Published in final edited form as:

J Am Geriatr Soc. 2012 February ; 60(2): 304–309. doi:10.1111/j.1532-5415.2011.03823.x.

Functional Status Does Not Predict Complicated Clinical Course in Older Emergency Department Adults with Infection

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Abstract

Background/objectives—To identify the relationship between functional status and complicated clinical course in older emergency department (ED) patients with suspected infection. The secondary objective was to identify other independent predictors of complicated clinical course.

Design—A prospective observational cohort study

Setting—An academic, tertiary care ED with 70,000 visits per year

Participants—Inclusion criteria included admitted ED patients age ≥ 65 years, blood cultures obtained in the ED, and final ED physician diagnosis of acute infection.

Measurements—Functional status was obtained using the Older Americans Resources Scale (OARS). Complicated clinical course was: in-hospital mortality, or need for ICU-level care or worsening in sepsis criteria within 48 hours. Analysis was by multivariable logistic regression.

Results—We enrolled 105 patients, 34 with the primary outcome. OARS was not predictive of complicated clinical course in univariate ($p=0.130$) or multivariable ($p=0.896$) models. OARS was also nonsignificant ($p=0.225$). Independent predictors were: immunosuppression (odds ratio [OR] 3.45, 95% CI 1.06–11.20), systolic pressure (OR 0.98, 95% CI 0.96–1.00), pulse (OR 1.03, 95% CI 1.00–1.06), metabolic acidosis (OR 3.46, 95% CI 1.08–11.09), severe sepsis/septic shock (OR 10.24, 95% CI 1.44–72.79), suspected bloodstream infection (OR 3.56, 95% CI 1.13–11.16).

Conclusion—Among older ED patients admitted with infection, functional status did not predict complicated clinical course. However, several other variables were predictive including immunosuppression, several variables associated with hypoperfusion, and suspected bloodstream infection. Emergency physicians could consider these variables as potential indicators of complicated clinical course when making disposition decisions for this patient population.

Keywords

elder; emergency department; infection; functional status

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Conflict of interest: The authors declare that they have no conflicts of interest.

Author contributions: JMC designed the study, oversaw collection of the data, performed the data analysis, and authored the manuscript. RAM collaborated in study design and critically reviewed the manuscript. KBS collaborated in study design, aided in conduct of the study, and critically reviewed the manuscript.

INTRODUCTION

Older adults ≥ 65 years of age account for over 15 million US Emergency Department (ED) visits each year (1). A large percentage present with severe infections, the 6th leading cause of death in older adults (2). Delivering appropriate care to older adults with infection requires accurate determination of disease severity which is crucial to identifying appropriate level of care and resource allocation. Determining the need for intensive care unit (ICU)-level care in infected older adults is important due to their increased mortality compared to younger patients (3), the need to avoid inappropriately admitting patients from the ED to the ward rather than ICU (4), and the proven benefits of applying early, aggressive care to patients most at risk of poor outcomes (5). Inappropriately admitting patients to a ward worsens outcomes as compared to direct ED to ICU admission (4;6).

Unfortunately, severity of infection is difficult to assess in older ED patients. First, infection in older adults often presents with non-specific signs and symptoms (3;7–9). Second, illness severity scores derived in general populations are less accurate in these patients (10–12). Third, most available ED-derived outcome prediction models predict mortality only. Equally relevant to ED physicians are short-term outcomes which aid the physician in determining destination and resource uses. One such outcome is complicated clinical course which can be represented as requirements for aggressive therapy and higher levels of care. Attempts have been made to predict clinical deterioration in infected ED patients but these have not focused specifically on older patients (13). A focus on older ED patients is advisable as previous work has demonstrated differences in outcome prediction models between those created for older and younger patients (14).

For predicting outcomes in older adults, the importance of using unique characteristics of this population, particularly functional status assessment, has been recognized (9). Infected older adults present more commonly with decreased functional status than classic symptoms (9) and this decrease has been associated with morbidity and mortality (12;15). We hypothesized that declining functional status would be predictive of complicated clinical course and thus appropriately guide patient care and disposition decisions in older ED patients with infection. Our primary objective was to identify the relationship between functional status and complicated clinical course (defined as need for ICU-level care within 48 hours of hospitalization, worsening in sepsis criteria within 48 hours, or in-hospital mortality) in older ED patients with suspected infection. The secondary objective was to identify independent predictors of complicated clinical course in study patients.

METHODS

We conducted a prospective observational cohort study of ED patients ≥ 65 years of age who were suspected of acute, systemic infection and were admitted to the hospital. The study was conducted from 1/1/2006 to 5/31/2009 in an academic, tertiary care ED with 70,000 visits per year. It was approved by the hospital's Institutional Review Board. Informed consent was obtained from the patient or an appropriate proxy.

Inclusion criteria included age ≥ 65 years, admitted to the hospital, blood cultures obtained in the ED, and final ED attending physician diagnosis of confirmed or suspected acute infection. Exclusion criteria included subject incarcerated, subject non-English speaking, lack of patient or proxy ability to give consent, ED visit or admission within the previous 7 days for the same condition, previous enrollment in the study, or trauma team activation.

Data was collected from patient surveys, physician surveys, and from ED and inpatient medical records. Enrollment and survey administration was by trained research associates on a sample of shifts between 8 AM and midnight on all days of the week when a research

assistant was available, with an average of 20 hours of coverage per week. In the ED, a functional status survey was administered by research assistants to patients after initial evaluation and an ED physician survey was administered to the treating physician. The survey could be answered either by the patient or a family member in the room. In cases where respondents did not agree, the worst reported functional status was used. The physician survey confirmed medical history, presence of an acute infection, and suspected location of the infection after ED evaluation. Physicians were instructed to indicate an infection was present if they thought one was confirmed, likely, or possible from a specific source.

Additional data were gathered by chart review of the ED record and the first 48 hours of the inpatient record. Review techniques included an initial abstractor training session, creation of a data dictionary, and blinding of abstractors both to study hypotheses and functional status results. Ten percent of charts were re-abstracted by one investigator (JMC) and agreement was measured. Variables chosen for re-abstractation included immunosuppression, altered mental status, fever, and severe sepsis/septic shock. Medical record data collected included demographics, extended care facility residence, vital signs, past medical history, medications, patient complaints, physical exam, fluid administration, medications, transfusions, laboratory results, and imaging data.

The primary outcome measure was complicated clinical course within 48 hours of admission which was defined as any one of the following: in-hospital mortality, requirement for ICU admission or ICU-level care within the first 48 hours of admission, or progression in sepsis category (e.g. from sepsis to severe sepsis or septic shock) within the first 48 hours. These factors have been previously used to define complicated clinical course (16–18). We limited the time considered to <48 hours from admission to reflect the direct effect that decisions on admission destination made in the ED may have. We included ICU-level care both because our institution's ICU is often filled, with seriously ill patients admitted to a step-down unit and to prevent incorrect outcome assignment in patients admitted inappropriately to the floor. ICU-level care was defined as any of: mechanical ventilation, vasopressor or inotrope use, large volume fluid resuscitation (≥4L fluid in any 24 hour period), or large volume transfusion (≥4 units in any 24 hour period). Previously described sepsis definitions were used (19). Progression of sepsis was chosen as a marker of worsening outcomes and increased resource use as done previously (6). In-hospital mortality is a common marker of illness severity (16;17).

The independent variable of interest was functional status which was assessed using the Older Americans Resources and Services (OARS) assessment of Activities of Daily Living (ADL) and Instrumental Activities of Daily Living (IADL). Seven ADLs and seven IADLs are tested (20). The OARS score has been validated in the ED with abnormal functional status described as a decline of 3 points. A score of 28 is normal and a score ≤25 is a clinically significant decrease in functional status (21).

Age was recorded by decade (65–74, 75–84, ≥84 years). Extended care facility residence included presentation from nursing home, inpatient rehabilitation, or extended-stay hospital. The Charlson co-morbidity (CCM) index was calculated (22). Immunosuppression was defined as: HIV/AIDS, multiple myeloma, systemic steroid use (past 30 days), malignancy, organ transplant, or use of immunosuppressive medication. Initial ED vital signs were collected. Respiratory distress was defined as: oxygen saturation <93%, respiratory rate ≥24/min, or oxygen requirement ≥4 lpm. Laboratory data were examined both as continuous and dichotomous variables. Abnormal white blood cell (WBC) count was defined as white blood cell count <5,000 or ≥10,000/mm³, low platelets as <150,000/mm³, and metabolic

acidosis as either serum lactate ≥ 4 mmol/L, serum bicarbonate <20 mmol/L, or anion gap ≥ 16 .

Statistical analysis

Data analysis was performed using STATA, version 11 (STATA Corp, College Station, TX). Characteristics of the study population were reported as number with percentage or as median with interquartile range. Their association with complicated clinical course was examined in univariate logistic regression models.

We then created a series of multivariable logistic regression models. Model 1 included OARS unadjusted. Model 2 added CCM score. Model 3 was created using a forward stepwise technique. OARS score was forced into this model. Variables with univariate p values <0.3 were considered for inclusion. Variable choice was not automated but proceeded rationally based on p value, clinical plausibility, and effect on the OARS coefficient. Individual variables were added until no further variables were significant at a $p<0.05$ and/or no further variables caused a change in coefficient in OARS of $>20\%$. Then, all variables with initial $p<0.3$ were again tested to ensure that none had become significant. For variables measuring the same characteristic (e.g. bicarbonate level and metabolic acidosis), one was chosen for inclusion based on significance and clinical relevance.

We tested for linearity in the logit using graphical and fractional polynomial analysis, for plausible interactions, for fit using the Hosmer-Lemeshow test, and for discrimination using ROC curves. As a sensitivity analysis, we reran the models both with the dichotomous OARS ≥ 25 and using the patient's reported functional status at baseline, one week prior to the ED visit.

RESULTS

We identified 257 potentially eligible patients on initial screening. Of these, 157 were not enrolled: 42 patient refused, 30 patient was too ill, 45 with altered mental status with no family present or otherwise unable to give consent, 27 missed (e.g., end of research assistant shift, patient transferred out of the ED prior to enrollment), 2 non-English speaking, 1 trauma, 4 recent ED visit for the same condition, 4 prior enrollment, and 2 incarcerated. Of the 118 patients who consented, two were dropped for lack of recorded OARS data and eleven were excluded after the ED physician survey revealed that the physician did not suspect infection. The remaining 105 patients constitute the study population. Inter-rater reliability was good with complete agreement for altered mental status and severe sepsis/septic shock. The kappa was 0.78 for immunosuppression and of fever.

Patient characteristics are shown in Table 1. Of note, there were a high proportion of immunosuppressed patients (56.2%) in our cohort. The mean OARS score was 19 (interquartile [IQ] range 12–26) with 72.3% of patients having an abnormal OARS score ≤ 25 . Complicated clinical course was present in 34 patients (32.4%). Of the 3 patients with septic shock, 2 were admitted to an ICU and all 3 received ICU-level care. Of the 7 patients with severe sepsis, none were admitted to an ICU and 5 received ICU-level care. Of the 35 patients with sepsis, 2 were admitted to an ICU and 8 received ICU level of care.

The results of the univariate analyses are shown in Table 2. As the two youngest age categories had equivalent odds ratios, they were combined and age made a dichotomous variable with a cutoff of 85 years to improve efficiency in the modeling. Table 3 displays the results of the multivariable logistic regression models with complicated clinical course as the dependent variable and OARS score as the primary independent variable of interest. OARS score was not significantly associated with complicated clinical course in any model.

For Model 3, variables found to be predictors of complicated clinical course included immunosuppression (OR 3.45, 95% CI 1.06–11.20), SBP (OR 0.98, 95% CI 0.96–1.00), pulse (OR 1.03, 95% CI 1.00–1.06), metabolic acidosis (OR 3.46, 95% CI 1.08–11.09), severe sepsis/septic shock (OR 10.24, 95% CI 1.44–72.79), and suspected bloodstream infection (OR 3.56, 95% CI, 1.13–11.16).

All models demonstrated adequate linearity, fit, and discrimination. There were no interactions. In the sensitivity analysis, use of OARS divided into quartiles, dichotomized at an OARS score ≥ 5 , or measured by patient self-report of condition one week prior to the ED visit did not result in significant changes to any model. For example, in those with an OARS score ≥ 5 there was no significant relationship with complicated clinical course in the unadjusted model (OR 2.23, 95% CI 0.81–6.15) ($p=0.119$) or the full stepwise model (OR 2.16, 95% CI 0.62–7.50) ($p=0.225$).

DISCUSSION

We found that functional status did not predict complicated clinical course among older ED patients admitted with infection even after examining functional status as a continuous variable, at a dichotomous cutoff, and by quartiles. We did identify other variables independently associated with complicated clinical course including immunosuppression, systolic blood pressure, pulse, metabolic acidosis, severe sepsis/septic shock in the ED, and suspected bloodstream infection.

There is no widely accepted definition for complicated clinical course in the literature, but it should encompass markers of increased resource use and poor outcome in a time period which could reasonably be associated with the ED visit. Using such an outcome rather than a more long-term one such as mortality allows one to identify components of the ED visit which relate to or affect the outcome and limits confounding by factors unrelated to the ED visit. Previous studies have defined complicated clinical course using various criteria including transfer to an ICU within 48 hours of admission (4;6;13;23). Our definition included ICU admission, markers of ICU level care, and worsening of sepsis category. These were included to capture those patients requiring high levels of care or continuing to deteriorate after admission. They were included both because ICU beds are not always available and because ICU admission depends on physician recognition of severity. Timely recognition of severity by the emergency physician is key to limiting morbidity and mortality as transfer from a ward to an ICU is associated with greater mortality than direct admission to the ICU (4;6).

Currently, it is difficult to predict complicated clinical course in ED patients, and a large proportion of patients initially stable in the ED have worsening of clinical status (24). In one study, almost 50% of patients who progressed to severe sepsis were initially admitted to a ward (17). This number may be higher in older adults with non-specific signs and symptoms. The failure to find an association between functional status and complicated clinical course in our older ED population was surprising given previously identified associations of functional status and mortality in older infected ED patients (12;25). These studies' use of a different outcome measure may explain the negative findings in our study. Mortality is a longer-term outcome frequently associated with functional status (9;25–27); but our outcome was designed to reflect the effect of ED disposition decisions.

Although functional status was not predictive, the modeling we performed provided useful information regarding potential predictors of complicated clinical course. We have previously shown that predictors of mortality in older ED patients with infection differ from

those of other adults (14). To our knowledge, predictors of complicated clinical course have not previously been described specifically in the older ED population.

Previous work examining complicated clinical course in the general ED and inpatient population with infection has been reported, with results varying between studies (13;16;18;23). Direct comparison among these studies and with ours is limited by differing patient populations, confounders considered, and outcome definitions. Nevertheless, our results are generally consistent with these previous studies. Our models found immunosuppression, systolic blood pressure, pulse, metabolic acidosis, presence of severe sepsis/septic shock, and suspected blood stream infection to be predictors. Many of these factors have been previously recognized as predictors including hypotension (13;18), tachycardia (18), bacteremia (18), severe sepsis (16), and metabolic acidosis (23).

As the first examination of complicated clinical course in older ED adults, we now have some indication as to important prognostic factors. Further study in larger groups is necessary for validation and, potentially, creation of a predictive risk score that can assist disposition decisions by ED physicians. Additionally, we identified factors which seem unlikely to predict complicated clinical course in these patients. These included extended care facility residence, extremes of age, altered mental status, and suspected genitourinary or skin/soft tissue infection.

The study has several limitations. First, the study included only 105 patients with 34 events. Traditionally for logistic regression 10 events per variable are considered prudent. However, recent evidence indicates that 5–9 events per variable provides similar confidence interval coverage, Type I error rates, and relative bias as the traditional cutoff (28). This number of events per variable may increase Type II error rates. This is particularly concerning where p values and confidence intervals are near significance. However, the confidence intervals and p values for OARS score in our stepwise model is far from significant, making a Type II error unlikely. One exception is the p value observed when OARS was examined in the stepwise model as a dichotomized variable. Given the nonsignificant OR of 2.16 and p value of 0.225, it would not be unreasonable to evaluate OARS in this form in future studies. Regardless, we would suggest caution in interpreting the results of the large stepwise model and use it for purposes of hypothesis generation rather than as a validated clinical decision rule.

Patients who were too ill or had altered mental status were excluded if there was not a surrogate present. This may have led to a selection bias due to the failure to include these patients. The use of medical record review may also introduce bias. However, we took steps to ensure validity of the review and the kappa scores were adequate. Additionally, functional status was not obtained by chart review. As the study data was obtained from one tertiary care center, caution should be used in extrapolating it to other centers. The particular characteristics of our center are apparent in Table 1, for example the large number of immunosuppressed patients.

In conclusion, among older ED patients admitted with infection, functional status does not predict complicated clinical course. Functional status was not a useful marker of short-term need for ICU-level care or deterioration of clinical condition although there was a trend when the functional status measure was dichotomized. Several other variables were predictive including immunosuppression, systolic blood pressure, pulse, metabolic acidosis, presence of severe sepsis/septic shock, and suspected blood stream infection. Emergency physicians could consider these variables as potential indicators of complicated clinical course when making disposition decisions for this patient population. Future studies in large

groups are necessary to validate these factors and to potentially create and validate a predictive risk score that can assist disposition decisions by ED physicians.

Acknowledgments

This study was supported by a Dennis W. Jahnigen Career Development Award sponsored by the American Geriatrics Society, John A. Hartford Foundation, and Atlantic Philanthropies. The project was also supported by Award Number UL1RR025755 from the National Center For Research Resources. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Center For Research Resources, the National Institutes of Health, or other funding agencies.

Sponsor's role: The sponsors had no role in the design, methods, recruitment, data analysis, or preparation of the paper.

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Table 1**Characteristics of the Study Population**

Variable	Number of subjects *	Percent of total or median (interquartile range*)
Age		
65–74 years	57	54.3%
75–84 years	34	32.4%
>=85 years	14	13.3%
Gender		
Female	56	53.3%
Male	49	46.7%
Extended care facility residence	19	18.1%
Non-white race	20	19.0%
Hispanic ethnicity	3	3.1%
Charlson comorbidity score (continuous) (CCM)	--	3 (2–5)
Immunosuppression	59	56.2%
Functional status		
OARS score total (continuous)	--	19 (12–26)
Abnormal OARS score (≥ 25)	76	72.3%
Altered mental status or confusion in the ED	16	15.2%
Infection severity in the ED		
Sepsis	35	33.3%
Severe sepsis	7	6.7%
Septic shock	3	2.9%
Initial ED vital signs		
Hypotension (SBP <90mmHg)	16	15.3%
Systolic blood pressure (continuous)	--	123 (101–144)
Fever (temperature ≥ 38.0 celsius)	28	26.7%
Temperature (degrees celsius)	--	36.9 (36.6–37.6)
Pulse (beats/minute)	--	88 (78–104)
Respiratory rate (breaths/minute)	--	20 (17–20)
Respiratory distress	33	31.4%
Laboratory values in ED		
Abnormal white blood cell count (<5 or ≥10 K/microL)	76	72.4%
Platelets <150,000/mm ³	24	22.9%
Serum bicarbonate (continuous; mmol/L)	--	25 (22–27)
Metabolic acidosis	32	30.5%
Suspected source of infection		
Hematologic	25	23.8%
Central nervous system	1	1.0%
Pulmonary	55	52.4%
Skin and soft tissue	14	13.3%
Genitourinary	18	17.1%

Variable	Number of subjects *	Percent of total or median (interquartile range*)
Gastrointestinal	7	6.7%
Osteomyelitis	3	2.9%
Other	7	6.7%
Outcomes (subjects may have >1 outcome)		
Complicated clinical course	34	32.4%
ICU level care or admission †	26	24.8%
ICU admission	8	7.6%
ICU level care	23	21.9%
Worsening of sepsis criteria during first 48 hours	6	5.7%
Vasopressor use	3	3.0%
In-hospital mortality	7	6.7%

* Values expressed as number with percentage of total (for noncontinuous variables) or as median with interquartile range (for continuous variables)

† Represents combined ICU level care with ICU admission. Some patients met both criteria so numbers do not add to 26

OARS=Older Americans Resources Scale; ED=emergency department; ICU=intensive care unit; SBP=systolic blood pressure

Table 2

Univariate Analysis of Potential Predictors of Complicated Clinical Course

Variable	Odds ratio	95% Confidence Interval	p value
Functional status			
OARS score total (continuous)	0.96	0.92 – 1.01	0.130
Abnormal OARS score (≥ 25)	2.23	0.81 – 6.15	0.119
Age ≥85	0.53	0.14 – 2.03	0.350
Female gender	1.22	0.54 – 2.76	0.636
Extended care facility residence	0.96	0.33 – 2.78	0.934
Nonwhite race	1.15	0.41 – 3.23	0.781
Charlson comorbidity score	1.15	0.99 – 1.34	0.063
Immunosuppression	3.74	1.49 – 9.38	0.005
Altered mental status or confusion in the ED	0.66	0.19 – 2.21	0.495
Initial ED vital signs			
Systolic blood pressure	0.98	0.96 – 0.99	0.005
Hypotension (SBP <90mmHg)	3.29	1.11 – 9.79	0.032
Fever (temperature ≥38.0 celsius)	1.23	0.49 – 3.05	0.660
Temperature (degrees celsius)	1.02	0.97 – 1.06	0.515
Pulse (beats/minute)	1.03	1.01 – 1.05	0.009
Respiratory rate (breaths/minute)	0.95	0.86 – 1.05	0.332
Respiratory distress	0.71	0.28 – 1.74	0.450
Laboratory values in ED			
Abnormal white blood cell count (<5 or ≥10 K/microL)	4.07	1.29 – 12.89	0.011
Platelets <150,000/mm ³	1.34	0.52 – 3.48	0.542
Serum bicarbonate (continuous; mmol/L)	0.94	0.85 – 1.04	0.264
Metabolic acidosis	3.73	1.54 – 9.01	0.003
Severe sepsis or septic shock in the ED	10.6	2.11 – 53.31	0.004
Suspected source of infection			
Hematologic	3.81	1.49 – 9.75	0.005
Pulmonary	0.51	0.22 – 1.17	0.114
Skin and soft tissue	0.81	0.24 – 2.81	0.744
Genitourinary	1.88	0.66 – 5.29	0.234
Gastrointestinal	1.62	0.34 – 7.68	0.543
Osteomyelitis	1.04	0.09 – 11.95	0.971

OARS=Older Americans Resources Scale; ED=emergency department; SBP=systolic blood pressure

Table 3
Multivariable Logistic Regression Models with Complicated Clinical Course as the Dependent Variable

Variables	Odds Ratio	95% Confidence Interval	p value	Model fit p value	Model AUROC
Model 1 - OARS unadjusted					
OARS in ED (continuous)	0.96	0.92 – 1.01	0.130	0.829	0.590
Model 2 - OARS and Charlson index					
OARS in ED (continuous)	0.97	0.92 – 1.02	0.198	0.710	0.620
Charlson comorbidity index (CCM)	1.14	0.98 – 1.32	0.092		
Model 3 - Stepwise model building with OARS forced into model					
OARS in ED (continuous)	1.00	0.94 – 1.08	0.896	0.412	0.839
Immunosuppression	3.45	1.06 – 11.20	0.039		
Systolic blood pressure (continuous)	0.98	0.96 – 1.00	0.016		
Pulse (continuous)	1.03	1.00 – 1.06	0.025		
Metabolic acidosis	3.46	1.08 – 11.09	0.037		
Severe sepsis/septic shock in the ED	10.24	1.44 – 72.79	0.020		
Suspected bloodstream infection	3.56	1.13 – 11.16	0.029		

OARS=Older Americans Resources Scale; ED=emergency department; CCM=Charlson comorbidity index; AUROC=area under receiver operating characteristic curve