



ISSN: 2754-8880
Published 00 11 0000

Psoas Muscle Cross-Sectional Area and Outcomes Following Colorectal Cancer Surgery

Matthew Mouat¹, Ashok Gunawardene², Lisa Sweetman¹, Elizabeth Dennett^{1,2}, and Peter Larsen^{2*}

*Corresponding author: Associate Professor Peter Larsen, Department of Surgery Anaesthesia, University of Otago Wellington, New Zealand. Peter.Larsen@otago.ac.nz.

¹Capital & Coast District Health Board, New Zealand

²Department of Surgery and Anaesthesia, University of Otago, Wellington, New Zealand

ORIGINAL

Abstract

Background: Frailty and functional status are established risk factors for postoperative morbidity and mortality, but new data also suggest a link between sarcopenia and longer-term oncological outcomes in colorectal cancer. Cross-sectional imaging is performed routinely prior to elective resection and provides a means to measure psoas muscle cross-sectional area, which in turn is a surrogate marker of sarcopenia.

Methods: A retrospective cohort study of patients undergoing elective surgery with curative intent for colorectal cancer. Using automated software, psoas muscle cross-sectional area was measured and the relationship with five-year disease-free survival was evaluated using Kaplan-Meier survival curves.

Results: A significant relationship was found among patients with a low (below median) psoas muscle cross-sectional area, HR 1.57 (95% CI 1.1-2.5) p=0.04.

Conclusion: This study demonstrated a potential relationship between psoas muscle cross-sectional area and disease-free survival, highlighting the further utility of pre-operative staging CT in predicting prognosis in patients with colorectal cancer.

Introduction

Assessing the likelihood of postoperative morbidity and mortality is critical to informing the decision-making of both surgical teams and patients. One of the more complex tasks for clinicians is assessing the overall physical health of the preoperative patient, or when thinking about potential adverse outcomes, their frailty. Frailty can be described as “a state of a reduced physiologic reserve associated with increased susceptibility to disability” (1). Methods for measurement of frailty or functional status have included many variables such as the patient’s ability to perform activities of daily living, cognition, falls, anaemia, weight loss, physical fitness, and underlying medical conditions (1; 2; 3; 4; 5). One aspect of frailty is the loss of lean muscle mass, and many studies have shown that this can be used as a predictor of adverse post-surgical outcomes (4; 6; 7; 8; 9; 10; 11). A simple and reproducible method for loss of muscle mass is a measurement of the cross-sectional area of the psoas muscle in the lumbar spine (8; 9; 12).

Colorectal cancer is the second leading cause of cancer-related deaths in New Zealand. The incidence of colorectal cancer progressively increases with age. Over ninety percent of cases in New Zealand occur after the age of 50, and three-quarters of those patients are older than 65 (13). This age-related increase means that the greatest need for colorectal cancer surgery is in older patients who are also more likely to be frail, conferring a higher risk of adverse postoperative outcomes. Loss of lean muscle mass in this population has been associated with poor short-term

OPEN ACCESS

Edited by
A.Hussain

Submitted 30 Nov 2021

Accepted 04 Dec 2021

Citation

Matthew Mouat, Ashok Gunawardene, Lisa Sweetman, Elizabeth Dennett, Peter Larsen. Psoas Muscle Cross-Sectional Area and Outcomes Following Colorectal Cancer Surgery: BJOSS::2021:(1);39-45

outcomes, but not with a longer-term prognosis. To determine whether loss of mean muscle mass does predict longer-term outcomes, this study examined whether measurements of psoas muscle cross-sectional area in colorectal cancer surgery patients was a predictor of 5-year disease-free survival.

Methods

We retrospectively collated a cohort of all patients undergoing surgery with curative intent for colorectal at Wellington Hospital over the years 2010, 2011, and 2012. Baseline demographics and outcomes were recorded for all patients. Disease-free survival was defined as having neither recurrence nor death. Time-to-recurrence was calculated from the date of surgery to either histological confirmation or clinical-radiological evidence of loco-regional or metastatic disease recurrence on review at a multi-disciplinary meeting, where the date of the meeting was taken as the end-point (14). Patients that were alive and without evidence of disease recurrence on 1st November 2016 were censored.

For each patient, we accessed preoperative CT imaging which had been performed either in Wellington Hospital on 16 slice Siemens or GE CT scanners or by a local private radiology provider on 32 or 64 slice CT scanners. The images for these CT scans were then uploaded onto the workstation for the current 320 slices Toshiba Aquilion One Genesis CT at Wellington Hospital and the images were evaluated using the Toshiba workstation software. This software allowed for the region of interest (ROI) measurement of both psoas muscles at the level of the inferior endplate of L3 using maximum and minimum Hounsfield unit (HU) thresholds [Figure 1](#). The range of values used for measurement of psoas cross-sectional area was between +150HU and -29 HU (12). Measurements were taken by a single observer, a final year diagnostic radiology trainee. The ROI was defined manually using a drawing tool on the Toshiba software. Any operator error that inadvertently included bone (vertebral body or osteophyte) or retroperitoneal fat within the ROI was minimized by the HU threshold settings.

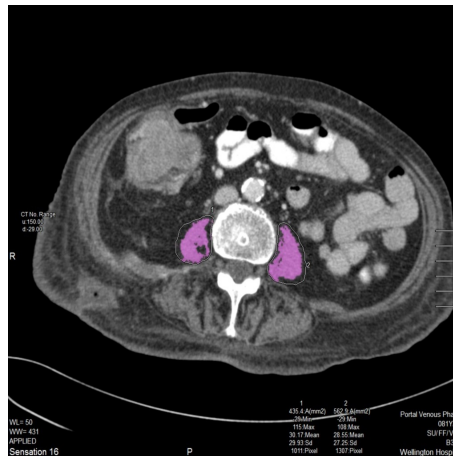


Figure 1. CT image for a representative subject at the inferior endplate of L3. The region of interest was defined manually (defined here as the green line). The Toshiba software then detected muscle tissue on the basis of HU threshold settings (area shaded pink), excluding bone or retroperitoneal fat.

Measurement error was further minimized by using multi-planar reconstruction software to account for curvature (anteroposterior or lateral) of the patient's lumbar spine, to standardize the level of measurement to the inferior endplate of L3. Repeat measurements were performed on images for 10 subjects selected at random, with the investigator blinded to the original measurement. The percentage variance between initial and repeat measurement averaged 1.7%, with a maximum variance of 5.9%.

We took the average of left and right psoas muscle area and divided this by patient height to give total psoas muscle (TPA) area (15). Sarcopenia was defined using gender-specific cutoff points of $<38.5\text{cm}^2/\text{m}^2$ for female patients and $<54.5\text{cm}^2/\text{m}^2$ for male patients based on an international consensus group definition (16).

Statistical analysis

Continuous variables are expressed as mean + standard deviation, and categorical variables are expressed as numbers (percentage). We examined disease-free survival based on quartiles and median cut-points for BMI and TPA, and those with and without sarcopenia. P values >0.05 were taken as statistically significant. Data analysis was performed using SPSS.

Results

During the study period, 237 patients underwent curative-intent surgery for the colorectal cancer cohort. Of this group, 218 patients had preoperative CT scans that were accessible and were included in the study. Demographic features of the patient cohort are given in Table 1. The mean age was 69, 49% were male, and 74% had colon cancer.

Table 1. Demographical and clinical characteristics of the patients

	All (n=218)
Age	69 (12)
Male Gender	108 (49%)
BMI	27 (7)
CCI	
0	117(54%)
1	46 (21%)
2	32 (15%)
3+	23 (10%)
Tumour Location Colon	161 (74%)
Rectum	57 (26%)
Cancer Stage	
1	37 (17%)
2	84 (39%)
3	87 (40%)
4	10 (5%)
Adjuvant Therapy	69 (32%)

The mean TPA in the cohort was $58.1 \pm 17.2 \text{ cm}^2/\text{m}^2$ and the mean BMI was $27.2 \pm 6.9 \text{ kg}/\text{m}^2$. While there was a correlation between BMI and TPA, this relationship was relatively weak ($r=0.36$, $p=0.0001$, Pearson's Correlation) Figure 2. There was a weak inverse relationship between TPA and age, and TPA was greater in male patients ($67.9 \pm 16.1 \text{ cm}^2/\text{m}^2$ versus $47.4 \pm 11.1 \text{ cm}^2/\text{m}^2$, $p=0.0001$, unpaired t-test). TPA was also greater in male patients than female patients and had a weak inverse relationship with age ($r=-0.22$, $p=0.001$, Pearson's Correlation). TPA did not differ by cancer stage, or between patients with colon or rectal cancer.

Applying the consensus definition of sarcopenia to the population, 23 patients were defined as sarcopenic. This group was older than the rest of the cohort (mean age 74 ± 7 versus 69 ± 12 , $p=0.04$) but did not differ from the rest of the cohort significantly by BMI.

At 5 years, disease free survival in the cohort was 62%. We examined rates of disease-free survival against TPA by quartile and by median Figure 3 and observed that there was a statistical difference in outcome in the group divided by median score. Those in the lower half had a 5-year disease-free survival of 55% compared to 66% in those in the upper half, giving a hazard ratio of

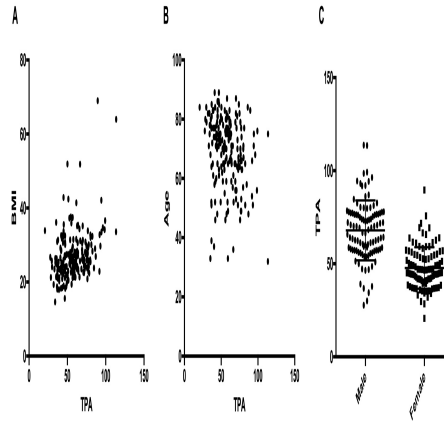


Figure 2. A shows the relationship between TPA in cm²/m² and BMI in kg/m² ($r=0.36$, $p=0.0001$, Pearson’s Correlation). B shows the relationship between age and TPA ($r=-0.22$, $p=0.001$, Pearson’s Correlation). C shows the difference in TPA between male and female patients ($p=0.0001$, unpaired t-test)

1.57 (95% CI 1.1 to 2.5) associated with being in the lower half of TPA scores ($p=0.04$, Mantel-Cox test). There was no significant difference in disease-free survival against BMI by either quartile or by median [Figure 4](#). In those with sarcopenia, we observed a 5-year disease-free survival rate of 54%, compared to 62% in those nonsarcopenic. This difference was not statistically significant [Figure 5](#).

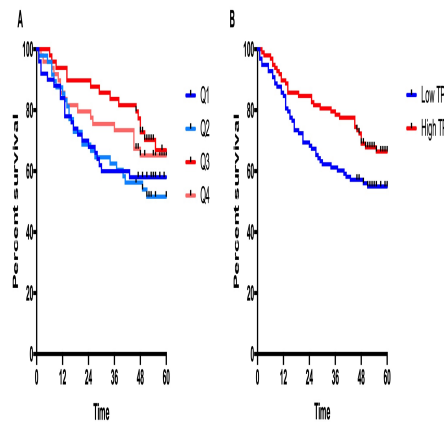


Figure 3. Disease free survival in the population segregated on the basis of TPA quartiles (A) and by the median (B). There was a significant difference between the survival curves segregated by the median, with a hazard ratio of 1.57 (95% CI 1.1 to 2.5) associated with being in the lower half of TPA scores ($p=0.04$, Mantel-Cox test)

Discussion

We have observed that low TPA is a predictor of poor 5-year disease-free survival in patients with colorectal cancer and a similar trend observed in analysis by sarcopenia, but the rate of sarcopenia was low and this result was not statistically significant. TPA did differ by gender, and was correlated with BMI and inversely correlated with age although these were weak relationships.

We observed that preoperative TPA was a statistically significant predictor of 5-year disease-free survival in colorectal cancer surgical patients. Patients in the high TPA group had a 66%

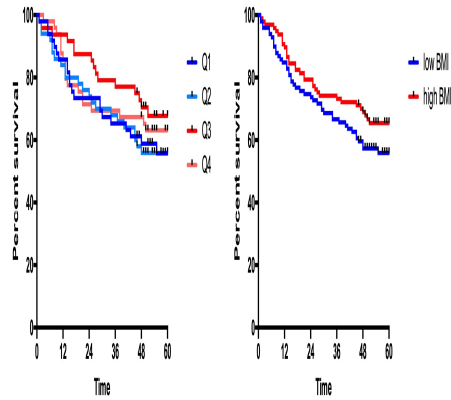


Figure 4. Disease free survival in the population segregated on the basis of BMI quartiles (A) and by the median (B). There were no significant differences in survival between these groups

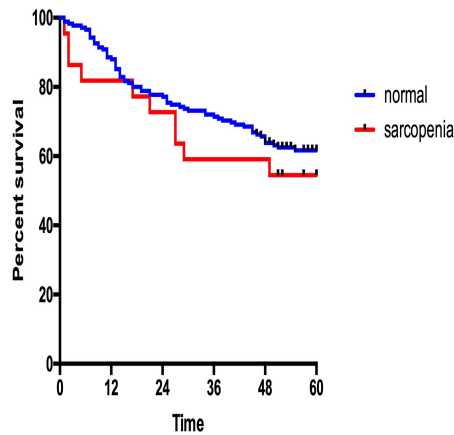


Figure 5. Disease free survival of groups with (n=23) and without (n=195) sarcopenia on the basis of TPA measurement. There was no statistical difference in survival outcomes between these groups

5-year survival compared with 55% in the low TPA group. While TPA was related to BMI, we did not observe the same association between BMI and disease-free survival, indicating that TPA measurement is providing information that is not gained from simple measurement of BMI.

The association between TPA and outcome is consistent with the findings of multiple previous studies linking low preoperative TPA to poor short-term post-surgical outcomes (4; 6; 7; 9; 11). While the majority of literature examining TPA in cancer patients has focused on short-term outcomes, a previous study in oesophageal cancer patients observed that low TPA was associated with worse 3-year survival (17). The only other study we are aware of to examine long term outcomes in colorectal cancer patients found no significant survival differences between those with and without sarcopenia, however, this was in a cohort of patients who had undergone liver resection for metastatic colorectal cancer, as opposed to surgery for the primary mass (7).

The findings of this study suggest that in addition to the previously demonstrated increased likelihood of adverse short-term outcomes, patients with low TPA have reduced 5-year survival. This provides additional information to clinicians and patients for the purposes of operative risk stratification and informed decision-making. It also reinforces the need to optimize patient resilience (reduce frailty) prior to surgery whenever possible.

Measurement of TPA is simple to perform and multiple studies have shown high inter-observer

reliability with minimal training (9; 11; 12). Jones et al also demonstrated that a simplified two-axis cross-sectional measurement significantly correlates with the measurements made using more complex software, as used in this study (9). This further simplifies the quantification of TPA and reduces additional software costs. The measurements take no more than a few minutes to perform and could easily be included in a template report for colorectal cancer staging CT scans.

It is not clear what the optimal threshold for determining low TPA should be. The international consensus document defines CT-based criteria for sarcopenia (16), but these come from a single study examining sarcopenia in obese cancer patients (15). A variety of different thresholds have been applied in the literature (9; 17; 18), and our quartile data suggest a graded risk may exist across the spectrum of TPA. Routine reporting of TPA in colorectal staging CT scans would provide large population data that could address how to quantify TPA. Gender and age-specific criteria may be appropriate, as our data show a degree of correlation with these demographic variables.

The study has several limitations. The data were collected retrospectively, which may affect its quality. Using only the area of the psoas muscles at the level of L3 as an indirect marker of sarcopenia and therefore frailty provides an incomplete assessment of patient health and functional status, and although it has been shown to correlate well with more comprehensive measures of sarcopenia, the addition of more variables such as body fat (to evaluate for the presence of sarcopenic obesity) may increase the predictive value (9; 15). Another limitation is that while the cohort is larger than some, with 218 patients, there were only 23 patients that met the criteria for sarcopenia, limiting the power of the findings for this group. The study was also insufficient in size to allow for detailed analysis of subgroups based on cancer stage, although TPA did not differ by this variable suggesting that our observed results were not attributable to the cancer stage alone.

Conclusion

Low TPA is a predictor of reduced 5-year survival in colorectal cancer surgical patients. Measurement of TPA on CT is reliable, quick, and easy to perform, and could be used to assist in preoperative risk assessment and planning.

References

- [1] Robinson TN, Wu DS, Pointer L, Dunn CL, Cleveland Jr JC, Moss M. Simple frailty score predicts postoperative complications across surgical specialties. *The American Journal of Surgery*. 2013;206(4):544-50.
- [2] Fagard K, Leonard S, Deschodt M, Devriendt E, Wolthuis A, Prenen H, et al. The impact of frailty on postoperative outcomes in individuals aged 65 and over undergoing elective surgery for colorectal cancer: a systematic review. *Journal of geriatric oncology*. 2016;7(6):479-91.
- [3] Makary MA, Segev DL, Pronovost PJ, Syin D, Bandeen-Roche K, Patel P, et al. Frailty as a predictor of surgical outcomes in older patients. *Journal of the American College of Surgeons*. 2010;210(6):901-8.
- [4] Garg L, Agrawal S, Pew T, Hanzel GS, Abbas AE, Gallagher MJ, et al. Psoas muscle area as a predictor of outcomes in transcatheter aortic valve implantation. *The American journal of cardiology*. 2017;119(3):457-60.
- [5] Clegg A, Young J, Iliffe S, Rikkert MO, Rockwood K. Frailty in elderly people. *The lancet*. 2013;381(9868):752-62.
- [6] Lieffers J, Bathe O, Fassbender K, Winget M, Baracos V. Sarcopenia is associated with postoperative infection and delayed recovery from colorectal cancer resection surgery. *British journal of cancer*. 2012;107(6):931-6.

- [7] Peng PD, Van Vledder MG, Tsai S, De Jong MC, Makary M, Ng J, et al. Sarcopenia negatively impacts short-term outcomes in patients undergoing hepatic resection for colorectal liver metastasis. *Hpb*. 2011;13(7):439-46.
- [8] Boutin RD, Yao L, Canter RJ, Lenchik L. Sarcopenia: current concepts and imaging implications. *American Journal of Roentgenology*. 2015;205(3):W255-66.
- [9] Jones K, Doleman B, Scott S, Lund JN, Williams JP. Simple psoas cross-sectional area measurement is a quick and easy method to assess sarcopenia and predicts major surgical complications. *Colorectal Disease*. 2015;17(1):O20-6.
- [10] Miller AL, Englesbe MJ, Diehl KM, Chan CL, Cron DC, Derstine BA, et al. Pre-operative Psoas Muscle Size Predicts Postoperative Delirium in Older: Surgical Patients: A Pilot Cohort Study. *Journal of the American Geriatrics Society*. 2017;65(1):e23.
- [11] Reisinger KW, van Vugt JL, Tegels JJ, Snijders C, Hulsewé KW, Hoofwijk AG, et al. Functional compromise reflected by sarcopenia, frailty, and nutritional depletion predicts adverse postoperative outcome after colorectal cancer surgery. *Annals of surgery*. 2015;261(2):345-52.
- [12] McClellan T, Allen BC, Kappus M, Bhatti L, Dafalla RA, Snyder LD, et al. Repeatability of computerized tomography-based anthropomorphic measurements of frailty in patients with pulmonary fibrosis undergoing lung transplantation. *Current problems in diagnostic radiology*. 2017;46(4):300-4.
- [13] Group NZG. Guidance on surveillance for people at increased risk of colorectal cancer [PDF on Internet]. Wellington: New Zealand Guidelines Group [Updated 2011];. <https://www.health.govt.nz/system/files/documents/publications/colorectal-cancer-surveillance-guidance.pdf>.
- [14] Birgisson H, Wallin U, Holmberg L, Glimelius B. Survival endpoints in colorectal cancer and the effect of second primary other cancer on disease free survival. *BMC cancer*. 2011;11(1):1-11.
- [15] Prado CM, Lieffers JR, McCargar LJ, Reiman T, Sawyer MB, Martin L, et al. Prevalence and clinical implications of sarcopenic obesity in patients with solid tumours of the respiratory and gastrointestinal tracts: a population-based study. *The lancet oncology*. 2008;9(7):629-35.
- [16] Fearon K, Strasser F, Anker SD, Bosaeus I, Bruera E, Fainsinger RL, et al. Definition and classification of cancer cachexia: an international consensus. *The lancet oncology*. 2011;12(5):489-95.
- [17] Park SY, Yoon JK, Lee SJ, Haam S, Jung J. Prognostic value of preoperative total psoas muscle area on long-term outcome in surgically treated oesophageal cancer patients. *Interactive cardiovascular and thoracic surgery*. 2017;24(1):13-9.
- [18] Hanaoka M, Yasuno M, Ishiguro M, Yamauchi S, Kikuchi A, Tokura M, et al. Morphologic change of the psoas muscle as a surrogate marker of sarcopenia and predictor of complications after colorectal cancer surgery. *International journal of colorectal disease*. 2017;32(6):847.