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# Point-of-Care Ultrasound Frailty Assessments: Comment

## To the Editor:

We read with great interest the article by Canales *et al.*,[1] who benchmarked the predictive value of four surrogates of preoperative sarcopenia and the Fried phenotype frailty tool for predefined adverse postoperative outcomes. We salute the authors on this pioneering and important investigation and would like to highlight several points.

First, the authors used three novel, bedside, sonographic measurements of the quadriceps muscle, as well as a tomographic assessment of the psoas muscle. For the assessment of generalized sarcopenia, the abdominal muscles, including the psoas, are preferable to appendicular muscles due to the former relative independence of activity level.[2] Moreover, dual-energy x-ray has been the standard quantitative measure for total appendicular muscle mass and appears in nearly 500 publications.[3] The advantage of bedside appendicular muscle sonography should be further explored.

Second, females comprised 71 and 61% of the "Not Frail" and "Frail" study groups. The authors adjusted psoas muscle area values according to body surface area and body mass index, but not by sex. The prevailing consensus, however, is to use sex-specific cutoffs for low values due to significant sex variation of human spinal and paraspinal muscles at all body habitus.[4] This fact independently underscores the importance of equal representation of both sexes in the cohort.

Third, for the sample power analysis, the authors provide the desired discriminative magnitude and CI; the expected frequency of frailty in the study population and expected sensitivity and specificity of sonography, however, are not given.[5] Additionally, the areas under the receiver operating curves (AUCs) for each frailty surrogate and outcome measurement are presented (table 1 of Canales *et al.*[1]). The false discovery rate for these 40 statistical tests was not reported, and the authors did not analyze whether differences in AUC between the frailty surrogates were statistically significant.[6]

Last, for comparison purposes, the study provided sonographic muscle mass measurements of healthy controls. However, the race/ethnicity makeup of the cohort and controls were very different (*e.g.*, 79% Caucasians *vs.* 35%, respectively), even though skeletal muscle mass differs significantly between ethnicities at all adult ages.[7] As expected, all controls were "Not Frail" per the Friend phenotype frailty assessment (table 2 of Canales *et al.*[1]), and therefore, the diagnostic quality of a frailty test cannot be assessed in this group. Simply put, a frailty test when performed on nonfrail controls would yield specificity and negative predictive values of 1, but the test's sensitivity, positive predictive value, and AUC cannot be determined. However, sensitivity, specificity, positive and negative predictive values, AUC, and cutoff point are provided for each sonographic frailty surrogate in the controls (table 3 of Canales *et al.*[1]). Likewise, computed tomography was not performed in the controls (see, "Methods" and fig. 3A of Canales *et al.*[1]), yet the aforementioned statistical parameters are provided for psoas muscle area in controls. Perhaps table 3 should read "study cohort" instead of "heathy controls."

The authors did not comment on the surprisingly poor ability of the well established Fried phenotype frailty assessment to predict unplanned intensive care unit admission, prolonged intensive care unit and hospital length of stay, and rehospitalization (AUCs of 0.61, 0.54, 0.65, and 0.52, respectively). The sonographic and the tomographic sarcopenia assessments also seem to lack adequate discriminatory value for a prolonged hospital length of stay and rehospitalization. Unexpectedly prolonged postoperative hospitalization frequently precedes and portends unplanned nursing facility admission. The unexpected dichotomous discriminatory ability of these frailty assessments to predict the latter but not the former warrants further exploration. While we appreciate the authors' objective to determine whether appendicular skeletal sonography could be used reliably in a preoperative setting to identify frailty, addressing these points would further strengthen their findings.

### Competing Interests

The authors declare no competing interests.

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# Point-of-Care Ultrasound Frailty Assessments: Comment

## To the Editor:

We congratulate Canales *et al.*[1] on their innovative application of bedside ultrasound to identify frailty preoperatively. Their study adds to the accruing evidence base that patients with reduced skeletal muscle mass are at increased risk of poorer outcomes after surgery. The authors present results for raw unadjusted measures and for body surface area– and body mass index–adjusted measures, which is a helpful comparison. However, this highlights one frequent inconsistency emerging in studies of this type: how to adequately account for indexation of muscle size to differences in body shape, sex, and ethnicity and whether to undertake such indexation at all.

As an example, Mueller *et al.*[2] used a coefficient adjustment of 1.484 for female participants. This figure was derived from a single study of healthy patients predominantly under the age of 60.[3] The study by Salim *et al.*[4] standardized rectus femoris and vastus intermedius to thigh length and lumbar skeletal muscle cross-sectional area to patient height. In another study investigating mortality in critically ill patients, rectus femoris muscle was adjusted for body surface area only.[5] In other studies exploring the association between psoas muscle size and outcomes, muscle size has been stratified into tertiles or quartiles by sex or by both body surface area and sex.[6]

To further obfuscate the utility of such skeletal muscle measurements, ethnic disparities may occur.[7] In all the above cited studies, where reported, the majority of patients have been Caucasian. The study by Canales *et al.*[1] was a small pilot study, but it is interesting to note that all Hispanic patients (five participants) were classed as frail, when Hispanics, especially males, have significantly less skeletal muscle mass and a higher rate of decline with ageing when compared to other groups.[7]

Ultrasound measurement of major muscles is a conceptually and logistically attractive surrogate for sarcopenia and/or frailty and holds the promise of providing an objective outcome for prehabilitation programs. It is hard to envisage how such a measure will move beyond an interesting association found in the separate and disparate populations that have been studied. There is much work to be done to find, if at all possible, universally acceptable measurements that are generalizable. We hope future researchers report multiple methods of indexation and raw data for comparison, as Canales *et al.*[1] have done, and that larger studies attempt to unravel some of these unknowns to enable a more evidence-based standard of reporting.

### Competing Interests

The authors declare no competing interests.

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# Point-of-Care Ultrasound Frailty Assessments: Reply

## In Reply:

We thank Raveh *et al.*[1] and Ben-Menachem and Ashes[2] for their interest in our research. We are pleased that our article on preoperative point-of-care ultrasound to identify frailty[3] has generated discussions on best practices for measuring and reporting muscle mass as a predictor of patient outcomes. Increasing awareness of the varied approaches to measuring muscle mass and creating a collective body of work by different investigatory groups are paramount to moving research forward from associations to defining targeted interventions to improve patient outcomes.

Raveh *et al.*[1] question the utility of point-of-care ultrasound in general over dual-energy x-rays or computer tomography of psoas muscles or total appendicular muscle mass, given the vast number of publications supporting these more invasive assessments. Although we agree with Raveh *et al.*[1] that the current standard for measuring total appendicular muscle mass includes radiation emitting techniques that require scheduled time in the scanner, the goal of our pilot project was to explore a bedside model that would allow the clinician to perform assessments at the bedside to (1) allow rapid risk stratification, (2) provide a radiation-free methodology, and (3) not be limited by resource (scanner) utilization.

In addition, Ben-Menachem and Ashes[2] point out the lack of standardization regarding how to adequately account for indexation of muscle size to different body shape, sex, and ethnicity. We reported raw data in addition to indexed values specifically because of the varied reporting practices. Ideally, a study adequately powered to account for ethnicity, body shape, sex, and frailty status should be undertaken. This information would be high yield as more of us explore sarcopenia, muscle loss, and health outcomes.

We also thank Raveh *et al.*[1] for bringing up the false discovery rate, which we inadvertently omitted from the article. Using a $P$ value threshold of 0.05 for table 3 (40 possible tests), the false discovery rate was estimated to be 25%, meaning that of the six tests we are calling significant, it is likely that around two are false positives (using the methods of false discovery rate described by Storey[4]). It is also true we did not analyze whether differences in the AUC between the frailty surrogates were statistically significant. We felt that given the exploratory nature of this study and the relatively small sample size/event rates, this would be a somewhat underpowered endeavor. For your curiosity, we have now computed these comparisons for you (table 1). As expected, none of the differences were statistically significant.

**Table 1.** Paired-sample Area Difference under the Receiver Operating Characteristics Curves

| Characteristic | Area under the Curve (95% CI) |
|---|---|
| 1 Quadriceps depth, cm | 0.80 (0.64, 0.97) |
| 2 Rectus femoris cross-sectional area, $cm^2$ | 0.70 (0.49, 0.91) |
| 3 Psoas muscle area, $cm^2$ | 0.88 (0.76, 1.00) |
| 4 Rectus femoris circumference, cm | 0.67 (4.46, 0.88) |

1 *versus* 2, $P = 0.088$; 1 *versus* 3, $P = 0.346$; 1 *versus* 4, $P = 0.106$; 2 *versus* 3, $P = 0.133$; 2 *versus* 4, $P = 0.439$; 3 *versus* 4, $P = 0.090$.

We could not agree more with Raveh *et al.*[1] and Ben-Menachem and Ashes[2] that more work needs to be done to standardize measurement and reporting strategies. Our goal with the pilot study was to determine feasibility and hope that further work by us and other groups will bring us closer to identifying best practices for measurements and reporting strategies.

## Competing Interests

Dr. Cannesson has unrelated financial relationships with Sironis, Edwards Lifesciences (Irvine, California), Masimo (Irvine, California). The authors declare no competing interests.

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