

PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Performance-based functional impairment and readmission and death: a prospective study
AUTHORS	Aubert, Carole; Folly, Antoine; Mancinetti, Marco; Hayoz, Daniel; Donz�, Jacques

VERSION 1 - REVIEW

REVIEWER	Erik Hoyer Johns Hopkins University, USA
REVIEW RETURNED	10-Feb-2017

GENERAL COMMENTS	<p>This was a single center prospective study in a medicine population looking at the association between TUG and readmission and mortality. The effort these researchers took is greatly appreciated towards studying this important topic. This is a well written paper but there are limitations:</p> <ul style="list-style-type: none">- single center in medicine patients only is a limitation of study design.- Introduction – the Author’s haven’t made a compelling argument about the mechanism of the TUG to predict readmissions and mortality. The intro reads more as exploratory analysis rather than the fact the authors had an apriori hypothesis.- In the discussion there is a discussion about the TUG as an assessment tool but there is no real explanation WHY the TUG may be better than other functional assessment tools to specifically predict readmissions and mortality.- The take home points about diagnoses and functional status and outcomes is not clear to the reader. There is no discussion about the reason for the association of infection and functional status and outcomes, which seemed notable.- Rate of readmissions is higher than typically cited in the literature, and it is unclear why?- The problem with looking at 6 months after hospitalization is that the reasons for these outcomes are less likely related to the index hospitalization when you go far out.- The authors argue that the TUG is a simple test, which is done by physiotherapists in this study. This seems like a significant limitation to feasibility. Many hospitals have limited physiotherapy resources, so to expect them to perform this on every patient is unlikely in real practice. If the authors wanted to argue that this is a feasible methodology, it would have been better to have a staff resource that is more available such as nursing or similar.- The patients that are evaluated is a very specific/limited cohort, which potentially limits the generalizability. TUG assumes patients can ambulate without physical assistance, which really limits the patient’s that are assessed. The authors excluded patients going to rehab, which means that the functionally impaired patients in this
-------------------------	---

	<p>study are: patients that are debilitated, but not too debilitated that they don't go to rehab or need physical assistance during ambulation. The authors should discuss the potential implications of this on their findings.</p> <ul style="list-style-type: none"> - Analysis plan needs development– It is unclear why the authors only adjusted for age and gender when they had other variables available. Additionally, they did not provide information on the modeling, such as model fit, variance inflation factors, appropriateness of using a linear approach to model the outcomes, and whether linear assumptions were reasonable for the covariates. Also the authors studied readmissions and mortality separately, but they could influence each other- i.e. a patient who dies cannot be readmitted. Was this accounted for? - The author seem to overstate the uniqueness of their study design. There are other studies looking at gait speed (a performance metric) and mortality and readmissions for example (i.e. Dodson 2016 J American Geriatric Society) - The 'So what' is not addressed. The application of the results (i.e. TUG) in real world practice is not discussed. How could clinicians use this data in a practical way to potentially affect the outcomes evaluated? <p>Other:</p> <p>Page 4 line 18 – it is not clear at this point in the article why it is INTUITIVE why functional status is associated with readmission</p> <p>Page 4 line 51 – typo - controversial.</p> <p>Page 5 line 15 – define large hospital.</p> <p>Page 5 line 55 – it is unclear whether the 'capture area' of these hospitals is large enough to account for the low possibility that someone could be readmitted outside this area.</p> <p>Page 6 line 51, although this approach for cutoff is not unreasonable, it would have been good for the authors to have done additional sensitivity analyses to see if other cutoffs were associated with these outcomes.</p> <p>Page 7, covariates – Given that this is a prospective study the reader would expect a higher degree of accounting for potential confounding. For example the authors state that readmissions are due to many complex reason. However, there is no information on potentially important factors such as prehospital functional status, the severity of illness from the hospitalization, or other psychosocial factors that could influence risk for readmission (i.e. care giver support, literacy, etc).</p> <p>Page 10, line 55 – how is their risk influenced by rehabilitation? This is not clear.</p>
--	---

REVIEWER	Alison Mudge Royal Brisbane and Women's Hospital, Brisbane, Australia
REVIEW RETURNED	27-Feb-2017

GENERAL COMMENTS	<p>This paper addresses the question: Is a physical performance measure (TUG) at discharge associated with higher risk of death or unplanned readmission in medical patients aged 50 years and older?</p> <p>The findings are of some merit but there are some significant omissions that need addressing, and the tables are presented in a manner that does not relate directly to the research question. I suggest the authors consider the following:</p>
-------------------------	---

	<p>Background: It is important to distinguish between self-report and physical performance measures, as they are conceptually different, and I would make this clearer by not using data from studies using ADL measures.</p> <p>There is substantial evidence that TUG (and other performance measures) are strong predictors of mortality in various inpatient and community populations, and indeed are often part of various frailty measures which are strongly associated with mortality...this literature is missing from background and discussion.</p> <p>Methods:</p> <p>Death and readmission are appropriately defined and measured. It is unclear why TUG has been dichotomised when it is a continuous variable (and agree there is little agreement on a cut-point in the literature); using more groupings eg quartiles may have provided a more meaningful analysis.</p> <p>The reason for the choice of the other co-variables is unclear, although they include variables associated with readmission and/or mortality. Are they considered potential confounders? If so, then it is unclear why only age and gender were included in the multivariate analysis rather than all potential confounders.</p> <p>Results</p> <p>Table 1 is not really related to the research question. A more conventional approach would be to compare characteristics including the variable under study (TUG) and other likely associated variables between participants with and without the outcome of interest (readmission in one table and death in another). Other significantly associated variables would then be included in a multivariable model as potential confounders or mediators in order to identify the independent contribution of TUG to each outcome of interest.</p> <p>I am unclear the justification for presenting the different readmission diagnostic groups by functional status and how this relates to the research question.</p> <p>Discussion:</p> <p>First sentence: the "150%" is a function of how the TUG was dichotomised and this should be clear.</p> <p>Again, I do not think it is useful to compare self-report and performance based testing.</p> <p>I do not really understand why an increase in readmission with impaired function would be reflected in different diagnostic patterns. The clinical implications have not been discussed i.e. how would this information be used in practice?.</p> <p>References:</p> <p>There is a large literature on TUG and mortality which is missing, and there are a large number of references included about TUG and falls risk which are of limited relevance to this paper.</p> <p>Language:</p> <p>There are some minor language issues throughout the manuscript that would benefit from editing</p>
--	---

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Erik Hoyer

Johns Hopkins University, USA

Please state any competing interests or state 'None declared': none declared.

Please leave your comments for the authors below This was a single center prospective study in a medicine population looking at the association between TUG and readmission and mortality. The effort these researchers took is greatly appreciated towards studying this important topic. This is a well written paper but there are limitations:

1) single center in medicine patients only is a limitation of study design.

We agree that this is a limitation of our study design, as already stated in the limitations (page 14, paragraph 2): “Second, the study was conducted in a single center and included only medical patients, limiting the generalizability of our results.” However, because the relation between a valid functional status measure and readmission has been very few studied, a single-center study is still a valuable contribution. We agree as mentioned that the results may not be generalizable to other populations than medical patients, however, because medical and surgical patients have each their own particularities, we believe that the TUG test may need to be tailored anyway to groups of patients. To illustrate such a difference, the TUG test is expected to have a different threshold of readmission prediction in orthopedic patients after a hip replacement than in medical patients.

2) Introduction – the Author’s haven’t made a compelling argument about the mechanism of the TUG to predict readmissions and mortality. The intro reads more as exploratory analysis rather than the fact the authors had an a priori hypothesis.

Thank you for the suggestion. We added some explanation on our hypothesis in the introduction (page 4, paragraph 3):

“Unlike many tools to assess functional status, the TUG test gives information both on balance and cardiorespiratory capacity, and was associated with overall health decline. It has been also shown not to suffer from ceiling effect limitations, and to be related to executive function. These characteristics make it a good potential tool to assess the risk of readmission. We hypothesized that the TUG test may be a good predictor of adverse health outcomes in medical patients.”

3) In the discussion there is a discussion about the TUG as an assessment tool but there is no real explanation WHY the TUG may be better than other functional assessment tools to specifically predict readmissions and mortality.

We appreciate the comment. We suggest that the TUG test may be better than other functional assessment tools for several reasons: 1) it is objective and has a very high inter-rater and test-retest reliability;1-3 2) it does not suffer from ceiling or floor effects;4 3) it evaluates both balance and cardiorespiratory function, so that it may predict overall health decline;5 4) it is simple and can be performed not only by physiotherapists, but also by nurses or nursing assistants;6,7 5) despite its apparent simplicity, it actually evaluates multiple aspects needed for adequate functional status (such as balance, mobility, coordination, cardiorespiratory reserve), so that it may capture many factors such as disease severity, independently of the kind of disease, and may as such be a good proxy to predict overall health decline.5,8,9 We clarified this in the conclusions (page 12, paragraph 3):

“First, we used the TUG test, which has been largely validated as a simple, quick, and reliable clinical method to assess functional status and presents several advantages in comparison with other tools to assess functional status. The TUG test has been largely validated as a simple, quick, and reliable clinical method to assess functional status, and presents several advantages in comparison with other tools to assess functional status. The TUG test is objective, and its very high inter-rater and test-retest reliability allows better comparability than other tools. Although this measure is very simple, it is actually constituted of several complex sequences (e.g. moving from the sitting to the standing position), each of which evaluating multiple aspects needed for adequate functional status, including

balance, mobility, cardiorespiratory function and coordination. It may therefore capture several factors such as disease severity, independently of the kind of disease, and may as such be a good proxy to predict overall health decline. Moreover, as opposed to other tools used to assess functional status, the TUG test does not suffer from ceiling or floor effects in healthy older adults. Furthermore, a physiotherapist is not absolutely needed, as it can be performed by nursing personal as well."

4) The take home points about diagnoses and functional status and outcomes is not clear to the reader. There is no discussion about the reason for the association of infection and functional status and outcomes, which seemed notable.

We appreciate this comment. As outlined by Reviewer 2 also (comment 5), presenting and discussing diagnoses of readmission according to functional status didn't tightly relate to our research question. Furthermore, it seems from this comment that the results presented in Table 2 were confusing for the reader. We indeed presented percentages of columns, showing that 19.6% of the patients with functional impairment were readmitted for an infection, but only 11.5% of those without functional impairment. However, when comparing only patients readmitted for an infection, the number of patients with or without functional impairment was not different (n=9 versus n=7, P = 0.13). To remain focused on our research question, avoid confusion, and answer comment 5 of Reviewer 2 also, we removed Table 2 and the text related to diagnoses of readmission.

5) Rate of readmissions is higher than typically cited in the literature, and it is unclear why?

Thank you for the comment. We think that there is confusion between 30-day and 6-month readmission rates. Literature typically reports readmission rates of 14-22% within 30 days after hospital discharge.¹⁰⁻¹³ There is less data for 6-month readmission rate, but it reaches 20 to 50% according to the study population.¹⁴⁻¹⁷ In our study, 31.7% of the patients had an unplanned readmission within 6 months, and 10.7% within 30 days after discharge, which is therefore in line with previous literature.

6) The problem with looking at 6 months after hospitalization is that the reasons for these outcomes are less likely related to the index hospitalization when you go far out.

Thank you for the comment. First, as pointed out by several well-conducted studies,^{11,12} patients are mostly readmitted for reasons that are not related to the initial diagnosis of the index admission. Therefore, the relation is anyway weak even at 30 days, and it was not our aim to look at the relationship between the causes of admission and of readmission, but rather to evaluate whether functional status is associated with adverse health outcome. Second, a predictor not able to identify the risk of readmission at 6 months is unlikely to identify it at 30 days. And indeed, a sensitivity analysis for readmission at 30 days yielded similar results (OR: 1.64, 95%CI 0.76-3.53). Finally, several studies assessed the relationship between functional status and readmission with longer term outcomes.¹⁸⁻²¹ Concerning the outcome "death", most studies assessed this outcome after an even longer follow-up period, which may be useful when wanting to tailor care according to life expectancy.²²⁻³⁰ We therefore think that our outcomes are relevant.

7) The authors argue that the TUG is a simple test, which is done by physiotherapists in this study. This seems like a significant limitation to feasibility. Many hospitals have limited physiotherapy resources, so to expect them to perform this on every patient is unlikely in real practice. If the authors wanted to argue that this is a feasible methodology, it would have been better to have a staff resource that is more available such as nursing or similar.

The test was indeed performed by physiotherapists to guaranty a high standardization for study purposes. However, this test can be performed by nurses or nursing assistants as well.^{6,7} We added

a comment on this topic in the conclusions (page 12, paragraph 3):

“Furthermore, a physiotherapist is not absolutely needed, as it can be performed by nursing personal as well.”

8) The patients that are evaluated is a very specific/limited cohort, which potentially limits the generalizability. TUG assumes patients can ambulate without physical assistance, which really limits the patient's that are assessed. The authors excluded patients going to rehab, which means that the functionally impaired patients in this study are: patients that are debilitated, but not too debilitated that they don't go to rehab or need physical assistance during ambulation. The authors should discuss the potential implications of this on their findings.

We appreciate this comment. We agree that our findings may not apply to patients discharged to a rehabilitation facility. However, we excluded these patients because the rehabilitation stay will certainly improve their functional status. We believe that functional status must be assessed at a comparable point in time for all patients in order to evaluate its predictive performance. The best comparable point in time being “before discharge home for all patients”, the patients transferred to another acute care or to rehabilitation center shouldn't be included in our study. A specific study for patients discharged to rehabilitation would be needed to answer the question of the Reviewer. We stated this as a limitation (page 14, paragraph 2) and added some discussion (see answer to comment 18 of Reviewer 1):

“Third, we excluded patients who were discharged to a rehabilitation facility, because we hypothesized that their functional status at discharge of the acute care setting would not reflect their actual functional status at discharge of the rehabilitation clinic. Our findings may therefore not apply to these patients.”

Concerning patients that are too debilitated to perform the TUG test, they get 6 points on the global quotation of the test. We classified them as having functional impairment. It concerned only 12 patients in our population. A sensitivity analysis excluding them yielded similar results for both outcomes (OR 4.16, 95% CI 1.76-9.83 for death; OR 1.50, 95% CI 0.88-2.55 for readmission). We therefore may suppose that our findings could apply to those debilitated patients as well. We clarified how these patients were handled, added this sensitivity analysis, and discussed the application of these results:

Page 7, paragraph 2:

“Patients who were too debilitated to perform the test were classified as having functional impairment.”

Page 9, paragraph 1:

“We finally performed a sensitivity analysis excluding the patients who were too debilitated to perform the test.”

Page 11, paragraph 2:

“Results were similar ... in the sensitivity analysis excluding 12 patients who were too debilitated to perform the TUG test (OR 4.16, 95% CI 1.76-9.83 for death; OR 1.50, 95% CI 0.88-2.55 for readmission).”

Page 14, paragraph 1

“As results were similar when including or excluding patients who were too debilitated to perform the test, it suggests that our findings may apply to those patients also, if classified as functionally impaired.”

9) Analysis plan needs development–

a) It is unclear why the authors only adjusted for age and gender when they had other variables available.

Thank you for this comment. Concerning the variables we adjusted for, we agree that there may be other potential confounding variables. However, our study question was not to answer whether functional status is an independent risk factor for readmission or death, but if functional status as stand-alone measure can be used to predict the overall risk of readmission or death. A predictor is not expected to be free from potential confounders, but to be a simple measure to predict a certain outcome.

As discussed in response to comment 3 of Reviewer 1, the TUG test may be a proxy for several factors that are otherwise anyway difficult or impossible to capture, such as disease severity.

Therefore, it makes the TUG test even more interesting as a predictor, because this simple measure is able to capture many factors related to the risk of readmission or death.

We decided to adjust for age and gender only, because functional status is not similar according to these two factors in otherwise healthy adults. For your interest, even if adjusting for other main potential confounders such as the Charlson comorbidity index in a sensitivity analysis, we obtain similar results (OR 1.25, 95% CI 0.73-2.16 for readmission, and OR 2.42, 95% CI 1.00-5.87 for death).

We are discussing this aspect in the conclusions (page 12, paragraph 3, and page 14, paragraph 2):

“It may therefore capture several factors such as disease severity, independently of the kind of disease, and may as such be a good proxy to predict overall health decline.”

“Fourth, although we may not exclude residual confounding factors, the aim of our study was to evaluate the performance of the TUG test as a simple overall prediction measure and not as an independent risk factor. Therefore, we adjusted only for age and gender.”

b) Additionally, they did not provide information on the modeling, such as model fit, variance inflation factors, appropriateness of using a linear approach to model the outcomes, and whether linear assumptions were reasonable for the covariates.

Thank you for the comment. The collinearity diagnostic measurement³¹ showed that the variance inflation factors and the tolerance were near 1.00 for each variable included in the model (TUG test, age, gender), meaning that the variables were not correlated. We performed a link test that confirmed that our linear approach to model the outcomes was correct.³² To assess the linear assumption, we tested the relationship of age with the outcome using a cubic or quadratic transformation, as well as age categories. This yielded similar results, so that we kept age as a continuous variable. Model fit was assessed using the Hosmer-Lemeshow goodness-of-fit test,³³ which showed not significant P, meaning good fit.

We added this in the methods and results (page 8, paragraph 3, and page 11, paragraph 1):

“A collinearity diagnostic measurement was performed to detect collinearity between the variables included in the model. A link test was used to confirm that the linear approach to model the outcome was correct. We used age as a continuous variable because assessing the variable in categories or after cubic or quadratic transformation yielded similar results. Model fit was assessed using the Hosmer-Lemeshow goodness-of-fit test.”

“P for the Hosmer-Lemeshow goodness-of-fit test was >0.05 for both adjusted models, indicating good fit. The variance inflation factors and tolerance were near 1.00 for all variables, excluding

significant collinearity. The link test confirmed that the linear approach to model the outcomes was correct.”

c) Also the authors studied readmissions and mortality separately, but they could influence each other- i.e. a patient who dies cannot be readmitted. Was this accounted for?

We decided to study the outcomes “readmission” and “death” separately, because grouping both may have yielded false positive or false negative results driven by one of the outcomes. However, in a survival analysis using a competing-risks regression model based on Fine and Gray’s method, which takes into account the incidence of death,³⁴⁻³⁶ results were similar (sub-hazard ratio for readmission 1.50, 95% CI 0.95-2.35).

10) The author seem to overstate the uniqueness of their study design. There are other studies looking at gait speed (a performance metric) and mortality and readmissions for example (i.e. Dodson 2016 J American Geriatric Society)

Thank you for this comment. To answer comments 1 and 11 of Reviewer 2 also, we added literature studying the association between performance-based functional impairment and readmission or death, among which the suggested paper. However, most of the studies assessing the association between functional impairment and readmission were limited by or retrospective design, or by focusing on a specific setting such as surgical ward or rehabilitation clinics, or on specific patients populations (older adults, patients with specific diseases such as COPD or myocardial infarction).^{18-21,26,37-40} Furthermore, the study by Dodson assessed patients one month after discharge following a myocardial infarction, and not at the time of discharge, so that this study may be little comparable with our study.

Studies looking at the association between functional impairment and mortality were mostly performed in ambulatory care settings,^{22-26,28-30,41} while those evaluating the risk of death after a hospitalization found controversial results.^{19,27,40}

In summary, although the association between the TUG test and readmission or death has been assessed in some specific populations, few studies looked at the predictability of the TUG test in a broader population such as general medical inpatients.

We modified the introduction and conclusions accordingly:

Page 4, paragraph 2:

“Few studies assessed the association between performance-based functional impairment and readmission. Although those studies reported mainly a significant association between functional impairment and readmission, they were often limited by a retrospective design, or by focusing on a specific setting such as surgical ward or rehabilitation care facilities, or on specific populations such as older adults or patients with chronic obstructive pulmonary disease or myocardial infarction. Functional impairment has also been associated with mortality in several studies in ambulatory care settings, while the few studies assessing this outcome after a hospitalization found controversial results.”

Page 5, paragraph 1:

“In summary, although the TUG test has been associated with death and to a lesser extent with readmission, few studies looked at the predictability of the TUG test in a broader population such as general medical inpatients.”

Page 13, paragraph 1:

“Similarly, other authors evaluated functional status at admission before an elective operation, at the time of discharge from the emergency department, or one month after discharge.”

Page 13, paragraph 2:

“Third, we focused on medical patients aged 50 years or older, while others studied older adults, or patients with a specific disease, such as chronic obstructive pulmonary disease or myocardial infarction.”

Page 13, paragraph 3 :

“Only few studies looked at this relationship between functional impairment and mortality following discharge. Two of them, which included 135 geriatric and 495 medical inpatients, respectively, were negative, while another study using the TUG test in 147 geriatric inpatients found an association. Our results are consistent with studies performed in ambulatory care settings.”

11) The ‘So what’ is not addressed. The application of the results (i.e. TUG) in real world practice is not discussed. How could clinicians use this data in a practical way to potentially affect the outcomes evaluated?

Thank you for the suggestion. We think that our findings may have two main clinical implications. First, it may help to identify patients at higher risk of adverse health outcome, who would benefit the most of interventions to improve functional status. Second, it may help clinicians to assess life expectancy of their patients, and to avoid prescribing drugs or screenings when the patients will probably not survive the time to benefit. We added this in the conclusions (page 13, paragraph 4, and page 14, paragraph 1):

“If confirmed by larger studies, our findings may have two main clinical implications. First, it may help to identify high-risk patients who would most likely benefit from interventions that have been shown to improve functional status. However, further studies are needed to assess if these interventions can improve patients’ outcome also. Second, it may help clinicians to assess the risk of short-term death of their patients, and to consequently tailor preventive and therapeutic care to each patient. Some drugs or preventive prescriptions, such as cancer screening, may indeed more harm than benefit to those high-risk patients unlikely to survive long enough to benefit from the intervention. The TUG test may therefore represent an easy-to-use and reliable tool for clinicians to improve assessment of patients’ life expectancy. As our results were similar when including or excluding patients who were too debilitated to perform the test, our findings may apply to those patients also, if classified as functionally impaired.”

Other:

12) Page 4 line 18 – it is not clear at this point in the article why it is INTUITIVE why functional status is associated with readmission

Thank you for the comment. We clarified this point in the introduction (page 4, paragraph 1):

“In this complex equation, patient’s functional impairment could intuitively be considered as a potential risk factor for readmission, as it may capture overall health status, including cardiorespiratory reserve and risk of falls altogether.”

13) Page 4 line 51 – typo - controversial.

Thank you, this word was removed in the revised version.

14) Page 5 line 15 – define large hospital.

We clarified this point in the methods (page 6, paragraph 2):

“In a prospective cohort study, we included all consecutive patients aged ≥ 50 years admitted to the Department of General Internal Medicine of a large secondary care hospital in Switzerland (Fribourg Cantonal Hospital, 115 beds, 4400 admissions/year), between April and September 2013.”

15) Page 5 line 55 – it is unclear whether the ‘capture area’ of these hospitals is large enough to account for the low possibility that someone could be readmitted outside this area.

As already mentioned in the methods, we first called each patient, and, if we failed to reach the patient directly after several attempts, we phoned the general practitioner, a next of kin or the nursing home, according to which was available. We were successful in reaching someone for all participants. We further checked the electronic health records only additionally to increase results reliability. However, most patients were readmitted to a hospital within Fribourg network, which covers a large area. We clarified this point in the results (page 10, paragraph 1):

“...and had no lost to follow-up, as we managed to get the outcome information per phone call (to the patient or to the general practitioner, a next of kin, or the nursing home) for all patients.”

16) Page 6 line 51, although this approach for cutoff is not unreasonable, it would have been good for the authors to have done additional sensitivity analyses to see if other cutoffs were associated with these outcomes.

We appreciate this suggestion. When dichotomizing a variable, we think that it is better to use a validated method, rather than to explore any possible cutoff point until finding an association. That is why we used the point closest to the top left corner of the ROC curve, which represents the best compromise between sensitivity and specificity and is a validated method to select a cutoff point.⁴² However, to answer the request and since there was no agreement in the literature for a specific cutoff when dichotomizing TUG test duration,⁸ we now performed two sensitivity analyses using two cutoff points previously used in other studies,^{19,40,41} i.e. >10 and >20 seconds, respectively. These analyses yielded similar results, supporting our findings. We added and discussed these additional analyses:

Page 2, paragraph 2:

“Sensitivity analyses using a cutoff at >10 and >20 seconds were performed.”

Page 9, paragraph 1:

“As there was no agreement for a specific cutoff when dichotomizing the TUG test duration, although we used a validated method to select it, we also performed additional sensitivity analyses with the cutoff set at >10 and >20 seconds, respectively, as done in previous studies.”

Page 11, paragraph 2:

“Results were similar in the sensitivity analyses setting the cutoff point at >10 or >20 seconds, respectively: OR 1.67 (95% CI 0.97-2.86) and 1.32 (95% CI 0.74-2.35) for readmission, and 2.69 (95%CI 1.09-6.67) and 2.64 (95% CI 1.11-6.30) for death,”

Page 13, paragraph 2:

“Second, sensitivity analyses using other cutoff points to define functional impairment yielded similar results.”

17) Page 7, covariates – Given that this is a prospective study the reader would expect a higher degree of accounting for potential confounding. For example the authors state that readmissions are due to many complex reason. However, there is no information on potentially important factors such as prehospital functional status, the severity of illness from the hospitalization, or other psychosocial

factors that could influence risk for readmission (i.e. care giver support, literacy, etc).

Thank you for this comment. Please refer to our answer to comment 9 of Reviewer 1.

18) Page 10, line 55 – how is their risk influenced by rehabilitation? This is not clear.

We appreciate this comment. We may reasonably suppose that a rehabilitation is expected to modify patients' functional status. Assessment of functional status at discharge of the acute care setting and at discharge of the rehabilitation setting will then be different. We hypothesize that improvement of functional status through rehabilitation would improve health outcome. We now clarified this point in the conclusions (page 12, paragraph 4, and page 13, paragraph 1):

“Patients discharged to a rehabilitation clinic may be more functionally impaired and have a higher morbidity level than other patients at discharge from the acute care setting. Conversely, we can suppose that functional status will be improved by the rehabilitation stay, which may consequently lower the following risk of readmission or death. ... We may suppose that all these patients have a better functional status than ours, as the acute care hospitalization may affect functional status, limiting comparability with our study.”

Reviewer: 2

Alison Mudge

Royal Brisbane and Women's Hospital, Brisbane, Australia Please state any competing interests or state 'None declared': none declared

Please leave your comments for the authors below This paper addresses the question: Is a physical performance measure (TUG) at discharge associated with higher risk of death or unplanned readmission in medical patients aged 50 years and older?

The findings are of some merit but there are some significant omissions that need addressing, and the tables are presented in a manner that does not relate directly to the research question. I suggest the authors consider the following:

1) Background: It is important to distinguish between self-report and physical performance measures, as they are conceptually different, and I would make this clearer by not using data from studies using ADL measures. There is substantial evidence that TUG (and other performance measures) are strong predictors of mortality in various inpatient and community populations, and indeed are often part of various frailty measures which are strongly associated with mortality...this literature is missing from background and discussion.

Thank you for this comment. We agree that self-reported and performance-based evaluations of functional status are conceptually different. We now removed studies using self-reported, and added literature using performance-based measures of functional status (see answer to comment 10 of Reviewer 1 for more details).

Methods:

2) Death and readmission are appropriately defined and measured. It is unclear why TUG has been dichotomised when it is a continuous variable (and agree there is little agreement on a cut-point in the literature); using more groupings eg quartiles may have provided a more meaningful analysis.

Thank you for this comment. We agree that the TUG test is a continuous variable. However, we thought that dichotomizing the patients as having a low versus high risk of readmission or death according to a specific cutoff point for the TUG test would be easier to use and interpret for clinicians,

in comparison with a continuous relationship or a higher number of risk categories. That is why we chose to analyze the TUG test as a dichotomized variable, as also done in previous studies.^{19,22,39-41} We now clarified this point in the methods section (page 7, paragraph 3):

“We decided to dichotomize the results of the TUG test instead of using it as a continuous variable or in a higher number of categories, because we thought that classifying patients at high versus low risk of readmission or death would be more useful to interpret for clinicians.”

Additionally, in answer to comment 16 of Reviewer 1, we now provide two sensitivity analyses using other cutoffs for the TUG test, i.e. >10 and >20 seconds, which yielded similar results (see answer to comment 16 of Reviewer 1).

3) The reason for the choice of the other co-variables is unclear, although they include variables associated with readmission and/or mortality. Are they considered potential confounders? If so, then it is unclear why only age and gender were included in the multivariate analysis rather than all potential confounders.

Thank you for this comment. Please refer to our answer to comment 9 of Reviewer 1.

Results

4) Table 1 is not really related to the research question. A more conventional approach would be to compare characteristics including the variable under study (TUG) and other likely associated variables between participants with and without the outcome of interest (readmission in one table and death in another). Other significantly associated variables would then be included in a multivariable model as potential confounders or mediators in order to identify the independent contribution of TUG to each outcome of interest.

Thank you for the comment. We modified the description of baseline characteristics. We now provide as suggested a Table 1 with baseline characteristics according to 6-month readmission, and a Table 2 with baseline characteristics according to 6-month death. We adapted the text accordingly in the results (page 10, paragraph 1):

“Table 1 and Table 2 show the baseline characteristics according to the presence or absence of readmission or death, respectively.”

5) I am unclear the justification for presenting the different readmission diagnostic groups by functional status and how this relates to the research question.

Thank you for this comment. We agree that presenting the readmission diagnostic groups did not tightly relate to our research question. We therefore removed Table 2 and the text related to readmission diagnostic groups (see answer to comment 4 of Reviewer 1 also).

Discussion:

6) First sentence: the “150%” is a function of how the TUG was dichotomised and this should be clear.

Thank you for this comment. We clarified this in the conclusions (page 12, paragraph 1):

“In this prospective cohort study, we found that functional impairment, defined as ≥ 15 seconds to perform the validated performance-based “Timed Up and Go test” before acute care hospital discharge, was associated with an almost 150% increase in the risk of death within 6 months after hospital discharge.”

7) Again, I do not think it is useful to compare self-report and performance based testing.

Please refer to our answer to comment 1 of Reviewer 2.

8) I do not really understand why an increase in readmission with impaired function would be reflected in different diagnostic patterns.

We agree that this was not clear. To answer comment 3 of Reviewer 2 also, we now removed this section from the manuscript.

10) The clinical implications have not been discussed i.e. how would this information be used in practice?.

Thank you for the suggestion. Please refer to our answer to comment 11 of Reviewer 1.

11) References:

There is a large literature on TUG and mortality which is missing, and there are a large number of references included about TUG and falls risk which are of limited relevance to this paper.

Thank you for this comment. We added literature on the association between the TUG test and mortality, and removed some references on the association between the TUG test and the risk of fall in the introduction and in the conclusions (see also answer to comment 10 of Reviewer 1).

12) Language:

There are some minor language issues throughout the manuscript that would benefit from editing

Thank you for the comment. We carefully reread the manuscript and hope to have corrected most language issues.

References

1. Shumway-Cook A, Brauer S, Woollacott M. Predicting the probability for falls in community-dwelling older adults using the Timed Up & Go Test. *Physical therapy*. 2000;80(9):896-903.
2. Podsiadlo D, Richardson S. The timed "Up & Go": a test of basic functional mobility for frail elderly persons. *Journal of the American Geriatrics Society*. 1991;39(2):142-148.
3. Steffen TM, Hacker TA, Mollinger L. Age- and gender-related test performance in community-dwelling elderly people: Six-Minute Walk Test, Berg Balance Scale, Timed Up & Go Test, and gait speeds. *Physical therapy*. 2002;82(2):128-137.
4. Herman T, Giladi N, Hausdorff JM. Properties of the 'timed up and go' test: more than meets the eye. *Gerontology*. 2011;57(3):203-210.
5. Roedl KJ, Wilson LS, Fine J. A systematic review and comparison of functional assessments of community-dwelling elderly patients. *Journal of the American Association of Nurse Practitioners*. 2016;28(3):160-169.
6. Mueller K, Hamilton G, Rodden B, DeHeer HD. Functional Assessment and Intervention by Nursing Assistants in Hospice and Palliative Care Inpatient Care Settings: A Quality Improvement Pilot Study.

- The American journal of hospice & palliative care. 2016;33(2):136-143.
7. Murphy K, Lowe S. Improving fall risk assessment in home care: interdisciplinary use of the Timed Up and Go (TUG). *Home healthcare nurse*. 2013;31(7):389-396; quiz 396-388.
 8. Beauchet O, Fantino B, Allali G, Muir SW, Montero-Odasso M, Annweiler C. Timed Up and Go test and risk of falls in older adults: a systematic review. *The journal of nutrition, health & aging*. 2011;15(10):933-938.
 9. Janssen WG, Bussmann HB, Stam HJ. Determinants of the sit-to-stand movement: a review. *Physical therapy*. 2002;82(9):866-879.
 10. Donzé J, Aujesky D, Williams D, Schnipper JL. Potentially avoidable 30-day hospital readmissions in medical patients: derivation and validation of a prediction model. *JAMA internal medicine*. 2013;173(8):632-638.
 11. Donzé J, Lipsitz S, Bates DW, Schnipper JL. Causes and patterns of readmissions in patients with common comorbidities: retrospective cohort study. *BMJ (Clinical research ed)*. 2013;347:f7171.
 12. Jencks SF, Williams MV, Coleman EA. Rehospitalizations among patients in the Medicare fee-for-service program. *The New England journal of medicine*. 2009;360(14):1418-1428.
 13. Kansagara D, Englander H, Salanitro A, et al. Risk Prediction Models for Hospital Readmission: A Systematic Review. *JAMA* 2011;306(15):1688-1698.
 14. Linne AB, Liedholm H. Effects of an interactive CD-program on 6 months readmission rate in patients with heart failure - a randomised, controlled trial [NCT00311194]. *BMC cardiovascular disorders*. 2006;6:30.
 15. Krumholz HM, Parent EM, Tu N, et al. Readmission after hospitalization for congestive heart failure among Medicare beneficiaries. *Archives of internal medicine*. 1997;157(1):99-104.
 16. Friedman B, Basu J. The rate and cost of hospital readmissions for preventable conditions. *Medical care research and review : MCRR*. 2004;61(2):225-240.
 17. Lupon J, Valle V, Marrugat J, et al. Six-month outcome in unstable angina patients without previous myocardial infarction according to the use of tertiary cardiologic resources. RESCATE Investigators. *Recursos Empleados en el Síndrome Coronario Agudo y Tiempos de Espera*. *Journal of the American College of Cardiology*. 1999;34(7):1947-1953.
 18. Walker KJ, Bailey M, Bradshaw SJ, et al. Timed Up and Go test is not useful as a discharge risk screening tool. *Emergency medicine Australasia : EMA*. 2006;18(1):31-36.
 19. Wong RY, Miller WC. Adverse outcomes following hospitalization in acutely ill older patients. *BMC geriatrics*. 2008;8:10.
 20. Peel NM, Navanathan S, Hubbard RE. Gait speed as a predictor of outcomes in post-acute transitional care for older people. *Geriatrics & gerontology international*. 2014;14(4):906-910.
 21. Kon SS, Jones SE, Schofield SJ, et al. Gait speed and readmission following hospitalisation for acute exacerbations of COPD: a prospective study. *Thorax*. 2015;70(12):1131-1137.
 22. Antonini TC, de Paz JA, Ribeiro EE, et al. Impact of functional determinants on 5.5-year mortality in Amazon riparian elderly. *Revista panamericana de salud publica = Pan American journal of public health*. 2016;40(1):9-15.
 23. Bergland A, Jorgensen L, Emaus N, Strand BH. Mobility as a predictor of all-cause mortality in older men and women: 11.8 year follow-up in the Tromso study. *BMC health services research*. 2017;17(1):22.
 24. Castro-Rodriguez M, Carnicero JA, Garcia-Garcia FJ, et al. Frailty as a Major Factor in the Increased Risk of Death and Disability in Older People With Diabetes. *Journal of the American Medical Directors Association*. 2016.
 25. De Buyser SL, Petrovic M, Taes YE, Toye KR, Kaufman JM, Goemaere S. Physical function measurements predict mortality in ambulatory older men. *European journal of clinical investigation*. 2013;43(4):379-386.
 26. Dodson JA, Arnold SV, Gosch KL, et al. Slow Gait Speed and Risk of Mortality or Hospital Readmission After Myocardial Infarction in the Translational Research Investigating Underlying Disparities in Recovery from Acute Myocardial Infarction: Patients' Health Status Registry. *Journal of the American Geriatrics Society*. 2016;64(3):596-601.

27. Nikolaus T, Bach M, Oster P, Schlierf G. Prospective value of self-report and performance-based tests of functional status for 18-month outcomes in elderly patients. *Aging (Milan, Italy)*. 1996;8(4):271-276.
28. Roshanravan B, Robinson-Cohen C, Patel KV, et al. Association between physical performance and all-cause mortality in CKD. *Journal of the American Society of Nephrology : JASN*. 2013;24(5):822-830.
29. Studenski S, Perera S, Patel K, et al. Gait speed and survival in older adults. *Jama*. 2011;305(1):50-58.
30. Tice JA, Kanaya A, Hue T, et al. Risk factors for mortality in middle-aged women. *Archives of internal medicine*. 2006;166(22):2469-2477.
31. Belsley DA, E. Kuh, and R. E. Welsch. 1980. *Regression Diagnostics: Identifying Influential Data and Sources of Collinearity*. New York: Wiley.
32. Pregibon D. Goodness of link tests for generalized linear models. *Applied Statistics* 29: 15–24.
33. Steyerberg EW, Vickers AJ, Cook NR, et al. Assessing the performance of prediction models: a framework for traditional and novel measures. *Epidemiology (Cambridge, Mass)*. 2010;21(1):128-138.
34. Andersen PK, Geskus RB, de Witte T, Putter H. Competing risks in epidemiology: possibilities and pitfalls. *International journal of epidemiology*. 2012;41(3):861-870.
35. Hinchliffe SR, Lambert PC. Flexible parametric modelling of cause-specific hazards to estimate cumulative incidence functions. *BMC medical research methodology*. 2013;13:13.
36. Fine JPG, R.J. A Proportional Hazards Model for the Subdistribution of a Competing Risk *Journal of the American Statistical Association* 1999;94(46):496-509.
37. Burke RE, Whitfield EA, Hittle D, et al. Hospital Readmission From Post-Acute Care Facilities: Risk Factors, Timing, and Outcomes. *Journal of the American Medical Directors Association*. 2016;17(3):249-255.
38. Tonkikh O, Shadmi E, Flaks-Manov N, Hoshen M, Balicer RD, Zisberg A. Functional status before and during acute hospitalization and readmission risk identification. *Journal of hospital medicine*. 2016;11(9):636-641.
39. Robinson TN, Wu DS, Pointer L, Dunn CL, Cleveland JC, Jr., Moss M. Simple frailty score predicts postoperative complications across surgical specialties. *American journal of surgery*. 2013;206(4):544-550.
40. Belga S, Majumdar SR, Kahlon S, et al. Comparing three different measures of frailty in medical inpatients: Multicenter prospective cohort study examining 30-day risk of readmission or death. *Journal of hospital medicine*. 2016;11(8):556-562.
41. Idland G, Engedal K, Bergland A. Physical performance and 13.5-year mortality in elderly women. *Scandinavian journal of public health*. 2013;41(1):102-108.
42. Zweig MH, Campbell G. Receiver-operating characteristic (ROC) plots: a fundamental evaluation tool in clinical medicine. *Clinical chemistry*. 1993;39(4):561-577.