Frailty and associated prognosis among older emergency department patients with suspected infection: A prospective, observational cohort study

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CLINICIAN'S CAPSULE

What is known about the topic?
Older emergency department (ED) patients with suspected infection are at risk of future deterioration, and often difficult to disposition.

What did this study ask?
What was the association between clinical frailty and 30-day mortality among older ED patients presenting with suspected infection?

What did this study find?
Patients with frailty had higher development of septic shock and increased 30-day mortality, compared with patients without frailty.

Why does this study matter to clinicians?
Frailty can be quickly and easily measured in ED patients, and can be used particularly to risk stratify older patients with suspected infection.

ABSTRACT

Background: Prognosis and disposition among older emergency department (ED) patients with suspected infection remains challenging. Frailty is increasingly recognized as a predictor of poor prognosis among critically ill patients; however, its association with clinical outcomes among older ED patients with suspected infection is unknown.

Methods: We conducted a multicenter prospective cohort study at two tertiary care EDs. We included older ED patients (≥75 years) with suspected infection. Frailty at baseline (before index illness) was explicitly measured for all patients by the treating physicians using the Clinical Frailty Scale (CFS). We defined frailty as a CFS 5–8. The primary outcome was 30-day mortality. We used multivariable logistic regression to adjust for known confounders. We also compared the prognostic accuracy of frailty with the Systemic Inflammatory Response Syndrome (SIRS) and Quick Sequential Organ Failure Assessment (qSOFA) criteria.

Results: We enrolled 203 patients, of whom 117 (57.6%) were frail. Frail patients were more likely to develop septic shock (adjusted odds ratio [aOR], 1.83; 95% confidence interval [CI], 1.08–2.51) and more likely to die within 30 days of ED presentation (aOR 2.05; 95% CI, 1.02–5.24). Sensitivity for mortality was highest among the CFS (73.1%; 95% CI, 52.2–88.4), compared with SIRS ≥ 2 (65.4%; 95% CI, 44.3–82.8) or qSOFA ≥ 2 (38.4; 95% CI, 20.2–59.4).

Conclusions: Frailty is a highly prevalent prognostic factor that can be used to risk-stratify older ED patients with suspected infection. ED clinicians should consider screening for frailty to optimize disposition in this population.

RÉSUMÉ

Contexte: Il n'est pas facile de déterminer le pronostic et les suites à donner chez les personnes âgées souffrant d'une infection présumée, au service des urgences (SU). La fragilité est de plus en plus reconnue comme un facteur prévisionnel de pronostic sombre chez les personnes gravement malades; toutefois, on ne sait pas s'il existe une association entre les résultats cliniques observés chez les personnes âgées au SU et les infections présumées.

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Méthode: Il s'agit d'une étude de cohorte, prospective et multicentrique, réalisée dans deux SU de soins tertiaires. Ont été retenus des patients âgées (≥ 75 ans) examinés au SU pour une infection présumée. Le degré de fragilité au départ (avant la maladie de référence) a été explicitement mesuré chez tous les patients par le médecin traitant à l'aide d'une échelle de fragilité clinique, la Clinical Frailty Scale (CFS). La fragilité a été définie comme une valeur variant de 5 à 8 sur la CFS. Le principal critère d'évaluation était la mortalité au bout de 30 jours. Les chercheurs ont utilisé un modèle de régression logistique plurifactorielle pour tenir compte des variables de confusion connues. L'exactitude du pronostic de fragilité selon la CFS a également été comparée avec celle de deux autres outils, soit les Systemic Inflammatory Response Syndrome (SIRS) et Quick Sequential Organ Failure Assessment (qSOFA).

Résultats: Ont participé à l'étude 203 patients, dont 117 (57,6%) étaient considérés comme fragiles. Ces derniers étaient plus susceptibles que les autres de subir un choc septique (risque relatif approché rajusté [RRAr] : 1,83; intervalle de confiance [IC] à 95% : 1,08-2,51) et de succomber à la maladie dans les 30 jours suivant la consultation au SU (RRAr : 2,05; IC à 95% : 1,02-5,24). C'est la CFS qui a révélé la plus forte sensibilité à l'égard de la mortalité (73,1%; IC à 95% : 52,2-88,4), comparativement à l'échelle SIRS ≥ 2 (65,4%; IC à 95% : 44,3-82,8) et à la qSOFA ≥ 2 (38,4; IC à 95% : 20,2-59,4).

Conclusion: La fragilité est un facteur de pronostic très courant qu'on peut utiliser pour classer les patients âgés atteints d'une infection présumée, en fonction du risque, au SU. Les urgentologues devraient envisager la possibilité de mesurer le degré de fragilité dans la population concernée afin d'optimiser les suites à donner.

Keywords: Frailty, geriatrics, infection, sepsis, septic shock

INTRODUCTION

Severe infection, resulting in sepsis and septic shock, remains a major cause of death.[1] In the emergency department (ED), early identification of patients with sepsis has been associated with improved outcomes,[2] while inappropriate disposition has been linked to worse outcomes and increased costs.[3] Older patients with suspected infection often present with nonspecific signs,[4,5] making risk-stratification in this population challenging. Frailty, a clinical state characterized by reduced physiologic reserve, has been associated with poor outcome among intensive care unit (ICU) patients.[4,6] In the ED, frailty can be easily measured and used to risk-stratify patients. We evaluated the association between frailty and outcomes of ED patients with suspected infection, and compared frailty with other prognostic tools, including the Systemic Inflammatory Response Syndrome (SIRS) criteria, and the Quick Sequential Organ Failure Assessment (qSOFA).[7]

METHODS

Study approval was received from The Ottawa Health Science Network Research Ethics Board. Further methodological detail is included in the online Supplemental Table 1.

Study design, setting, and subjects

We conducted this prospective cohort study in the EDs of two university-affiliated hospitals within The Ottawa Hospital network (Ottawa, ON) from September 2018 to February 2019. We recruited a convenience sample of patients ≥75 years of age, presenting with suspected infection. We defined "suspected infection" by administration of antimicrobial therapy, and either (A) drawing of body fluid cultures (including blood, urine, and cerebrospinal fluid); or (B) chest radiography interpreted by the ED physician to represent pneumonia. We defined "septic shock" as serum lactate > 2.0 mmol/L, and persistent hypotension below a mean arterial pressure of 65 mmHg, despite fluid resuscitation. These definitions of "suspected infection" and "septic shock" largely match those used in the Third International Consensus Definitions for Sepsis and Septic Shock.[7]

Identifying frailty

Treating ED physicians or residents were asked to identify the presence of frailty, before patient disposition. This was done using the Clinical Frailty Scale (CFS), a 9-point global frailty scale that evaluates baseline mobility, energy, physical activity, and function (before consultation or discharge)[8] (Supplemental Figure 1), and has been applied in the ED with good inter-rater reliability.[9] Consistent with previous research, a CFS ≥ 5

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was used to identify the presence of frailty. Patients with a CFS of 9 were excluded due to the high likelihood of short-term mortality.

Data collection and outcomes measures

Following enrollment, patients were approached by a trained research assistant, who gathered data related to baseline characteristics, and calculated SIRS and qSOFA scores at the time of physician assessment. Patients were phoned by a single investigator (K.H.G.) at 30 days following enrollment. The primary outcome was 30-day mortality. Secondary outcomes included need for hospital admission, development of septic shock, and disposition to long-term care facilities.

Statistical analysis

We present data as mean values, with standard deviation (SD), or medians, with interquartile range (IQR), where appropriate. We performed the Student's t-test, Mann-Whitney test, and χ^2 to determine between-group differences. As recommended for observational studies (Supplemental Table 1), we determined confounders a priori, and used multivariable logistic regression modeling to adjust for important continuous (age, Canadian Triage and Acuity Score [CTAS]) and categorical (sex, treatment limitations) variables. We present adjusted odds ratios (aOR) with 95% confidence intervals (CIs). A p value of ≤ 0.05 was considered statistically significant. We calculated the sensitivity, specificity, and likelihood ratios with 95% CIs for the CFS, SIRS, and qSOFA for 30-day mortality.

RESULTS

We recruited 205 older ED patients presenting with suspected infection. Two (1.0%) were lost to follow-up at 30-days, leaving 203 patients available for analysis (Supplemental Figure 2). Of these, 117 (57.6%) were identified as being frail. Baseline characteristics are shown in Supplemental Table 2. Frail patients were older (mean age 86.5 v. 83.0 years; $p < 0.001$), and were more likely to have bladder and bowel incontinence, cognitive impairment, and require assistance with mobility and activities of daily living. Frail patients were less likely to be from home, and more likely to have limitations with regard to critical care interventions. No differences were seen in initial CTAS score, suspected source of infection, or initial ED vital signs. Outcomes are displayed in Supplemental Table 3. In this cohort, 26 patients (12.8%) died before day 30. Frailty was associated with development of septic shock (aOR, 1.83 [95% CI, 1.08–2.51]) and increased 30-day mortality (aOR, 2.05 [95% CI, 1.02–5.24]; Supplemental Table 4).

Prognostic accuracy of the CFS, SIRS, and qSOFA criteria for 30-day mortality are shown in Table 1. CFS ≥ 5 had a sensitivity of 73.1% (95% CI, 52.2–88.4) and specificity of 44.6% (95% CI, 37.2–55.3). SIRS ≥ 2 had a sensitivity of 65.4% (95% CI, 44.3–82.8) and specificity of 57.1% (95% CI, 49.4–64.5). Finally, qSOFA ≥ 2 had a sensitivity of 38.4% (95% CI, 20.2–59.4%) and a specificity of 91.5% (95% CI, 86.4–95.2). A qSOFA ≥ 2 was only seen in 12.8% of patients. Presence of frailty combined with a qSOFA ≥ 2 had an odds ratio of 7.83 (95% CI, 2.99–19.5) for 30-day mortality.

DISCUSSION

Risk-stratification of older ED patients with suspected infection is difficult. The SIRS criteria are commonly used to screen for initiation of therapy[2]; however, these criteria are less reliable in older patients, who may not mount the same compensatory response seen from systemic inflammation.[5] We found that a CFS 5–8 had superior sensitivity to the SIRS criteria ≥ 2, making it potentially more valuable in the ED setting. In keeping with existing research, qSOFA ≥ 2 was found to have particularly poor sensitivity for mortality,[10] and only a minority of patients met this criteria. Regardless, the high odds ratio of qSOFA suggests that it may be valuable in identifying very high-risk patients, and synergistic combination with the CFS identified patients with the highest odds of dying. Interestingly, our results show that frail patients are at increased risk of deterioration to septic shock, suggesting a potential underlying relationship between the poor physiologic reserve associated with frailty, immunosenesence, and specific features such as an overwhelming systemic host response to infection. Whether this population may benefit from earlier and more aggressive interventions could be an important avenue of future research.

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Table 1. Prognostic accuracy of Clinical Frailty Scale, Systemic Inflammatory Response Syndrome, and Quick Sequential Organ Failure Assessment for 30-day mortality among older patients with suspected infection (n = 203)

Characteristic	Value
Clinical Frailty Scale (CFS) ≥ 5	
Prevalence, %	57.6
Sensitivity, % (95% CI)	73.1 (52.2-88.4)
Specificity, % (95% CI)	44.6 (37.2-52.3)
Positive likelihood ratio (95% CI)	1.3 (1.0-1.7)
Negative likelihood ratio (95% CI)	0.6 (0.3-1.2)
Positive predictive value, % (95% CI)	16.2 (12.9-20.2)
Negative predictive value, % (95% CI)	91.9 (85.4-95.6)
Odds ratio (95% CI)	2.19 (0.92-5.62)
Odds ratio (95% CI), CFS ≥ 5 + SIRS ≥ 2	3.50 (1.53-8.38)
Odds ratio (95% CI), CFS ≥ 5 + qSOFA ≥ 2	7.83 (2.99-19.5)
Systemic Inflammatory Response Syndrome (SIRS) ≥ 2	
Prevalence, %	45.8
Sensitivity, % (95% CI)	65.4 (44.3-82.8)
Specificity, % (95% CI)	57.1 (49.4-64.5)
Positive likelihood ratio (95% CI)	1.5 (1.1-2.1)
Negative likelihood ratio (95% CI)	0.6 (0.4-1.0)
Positive predictive value, % (95% CI)	18.3 (13.9-23.7)
Negative predictive value, % (95% CI)	91.8 (86.7-95.1)
Odds ratio (95% CI)	2.51 (1.11-6.12)
Quick Sequential Organ Failure Assessment (qSOFA) ≥ 2	
Prevalence, %	12.8
Sensitivity (95% CI)	38.4 (20.2-59.4)
Specificity (95% CI)	91.5 (86.4-95.2)
Positive likelihood ratio (95% CI)	4.5 (2.3-9.0)
Negative likelihood ratio (95% CI)	0.7 (0.5-0.9)
Positive predictive value (95% CI)	40.0 (25.1-57.0)
Negative predictive value (95% CI)	91.0 (88.2-93.2)
Odds ratio (95% CI)	6.75 (2.43-17.2)

CI = confidence interval.

Our study has important limitations. First, we enrolled a convenience sample of patients on the basis of research assistant availability, leaving open the possibility for selection bias. We do not know what proportion of patients with "suspected infection" were missed. Second, the majority of patients had pulmonary or urinary infections, and how our findings extend to other infection sources is unclear. Third, we included initial goals-of-care in our regression models, but do not have data related to how goals-of-care may have changed throughout hospital admission, as clinicians may be more likely to engage with frail patients and their families in conversations about prognosis. Finally, our study was conducted at two hospitals within the same city and is potentially susceptible to bias from regional practice.

CONCLUSION

Pre-admission frailty was associated with increased odds of development of septic shock and 30-day mortality in older ED patients with suspected infection. The CFS had higher sensitivity than SIRS or qSOFA for prognosis of 30-day mortality. ED clinicians should consider use of the CFS for quick screening, prognostication, and disposition.

Supplemental material: The supplemental material for this article can be found at https://doi.org/10.1017/cem.2020.377.

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Author Contributions: S.M.F. and J.J.P. designed the study. S.M.F. and K.H.G. gathered the data. All authors analyzed and interpreted the data. All authors wrote the manuscript.

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