Article details: 2022-0094
Title: Using the Hospital Frailty Risk Score to assess mortality risk in older medical patients admitted to the intensive care unit
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Reviewer 1: Ms. Carmel Montgomery
Institution: University of Alberta
General comments (author response in bold)

Thank you for the opportunity to review this manuscript describing hospital 12-month readmissions among a cohort of patients ≥75 years of age with previous hospital discharge Hospital Frailty Risk score in Ontario. Outcomes included ICU admission and mortality during hospital readmission. This manuscript is well written with sound methods. I have a few suggestions for your consideration.

2.1 Major comments:
1. Page 7, line 31 The logistic regression models included age, sex, hospital, weekday, admit time, LAPS. My concern with LAPS score is its variability over time yet lack of variability across severity of frailty (HFRS in Table 1). A single score from a single point in time may not represent the risk of ICU and hospital mortality. More explanation is needed to justify the use of LAPS and details on timing of LAPS calculation.
1R. While we agree that the LAPS is a single score that is collected at the time of admission, it has been widely cited (the original paper has been referenced 281 times to date) as a predictor of in hospital mortality, when used in the way we have, as a single baseline measure, which is why we included it in our model. We completely agree that risk of mortality changes over time, but all of the data points we collect are static. We also believe that a patient's baseline frailty risk may not be reflected in their acute clinical state at the time of admission, which is intended to be reflected using the LAPS. There is also a challenge of collecting data points at different time points in a hospital admission as it may not reflect data that is available at the time at which an assessment for risk is being made.

2. Page 8, line 9, The author reports a Charlson Comorbidity Index in the results. It is the first mention of this available index. Readers would be interested to know why it was not included in the logistic regression models. It should also appear in the data collection portion of the methods section.
2R. We agree with this comment, that mirrors comment 3 from the statistician. We have now included the Charlson Comorbidity Index to the model. We have also modified the text in the methods section to highlight that the Charlson Comorbidity Index was collected/calculated.

3. Page 10, line 22, While discussions about goals of care should consistently occur in the ambulatory setting, ambulatory care clinicians will argue they don't have time for high quality discussions. Patients with predictable chronic disease trajectories may have discussions outside of the acute care environment (i.e., primary care, outpatients), but those discussions and decisions need to be reviewed, updated, confirmed, and supported when acute events occur. Is it possible that every encounter is an opportunity to help a patient avoid an unwanted/unhelpful ICU admission?

3R. We highlighted some of the potential advantages of having these discussions in the ambulatory setting and some of the potential disadvantages of having these discussions in the inpatient environment. We agree that some ambulatory clinicians may not have the time for high quality discussions but that suggests that perhaps these discussions should be prioritized and time is made for the discussions. We have added to this discussion based on this comment. This paragraph now has a sentence that reads; "Interventions addressing goals of care discussions in the outpatient setting that can include palliative care consultation and/or advanced care planning, can reduce both unwanted ICU admissions and ICU length of stay."

2.2 Minor comments:
Abstract, results, line 29-30, include confidence interval with aOR
We initially had to leave these out because of the word limits to the abstract. Based on this comment, we will now include the 95% CI. We have also modified the results based on the prior reviewer comments. The last sentence of the results section of the abstract now reads; "After multivariable adjustment, the risk of mortality after ICU admission was higher for high frailty risk patients patients compared to and low frailty risk patients (adjusted Odds Ratio=2.86, 95% Confidence Interval: 1.77-4.77)."

Page 10, line 20, repeat word 'goals'
Deleted

Page 11, line 6, repeated 'and values'
Deleted

Page 13-14, line 15 and 48, repeat reference (Hill)
Page 13-14, line 19 and 52, repeat reference (Zampieri)
These repeated references were deleted and the rest of the references were adjusted accordingly.

Page 19, line 31, repeat definition 'inpatient chronic care'
These were deleted. This repeat definition was also noted in Table 4 as well so that was also deleted.

Reviewer 2: Dr. Hélène Vallet
Institution: Sorbonne Université Faculté de Médecine, Hôpital Saint-Antoine
General comments (author response in bold)

The authors have performed a very interesting study about the impact of frailty on prognosis of older patients after a second hospitalization. Their main results are that frailty is associated with higher mortality in ICU but also out of ICU.

The benefit of ICU admission for older patients is a hot topic, and raise the question how to identify patients able to survive an ICU stay without disabilities? Frailty is an important factor associated with short- and long-term mortality after ICU stay. The originality of the present work is the impact on prognosis after a rehospitalisation.

I have some questions and comments

1. I am very surprised about the low proportion of high frailty risk patients. In fact, only 8% of patients are in this category. In geriatric hospitalized population, this proportion should be higher, did you have an explanation? I think this point should be discussed.
1R. This is an important comment and echoes comment 1 from the editor. Much of this has been addressed above because these comments are very similar. We have modified the text based on these two comments to reflect this. The fourth paragraph in the discussion now has a section that reads; "While the HFRS can be used to predict the risk of adverse outcomes, it may have variable correlation with traditional measures of frailty used, like the clinical frailty scale (30). The advantage to using the clinical frailty scale is that it incorporates different quantitative and qualitative elements of a patients clinical and functional status to summarize a patients overall clinical status, which requires time and expertise (31). The advantage to the HFRS is that it uses administrative data that can be collected automatically using electronic medical records (9). Traditional measures of frailty, like the clinical frailty scale, and the HFRS are different scales with different intended uses that are ultimately used to try and assess a patient's risk of experiencing adverse outcomes."

2. Most of studies evaluating the impact of frailty on prognosis in older patients admitted in ICU used the Clinical Frailty Score. For an anderstandable reason you have used the HFRS. However, you should more discuss this point and the overlap between HFRS and CFS
2R. We agree and believe the response to editor comment 1 and reviewer comment 1 above applies to this comment as well. This includes the changes to the text of the manuscript in the comment above.

3. You don't speck about the first hospitalisation. Which proportion of patients were in admitted in ICU?
3R. Thank you for this comment. We have now included the proportion of patients who were admitted in the ICU on the prior hospitalization. The results are presented below but are now also included in Table 1.

Of the 22,178 patients with a previous admission, 854 patients (3.85%) were previously admitted to ICU.

	High N=1,767	**Moderate N=9,464**	**Low N=10,947**
Admitted to ICU in previous hospitalization	110 (6.23%)	393 (4.15%)	351 (3.21%)

4. In table 2, you give the details of patients dead with and without ICU that is redundant with table 3 and 4 and the p value for patients dead in ICU is not the same in table 2 and 3 (0.086 in table 2 an <0.001 in table 3), can you modify or remove?
4R. The difference between the p values in table 2 and table 3 reflect differences in the denominators between these two tables, thus making the p values different.

5. Severity at ICU admission in an important factor associated with prognosis of older patients. You choose to use the LAPS. Why did you not use a more usual severity index as SAPSII/III or APACHE? It could induce a bias and should be discuss

5R. There are numerous indices of severity of illness that could be used. Unfortunately different iterations of SAPS or APACHE are not part of the GEMINI dataset because we lack complete sets of vital signs for all patients.

6. Furthermore, early readmission is associated with lower prognosis in old patients, could you append the length between the 2 hospitalizations in your adjusted model?
6R. The goal of our model was to predict outcomes at the time of hospital discharge, so that they could inform discussions prior to the next hospitalization, thus we are choosing to not include time between hospitalizations in our model. However, for the reviewers interest, we did perform the analysis to see if there is any change in the results. The eTables are listed below and the results are very similar to the model that does not include time between hospitalizations.

eTable 2. Adjusted Odds Ratios Hospital Frailty Risk Score and ICU Admission

Predictor	Adjusted OR (95% CI)	p
Intercept	5.02 (2.11 – 12.01)	<0.001
Moderate Frailty	0.96 (0.85 – 1.08)	0.514
High Frailty	1.00 (0.79 – 1.25)	0.999
Charlson Comorbidity Index – 1	1.28 (1.03 – 1.58)	0.023
Charlson Comorbidity Index – 2+	1.54 (1.31 – 1.81)	<0.001
Age	0.94 (0.94 – 0.95)	<0.001
Sex – Male	1.24 (1.11 – 1.39)	<0.001
Day of Admission - Weekend	1.54 (1.31 – 1.81)	<0.001
Time of Admission - Night	0.86 (0.76 – 0.97)	0.014
LAPS	1.02 (1.02 – 1.03)	<0.001
Hospital – A	0.43 (0.35 – 0.53)	<0.001
Hospital – B	0.91 (0.73 – 1.14)	0.427
Hospital – C	0.50 (0.39 – 0.63)	<0.001
Hospital – D	1.05 (0.88 – 1.27)	0.57
Hospital – E	0.77 (0.62 – 0.97)	0.025
Hospital – F	0.95 (0.77 – 1.17)	0.604
Prior Location – Inpatient Chronic Care	0.64 (0.55 – 0.75)	<0.001
Prior Location – Rehab	0.99 (0.65 – 1.45)	0.959
Prior Location – Other	1.63 (1.19 – 2.19)	0.002
Heart Failure	1.20 (1.00 – 1.42)	0.042
Neurocognitive Disorders	0.35 (0.23 – 0.51)	<0.001
Pneumonia	0.88 (0.68 – 1.13)	0.343
Urinary Tract Infection	0.24 (0.14 – 0.37)	<0.001

Chronic Obstructive Pulmonary Disease	1.28 (1.01 – 1.60)	0.033
Time from Last Hospitalization	1.00 (1.00 – 1.00)	0.332

N = 22,178, C-statistic = 0.7155, R^2 without HFRS = 0.7154
LAPS=Lab and acute physiology score
Reference levels include frailty (low), Charlson Comorbidity Index (0), sex (female), day of admission (weekday), time of admission (daytime), hospital (G), prior location (home), and Charlson comorbidity index (0)

eTable 3. Adjusted Odds Ratios for Hospital Frailty Risk Score and Death Among Patients Admitted to the ICU

Predictor	**Adjusted OR (95% CI)**	**p**
Intercept	0.09 (0.01 – 0.52)	0.008
Moderate Frailty	1.09 (0.86 – 1.38)	0.478
High Frailty	2.73 (1.68 – 4.57)	<0.001
Charlson Comorbidity Index – 1	1.27 (0.83 – 1.94)	0.266
Charlson Comorbidity Index – 2+	2.00 (1.44 – 2.78)	<0.001
Age	1.02 (1.00 – 1.05)	0.025
Sex – Male	1.10 (0.88 – 1.37)	0.396
Day of Admission - Weekend	1.23 (0.95 – 1.59)	0.114
Time of Admission - Night	1.15 (0.90 – 1.47)	0.258
LAPS	1.01 (1.00 – 1.01)	0.004
Hospital – A	1.20 (0.78 – 1.86)	0.409
Hospital – B	0.56 (0.36 – 0.86)	0.01
Hospital – C	1.03 (0.65 – 1.65)	0.901
Hospital – D	0.97 (0.68 – 1.40)	0.878
Hospital – E	0.90 (0.58 – 1.41)	0.656
Hospital – F	0.80 (0.53 – 1.21)	0.291
Prior Location – Inpatient Chronic Care	0.76 (0.55 – 1.04)	0.084
Prior Location – Rehab	1.22 (0.54 – 2.94)	0.645
Prior Location – Other	0.67 (0.37 – 1.21)	0.187
Heart Failure	0.80 (0.57 – 1.13)	0.206
Neurocognitive Disorders	1.78 (0.75 – 4.58)	0.208
Pneumonia	1.07 (0.63 – 1.82)	0.805
Urinary Tract Infection	0.59 (0.20 – 1.61)	0.31
Chronic Obstructive Pulmonary Disease	0.75 (0.48 – 1.16)	0.194
Time from Last Hospitalization	1.00 (1.00 – 1.00)	0.001

N = 1,456, C-statistic = 0.6494, R^2 without HFRS = 0.6375
LAPS=Lab and acute physiology score
Reference levels include frailty (low), Charlson Comorbidity Index (0), sex (female), day of admission (weekday), time of admission (daytime), hospital (G), prior location (home), and Charlson comorbidity index (0)

eTable 4. Adjusted Odds Ratios for Hospital Frailty Risk Score and Death Among Patients Not Admitted to the ICU

Predictor	Adjusted OR (95% CI)	p
Intercept	0.00 (0.00 – 0.01)	<0.001
Moderate Frailty	1.15 (1.06 – 1.24)	0.001
High Frailty	1.22 (1.06 – 1.40)	0.004
Charlson Comorbidity Index – 1	0.99 (0.85 – 1.14)	0.862
Charlson Comorbidity Index – 2+	1.99 (1.79 – 2.21)	<0.001
Age	1.04 (1.03 – 1.04)	<0.001
Sex – Male	1.19 (1.10 – 1.28)	<0.001
Day of Admission - Weekend	1.04 (0.96 – 1.13)	0.322
Time of Admission - Night	0.81 (0.75 – 0.88)	<0.001
LAPS	1.04 (1.03 – 1.04)	<0.001
Hospital – A	0.71 (0.61 – 0.83)	<0.001
Hospital – B	1.51 (1.27 – 1.78)	<0.001
Hospital – C	1.28 (1.11 – 1.49)	0.001
Hospital – D	1.31 (1.13 – 1.51)	<0.001
Hospital – E	1.57 (1.33 – 1.84)	<0.001
Hospital – F	1.82 (1.57 – 2.12)	<0.001
Prior Location – Inpatient Chronic Care	1.13 (1.04 – 1.24)	0.005
Prior Location – Rehab	1.01 (0.75 – 1.34)	0.959
Prior Location – Other	1.36 (1.07 – 1.71)	0.011
Heart Failure	0.64 (0.56 – 0.73)	<0.001
Neurocognitive Disorders	0.55 (0.45 – 0.65)	<0.001
Pneumonia	0.89 (0.76 – 1.04)	0.153
Urinary Tract Infection	0.23 (0.18 – 0.29)	<0.001
Chronic Obstructive Pulmonary Disease	0.82 (0.69 – 0.98)	0.034
Time from Last Hospitalization	1.00 (1.00 – 1.00)	<0.001

N = 20,722, C-statistic = 0.7290, R^2 without HFRS = 0.7282

LAPS=Lab and acute physiology score

Reference levels include frailty (low), Charlson Comorbidity Index (0), sex (female), day of admission (weekday), time of admission (daytime), hospital (G), prior location (home), and Charlson comorbidity index (0)

7. In the method, you report that comorbidities were collect using the ICD-10 codes but the Charlson comorbidity index is not mentioned (compared to table 1)
7R. Based on this comment, we have included mention of the charlson comorbidity index in the methods. The sentence in the 'data collection' paragraph of the methods section now reads; "…comorbidities, including the Charlson Comorbidity Index."

8. Could you mentioned the PROBE Statement in the method?
8R. We are assuming this is minor typo and PROBE refers to STROBE statement. We have included the STROBE statement but are also including the now are including the RECORD checklist as well. If the editors want us to include a statement showing we followed this we would be pleased to include this statement with either the STROBE or RECORD checklist. IF PROBE is the intended word, we would need some specific clarification on what this refers to. Thank you!