Sepsis in nonagenarians admitted to Internal Medicine departments: a comparative study of outcomes

M. VARDI1,2,3, N.O. GHANEM-ZOUBI2, H. BITTERMAN2,3, N. ABO-HELO2, V. YURIN2, G. WEBER2,3 and A. LAOR2,3

From the 1Harvard Clinical Research Institute, 930 Commonwealth Ave., Boston, MA 02110, USA, 2Department of Medicine, Carmel Medical Center, 7 Michal St., Haifa 34362, Israel and 3The Ruth and Bruce Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, P.O.B. 9649, Haifa, 31096, Israel

Address correspondence to Dr M. Vardi, Harvard Clinical Research Institute, 930 Commonwealth Ave., Boston, MA 02110, USA. email: vardi.moshe@gmail.com

Received 23 July 2012 and in revised form 18 October 2012

Summary

Background: Elderly patients are at a higher risk of acquiring sepsis, and are largely being treated in Internal Medicine (IM) departments.

Aim: To characterize the differences between nonagenarians and other age groups in patients admitted to IM departments with sepsis, and to assess predictors for survival in patients older than 90 years of age.

Design and methods: A prospective registry of all-comers with sepsis admitted to IM departments in a community-based Medical Center was built. Patients’ demographics, medical history, clinical presentation and outcomes were recorded and analyzed according to age groups.

Results: One thousand and eighty patients were followed for a mean of 83.63 ± 65.90 days. Nonagenarians constituted 10.93% (118/1080) of our cohort. Of these, 70.48% had a cognitive impairment and 82.60% had reduced functional state. Of these, 5.61 and 10.50% fulfilled the criteria of septic shock and severe sepsis, respectively. Sepsis category was significantly influenced by age groups (P<0.001). Complications secondary to sepsis at admission and throughout hospitalization, and mortality rates, were higher in the nonagenarian population (61.86 vs. 51.14%, P=0.032 and 37.29 vs. 20.06%, P<0.001, respectively), and overall survival was significantly lower in the nonagenarian population (40.68 vs. 66.84%, P<0.001).

Conclusions: Patients treated in IM departments for sepsis are old, and a significant percentage is older than 90 years of age with reduced function and mental status at baseline. These frail patients are afflicted by a worse outcome, which is most likely associated with poor functional status at baseline and severe deconditioning during the acute illness. Prognostic tools are needed to address today’s trends in patient-mix and disease severity, specifically for very-old patients admitted with sepsis cared for in IM departments.

Introduction

Aging people now constitute a significantly larger portion of the population than they did before. People aged >85 years now constitute 1.8% of the US population.1 Concomitant with the prolonged longevity of the population in developed countries, there is a rapid increase in the hospitalization rates of the oldest population. Recent studies have shown this trend. In Spain, the percentage of nonagenarian patients admitted to the medical services is gradually increasing and is already ~6%.2 This trend and its effect on patient complexity were also shown in a recent survey of hospitalized patients.
in Internal Medicine (IM) departments across Europe,\textsuperscript{3} in which the median age of admitted patients was 67 years (ranging up to 99). They carried a median of three chronic medical diagnoses at admission (ranging up to 18), and had a median of four prescribed drugs at the time of admission (ranging up to 21). In this survey, infection was the second leading diagnosis at discharge.

Nonagenarian patients have distinct characteristics. A previous report on 482 admissions of 333 patients aged >90 years from our department revealed a high rate of residency in nursing institutions (50%).\textsuperscript{4} Acute infectious disease was the leading hospitalization diagnosis (57%), and in-hospital mortality rate was 22%. Admission due to an infectious disease was significantly correlated to in-hospital and post-discharge mortality.

Sepsis is a prevalent, serious and resource-consuming medical condition. The incidence of sepsis has increased by 8.7% annually over the years between 1979 and 2000.\textsuperscript{5} Sepsis is the 10th leading cause of overall death in the USA, rising to sixth place when pneumonia and influenza are included.\textsuperscript{6} Although the in-hospital mortality rate from sepsis had decreased from 27.8% between 1979 and 1984 to 17.9% between 1995 and 2000, the absolute number of deaths had increased due to its increasing incidence.\textsuperscript{5} As the population is getting older, more septic patients in the very old-age group are expected to be cared by internists in IM wards.\textsuperscript{7} The purpose of the current study was to assess the differences in outcomes in patients older than 90 years vs. younger patients, admitted to IM wards with sepsis, and to assess predictors for survival in nonagenarians.

**Data collection**

The prospective collection of data through the electronic medical record system has been previously described.\textsuperscript{9} In short, we collected demographic and clinical data, as well as rates of death for a mean follow-up period of 86.63 ± 65.9 days. For the purpose of this analysis, we collected additional data from patient’s charts, which included information on chronic medical conditions, and rates of in-hospital complications. Baseline functional and cognitive statuses were collected from patients’ medical records. A more formal assessment was impossible in the setting of this study. Complications were recorded according to predefined strict criteria as described in Supplementary Table S1, and in accordance with acceptable guidelines of leading medical associations.

**Statistical methods**

A comparison between nonagenarians and other patients was performed. Continuous variables were assessed with the student’s \(t\)-test. Variables that cannot be claimed to have a normal distribution were compared via the Mann–Whitney test. Categorical variables were compared with the Chi-square test. Survival analysis was performed with Cox’s proportional hazards model. For analyzing predictors of in-hospital death, we used logistic regression. All analyses were performed by SAS software (version 9.2) and SAS procedures are MEANS, FREQ, TTEST, LOGISTIC, LIFETEST and PHREG.\textsuperscript{10} The study was approved by the Carmel Medical Center Institutional Review Board Committee. The need for informed consent was waived.

**Results**

For this current analysis, we included data of 1080 patients admitted to the division of IM throughout the 15-month study period that met criteria of sepsis on admission. The mean age of our study group was 74.7 ± 16.1. One hundred and eighteen patients (10.93%) aged >90 years and five (0.46%) aged >100 years. Table 1 details the demographics of our patient population. In the nonagenarian patient cohort, more patients were of female gender (58.78 vs. 46.67%, \(P=0.038\)), more resided in long-term care facilities (43.22 vs. 17.66%, \(P<0.001\)), more had a decreased functional status (82.60 vs. 48.37%, \(P<0.001\)) and more had cognitive impairment (70.48 vs. 33.45%, \(P<0.001\)). Additionally, more patients aged >90 years had hypertension (77.12 vs. 64.45%, \(P=0.006\)) and chronic kidney disease (33.90 vs. 24.12%, \(P=0.020\)), but fewer

**Methods**

**Patients**

We prospectively collected data of consecutive patients admitted to a 110-bed division of IM from 1 February 2008 to 30 April 2009 in a 450-bed community-based university affiliated hospital in Haifa, Israel. All patients were aged >18 years, and had a presumed diagnosis compatible with sepsis. The patients were identified automatically using the definition of sepsis determined by the American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference in 1991,\textsuperscript{8} i.e. any patient admitted with suspected infection and clinical criteria of systemic inflammatory response syndrome (SIRS).
had diabetes mellitus (16.49 vs. 38.57%, \(P < 0.001\)) or cancer (12.71 vs. 21.21%, \(P = 0.030\)).

Most of our study population (96.20%) was admitted to IM through the Emergency Department, with the rest being transferred from other departments in the hospital. Leading suspected sources of infection on admission for the entire cohort and for the nonagenarian cohort were pneumonia (43.09 and 43.10%, respectively) and urinary tract infection (27 and 41.38%, respectively).

On admission, 5.61% of our study cohort fulfilled the criteria of septic shock and 10.50% met criteria of severe sepsis. Sepsis category was significantly influenced by age groups, with elderly patients being admitted in a worse clinical condition (\(P < 0.001\)) (Figure 1).

During the course of their hospitalization, patients aged >90 years incurred more complications than younger patients. In the nonagenarian population, 61.86% were diagnosed with at least one complication at admission or during the hospital course, vs. 51.14% in the younger cohort (\(P = 0.032\)). Specifically, older patients were more likely to be diagnosed at admission with acute myocardial infarction (9.32 vs. 3.22%, \(P = 0.001\)) and acute renal failure (33.90 vs. 24.12%, \(P = 0.020\)). In-hospital mortality was significantly higher in the nonagenarian population (37.29 vs. 20.06%, \(P < 0.001\)). Overall survival in a mean follow-up of 83.63 ± 65.90 days (range 0–452) was also significantly affected by age (40.68 vs. 66.84%, for nonagenarians vs. others, respectively; \(P < 0.001\)). Figure 2 shows the survival curves for nonagenarians and for the different age groups. Analyses of survival for nonagenarians vs. younger patients and for the different age groups, showed a statistically significant difference among the groups (\(P < 0.001\)). Patients >90 years of age died sooner. The median day of death of the 25th percentile for nonagenarians was 8 days \([95\% \text{ confidence interval (CI) 4–18}]\), compared to 40 days \((95\% \text{ CI 28–58})\) in the younger cohort.

We analyzed predictors for overall survival in patients older than 90 years of age. Higher urea and a higher respiratory rate were associated with poor outcome [hazard ratio (HR): 1.01, \(P < 0.001\) and HR: 1.05, \(P = 0.013\), respectively], while a higher Glasgow Coma Scale upon admission and a higher systolic blood pressure were associated with a better prognosis (HR: 0.91, \(P < 0.003\) and HR: 0.99, \(P = 0.040\), respectively). Baseline functional status was a significant predictor of survival in patient younger than 90 years of age (\(P < 0.001\)). This trend was also found in the older patients group, but did not reach statistical significance (\(P = 0.06\)).

### Table 1  Baseline characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Overall (n = 118)</th>
<th>Age ≥90 years (n = 962)</th>
<th>(P)-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>516 (47.78)</td>
<td>67 (58.78)</td>
<td>449 (46.67)</td>
</tr>
<tr>
<td>Residency at long-term care facilities</td>
<td>221 (20.46)</td>
<td>51 (43.22)</td>
<td>170 (17.66)</td>
</tr>
<tr>
<td>Functional status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Debilitated</td>
<td>438 (41.17)</td>
<td>82 (71.30)</td>
<td>356 (37.51)</td>
</tr>
<tr>
<td>Partially debilitated</td>
<td>116 (10.90)</td>
<td>13 (11.30)</td>
<td>103 (10.85)</td>
</tr>
<tr>
<td>Normal</td>
<td>510 (47.93)</td>
<td>20 (17.39)</td>
<td>490 (51.63)</td>
</tr>
<tr>
<td>Cognitive status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>609 (61.70)</td>
<td>31 (29.52)</td>
<td>578 (58.56)</td>
</tr>
<tr>
<td>Impaired</td>
<td>369 (37.39)</td>
<td>74 (70.48)</td>
<td>295 (33.45)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>710 (65.74)</td>
<td>91 (77.12)</td>
<td>619 (64.35)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>387 (35.83)</td>
<td>23 (19.49)</td>
<td>364 (37.84)</td>
</tr>
<tr>
<td>Smoking</td>
<td>151 (13.98)</td>
<td>5 (4.24)</td>
<td>146 (15.18)</td>
</tr>
<tr>
<td>Ischemic heart disease</td>
<td>441 (40.83)</td>
<td>54 (45.76)</td>
<td>387 (40.23)</td>
</tr>
<tr>
<td>CHF</td>
<td>375 (34.72)</td>
<td>46 (38.98)</td>
<td>329 (34.20)</td>
</tr>
<tr>
<td>COPD</td>
<td>144 (13.33)</td>
<td>9 (7.63)</td>
<td>135 (14.03)</td>
</tr>
<tr>
<td>Bronchial asthma</td>
<td>30 (2.78)</td>
<td>2 (1.69)</td>
<td>28 (2.91)</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>304 (28.15)</td>
<td>46 (38.98)</td>
<td>258 (26.82)</td>
</tr>
<tr>
<td>Dialysis treatment</td>
<td>32 (2.96)</td>
<td>6 (5.08)</td>
<td>26 (2.70)</td>
</tr>
<tr>
<td>Liver cirrhosis</td>
<td>19 (1.76)</td>
<td>1 (0.85)</td>
<td>18 (1.87)</td>
</tr>
<tr>
<td>Active cancer</td>
<td>223 (20.65)</td>
<td>15 (12.71)</td>
<td>208 (21.62)</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>70 (6.48)</td>
<td>0 (0.0)</td>
<td>70 (7.28)</td>
</tr>
</tbody>
</table>

Data are given in number of patients (%). CHF: congestive heart failure; COPD: chronic obstructive pulmonary disease.
In this study, we examined the differences in characteristics and outcomes of a distinct age group (nonagenarians) in a large prospective cohort of patients with sepsis treated in IM departments in a single community-based institute. Our results show that the very old patient population, i.e. those aged >90 years of age, bare more chronic medical disorders, are admitted in a worse clinical

**Figure 1.** Severity of presentation in different age group.

**Figure 2.** Effect of age on overall survival in different age groups.

**Discussion**

In this study, we examined the differences in characteristics and outcomes of a distinct age group (nonagenarians) in a large prospective cohort of patients with sepsis treated in IM departments in a single community-based institute. Our results show that the very old patient population, i.e. those aged >90 years of age, bare more chronic medical disorders, are admitted in a worse clinical
condition, suffer from a higher rate of complications throughout their hospital course and are more likely to die within and after the hospitalization.

Each year, ~750,000 patients in the USA develop severe sepsis, and >60% of these patients with sepsis are >65 years of age. In the USA, ~2500 cases of sepsis occur per 100,000 persons aged 85 years or older. The number of octogenarians with sepsis is expected to double by the year 2300. The annual incidence of severe sepsis is reported to be >100 times greater in individuals older than 85 years than the incidence noted among individuals 5–14 years of age. Moreover, patients with sepsis admitted to Emergency Departments are hospitalized in 84% of the cases, but only a fraction of these (12%) are eventually hospitalized in intensive care settings, while the rest are treated in general wards. Thus, understanding the specific characteristics of this growing population, their overall outcome and the risk factors for mal-prognosis is of importance.

Risk factors for sepsis in the old are diverse and include co-morbid illnesses, exposure to instrumentation and procedures, institutionalization, malnutrition and poor performance status. Given the number of co-morbidities in today’s IM patients, the high rate of residence in long-term care facilities, the low baseline functional status and the effect of immunosenescence (i.e., gradual deterioration of the immune response in elderly patients), it is not surprising that hospitals are facing increased resource allocations toward treating the very old. In 1995, >52% of the costs associated with sepsis were attributable to the care of patients older than 65 years of age, and 30.8% of that cost was attributable to the care of patients older than 75 years of age.

In our cohort, patients older than 90 years died in excess and sooner, compared to younger patients. Angus et al. reported a 28.6% overall mortality rate associated with sepsis, whereas among patients older than 85 years mortality rate was 38.4%. These figures are similar to those found in the current analysis. Older patients who are admitted to hospital with sepsis are also prone to severe deconditioning, and hence may eventually be released to institutions rather than back to their homes. Indeed, the overall survival in our cohort of patients in a follow-up of up to 452 days was only slightly higher than 40% in patients >90 years of age, compared to ~60% in the control group. Therefore, surviving hospitalization in these frail patients does not necessarily predict the true consequences of sepsis.

In the very old patient population, there were no strong predictors of survival. Those that were found to be statistically significant in our analysis had a subtle clinical effect. It is likely that the overall status of the very old, including their co-morbidities, functional and mental status and type of residence dilute any other direct effects that can be observed in this population. In a report based on a cohort of 137 patients aged >70 years with sepsis, Regazzoni et al. found that the functional status and organ failure were independent predictors of survival. We have found that the baseline functional status was indeed a predictor for survival in patients younger than 90 years, but this trend was no longer statistically significant when the analysis was confined to nonagenarians. In a previous analysis from this cohort of patients, we analysed the applicability of four scoring systems in IM patients with sepsis: the Modified Early Warning Score, the Simple Clinical Score, the Mortality in Emergency Department Sepsis and the Rapid Emergency Medicine Score. These tools should be re-assessed to validate their applicability in the nonagenarian population.

Our study has some limitations. Despite being prospective in design, the current analysis is a post hoc analysis. Only a limited number of data items were collected retrospectively from electronic medical records to comply with the objectives of the current analysis, while death, which was defined as the primary objective for this analysis was collected prospectively. This limitation is mitigated by the use of Ofek system, which has the strength of covering full hospital and community patient level clinical, laboratory and imaging data, and by the fact that most of our patients are likely to be readmitted to our services if needed. Of note is the lack of formal assessment of patient cognitive impairment, dictated by the nature of patient presentation at enrollment. These data were collected prospectively from patients and families, referral notes and the Ofek system. Additional relevant baseline clinical characteristics not collected in this study may also affect the outcomes in this patient cohort. Those collected are mainly driven by their inclusion in the clinical risk assessment scores relevant to admission of septic patient in IM departments. Additional research into this patient population is warranted to deepen our understanding of this group of patients. The size of the current cohort of patients, being one of the biggest prospective representations of septic patients treated in a community-based IM service is unique. Additionally, we had no exclusion criteria and all consecutive patients with sepsis were included. Thus, our cohort is likely to be externally valid, reflecting the trends in sepsis care both in terms of complexity of patients, and outcomes. The cohort of patients represented in this analysis...
is old, and some may argue may not accurately reflect current IM admittance characteristics. We believe that the data represent the demographics of patients in a growing number of community-based medical centers, and in view of life longevity trends are likely to become even more relevant in the near future.

To conclude, this study shows the complex and fragile nature of nonagenarians admitted to IM departments with sepsis. As more and more patients with sepsis are treated in IM departments, and as the overall population admitted to IM wards is ageing, it is of utmost importance to continue and study this age group in the current setting as well as in other clinical domains.

**Supplementary Material**

Supplementary material is available at QJMED online.

**Conflict of interest:** None declared.

**References**


