and Fisher's exact test was used to compare categorical variables. The relationship between burden of comorbid disease, morphometric age, and chronologic age was further assessed. Patients were assigned a point for each comorbid condition collected by the Michigan Surgical Quality Collaborative. Three groups of patients were selected: the 10% oldest chronologic age, the 10% oldest morphometric age, and the 10% with the most comorbidities. These groups were compared using a Venn diagram.

In order to determine whether chronologic and morphometric age were independently associated with mortality and LOS, multivariable logistic and linear regression was performed using stepwise backward selection to identify a set of model covariates from the

candidate variables previously detailed. Each patient was put into a tertile for both chronologic age and morphometric age. Separate models were created for chronologic age (mortality and LOS) and morphometric age (mortality and LOS). For the logistic models, the reference age population was the middle tertile and the outputs are expressed as odds ratios (OR) ± 95% CI compared with the middle tertile group.

The implications of age adjustment were then assessed by comparing patients of the same chronologic age group, but who "jumped" into older and younger age groups after morphometric age adjustment. First, we compared outcomes among patients from the middle chronologic age group who jumped either to the young or the old morphometric age group. Next, we compared the outcomes of patients from the youngest chronologic age group who jumped to the oldest morphometric age group and the patients from the oldest chronologic age group who jumped into the youngest morphometric age group. These comparisons used a *t*-test or Fischer's exact test.

All analyses were performed using SAS v9.1. A 2-sided significance of alpha = 0.05 was used for all analyses. This study was approved by the University of Michigan Institutional Review Board with a waiver of informed consent for subjects.

RESULTS

Control population

The mean (± SD) chronologic age of this group was 41.1 ± 14.8 years and 54.7% were male. The mean psoas muscle area for men was (3,266.3 ± 725.1 mm^2) and for women was (1,919.7 ± 447.2 mm^2). The mean psoas muscle density for men was (57.1 ± 7.5 HU) and for women was (54.5 ± 7.4 HU). The mean percent aortic wall calcification for men was (2.5% ± 7.3%) and for women was (1.9% ± 6.8%). There was a linear relationship between chronologic age and mean psoas muscle area for men ($y = -20.69x + 4098.4$, $r = -0.43$) and for women ($y = -12.84x + 2461$, $r = -0.41$). There was a linear relationship between chronologic age and mean psoas density for men ($y = -0.23x + 66.24$, $r = -0.46$) and for women ($y = -0.17x + 61.55$, $r = -0.32$). There was a linear relationship between age and aortic calcification for men ($y = 0.26x - 7.96$, $r = 0.54$) and for women ($y = 0.21x - 7.23$, $r = 0.46$). A linear regression model for morphometric age (covariates included total psoas area [TPA], psoas density, and aortic calcification) resulted in the following equation for men (Age = 87.56 − 0.006*TPA − 0.397*psoas density + 0.588*calcification, $r = 0.67$, $p < 0.001$ for all covariates) and for women (Age = 93.39 − 0.012*TPA − 0.461*psoas density + 0.62*calcification, $r = 0.64$, $p < 0.001$ for all covariates).

The study population

Patients in the study group (n = 1,370) were separated into 3 groups based on chronologic age (youngest, middle, oldest chronologic age groups). Descriptive and clinical characteristics for these groups are detailed in Table 1. For the study group overall, case mix included 60 liver cases (4.4%), 79 major vascular cases (5.8%), 136 pancreas cases (9.9%), and 1,095 cases categorized as "other" major general surgery (79.9%). The chronologic oldest patients were 55.1% male, had an average body mass index of 28.3 kg/m^2, an average albumin of 3.8 g/dL, and an average age of 71.6 years. Of these patients, 10.1% were functionally nonindependent, 7.9% were taking steroids preoperatively, and 6.3% had preoperative sepsis.

Patients were also separated into 3 groups based on morphometric age (youngest, middle, oldest morphometric age groups), and their descriptive and clinical characteristics are detailed in Table 2. The morphometric oldest patients were 57.5% male, had an average body mass index of 27.7 kg/m^2, an average albumin of 3.6 g/dL, and an average chronologic age of 65.3 years. Among these patients, 16.6% were functionally nonindependent, 12.7% were taking steroids preoperatively, and 12.0% had preoperative sepsis.

We then investigated the relationship between chronologic age, preoperative comorbidities, and morphometric age. We compared the 10% of patients with the greatest morphometric age with the 10% of patients with the greatest chronologic age and the largest number of preoperative comorbidities (Fig. 1). We noted that 57.2% of patients within the group with the oldest morphometric age were not in the oldest chronologic age group. Similarly, 73.0% of patients within the group of the oldest morphometric age were not in the group with the most medical comorbidities.

Mortality analysis

We then compared chronologic and morphometric age as independent risk factors for postoperative mortality. Independent of other covariates, morphometric age is a better predictor of mortality than chronologic age (area under the receiver operating characteristic curve [AUROC] = 0.75 vs AUROC = 0.63). Per 1-year increase, the odds of mortality increase 1.06 times ($p < 0.001$, 95% CI 1.04 to 1.07) for morphometric age compared with an OR = 1.03 for chronologic age ($p < 0.001$, 95% CI 1.02 to 1.05). When stratifying patients into tertiles of age and using the middle group for comparison, the

Table 2. Patient Characteristics of the Study Population (n = 1,370) Stratified by Tertiles of Morphometric Age

Characteristic	Morphometric tertile		
	Youngest	Middle	Oldest
Demographic characteristics			
n	456	457	457
Age, y, mean ± SD	44.2 ± 13.6	54.9 ± 13.4	65.3 ± 12.5
Height, cm, mean ± SD	169.6 ± 10.9	171.5 ± 10.2	169.8 ± 11.0
Weight, kg, mean ± SD	86.3 ± 25.4	84.0 ± 22.5	80.0 ± 20.5
Body mass index, kg/m^2, mean ± SD	30.1 ± 8.8	28.5 ± 7.0	27.7 ± 6.6
Preoperative albumin, g/dL, mean ± SD	4.2 ± 0.5	4.0 ± 0.7	3.6 ± 0.8
Clinical characteristics, n (%)			
Male sex	186 (40.8)	271 (59.3)	263 (57.5)
Nonwhite race	87 (19.1)	81 (17.7)	54 (11.8)
Diabetes mellitus	46 (10.1)	76 (16.6)	126 (27.6)
Smoker	70 (15.4)	66 (14.4)	84 (18.4)
Nonindependent functional status	6 (1.3)	20 (4.4)	76 (16.6)
COPD	6 (1.3)	18 (3.9)	35 (7.7)
Recent transient ischemic attack	1 (0.2)	9 (2.0)	14 (3.1)
Cancer diagnosis	24 (5.3)	38 (8.3)	39 (8.5)
Currently receiving radiotherapy	10 (2.2)	15 (3.3)	17 (3.7)
Currently receiving chemotherapy	13 (2.9)	23 (5.0)	25 (5.5)
Taking preoperative steroids	23 (5.0)	41 (9.0)	58 (12.7)
Preoperative sepsis	21 (4.6)	34 (7.4)	55 (12.0)
Peripheral vascular disease	2 (0.4)	7 (1.5)	20 (4.4)
Ascites	2 (0.4)	7 (1.5)	9 (2.0)
Case mix characteristics, n (%)			
Emergent priority	55 (12.1)	42 (9.2)	71 (15.5)
Liver resection	21 (4.6)	19 (4.2)	20 (4.4)
Pancreatic resection	38 (8.3)	54 (11.8)	44 (9.6)
Major vascular	15 (3.3)	23 (5.0)	41 (9.0)
Other general surgery	382 (83.8)	361 (79.0)	352 (77.0)

chronologic oldest patients were not at significantly greater risk of mortality than the middle age patients ($p = 0.11$, OR 1.39, 95% CI 0.93 to 2.07). The chronologic youngest patients did have significantly less mortality risk than the middle age patients ($p = 0.002$, OR 0.43, 95% CI 0.26 to 0.73). The morphometric oldest had significantly greater mortality risk than the middle age group ($p < 0.001$, OR 3.30, 95% CI 2.16 to 5.06), and the morphometric youngest group had significantly less mortality risk ($p = 0.002$, OR 0.33, 95% CI 0.16 to 0.66).

For multivariable analysis, the comparison group was also the middle age group. The risk of postoperative mortality was significantly smaller for the chronologic youngest group compared with the chronologic middle age group (OR 0.44, 95% CI 0.24 to 0.79, $p = 0.009$). Conversely, patients in the oldest chronologic age group did not have a significantly higher mortality than patients in the middle chronologic age group (OR 1.36, 95% CI 0.86 to 2.15, $p = 0.19$). When input as a continuous variable, chronologic age was statistically significant ($p < 0.001$, OR 1.03, 95% CI 1.02 to 1.05). Other significant covariates in this model included emergent priority status ($p = 0.003$, OR 2.28, 95% CI 1.33 to 3.89), dialysis ($p < 0.001$, OR 4.41, 95% CI 1.98 to 9.86), nonwhite race ($p = 0.006$, OR 0.36, 95% CI 0.17 to 0.74), cancer ($p < 0.001$, OR 3.01, 95% CI 1.66 to 5.47), albumin ($p < 0.001$, OR 0.51 per g/dL, 95% CI 0.38 to 0.69), operation time ($p < 0.001$, OR 1.17 per hour, 95% CI 1.07 to 1.27), dyspnea ($p = 0.001$, OR 2.35, 95% CI 1.39 to 3.97), bleeding ($p = 0.016$, OR 2.14, 95% CI 1.15 to 3.96), steroid use ($p = 0.02$, OR 1.99, 95% CI 1.11 to 3.55), chemotherapy ($p = 0.001$, OR 3.38, 95% CI 1.65 to 6.93), and nonindependent functional status ($p = 0.035$, OR 1.96, 95% CI 1.05 to 3.67). The AUROC for this model was 0.84. After adjusting for covariates, the mortality

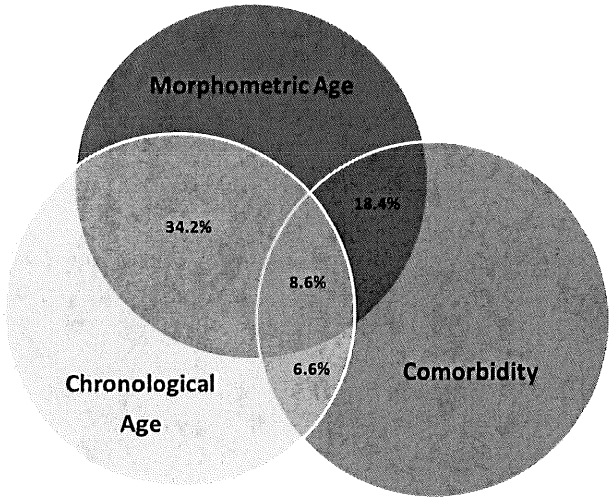

Figure 1. Morphometric age as an independent domain of surgical risk. Red circle, the 10% oldest patients by morphometric age; green circle, the 10% oldest patients by chronologic age; blue circle, the 10% with the most comorbidities. Note that 57.2% of patients within the group with the oldest morphometric age were not in the oldest chronologic age group. Similarly, 73.0% of patients within the group of the oldest morphometric age were not in the group with the most medical comorbidities.

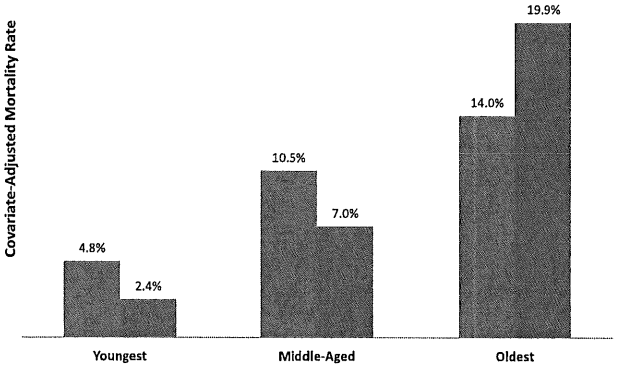

Figure 2. Covariate-adjusted 1-year mortality rates stratified by tertiles of morphometric and chronologic age. Blue bar, chronologic age; red bar, morphometric age. Mortality was adjusted for the covariates listed in Table 3, determined by logistic regression. Morphometric age was a significant predictor of 1-year mortality; chronologic age was not. The morphometric youngest had half the risk of 1-year mortality compared with the chronologic youngest; the morphometric oldest had greater risk than the chronologic oldest.

rate of the chronologic oldest patients was 14.0% compared with 4.8% for the chronologic youngest patients (Fig. 2).

The risk of postoperative mortality was significantly smaller for the morphometric youngest group compared with the morphometric middle age group (OR 0.47, 95% CI 0.23 to 0.98, $p = 0.045$). In addition, patients in the oldest morphometric age group had a significantly higher mortality than patients in the middle morphometric age group (OR 2.42, 95% CI 1.52 to 3.84, $p < 0.001$). As a continuous variable, morphometric age remained a significant predictor ($p < 0.001$, OR 1.04, 95% CI 1.02 to 1.05). The results of this multivariable model are summarized in Table 3. The AUROC for this model was 0.83. After adjusting for covariates, the mortality rate of the morphometric oldest patients was 19.9% compared with 2.4% for the morphometric youngest patients (Fig. 2).

Length of stay analysis

We then compared chronologic and morphometric ages as independent risk factors for LOS. Independent of other covariates, morphometric age is a better predictor of LOS than chronologic age (Pearson-product moment correlation coefficient = 0.27 vs 0.09). For multivariable analysis, age was stratified into tertiles. Chronologic age was not a significant predictor of LOS ($p = 0.30$, $\beta = 0.43$ per tertile). Chronologic age remained insignificant as a continuous variable ($p = 0.20$, $\beta = 0.03$ per year). Significant covariates included relative value unit (RVU) ($p = 0.04$, $\beta = 0.10$ per unit), dyspnea ($p = 0.023$, $\beta = 2.52$), ventilator dependency ($p = 0.005$, $\beta = 6.36$), pneumonia ($p = 0.024$, $\beta = 9.03$), ascites ($p < 0.001$, $\beta = 10.72$), congestive heart failure ($p = 0.009$, $\beta = 7.86$), acute renal failure ($p = 0.036$, $\beta = 7.73$), sensorium ($p = 0.001$, $\beta = 14.07$), bleeding ($p < 0.001$, $\beta = 5.76$), sepsis ($p = 0.021$, $\beta = 3.38$), peripheral vascular disease ($p = 0.008$, $\beta = 5.83$), albumin ($p < 0.001$, $\beta = -3.88$ per g/dL), operation time ($p < 0.001$, $\beta = 1.01$ per hour), nonindependent functional status ($p = 0.01$, $\beta = 4.15$), and contaminated or dirty wound classification ($p < 0.001$, $\beta = 3.96$). The overall correlation coefficient for this model was 0.59. The covariate-adjusted LOS was then computed for

Table 3. Logistic Regression Model Covariates for 1-Year Mortality and Morphometric Age

Covariate	p Value	Odds ratio (95% CI)
Morphometric age (reference = middle group)		
Youngest tertile	0.044	0.47 (0.23–0.98)
Oldest tertile	<0.001	2.42 (1.52–3.84)
Emergent status	0.003	2.18 (1.30–3.64)
Dialysis	0.002	3.16 (1.53–6.55)
Cancer	<0.001	3.90 (2.24–6.77)
Dyspnea	<0.001	2.44 (1.49–4.00)
Bleeding disorder	0.008	2.22 (1.24–3.99)
Albumin per g/dL	<0.001	0.54 (0.41–0.71)
Operation time per h	0.001	1.15 (1.06–1.25)

each tertile. The adjusted LOS for the chronologic oldest patients was 11.3 days compared with 8.5 days for the chronologic youngest (Fig. 3).

Morphometric age was a significant predictor of LOS ($p = 0.032$, $\beta = 0.93$ per tertile) in the presence of other covariates. So, holding all other model covariates equal, a patient in the oldest tertile would be predicted to have an LOS 1.86 days longer than a patient in the youngest tertile. Morphometric age remained a significant predictor as a continuous variable ($p = 0.002$, $\beta = 0.09$ per morphometric year). The overall correlation coefficient for this model was 0.60. The results of the multivariable models are summarized in Table 4. The covariate-adjusted LOS for the morphometric oldest patients was 14.2 days compared with 5.8 days for the morphometric youngest patients (Fig. 3).

Clinical implications of morphometric age adjustment

We then assessed the clinical implications of morphometric age adjustment on patients within the chronologic middle tertile. Patients in the chronologic middle age tertile who jumped into the old morphometric age group had significantly inferior outcomes (mortality 21.4% and mean LOS 13.8 days) compared with patients in the chronologic middle age tertile who jumped into the morphometric young group (mortality 4.5% and mean LOS 6.3 days, $p < 0.001$ for both comparisons) (Fig. 4A). There was no significant difference in chronologic age or case mix complexity (23.5 vs 23.8 RVU, $p = 0.82$) among patients in the chronologic middle tertile who jumped into the morphometric oldest and morphometric youngest groups, respectively.

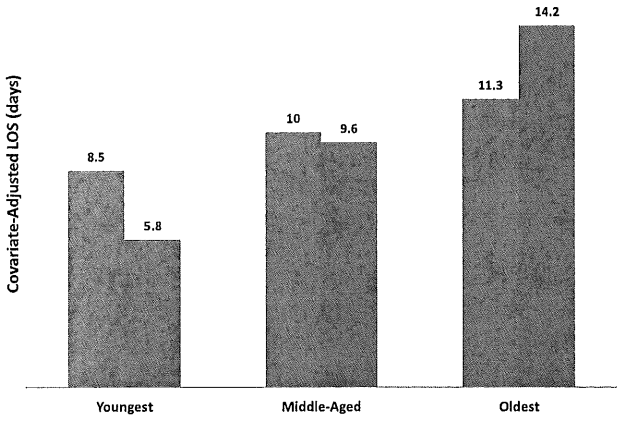

Figure 3. Covariate-adjusted length of stay stratified by tertiles of morphometric and chronologic age. Blue bar, chronologic age; red bar, morphometric age. Length of stay was adjusted for the covariates listed in Table 4, determined by linear regression. Patients in the youngest morphometric tertile were predicted to have shorter length of stay (LOS) than those in the youngest chronologic tertile; patients in the oldest morphometric tertile were predicted to have longer LOS than the chronologic oldest patients.

Table 4. Linear Regression Model Covariates for Length of Stay and Morphometric Age

Covariate	p Value	Coefficient, β (95% CI)
Morphometric age tertile	0.032	0.93 (0.08–1.78)
Operative complexity (measured as RVU)	0.005	0.09 (0.03–0.16)
Dyspnea	0.031	2.38 (0.22–4.55)
Ventilator dependency	0.004	6.55 (2.14–10.96)
Pneumonia	0.026	8.87 (1.07–16.67)
Ascites	<0.001	10.75 (5.13–16.37)
Congestive heart failure	0.010	7.70 (1.85–13.54)
Acute renal failure	0.037	7.67 (0.46–14.89)
Impaired sensorium	<0.001	13.92 (8.04–19.79)
Bleeding disorder	<0.001	5.58 (2.95–8.21)
Sepsis	0.018	3.44 (0.59–6.29)
Peripheral vascular disease	0.012	5.58 (1.25–9.92)
Albumin per g/dL	<0.001	−3.61 (−4.69 to −2.52)
Operation time per h	<0.001	1.02 (0.64–1.39)
Nonindependent functional status	0.016	3.91 (0.75–7.08)
Wound classification, contaminated or dirty/infected	<0.001	3.91 (2.04–5.78)
Constant	<0.001	13.53 (8.25–18.81)

RVU, relative value unit.

Patients in the chronologic youngest tertile (mean age 40.6 years) but morphometric oldest tertile had poor surgical outcomes, including a mortality rate of 17.8% and a mean LOS of 21.5 days (Fig. 4B). Conversely, patients in the chronologic oldest tertile (mean age 66.9 years) but the morphometric youngest tertile had good surgical outcomes, including a mortality of 3.0% and a mean LOS of 3.9 days ($p < 0.001$ for both comparisons). Measures of case complexity were similar between the 2 groups (21.1 vs 21.8 RVU, $p = 0.81$).

DISCUSSION

This study demonstrated that cross-sectional imaging can be used to assign a morphometric age to surgical patients. Morphometric age appears distinct from chronologic age and comorbidity. Morphometric age appears to be more strongly associated than chronologic age with the outcomes of 1-year mortality and LOS. Patients who "jump" from young to old when comparing morphometric age to chronologic age appear to have particularly poor postoperative outcomes, with 1-year mortality of approximately 20%. In contrast, chronologically older

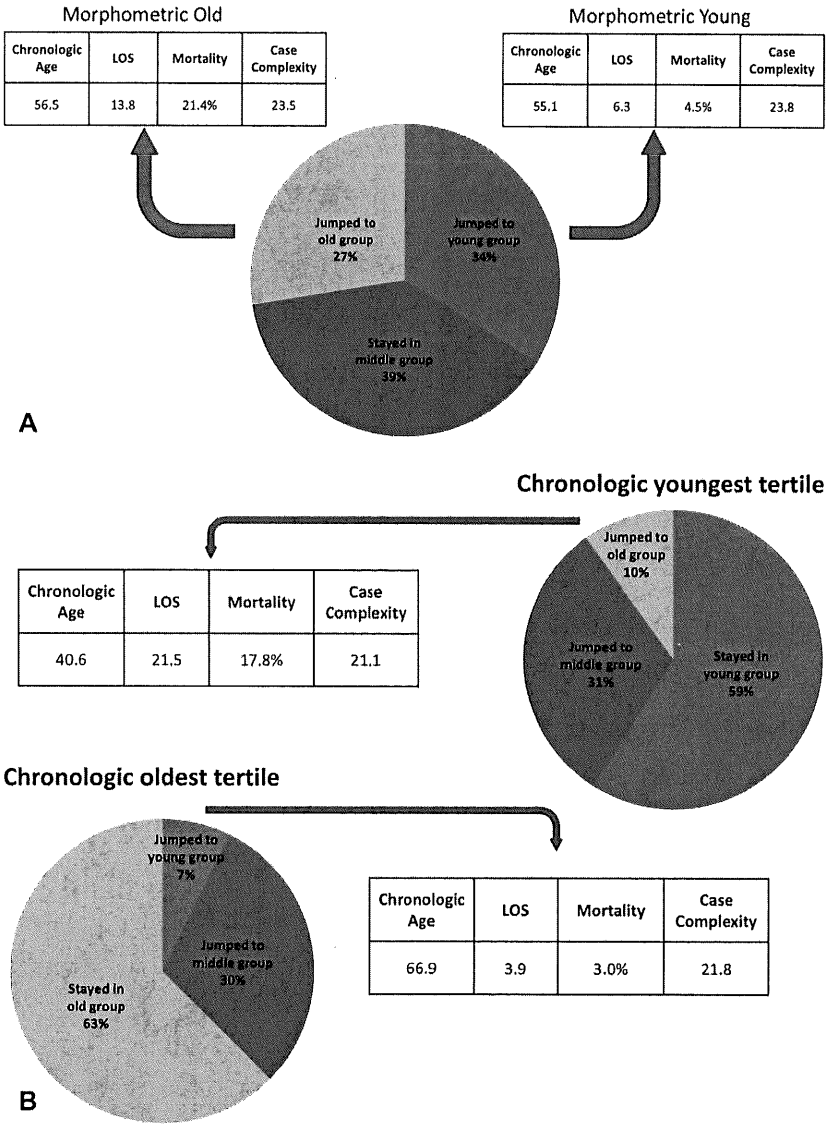

Figure 4. (A) Clinical implications of morphometric age adjustment on patients within the chronologic middle tertile. Patients in the chronologic middle age tertile who jumped into the old morphometric age group had remarkably inferior outcomes (mortality 21.4%) compared with patients in the chronologic middle age tertile who jumped into the morphometric young group (mortality 4.5%, $p < 0.001$). Note that there was no significant difference in the patients who jumped with respect to chronologic age and case complexity. (B) Patients in the chronologic youngest tertile (mean age 40.6 y) but morphometric oldest tertile had poor surgical outcomes, including a mortality rate of 17.8%. Conversely, patients in the chronologic old tertile (mean age 66.9 y) but the morphometric young tertile had good surgical outcomes, including a mortality of 3.0% ($p < 0.001$). LOS, length of stay.

patients who are morphometrically young have a low risk of mortality and a shorter LOS.

This study suggests that cross-sectional imaging can be used to reliably assess morphometric changes associated with aging. Furthermore, preoperative imaging can be used to assign a morphometric age to patients, which more accurately predicts surgical morbidity and mortality than chronologic age. The techniques used in this study, specifically quantitative analysis of medical imaging data called "analytic morphomics," represent a novel approach to the assessment of preoperative risk. Our impression is that this assessment of a patient's physical condition

may provide an objective metric that supports the surgeon's subjective assessment of fitness for surgery, imitating the "eyeball test." In addition, expressing this assessment as "age" provides an intuitive risk measure for clinicians and patients.

It is well established that older patients have inferior surgical outcomes.[18-20] Underpinning these inferior outcomes are discrete physiologic changes associated with aging, including muscle loss and increased atherosclerosis. Previous work has demonstrated that these physiologic changes can be accelerated in chronic disease states, have been correlated with overall survival and functional status, and may be associated with postoperative mortality.[2,3,10] Certainly, all clinicians appreciate the wide variation in physiologic reserve among older patients, and many older patients do very well, even after the most physiologically demanding surgical procedures. Similarly, our work has demonstrated wide variation in morphometric changes of aging. This fact enables this novel measure to identify relatively low-risk older patients, as well as high-risk younger patients.

When a clinician comments that patient appears "older than stated age," one envisions a frail patient who would be high risk for a major surgical procedure. It is certainly too simple an approach to distill the complex physiologic changes of aging into 3 simple morphometric measures. Alternatively, we could have described the relationship between each morphometric characteristic and surgical outcomes, without filtering these risk factors into a single variable related to patient age. We have chosen to express morphometric patient characteristics as age, in order to leverage the unique characteristics of age as an intuitive perioperative risk factor for patients and clinicians. Additional work is needed to elucidate additional morphometric characteristics, determine how best to communicate morphometric risk assessment to patients and clinicians, and more broadly, how preoperative imaging can inform clinical decision-making.

There are some important limitations of this work. First, not all patients get a preoperative cross-sectional imaging study. Further, this study is retrospective and involves patients from a single center and is not designed to attribute causality between morphometric age and poor surgical outcomes. In addition, the best methods to determine morphometric age are debatable. We chose a cohort of kidney donors and trauma patients as a "healthy" patient population to serve as the reference population for the "normal" morphometric changes of aging. Including patients with acute or chronic illness being assessed for surgical intervention in our reference population may or may not have improved the generalizability of our morphometric age assessment.

CONCLUSIONS

Overall, this study demonstrated the potential benefit of quantifying morphometric age and emphasized the rich source of additional data contained in preoperative imaging studies. Better understanding of the complex milieu of preoperative risk factors offers opportunities for improved risk stratification and informs shared decision-making between patients and surgeons. Further, analytic morphomics may elucidate mechanisms of adverse surgical outcomes, informing novel approaches to mitigate these risks. Unlike standard risk factors, morphometric measures available on preoperative imaging may highlight potentially remediable preoperative risks. For example, low core muscle size may identify patients who will benefit from preoperative strength training. Preoperative imaging may also reveal previously unappreciated surgical risk, as in patients with no known cardiovascular risk factors but significant abdominal aortic calcification. It is possible that in time, surgeons will use imaging studies as a routine part of the preoperative evaluation of fitness for surgery.

Author Contributions

Study conception and design: Englesbe, Terjimanian, Harbaugh, Sullivan, Wang, Sonnenday

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Critical revision: Englesbe, Campbell, Wang, Sonnenday

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