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Clinical Research

Frailty and Outcome in Elderly Patients With Acute Coronary Syndrome

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ABSTRACT

Background: Frailty is superior to chronological age as a predictor of outcome. The Edmonton Frail Scale (EFS) is a simple valid measure of frailty, covering multiple important domains, with scores ranging from 0 (not frail) to 17 (very frail). The purpose of this pilot study was to assess the EFS in a group of elderly patients with acute coronary syndrome (ACS).

Methods: The EFS was administered to 183 consecutive patients with ACS aged $\geq$ 65 years admitted to a single centre in Edmonton, Alberta, Canada.

Results: Scores ranged from 0-13. Patients with higher EFS scores were older, with more comorbidities, longer lengths of stay (EFS 0-3: mean, 7.0 days; EFS 4-6: mean, 9.7 days; and EFS $\geq$ 7: mean, 12.7 days; $P = 0.03$), and decreased procedure use. Crude mortality rates at 1 year were 1.6% for EFS 0-3, 7.7% for EFS 4-6, and 12.7% for EFS $\geq$ 7 ($P = 0.05$). After adjusting for baseline risk differences using a "burden of illness" score, the hazard ratio for mortality for EFS $\geq$ 7 compared with EFS 0-3 was 3.49 (95% confidence interval [CI], 1.08-7.61; $P = 0.002$).

Conclusions: The EFS is associated with increased comorbidity, longer lengths of stay, and decreased procedure use. After adjustment for burden of illness, the highest frailty category is independently

RÉSUMÉ

Introduction : La fragilité est supérieure à l'âge chronologique en matière de prédicteur des résultats cliniques. L'Edmonton Frail Scale (EFS) est une mesure fiable et simple de la fragilité, couvrant plusieurs domaines importants et utilisant des scores allant de 0 (non fragile) à 17 (très fragile). Le but de cette étude pilote était d'évaluer l'EFS chez un groupe de patients âgés ayant un syndrome coronarien aigu (SCA).

Méthodes : Cent quatre-vingt-trois (183) patients consécutifs âgés $\geq$ 65 ans ayant un SCA et étant admis à un seul centre d'Edmonton, en Alberta, au Canada, ont rempli l'EFS.

Résultats : Les scores allaient de 0 à 13. Les patients ayant des scores plus élevés à l'EFS étaient plus âgés, avaient plus de comorbidités, des séjours plus longs (EFS, 0 à 3 : moyenne, 7,0 jours; EFS, 4 à 6 : moyenne, 9,7 jours; EFS $\geq$ 7 : moyenne, 12,7 jours; $P =$ 0,03) et une diminution de l'utilisation d'interventions. Les taux de mortalité bruts à 1 an étaient de 1,6 % pour un score de 0 à 3 à l'EFS, de 7,7 % pour un score de 4 à 6 à l'EFS et de 12,7 % pour un score $\geq$ 7 à l'EFS ($P =$ 0,05). Après l'ajustement des différences de risque initial au moyen du score du « fardeau de la maladie », le rapport de risque de mortalité quant à un score $\geq$ 7 à l'EFS comparativement à un score de 0 à 3 à l'EFS était de 3,49 (intervalle de confiance [IC] à 95 %, 1,08-7,61; $P =$ 0,002).

Cardiovascular disease is a leading cause of morbidity and mortality in older individuals, and managing elderly patients can be challenging. Chronological age is an independent risk factor for adverse outcomes in many conditions and is often included in risk indices.[1-3] However, the assessment of frailty in elderly patients is emerging as a superior predictor when compared with chronological age. Frailty can be conceptualized as a phenotype of weight loss, fatigue, and weakness or a multidimensional state of vulnerability arising from a complex interplay of biological, cognitive, and social factors.[4-8] Compared with age-matched cohorts, frail individuals are at higher risk of functional disability, institutionalization, and death. Unfortunately, methods used to assess frailty can be impractical in busy clinical settings, because the phenotype model is narrow in scope and requires special equipment,[4] and most multidimensional models

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associated with mortality in elderly patients with ACS. Further work is needed to determine whether the use of a validated frailty instrument would better delineate medical decision making in this important, often disadvantaged population.

Conclusions : L'EFS est associée à une augmentation de la comorbidité, à des séjours plus longs et à une diminution de l'utilisation d'interventions. Après l'ajustement du fardeau de la maladie, la catégorie la plus élevée de fragilité est indépendamment associée à la mortalité chez les patients âgés ayant un SCA. D'autres recherches sont nécessaires pour déterminer si l'utilisation d'un instrument de fragilité fiable pourrait mieux orienter la prise de décision médicale chez cette importante population, souvent défavorisée.

require comprehensive geriatric assessment or special training, or both.[5-8]

A brief user-friendly screening interview for frailty in seniors (the Edmonton Frail Scale [EFS]) was developed and validated for use by nongeriatricians.[9,10] The purpose of this pilot cohort study was to expand the validation of the EFS to a group of elderly patients with acute coronary syndrome (ACS) and to determine the association of frailty, as measured by the EFS, with mortality.

Methods

The EFS

Using a series of simple questions or tasks, the EFS (Table 1) assesses cognitive impairment, dependence for activities of daily living, burden of illness, self-perceived health, depression, weight loss, medication issues, incontinence, social support, and mobility (using the timed "get up and go" test). Scores range from 0 (not frail) to a maximum of 17 (very frail). The EFS does not depend on formal medical training to administer, requires less than 5 minutes of the patient's time, and is a valid measure of frailty compared with the clinical impression of geriatric specialists after their more comprehensive assessment.[9,10]

We approached all patients aged 65 years or older with a diagnosis of ACS who were admitted over a period of 6 months to the cardiology inpatient unit at the University of Alberta Hospital, which is an academic tertiary care centre in Edmonton, Alberta, Canada. Exclusion criteria were mechanical ventilation, hemodynamic instability requiring urgent/emergent treatment, and inability to give consent for reasons of language barrier, delirium, known pre-existing cognitive impairment, or significant visual or hearing impairment. Patients were approached as soon as possible after admission, and the EFS was administered before any invasive testing was completed. For those patients who were prescribed strict bed rest, mobility assessment using the timed get up and go test was performed as soon as this clinical restriction was lifted. Health care providers were blinded to the results of the EFS assessment. The study protocol was approved by the Institutional Review board of the University of Alberta.

Because this was a pilot study with a relatively small cohort, a decision was made to categorize the EFS into

Table 1. Domains of the Edmonton Frail Scale

Frailty domain	Item	0 points	1 point	2 points
Cognition	Clock diagram: Place the numbers in the correct positions then place the hands to indicate a time of "10 after 11"	No errors	Minor spacing errors	Other errors
General health status	Hospital admissions in past year	0	1-2	≥ 2
	General health description	Excellent, very good, good	Fair	Poor
Functional independence	Requires assistance with activities such as meal preparation, shopping, transportation, dialing telephone, housekeeping, laundry, managing money, taking medications	0-1	2-4	5-8
Social support	Availability of individuals who are willing and able to support patient needs	Always	Sometimes	Never
Medication use	Five or more different prescription medications on a regular basis	No	Yes	
	Forgetfulness about taking prescription medications	No	Yes	
Nutrition	Weight loss	No	Yes	
Mood	Reported feelings of sadness or depression	No	Yes	
Continence	Unexpected urinary incontinence	No	Yes	
Functional performance (timed get up and go test)	Patient begins by sitting in a chair with back and arms resting, then stands up and walks approximately 3 m, and returns to the chair and sits down	0-10 s	11-20 s	$>$ 20 s, patient unwilling or requires assistance
Totals	Final score is sum of column totals			

3 groups, as was done by previous investigators using the EFS in patients undergoing noncardiac surgery.[11] The following categories were established: EFS 0-3, EFS 4-6, and EFS ≥ 7 to ensure relatively equal numbers of patients in each of the 3 groups.

Real-time chart review conducted during hospital admission confirmed the diagnosis of ACS. Baseline patient data were then collected and entered into the admissions module of the **A**lberta **P**rovincial **Pro**ject for **O**utcomes **A**ssessment in **C**oronary **H**eart Disease (APPROACH registry). APPROACH is a clinical data collection initiative capturing all patients undergoing cardiac catheterization in Alberta, Canada since 1995,[12] and expanded to collect data related to cardiac admissions in 2004. APPROACH contains detailed demographic and clinical information and tracks therapeutic interventions and revascularization procedures. Data collected in the admissions module correspond to the baseline predictor variables collected in APPROACH: age, sex, ejection fraction, the presence or absence of previous myocardial infarction, congestive heart failure, diabetes, cerebrovascular disease, peripheral vascular disease, chronic pulmonary disease, elevated creatinine levels, need for dialysis, hyperlipidemia, hypertension, liver or gastrointestinal disease, and malignancy. Previous therapeutic interventions such as medications, thrombolytic therapy, revascularization including coronary artery bypass grafting (CABG) or percutaneous coronary intervention (PCI) are also tracked. Patients undergoing cardiac catheterization have coronary anatomy and procedural data (including revascularization procedures) collected. Follow-up mortality is ascertained through quarterly linkage to data from the Alberta Bureau of Vital Statistics.

Table 2. Patient characteristics

Characteristic	EFS 0-3 n = 63	EFS 4-6 n = 65	EFS ≥ 7 n = 55	*P* value
Mean age (y)	73.9	75.3	77.2	0.031
Sex (% female)	22.2	38.5	38.2	0.088
Hypertension (%)	61.3	86.2	96.4	< 0.001
Dyslipidemia (%)	84.1	92.3	85.5	0.328
Diabetes (%)	14.3	27.7	45.5	0.001
Smoking (%)	7.9	12.3	16.4	0.571
Renal disease (%)	6.7	14.1	29.6	0.003
Congestive heart failure (%)	4.8	9.2	35.2	< 0.001
Peripheral vascular disease (%)	4.8	7.7	9.1	0.642
Cerebrovascular disease (%)	7.9	10.8	25.5	0.015
Previous MI (%)	22.2	40.0	43.6	0.030
Previous PCI (%)	17.5	29.2	34.5	0.096
Previous CABG (%)	8.1	18.5	18.5	0.203
STEMI (%)	23.8	18.5	14.5	0.436
Malignancy (%)	8.1	9.2	11.1	0.854
Pulmonary disease (%)	11.3	16.9	29.6	0.113
Liver disease (%)	0.0	0.0	1.9	0.448
GI disease (%)	10.0	9.2	14.8	0.734
Treatment received				
Cardiac catheterization (%)	88.9	86.2	58.2	< 0.001
PCI (%)	36.5	26.2	16.4	0.047
CABG (%)	12.7	18.5	9.1	0.364
Length of stay (mean d)	7.0	9.7	12.7	0.026

CABG, coronary artery bypass grafting; CAD, coronary artery disease; EFS, Edmonton Frail Scale; GI, gastrointestinal; LV, left ventricle; MI, myocardial infarction; PCI, percutaneous intervention; STEMI, ST-segment elevation MI.

Statistical analysis

Patient characteristics among the 3 frailty groups were compared using *t* tests and χ^2 tests. Kaplan-Meier plots and log-rank tests were used to determine and compare crude mortality rates. Using linear regression and age as the outcome variable, a model was developed that included all of the clinical variables contained in Table 2. The predicted "age" of the modelling process was saved and used as a surrogate for the "burden of illness" score in subsequent regression analyses. A Cox regression analysis was then conducted using the burden of illness variable and the frailty categories to assess the association of these variables with survival. To fit the small sample size, bootstrapping was used to derive robust estimates of the standard errors and confidence intervals for the regression coefficient (hazard ratios).

Secondary outcomes of interest included length of hospitalization (also assessed with the EFS as a continuous variable), use of cardiac catheterization, and revascularization procedures (CABG and PCI).

Statistical analyses were performed using IBM SPSS Statistics, version 20 (SPSS, Chicago, IL).

Results

Over a 6-month period, the EFS was administered to 183 consecutive patients aged ≥ 65 years who were admitted with a confirmed diagnosis of ACS. The EFS on average required < 5 minutes to administer. Scores ranged from 0-13 (maximum 17 points), with higher scores indicating higher levels of frailty. Categorization of the patient cohort into tertiles resulted in 63 patients with an EFS score of 0-3, 65 patients with an EFS score of 4-6, and 55 patients with an EFS score of ≥ 7.

Table 2 shows the baseline characteristics of these patients. Patients with higher EFS scores were older and more likely to have a history of hypertension, previous myocardial infarction, congestive heart failure, and chronic kidney disease. EFS scores ≥ 7 were associated with a substantial proportion of congestive heart failure in $> 33\%$ of patients and cerebrovascular disease in 25%. Higher EFS scores were also associated with longer mean hospital lengths of stay (7.0 days for EFS 0-3, 9.7 days for EFS 4-6, and 12.7 days for EFS ≥ 7; $P = 0.03$).

Table 2 also illustrates that patients in the highest EFS category were less likely to undergo cardiac catheterization (58% of patients with EFS ≥ 7 compared with $> 86\%$ of patients in the other EFS categories with lower scores). Patients in this highest EFS category group were also less likely to receive subsequent revascularization procedures, particularly PCI, although this finding was not statistically significant for CABG.

Figure 1 presents the Kaplan-Meier curves for survival to 1 year of follow-up after hospitalization for ACS. Crude mortality rates at 1 year were 1.6% for EFS 0-3, 7.7% for EFS 4-6, and 12.7% for EFS ≥ 7 ($P = 0.05$).

Using all the clinical characteristics found in Table 2, a linear regression model was run, with age at assessment as the outcome variable. The predicted scores were used as a proxy variable, which we labelled "burden of illness." Cox regression analysis, including the burden of illness variable and the EFS categories, was then performed. Using the EFS ≤ 3 category as a referent, the adjusted hazard ratio for EFS 4-6

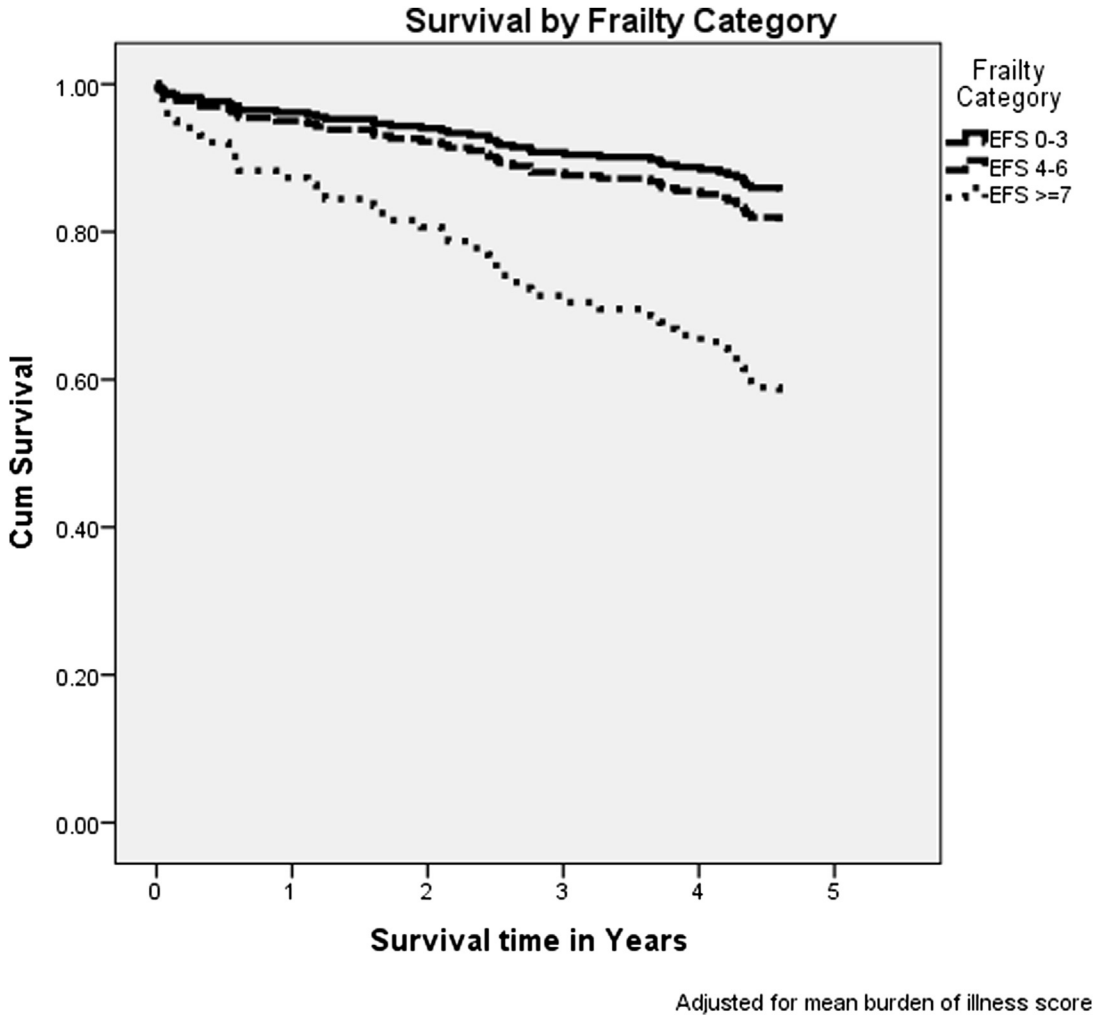

Figure 1. Kaplan-Meier survival curves for the 3 different frailty groups followed up to 3 years after admission for acute coronary syndrome (ACS).

was 1.31 (95% CI, 0.55-3.13) and for EFS $\geq$ 7, it was 3.49 (95% CI, 1.08-7.61), indicating that after adjustment for burden of illness, the highest frailty category remained independently associated with mortality in this ACS cohort.

Discussion

In this pilot study, we demonstrated that a simple user-friendly instrument to assess frailty at the bedside is associated with increasing comorbidity, hospital lengths of stay, lower use of invasive procedures, and increased mortality in a known high-risk population—elderly patients with ACS. The EFS has been successfully used in other important clinical situations, including noncardiac surgery, in which higher EFS scores were associated with an increase in postoperative complications, increased length of stay, and an inability to be discharged home.[11] Most recently, frailty as measured by the EFS was found to be associated with lower use of warfarin for stroke prevention in atrial fibrillation and an increased rate of embolic stroke.[13]

A recent systematic review demonstrated that > 50% of elderly patients with cardiovascular disease are frail, and frailty is known to be associated with an increase in mortality in community-dwelling patients with cardiovascular disease.[14] The complexity of some methods of frailty assessment does make more simple tools attractive from the perspective of ease of use and time required to administer tests. Although simple tools may lose some nuances, they can still be predictive, as was demonstrated when the simple Study of Osteoporotic Fracture Index, with 3 domains, was found to predict the risk of falls, disability, fractures, and mortality as well as the more complex Cardiovascular Health Study Index.[15,16] Gait speed (1 simpler measure of frailty) in hospitalized older patients with known coronary artery disease was found to be the strongest predictor of 6-month mortality.[17] Similarly, the 6-minute walk test administered in older adults with heart failure was found to be independently predictive of mortality.[18] However, although easy to administer, gait speed and the 6-minute walk test do not assess the other critical domains associated with frailty. Freiheit et al. recently developed a frailty index in elderly patients undergoing cardiac catheterization, which includes physical, cognitive. and psychosocial criteria.[19] However, this model has not yet been validated in other settings. The EFS therefore has advantages because it has been validated in multiple clinical situations and assesses multiple domains.

In our cohort, there were significant differences in baseline characteristics according to degree of frailty, with an increase in clinically significant comorbidities, which would by their very nature correlate with increased cardiovascular risk. Correspondingly, these patients were less likely to receive cardiac catheterization and revascularization procedures and had significantly higher mortality rates. Clinical trials and large observational studies suggest that invasive investigation and revascularization in appropriately selected elderly patients with coronary artery disease leads to decreased mortality and major adverse cardiac events and improved quality of life.[20-23] However, patient selection is critical, and Yan et al. previously demonstrated that physicians may not be incorporating readily available adverse prognosticators into patient risk assessment.[24] Furthermore, these studies did not include objective measures of frailty. The risks of increasing morbidity and mortality with revascularization procedures have collectively raised clinical thresholds for considering these procedures in the elderly. Indeed, a recent study also demonstrated that patients who are objectively identified as being frail but who undergo major cardiac surgical procedures have significantly increased risk for in-hospital and midterm mortality. In addition, these frail surgical patients are more likely to experience postoperative complications and require discharge to institutional care.[25] In very frail patients, therefore, the use of fewer invasive procedures may be completely appropriate, because the risks of procedures begin to outweigh the benefits. This emphasizes the importance of individually tailored informed consent and highlights the potential advantage of incorporating frailty into risk assessments.

Another consideration is the potential of a simple frailty assessment to identify issues in individual patients that are possibly modifiable. For example, one could envision interventions through social work and home care to improve functional independence, social support, medication compliance, and nutrition. Such interventions have previously been demonstrated to be effective in elderly patients with heart failure.[26] Cardiac rehabilitation programs are associated with improved outcomes, even in older individuals.[27,28] Cardiac rehabilitation is also associated with improvements in depressive symptoms in older patients.[29] Finally, recent studies have shown that resistance training can improve cognitive performance in patients with subjective memory impairment, potentially at a cost savings.[30,31] Although older patients are less likely to participate in these programs,[32] investigators have also found that simple interventions such as early appointments after discharge improve attendance.[33] Further work is therefore required to determine whether it is possible to "defrail" a frail patient and to identify the relationship potential frailty interventions may have to outcomes.

There are limitations to this study. It is a single-centre pilot study involving a relatively small number of patients, with limited power to evaluate other important major adverse outcomes; therefore, generalizability may be a concern. However, our findings are in keeping with other studies of frailty in general, and furthermore all CIs and significance tests were computed based on the standard errors of the bootstrap samples. The small numbers also prevent assessment of the relative contributions of the individual domains measured in the EFS to outcome. Finally, the relationship between frailty and quality of life is an important consideration that requires further research.

Conclusions

In conclusion, we have expanded the use of a simple frailty assessment tool administered by nongeriatricians to a group of elderly patients with ACS. Higher EFS scores are associated with increased comorbidity, longer lengths of stay, and decreased procedure use. Furthermore, after adjusting for baseline risk factor differences using a burden of illness variable, high EFS scores are associated with increased mortality. This simple tool therefore has the potential to serve as a practical and clinically meaningful measure of frailty in a variety of settings. Further work is needed to determine whether the use of a validated frailty instrument to better delineate some of the "unmeasured factors" involved in medical decision making in elderly patients with cardiovascular disease would provide more transparent and refined discussions of risk and the opportunity for interventions to improve this risk in this important, often disadvantaged, population.

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Disclosures

The authors have no conflicts to disclose.

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