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Validation of the Hospital Frailty Risk Score in a Tertiary Care Hospital in Switzerland: results of a prospective, observational study

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ABSTRACT

Objectives: Recently, the Hospital Frailty Risk Score based on a derivation and validation study in the United Kingdom has been proposed as a low-cost, systematic screening tool to identify elderly patients who are at greater risk of adverse outcomes and for whom a frailty-attuned approach might be useful. We aimed to validate this Score in an independent cohort in Switzerland.

Design: Secondary analysis of a prospective, observational study (TRIAGE study).

Setting: One 600-bed tertiary care hospital in Aarau, Switzerland

Participants: Consecutive medical inpatients aged 75 years or older that presented to the emergency department or were electively admitted between October 2015 and April 2018.

Primary and secondary outcome measures: The primary endpoint was all-cause 30-day mortality. Secondary endpoints were length of hospital stay, hospital readmission, functional impairment, and quality of life measures. We used multivariate regression analyses.

Results: Of 4957 included patients, 3150 (63.5%) were classified as low risk, 1663 (33.5%) intermediate risk, and 144 (2.9%) high risk for frailty. Compared to the low-risk group, patients in the moderate risk and high-risk groups had increased risk for 30-day mortality (odds ratio [OR] 2.53, 95%CI 2.09 to 3.06, P<0.001 and OR 4.40, 95%CI 2.94 to 6.57, P<0.001) with overall moderate discrimination (area under the ROC curve 0.66). The results remained robust after adjustment for important confounders. Similarly, we found longer length of hospital stay, more severe functional impairment and a lower quality of life in higher risk group patients.

Conclusion: Our data confirms the prognostic value of the Hospital Frailty Risk Score to identify frail, elderly people at risk for mortality and adverse outcomes in an independent patient population.

Trial registration number: ClinicalTrials.gov; Identifier: NCT01768494

STRENGTHS AND LIMITATIONS OF THE STUDY

Strength and limitations of this study

- This is the first study to validate the Hospital Frailty Risk Score following its publication and initial validation.
- The validation in a Swiss Tertiary care hospital is a first step in assessing the applicability of the risk score in multinational settings.
- In addition to associations with adverse clinical outcomes we assess associations of higher hospital frailty risk scores with functional impairment, quality of life, and need for post-acute care.
- Due to the study design there was no routine frailty assessment in our patients and we were not able to compare the score with other frailty assessments or screening scores.
- As the score is dependent of documentation and coding of ICD-10, variation in coding could contribute to misclassification.

INTRODUCTION

With the increase in the ageing, multimorbidity patient population, the proportion of frail patients is expected to further raise.[1] Frailty describes a state of increased risk for decline in health after an exposure to a stressor event (e.g., hospitalization for an acute illness) increasing the risk for adverse events such as falls, delirium, disability and death.[2-4] Importantly, identifying patients at risk for frailty early during the course of hospitalization may help to improve treatment strategies including a comprehensive geriatric assessment to improve the care and outcomes of patients.[5] Several tools to identify frailty have been developed in the last 20 years.[6] Yet none has emerged as a gold standard. Current instruments show only a moderate power to identify frailty,[7] and some tools require time consuming manual assessment [8 9]. Moreover, in most hospitals there is no routine assessment of the elderly and only a subset of patients is screened for frailty[6]. For these reasons, patients who may benefit from a specific frailty-directed treatment approach may be missed in usual hospital care. To improve the care of frail patients, the recently published Hospital Frailty Risk score[10] was developed for early identification of patients with characteristics of frailty, who are at risk of adverse health-care outcomes and who could be identified without any additional assessment apart from routinely collected data. The score relies on the diagnostic codes from the International Statistical Classification of Diseases and Related Health Problems, Tenth Revision (ICD-10), a coding system that is implemented in many administrative hospital databases worldwide. This provides the opportunity to systematically screen elderly patients in a low-cost manner [10]. In a three-step approach, this score was developed and later validated within three patient populations from the United Kingdom showing high prognostic performance. Still, international validation is needed before more wide-spread use of this score in other health care systems. Herein, we aimed to validate

the Hospital Frailty Risk Score in a Swiss tertiary care hospital. We investigated associations of the score with adverse clinical outcomes such as 30-day mortality, length of hospital stay, and 30-day readmission, as well as functional outcomes including functional impairment, quality of life and discharge location.

METHODS

Study design and study population

This is a secondary analysis of the TRIAGE study, a prospective, observational cohort study initially designed to understand the value of admission biomarkers to predict later adverse outcomes.[11 12] We included consecutive medical patients presenting with a medical urgency at the Kantonsspital in Aarau (Switzerland), a 600-bed tertiary care hospital with most medical admissions entering the hospital over the ED. As an observational quality control study, the Institutional Review Boards (IRB) of the hospital approved the study and waived the need for individual informed consent (main Swiss IRB: Ethikkommission Kanton Aargau (EK 2012/059). The study was registered at the "ClinicalTrials.gov" registration website (http://www.clinicaltrials.gov/ct2/show/NCT01768494) and the study protocol has been published previously.[13]

In accordance with the initial study, we selected medical inpatients aged 75 years or older, that were admitted between October 2015 and April 2018. The cohort includes elective and emergency admissions. In case of multiple admissions of the same patient, only the first admission was used for the analysis.

Patient and Public Involvement

Patients were not involved in the development of the research question or the design of the study.

Follow-up and initial data collection

We used ICD-10 diagnostic codes assigned to patients after discharge by professional hospital coders according to the information of medical records. The electronic records contained up to 38 diagnosis fields coded according to ICD-10.

Regarding follow-up, 30 days after hospital admission patients were contacted by telephone for a structured interview to obtain information on vital status, clinical outcomes, location of living and functional measurements. Functional status was obtained using the EQ-5D-3L standardized measure of health, which was administered as recommended [14]. We assessed mobility, self-care, usual activities, pain or discomfort, and anxiety and depression, using dichotomized data with levels 2 and 3 indicating "impairment" and level 1 indicating "no impairment". Moreover, we used the EQ-VAS, recording the self-rated health on a visual analogue scale with values between 0 and 100 with higher points indicating better health states.

We used the Barthel Index to measure activities of daily living (ADL)[15], with a cutoff <95 points indicating functional impairment. We assessed location after discharge and identified patients who were living at home before hospital admission and were discharged to a location other than home.

All information was stored in a centralized, password-secured database (SecuTrial®; interActive Systems GmbH, Berlin, Germany).

Calculation of the Hospital Frailty Risk Score

For each patient the Hospital Frailty Risk Score was calculated retrospectively using all available ICD-10 diagnostic codes that were documented for the particular admission as recommended [10]. The score is an aggregate of 109 ICD-10 diagnostic codes that were found to be associated with frailty risk. Each of these ICD-10 diagnostic codes were awarded with specific values proportional to how strongly they predicted frailty. According to the aggregate score, patients were divided into the three frailty risk categories low risk (<5 points), intermediate risk (5-15 points), and high risk (> 15 points) as recommended [10].

Research aims and statistical approach

We investigated associations of the Hospital Frailty Risk with adverse clinical outcomes. Our primary endpoint is all-cause 30-day mortality. Secondary endpoints include hospital length of stay, long hospital stay (>10 days), and hospital readmission within 30 days. Moreover, we examined associations with functional impairment using the Barthel-Index (<95 points indicating impairment), Quality of Life measurements using the EQ-5D standardized measure, and discharge location other than home, for patients that were living at home before admission.

Statistical analysis

We expressed patient characteristics using descriptive statistics including mean with standard deviation (SD), median with interquartile range (IQR), and frequencies, as appropriate. Frequency comparison was done using the χ^2 test.

To investigate associations of the Hospital Frailty Risk Score with outcomes we used univariate and multivariate regression analyses. Models were stepwise adjusted for age (model 1), age and gender (model 2), and age, gender and comorbidities that were not included in the calculation of the frailty risk score (model 3). We provide odds ratios (ORs) or regression coefficients (RCs) with 95% confidence intervals (95% CIs) as appropriate. We used receiver operating statistics reporting area under the curve (AUC) as a measure of discrimination. We considered AUCs of 0.6 to 0.7 as moderate, 0.7 to 0.8 as fair, 0.8 to 0.9 as good, and >0.9 as excellent. Also, for graphical illustration we generated Kaplan-Meier survival estimates stratified by frailty risk groups.

We repeated analyses in predefined subgroups stratified by age and gender.

All tests were two-tailed and carried out at 5% significance levels. Analyses were performed with STATA 12.1 (Stata Corp., College Station, TX, USA).

RESULTS

Patient Population

A total of 4957 Patients with a median age of 82 years were included in this analysis. At time of admission the majority of patients (63.4%) resided at home. A total of 63.5% (3150) of patients were in the low frailty risk group, 33.5% (1663) in the intermediate risk group, and 2.9% (144) were in the high-risk group. Baseline characteristics of the general population and stratified by Hospital Frailty Risk categories are listed in **Table 1**.

Table1 Baseline characteristics of the total cohort and stratified by frailty risk group

Characteristics	Total cohort	Frailty risk (points)			p-value
		Low risk (<5)	Intermediate risk (5-15)	High risk (>15)	
N (%)	4957	3150 (63.5%)	1663 (33.5%)	144 (2.9%)	
Male gender, n (%)	2426 (49.0%)	1634 (52.0%)	733 (44.2%)	59 (41.0%)	<0.001
Age (years), median (IQR)	82 (78, 86)	82 (78, 85)	83 (79, 87)	83 (79, 87)	<0.001
Vital signs, median (IQR)					
Blood pressure systolic (mmHg)	148 (129, 168)	149 (131, 168)	147 (125, 166)	151 (132, 176.5)	0.007
Blood pressure diastolc (mmHg)	80 (68, 93)	80 (69, 93)	80 (68, 92)	80 (69, 97)	0.25
Pulse rate (bpm)	81.5 (70, 95.2)	80.5 (69, 94.8)	82 (70.9, 96)	85 (73, 101)	0.009
Oxygen saturation (%)	95.8 (92.8, 98)	96 (93.5, 98)	95.4 (92.1, 97.6)	95.05 (92, 97.4)	<0.001
Temperature (°C)	36.8 (36.4, 37.3)	36.8 (36.4, 37.3)	36.8 (36.4, 37.4)	36.6 (36.4, 37.1)	0.007
Comorbidities, n (%)					
Diabetes	698 (14.1%)	486 (15.4%)	205 (12.3%)	7 (4.9%)	<0.001
Malignant disease	494 (10.0%)	354 (11.2%)	131 (7.9%)	9 (6.2%)	<0.001
Chronic heart failure	699 (14.1%)	436 (13.8%)	249 (15.0%)	14 (9.7%)	0.17
COPD	257 (5.2%)	178 (5.7%)	75 (4.5%)	4 (2.8%)	0.099
Dementia	338 (6.8%)	104 (3.3%)	218 (13.1%)	16 (11.1%)	<0.001
Chronic renal disease	1282 (25.9%)	715 (22.7%)	540 (32.5%)	27 (18.8%)	<0.001
Hypertension	2608 (52.6%)	1726 (54.8%)	826 (49.7%)	56 (38.9%)	<0.001
Coronary heart disease	531 (10.7%)	424 (13.5%)	100 (6.0%)	7 (4.9%)	<0.001
Stroke	668 (13.5%)	193 (6.1%)	396 (23.8%)	79 (54.9%)	<0.001

Location prior to admission, n (%)					
Home	3144 (63.4%)	2194 (69.7%)	895 (53.8%)	55 (38.2%)	<0.001
Home with assistance service	264 (5.3%)	107 (3.4%)	142 (8.5%)	15 (10.4%)	
Nursing home	370 (7.5%)	161 (5.1%)	190 (11.4%)	19 (13.2%)	
Other hospital	457 (9.2%)	275 (8.7%)	161 (9.7%)	21 (14.6%)	
Unknown or other	722 (14.6%)	413 (13.1%)	275 (16.5%)	34 (23.6%)	

COPD chronic obstructive pulmonary disease; IQR interquartile range

Associations of frailty risk score with mortality

A total of 524 (10.7%) patients died within 30 days of admission, consisting of 221 (7.1%) of those in the low risk group, 267 (16.2%) in the intermediate risk group and 36 (25.2%) in the high-risk group. Regression analyses showed corresponding ORs of 2.53 (95% CI 2.09 to 3.06, P<0.001) for the intermediate risk group and 4.40 (95% CI 2.94 to 6.57, P<0.001) for the high-risk group, respectively, compared to the low risk group. Results remained robust after adjustment for confounders (age, gender, and comorbidities not included in the score) (**Table 2, Figure 1**).

We also investigated the discriminative performance of the score and found only moderate results for mortality (AUC 0.66) (**Table 3**).

Table 2 Associations of elevated frailty risk groups with adverse clinical outcomes compared to the low frailty risk group

Outcome	Overall n (%)	Low Risk n (%)	Intermediate Risk, n (%)	High Risk n (%)	P value	Intermediate Risk, OR (95% CI), P-value unadjusted	Intermediate Risk, OR (95% CI), P-value fully adjusted	High Risk, OR (95% CI), P-value unadjusted	High Risk, OR (95% CI), P-value fully adjusted
all-cause 30-day mortality	524 (10.7%)	221 (7.1%)	267 (16.2%)	36 (25.2%)	<0.001	2.53 (2.09 to 3.06), p<0.001	2.65 (2.17 to 3.25), p<0.001	4.4 (2.94 to 6.57), p<0.001	4.83 (3.17 to 7.37), p<0.001
Length of stay, median (IQR)*	5 (2, 9)	4 (2, 7)	7 (4, 12)	11.5 (7, 18)	<0.001	3.74 (3.34 to 4.14), p<0.001	3.77 (3.39 to 4.15), p<0.001	10.04 (8.92 to 11.16), p<0.001	10.07 (9.02 to 11.13), p<0.001
Long hospital stay >10 days	1010 (20.4%)	386 (12.3%)	543 (32.7%)	81 (56.2%)	<0.001	3.47 (2.99 to 4.02), p<0.001	3.66 (3.14 to 4.28), p<0.001	9.21 (6.51 to 13.01), p<0.001	9.75 (6.83 to 13.92), p<0.001
30-day readmission	586 (11.8%)	372 (11.8%)	195 (11.7%)	19 (13.2%)	0.87	1.04 (0.88 to 1.24), p=0.643	1.04 (0.87 to 1.24), p=0.69	1.47 (0.95 to 2.26), p=0.081	1.67 (1.08 to 2.59), p=0.022
Functional impairment, n (%)									
Barthel Index, median (IQR)*	95 (70, 100)	100 (85, 100)	80 (55, 100)	50 (20, 75)	<0.001	-15.76 (-17.87 to -13.64), p<0.001	-14.59 (-16.69 to -12.48), p<0.001	-40.55 (-47.01 to -34.09), p<0.001	-39.7 (-46.06 to -33.33), p<0.001
Barthel Index <95 points	1052 (46.5%)	529 (36.3%)	472 (62.9%)	51 (92.7%)	<0.001	2.98 (2.48 to 3.58), p<0.001	2.87 (2.37 to 3.47), p<0.001	22.37 (8.04 to 62.23), p<0.001	25.03 (8.91 to 70.32), p<0.001
Quality of Life, n(%)									
Impairment of mobility	408 (18.0%)	162 (11.1%)	217 (28.9%)	29 (51.8%)	<0.001	3.25 (2.59 to 4.08), p<0.001	3.1 (2.46 to 3.92), p<0.001	8.61 (4.97 to 14.91), p<0.001	8.45 (4.82 to 14.81), p<0.001
Impairment of self-care	1010 (44.5%)	480 (32.9%)	484 (64.4%)	46 (82.1%)	<0.001	3.69 (3.07 to 4.44), p<0.001	3.63 (2.99 to 4.4), p<0.001	9.40 (4.7 to 18.79), p<0.001	9.59 (4.74 to 19.41), p<0.001
Impairment of usual activities	1366 (60.2%)	767 (52.5%)	553 (73.5%)	46 (82.1%)	<0.001	2.51 (2.08 to 3.05), p<0.001	2.35 (1.92 to 2.87), p<0.001	4.16 (2.08 to 8.31), p<0.001	3.98 (1.97 to 8.06), p<0.001
Pain/discomfort	910 (42.7%)	574 (40.8%)	314 (46.3%)	22 (48.9%)	0.039	1.25 (1.04 to 1.51), p=0.017	1.21 (1 to 1.47), p=0.047	1.39 (0.77 to 2.52), p=0.278	1.28 (0.7 to 2.33), p=0.43
Anxiety/depression	629 (30.3%)	394 (28.2%)	213 (33.2%)	22 (56.4%)	<0.001	1.26 (1.03 to 1.55), p=0.023	1.26 (1.02 to 1.55), p=0.029	3.29 (1.73 to 6.26), p<0.001	3.11 (1.62 to 5.99), p=0.001
EQ-VAS, mean (SD)*	70.8 (18.3)	72.1 (17.9)	68.2 (19.0)	61.8 (17.6)	<0.001	-3.9 (-5.83 to -1.97), p<0.001	-3.75 (-5.69 to -1.81), p<0.001	-10.3 (-17.53 to -3.08), p=0.005	-11.12 (-18.29 to -3.94), p=0.002
discharge other than home	1092 (22.0%)	504 (16.0%)	530 (31.9%)	58 (40.3%)	<0.001	2.46 (2.13 to 2.83), p<0.001	2.53 (2.18 to 2.92), p<0.001	3.54 (2.5 to 5.01), p<0.001	3.81 (2.68 to 5.42), p<0.001

95% CI confidence interval; EQ-VAS EuroQol visual analog health scale; IQR interquartile range; OR odds ratio; SD standard deviation;

Quality of life measures were adapted from EQ-5D. We dichotomized levels into "no impairment" (level 1) and "impairment" (levels 2 and 3). Frequencies of reported impairment (level 2 and 3) were analyzed.

The fully adjusted model was adjusted for age, gender, and comorbidities not included in the score

* linear regression analyses were calculated reporting regression coefficient, 95% confidence interval, P-value

Table 3 Discriminative Performance of the Hospital frailty Risk Score regarding clinical and functional outcomes

Outcome	AUC (95% CI)
Clinical outcomes	
all-cause 30-day mortality	0.66 (0.63 to 0.68)
Long hospital stay (>10 days)	0.72 (0.7 to 0.74)
30-day readmission	0.54 (0.51 to 0.56)
Functional impairment	
Barthel Index <95 points, n (%)	0.69 (0.67 to 0.71)
Quality of Life, n (%)	
Impairment of mobility	0.71 (0.68 to 0.74)
Impairment of self-care	0.71 (0.69 to 0.73)
Impairment of usual activities	0.66 (0.63 to 0.68)
Pain/discomfort	0.54 (0.51 to 0.56)
Anxiety/depression	0.56 (0.53 to 0.58)
discharge other than home, n (%)	0.64 (0.63 to 0.66)

AUC area under the receiver operating curve; 95% CI 95% confidence interval

Quality of life measures were adapted from EQ-5D. We dichotomized levels into "no impairment" (level 1) and "impairment" (levels 2 and 3). Frequencies of reported impairment (level 2 and 3) were analyzed.

Associations of frailty risk score with other adverse clinical outcomes

We also found significant results regarding length of hospital stay and long hospital stay (>10 days). Compared to the low risk group corresponding ORs for long hospital stay were 3.47 (95% CI 2.99 to 4.02, P<0.001) for the intermediate risk group and 9.21 (95% CI 6.51 to 13.01, P<0.001) for the high-risk group. Again, results remained robust after adjustment for the confounders mentioned.

Regarding hospital readmission within 30 days we did only find a significant association for the high-risk group compared to the low-risk group in the fully adjusted model (fully adjusted OR 1.67, 95% CI 1.08 to 2.59, P=0.022) (**Table 2**).

Associations with functional Impairment, quality of life, and location after discharge

Regarding functional status, we found significantly higher proportions of impairment (Barthel Index < 95 points) in higher frailty risk groups with corresponding ORs of 2.98 (95% CI 2.48 to 3.58, P<0.001) and 22.37 (95% CI 8.04 to 62.23, P<0.001). Similar results were found for quality of life measures 30 days after admission with corresponding ORs for the high-risk group of 8.61 (95% CI 4.97 to 14.91, P<0.001) for impairment of mobility, 9.40 (95% CI 4.7 to 18.79, P<0.001) for impaired self-care, 4.16 (95% CI 2.08 to 8.31, P<0.001) for impairment of usual activities, and 3.29 (95% CI 1.73 to 6.26, P<0.001) for suffering from anxiety or depression.

Compared to patients in the low risk group, patients in the high-risk group that resided home at time of admission had a 3.5 fold increased risk of not being able to be discharged back home (OR 3.54 (95% CI 2.5 to 5.01, P<0.001) (**Table 2**).

Additional results of regression analyses of all models with stepwise adjustment for confounders are shown in the supplemental material (**Tables A1 & A2**).

Subgroup analyses

Analyses of subgroups showed similar associations of the Hospital Frailty Risk Score with 30-day mortality, long hospital stay, and hospital readmission among different age groups and stratified by gender with no evidence for effect modification (**Figure 2**).

DISCUSSION

Within this independent validation study including medical inpatients >75 years of age in a Swiss tertiary care setting, we found significant associations between the Hospital frailty risk scores and several adverse clinical outcomes, specifically all-cause 30-day mortality, hospital length of stay, and long hospital stay (>10 days). Moreover, we found significant associations of the intermediate and high-risk group with functional impairment, measured by the Barthel Index, and reduced quality of life, as assessed by the EQ-5D. Last, we found patients of the higher risk group that were admitted from home significantly less likely to return back home at time of discharge.

Compared to the three cohorts of the original publication (one development cohort and two validation cohorts) by Gilbert et al.[10] a similar proportion of patients were classified in the intermediate-risk group (33.5% vs. 20.3 to 37.6%) but a smaller proportion of patients were classified in the high-risk group (2.9% vs. 9.0 to 20.0%). This might be due to different health care systems, different patient populations studied and variation in ICD-10 coding. However, compared to the results of Gilbert et al., we found even stronger associations of the high frailty risk group compared to the low-risk group with regard to 30-day mortality (adjusted OR 4.83, 95% CI 3.17 to 7.37, p<0.001 vs. adjusted OR 1.71, 95% CI 1.68 to 1.75), and long hospital stay (adjusted OR 9.75, 95% CI 6.83 to 13.92, p<0.001 vs. adjusted OR 6.03, 95% CI 5.92 to 6.10).

Regarding the discriminative performance of the Hospital frailty risk score we found similar results as Gilbert et al. with regard to 30-day mortality (AUC 0.66 vs. 0.60), long hospital stay (AUC 0.72 vs. 0.68), and hospital readmission within 30 days (AUC 0.54 vs. 0.56). Overall, these results show significant associations of the Hospital frailty risk score with adverse outcomes, however, with moderate discriminatory

ability. Thus, future studies should aim to further refine the score to increase its sensitivity and specificity.

To the best of our knowledge, this is the first study to validate the Hospital Frailty Risk Score following its publication and initial validation. Moreover, the validation in a Swiss tertiary care hospital in an unselected medical cohort including emergency admissions and elective admissions is a first step in assessing whether the risk score is applicable in multinational settings.

In addition to Gilbert et al. we were able to show associations of higher hospital frailty risk scores not only with adverse clinical outcomes but also with functional impairment, quality of life, and need for post-acute care. Our data thus extend the prior study and provides new evidence that the score is valuable in risk stratification of patients based on ICD10 codes.

A general strength of the score is the easy calculation using routine hospital data which provides a systematic method to screen for patients at risk for frailty without any need to apply a manual score bringing along resource intensive assessment and potential inter-operator reliability issues [8 9 16]. Moreover, instead of focusing only on symptoms and diagnoses that are known to be related to frailty, the score contains a wider set of ICD-10 codes focusing on codes that are actually in routine use.

Our report has several limitations. Firstly, this is a secondary analysis of a former prospective study. We did address this limitation by adjusting for confounders. Furthermore, as we were able to externally validate the previous findings accurately, we are confident that there is no additional bias. Second, due to the study design there was no routine frailty assessment in our patients. As a consequence, we were not able to compare the Hospital Frailty Risk score with other frailty assessments or screening scores. Yet, so far there is no gold standard in frailty screening to compare it to [2 16 17]. In addition, Gilbert et al. found fair overlap of the score with the

established frailty assessment tools Fried and Rockwood scales [9 10 17]. Using multiple clinical and functional outcomes as well as quality of life measures, we tried to address a broad variety of potential adverse outcomes associated with frailty.

Thirdly, though we had a large sample size, only few patients were in the high frailty risk group, which may impact confidence intervals. Lastly, the score is dependent of documentation and coding of ICD-10. Thus, variation in coding could contribute to misclassification. Moreover, important components of frailty such as polypharmacy or general weakness might not be adequately reflected in ICD-10 codes.

The development of a gold standard for frailty risk assessment has proven to be a challenging task [16 17]. The attempt has left us with a multitude of screening tools, suited for a variety of patient populations and a large variability of application methods [6]. Recent research suggests that a single universal frailty measurement method may not be the best approach. As some methods are useful for broad population screenings whilst others are based on clinical assessment, a two-tiered system may be the way forward [18]. The Hospital Frailty Risk Score could be used as a screening tool to assess all elderly patients admitted to a hospital using all previously and currently documented ICD-10 codes. This could easily identify high-risk patients in need of a complete in-depth clinical assessment. As a low-cost, swift and consecutively widely used tool, the Hospital Frailty Risk Score could ensure that less patients with frailty are missed. Identifying frail patients is vital, as they may benefit from improved outcomes when they undergo geriatric assessment and receive a particular frailty-adjusted treatment approach [19].

The frailty risk score needs further validation in a wide variety of patient settings. Its place in the screening of geriatric patients, possibly in combination with other frailty assessment methods, as well as the practicability in clinical practice, has yet to be

investigated. Furthermore, it remains unclear whether its theoretical benefits can be translated into improved patient care and patient outcome.

CONCLUSION

The Hospital Frailty Risk Score is an easy to use and low-cost tool using administrative hospital data to identify frail, elderly people at risk for adverse outcomes who might benefit from a standardized geriatric assessment and from a particular frailty-adjusted treatment approach. Our data further validate this score in an independent patient population.

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Author contributions

All authors made substantive intellectual contributions to this study regarding conception and design, have taken an active part in acquisition, analysis, and interpretation of data, and approved the final version of the manuscript. AE, SH, and PS conducted the statistical analyses and initially drafted the manuscript. AE and SH contributed equally to this work.

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Competing interests

All authors have no conflicts of interest relevant to this paper. The funding organization had no role in the design or conduct of the study, analysis and interpretation of the data, writing of the manuscript, or the decision to submit the manuscript for publication.

Data sharing statement:

Part of the dataset will be available from the Dryad repository.

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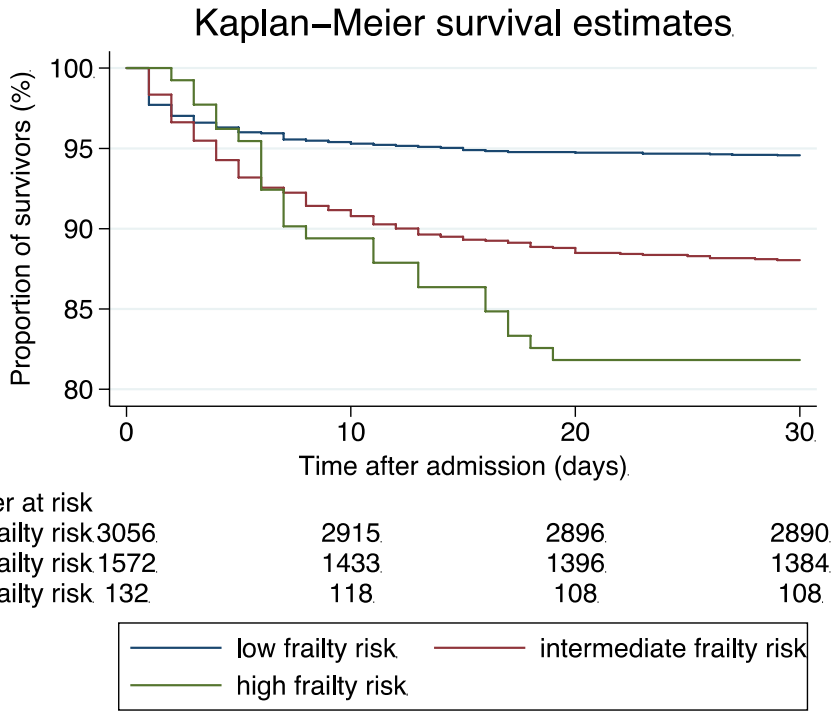
FIGURES

Figure 1 Survival estimates stratified by the three Hospital Frailty Risk group

Figure 2 Associations of elevated hospital frailty risk with adverse clinical outcomes stratified by age and gender

OR odds ratio, 95% CI 95% confidence interval



Number at risk				
low frailty risk	3056	2915	2896	2890
intermediate frailty risk	1572	1433	1396	1384
high frailty risk	132	118	108	108

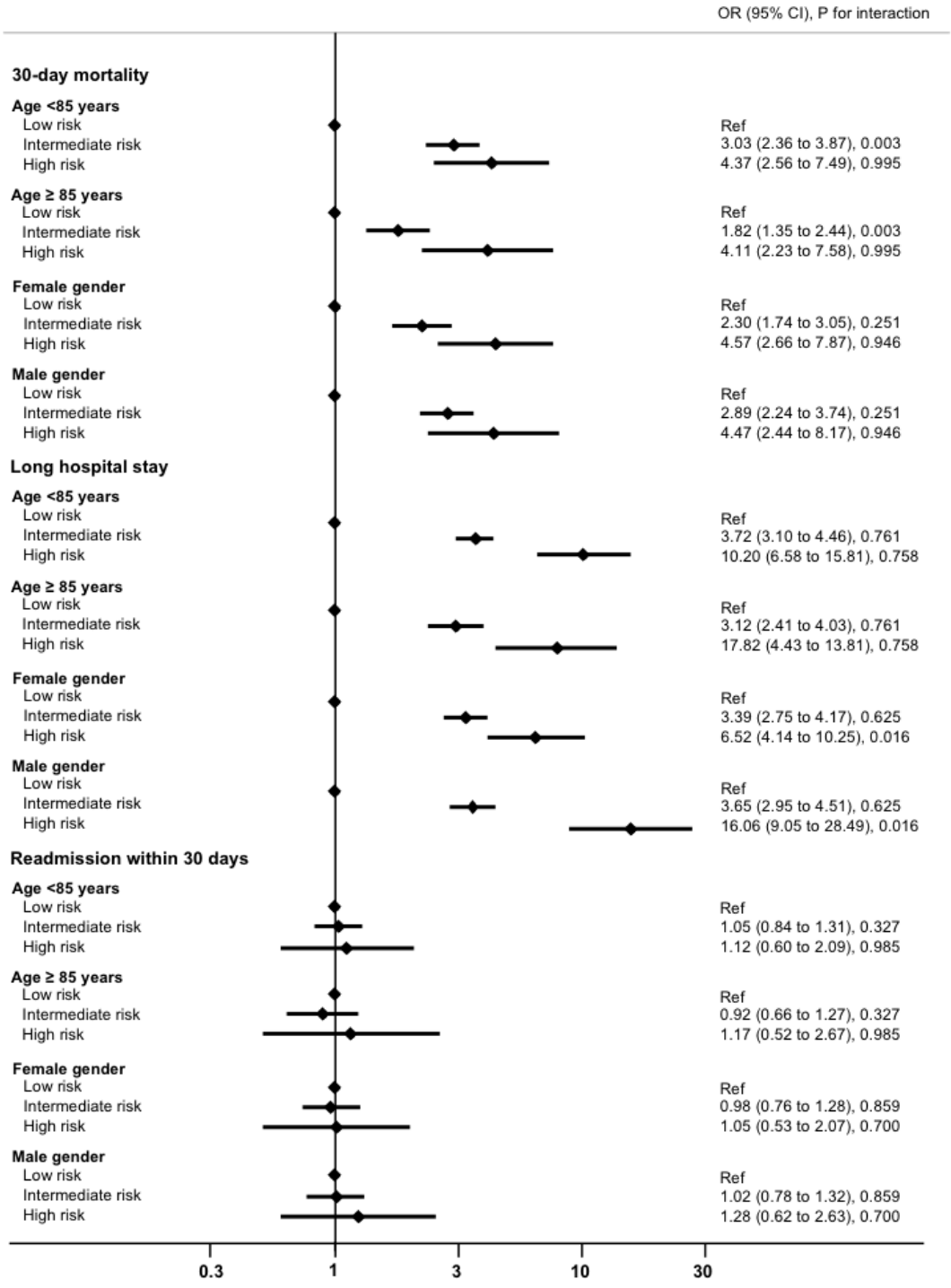

OR (95% CI), P for interaction
30-day mortality
Age <85 years
Low risk
Ref
Intermediate risk
3.03 (2.36 to 3.87), 0.003
High risk
4.37 (2.56 to 7.49), 0.995
Age ≥ 85 years
Low risk
Ref
Intermediate risk
1.82 (1.35 to 2.44), 0.003
High risk
4.11 (2.23 to 7.58), 0.995
Female gender
Low risk
Ref
Intermediate risk
2.30 (1.74 to 3.05), 0.251
High risk
4.57 (2.66 to 7.87), 0.946
Male gender
Low risk
Ref
Intermediate risk
2.89 (2.24 to 3.74), 0.251
High risk
4.47 (2.44 to 8.17), 0.946
Long hospital stay
Age <85 years
Low risk
Ref
Intermediate risk
3.72 (3.10 to 4.46), 0.761
High risk
10.20 (6.58 to 15.81), 0.758
Age ≥ 85 years
Low risk
Ref
Intermediate risk
3.12 (2.41 to 4.03), 0.761
High risk
17.82 (4.43 to 13.81), 0.758
Female gender
Low risk
Ref
Intermediate risk
3.39 (2.75 to 4.17), 0.625
High risk
6.52 (4.14 to 10.25), 0.016
Male gender
Low risk
Ref
Intermediate risk
3.65 (2.95 to 4.51), 0.625
High risk
16.06 (9.05 to 28.49), 0.016
Readmission within 30 days
Age <85 years
Low risk
Ref
Intermediate risk
1.05 (0.84 to 1.31), 0.327
High risk
1.12 (0.60 to 2.09), 0.985
Age ≥ 85 years
Low risk
Ref
Intermediate risk
0.92 (0.66 to 1.27), 0.327
High risk
1.17 (0.52 to 2.67), 0.985
Female gender
Low risk
Ref
Intermediate risk
0.98 (0.76 to 1.28), 0.859
High risk
1.05 (0.53 to 2.07), 0.700
Male gender
Low risk
Ref
Intermediate risk
1.02 (0.78 to 1.32), 0.859
High risk
1.28 (0.62 to 2.63), 0.700
0.3
1
3
10
30

Table A1 Associations of intermediate frailty risk with adverse clinical outcomes compared to the low frailty risk group.

Outcome	Overall n (%)	Low Risk n (%)	Intermediate Risk, n (%)	Intermediate Risk, OR (95% CI), P-value unadjusted	Model 1	Model 2	Model 3
all-cause 30-day mortality	524 (10.7%)	221 (7.1%)	267 (16.2%)	2.53 (2.09 to 3.06), p<0.001	2.45 (2.03 to 2.97), p<0.001	2.52 (2.08 to 3.06), p<0.001	2.65 (2.17 to 3.25), p<0.001
Length of stay, median (IQR)*	5 (2, 9)	4 (2, 7)	7 (4, 12)	3.74 (3.34 to 4.14), p<0.001	3.76 (3.36 to 4.16), p<0.001	3.83 (3.45 to 4.21), p<0.001	3.77 (3.39 to 4.15), p<0.001
Long hospital stay >10 days	1010 (20.4%)	386 (12.3%)	543 (32.7%)	3.47 (2.99 to 4.02), p<0.001	3.50 (3.02 to 4.06), p<0.001	3.55 (3.06 to 4.12), p<0.001	3.66 (3.14 to 4.28), p<0.001
30-day readmission	586 (11.8%)	372 (11.8%)	195 (11.7%)	1.04 (0.88 to 1.24), p=0.643	1.06 (0.89 to 1.26), p=0.521	1.06 (0.89 to 1.26), p=0.503	1.04 (0.87 to 1.24), p=0.69
Functional impairment, n (%)							
Barthel Index, median (IQR)*	95 (70, 100)	100 (85, 100)	80 (55, 100)	-15.76 (-17.87 to -13.64), p<0.001	-15.01 (-17.1 to -12.92), p<0.001	-14.87 (-16.97 to -12.78), p<0.0010	-14.59 (-16.69 to -12.48), p<0.001
Barthel Index <95 points	1052 (46.5%)	529 (36.3%)	472 (62.9%)	2.98 (2.48 to 3.58), p<0.001	2.89 (2.4 to 3.47), p<0.001	2.85 (2.36 to 3.43), p<0.001	2.87 (2.37 to 3.47), p<0.001
Quality of Life, n(%)							
Impairment of mobility	408 (18.0%)	162 (11.1%)	217 (28.9%)	3.25 (2.59 to 4.08), p<0.001	3.14 (2.50 to 3.95), p<0.001	3.13 (2.49 to 3.94), p<0.001	3.1 (2.46 to 3.92), p<0.001
Impairment of self-care	1010 (44.5%)	480 (32.9%)	484 (64.4%)	3.69 (3.07 to 4.44), p<0.001	3.60 (2.99 to 4.35), p<0.001	3.56 (2.95 to 4.30), p<0.001	3.63 (2.99 to 4.4), p<0.001
Impairment of usual activities	1366 (60.2%)	767 (52.5%)	553 (73.5%)	2.51 (2.08 to 3.05), p<0.001	2.41 (1.99 to 2.93), p<0.001	2.35 (1.93 to 2.87), p<0.001	2.35 (1.92 to 2.87), p<0.001
Pain/discomfort	910 (42.7%)	574 (40.8%)	314 (46.3%)	1.25 (1.04 to 1.51), p=0.017	1.26 (1.04 to 1.51), p=0.015	1.22 (1.01 to 1.47), p=0.036	1.21 (1 to 1.47), p=0.047
Anxiety/depression	629 (30.3%)	394 (28.2%)	213 (33.2%)	1.26 (1.03 to 1.55), p=0.023	1.28 (1.04 to 1.56), p=0.018	1.25 (1.02 to 1.53), p=0.032	1.26 (1.02 to 1.55), p=0.029
EQ-VAS, mean (SD)*	70.8 (18.3)	72.1 (17.9)	68.2 (19.0)	-3.9 (-5.83 to -1.97), p<0.001	-3.87 (-5.81 to -1.93), p<0.001	-3.78 (-5.73 to -1.84), p<0.001	-3.75 (-5.69 to -1.81), p<0.001
discharge other than home	1092 (22.0%)	504 (16.0%)	530 (31.9%)	2.46 (2.13 to 2.83), p<0.001	2.39 (2.07 to 2.75), p<0.001	2.39 (2.07 to 2.75), p<0.001	2.53 (2.18 to 2.92), p<0.001

95% CI confidence interval; EQ-VAS EuroQol visual analog health scale; IQR interquartile range; OR odds ratio; SD standard deviation;

Quality of life measures were adapted from EQ-5D. We dichotomized levels into "no impairment" (level 1) and "impairment" (levels 2 and 3). Frequencies of reported impairment (level 2 and 3) were analyzed.

adjusted for age (model 1), age and gender (model 2), and age, gender and comorbidities that were not included in the calculation of the frailty risk score (model 3)

* linear regression analyses were calculated reporting regression coefficient, 95% confidence interval, P-value

Table A2 Associations of high frailty risk with adverse clinical outcomes compared to the low frailty risk group.

Outcome	Overall n (%)	Low Risk n (%)	High Risk n (%)	High Risk, OR (95% CI), P-value unadjusted	Model 1	Model 2	Model 3
all-cause 30-day mortality	524 (10.7%)	221 (7.1%)	36 (25.2%)	4.40 (2.94 to 6.57), p<0.001	4.28 (2.86 to 6.41), p<0.001	4.49 (2.99 to 6.73), p<0.001	4.83 (3.17 to 7.37), p<0.001
Length of stay, median (IQR)*	5 (2, 9)	4 (2, 7)	11.5 (7, 18)	10.04 (8.92 to 11.16), p<0.001	10.06 (8.94 to 11.18), p<0.001	10.12 (9.06 to 11.19), p<0.001	10.07 (9.02 to 11.13), p<0.001
Long hospital stay >10 days	1010 (20.4%)	386 (12.3%)	81 (56.2%)	9.21 (6.51 to 13.01), p<0.001	9.28 (6.56 to 13.12), p<0.001	9.42 (6.66 to 13.33), p<0.001	9.75 (6.83 to 13.92), p<0.001
30-day readmission	586 (11.8%)	372 (11.8%)	19 (13.2%)	1.47 (0.95 to 2.26), p=0.081	1.49 (0.97 to 2.29), p=0.070	1.49 (0.97 to 2.30), p=0.069	1.67 (1.08 to 2.59), p=0.022
Functional impairment, n (%)							
Barthel Index, median (IQR)*	95 (70, 100)	100 (85, 100)	50 (20, 75)	-40.55 (-47.01 to -34.09), p<0.001	-40.29 (-46.66 to -33.93), p<0.001	-40.01 (-46.37 to -33.64), p<0.001	-39.70 (-46.06 to -33.33), p<0.001
Barthel Index <95 points	1052 (46.5%)	529 (36.3%)	51 (92.7%)	22.37 (8.04 to 62.23), p<0.001	23.74 (8.48 to 66.44), p<0.001	22.9 (8.19 to 64.06), p<0.001	25.03 (8.91 to 70.32), p<0.001
Quality of Life, n(%)							
Impairment of mobility	408 (18.0%)	162 (11.1%)	29 (51.8%)	8.61 (4.97 to 14.91), p<0.001	8.62 (4.95 to 15.01), p<0.001	8.57 (4.92 to 14.93), p<0.001	8.45 (4.82 to 14.81), p<0.001
Impairment of self-care	1010 (44.5%)	480 (32.9%)	46 (82.1%)	9.40 (4.70 to 18.79), p<0.001	9.67 (4.8 to 19.48), p<0.001	9.39 (4.66 to 18.90), p<0.001	9.59 (4.74 to 19.41), p<0.001
Impairment of usual activities	1366 (60.2%)	767 (52.5%)	46 (82.1%)	4.16 (2.08 to 8.31), p<0.001	4.19 (2.08 to 8.44), p<0.001	3.88 (1.92 to 7.82), p<0.001	3.98 (1.97 to 8.06), p<0.001
Pain/discomfort	910 (42.7%)	574 (40.8%)	22 (48.9%)	1.39 (0.77 to 2.52), p=0.278	1.39 (0.77 to 2.52), p=0.276	1.28 (0.70 to 2.34), p=0.413	1.28 (0.70 to 2.33), p=0.430
Anxiety/depression	629 (30.3%)	394 (28.2%)	22 (56.4%)	3.29 (1.73 to 6.26), p<0.001	3.29 (1.73 to 6.27), p<0.001	3.08 (1.61 to 5.89), p=0.001	3.11 (1.62 to 5.99), p=0.001
EQ-VAS, mean (SD)*	70.8 (18.3)	72.1 (17.9)	61.8 (17.6)	-10.3 (-17.53 to -3.08), p=0.005	-10.3 (-17.53 to -3.07), p=0.005	-10.13 (-17.37 to -2.90), p=0.006	-11.12 (-18.29 to -3.94), p=0.002
discharge other than home	1092 (22.0%)	504 (16.0%)	58 (40.3%)	3.54 (2.50 to 5.01), p<0.001	3.46 (2.44 to 4.90), p<0.001	3.46 (2.44 to 4.90), p<0.001	3.81 (2.68 to 5.42), p<0.001

95% CI confidence interval; EQ-VAS EuroQol visual analog health scale; IQR interquartile range; OR odds ratio; SD standard deviation;

Quality of life measures were adapted from EQ-5D. We dichotomized levels into "no impairment" (level 1) and "impairment" (levels 2 and 3). Frequencies of reported impairment (level 2 and 3) were analyzed.

adjusted for age (model 1), age and gender (model 2), and age, gender and comorbidities that were not included in the calculation of the frailty risk score (model 3)

* linear regression analyses were calculated reporting regression coefficient, 95% confidence interval, P-value

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3-4
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5
Objectives	3	State specific objectives, including any prespecified hypotheses	5-6
Methods			
Study design	4	Present key elements of study design early in the paper	7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	7
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	n/a
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	8-9
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*8-9*
Bias	9	Describe any efforts to address potential sources of bias	8-9
Study size	10	Explain how the study size was arrived at	7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7-8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	9
		(*b*) Describe any methods used to examine subgroups and interactions	9
		(*c*) Explain how missing data were addressed	9
		(*d*) If applicable, explain how loss to follow-up was addressed	n/a
		(*e*) Describe any sensitivity analyses	9
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7
		(b) Give reasons for non-participation at each stage	7
		(c) Consider use of a flow diagram	n/a
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	10-11
		(b) Indicate number of participants with missing data for each variable of interest	n/a
		(c) Summarise follow-up time (eg, average and total amount)	n/a
Outcome data	15*	Report numbers of outcome events or summary measures over time	11-14
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	11-14
		(*b*) Report category boundaries when continuous variables were categorized	11-14
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	14
Discussion			
Key results	18	Summarise key results with reference to study objectives	15-16
Limitations			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	16-17
Generalisability	21	Discuss the generalisability (external validity) of the study results	17
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	19

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Validation of the Hospital Frailty Risk Score in a Tertiary Care Hospital in Switzerland: results of a prospective, observational study

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Validation of the Hospital Frailty Risk Score in a Tertiary Care Hospital in Switzerland: results of a prospective, observational study

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ABSTRACT

Objectives: Recently, the Hospital Frailty Risk Score based on a derivation and validation study in the United Kingdom has been proposed as a low-cost, systematic screening tool to identify older, frail patients who are at greater risk of adverse outcomes and for whom a frailty-attuned approach might be useful. We aimed to validate this Score in an independent cohort in Switzerland.

Design: Secondary analysis of a prospective, observational study (TRIAGE study).

Setting: One 600-bed tertiary care hospital in Aarau, Switzerland

Participants: Consecutive medical inpatients aged 75 years or older that presented to the emergency department or were electively admitted between October 2015 and April 2018.

Primary and secondary outcome measures: The primary endpoint was all-cause 30-day mortality. Secondary endpoints were length of hospital stay, hospital readmission, functional impairment, and quality of life measures. We used multivariate regression analyses.

Results: Of 4957 included patients, 3150 (63.5%) were classified as low risk, 1663 (33.5%) intermediate risk, and 144 (2.9%) high risk for frailty. Compared to the low-risk group, patients in the moderate risk and high-risk groups had increased risk for 30-day mortality (odds ratio [OR] 2.53, 95%CI 2.09 to 3.06, P<0.001 and OR 4.40, 95%CI 2.94 to 6.57, P<0.001) with overall moderate discrimination (area under the ROC curve 0.66). The results remained robust after adjustment for important confounders. Similarly, we found longer length of hospital stay, more severe functional impairment and a lower quality of life in higher risk group patients.

Conclusion: Our data confirms the prognostic value of the Hospital Frailty Risk Score to identify older, frail people at risk for mortality and adverse outcomes in an independent patient population.

Trial registration number: ClinicalTrials.gov; Identifier: NCT01768494

STRENGTHS AND LIMITATIONS OF THE STUDY

Strength and limitations of this study

- This is the first study to validate the Hospital Frailty Risk Score following its publication and initial validation.
- The validation in a Swiss Tertiary care hospital is a first step in assessing the applicability of the risk score in multinational settings.
- In addition to associations with adverse clinical outcomes we assess associations of higher hospital frailty risk scores with functional impairment, quality of life, and need for post-acute care.
- Due to the study design there was no routine frailty assessment in our patients and we were not able to compare the score with other frailty assessments or screening scores.
- As the score is dependent of documentation and coding of ICD-10, variation in coding could contribute to misclassification.

INTRODUCTION

With the increase in the ageing, multimorbidity patient population, the proportion of frail patients is expected to further raise.[1] Frailty describes a state of increased risk for decline in health after an exposure to a stressor event (e.g., hospitalization for an acute illness) increasing the risk for adverse events such as falls, delirium, disability and death.[2-4] Importantly, identifying patients at risk for frailty early during the course of hospitalization may help to improve treatment strategies including a comprehensive geriatric assessment to improve the care and outcomes of patients.[5] Several tools to identify frailty have been developed in the last 20 years.[6] Yet none has emerged as a gold standard. Current instruments show only a moderate power to identify frailty,[7] and some tools require time consuming manual assessment [8 9]. Moreover, in most hospitals there is no routine assessment of older patients and only a subset of patients is screened for frailty[6]. For these reasons, patients who may benefit from a specific frailty-directed treatment approach may be missed in usual hospital care. To improve the care of frail patients, the recently published Hospital Frailty Risk score[10] was developed for early identification of patients with characteristics of frailty, who are at risk of adverse health-care outcomes and who could be identified without any additional assessment apart from routinely collected data. The score relies on the diagnostic codes from the International Statistical Classification of Diseases and Related Health Problems, Tenth Revision (ICD-10), a coding system that is implemented in many administrative hospital databases worldwide. This provides the opportunity to systematically screen older patients in a low-cost manner [10]. In a three-step approach, this score was developed and later validated within three patient populations from the United Kingdom showing high prognostic performance. Still, international validation is needed before more wide-spread use of this score in other health care systems. Herein, we aimed to validate

the Hospital Frailty Risk Score in a Swiss tertiary care hospital. We investigated associations of the score with adverse clinical outcomes such as 30-day mortality, length of hospital stay, and 30-day readmission, as well as functional outcomes including functional impairment, quality of life and discharge location.

METHODS

Study design and study population

This is a secondary analysis of the TRIAGE study, a prospective, observational cohort study initially designed to understand the value of admission biomarkers to predict later adverse outcomes.[11 12] We included consecutive medical patients presenting with a medical urgency at the Kantonsspital in Aarau (Switzerland), a 600-bed tertiary care hospital with most medical admissions entering the hospital over the ED. As an observational quality control study, the Institutional Review Boards (IRB) of the hospital approved the study and waived the need for individual informed consent (main Swiss IRB: Ethikkommission Kanton Aargau (EK 2012/059). The study was registered at the "ClinicalTrials.gov" registration website (http://www.clinicaltrials.gov/ct2/show/NCT01768494) and the study protocol has been published previously.[13]

In accordance with the initial study, we selected medical inpatients aged 75 years or older, that were admitted between October 2015 and April 2018. The cohort includes elective and emergency admissions. In case of multiple admissions of the same patient, only the first admission was used for the analysis.

Patient and Public Involvement

Patients were not involved in the development of the research question or the design of the study.

Follow-up and initial data collection

We used ICD-10 diagnostic codes of the incident admission assigned to patients after discharge by professional hospital coders according to the information of medical records. The electronic records contained up to 38 diagnosis fields coded

according to ICD-10. Regarding follow-up, 30 days after hospital admission patients were contacted by telephone for a structured interview to obtain information on vital status, clinical outcomes, location of living and functional measurements. Functional status was obtained using the EQ-5D-3L standardized measure of health, which was administered as recommended [14]. We assessed mobility, self-care, usual activities, pain or discomfort, and anxiety and depression, using dichotomized data with levels 2 and 3 indicating "impairment" and level 1 indicating "no impairment". Moreover, we used the EQ-VAS, recording the self-rated health on a visual analogue scale with values between 0 and 100 with higher points indicating better health states.

We used the Barthel Index to measure activities of daily living (ADL)[15], with a cutoff <95 points indicating functional impairment. We assessed readmission to any facility, location after discharge and identified patients who were living at home before hospital admission and were discharged to a location other than home.

All information was stored in a centralized, password-secured database (SecuTrial®; interActive Systems GmbH, Berlin, Germany).

Calculation of the Hospital Frailty Risk Score

For each patient the Hospital Frailty Risk Score was calculated retrospectively using all available ICD-10 diagnostic codes that were documented for the particular admission as recommended [10]. The score is an aggregate of 109 ICD-10 diagnostic codes that were found to be associated with frailty risk. Each of these ICD-10 diagnostic codes were awarded with specific values proportional to how strongly they predicted frailty. According to the aggregate score, patients were divided into the three frailty risk categories low risk (<5 points), intermediate risk (5-15 points), and high risk (> 15 points) as recommended [10].

Research aims and statistical approach

We investigated associations of the Hospital Frailty Risk with adverse clinical outcomes. Our primary endpoint is all-cause 30-day mortality. Secondary endpoints include hospital length of stay, long hospital stay (>10 days), and hospital readmission within 30 days. Moreover, we examined associations with functional impairment using the Barthel-Index (<95 points indicating impairment), Quality of Life measurements using the EQ-5D standardized measure, and discharge location other than home, for patients that were living at home before admission.

Statistical analysis

We expressed patient characteristics using descriptive statistics including mean with standard deviation (SD), median with interquartile range (IQR), and frequencies, as appropriate. Frequency comparison was done using the χ^2 test.

To investigate associations of the Hospital Frailty Risk Score with outcomes we used univariate and multivariate regression analyses. Models were adjusted for age (model 1), age and gender (model 2), and age, gender and comorbidities that were not included in the calculation of the frailty risk score (model 3). We performed another analysis adjusting for the structured early warning score NEWS (national early warning score) to comprise physiological parameters that might be an important modifier of outcomes. NEWS was calculated retrospectively as recommended [16] based on admission data. We provide odds ratios (ORs) or regression coefficients (RCs) with 95% confidence intervals (95% CIs) as appropriate. We used receiver operating statistics reporting area under the curve (AUC) as a measure of discrimination. We considered AUCs of 0.6 to 0.7 as moderate, 0.7 to 0.8 as fair, 0.8 to 0.9 as good, and >0.9 as excellent. Also, for graphical illustration we generated Kaplan-Meier survival estimates stratified by frailty risk groups.

We repeated analyses in predefined subgroups stratified by age and gender.

All tests were two-tailed and carried out at 5% significance levels. Analyses were performed with STATA 12.1 (Stata Corp., College Station, TX, USA).

RESULTS

Patient Population

A total of 4957 Patients with a median age of 82 years were included in this analysis. At time of admission the majority of patients (63.4%) resided at home. A total of 63.5% (3150) of patients were in the low frailty risk group, 33.5% (1663) in the intermediate risk group, and 2.9% (144) were in the high-risk group. Minimum score was 0 points, maximum score 30.3 points, quartiles were 1.4, 3.4, and 6.7 points, mean 4.5 points (SD 4.3). Baseline characteristics of the general population and stratified by Hospital Frailty Risk categories are listed in **Table 1**.

Table1 Baseline characteristics of the total cohort and stratified by frailty risk group

Characteristics	Total cohort	Frailty risk (points)			p-value
		Low risk (<5)	Intermediate risk (5-15)	High risk (>15)	
N (%)	4957	3150 (63.5%)	1663 (33.5%)	144 (2.9%)	
Male gender, n (%)	2426 (49.0%)	1634 (52.0%)	733 (44.2%)	59 (41.0%)	<0.001
Age (years), median (IQR)	82 (78, 86)	82 (78, 85)	83 (79, 87)	83 (79, 87)	<0.001
Vital signs, median (IQR)					
Blood pressure systolic (mmHg)	148 (129, 168)	149 (131, 168)	147 (125, 166)	151 (132, 176.5)	0.007
Blood pressure diastolc (mmHg)	80 (68, 93)	80 (69, 93)	80 (68, 92)	80 (69, 97)	0.25
Pulse rate (bpm)	81.5 (70, 95.2)	80.5 (69, 94.8)	82 (70.9, 96)	85 (73, 101)	0.009
Oxygen saturation (%)	95.8 (92.8, 98)	96 (93.5, 98)	95.4 (92.1, 97.6)	95.05 (92, 97.4)	<0.001
Temperature (°C)	36.8 (36.4, 37.3)	36.8 (36.4, 37.3)	36.8 (36.4, 37.4)	36.6 (36.4, 37.1)	0.007
Comorbidities, n (%)					
Diabetes	698 (14.1%)	486 (15.4%)	205 (12.3%)	7 (4.9%)	<0.001
Malignant disease	494 (10.0%)	354 (11.2%)	131 (7.9%)	9 (6.2%)	<0.001
Chronic heart failure	699 (14.1%)	436 (13.8%)	249 (15.0%)	14 (9.7%)	0.17
COPD	257 (5.2%)	178 (5.7%)	75 (4.5%)	4 (2.8%)	0.099
Dementia	338 (6.8%)	104 (3.3%)	218 (13.1%)	16 (11.1%)	<0.001
Chronic renal disease	1282 (25.9%)	715 (22.7%)	540 (32.5%)	27 (18.8%)	<0.001
Hypertension	2608 (52.6%)	1726 (54.8%)	826 (49.7%)	56 (38.9%)	<0.001
Coronary heart disease	531 (10.7%)	424 (13.5%)	100 (6.0%)	7 (4.9%)	<0.001
Stroke	668 (13.5%)	193 (6.1%)	396 (23.8%)	79 (54.9%)	<0.001
Location prior to admission, n (%)					

Home	3144 (63.4%)	2194 (69.7%)	895 (53.8%)	55 (38.2%)	<0.001
Home with assistance service	264 (5.3%)	107 (3.4%)	142 (8.5%)	15 (10.4%)	
Nursing home	370 (7.5%)	161 (5.1%)	190 (11.4%)	19 (13.2%)	
Other hospital	457 (9.2%)	275 (8.7%)	161 (9.7%)	21 (14.6%)	
Unknown or other	722 (14.6%)	413 (13.1%)	275 (16.5%)	34 (23.6%)	

COPD chronic obstructive pulmonary disease; IQR interquartile range

Associations of frailty risk score with mortality

A total of 524 (10.7%) patients died within 30 days of admission, consisting of 221 (7.1%) of those in the low risk group, 267 (16.2%) in the intermediate risk group and 36 (25.2%) in the high-risk group. Regression analyses showed corresponding ORs of 2.53 (95% CI 2.09 to 3.06, P<0.001) for the intermediate risk group and 4.40 (95% CI 2.94 to 6.57, P<0.001) for the high-risk group, respectively, compared to the low risk group. Results remained robust after adjustment for confounders (age, gender, and comorbidities not included in the score) (**Table 2, Figure 1**).

We also investigated the discriminative performance of the score and found only moderate results for mortality (AUC 0.66) (**Table 3**).

Table 2 Associations of elevated frailty risk groups with adverse clinical outcomes compared to the low frailty risk group

Outcome	Overall n (%)	Low Risk n (%)	Intermediate Risk, n (%)	High Risk n (%)	P value	Intermediate Risk, OR (95% CI), P-value unadjusted	Intermediate Risk, OR (95% CI), P-value fully adjusted	High Risk, OR (95% CI), P-value unadjusted	High Risk, OR (95% CI), P-value fully adjusted
all-cause 30-day mortality	524 (10.7%)	221 (7.1%)	267 (16.2%)	36 (25.2%)	<0.001	2.53 (2.09 to 3.06), p<0.001	2.65 (2.17 to 3.25), p<0.001	4.4 (2.94 to 6.57), p<0.001	4.83 (3.17 to 7.37), p<0.001
Length of stay, median (IQR)*	5 (2, 9)	4 (2, 7)	7 (4, 12)	11.5 (7, 18)	<0.001	3.74 (3.34 to 4.14), p<0.001	3.77 (3.39 to 4.15), p<0.001	10.04 (8.92 to 11.16), p<0.001	10.07 (9.02 to 11.13), p<0.001
Long hospital stay >10 days	1010 (20.4%)	386 (12.3%)	543 (32.7%)	81 (56.2%)	<0.001	3.47 (2.99 to 4.02), p<0.001	3.66 (3.14 to 4.28), p<0.001	9.21 (6.51 to 13.01), p<0.001	9.75 (6.83 to 13.92), p<0.001
30-day readmission	586 (11.8%)	372 (11.8%)	195 (11.7%)	19 (13.2%)	0.87	1.04 (0.88 to 1.24), p=0.643	1.04 (0.87 to 1.24), p=0.69	1.47 (0.95 to 2.26), p=0.081	1.67 (1.08 to 2.59), p=0.022
Functional impairment, n (%)									
Barthel Index, median (IQR)*	95 (70, 100)	100 (85, 100)	80 (55, 100)	50 (20, 75)	<0.001	-15.76 (-17.87 to -13.64), p<0.001	-14.59 (-16.69 to -12.48), p<0.001	-40.55 (-47.01 to -34.09), p<0.001	-39.7 (-46.06 to -33.33), p<0.001
Barthel Index <95 points	1052 (46.5%)	529 (36.3%)	472 (62.9%)	51 (92.7%)	<0.001	2.98 (2.48 to 3.58), p<0.001	2.87 (2.37 to 3.47), p<0.001	22.37 (8.04 to 62.23), p<0.001	25.03 (8.91 to 70.32), p<0.001
Quality of Life, n(%)									
Impairment of mobility	408 (18.0%)	162 (11.1%)	217 (28.9%)	29 (51.8%)	<0.001	3.25 (2.59 to 4.08), p<0.001	3.1 (2.46 to 3.92), p<0.001	8.61 (4.97 to 14.91), p<0.001	8.45 (4.82 to 14.81), p<0.001
Impairment of self-care	1010 (44.5%)	480 (32.9%)	484 (64.4%)	46 (82.1%)	<0.001	3.69 (3.07 to 4.44), p<0.001	3.63 (2.99 to 4.4), p<0.001	9.40 (4.7 to 18.79), p<0.001	9.59 (4.74 to 19.41), p<0.001
Impairment of usual activities	1366 (60.2%)	767 (52.5%)	553 (73.5%)	46 (82.1%)	<0.001	2.51 (2.08 to 3.05), p<0.001	2.35 (1.92 to 2.87), p<0.001	4.16 (2.08 to 8.31), p<0.001	3.98 (1.97 to 8.06), p<0.001
Pain/discomfort	910 (42.7%)	574 (40.8%)	314 (46.3%)	22 (48.9%)	0.039	1.25 (1.04 to 1.51), p=0.017	1.21 (1 to 1.47), p=0.047	1.39 (0.77 to 2.52), p=0.278	1.28 (0.7 to 2.33), p=0.43
Anxiety/depression	629 (30.3%)	394 (28.2%)	213 (33.2%)	22 (56.4%)	<0.001	1.26 (1.03 to 1.55), p=0.023	1.26 (1.02 to 1.55), p=0.029	3.29 (1.73 to 6.26), p<0.001	3.11 (1.62 to 5.99), p=0.001
EQ-VAS, mean (SD)*	70.8 (18.3)	72.1 (17.9)	68.2 (19.0)	61.8 (17.6)	<0.001	-3.9 (-5.83 to -1.97), p<0.001	-3.75 (-5.69 to -1.81), p<0.001	-10.3 (-17.53 to -3.08), p=0.005	-11.12 (-18.29 to -3.94), p=0.002
discharge other than home	1092 (22.0%)	504 (16.0%)	530 (31.9%)	58 (40.3%)	<0.001	2.46 (2.13 to 2.83), p<0.001	2.53 (2.18 to 2.92), p<0.001	3.54 (2.5 to 5.01), p<0.001	3.81 (2.68 to 5.42), p<0.001

95% CI confidence interval; EQ-VAS EuroQol visual analog health scale; IQR interquartile range; OR odds ratio; SD standard deviation;

Quality of life measures were adapted from EQ-5D. We dichotomized levels into "no impairment" (level 1) and "impairment" (levels 2 and 3). Frequencies of reported impairment (level 2 and 3) were analyzed.

The fully adjusted model was adjusted for age, gender, and comorbidities not included in the score

* linear regression analyses were calculated reporting regression coefficient, 95% confidence interval, P-value

Table 3 Discriminative Performance of the Hospital frailty Risk Score regarding clinical and functional outcomes

Outcome	AUC (95% CI)
Clinical outcomes	
all-cause 30-day mortality	0.66 (0.63 to 0.68)
Long hospital stay (>10 days)	0.72 (0.7 to 0.74)
30-day readmission	0.54 (0.51 to 0.56)
Functional impairment	
Barthel Index <95 points, n (%)	0.69 (0.67 to 0.71)
Quality of Life, n (%)	
Impairment of mobility	0.71 (0.68 to 0.74)
Impairment of self-care	0.71 (0.69 to 0.73)
Impairment of usual activities	0.66 (0.63 to 0.68)
Pain/discomfort	0.54 (0.51 to 0.56)
Anxiety/depression	0.56 (0.53 to 0.58)
discharge other than home, n (%)	0.64 (0.63 to 0.66)

AUC area under the receiver operating curve; 95% CI 95% confidence interval

Quality of life measures were adapted from EQ-5D. We dichotomized levels into "no impairment" (level 1) and "impairment" (levels 2 and 3). Frequencies of reported impairment (level 2 and 3) were analyzed.

Associations of frailty risk score with other adverse clinical outcomes

We also found significant results regarding length of hospital stay and long hospital stay (>10 days). Compared to the low risk group corresponding ORs for long hospital stay were 3.47 (95% CI 2.99 to 4.02, P<0.001) for the intermediate risk group and 9.21 (95% CI 6.51 to 13.01, P<0.001) for the high-risk group. Again, results remained robust after adjustment for the confounders mentioned.

Regarding hospital readmission within 30 days we did only find a significant association for the high-risk group compared to the low-risk group in the fully adjusted model (fully adjusted OR 1.67, 95% CI 1.08 to 2.59, P=0.022) (**Table 2**).

Associations with functional Impairment, quality of life, and location after discharge

Regarding functional status, we found significantly higher proportions of impairment (Barthel Index < 95 points) in higher frailty risk groups with corresponding ORs of 2.98 (95% CI 2.48 to 3.58, P<0.001) and 22.37 (95% CI 8.04 to 62.23, P<0.001). Similar results were found for quality of life measures 30 days after admission with corresponding ORs for the high-risk group of 8.61 (95% CI 4.97 to 14.91, P<0.001) for impairment of mobility, 9.40 (95% CI 4.7 to 18.79, P<0.001) for impaired self-care, 4.16 (95% CI 2.08 to 8.31, P<0.001) for impairment of usual activities, and 3.29 (95% CI 1.73 to 6.26, P<0.001) for suffering from anxiety or depression.

Compared to patients in the low risk group, patients in the high-risk group that resided home at time of admission had a 3.5 fold increased risk of not being able to be discharged back home (OR 3.54 (95% CI 2.5 to 5.01, P<0.001) (**Table 2**).

Additional results of regression analyses of all models with stepwise adjustment for confounders are shown in the supplemental material (**Tables A1 & A2**).

Subgroup analyses and cut-offs

Analyses of subgroups showed similar associations of the Hospital Frailty Risk Score with 30-day mortality, long hospital stay, and hospital readmission among different age groups and stratified by gender with no evidence for effect modification (**Figure 2**).

ROC analyses of modified cut-offs of the risk score did not show significant differences in AUCs for the outcome 30-day mortality compared to the initial cut-offs (Supplementary material, **Table A3**).

DISCUSSION

Within this independent validation study including medical inpatients >75 years of age in a Swiss tertiary care setting, we found significant associations between the hospital frailty risk scores and several adverse clinical outcomes, specifically all-cause 30-day mortality, hospital length of stay, and long hospital stay (>10 days). Moreover, we found significant associations of the intermediate and high-risk group with functional impairment, measured by the Barthel Index, and reduced quality of life, as assessed by the EQ-5D. Last, we found patients of the higher risk group that were admitted from home significantly less likely to return back home at time of discharge.

Compared to the three cohorts of the original publication (one development cohort and two validation cohorts) by Gilbert et al.[10] a similar proportion of patients were classified in the intermediate-risk group (33.5% vs. 20.3 to 37.6%) but a smaller proportion of patients were classified in the high-risk group (2.9% vs. 9.0 to 20.0%). This might be due to variation in ICD-10 coding and different health care systems and patient populations studied. Regarding the tertiary nature of the setting, it can be expected that some older people with severe frailty might have been managed in other secondary care settings or geriatric clinics. However, compared to the results of Gilbert et al., we found even stronger associations of the high frailty risk group compared to the low-risk group with regard to 30-day mortality (adjusted OR 4.83, 95% CI 3.17 to 7.37, p<0.001 vs. adjusted OR 1.71, 95% CI 1.68 to 1.75), and long hospital stay (adjusted OR 9.75, 95% CI 6.83 to 13.92, p<0.001 vs. adjusted OR 6.03, 95% CI 5.92 to 6.10). Besides, results remained robust when adjusting for NEWS, a structured early warning score that comprises physiological parameters that might be an important modifier of outcomes.

Regarding the discriminative performance of the Hospital frailty risk score we found similar results as Gilbert et al. with regard to 30-day mortality (AUC 0.66 vs. 0.60), long hospital stay (AUC 0.72 vs. 0.68), and hospital readmission within 30 days (AUC 0.54 vs. 0.56). Overall, these results show significant associations of the Hospital frailty risk score with adverse outcomes, however, with moderate discriminatory ability. Thus, future studies should aim to further refine the score to increase its sensitivity and specificity.

While we found the score to be helpful with strong prognostic abilities, in our cohort there were only few patients in the highest risk category with thus limited sensitivity. It is thus possible that the score could be further improved by changing the risk categories for specific patient populations.

To the best of our knowledge, this is the first study to validate the Hospital Frailty Risk Score following its publication and initial validation. Moreover, the validation in a Swiss tertiary care hospital in an unselected medical cohort including emergency admissions and elective admissions is a first step in assessing whether the risk score is applicable in multinational settings.

In addition to Gilbert et al. we were able to show associations of higher hospital frailty risk scores not only with adverse clinical outcomes but also with functional impairment, quality of life, and need for post-acute care. Our data thus extend the prior study and provides new evidence that the score is valuable in risk stratification of patients based on ICD10 codes.

A general strength of the score is the easy calculation using routine hospital data which provides a systematic method to screen for patients at risk for frailty without any need to apply a manual score bringing along resource intensive assessment and potential inter-operator reliability issues [8 9 17]. Moreover, instead of focusing only on

symptoms and diagnoses that are known to be related to frailty, the score contains a wider set of ICD-10 codes focusing on codes that are actually in routine use. However, dependency of the ICD-10 codes from administrative databases is also a weakness of the score as they are coded only after hospital discharge and the score can only be applied early in the admission process to those with prior ICD-10 code records. In addition to that calculating the score based on previous admissions has potential to miss or misclassify frailty. Moreover, important components of frailty such as polypharmacy, general weakness and dependence with activities of daily living might not be adequately reflected in ICD-10 codes. Their absence may in part explain the relatively poor overlap of the score with the established frailty assessment tools Fried [18] and Rockwood scales [9] in the original study by Gilbert et al [10]. This raises the question of whether the "hospital frailty risk score" is in fact measuring frailty, or whether it is predominantly a measure of comorbid disease and adverse outcome.

Our report has several limitations. Firstly, this is a secondary analysis of a former prospective study. We did address this limitation by adjusting for confounders. Furthermore, as we were able to externally validate the previous findings accurately, we are confident that there is no additional bias. Second, due to the study design there was no routine frailty assessment in our patients. As a consequence, we were not able to compare the Hospital Frailty Risk score with other frailty assessments or screening scores. Yet, there is no unique accepted gold standard in frailty screening to compare it to as there are two major paradigms of frailty (frailty phenotype vs. frailty index) [2 17 19 20]. Using multiple clinical and functional outcomes as well as quality of life measures, we tried to address a broad variety of potential adverse outcomes associated with frailty.

Thirdly, though we had a large sample size, only few patients were in the high frailty risk group, which may impact confidence intervals. Lastly, the score is dependent of documentation and coding of ICD-10. Thus, variation in coding could contribute to misclassification.

The development of a gold standard for frailty risk assessment has proven to be a challenging task [17 19]. The attempt has left us with a multitude of screening tools, suited for a variety of patient populations and a large variability of application methods [6]. Recent research suggests that a single universal frailty measurement method may not be the best approach. As some methods are useful for broad population screenings whilst others are based on clinical assessment, a two-tiered system may be the way forward [20]. The Hospital Frailty Risk Score could be used as a screening tool to assess all older patients admitted to a hospital using all previously and currently documented ICD-10 codes. This could easily identify high-risk patients in need of a complete in-depth clinical assessment. As a low-cost, swift and consecutively widely used tool, the Hospital Frailty Risk Score could ensure that less patients with frailty are missed. Identifying frail patients is vital, as they may benefit from improved outcomes when they undergo geriatric assessment and receive a particular frailty-adjusted treatment approach [21].

The frailty risk score needs further validation in a wide variety of patient settings. Its place in the screening of geriatric patients, possibly in combination with other frailty assessment methods, as well as the practicability in clinical practice, has yet to be investigated. Furthermore, it remains unclear whether its theoretical benefits can be translated into improved patient care and patient outcome.

CONCLUSION

The Hospital Frailty Risk Score is an easy to use and low-cost tool using administrative hospital data to identify frail people at risk for adverse outcomes who might benefit from a standardized geriatric assessment and from a particular frailty-adjusted treatment approach. Our data further validate this score in an independent patient population.

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Author contributions

Prof. Philipp Schuetz had complete access to all study data and takes full responsibility for the integrity of the data and the accuracy of the analyses. BM and PS were involved in the conceptualization and design of the study. SH, AK, DK, BM and PS were responsible for the acquisition, analysis, or interpretation of the data. AE, SIH, and PS performed the statistical analyses and drafted the manuscript. TS, MAM, and ON reviewed the draft and revised the manuscript for important intellectual content. All authors approved the final version of the manuscript and the decision to submit the manuscript for publication. AE and SIH contributed equally to this work.

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Competing interests

All authors have no conflicts of interest relevant to this paper. The funding organization had no role in the design or conduct of the study, analysis and interpretation of the data, writing of the manuscript, or the decision to submit the manuscript for publication.

Data sharing statement:

Extra data can be accessed via the Dryad data repository at http://datadryad.org/ with the doi:10.5061/dryad.71638rk

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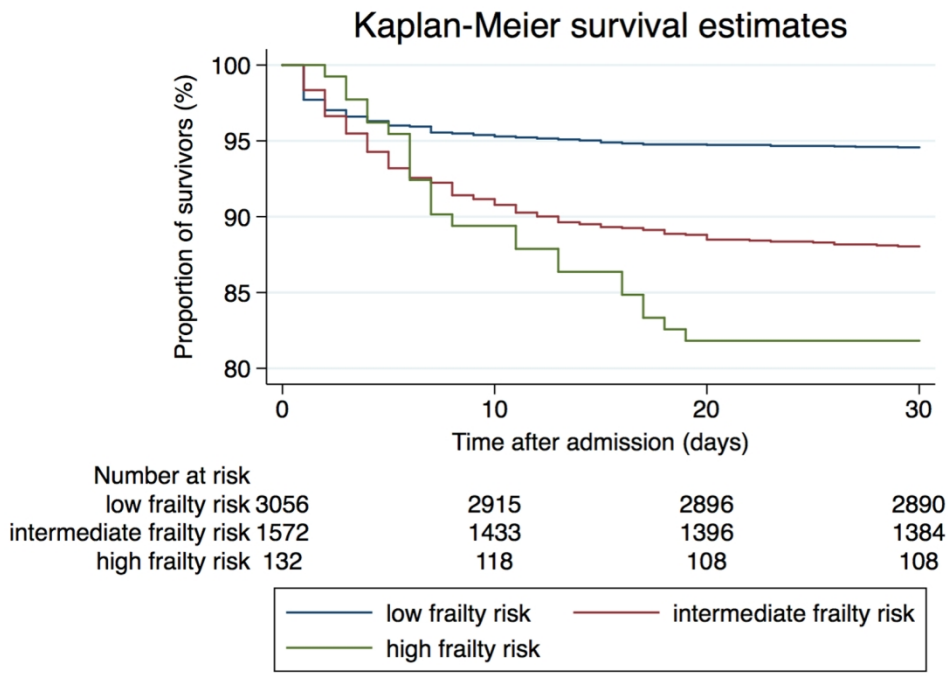
FIGURES

Figure 1 Kaplan Meier survival estimates stratified by the three Hospital Frailty Risk Score groups

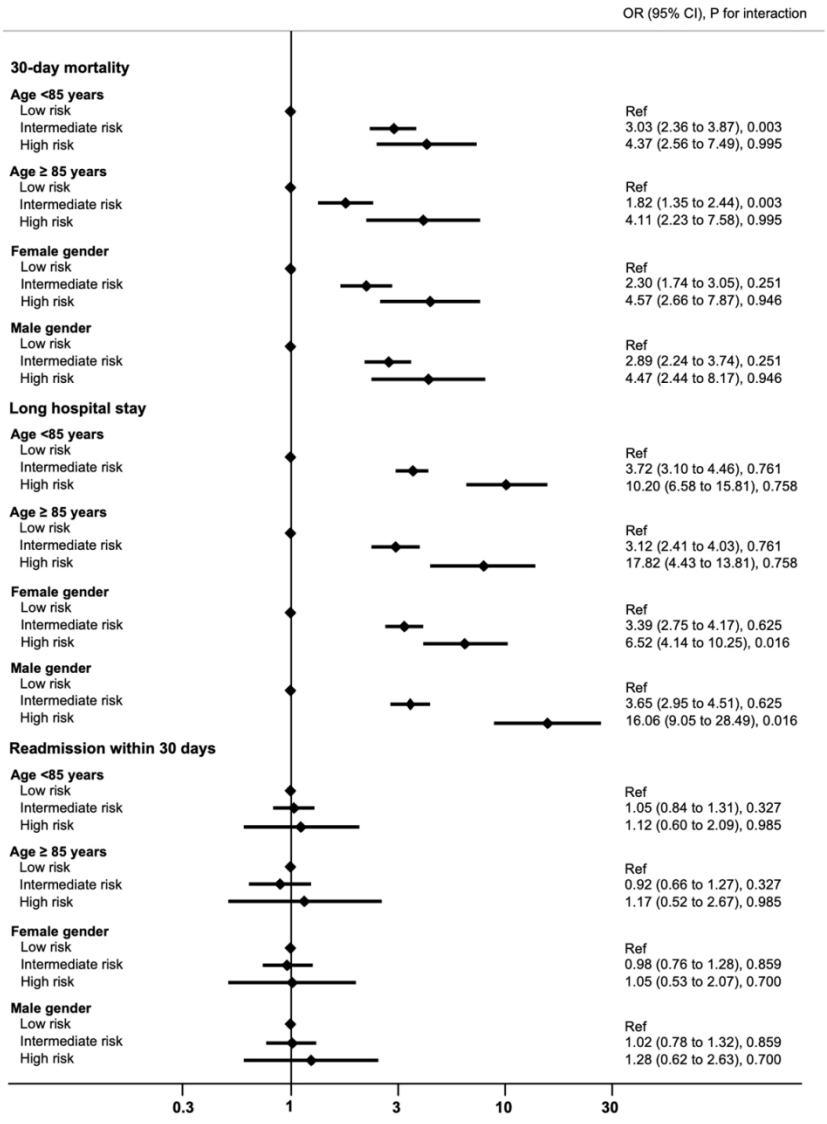
Figure 2 Associations of elevated hospital frailty risk with adverse clinical outcomes in subgroups stratified by age and gender

Legend: OR odds ratio, 95% CI 95% confidence interval



Kaplan Meier survival estimates stratified by the three Hospital Frailty Risk Score groups

150x109mm (300 x 300 DPI)



Associations of elevated hospital frailty risk with adverse clinical outcomes in subgroups stratified by age and gender

Legend: OR odds ratio, 95% CI 95% confidence interval

Table A1 Associations of intermediate frailty risk with adverse clinical outcomes compared to the low frailty risk group.

	Intermediate Risk, OR (95% CI), P-value				
Outcome	**unadjusted**	**Model 1**	**Model 2**	**Model 3**	**NEWS-adjusted**
all-cause 30-day mortality	2.53 (2.09 to 3.06), p<0.001	2.45 (2.03 to 2.97), p<0.001	2.52 (2.08 to 3.06), p<0.001	2.65 (2.17 to 3.25), p<0.001	2.05 (1.69 to 2.50), p<0.001
Length of stay, median (IQR)*	3.74 (3.34 to 4.14), p<0.001	3.76 (3.36 to 4.16), p<0.001	3.83 (3.45 to 4.21), p<0.001	3.77 (3.39 to 4.15), p<0.001	3.69 (3.28 to 4.09), p<0.001
Long hospital stay >10 days	3.47 (2.99 to 4.02), p<0.001	3.50 (3.02 to 4.06), p<0.001	3.55 (3.06 to 4.12), p<0.001	3.66 (3.14 to 4.28), p<0.001	3.44 (2.96 to 3.99), p<0.001
30-day readmission	1.04 (0.88 to 1.24), p=0.643	1.06 (0.89 to 1.26), p=0.521	1.06 (0.89 to 1.26), p=0.503	1.04 (0.87 to 1.24), p=0.69	0.99 (0.83 to 1.18), p=0.883
Functional impairment, n (%)					
Barthel Index, median (IQR)*	-15.76 (-17.87 to -13.64), p<0.001	-15.01 (-17.1 to -12.92), p<0.001	-14.87 (-16.97 to -12.78), p<0.0010	-14.59 (-16.69 to -12.48), p<0.001	-15.45 (-17.59 to -13.31), p<0.001
Barthel Index <95 points	2.98 (2.48 to 3.58), p<0.001	2.89 (2.4 to 3.47), p<0.001	2.85 (2.36 to 3.43), p<0.001	2.87 (2.37 to 3.47), p<0.001	2.87 (2.38 to 3.45), p<0.001
Quality of Life, n(%)					
Impairment of mobility	3.25 (2.59 to 4.08), p<0.001	3.14 (2.50 to 3.95), p<0.001	3.13 (2.49 to 3.94), p<0.001	3.1 (2.46 to 3.92), p<0.001	3.17 (2.52 to 3.99), p<0.001
Impairment of self-care	3.69 (3.07 to 4.44), p<0.001	3.60 (2.99 to 4.35), p<0.001	3.56 (2.95 to 4.30), p<0.001	3.63 (2.99 to 4.4), p<0.001	3.55 (2.95 to 4.28), p<0.001
Impairment of usual activities	2.51 (2.08 to 3.05), p<0.001	2.41 (1.99 to 2.93), p<0.001	2.35 (1.93 to 2.87), p<0.001	2.35 (1.92 to 2.87), p<0.001	2.45 (2.02 to 2.98), p<0.001
Pain/discomfort	1.25 (1.04 to 1.51), p=0.017	1.26 (1.04 to 1.51), p=0.015	1.22 (1.01 to 1.47), p=0.036	1.21 (1 to 1.47), p=0.047	1.29 (1.07 to 1.55), p=0.008
Anxiety/depression	1.26 (1.03 to 1.55), p=0.023	1.28 (1.04 to 1.56), p=0.018	1.25 (1.02 to 1.53), p=0.032	1.26 (1.02 to 1.55), p=0.029	1.22 (1.00 to 1.50), p=0.053
EQ-VAS, mean (SD)*	-3.9 (-5.83 to -1.97), p<0.001	-3.87 (-5.81 to -1.93), p<0.001	-3.78 (-5.73 to -1.84), p<0.001	-3.75 (-5.69 to -1.81), p<0.001	-3.57 (-5.52 to -1.61), p<0.001
discharge other than home	2.46 (2.13 to 2.83), p<0.001	2.39 (2.07 to 2.75), p<0.001	2.39 (2.07 to 2.75), p<0.001	2.53 (2.18 to 2.92), p<0.001	2.15 (1.86 to 2.48), p<0.001

95% CI confidence interval; EQ-VAS EuroQol visual analog health scale; IQR interquartile range; NEWS national early warning score; OR odds ratio; SD standard deviation;
Quality of life measures were adapted from EQ-5D. We dichotomized levels into "no impairment" (level 1) and "impairment" (levels 2 and 3). Frequencies of reported impairment (level 2 and 3) were analyzed.
Models were adjusted for age (model 1), age and gender (model 2), age, gender, and comorbidities not included in the score (model 3), and for NEWS which was calculated retrospectively based on admission data.
* linear regression analyses were calculated reporting regression coefficient, 95% confidence interval, P-value

Table A2 Associations of high frailty risk with adverse clinical outcomes compared to the low frailty risk group.

	High Risk, OR (95% CI), P-value				
Outcome	**unadjusted**	**Model 1**	**Model 2**	**Model 3**	**NEWS adjusted**
all-cause 30-day mortality	4.40 (2.94 to 6.57), p<0.001	4.28 (2.86 to 6.41), p<0.001	4.49 (2.99 to 6.73), p<0.001	4.83 (3.17 to 7.37), p<0.001	3.68 (2.41 to 5.60), p<0.001
Length of stay, median (IQR)*	10.04 (8.92 to 11.16), p<0.001	10.06 (8.94 to 11.18), p<0.001	10.12 (9.06 to 11.19), p<0.001	10.07 (9.01 to 11.13), p<0.001	9.98 (8.86 to 11.10), p<0.001
Long hospital stay >10 days	9.21 (6.51 to 13.01), p<0.001	9.28 (6.56 to 13.12), p<0.001	9.42 (6.66 to 13.33), p<0.001	9.75 (6.83 to 13.92), p<0.001	9.10 (6.43 to 12.88), p<0.001
30-day readmission	1.47 (0.95 to 2.26), p=0.081	1.49 (0.97 to 2.29), p=0.070	1.49 (0.97 to 2.30), p=0.069	1.67 (1.08 to 2.59), p=0.022	1.38 (0.90 to 2.13), p=0.141
Functional impairment, n (%)					
Barthel Index, median (IQR)*	-40.55 (-47.01 to -34.09), p<0.001	-40.29 (-46.66 to -33.93), p<0.001	-40.01 (-46.37 to -33.64), p<0.001	-39.70 (-46.06 to -33.33), p<0.001	-40.06 (-46.54 to -33.58), p<0.001
Barthel Index <95 points	22.37 (8.04 to 62.23), p<0.001	23.74 (8.48 to 66.44), p<0.001	22.9 (8.19 to 64.06), p<0.001	25.03 (8.91 to 70.32), p<0.001	21.12 (7.58 to 58.83), p<0.001
Quality of Life, n(%)					
Impairment of mobility	8.61 (4.97 to 14.91), p<0.001	8.62 (4.95 to 15.01), p<0.001	8.57 (4.92 to 14.93), p<0.001	8.45 (4.82 to 14.81), p<0.001	8.29 (4.77 to 14.40), p<0.001
Impairment of self-care	9.40 (4.70 to 18.79), p<0.001	9.67 (4.8 to 19.48), p<0.001	9.39 (4.66 to 18.90), p<0.001	9.59 (4.74 to 19.41), p<0.001	8.85 (4.42 to 17.73), p<0.001
Impairment of usual activities	4.16 (2.08 to 8.31), p<0.001	4.19 (2.08 to 8.44), p<0.001	3.88 (1.92 to 7.82), p<0.001	3.98 (1.97 to 8.06), p<0.001	4.00 (2.00 to 8.00), p<0.001
Pain/discomfort	1.39 (0.77 to 2.52), p=0.278	1.39 (0.77 to 2.52), p=0.276	1.28 (0.70 to 2.34), p=0.413	1.28 (0.70 to 2.33), p=0.430	1.45 (0.80 to 2.63), p=0.225
Anxiety/depression	3.29 (1.73 to 6.26), p<0.001	3.29 (1.73 to 6.27), p<0.001	3.08 (1.61 to 5.89), p=0.001	3.11 (1.62 to 5.99), p=0.001	3.11 (1.63 to 5.95), p=0.001
EQ-VAS, mean (SD)*	-10.3 (-17.53 to -3.08), p=0.005	-10.3 (-17.53 to -3.07), p=0.005	-10.13 (-17.37 to -2.90), p=0.006	-11.12 (-18.29 to -3.94), p=0.002	-9.77 (-17.01 to -2.54), p=0.008
discharge other than home	3.54 (2.50 to 5.01), p<0.001	3.46 (2.44 to 4.90), p<0.001	3.46 (2.44 to 4.90), p<0.001	3.81 (2.68 to 5.42), p<0.001	3.09 (2.17 to 4.41), p<0.001

95% CI confidence interval; EQ-VAS EuroQol visual analog health scale; IQR interquartile range; NEWS national early warning score; OR odds ratio; SD standard deviation;
Quality of life measures were adapted from EQ-5D. We dichotomized levels into "no impairment" (level 1) and "impairment" (levels 2 and 3). Frequencies of reported impairment (level 2 and 3) were analyzed.
Models were adjusted for age (model 1), age and gender (model 2), age, gender, and comorbidities not included in the score (model 3), and for NEWS which was calculated retrospectively based on admission data.
* linear regression analyses were calculated reporting regression coefficient, 95% confidence interval, P-value

Table A3 ROC analyses of different frailty score cut-offs for the outcome 30-day mortality

low risk		intermediate risk		high risk		AUC (95% CI)
Cut-off	No of patients	Cut-off	No of patients	Cut-off	No of patients	
	63.55 %	5-15	33.55 %	>15	2.9 %	0.624 (0.601 to 0.647)
<5	63.55 %	5-10	24.69 %	>10	11.76 %	0.629 (0.605 to 0.652)
<4	55.09 %	4-10	33.15 %	>10	11.76 %	0.636 (0.613 to 0.660)
<4	55.09 %	4-9	30.18 %	>9	14.73 %	0.637 (0.613 to 0.660)

AUC, area under the receiver operating curve; 95% CI, 95% confidence interval

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3-4
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5
Objectives	3	State specific objectives, including any prespecified hypotheses	5-6
Methods			
Study design	4	Present key elements of study design early in the paper	7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	7
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	n/a
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	8-9
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*8-9*
Bias	9	Describe any efforts to address potential sources of bias	8-9
Study size	10	Explain how the study size was arrived at	7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7-8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	9
		(*b*) Describe any methods used to examine subgroups and interactions	9
		(*c*) Explain how missing data were addressed	9
		(*d*) If applicable, explain how loss to follow-up was addressed	n/a
		(*e*) Describe any sensitivity analyses	9
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7
		(b) Give reasons for non-participation at each stage	7
		(c) Consider use of a flow diagram	n/a
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	10-11
		(b) Indicate number of participants with missing data for each variable of interest	n/a
		(c) Summarise follow-up time (eg, average and total amount)	n/a
Outcome data	15*	Report numbers of outcome events or summary measures over time	11-14
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	11-14
		(*b*) Report category boundaries when continuous variables were categorized	11-14
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	14
Discussion			
Key results	18	Summarise key results with reference to study objectives	15-16
Limitations			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	16-17
Generalisability	21	Discuss the generalisability (external validity) of the study results	17
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	19

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.