Comparing three methods of assessment of psoas area as a proxy for sarcopenia in predicting short-term outcomes in trauma patients 55 years and older

A thesis submitted by

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ABSTRACT

Objective: Psoas cross-sectional area (CSA) is a proxy for sarcopenia and frailty, and prior studies have suggested an association with long-term adverse surgical outcomes. The objectives of this study were 1) to optimize methods of CSA measurement and evaluate the population distribution; 2) to determine whether psoas CSA is associated with short-term outcomes in older trauma patients, and if added to traditional predictive models CSA improves their performance.

Design: Retrospective cohort study using medical records and stored images.

Setting: Level 1 Trauma Center, 2015-2019.

Participants: Trauma patients age 55+ who underwent computed tomography (CT) of the pelvis

Exposure: Psoas muscle CSA as measured on CT pelvis

Outcome measures: 1) Combined outcome of death or serious complication during index hospitalization; 2) Unfavorable discharge disposition

Results: 1207 patients met inclusion criteria. 146 patients (13.3%) had the outcome of composite in-hospital complications/mortality with an overall mortality rate of 5.7% (69). Median age was 75 [IQR 64, 84], 49% were male, and 97% were white. Median Injury Severity Score (ISS) was 9, median Glasgow Coma Scale (GCS) was 15, and median Charlson Comorbidity Score (CCS) was 1. Psoas CSA could not be determined for 80 patients due to anatomic factors or missing CT. Median psoas CSA was 11.95 (9.46, 14.8) cm^2, with a nearly symmetric distribution.

A surgical and a radiology resident initially required 2 minutes to measure PCSA, but after 40 cases the time required decreased to 1 minute. There was a high level of

agreement between the two (ICC 0.97, 95% CI 0.93 to 0.98, ($F(38,39)=55.9$, $p<0.01$)) and with an experienced emergency radiologist (ICC 0.97, 95% CI 0.87 to 1.0, ($F(4, 10)=96.4$, $p<0.01$)). Measurement at the L4 level was most reliable and most practical. Psoas CSA adjusted for height and/or body surface area were highly correlated with the unadjusted measurement, with ($r_s = 0.9$, $p < 0.01$) for both.

In the univariate analysis, psoas CSA was not associated with the composite outcome of in-hospital complications or mortality ($p=0.19$). After adjusting for multiple covariates using logistic regression, psoas CSA was not associated with adverse short-term outcomes. Although psoas CSA was associated with unfavorable discharge disposition in the univariate analysis ($p<0.05$), the effect became nonsignificant after adjusting for other covariates ($p=0.19$).

Conclusions: Psoas CSA is easily measured and standardizable. We found that in our population, it does not predict short-term outcomes in models that already contain other important predictors. Other methods of measuring frailty including in-person or EMR automated tools should be tested.

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DEDICATION

For the women in medicine who paved the way for me, and for my daughter, for whom I hope the road may be even better paved.

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LIST OF ABBREVIATIONS

ACS	American College of Surgeons
AP	Anterior-Posterior
CCS	Charlson Comorbidity Score
CSA	Average psoas Cross Sectional Area
CSA-H	Average psoas CSA adjusted for height
CSA-BSA	Average psoas CSA adjusted for body surface area
CT	Computed Tomography
Delta AUC	Change in the area under the receiver-operator curve
EMR	Electronic Medical Record
FRAIL	Fatigue, Resistance, Ambulation, Illnesses, & Loss of Weight scale
GCS	Glasgow Coma Scale
ICD	International Classification of Diseases, Ninth or Tenth revision
IMAT	Intermuscular Adipose Tissue
IQR	Interquartile Range
ISS	Injury Severity Score
MMC	Maine Medical Center
NSQIP	National Surgical Quality Improvement Program
ROC	Receiver Operator Characteristic Curve
SMD	Skeletal Muscle Density
TSFI	Trauma Specific Frailty Index
TRIPOD	Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis
VIF	Variance Inflation Factor

1. INTRODUCTION

As Americans are living longer there are a growing number of older patients requiring treatment for traumatic injuries. The number of Americans ages 65 and older is projected to more than double from 46 million in 2016 to over 98 million by 2060, and the 65-and-older age group's share of the total population will rise to nearly 24 percent from 15 percent.[1–3] While the overall mortality rate after traumatic injury for patients under the age of 55 has been estimated at 10%, the rate increases dramatically with age, with a rate of >15% in patients over 65 years, and >20% in patients over 75 years of age.[4,5]

The high morbidity and mortality seen in older trauma patients has been attributed to the presence of comorbidities, diminished physiologic reserve, and inability to compensate for severe injury.[4,6] Although chronological age is often used as a surrogate marker for vulnerability, there is large variability in health status within age strata. Frailty, defined as a decrease in physiologic reserve and resistance to stressors, has been shown to be predictive of poor outcomes and slow recovery in older patients.[7,8]

Given the heterogeneity of health status amongst older trauma patients, a major challenge lies in the rapid objective identification of frailty. Although there is widespread agreement regarding the clinical significance of frailty, and international guidelines recommend routine identification of frailty in patients ≥65 years, frailty is not systematically assessed in the trauma setting. Clinicians generally rely on visual inspection and clinical judgement to assess frailty, but this approach is unreliable.[9] While

frailty scales such as the five-item Fatigue, Resistance, Ambulation, Illnesses, & Loss of Weight (FRAIL) scale,[10] and the fifteen item Trauma Specific Frailty Index (TSFI)[11] have been found to be predictive of frailty and poor outcomes, there is no consensus on which frailty score is best. Furthermore, such questionnaires are time intensive, and their use may not be practical for patients with physiologic instability, cognitive impairment, or emotional distress after trauma.[7,12,13] Claims-based frailty indicators using International Classification of Diseases, Ninth or Tenth revision (ICD) diagnostic codes have recently been developed but cannot be used at the point of care unless they are automated in the electronic medical record (EMR).[14]

Due to the limitations in current frailty measures, there has been a surge of interest in surrogate markers of frailty, such as muscle mass, as predictive factors of poor outcomes after trauma. Sarcopenia, defined as a loss of skeletal muscle mass and strength which accompanies aging, is one of the components of the frailty phenotype and can be objectively measured on computed tomography (CT) imaging. [15,16] The cross sectional area (CSA) of the psoas major muscle has previously been investigated as a measure of sarcopenia, [17–21] and can easily be measured manually, even by nonradiologists.[22]

In order to appropriately categorize patients as sarcopenic, the population distribution of psoas CSA on CT in individuals 55 years and older must be established. Estimates of the prevalence of sarcopenia among trauma patients vary across studies due to differences in definition and sample characteristics.[17,23,24] To classify an individual as sarcopenic, one must have a measure of muscle mass relative to sex and stature in order

to define muscle mass as "deficient."[25] In an analysis of a population of Dutch men and women, it was demonstrated that the estimate of the prevalence of sarcopenia varied widely depending on the diagnostic criteria used, attributed to different reference populations and differing methods of adjustment.[26] An additional area of concern is that the psoas measurement that best correlates with outcomes has yet to be determined, and it is unclear which measurement should be implemented in usual practice. An area of concern with the study of sarcopenia in relation to trauma outcomes are the multiple methods of ascertaining psoas CSA. The psoas size has been measured cross sectionally at the level of the 3rd, 4th or 5th lumbar vertebra.[27] Measurements are typically averaged between left and right, and in some studies have been adjusted by height or body surface area.

The identification of the method of psoas measurement with the strongest association to poor outcomes in trauma patients is essential to recognize those patients at highest risk post injury, for whom targeted interventions may make the greatest difference. Use of this measurement as a rapid screening test could allow trauma providers to identify those patients with most vulnerable status at the time of admission. This would facilitate improved patient triage, better targeting of high intensity services such as increased monitoring, care management, transition of care services and geriatric services to those most likely to benefit, and help to facilitate goals of care discussions with patients and their families.

The first objective of this research was to establish the population distribution of psoas muscle CSA in adults 55 years and older in order to provide the basis for which imaging definitions of sarcopenia can be better specified. We also evaluated the feasibility and reproducibility of different methods for quantifying psoas CSA. The second objective was to determine whether psoas CSA is associated with short-term outcomes in older trauma patients and if its addition to a clinical prediction model adjusted for demographics, comorbidities, and severity of trauma improves model performance for adverse outcomes. We hypothesized that the addition of psoas CSA to a predictive model would improve the ability to predict in-hospital complications and mortality in a population of trauma patients 55 years and older.

2. METHODS

2.1 Data Source, Setting, and Patients

We conducted a retrospective study of patients admitted to Maine Medical Center (MMC) in Portland, the only American College of Surgeons verified Level-1 trauma center in Maine. We queried the MMC Trauma Registry for all adults 55 years and older who underwent evaluation by the Trauma Service between January 1, 2015 and January 1, 2019. The MMC EPIC electronic medical record (EMR) was queried for additional demographic and clinical information including the diagnosis codes associated with each patient encounter.

2.2 Inclusion and Exclusion Criteria

We included all trauma patients ages 55 and older evaluated by the Maine Medical Center Trauma Service who underwent CT imaging of the abdomen and pelvis. The decision to broaden the age criteria to 55 or older was based on:

1) previous literature demonstrating that in the critically ill population that 50% of frail patients are under the age of 65[28]

2) previously documented increase in mortality after trauma starting as early as age 55.[4,5]

In the case of multiple admissions within the study time period, only a patient's first admission was used.

We excluded patients who did not undergo CT imaging of the pelvis, patients with a history of muscular dystrophy or myopathy as identified by ICD diagnostic codes,

and patients with psoas muscle hemorrhage, abscess, or tumor of the psoas identified on CT. Patients with poor imaging quality preventing accurate measurement of the psoas muscle cross sectional area on CT were noted but not excluded; the reasons for poor imaging quality included severe lumbar scoliosis, lumbar vertebral body fracture, artifact from lumbar hardware, and motion artifact. Multiple imputation was used to estimate psoas data points for these patients, due to the risks of introducing bias were these patients to be excluded; patient characteristics were compared between those with recorded psoas data and those with imputed psoas data.

2.3 Sample Size

The sample size calculation was based on sarcopenia as an imbalanced variable (prevalence of 25-35%) with a marginal odds ratio for hospital complication rate of 1.21 and an in-hospital complication rate ranging from 11%-24% depending on sarcopenic status (19% overall) as reported by McCusker et al.[23] It was determined that to achieve the standard of 20 events per variable (EPV) in an estimated 5 variable model with 5 degrees of freedom would require at least 526 patients.[29,30]

2.4 Data Points and Definitions

Data collected retrospectively from the Trauma Registry included patient demographics (age, sex, ethnicity, height, weight), injury characteristics (mechanism of injury, Injury Severity Score (ISS)[31], Glasgow Coma Scale (GCS))[32], in-hospital complications, mortality, and discharge disposition. The ICD codes associated with each

patient encounter were extracted from the MMC EMR and used to calculate the Charlson Comorbidity Score (CCS).[33] Admission source was also obtained from the EMR.

2.5 Psoas Muscle Measurement

Each patient's initial CT from the time of admission was evaluated for measurement of bilateral psoas muscle CSA using MaineHealth Agfa IMPAX imaging software (Agfa HealthCare NV, Mortsel, Belgium).

The methods of psoas muscle CSA measurement were based on those evaluated in prior literature, and included:

1. Total psoas area measured at the L4 level, averaged between left and right[18]
2. Total psoas area measured at the L4 level adjusted for height (total psoas area/ height^2), averaged between left and right[23]
3. Total psoas area at the L4 level adjusted for body surface area (Mosteller formula, [(weight (kg)*height(cm)) / 3600] ^ 1/2),[34] averaged between left and right (otherwise referred to as the "psoas index.")[17]

These methods of psoas CSA measurement will be abbreviated as the following:

1. CSA: Average psoas CSA
2. CSA-H: Average psoas CSA adjusted for height
3. CSA-BSA: Average psoas CSA adjusted for body surface area

Throughout this manuscript, the term "measurements of psoas CSA" refers to these three measures.

2.6 Training for CSA Measurement

In a one-hour session, the Maine Medical Center ER/Trauma Radiologist trained the study PI (a resident in General Surgery) and a third-year radiology resident in accurate measurement of psoas cross sectional area. Using IMPACS imaging software, the patient psoas muscle was visualized in the axial and sagittal planes at the level of the superior aspect of the L3 and L4 vertebral body. In the axial plane, anterior-posterior (AP) and lateral measurements of the muscle body were performed at its greatest diameter for both L3 and L4 levels. The AP and lateral measurements were multiplied to calculate the cross-sectional area of the muscle body.

To evaluate the timeline to proficiency of measurement, for patient 1, 5, 10, 15, 20, 30, and 40, each CT reviewer was timed to determine the amount of time required to perform measurement of bilateral psoas CSA at the L4 level.

Both the study PI and the Radiology resident measured the bilateral psoas CSA of the first 40 patients, each blinded to the other's results. The interrater reliability was assessed at 10, 20, 30, and 40 patients. Adequate inter-rater reliability was achieved, after which the remaining patient measurements were performed by the study PI.

For the first 40 patients, psoas CSA was measured by both evaluators at level of the superior border of L3 and L4 vertebral bodies and measurements compared; no significant difference was found, but it was noted that due to anatomical variation and windowing of pelvic CT, measurements were more complete at the L4 level, and

thereafter measurement was standardized at this level. Psoas muscle cross sectional area in the axial plane at the level of the superior aspect of the L4 vertebral body was recorded for the left and right psoas for all patients.

Bilateral psoas muscle CSA was measured by the study PI, radiologist, and radiology resident without knowledge of the outcome.

2.7 Outcome Measures

The primary outcome was a composite of in-hospital complications or mortality. In-hospital complications were defined based on the American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) categories as neurological (cerebrovascular accident, seizure), respiratory (acute respiratory distress syndrome, pneumonia, unplanned intubation or reintubation), cardiovascular (myocardial infarction, arrhythmia), infectious (sepsis, urinary tract infection, surgical site infection), hematological (deep venous thrombosis, pulmonary embolus), renal (acute kidney injury, acute renal failure), and soft tissue/musculoskeletal (pressure ulcer, compartment syndrome). The secondary outcome was discharge disposition, categorized as favorable or unfavorable. Post-discharge dispositions included home, home with services, acute rehabilitation center, transfer for higher level of care, dependent care (including skilled nursing facility, long term care), hospice care, and death. Discharge was considered favorable if a patient was discharged to the same or a lesser level of care than their admission source, with the exception that a patient who originated from home and was discharged to acute rehab was considered a favorable discharge. Discharge was

considered unfavorable if a patient was discharged to a higher level of care than their admission source.

2.8 Statistical Analysis

Data analysis was performed using R statistical software (R project, Vienna, Austria).

2.8.1 Aim 1

Inter-rater reliability of psoas muscle measurements by the radiology resident and general surgery resident at two anatomic levels (L3, L4) were evaluated using intra-class correlation (R package "irr") with a one-way random effects, single rater model evaluating agreement. The same intra-class correlation model was used in a pairwise fashion to evaluate the inter-rater reliability between the radiology resident, surgical resident, and gold-standard attending radiologist.

The agreement between the three methods of quantifying psoas CSA was evaluated using Spearman correlation (R package "stats").

Different cutoff values of the psoas CSA variable were evaluated for estimates of sarcopenia according to previously published definitions; <2sd below mean[17], <20th percentile[26,35], <25th percentile[19,23], less than the median[20].

The sex distribution of psoas CSA was evaluated for all three measures, with sex strata defined as male and female. The psoas CSA median and interquartile range were reported by sex strata.

The data were assessed for missingness. Multiple imputation was used to account for any missing data (R package "mice"). Dataset imputation was performed 5 times, generating 5 imputed datasets.

2.8.2 Aim 2

Development of the prediction models was informed by the "Transparent Reporting of a multivariable prediction model for Individual Prognosis or Diagnosis" (TRIPOD) statement (Appendix A).[36] Stepwise variable selection was performed according to Rubin's rules on each imputed dataset (R package "MASS"). Candidate variables included sex (male, female) and race (White, non-White) as binary variables, age, injury severity score (ISS) (range 1- 75), Glasgow Coma Scale (GCS) (range 3-15),[32] and Charlson Comorbidity Score (CCS) (range 0 – 33)[33] as continuous variables, and mechanism of injury (fall from standing, fall from height, motor vehicle crash, motorcycle crash, pedestrian struck by vehicle, cyclist struck by vehicle, other blunt injury, burn, penetrating injury) as a categorical variable.

2.8.3 Development of the prediction models for the composite outcome of death or serious complication during index hospitalization

Univariate logistic regression was used to evaluate the relationship of psoas CSA with the primary outcome of in-hospital complications and mortality.

For each of the five imputed datasets, using stepwise variable selection the covariates selected were the same: ISS, CCS, and GCS.

Prediction models for the composite outcome of in-hospital complications and mortality were constructed using logistic regression. Bootstrapping with 150 and 200 bootstrap samples was used to avoid overfitting (R package "rms") and uniform shrinkage used to account for model optimism.

The baseline model for the primary outcome of in-hospital complications or mortality included age, sex, and variables found to be significant in the stepwise selection process, not including CSA. The full models included psoas CSA data as a continuous variable; individual models were constructed for CSA, CSA-H, and CSA-BSA. CSA, CSA-H, and CSA-BSA were evaluated as continuous variables to maximize power to detect an association with the outcome. For each of the 5 imputed datasets, multivariable logistic regression was performed for the baseline model and for each of the three methods of measurement of psoas CSA.

Table 2.1 Components of Prediction Model for death or in-hospital complications

Measure of CSA	Baseline Model	Full Model
CSA	Age, Sex, ISS, GCS, CCS	Baseline Model + CSA
CSA-H	Age, Sex, ISS, GCS, CCS	Baseline Model + CSA-H
CSA-BSA	Age, Sex, ISS, GCS, CCS	Baseline Model + CSA-BSA

2.8.4 Development of the prediction models for the secondary outcome of discharge disposition

Univariate logistic regression was used to evaluate the relationship of psoas CSA with the secondary outcome of unfavorable discharge destination.

Patients for whom discharge disposition could not be determined were excluded from multivariate prediction modeling of the secondary outcome, leaving 807 patients in the analysis. For each of the five imputed datasets, using stepwise variable selection the covariates selected were the same: Age, ISS, CCS, GCS, and mechanism. We evaluated interactions for inclusion in the model.

Prediction models for the secondary outcome of unfavorable discharge were constructed using logistic regression. Bootstrapping with 150 and 200 bootstrap samples was used to avoid overfitting (R package "rms") and uniform shrinkage used to account for model optimism.

The baseline model for the secondary outcome of discharge disposition included age, sex, ISS, CCS, GCS, and mechanism. The full models included psoas CSA as a continuous variable; individual models were constructed for CSA, CSA-H, and CSA-

BSA. For each of the 5 imputed datasets, multivariable logistic regression was performed for the baseline model and for each of the three methods of measurement of psoas CSA.

2.8.5 Evaluation of Prediction Models

Model fit was evaluated for the baseline and three psoas CSA models using the Hosmer-Lemeshow test and calibration plots. Discrimination was evaluated with the C-statistic.[37,38] To examine whether the psoas CSA measurement added additional predictive ability to the baseline model, we compared each psoas model to the baseline using change in the area under the receiver-operator curve (delta AUC).

3. RESULTS

3.1 Cohort Characteristics

1207 patients met the inclusion criteria and were included in the analysis and are described in Table 1. The median age of the cohort was 75, 49% were male, and 97% were white. The median ISS was 9 [IQR 5, 14], the median GCS was 15 [IQR 15, 15].

Table 3.1 Cohort demographics and injury characteristics by sex.
Statistics are given as median [IQR].

	Female	Male
n=1207	619	588
Age (years)	78.00 [67.00, 87.00]	71.00 [62.00, 82.00]
White Race (%)	604 (97.6)	570 (96.9)
ISS	9.00 [5.00, 13.00]	9.00 [5.00, 14.00]
GCS	15.00 [15.00, 15.00]	15.00 [15.00, 15.00]
CCS	1.00 [0.00, 2.00]	1.00 [0.00, 2.00]
BMI	25.38 [21.30, 29.84]	26.81 [23.74, 30.42]
Height (cm)	160.00 [154.90, 165.10]	177.00 [170.65, 182.00]
Weight (kg)	65.00 [54.00, 77.10]	82.60 [73.20, 95.30]
CSA	9.86 [8.28, 11.74]	14.64 [12.47, 17.87]
CSA-H	3.86 [3.23, 4.55]	4.76 [4.03, 5.63]
CSA-BSA	5.82 [5.02, 6.62]	7.27 [6.30, 8.36]

ISS=Injury Severity Score, GCS = Glasgow Coma Scale, CCS = Charlson Comorbidity Score, BMI=Body Mass Index, CSA=average psoas muscle cross sectional area in cm^2, CSA-H=average psoas CSA adjusted for height (cm^2/m^2), CSA-BSA=average psoas CSA adjusted for body surface area (cm^2/m^2)

3.2 Inter-Rater Reliability

At the L3 level, a high degree of reliability was found between the measurement of the radiology resident and the surgical resident, with an ICC of 0.89, with a 95% confidence interval from 0.80 to 0.95, ($F(34, 35)=17.8$, $p<0.01$). The inter rater reliability of measurement between the radiology resident and attending radiologist (considered the

"gold standard" for measurement) was fair with an ICC of 0.65, with a 95% confidence interval from 0.22 to 0.96, ($F(4,5)=4.69$, $p=0.06$). The inter rater reliability of measurement between the surgery resident and attending radiologist was fair with an ICC of 0.70, with a 95% confidence interval from 0.13 to 0.96, ($F(4,5)=5.74$, $p=0.04$). Overall, inter-rater reliability of measurement between both residents and attending radiologist was fair at the L3 level with an ICC of 0.80, with a 95% confidence interval from 0.39 to 0.97, ($F(4, 10)=12.9$, $p<0.01$) (Table 3.2).

Table 3.2 Intraclass correlation measures between CT interpreters at the L3 level

CT Interpreters	ICC (95% CI)	p-value
Radiology Resident, Surgery Resident	0.89 (0.80, 0.95)	$p<0.05$
Radiology Resident, Attending Radiologist	0.648 (0.22, 0.96)	$p=0.06$
Surgery Resident, Attending Radiologist	0.70 (0.13, 0.96)	$P<0.05$
Both Residents, Attending Radiologist	0.80 (0.39, 0.97)	$P<0.05$

At the L4 level, there was a high degree of reliability between the measurements of the radiology resident and the surgical resident, with an ICC of 0.965, with a 95% confidence interval from 0.934 to 0.981, ($F(38,39)=55.9$, $p<0.01$). The inter rater reliability of measurement between the radiology resident and attending radiologist was high with an ICC of 0.97, with a 95% confidence interval from 0.788 to 0.997, ($F(4,5)=62.3$, $p<0.01$). The inter rater reliability of measurement between the surgery resident and attending radiologist was high with an ICC of 0.97, with a 95% confidence interval from 0.824 to 0.997, ($F(4,5)=76.3$, $p<0.01$). Overall, the inter-rater reliability of measurement between both residents and attending radiologist was high at the L4 level

with an ICC of 0.97, with a 95% confidence interval from 0.873 to 0.996 ($F(4, 10)=96.4$, $p<0.01$) (Table 3.3).

Table 3.3 Intraclass correlation measures between CT interpreters at the L4 level

CT Interpreters	ICC (95% CI)	p-value
Radiology Resident, Surgery Resident	0.97 (0.93, 0.98)	p<0.01
Radiology Resident, Attending Radiologist	0.97 (0.79, 1.00)	p<0.01
Surgery Resident, Attending Radiologist	0.97 (0.82, 1.00)	p<0.01
Both Residents, Attending Radiologist	0.97 (0.87, 1.00)	p<0.01

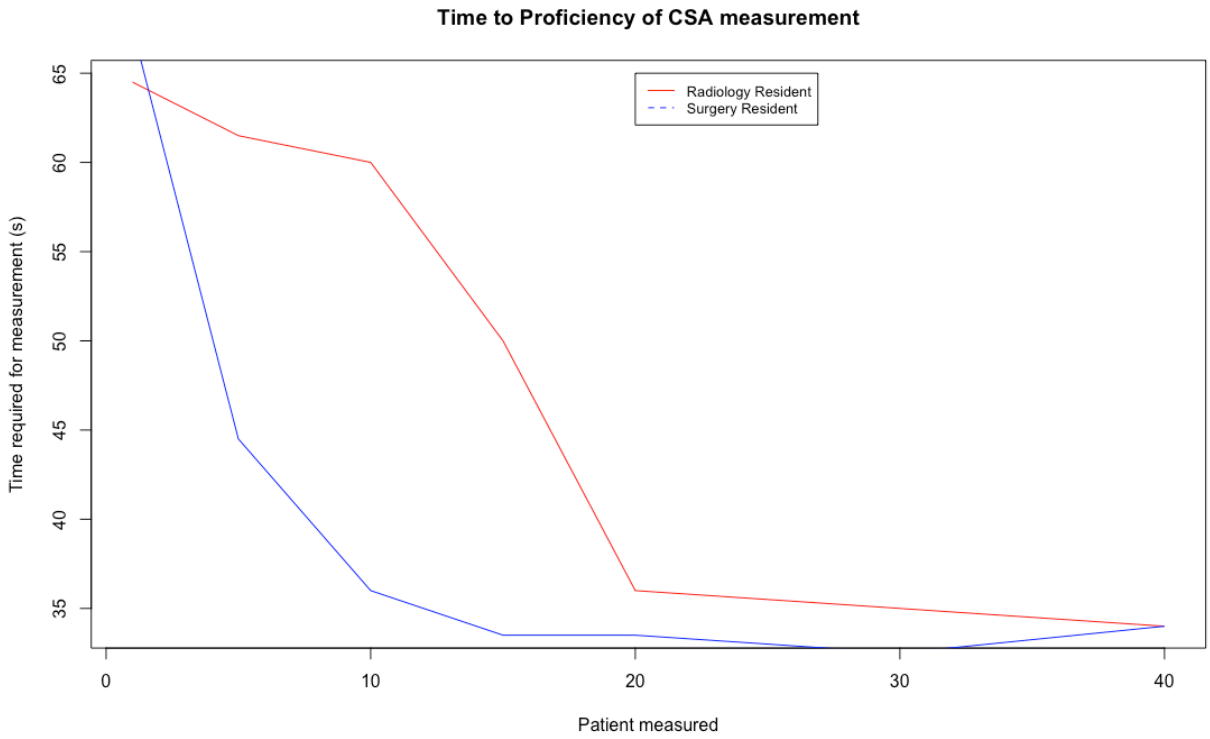
Measurements of psoas CSA at the L3 and L4 levels were found to have a strong positive correlation when evaluated with a Pearsons product-moment correlation coefficient, $r(33)=0.91$, $p<0.01$. Given a higher rate of interrater agreement at the L4 level as well as a better ability to capture psoas muscle cross sectional area at the L4 level due to CT slice capture in the majority of patients, and the high degree of correlation between psoas CSA values at L3 and L4, the remainder of the cohort underwent measurement of bilateral psoas muscle cross sectional area at the level of the superior aspect of the L4 vertebral body, and all calculations were performed using the L4 level data.

3.3 Timeline to Proficiency of Measurement:

The first measurement of bilateral psoas CSA at the L4 level took 64.5 seconds for the radiology resident and 67.5 seconds for the surgical resident. The time required for measurement decreased until patient 20 at which point the measurement took the

radiology resident 36 seconds and the surgical resident 33.5 seconds. Time required for measurements then plateaued, with both residents requiring 34 seconds to perform measurements on patient 40 (Fig. 3.1).

Figure 3.1 Line chart of the timeline to proficiency of CSA measurement



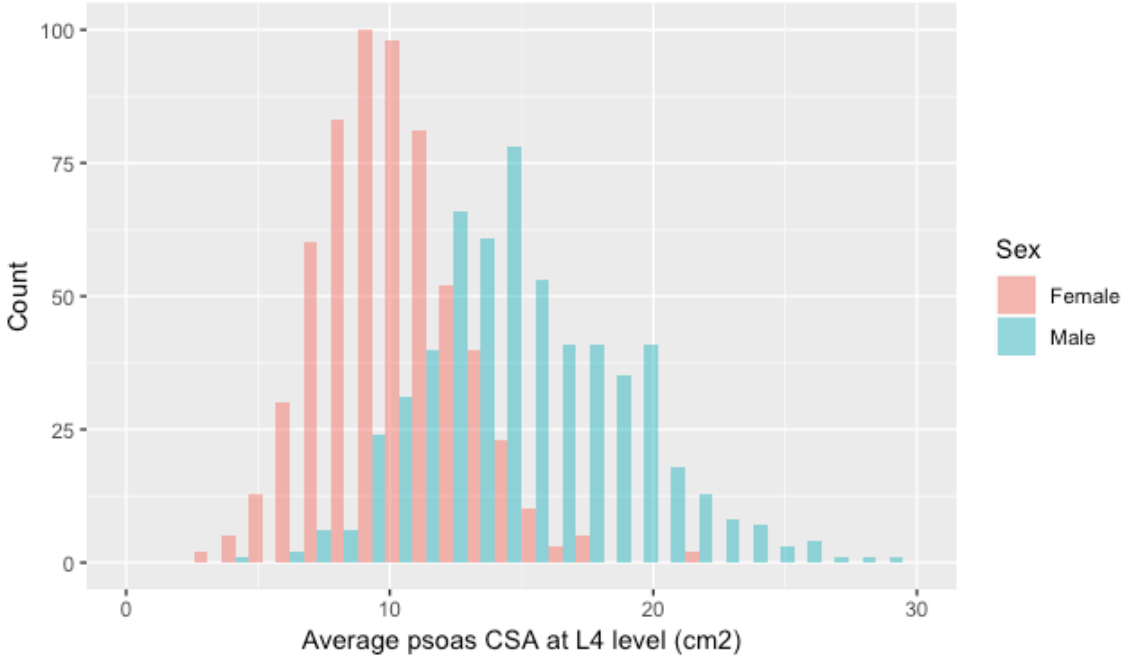
3.4 Agreement between Methods of Quantifying Psoas CSA

Results of the Spearman correlation indicated that there was a significant association between CSA and CSA-H, ($r_s = 0.898$, $p < 0.01$), as well as between CSA and CSA-BSA ($r_s=0.883$, $p<0.01$). There was also significant association between CSA-BSA and CSA_H ($r_s=0.890$, $p<0.01$).

3.5 Population Distribution

The median psoas CSA in the cohort was 11.95cm^2, with an interquartile range of 9.46cm^2 to 14.8cm^2. The minimum psoas CSA was 2.94cm^2, and the maximum psoas CSA was 29.4cm^2. Overall, males in the cohort had higher median psoas CSA 14.64 [12.47, 17.87] as compared to females 9.86 [8.28, 11.74] (Figure 3.2).

Figure 3.2 Population distribution of average psoas CSA at the L4 level by sex



3.6 Population Estimates of Sarcopenia

While in this cohort CSA was evaluated as a continuous measure in prediction modeling, the psoas CSA variable was evaluated according to the various cutoffs previously published for estimates of sarcopenia. For males, the number of patients considered sarcopenic according to the various definitions would vary from 13 (2%) to 293 (50%) out of 588 patients. For females, the number of patients would vary from 13

(2%) to 308 (50%) out of 619 patients. Within-cohort threshold psoas CSA values for varying definitions of sarcopenia are given in Table 3.4.

Table 3.4 Threshold values for psoas sarcopenia definitions
CSA values (cm^2) for varying sarcopenia cutoff definitions

Cutoff	Male	Female
< 2 SD below mean	7.3	3
<20th percentile	11.9	7.8
<25th percentile	12.5	8.3
<30th percentile	12.9	8.6
< Median	14.6	9.9

CSA-H values (cm2/m2) for varying sarcopenia cutoff definitions

Cutoff	Male	Female
< 2 SD below mean	2.5	1.4
<20th percentile	3.8	3.1
<25th percentile	4.0	3.3
<30th percentile	4.1	3.4
< Median	4.7	3.9

CSA-BSA values (cm2/m2) for varying sarcopenia cutoff definitions

Cutoff	Male	Female
< 2 SD below mean	3.8	2.5
<20th percentile	6.0	4.9
<25th percentile	6.3	5.0
<30th percentile	6.5	5.2
< Median	7.3	5.8

3.7 Outcome Proportions

Overall, 146 patients (13.3%) had the outcome of composite in-hospital complications/mortality with an overall mortality rate of 5.7% (69). Respiratory complications were the most common (39 patients), followed by infectious (33) and cardiac (22). Significant differences were found between those with the composite

outcome and those without, with those suffering the composite outcome more likely to be male, have a higher ISS, higher CCS, lower GCS, and male gender ($p<0.05$). CSA was found to be slightly higher in the group with the composite outcome (13.0cm^2 vs 12.4cm^2), though this was not a statistically significant difference. (Table 3.5)

Table 3.5 Cohort demographics and injury characteristics by primary outcome. Statistics are given as mean (standard deviation).

	Without Composite Outcome (88%)	With Composite Outcome (12%)	p
n=1207	1061	146	
Age	74.6 (11.9)	73.4 (11.5)	0.24
Male Sex (%)	502 (47.3%)	86 (58.9%)	0.01
White Race (%)	1033 (97.4%)	141 (96.6%)	0.74
ISS	9.5 (6.2)	17.2 (10.8)	<0.001
GCS	14.6 (1.7)	12.0 (4.6)	<0.001
CCS	1.0 (1.2)	1.5 (1.4)	<0.001
BMI	27.06 (7.0)	27.3 (6.5)	0.68
Height (cm)	167.6 (11.4)	169.5 (11.4)	0.06
Weight (kg)	76.4 (22.2)	78.6 (19.7)	0.26
CSA	12.4 (4.4)	13.0 (4.4)	0.19
CSA-H	4.4 (1.4)	4.5 (1.4)	0.50
CSA-BSA	6.5 (1.8)	6.8 (1.9)	0.19

ISS=Injury Severity Score, GCS = Glasgow Coma Scale, CCS = Charlson Comorbidity Score, BMI=Body Mass Index, CSA=average psoas muscle cross sectional area (cm^2), CSA-H=average psoas CSA adjusted for height (cm^2/m^2), CSA-BSA=average psoas CSA adjusted for body surface area (cm^2/m^2)

With respect to the secondary outcome, 308 of 807 (38%) patients had an unfavorable discharge. Those with unfavorable discharge were more likely to be female, older, with higher ISS, lower GCS, higher CCS, shorter in stature, lower in weight, and with smaller CSA values. (Table 3.6).

Table 3.6 Cohort demographics and injury characteristics by secondary outcome. Statistics are given as mean (standard deviation).

	Favorable Discharge (62%)	Unfavorable Discharge (38%)	p
n=807	499	308	
Age	71.5 (11.5)	80.9 (10.7)	<0.001
Male Sex (%)	254 (50.9%)	126 (40.9%)	<0.05
White Race (%)	483 (96.8%)	303 (98.4%)	0.30
ISS	9.4 (6.3)	10.8 (7.9)	<0.05
GCS	14.8 (0.9)	14.11 (2.63)	<0.001
CCS	0.8 (1.2)	1.4 (1.3)	<0.001
BMI	27.3 (6.4)	25.3 (6.2)	<0.001
Height (cm)	168.5 (11.4)	165.9 (11.4)	<0.05
Weight (kg)	78.0 (21.5)	70.0 (20.3)	<0.001
CSA	12.9 (4.5)	11.3 (4.2)	<0.001
CSA-H	4.5 (1.5)	4.0 (1.3)	<0.001
CSA-BSA	6.7 (1.9)	6.3 (1.8)	<0.001

ISS=Injury Severity Score, GCS = Glasgow Coma Scale, CCS = Charlson Comorbidity Score, BMI=Body Mass Index, CSA=average psoas muscle cross sectional area (cm^2), CSA-H=average psoas CSA adjusted for height (cm^2/m^2), CSA-BSA=average psoas CSA adjusted for body surface area (cm^2/m^2)

3.8 Missing Data

Prior to imputation, the data was assessed for missingness. With respect to clinical characteristics, measurements of psoas CSA had the greatest number missing (80 patients), followed by GCS (27), and ISS (7). Those patients missing psoas CSA data tended to be older (77.5 vs 75 years, $p<0.05$), have lower BMI (24.8 vs 26.3, $p<0.05$), and be smaller in stature with lower height (164 vs 168cm, $p<0.05$) and lower weight (68kg vs 75kg, $p<0.05$) (Table 3.7).

Table 3.7 Examination of the cohort subset missing psoas CSA data.
Statistics are given as median [IQR].

	Complete psoas data	Missing psoas data
n=1207	1127	80
Age	75.00 [64.00, 84.00]	77.50 [67.00, 86.25]
White Race (%)	1096 (97.2)	78 (97.5)
ISS	9.00 [5.00, 14.00]	9.00 [4.00, 10.00]
GCS	15.00 [15.00, 15.00]	15.00 [15.00, 15.00]
CCS	1.00 [0.00, 2.00]	1.00 [0.00, 2.00]
BMI	26.27 [22.77, 30.26]	24.81 [20.69, 27.41]
Height (cm)	167.60 [160.00, 177.00]	163.80 [157.38, 173.25]
Weight (kg)	75.20 [62.00, 88.50]	67.55 [57.28, 77.03]

ISS=Injury Severity Score, GCS = Glasgow Coma Scale, CCS = Charlson Comorbidity Score, BMI=Body Mass Index

Favorable versus unfavorable discharge disposition could not be determined for 400 patients; 393 patients were missing or had nonspecific admission source data and 11 patients were missing discharge destination data (excluding mortality). Patients for whom discharge disposition could not be determined were younger (74 vs 76 years, $p<0.05$), have higher BMI (27.1 vs 25.8, $P<0.05$), higher weight (77.6 vs 73.4kg, $p<0.05$), and have higher psoas CSA (12.4 vs 11.8 cm^2, $p<0.05$) (Table 3.8).

Table 3.8 Examination of the cohort subset missing admission source or discharge data.
Statistics are given as median [IQR].

	Complete disposition data	Missing disposition data
n=1207	807	400
Age	76.0 [65.0, 85.5]	74 [63.0, 83.0]
Male Sex (%)	380 (47.1)	207 (52)
White Race (%)	786 (97.4)	388 (97.0)
ISS	9.00 [5.00, 13.00]	9.00 [5.00, 16.00]
GCS	15.00 [15.00, 15.00]	15.00 [15.00, 15.00]
CCS	1.00 [0.00, 2.00]	1.00 [0.00, 2.00]
BMI	25.8 [22.4, 29.6]	27.1 [23.4, 31.5]
Height (cm)	167.0 [160.00, 177.0]	168.9 [160.0, 177.0]
Weight (kg)	73.4 [59.4, 87.0]	77.6 [66.0, 90.0]
CSA	11.8 [9.3, 14.8]	12.4 [9.9, 15.3]

ISS=Injury Severity Score, GCS = Glasgow Coma Scale, CCS = Charlson Comorbidity Score, BMI=Body Mass Index, CSA= average psoas muscle cross sectional area (cm^2)

3.9 Prediction Models

3.9.1 Prediction Models for the outcome of in-hospital complications or mortality

The variance inflation factor (VIF) of all covariates were < 2.5, suggestive of no strong evidence of collinearity. Univariate screening of psoas CSA demonstrated no significant prediction of the composite outcome (Coefficient 0.03, OR 1.03, p=0.189).

While age and sex are considered clinically relevant and important in the evaluation and treatment of the trauma population, neither was found to be predictive of the composite outcome. It is unusual that age was not found to have a significant relationship with the outcome given the breadth of prior evidence that age plays a substantial role in trauma clinical outcomes. Given concern for index event bias[39] due to the potential association of age with prognostic factors including mechanism, correlation between age and mechanism was evaluated with a Spearman rank-order correlation coefficient (R package "stats"), yielding significant correlation, with older age more strongly associated with lower impact mechanisms of injury including fall from less than 3 meters (r_s= -0.43, $p<0.05$). Subsequently, the interaction between age and mechanism of injury was evaluated for inclusion in the model; this interaction was not found to be a significant predictor of outcome in subsequent stepwise selection. Additional interactions were evaluated, including age and injury severity score, age and CSA, sex and CSA, sex and mechanism of injury, and sex and injury severity score, and were not found to be predictive of the composite outcome. Age (as a continuous variable for optimal power)

was forced into the model in a restricted stepwise selection. Sex was forced into the model given the importance of sex as a biological variable.

For each imputed dataset the C-statistic was calculated for each model and then pooled. Discrimination of the ROC curves was minimally different for each of the four models, with minimal change in AUC with the addition of psoas area data to the model (Table 3.9).

Table 3.9 ROC data for the outcome of in-hospital complications or mortality

Model	AUC	Delta AUC as compared to baseline
Baseline	0.7938	
Basline+CSA	0.7944	0.0006
Baseline+CSA-H	0.7946	0.0008
Baseline+CSA-BSA	0.7944	0.0006

With 200 bootstrapped samples, coefficients from the 5 datasets were pooled. A shrinkage factor of 0.97 was applied to correct for any model optimism, and shrunk coefficients were calculated (Tables 3.10-3.13).

Table 3.10 Adjusted Coefficients and Odds Ratios for Baseline Model for outcome of in-hospital complications or mortality

Covariate	Coefficient (95% CI)	Odds Ratio (95% CI)	p-value
Intercept	-1.33 (-2.96, 0.31)		
Age	0.002 (-0.016, 0.019)	1.00 (0.98, 1.02)	0.87
Gender	0.25 (-0.14, 0.65)	1.28 (0.88, 1.99)	0.18
ISS	0.09 (0.06, 0.11)	1.09 (1.07, 1.12)	<0.05
GCS	-0.16 (-0.23, -0.11)	0.84 (0.80, 0.91)	<0.05
CCS	0.25 (0.12, 0.40)	1.30 (1.12, 1.48)	<0.05

ISS=Injury Severity Score, GCS = Glasgow Coma Scale, CCS= Charlson Comorbidity Score

Table 3.11 Adjusted Coefficients and Odds Ratios for Baseline+CSA Model for outcome of in-hospital complications or mortality

Covariate	Coefficient (95% CI)	Odds Ratio (95% CI)	p-value
Intercept	-0.73 (-2.67, 1.17)		
Age	0.002 (-0.020, 0.016)	1.00 (0.98, 1.02)	0.84
Gender	0.40 (-0.07, 0.86)	1.48 (0.93, 2.37)	0.11
ISS	0.09 (0.06, 0.11)	1.09 (1.07, 1.12)	<0.05
GCS	-0.17 (-0.23, -0.11)	0.84 (0.80, 0.90)	<0.05
CCS	0.26 (0.12, 0.40)	1.30 (1.13, 1.49)	<0.05
CSA	-0.04 (-0.09, 0.02)	0.97 (0.92, 1.02)	0.28

ISS=Injury Severity Score, GCS = Glasgow Coma Scale, CCS= Charlson Comorbidity Score, CSA = average psoas CSA (cm^2)

Table 3.12 Adjusted Coefficients and Odds Ratios for Baseline+CSA-H Model for outcome of in-hospital complications or mortality

Covariate	Coefficient (95% CI)	Odds Ratio (95% CI)	p-value
Intercept	-0.87 (-2.72, 1.04)		
Age	0.001 (-0.019, 0.017)	1.00 (0.98, 1.02)	0.91
Gender	0.32 (-0.09, 0.74)	1.38 (0.91, 2.09)	0.14
ISS	0.09 (0.06, 0.11)	1.09 (1.07, 1.12)	<0.05
GCS	-0.17 (-0.23, -0.11)	0.85 (0.80, 0.90)	<0.05
CCS	0.26 (0.12, 0.40)	1.30 (1.13, 1.50)	<0.05
CSA-H	-0.08 (-0.23, 0.07)	0.97 (0.92, 1.02)	0.32

ISS=Injury Severity Score, GCS = Glasgow Coma Scale, CCS = Charlson Comorbidity Score, BMI=Body Mass Index, CSA-H=average psoas CSA adjusted for height (cm^2/m^2)

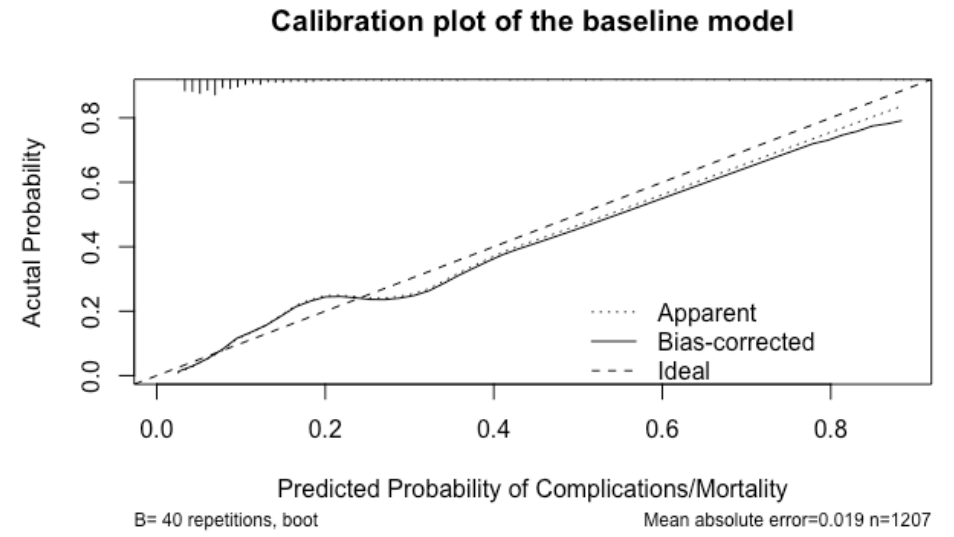
Table 3.13 Adjusted Coefficients and Odds Ratios for Baseline+CSA-BSA Model for outcome of in-hospital complications or mortality

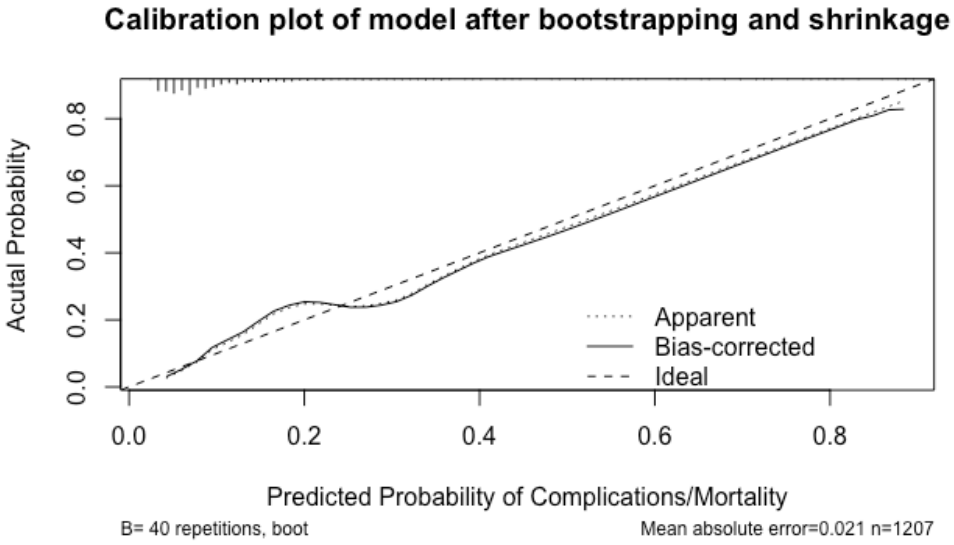
Covariate	Coefficient (95% CI)	Odds Ratio (95% CI)	p-value
Intercept	-0.99 (-2.86, 0.88)		
Age	0.0002(-0.018, 0.018)	1.00 (0.98, 1.02)	0.99
Gender	0.32 (-0.11, 0.74)	1.37 (0.89, 2.11)	0.16
ISS	0.09 (0.06, 0.11)	1.09 (1.07, 1.12)	<0.05
GCS	-0.17 (-0.23, -0.11)	0.84 (0.80, 0.90)	<0.05
CCS	0.26 (0.12, 0.40)	1.30 (1.13, 1.49)	<0.05
CSA-BSA	-0.04 (-0.16, 0.07)	0.96 (0.85, 1.08)	0.49

ISS=Injury Severity Score, GCS = Glasgow Coma Scale, CCS = Charlson Comorbidity Score, BMI=Body Mass Index, CSA-BSA=average psoas CSA adjusted for body surface area (cm^2/m^2)

The Hosmer-Lemeshow test was performed on each model for evaluation of calibration; all models demonstrated good fit with nonsignificant p-values. Calibration plots were additionally used to evaluate the models before and after bootstrapping and shrinkage (Figure 3.3).

Figure 3.3 Calibration plots of the baseline model for outcome of in-hospital complications or mortality before and after bootstrapping and shrinkage





3.9.2 Prediction Models for the outcome of unfavorable discharge disposition

The variance inflation factor (VIF) of all covariates were < 2.5, suggestive of no strong evidence of collinearity. Univariate screening of psoas CSA demonstrated a significant relationship with the outcome of discharge disposition (Coefficient -0.08, OR 0.92, $p<0.05$); larger CSA was associated with reduced odds of unfavorable discharge.

Interactions between age and mechanism of injury, age and injury severity score, sex and mechanism of injury, sex and injury severity score were not found to be predictive of unfavorable discharge. On univariate screen, sex was found to have a significant relationship with unfavorable discharge; a higher proportion of females had unfavorable discharge than males. However; sex was not included as a covariate in stepwise selection. Given concern for index event bias due to the potential association of sex with mechanism, correlation between sex and mechanism was evaluated with a Spearman rank-order correlation coefficient (R package "stats"), yielding a monotonic negative correlation, with female sex more strongly associated with lower impact mechanisms of injury including fall from less than 3 meters (r_s= -0.17, $p<0.05$). Because of its importance as a biologic variable, sex was forced into the model using restricted stepwise selection.

For each imputed dataset the C-statistic was calculated for each model and then pooled. Discrimination of the ROC curves was minimally different for each of the four

models, with minimal change in AUC with the addition of psoas area data to the model (Table 3.14).

Table 3.14 ROC data for outcome of unfavorable discharge disposition

Model	AUC	Delta AUC as compared to baseline
Baseline	0.788	
Basline+CSA	0.790	0.002
Baseline+CSA-H	0.791	0.003
Baseline+CSA-BSA	0.789	0.001

CSA = average psoas CSA (cm^2), CSA-H=average psoas CSA adjusted for height (cm^2/m^2), CSA-BSA=average psoas CSA adjusted for body surface area (cm^2/m^2)

With 200 bootstrapped samples, coefficients from the 5 datasets were pooled. A shrinkage factor of 0.96 was applied to correct for model optimism, and shrunk coefficients were calculated (Tables 3.15-3.18).

Table 3.15 Adjusted Coefficients and Odds Ratios, Baseline Model for outcome of unfavorable discharge disposition

Covariate	Coefficient (95% CI)	Odds Ratio (95% CI)	p-value
Intercept	-1.19 (-3.44, 0.97)		
Age	0.06 (0.05, 0.08)	1.06 (1.05, 1.08)	<0.05
Gender	-0.20 (-0.55, 0.13)	0.81 (0.58, 1.14)	0.25
ISS	0.03 (0.01, 0.06)	1.03 (1.01, 1.06)	<0.05
GCS	-0.26 (-0.39, -0.16)	0.76 (0.68, 0.85)	<0.05
CCS	0.24 (0.12, 0.38)	1.29 (1.13, 1.47)	<0.05
Mechanism	-0.21 (-0.3, -0.1)	0.81 (0.74, 0.88)	<0.05

ISS=Injury Severity Score, GCS = Glasgow Coma Scale, CCS= Charlson Comorbidity Score

Table 3.16 Adjusted Coefficients and Odds Ratios, Baseline+CSA-H Model for outcome of unfavorable discharge disposition

Covariate	Coefficient (95% CI)	Odds Ratio (95% CI)	p-value
Intercept	-0.70 (-3.03, 1.63)		
Age	0.06 (0.04, 0.08)	1.06 (1.04, 1.08)	<0.05
Gender	-0.06 (-0.46, 0.33)	0.93 (0.63, 1.39)	0.75
ISS	0.03 (0.01, 0.06)	1.03 (1.01, 1.06)	<0.05
GCS	-0.26 (-0.39, -0.16)	0.76 (0.68, 0.86)	<0.05
CCS	0.24 (0.13, 0.38)	1.29 (1.13, 1.47)	<0.05
Mechanism	-0.21 (-0.30, -0.12)	0.81 (0.74, 0.89)	<0.05
CSA	-0.04 (-0.08, 0.01)	0.97 (0.92, 1.01)	0.19

ISS=Injury Severity Score, GCS = Glasgow Coma Scale, CCS = Charlson Comorbidity Score, BMI=Body Mass Index, CSA=average psoas CSA (cm^2)

Table 3.17 Adjusted Coefficients and Odds Ratios, Baseline+CSA-H Model for outcome of unfavorable discharge disposition

Covariate	Coefficient (95% CI)	Odds Ratio (95% CI)	p-value
Intercept	-0.56 (-3.03, 1.63)		
Age	0.06 (0.04, 0.08)	1.06 (1.04, 1.08)	<0.05
Gender	-0.12 (-0.47, 0.23)	0.88 (0.62, 1.26)	0.75
ISS	0.03 (0.01, 0.06)	1.03 (1.01, 1.06)	<0.05
GCS	-0.27 (-0.39, -0.16)	0.76 (0.68, 0.86)	<0.05
CCS	0.26 (0.13, 0.39)	1.30 (1.14, 1.48)	<0.05
Mechanism	-0.21 (-0.30, -0.12)	0.81 (0.74, 0.89)	<0.05
CSA-H	-0.12 (-0.24, 0.01)	0.89 (0.78, 1.01)	0.75

ISS=Injury Severity Score, GCS = Glasgow Coma Scale, CCS = Charlson Comorbidity Score, BMI=Body Mass Index, CSA-H=average psoas CSA adjusted for height (cm^2/m^2)

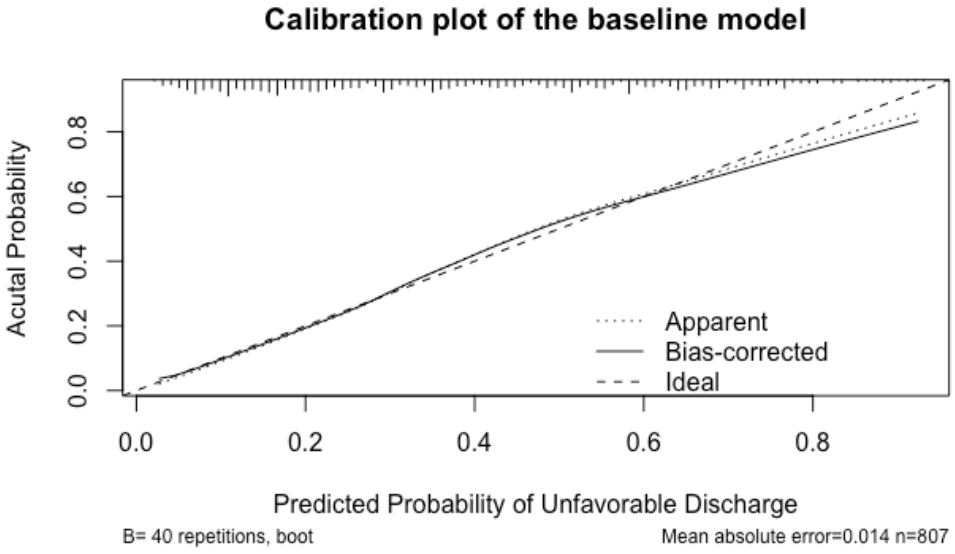
Table 3.18 Adjusted Coefficients and Odds Ratios, Baseline+CSA-BSA Model for outcome of unfavorable discharge disposition

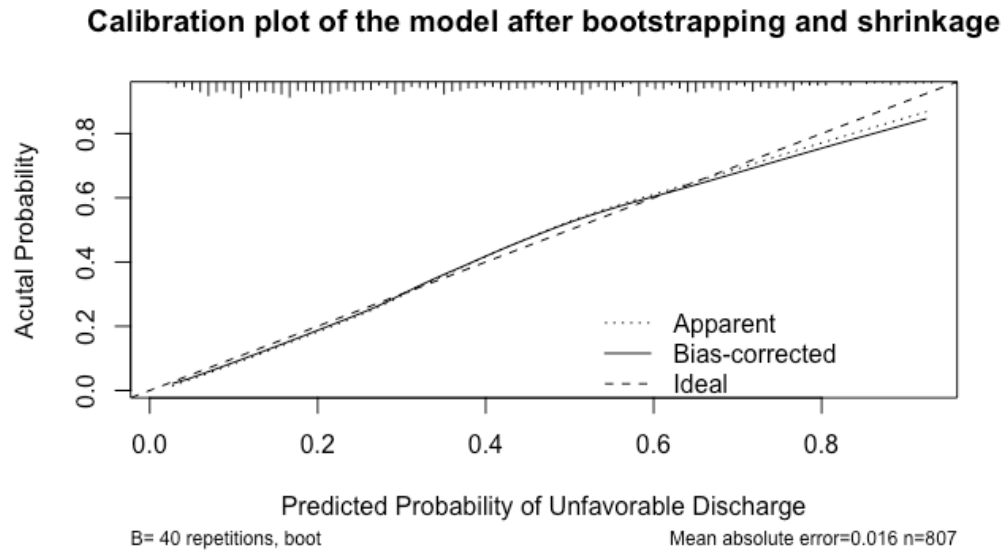
Covariate	Coefficient (95% CI)	Odds Ratio (95% CI)	p-value
Intercept	-0.78 (-3.03, 1.63)		
Age	0.06 (0.04, 0.08)	1.06 (1.04, 1.08)	<0.05
Gender	-0.13 (-0.49, 0.23)	0.88 (0.61, 1.25)	0.48
ISS	0.03 (0.01, 0.06)	1.03 (1.01, 1.06)	<0.05
GCS	-0.27 (-0.39, -0.16)	0.76 (0.68, 0.85)	<0.05
CCS	0.25 (0.13, 0.38)	1.29 (1.13, 1.47)	<0.05
Mechanism	-0.21 (-0.30, -0.12)	0.81 (0.74, 0.89)	<0.05
CSA-BSA	-0.06 (-0.16, 0.04)	0.94 (0.85, 1.04)	0.24

ISS=Injury Severity Score, GCS = Glasgow Coma Scale, CCS = Charlson Comorbidity Score, BMI=Body Mass Index, CSA-BSA=average psoas CSA adjusted for body surface area (cm^2/m^2)

The Hosmer-Lemeshow test was performed on each model for evaluation of calibration; all models demonstrated good fit with nonsignificant p-values. Calibration plots were additionally used to evaluate the models before and after bootstrapping and shrinkage (Figure 3.4).

Figure 3.4 Calibration plots of the baseline model for secondary outcome before and after bootstrapping and shrinkage





4. DISCUSSION

Psoas CSA is easily measured and standardizable. In the univariate analysis, psoas CSA was not associated with the composite outcome of in-hospital complications or mortality. Although psoas CSA was associated with unfavorable discharge disposition in the univariate analysis, the effect became nonsignificant after adjusting for other covariates.

4.1 Population distribution

In this study of 1207 trauma patients age 55 and older, we evaluated the population distribution of psoas CSA in males and females. Overall the median psoas CSA in the cohort was 11.95cm^2, with an interquartile range of 9.46cm^2 to 14.8cm^2. Males had larger psoas CSA than females, with median psoas CSA 14.64 cm^2 [12.47, 17.87] as compared to females 9.86 [8.28, 11.74]. The finding of a sex-based difference in psoas CSA is in line with prior research demonstrating variation in anthropometric measurements by sex,[40] and consistent with prior literature evaluating psoas CSA.[18,21] This is likely reflective of overall differences in body habitus between males and females, as males in this study were taller and heavier than females.

4.2 Psoas CSA measurement

Because time spent in measuring psoas CSA is key to achieve acceptance and uptake from providers, the timeline to proficiency of measurement was evaluated for both the radiology resident and surgical resident involved in measurement of psoas CSA on

CT; the methods of psoas measurement in this study involved evaluation of muscle mass and not muscle quality. While selected prior studies have used CT imaging to evaluate skeletal muscle quality and the degree of fatty infiltration via Hounsfield units, evaluation of skeletal muscle quality by Hounsfield units involves characterization of skeletal muscle density (SMD) to evaluate myosteatosis within muscle bodies as well as characterizing intermuscular adipose tissue (IMAT) to evaluate myosteatosis between muscle fibers. While this is valuable information in the workup of patients such as those who are mechanically ventilated or undergoing oncologic staging,[41,42] the process is time-consuming, and not practical for rapid evaluation by a clinician. Our study used standard imaging software to quantify psoas CSA, demonstrating that measurement of the psoas CSA in cross-sectional CT imaging takes little time, with a brief learning curve of approximately 20 patients. Psoas CSA is easily measured and standardizable. The greater level of agreement at the L4 level than the L3 level is likely due better anatomical capture due to differences in CT slicing between CT abdomen and CT pelvis, with the L4 level more often captured. While in this study it was not found to add significant predictive ability to a model of short-term outcomes (in hospital complications or mortality), it was associated with unfavorable discharge on univariate analysis, and it may add predictive ability to a model for longer term outcomes such as 1 year mortality.

4.3 Prevalence estimates of sarcopenia

Our cohort was examined for variability in prevalence of sarcopenia according to previously published definitions, with a high degree of variability in potential numbers of patients considered sarcopenic based on prior definitions. A more stringent cutoff of less

than two standard deviations below the mean would result in 13 of 588 males and 13 of 619 females categorized as sarcopenia, whereas a more generous cutoff of psoas CSA less than the median would result in 293 of 588 males and 308 of 619 females categorized as sarcopenic. With respect to the psoas area used as a threshold for the definition of sarcopenia, for CSA-H our study would define a threshold of the lowest sex-specific quartile as 4.0 cm^2/m^2 for males and 3.3 cm^2/m^2 for females; a prior retrospective review of 651 trauma patients ages 65 and older defined the threshold of the sex specific quartile as <3.51 cm^2/m^2 for males and <2.42 cm^2/m^2 for females.[23.] For CSA-BSA, our cohort threshold of <2SD below the mean would define sarcopenia as < 3.8 cm^2/m^2 for males and <2.5 cm^2/m^2 for females, as opposed to a prior retrospective review of 6874 patients 65 and older in which <2SD below the mean defined sarcopenia as < 5.2 cm^2/m^2 for males and <3.9 cm^2/m^2 for females.[17] In a previous study of a population of Dutch men and women "middle aged to older", it was demonstrated that the estimate of the prevalence of sarcopenia varied widely depending on the diagnostic criteria used, attributed to different reference populations and differing methods of adjustment.[26] The high degree of variability based on different psoas CSA cutoff definitions for sarcopenia emphasizes the need for a more standardized definition. This could be achieved by the creation of a large dataset combining patient data from our study as well as the multiple prior studies in order to better estimate the population distribution with a more representative sample.

4.4 Predictive ability of psoas CSA

4.4.1 Primary Outcome:

With nominal improvement in AUC after the addition of psoas CSA data to the prediction model, it appears that psoas CSA data adds minimal predictive ability to a model for in-hospital complications and mortality. Despite a variance inflation factor demonstrating lack of collinearity, the strong correlation of CSA with ISS and GCS may contribute to its minimal additive benefit to a predictive model.

Several studies of elderly trauma patients have evaluated the association of psoas CSA with post injury morbidity and mortality and most reported an association with outcomes. A retrospective, single-center study of 6874 adult patients hospitalized with trauma, evaluating CSA-BSA measured at L3, found that lower psoas CSA-BSA was associated with increased mortality after falls in patients 65 and older.[17] Additionally the study examined the prevalence of sarcopenia in their cohort based on a definition of sarcopenia as <2 standard deviations below that of a healthy reference population[25]; 72.49% of males and 46.48% of females in their cohort met those criteria for sarcopenia. Our estimates of sarcopenia prevalence were based on within cohort definitions, as the population distribution of psoas CSA amongst persons 55 and older has not been well established. A different retrospective cohort demonstrated a significant correlation between masseter muscle CSA and psoas CSA in 487 patients age 65 and older with blunt trauma, finding that both decreased psoas area and decreased masseter area were associated with 2 year mortality in persons 65+.[18] While their measurements were also performed at the L4 level using standard imaging software, they included only those

patients with both head and abdominal CT. Our study results may differ from prior due to the broader inclusion criteria by age, as well as a lower complication and mortality rate in our cohort.

4.4.2 Secondary Outcome:

Despite an association of psoas CSA with the outcome of unfavorable discharge on univariate screen (OR 0.92, $p<0.05$), psoas CSA was not found to be a significant predictor of the outcome when added to a multivariate model. There was minimal improvement in AUC after the addition of psoas CSA data to the prediction model for discharge disposition, most likely secondary to the well documented strength of the additional covariates in the model. Whereas our study involved evaluation of muscle mass using typical CT imaging software, a retrospective cohort of 252 patients measured psoas CSA at the L4-L5 interspace with Slice-O-Matic software using boundary tracing and Hounsfield unit gating, finding a significant difference in psoas CSA between patients discharged to dependent vs independent care.[27]

In a secondary analysis of a prospectively maintained trauma database, psoas CSA-H was measured at the L3 level using standard imaging software for calculation of sarcopenia in patients 65 and older admitted after trauma, defining sarcopenic patients as those in the lowest sex-specific quartile. [23] They found no association between sarcopenia and in-hospital complications, mortality, or unfavorable discharge on regression analysis, though in addition to controlling for demographics, injury severity, and comorbidities

they also controlled for frailty as identified with the trauma specific frailty index. Our model did not control for frailty, as sarcopenia (for which psoas CSA is a proxy variable) is one of the components of frailty.

While these prior studies all evaluated the association of psoas CSA with outcomes, they did not use a consistent method of quantifying of psoas cross sectional area or a single threshold to define sarcopenia, and therefore are difficult to compare.

4.5 Study Strengths and Limitations

With a total of 146 events and 7 model covariates, the sample size recommendation of 20 events per variable was achieved, though overall in-hospital complications (8.3%) and mortality (5.7%) in this cohort was lower than anticipated from the prior literature, with McCusker et al reporting mortality of 7.7% and an in-hospital complication rate of 19.4%, and Leeper et al reporting a mortality rate of 12.86% in patients 65 years and older.[17,23]

Generalizability with respect to race is limited due to the majority of the cohort being Caucasian (98%). It is unusual that age was not found to be a significant predictor of the primary outcome in our cohort, as this contradicts what has previously been demonstrated in the literature. Possible explanations include a vigorous population of adults 55+ or suboptimal event capture due to the retrospective nature of the data. Additionally, age was found to be a predictor of mortality alone, but not the composite outcome.

4.6 Areas for future work

A better understanding of the population distribution in non-White populations will provide additional background in which to begin standardizing the definition of sarcopenia with respect to cross-sectional imaging.

The psoas measurement that best correlates with outcomes has yet to be determined, and it is unclear which measurement, if any, should be implemented in usual practice. The high degree of correlation between methods of quantifying CSA demonstrated in our cohort, as well as the nominal improvement in delta AUC when any of the measures was added to a prediction model may support the use in future research of the simplest method of measurement; average CSA. More research is needed to evaluate the possible incremental benefit of adding psoas CSA data to models for more long-term data, including 1-year and 3-year mortality.

While frailty has previously been shown to be predictive of poor outcomes and slow recovery in older surgical patients,[7,8] and frailty scales such as the five-item Fatigue, Resistance, Ambulation, Illnesses, & Loss of Weight (FRAIL) scale developed by the International Association of Nutrition and Aging,[10] and the 15 item Trauma Specific Frailty Index (TSFI)[11] have been found to be predictive of frailty and risk of poor outcomes, decreased psoas cross sectional area on CT imaging is reflective of only one component of frailty: sarcopenia. [15,16] A recent review of the frailty biomarker literature suggests the use and development of multimodal/multivariate approaches to capture the

multifaceted nature of frailty. It may be that due to the multiple physiologic processes involved in the development of frailty, a single biomarker such as psoas CSA fails to provide a comprehensive picture of an individual's physical frailty.

5. APPENDIX

5.1 TRIPOD Checklist for Prediction Model Development and Validation

Section/Topic	n		Checklist Item	Page
Title and abstract				
Title	1	D;V	Identify the study as developing and/or validating a multivariable prediction model, the target population, and the outcome to be predicted.	i
Abstract	2	D;V	Provide a summary of objectives, study design, setting, participants, sample size, predictors, outcome, statistical analysis, results, and conclusions.	ii-iii
Introduction				
Background and objectives	a	D;V	Explain the medical context (including whether diagnostic or prognostic) and rationale for developing or validating the multivariable prediction model, including references to existing models.	1-3
	b	D;V	Specify the objectives, including whether the study describes the development or validation of the model or both.	4
Methods				
Source of data	a	D;V	Describe the study design or source of data (e.g., randomized trial, cohort, or registry data), separately for the development and validation data sets, if applicable.	5
	b	D;V	Specify the key study dates, including start of accrual; end of accrual; and, if applicable, end of follow-up.	5
Participants	a	D;V	Specify key elements of the study setting (e.g., primary care, secondary care, general population) including number and location of centers.	5
	b	D;V	Describe eligibility criteria for participants.	5,6
	c	D;V	Give details of treatments received, if relevant.	n/a
Outcome	a	D;V	Clearly define the outcome that is predicted by the prediction model, including how and when assessed.	9,10
	b	D;V	Report any actions to blind assessment of the outcome to be predicted.	9
Predictors	a	D;V	Clearly define all predictors used in developing the multivariable prediction model, including how and when they were measured.	12, 13
	b	D;V	Report any actions to blind assessment of predictors for the outcome and other predictors.	9
Sample size	8	D;V	Explain how the study size was arrived at.	6
Missing data	9	D;V	Describe how missing data were handled (e.g., complete-case analysis, single imputation, multiple imputation) with details of any imputation method.	11, 13
	0a	D	Describe how predictors were handled in the analyses.	9

Statistical analysis methods	10b	D	Specify type of model, all model-building procedures (including any predictor selection), and method for internal validation.	9-13
	10c	V	For validation, describe how the predictions were calculated.	n/a
	10d	D;V	Specify all measures used to assess model performance and, if relevant, to compare multiple models.	14
	10e	V	Describe any model updating (e.g., recalibration) arising from the validation, if done.	n/a
Risk groups	11	D;V	Provide details on how risk groups were created, if done.	n/a
Development vs. validation	12	V	For validation, identify any differences from the development data in setting, eligibility criteria, outcome, and predictors.	n/a
Results				
Participants	13a	D;V	Describe the flow of participants through the study, including the number of participants with and without the outcome and, if applicable, a summary of the follow-up time. A diagram may be helpful.	n/a
	13b	D;V	Describe the characteristics of the participants (basic demographics, clinical features, available predictors), including the number of participants with missing data for predictors and outcome.	15, 22, 23
	13c	V	For validation, show a comparison with the development data of the distribution of important variables (demographics, predictors and outcome).	n/a
Model development	14a	D	Specify the number of participants and outcome events in each analysis.	21, 22
	14b	D	If done, report the unadjusted association between each candidate predictor and outcome.	24, 28
Model specification	15a	D	Present the full prediction model to allow predictions for individuals (i.e., all regression coefficients, and model intercept or baseline survival at a given time point).	22-23, 25-27 (Table 3.10-3.13, 3.15-3.18)
	15b	D	Explain how to use the prediction model.	25, 28
Model performance	16	D;V	Report performance measures (with CIs) for the prediction model.	25, 26, 29-31
Model-updating	17	V	If done, report the results from any model updating (i.e., model specification, model performance).	n/a
Discussion				
Limitations	18	D;V	Discuss any limitations of the study (such as nonrepresentative sample, few events per predictor, missing data).	38

Interpretation	9a	V	For validation, discuss the results with reference to performance in the development data, and any other validation data.	n/a
	9b	D;V	Give an overall interpretation of the results, considering objectives, limitations, results from similar studies, and other relevant evidence.	33, 35-37
Implications	10	D;V	Discuss the potential clinical use of the model and implications for future research.	35, 38, 39
Other information				
Supplementary information	11	D;V	Provide information about the availability of supplementary resources, such as study protocol, Web calculator, and data sets.	n/a
Funding	12	D;V	Give the source of funding and the role of the funders for the present study.	iii

*Items relevant only to the development of a prediction model are denoted by D, items relating solely to a validation of a prediction model are denoted by V, and items relating to both are denoted D;V.

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