The Surgeon

Association between psoas major muscle mass and CPET performance and long-term survival following major colorectal surgery: A retrospective cohort study

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Abstract:	Objectives: To evaluate whether computed tomography (CT) derived psoas major muscle measurements could predict preoperative cardiopulmonary exercise testing (CPET) performance and long-term mortality in patients undergoing major colorectal surgery and to compare predictive performance of psoas muscle measurements using 2D approach and 3D approach Methods: A retrospective cohort study compliant with STROCSS standards was conducted. Consecutive patients undergoing major colorectal surgery between January 2011 and January 2017 following CPET as part of their preoperative assessment were included. Regression analyses were modelled to investigate association between the CT-derived psoas major muscle mass variables [total psoas muscle area (TPMA), total psoas muscle volume (TPMV) and psoas muscle index (PMI)] and CPET performance and mortality (1-year, 3-year, and 5-year). Discriminative performances of the variables were evaluated using Receiver Operating Characteristic (ROC) curve analysis. Results: A total of 457 eligible patients were included. The median TPMA and TPMV were 21 cm2 (IQR: 15-27) and 274 cm3 (IQR: 201-362), respectively. The median PMI measured via 2D and 3D approaches were 7 cm2/m2 (IQR: 6-9) and 99 cm3/m2 (IQR: 76-120), respectively. The risks of 1-year, 3-year, and 5-year mortality were 7.4%, 17.5%, and 27.1%, respectively. Regression analyses showed TPMA, TPMV, and PMI can predict preoperative CPET performance and long-term mortality. However, ROC curve analyses showed no significant difference in predictive performance amongst TPMA, TPMV, and PMI. Conclusion: Radiologically-measured psoas muscle mass variables may predict preoperative CPET performance and may be helpful with informing more objective selection of patients for preoperative CPET and prehabilitation.

Cover Letter

Dear Editor,

Please find attached for your kind review our manuscript entitled: Association between psoas major muscle mass and CPET performance and long-term survival following major colorectal surgery: A retrospective cohort study.

One of the most widely used preoperative tests is cardiopulmonary exercise testing (CPET). It provides an objective assessment of physical fitness and has been validated in the colorectal surgery setting. Despite its benefits, there are significant cost implications with running a CPET service and it can lengthen the preoperative work-up. This has led investigators to seek alternative markers of poor physical fitness and frailty. While there is no doubt that radiological psoas muscle measurements have significant prognostic value, whether psoas muscle measurements can predict CPET performance remains poorly understood. On the other hand, it remains controversial whether psoas muscle should be measured using 2-dimensional (2D) approach or 3-dimensional (2D) approach. Consequently, this study has the following objectives:

- To evaluate whether radiological psoas major muscle measurement could predict CPET performance in patients undergoing major colorectal surgery
- To evaluate whether radiological psoas major muscle measurement could predict long-term mortality in patients undergoing major colorectal surgery
- To compare predictive performance of psoas muscle measurements using 2D approach and 3D approach in patients undergoing major colorectal surgery

We declare that this manuscript is original and has not been published before. We wish to confirm that there are no known conflicts of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome.

We confirm that the manuscript has been read and approved by all named authors and that there are no other persons who satisfied the criteria for authorship but are not listed. We further confirm that the order of authors listed in the manuscript has been approved by all of us.

We confirm that we have given due consideration to the protection of intellectual property associated with this work and that there are no impediments to publication, including the timing of publication, with respect to intellectual property. In so doing we confirm that we have followed the regulations of our institutions concerning intellectual property.

We understand that the Corresponding Author is the sole contact for the Editorial process (including Editorial Manager and direct communications with the office). He is responsible for communicating with the other authors about progress, submissions of revisions and final approval of proofs. Below we have provided a current, correct email address, postal address and contact details of the Corresponding Author.

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Look forward to your favourable consideration

Yours sincerely

Shahab Hajibandeh

Responses to Reviewers' Comments: SURGE-D-23-00414

Dear Editor,

Many thanks for the second opportunity to respond to the Reviewer's comments. We would also like to thank the Reviewer for the time they put into reading our manuscript and preparing their comments which definitely helped to improve the quality of our work.

Below we have provided our responses to the Reviewer's comments:

Reviewers Comments:

Reviewer 1:

Many thanks for the opportunity to assist with the preparation of this manuscript. This is a single centre review of patients undergoing "major colorectal surgery" with an evaluation of survival post operatively. The factors assessed related to CT assessment of Psoas muscle volume prior to surgery. Larger Psoas muscle is associated with better cardiopulmonary performance and improved survival. This is an article in a commonly studied domain. We are always looking to assess fitness for surgery, and there is interest in measures such as this in regard to long term survival also.

Our response: We thank Reviewer 1 for their supportive comments.

The results do not focus on the impact of the different surgical approaches or operative procedures. As I read the paper I was unclear what "major colorectal surgery" was until I came to the table at the end. As a surgical readership, it would be of interest to bring this angle more into the results section with a comment on open / lap / cancer emergency etc.

Our response: We are in agreement with Reviewer 1. In order to address Reviewer 1's comment, we highlighted the procedures in the methods and added the following paragraph to the results section:

"**Colorectal procedure**

In terms of colorectal procedures performed, 33% (150 out of 457) of patients underwent hemicolectomy; 32% (150 out of 457) underwent anterior resection, 7% (30 out of 457) underwent abdominoperineal resection; 6% (26 out of 457) underwent extended hemicolectomy; 6% (27 out of 457) underwent sigmoid colectomy; 2% (7 out of 457) underwent subtotal colectomy, 1% (5 out of 457) underwent panproctocolectomy; 1% (4 out of 457) underwent transverse colectomy; 13% (58 out of 457) underwent other procedures. All procedures performed in elective setting. In terms of surgical approach, 28% (126 out of 457) of the procedures were open; 44% (201 out of 457) were laparoscopic; 12% (55 out of 457) were laparoscopic-assisted; 16% (75 out of 457) started laparoscopically but were converted to open. Malignant colorectal pathology was the indication for surgery in 88% (402 out of 457) of cases."

In the methods you explore patients without CT measurements. You state that those unable to perform cardiopulmonary exercise were deemed high risk. Did you include patients unable to perform exercise tests? and if so how did you score / handle that? I don't see any where that they were an exclusion criteria group.

Our response: We thank Reviewer 1 for this important comment. We included all patients who were unable to perform CPET. Overall, 15 out of 457 patients were unable to perform CPET but underwent surgery. For this subgroup, the risk of 30-day mortality, 1-year mortality and 5-year mortality were 13% (2 out of 15), 33% (5 out of 15) and 47% (7 out of 15), respectively." We added these information to the methods and results section as below:

Methods→Cardiopulmonary exercise testing→ "The patients who were unable to perform CPET or were unable to reach AT but underwent surgery were included for analyses."

Results →Inability to perform CPET → "*Among the included patients, 15 were not able to perform CPET but underwent operation as high risk patients. For this subgroup, the risk of 30-day mortality, 1-year mortality and 5-year mortality were 13% (2 out of 15), 33% (5 out of 15) and 47% (7 out of 15), respectively."*

Surgeons like to seem operative mortality / 30 day mortality figures when looking at surgery procedures. Can you provide 30 day mortality results?

Our response: We reported 30-day mortality results in the results section as below:

"The risk of 30-day mortality, 1-year mortality and 5-year mortality were 2% (9 out of 457), (7.4% (34 out of 457) and 27.1% (124 out of 457), respectively."

What is the benefit of reporting 1, 3 and 5 year mortality. Is is necessary to include 3 year mortality? In reading the results, they are challenging to follow. I suggest you consider reporting this as 1 year and 5 year results only.

Our response: We are in agreement with this comment and removed 3 year mortality analyses.

Overall, although not new, this is an interesting topic and interesting study with good 5 year follow-up and reasonable numbers. I think the readership would found this interesting.

Our response: We thank Reviewer 1 again for their supportive comments.

Editor:

After 5 rounds of reviewer requests we have one completed review. This is less then we target, but in the interest of avoiding further delays, we would appreciate if you would address the comments above and on resubmission the editorial team will review.

Our response: We thank the Editor for the opportunity to revise the manuscript and for agreeing to review the revised manuscript.

Title page (including author details)

Association between psoas major muscle mass and CPET performance and long-term survival following major colorectal surgery: A retrospective cohort study

Shahab Hajibandeh,[1] Iain Gilham,[2,*] Winnie Tam,[2] Emma Kirby,[2] Adetona Obaloluwa Babs-Osibodu,[2] William Jones,[2] George A. Rose,[3] Damian M. Bailey,[3] Christopher Morris,[1] Rachel Hargest,[1] Amy Clayton,[2] Richard G. Davies[4]

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Keywords: colorectal surgery; cardiopulmonary exercise test; psoas muscle index; sarcopenia

Ethics approval and consent to participate: The study proposal was approved by the University of South Wales Ethics Committee (LSE1636GREO), and Cardiff and Vale University Health Board (15/AIC/6352). Written informed consent was waived as this study constituted a service evaluation of routinely collected data.

Availability of data and materials: The data and materials related to this study will be available upon reasonable request from the corresponding author

Funding: There were no funding resources for this study. Damian M. Bailey is supported by a Royal Society Wolfson Research Fellowship (WM170007).

Conflict of interest: Damian M. Bailey is Editor-in-Chief of *Experimental Physiology,* Chair of the Life Sciences Working Group, a member of the Human Spaceflight and Exploration Science Advisory Committee to the European Space Agency, a member of the Space Exploration Advisory Committee to the UK Space Agency, and a member of the National Cardiovascular Network for Wales and South East Wales Vascular Network. Damian M. Bailey is also affiliated to the companies FloTBI Inc. and Bexorg Inc., focused on the technological development of novel biomarkers of brain injury in humans. All other authors declare no conflict of interest.

Author contributions

Conception and design: RGD, AC
Data collection: IG, WT, EK, ABO,WJ, RGD, GAR, DMB
Analysis and interpretation: All authors
Writing the article: SH, RGD, IG
Critical revision of the article: All authors
Final approval of the article: All authors

Highlights

- Radiologically-measured psoas muscle mass variables may predict CPET performance
- They may also predict long-term mortality after elective major colorectal resection
- The 3D measurement approach may not provide an advantage to 2D approach
- The above may help more objective patient selection for preoperative CPET

Association between psoas major muscle mass and CPET performance and long-term survival following major colorectal surgery: A retrospective cohort study

Keywords: colorectal surgery; cardiopulmonary exercise test; psoas muscle index; sarcopenia

Abstract

Objectives: To evaluate whether computed tomography (CT) derived psoas major muscle measurements could predict preoperative cardiopulmonary exercise testing (CPET) performance and long-term mortality in patients undergoing major colorectal surgery and to compare predictive performance of psoas muscle measurements using 2D approach and 3D approach

Methods: A retrospective cohort study compliant with STROCSS standards was conducted. Consecutive patients undergoing major colorectal surgery between January 2011 and January 2017 following CPET as part of their preoperative assessment were included. Regression analyses were modelled to investigate association between the CT-derived psoas major muscle mass variables [total psoas muscle area (TPMA), total psoas muscle volume (TPMV) and psoas muscle index (PMI)] and CPET performance and mortality (1-year and 5-year). Discriminative performances of the variables were evaluated using Receiver Operating Characteristic (ROC) curve analysis.

Results: A total of 457 eligible patients were included. The median TPMA and TPMV were 21 cm^2 (IQR: 15-27) and 274 cm^3 (IQR: 201-362), respectively. The median PMI measured via 2D and 3D approaches were 7 cm^2/m^2 (IQR: 6-9) and 99 cm^3/m^2 (IQR: 76-120), respectively. The risks of 1-year, 3-year, and 5-year mortality were 7.4%, 17.5%, and 27.1%, respectively. Regression analyses showed TPMA, TPMV, and PMI can predict preoperative CPET performance and long-term mortality. However, ROC curve analyses showed no significant difference in predictive performance amongst TPMA, TPMV, and PMI.

Conclusion: Radiologically-measured psoas muscle mass variables may predict preoperative CPET performance and may be helpful with informing more objective selection of patients for preoperative CPET and prehabilitation.

Background

Despite advances in surgical techniques, major colorectal surgery carries a significant risk of morbidity and mortality.[1] While the risk factors for surgical complications are varied,[2] a key aspect of minimising peri-operative complications is accurately determining preoperative risk. This has an important role in determining suitability for surgery, in counselling prior to surgery, and in selecting patients for prehabilitation and enhanced recovery programmes. One of the most widely used preoperative tests is cardiopulmonary exercise testing (CPET). It provides an objective assessment of physical fitness and has been validated in the colorectal surgery setting.[3] Despite its benefits, there are significant cost implications with running a CPET service and it can lengthen the preoperative work-up. This has led investigators to seek alternative markers of poor physical fitness and frailty.

Role of muscle mass in predicting the risk of postoperative morbidity and mortality has been the area of interest in research recently. Sarcopenia, age-related low muscle mass with reduced strength or function, is linked to aging, inactivity, malnutrition and disease and has become increasingly relevant as populations age.[4-7] Computed tomography (CT) scan derived measurements of the psoas major muscle, as surrogate of overall muscle mass, have been widely studied[8] and there is now a large body of literature demonstrating an association between this and prognosis in patients with cancer,[9] chronic disease,[10] in trauma patients,[11] and in patients undergoing emergency or elective surgery.[12-15]

While there is no doubt that radiological psoas muscle measurements have significant prognostic value, whether psoas muscle measurements can predict CPET performance remains poorly understood. On the other hand, it remains controversial whether psoas muscle should be measured using 2-dimensional (2D) approach or 3-dimensional (2D) approach.[16-18] Consequently, this study has the following objectives:

- To evaluate whether radiological psoas major muscle measurement could predict CPET performance in patients undergoing major colorectal surgery
- To evaluate whether radiological psoas major muscle measurement could predict long-term mortality in patients undergoing major colorectal surgery
- To compare predictive performance of psoas muscle measurements using 2D approach and 3D approach in patients undergoing major colorectal surgery

Methods

The Strengthening the Reporting of Cohort Studies in Surgery (STROCSS) guideline[19] for observational studies was followed to protocol, conduct and present this study. The Helsinki medical research ethical principles were respected and the study proposal was approved by the University and Health Board Ethics Committees. Written informed consent was waived as this study constituted a service evaluation of routinely collected data.

Study design

A retrospective cohort study was conducted at a teaching hospital located in South Wales. A prospectively maintained hospital database was used to identify all consecutive patients undergoing major colorectal surgery following CPET as part of their preoperative assessment. The study period was between January 2011 and January 2017. Colorectal procedures of interest included open or laparoscopic right or left hemicolectomy, transverse colectomy, sigmoid colectomy, subtotal or total colectomy, panproctocolectomy, anterior resection, abdominoperineal resection, and Hartmann's procedures. Patients without available preoperative CT abdomen and pelvis scan were excluded.

Predictive factor of interest

Psoas major muscle mass measured by CT scan was considered as predictive factor of interest. It was expressed as total psoas muscle area, total psoas muscle volume (cm^3), and psoas muscle index. Total psoas muscle area (cm^2) was calculated via 2-dimensional (2D) approach by measuring cross-sectional area of both right and left psoas muscles at the level of the upper margin of L4. Total psoas muscle volume (cm^3) was calculated via 3-dimensional (3D) approach by measuring volume of both right and left psoas muscles between the lower margin of L1 and the roof of the acetabulum. Total psoas muscle area and volume were adjusted based on each patient's height to calculate psoas muscle index (2D: cm^2/m^2 or 3D: cm^3/m^2). The CT scans were analysed using SYNAPSE software (FUJIFILM Medical Corp. Ltd., Tokyo, Japan. Software: Synapse V5.7.240.16413). Analysis was performed on reformatted images with a slice thickness of 5mm. The measurements were obtained in a semi-automated fashion.

Outcomes of interest

Cardiopulmonary exercise testing (CPET) performance was considered as the primary outcome of interest. Mortality (1-year and 5-year) was considered as secondary outcome.

Cardiopulmonary exercise testing. Following clinical examination and flow loop spirometry, preoperative CPET was conducted using an electromagnetically-braked cycle ergometer (Lode, Gronigen, The Netherlands) and a Medgraphics Ultima metabolic cart (MedGraphics™, Gloucester, UK) as previously described.[20-22] Calibration was conducted in accordance with the manufacturer's guidelines using a three litre volume syringe (Hans Rudolph) and reference calibration gases. During data collection, the middle five of seven breaths were averaged. Following three minutes of resting data collection, patients cycled at 60 revolutions per minute for three minutes in an unloaded freewheeling state. A progressively ramped period of exercise (5–15 Watts. min^{-1} based on body mass, height, age and sex) was then undertaken to volitional exhaustion or symptom limited termination, followed by a three-minute recovery period.[23] The Medgraphics Breeze™ software automatically determined peak oxygen uptake ($\dot{V}O_2$ peak) as the highest $\dot{V}O_2$ during the final 30 seconds of exercise. Oxygen uptake efficiency slope (OUES) [24] and peak oxygen pulse ($\dot{V}O_2$ peak/heart rate) were automatically determined by the software. The anaerobic threshold (AT) was manually interpreted by the supervising consultant anaesthetist using the V-slope method,[25] confirmed by a second consultant anaesthetist, and supported by comparison of ventilatory equivalents for oxygen ($\dot{V}E/\dot{V}O_2$) and carbon dioxide ($\dot{V}E/\dot{V}CO_2$) plots. The ventilatory equivalents for carbon dioxide and for oxygen were identified at the AT ($\dot{V}E/\dot{V}CO_2$-AT and $\dot{V}E/\dot{V}O_2$-AT respectively). Additional allometric scaling [26] was applied to metrics divided by body mass (AT and $\dot{V}O_2$ peak). Sub-categories 'Unable to CPET' and 'AT not detected' were recorded if patients were unable to perform a CPET because of their clinical status, or if insufficient data was available for clear identification of the AT. At our centre, patients were classified 'high risk' if CPET indicated an AT <11mL O_2 kg^{-1} min^{-1} combined with $\dot{V}E/\dot{V}CO_2$-AT >34 because patients with reduced AT or ventilatory inefficiency are more likely to die after major intra-abdominal surgery, whether or not they have associated cardiovascular risk factors.[27-30] Patients unable to perform CPET were also classified as high risk, as these patients are often characterized by poor postoperative outcomes.[31] The patients who were unable to perform CPET or were unable to reach AT but underwent surgery were included for analyses.

Mortality. Mortality was defined as death due to any cause occurring after surgery. The mortality data were compared and matched with data from Office for National Statistics (ONS) records to calculate 1-year and 5-year mortality.

Data collection

The prospectively maintained electronic hospital records were used as the source for data collection. An electronic data collection sheet was created for data collection which included the following data: age, sex, height, weight, body mass index (BMI), smoking history, American Society of Anesthesiologists (ASA) physical status, comorbidities (hypertension, diabetes, ischemic heart disease, atrial fibrillation, valvular heart disease, cerebrovascular accident, peripheral arterial disease, chronic obstructive pulmonary disease, asthma, renal insufficiency, liver cirrhosis, anaemia), and outcome data.

Statistical analysis

Simple descriptive statistics were used to summarise and present the demographics, clinical characteristics and outcome data. Continuous variables were summarized with mean ± standard deviation (SD) or median and interquartile range (IQR) and were compared using t-test or Mann-Whitney test as appropriate. Dichotomous variables were summarized as percentages and were compared using chi-squared test. Regression analyses were modelled to investigate association between the psoas major muscle mass variables (total psoas muscle area, total psoas muscle volume and psoas muscle index) and CPET performance and mortality (1-year, 3-year, and 5-year). The psoas major muscle mass variables were considered as independent variables; CPET performance parameters and mortality were considered as dependent variables. When the dependent variable was a dichotomous variable, binary logistic regression was modelled and when the dependent variable was a continuous variable, linear regression was modelled. All statistical tests were two-tailed and statistical significance was assumed at $P < 0.05$. Discriminative performances of psoas major muscle mass variables were evaluated and compared via Receiver Operating Characteristic (ROC) curve analysis. The method described by DeLong et al.[32] was used to calculate the standard error of the Area Under the Curve (AUC) and to calculate an exact Binomial Confidence Interval for the AUC. The MedCalc 13.0 software was used for statistical analyses.

Results

A total of 640 patients underwent major colorectal surgery following CPET between January 2011 and January 2017. We excluded 183 patients due to unavailable preoperative CT scan of abdomen and pelvis; therefore, 457 patients were included for analysis. Five-year data was available for all patients and there was no lost to follow-up. Figure 1 demonstrates study flow diagram and Table 1 summarised baseline characteristics of the included population.

Colorectal procedure

In terms of colorectal procedures performed, 33% (150 out of 457) of patients underwent hemicolectomy; 32% (150 out of 457) underwent anterior resection, 7% (30 out of 457) underwent abdominoperineal resection; 6% (26 out of 457) underwent extended hemicolectomy; 6% (27 out of 457) underwent sigmoid colectomy; 2% (7 out of 457) underwent subtotal colectomy, 1% (5 out of 457) underwent panproctocolectomy; 1% (4 out of 457) underwent transverse colectomy; 13% (58 out of 457) underwent other procedures. All procedures performed in elective setting. In terms of surgical approach, 28% (126 out of 457) of the procedures were open; 44% (201 out of 457) were laparoscopic; 12% (55 out of 457) were laparoscopic-assisted; 16% (75 out of 457) started laparoscopically but were converted to open. Malignant colorectal pathology was the indication for surgery in 88% (402 out of 457) of cases.

Psoas major muscle mass measurements

The median total psoas muscle area and volume were 21 cm^2 (IQR: 15-27) and 274 cm^3 (IQR: 201-362), respectively. The median psoas muscle index measured via 2D and 3D approaches were 7 cm^2/m^2 (IQR: 6-9) and 99 cm^3/m^2 (IQR: 76-120), respectively.

Mortality

The risk of 30-day mortality, 1-year mortality and 5-year mortality were 2% (9 out of 457), (7.4% (34 out of 457) and 27.1% (124 out of 457), respectively.

Inability to perform CPET

Among the included patients, 15 were not able to perform CPET but underwent operation as high risk patients. For this subgroup, the risk of 30-day mortality, 1-year mortality and 5-year mortality were 13% (2 out of 15), 33% (5 out of 15) and 47% (7 out of 15), respectively.

Psoas major muscle mass and CPET performance

Total psoas muscle area. Linear regression analyses suggested that total psoas muscle area measured via 2D approach was predictor of the followings: $\dot{V}O_2$ AT (Coefficient: 0.0605, P<0.001), $\dot{V}O_2$ AT (allometric scaling) (Coefficient: 0.5496, P<0.001), $\dot{V}E/\dot{V}CO_2$-AT (Coefficient: -0.1832, P<0.001), $\dot{V}E/\dot{V}O_2$-AT (Coefficient: -0.2298, P<0.001), $\dot{V}O_2$ peak (Coefficient: 0.2353, P<0.001), $\dot{V}O_2$ peak (allometric scaling) (Coefficient: 1.398, P<0.001), % predicted $\dot{V}O_2$ peak (Coefficient: 0.272, P=0.043), exercise time (Coefficient: 7.43, P<0.001), maximum Work (Coefficient: 3.628, P<0.001), peak metabolic equivalents, METS (Coefficient: 0.06763, P<0.001), peak respiratory exchange ratio, RER (Coefficient: 0.00337, P= 0.003), and peak oxygen pulse (Coefficient: 0.2961, P<0.001) (Table 2). Binary logistic regression analyses suggested that total psoas muscle area measured via 2D approach predicts inability to perform CPET (OR: 0.8906, 95% CI 0.8124, 0.9764, P=0.007) and inability to reach AT (OR: 0.8876, 95% CI 0.8355, 0.9429, P<0.001) (Table 3).

Total psoas muscle volume. Linear regression analyses suggested that total psoas muscle volume measured via 3D approach was predictor of the followings: $\dot{V}O_2$ AT (Coefficient: 0.00468, P<0.001), $\dot{V}O_2$ AT (allometric scaling) (Coefficient: 0.03571, P<0.001), $\dot{V}E/\dot{V}CO_2$-AT (Coefficient: -0.0108, P<0.001), $\dot{V}E/\dot{V}O_2$-AT (Coefficient: -0.01449, P<0.001), $\dot{V}O_2$ peak (Coefficient: 0.01598, P<0.001), $\dot{V}O_2$ peak (allometric scaling) (Coefficient: 0.09087, P<0.001), % predicted $\dot{V}O_2$ peak (Coefficient: 0.01849, P=0.036), exercise time (Coefficient: 0.497, P<0.001), maximum Work (Coefficient: 0.2261, P<0.001), peak METS (Coefficient: 0.004634, P<0.001), peak RER (Coefficient: 0.000228, P= 0.002), and peak oxygen pulse (Coefficient: 0.01711, P<0.001) (Table 2). Binary logistic regression analyses suggested that total psoas muscle volume measured via 3D approach predicts inability to perform CPET (OR: 0.9943, 95% CI 0.9888, 0.9998, P=0.032) and inability to reach AT (OR: 0.9927, 95% CI 0.9889, 0.9964, P<0.001) (Table 3).

Psoas muscle index (2D approach). Linear regression analyses suggested that psoas muscle index measured via 2D approach was predictor of the followings: $\dot{V}O_2$ AT (Coefficient: 0.1563, P=0.007), $\dot{V}O_2$ AT (allometric scaling) (Coefficient: 1.519, P<0.001), $\dot{V}E/\dot{V}CO_2$-AT (Coefficient: -0.650, P<0.001), $\dot{V}E/\dot{V}O_2$-AT (Coefficient: -0.793, P<0.001), $\dot{V}O_2$ peak (Coefficient: 0.693, P<0.001), $\dot{V}O_2$ peak (allometric scaling) (Coefficient: 4.067, P<0.001), % predicted $\dot{V}O_2$ peak (Coefficient: 1.351, P=0.003), exercise time (Coefficient: 22.06, P<0.001), maximum Work (Coefficient: 10.426, P<0.001), peak METS (Coefficient: 0.1951, P<0.001), peak RER (Coefficient: 0.00919, P=0.015), and peak oxygen pulse (Coefficient: 0.8315, P<0.001) (Table 2). Binary logistic regression analyses suggested that psoas muscle index measured via 2D approach predicts inability to reach AT (OR: 0.6975, 95% CI 0.5736, 0.8483, P<0.001) (Table 3).

Psoas muscle index (3D approach). Linear regression analyses suggested that psoas muscle index measured via 3D approach was predictor of the followings: $\dot{V}O_2$ AT (Coefficient: 0.01349, P<0.001), $\dot{V}O_2$ AT (allometric scaling) (Coefficient: 0.1024, P<0.001), $\dot{V}E/\dot{V}CO_2$-AT (Coefficient: -0.03780, P<0.001), $\dot{V}E/\dot{V}O_2$-AT (Coefficient: -0.05039, P<0.001), $\dot{V}O_2$ peak (Coefficient: 0.04918, P<0.001), $\dot{V}O_2$ peak (allometric scaling) (Coefficient: 0.2738, P<0.001), % predicted $\dot{V}O_2$ peak (Coefficient: 0.0877, P=0.003), exercise time (Coefficient: 1.542, P<0.001), maximum Work (Coefficient: 0.6664, P<0.001), peak METS (Coefficient: 0.01408, P<0.001), maximum heart rate, HR (Coefficient: 0.0883, P=0.038), peak RER (Coefficient: 0.000686, P=0.005), and peak oxygen pulse (Coefficient: 0.04846, P<0.001) (Table 2). Binary logistic regression analyses suggested that psoas muscle index measured via 3D approach predicts inability to reach AT (OR: 0.9783, 0.9671, 0.9896, P<0.001) (Table 3).

Psoas major muscle mass and mortality

One-year mortality. Binary logistic regression analyses suggested that total psoas muscle area (OR: 0.9031, 95% CI 0.8485, 0.9613, P=0.001), total psoas muscle area (OR: 0.9940, 95% CI 0.9901, 0.9979, P=0.001), psoas muscle index via 2D approach (OR: 0.6790, 95% CI 0.5487, 0.8403, P<0.001), and psoas muscle index via 3D approach (OR: 0.9793, 95% CI 0.9673, 0.9915, P=0.001) predicted 1-year mortality (Table 3). ROC curve analyses showed AUC of 0.667 (95% CI 0.619 to 0.713) for total psoas muscle area, 0.666 (95% CI 0.618 to 0.12) for total psoas muscle volume, 0.690 (95% CI 0.643 to 0.735) for psoas muscle index via 2D approach and 0.681 (95% CI 0.634 to 0.726) for psoas muscle index via 3D approach (Figure 2).

Five-year mortality. Binary logistic regression analyses suggested that total psoas muscle area (OR: 0.9617, 95% 0.9317, 0.9926, P=0.014), total psoas muscle volume (OR: 0.9979, 95% CI 0.9958, 0.9999, P=0.039), psoas muscle index via 2D approach (OR: 0.8602, 95% CI 0.7715, 0.9592, P=0.005), and psoas muscle index via 3D approach (OR: 0.9918, 95% CI 0.9850, 0.9986, P=0.016) predicted 5-year mortality (Table 3). ROC curve analyses showed AUC of 0.572 (95% CI 0.522 to 0.620) for total psoas muscle area, 0.565 (95% CI 0.515 to 0.614) for total psoas muscle volume, 0.599 (95% CI 0.549 to 0.647) for total psoas muscle volume, 0.585 (95% CI 0.536 to 0.634) for psoas muscle index via 2D approach and 0.575 (95% CI 0.525 to 0.623) for psoas muscle index via 3D approach (Figure 2).

Pairwise comparisons of ROC curves for mortality

Pairwise comparison of ROC curves for 1-year and 5-year mortality did not suggest any significant difference in discriminative performance amongst total psoas muscle area, total psoas muscle volume and psoas muscle index and the radiological approach used for their measurements (2D vs 3D) (Table 4).

Discussion

We aimed to evaluate whether radiological psoas major muscle measurements could predict preoperative CPET performance and long-term mortality in patients undergoing major colorectal surgery and to compare predictive performance of psoas muscle measurements using 2D approach and 3D approach. Analysis of 457 patients suggested that psoas major muscle mass variables (total psoas muscle area, total psoas muscle volume and psoas muscle index) predict CPET performance and long-term mortality in patients undergoing major colorectal surgery. However, there was no significant difference in predictive performance amongst total psoas muscle area, total psoas muscle volume and psoas muscle index suggesting that 3D approach may not provide any advantage in comparison to 3D approach.

To date a wide variety of core and appendicular skeletal muscles have been studied as potential markers of sarcopenia, with measurements of the psoas major muscle predominating in the literature.[8] Several authors have investigated which measurement of the psoas major muscle provides the highest specificity as a marker of sarcopenia, and to this end, it has previously been reported that single slice measurements of the psoas major muscles are representative of the total psoas major muscle volume.[18] This study has extended this previous research by showing axial psoas area and psoas volume measurements are equivalent as markers of long-term outcome in a clinical setting. Using single slice measurements of psoas major muscle area has the advantages of being fast and easily performed. It avoids the need for specialist software, although machine learning algorithms which perform automatic segmentation exist, which can potentially further facilitate data extraction.[33]

We have also shown an association between CT derived psoas muscle measurements and CPET performance, which is consistent with published studies in other settings.[34, 35] While CPET is likely to remain an indispensable preoperative assessment tool where high risk surgery is being contemplated, it takes time to arrange and perform, whereas psoas major muscle measurements can be obtained from the baseline diagnostic CT. Our results suggest that CT-derived psoas muscle measurements may be promising to inform more objective selection of patients for CPET and in identifying appropriate patients for prehabilitation. Prehabilitation has already been shown to decrease the incidence of postoperative complications in patients undergoing abdominal surgery.[36]

Furthermore, in scenarios such as emergency surgery, preoperative CPET is not possible. It has already been shown that psoas muscle measurements are associated with outcome in patients undergoing emergency surgery.[14,15] The HAS model (Hajibandeh Index, ASA status and sarcopenia) emergency laparotomy mortality risk calculator is the first risk assessment tool which takes into account psoas muscle measurements in predicting the risk of mortality following emergency laparotomy.[37] The utility of CT derived muscle mass when CPET testing is unavailable is further emphasised by studies which have shown that it provides information not given by other clinical parameters such as body mass index,[38] and is more closely associated with a clinical frailty score than a questionnaire based screening tool (SARC-F).[39]

The current study has the following limitations. The retrospective nature of the study subject our results to inevitable selection bias. We only included patients who were fit enough to undergo major operation, hence the association between psoas muscle measurements and CPET performance or log-term mortality in patients who did not undergo operation were not included and could therefore be considered a selection bias. Among 640 patients who underwent major colorectal surgery, 183 patients were excluded as they did not meet the eligibility criteria; nevertheless, the remaining sample size was relatively large enough to make meaningful conclusions with minimal risk of type 2 error. Otherwise, adequate sample size, objective and structured methodology, robust radiological approach in measurement of psoas muscle mass, no loss to follow-up, and transparent analyses and reporting may be considered as strengths of this this study.

Conclusions

The results of this study suggests that radiologically-measured psoas muscle mass variables may predict CPET performance and long-term mortality in patients undergoing elective major colorectal resection. The 3D approach in measurement of psoas major muscle mass may not provide an advantage in comparison to 2D approach in this setting. Our results suggest that radiologically-measured psoas muscle mass may help to inform more objective selection of patients for preoperative CPET and prehabilitation.

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Legends for Figures and Tables

Figure 1. The study flow diagram

Figure 2. Results of ROC curve analyses for association between psoas muscle mass measurements and a) 1-year mortality; b) 5-year mortality.

Table 1. Baseline characteristics of the included population

Table 2. Results of linear regression analysis for association between psoas muscle mass measurements and CPET performance

Table 3. Results of binary logistic regression analysis for association between psoas muscle mass measurements, CPET performance, and mortality

Table 4. Results of pairwise comparison of ROC curves for 1-year and 5-year mortality

Table

Table 1. Baseline characteristics of the included population	
Number of patients	457
Age, median (IQR)	72 (64-78)
Male, n (%)	267 (58%)
Female, n (%)	190 (42%)
Height, median (IQR)	169 (162-175)
Weight, median (IQR)	79 (68-90)
BMI, median (IQR)	27 (25-31)
ASA, n (%)	
I	15 (3%)
II	273 (60%)
III	164 (36%)
IV	3 (1%)
Smoking, n (%)	
Current smoker	53 (12%)
Ex-smoker	235 (51%)
Never smoked	169 (37%)
Comorbidities, n (%)	
Hypertension	211 (46%)
Diabetes	79 (17%)
Ischemic heart disease	48 (11%)
Atrial fibrillation	51 (11%)
Valvular heart disease	25 (5%)
Cerebrovascular accident	40 (9%)
Peripheral arterial disease	18 (4%)
Chronic obstructive pulmonary disease	48 (11%)
Asthma	43 (9%)
Renal insufficiency	20 (4%)
Liver cirrhosis	3 (1%)
Anaemia	174 (38%)
Malignancy as indication for operation, n (%)	402 (88%)
Procedure, n (%)	
Hemicolectomy	150 (33%)
Extended hemicolectomy	26 (6%)
Transverse colectomy	4 (1%)
Sigmoid colectomy	27 (6%)
Subtotal colectomy	7 (2%)
Panproctocolectomy	5 (1%)
Anterior resection	150 (32%)
Abdominoperineal resection	30 (7%)
Other	58 (13%)
Surgical approach, n (%)	
Open	126 (28%)
Laparoscopic	201 (44%)
Laparoscopic-assisted	55 (12%)
Laparoscopic converted to open	75 (16%)

CI: confidence interval; ASA: American Society of Anesthesiologists; IQR: interquartile range

Table

Table 2. Results of linear regression analysis for association between psoas muscle mass measurements and CPET performance

CPET performance as dependent variable	Psoas muscle mass measurements as independent variable							
	Total psoas muscle area (2D approach)		Total psoas muscle volume (3D approach)		Psoas muscle index (2D approach)		Psoas muscle index (3D approach)	
	Coefficient	P-value	Coefficient	P-value	Coefficient	P-value	Coefficient	P-value
$\dot{V}O_2$ Rest	-0.00275	0.677	-0.00014	0.744	-0.0112	0.614	-0.00056	0.698
$\dot{V}O_2$ AT	0.0605	<0.001	0.00468	<0.001	0.1563	0.007	0.01349	<0.001
$\dot{V}O2$ AT (allometric scaling)	0.5496	<0.001	0.03571	<0.001	1.519	<0.001	0.1024	<0.001
$\dot{V}E/\dot{V}CO_2$ AT	-0.1832	<0.001	-0.0108	<0.001	-0.650	<0.001	-0.03780	<0.001
$\dot{V}E/\dot{V}O_2$ AT	-0.2298	<0.001	-0.01449	<0.001	-0.793	<0.001	-0.05039	<0.001
$\dot{V}O_2$ peak	0.2353	<0.001	0.01598	<0.001	0.693	<0.001	0.04918	<0.001
$\dot{V}O_2$ peak (allometric scaling)	1.398	<0.001	0.09087	<0.001	4.067	<0.001	0.2738	<0.001
$\dot{V}O_2$ peak/Predicted $\dot{V}O_2$ peak	0.272	0.043	0.01849	0.036	1.351	0.003	0.0877	0.003
$\dot{V}O_2$ peak Exercise Time	7.43	<0.001	0.497	<0.001	22.06	<0.001	1.542	<0.001
Max Work	3.628	<0.001	0.2261	<0.001	10.426	<0.001	0.6664	<0.001
$\dot{V}O_2$ peak METS	0.06763	<0.001	0.004634	<0.001	0.1951	<0.001	0.01408	<0.001
$\dot{V}O_2$ peak Max HR	0.27	0.166	0.024	0.059	0.936	0.154	0.0883	0.038
$\dot{V}O_2$ peak Max RER	0.00337	0.003	0.000228	0.002	0.00919	0.015	0.000686	0.005
$\dot{V}O_2$ peak Max VO2/HR	0.2961	<0.001	0.01711	<0.001	0.8315	<0.001	0.04846	<0.001

$\dot{V}O_2$: oxygen uptake; AT: anaerobic threshold; $\dot{V}E/\dot{V}O_2$: ventilatory equivalents for oxygen; $\dot{V}E/\dot{V}CO_2$: ventilatory equivalents for carbon dioxide; HR: hear rate; RER: respiratory rate; METS: metabolic equivalents; CPET: cardiopulmonary exercise testing

Table

Table 3. Results of binary logistic regression analysis for association between psoas muscle mass measurements, CPET performance, and mortality

Dependent variables	**Psoas muscle mass measurements as independent variable**							
	Total psoas muscle area (2D approach)		**Total psoas muscle volume (3D approach)**		**Psoas muscle index (2D approach)**		**Psoas muscle index (3D approach)**	
	OR (95% CI)	**P-value**	**OR (95% CI)**	**P-value**	**OR (95% CI)**	**P-value**	**OR (95% CI)**	**P-value**
Inability to perform CPET	0.8906 (0.8124, 0.9764)	0.007	0.9943 (0.9888, 0.9998)	0.032	0.7685 (0.5807, 1.0170)	0.055	0.9879 (0.9715, 1.0045)	0.146
Inability to reach AT	0.8876 (0.8355, 0.9429)	<0.001	0.9927 (0.9889, 0.9964)	<0.001	0.6975 (0.5736, 0.8483)	<0.001	0.9783 (0.9671, 0.9896)	<0.001
1-year Mortality	0.9031 (0.8485, 0.9613)	0.001	0.9940 (0.9901, 0.9979)	0.001	0.6790 (0.5487, 0.8403)	<0.001	0.9793 (0.9673, 0.9915)	0.001
5-year Mortality	0.9617 (0.9317, 0.9926)	0.014	0.9979 (0.9958, 0.9999)	0.039	0.8602 (0.7715, 0.9592)	0.005	0.9918 (0.9850, 0.9986)	0.016

OR: odds ratio; CI: Confidence intervals; CPET: cardiopulmonary exercise testing; AT: anaerobic threshold

Table 4. Results of pairwise comparison of ROC curves for 1-year and 5-year mortality

	1-Year Mortality	5-Year Mortality
Total Psoas Area (2D) vs Total Psoas Volume (3D)	P = 0.9666	P = 0.7178
Total Psoas Area (2D) vs Psoas Muscle Index (2D)	P = 0.0553	P = 0.1494
Total Psoas Area (2D) vs Psoas Muscle Index (3D)	P = 0.6634	P = 0.8716
Total Psoas Volume (3D) vs Psoas Muscle Index (2D)	P = 0.4467	P = 0.3508
Total Psoas Volume (3D) vs Psoas Muscle Index (3D)	P = 0.1655	P = 0.2188
Psoas Muscle Index (2D) vs Psoas Muscle Index (3D)	P = 0.7704	P = 0.5924

Figure

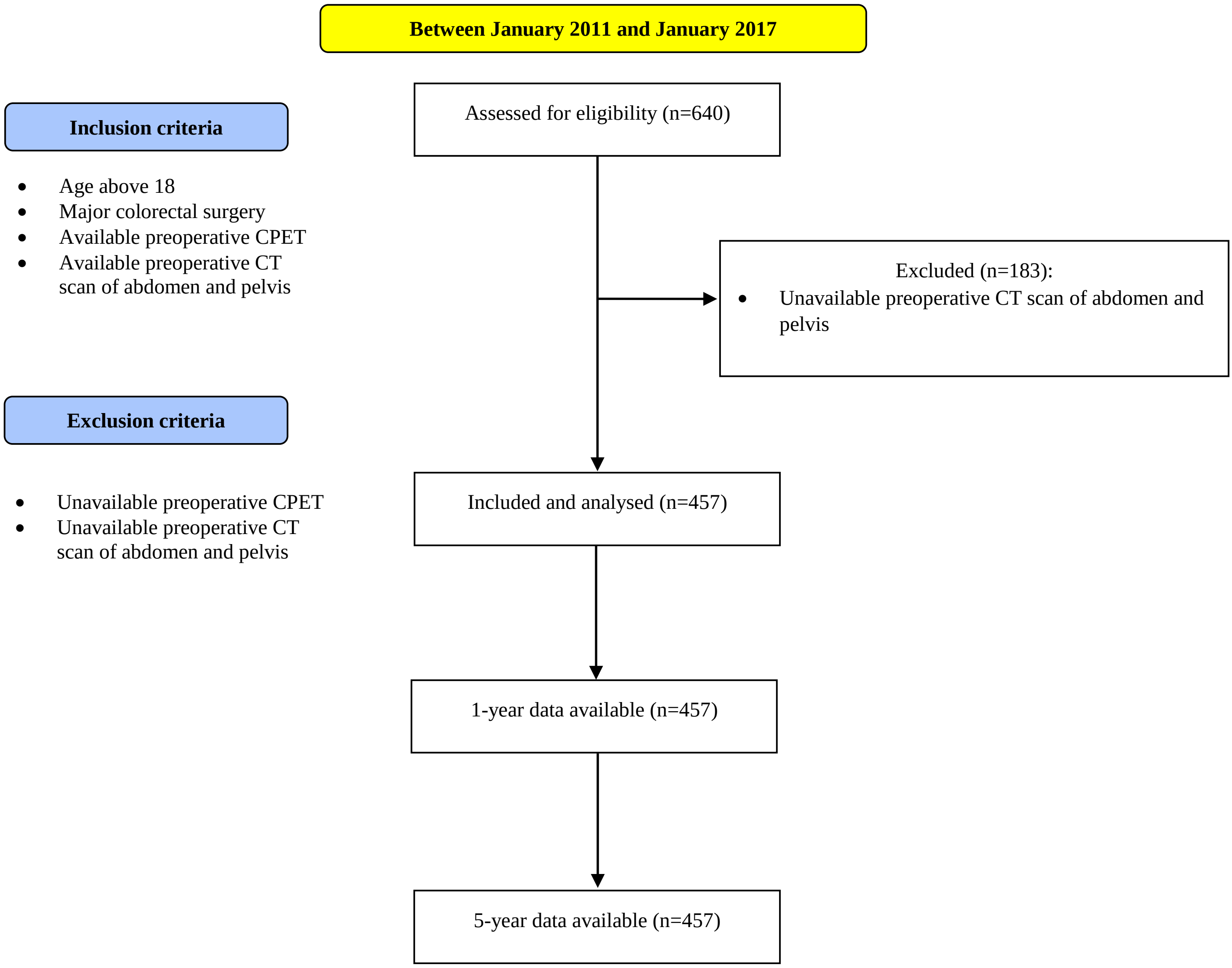
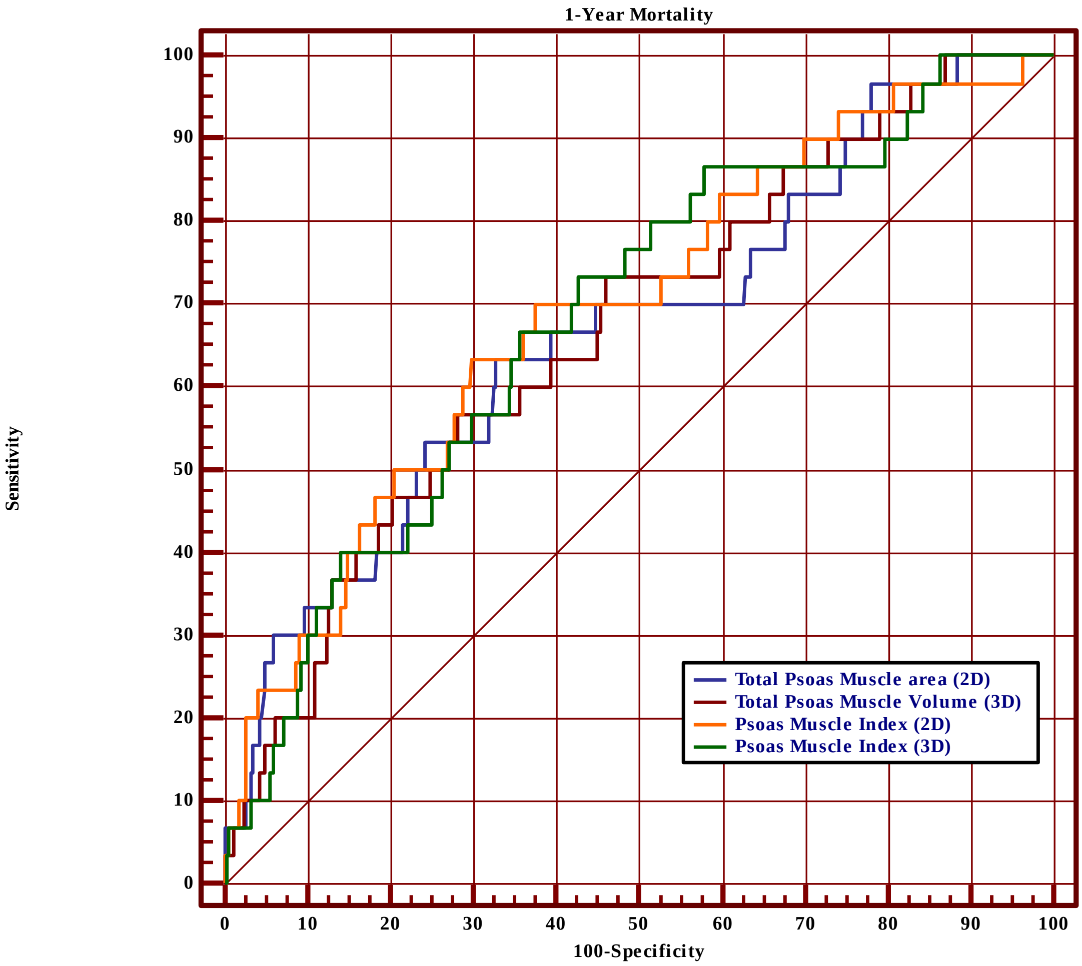


Figure 1. The study flow diagram

Figure

a) 1-year Mortality



b) 5-year Mortality

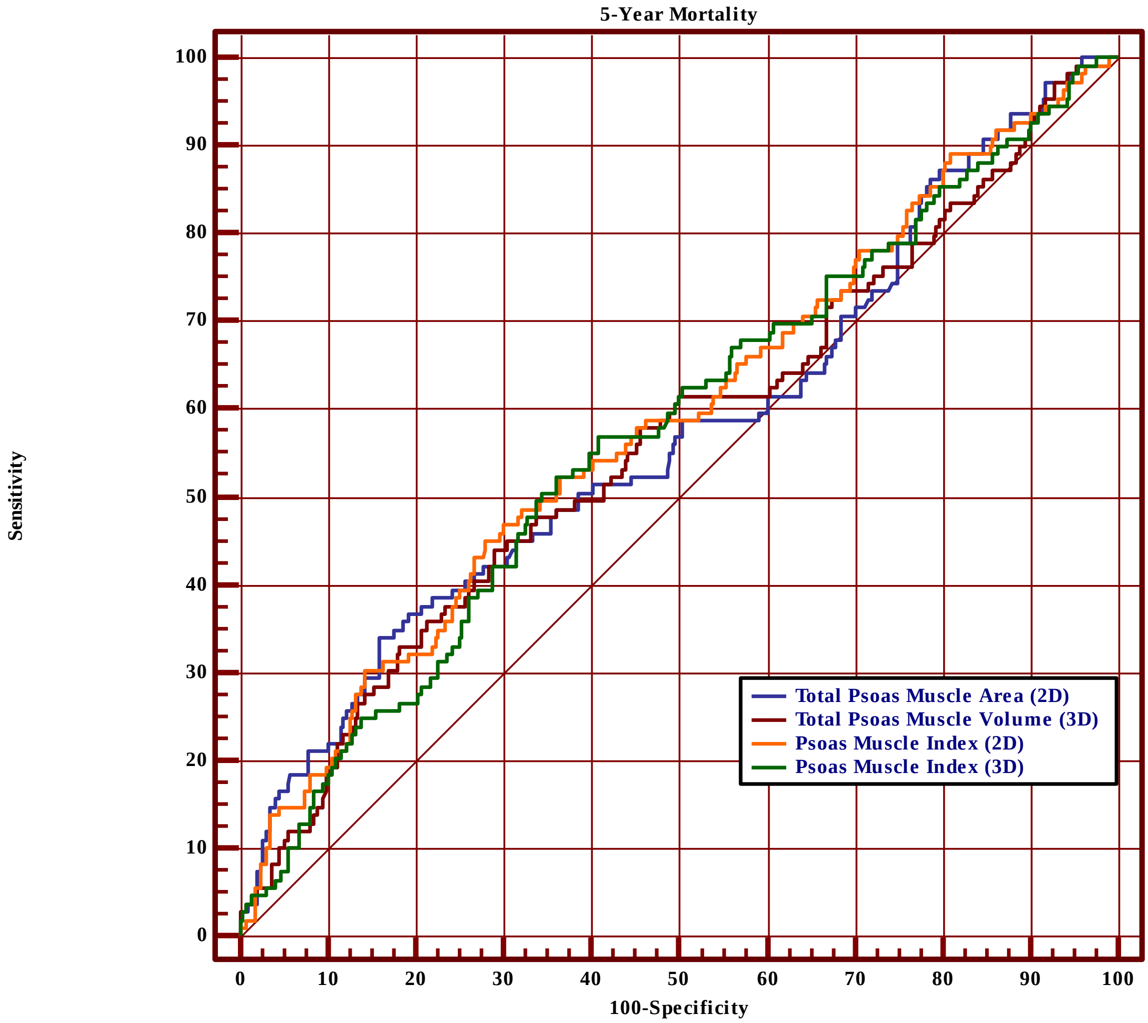


Figure 2. Results of ROC curve analyses for association between psoas muscle mass measurements and a) 1-year mortality; b) 5-year mortality

Conflict of interest statement

Damian M. Bailey is Editor-in-Chief of *Experimental Physiology*, Chair of the Life Sciences Working Group, a member of the Human Spaceflight and Exploration Science Advisory Committee to the European Space Agency, a member of the Space Exploration Advisory Committee to the UK Space Agency, and a member of the National Cardiovascular Network for Wales and South East Wales Vascular Network. Damian M. Bailey is also affiliated to the companies FloTBI Inc. and Bexorg Inc., focused on the technological development of novel biomarkers of brain injury in humans. All other authors declare no conflict of interest.