

# Nonagenarians in Internal Medicine: Characteristics, Outcomes and Predictors for In-hospital and Post-discharge Mortality

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**ABSTRACT:** **Background:** Parallel to increased life expectancy, the number of very elderly patients hospitalized in internal medicine departments is growing rapidly, although clinical data on hospital care are lacking.

**Objectives:** To investigate the sociodemographic data, hospitalization characteristics and outcomes of nonagenarian patients, as these measures are necessary for evaluating prognostic information and predictors of mortality.

**Methods:** We reviewed the medical records of all patients aged  $\geq 90$  hospitalized in our institute's Department of Internal Medicine. The data comprised 482 admissions of 333 patients hospitalized over a one year period.

**Results:** Half of the study patients were residents of nursing institutions. A high rate of atrial fibrillation was documented (106 patients, 32%). Acute infectious diseases constituted the leading diagnosis (276/482 admissions, 57%), followed by acute coronary syndrome (17% of admissions). In-hospital mortality occurred in 74 patients (22%). Chronic therapy with statins or acetylsalicylic acid was inversely related to mortality ( $P < 0.05$ ). The main predictors for in-hospital death of nonagenarians were pressure sores, older age, atrial fibrillation, malignant disease, and admission due to an acute infection, especially *Clostridium difficile*-associated diseases. In addition, mental decline, permanent urinary catheter, leukocytosis, renal failure and hypoalbuminemia predicted post-discharge mortality. Admission due to an infectious disease but not acute coronary syndrome was significantly correlated to in-hospital and post-discharge mortality ( $P < 0.001$ ).

**Conclusions:** Hospitalized nonagenarians comprise a growing group with distinct characteristics and increasing significance in the daily practice of internal medicine departments. Comprehensive assessment of the elderly at admission together with identification of the above clinical and laboratory risk factors for mortality will help determine in-hospital management, discharge planning and rehabilitation programs.

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**KEY WORDS:** nonagenarians, hospitalization, mortality, predictors, internal medicine

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In recent years we have been witnessing a reduction in late-life mortality, together with increased life expectancy and expansion of the older sector of the population. Nonagenarians (people in their nineties) now comprise a significantly larger population than they did before. The number of the oldest old in the United States is expected to double within 30 years [1]. Similarly, about 20% of people born in the last decade in Israel are expected to live at least to the age of 90 (assuming constant mortality patterns) [2]. In keeping with this trend, the saying "the nineties are the new eighties" is in fact becoming true [3]. Concomitant with the prolonged longevity of our society, there is a rapid increase in the hospitalization rates of the oldest population. Clinicians nowadays attend many more nonagenarian patients than before, especially in internal medicine departments. These departments are the major health care providers for the elderly in medical institutions, given the dearth of hospitalization beds in geriatric wards.

Aging itself is associated with deterioration in health status, and acute hospitalization of the elderly even more so. The latter can be a double-edged sword for this population, as it might be followed by progressive physical and functional decline and increased in-hospital and post-discharge mortality. Most of the literature data on this subset of nonagenarian patients are the result of community-based surveys [4-7], whereas hospitalization-based data in the literature focus on surgical patients, especially regarding issues of interventional procedures in the very old [8-10]. On the other hand, clinical data on the acute care of nonagenarian patients in internal medicine departments are lacking. Moreover, old age by itself is an exclusion criterion in many clinical trials and, commonly, the results of studies of younger patients are extrapolated to the very old population. Only a few studies have evaluated, independently, predictors of mortality in cohorts of nonagenarian patients in internal medicine [11,12].

The main objective of the present study was to evaluate the sociodemographic, functional and clinical data collected at the admission of nonagenarian patients, as well as hospitalization characteristics and outcomes. These measures provide

essential information on health status and hospital care of this population, enabling the evaluation of prognostic information and predictors of in-hospital and post-discharge mortality.

**PATIENTS AND METHODS**

For this observational cohort study, data were collected in the internal medicine department of the Carmel Medical Center, a 106-bed department in a 450-bed general community hospital affiliated with the Technion's Faculty of Medicine in Haifa, Israel. Included in the study were all patients aged 90 and above hospitalized in the internal medicine department during the year 2006 (total of 333 patients, admitted 482 times during the study period). The institutional ethics committee approved the study.

The medical records of all participants were collected from the department or hospital archive and examined by one researcher, using a predetermined data collection form. The following data were collected:

• **Sociodemographic and functional data**

Sociodemographic data included age, gender, and place of residency. Functional, mental and cognitive status at admission was assessed according to the Carmel Hospital nurses' admission scale, calculated for each patient at arrival (an expanded scaled assessment form based on the Norton risk assessment score [13] with additional cognitive assessment). Also recorded were medical data concerning urination, feeding, presence of pressure sores, and utilization of chronic oxygen therapy at home.

• **Medical status before hospitalization**

Patients' co-morbidities were documented. Each patient's chronic drug therapy and total number of drugs was recorded.

• **Clinical information during hospitalization**

This included the number of admissions during 2006, duration of hospitalizations, basic laboratory tests at admission, and major discharge diagnoses for each admission.

• **Hospitalization outcomes**

Discharge destination and mortality during hospitalization were documented for each patient. In addition, up to 2 year post-discharge mortality was examined by collecting computerized data on mortality from the health management organization.

**STATISTICAL ANALYSIS**

Continuous data are reported as means ± standard deviation, and categorical variables as numbers, percentages or proportions. Student's *t*-test was used to compare continuous variables. Chi-square tests were used to compare categorical variables, which were checked for correlation with in-hospital mortality. The main covariates, which were significantly associ-

ated with mortality, were analyzed using a multivariate logistic regression model in order to test the unique effect of patients and hospitalization variables on in-hospital mortality. An adjusted odds ratio with a 95% confidence interval was used. Predictive out-of-hospital survival analysis was performed using the Cox proportional hazard regression model. Adjusted hazard ratios and 95% CI were estimated. Survival curves were plotted by the Kaplan-Meier method. The results were considered statistically significant when the *P* value was < 0.05. Statistical analyses were performed using SAS software.

**RESULTS**

**PATIENTS' CHARACTERISTICS**

During the study period, a total of 482 admissions of 333 patients aged 90+ were documented in the internal medicine department. Baseline patient characteristics are presented in Table 1. The mean age of the study population was 93.1 ± 2.9

CI = confidence interval

**Table 1.** Baseline patient characteristics, and univariate correlation with in-hospital mortality

	No. (%) (n=333)	Discharged alive (n=259)	In-hospital mortality (n=74)	P value
Age (mean ± S.D)	93.1 ± 2.9	92.7 ± 2.6	94.2 ± 3.3	0.001
Gender: female	190 (57%)	152	38	0.288
Residence: nursing institution	168 (50.5%)	129	39	0.661
<b>Function</b>				
Independent	68 (20.4%)	61	7	
Mildly impaired	65 (19.5%)	56	9	
Moderately impaired	66 (19.8%)	54	12	
Fully dependent	134 (40.2%)	88	46	< 0.0001*
<b>Mental</b>				
Full consciousness	154 (46.2%)	134	21	
Mild confusion	80 (24%)	62	18	
Significant confusion	89 (26.7%)	59	30	
Unconsciousness	10 (3%)	4	5	< 0.0001*
<b>Cognitive</b>				
Full comprehension	164 (49.2%)	143	21	
Inadequate orientation	52 (15.6%)	33	19	
Dementia	117 (35%)	83	34	0.002*
Urination: urinary catheter or nephrostomy	54 (16.2%)	30	24	< 0.0001
Feeding: nasogastric tube or percutaneous gastrostomy	13 (4%)	11	2	0.246
Home oxygen therapy	15 (4.5%)	14	1	0.138
Pressure sores	69 (20.7%)	39	30	< 0.0001

\* *P* value calculated for ordinal variables in each group.

years (range 90–106) and the female/male ratio was 1.3. Half of the study population were residents of nursing homes. Forty percent of the patients were functionally independent or had mild impairment in activities of daily living functioning before hospitalization, and 154 (46%) and 164 (49%) were defined as having normal mental and cognitive functioning, respectively. Dementia was a past or present diagnosis in 117 patients (35%). Pressure sores of various degrees were documented in 69 patients (21%). Feeding and urination patterns are presented in Table 1. The leading co-morbid medical conditions were hypertension in 63% (209 patients), ischemic heart disease (45%) and chronic heart failure (38%). Atrial fibrillation was a past or present diagnosis in 106 patients (32%). The mean number of chronic drugs per patient was  $6 \pm 2.8$  (range 0–15), of which acetylsalicylic acid was the most common (45%), followed by beta-blockers (39%), angiotensin-converting enzyme inhibitors (35%), and calcium channel blockers (33%). In 29 patients (9%), antipsychotic drugs were newly added during hospitalization.

#### HOSPITALIZATION CHARACTERISTICS AND OUTCOME

The mean duration of hospitalization was  $6.3 \pm 3.9$  days (range 1–29 days). Basic laboratory blood tests on admission are presented in Table 2. About one-third of the patients had hypoalbuminemia  $< 3$  g/dl, and one-quarter had anemia with

hemoglobin levels  $< 10.3$  g/dl. More than half the patients had renal failure, with a mean creatinine/urea level of 1.53/76 mg/dl (median 1.21/61 mg/dl). Relatively low mean absolute lymphocyte counts of  $1.22 \pm 0.6$  ( $\times 10^3/\text{mm}^3$ ) were documented on admission.

Acute infectious disease was observed in 276 of 482 admissions (57%) and was the leading admission diagnosis. Urinary tract infection, observed in 151 admissions (31%), was the major infectious disease. Of the positive urinary cultures, 24 (20%) were positive for extended-spectrum beta-lactamase and required broad-spectrum antibiotics. Pneumonia was documented in 100 admissions (21%). Less common were bronchitis (6%), bacteremia, soft tissue infections, osteomyelitis, and pseudomembranous enterocolitis (4% each). Antibiotic treatment was initiated in the emergency room in 109 of the 276 patients with an acute infectious disease. The mean time to first antibiotic dose (from arrival to the emergency room) was  $4.6 \pm 3.2$  hours (range 0.5–18.5, median 4 hours). Acute coronary syndrome was less prevalent than acute infectious disease and was observed in 82 admissions (17%) only; most of them (73%) were classified as non ST-elevation myocardial infarction.

Overall, 74 patients died during hospitalization (22% of patients). Of the 482 admissions, 317 (66% of hospitalizations) ended with discharge back to the original site of residence, and in 51 admissions (11%) the patients were transferred to a subacute hospitalization unit in a geriatric institute for complete medical treatment, such as intravenous antibiotic therapy. The rest of the patients were transferred to the geriatric department (18 admissions, 4%) and to other in-hospital departments according to medical needs.

#### CORRELATIONS AND PREDICTORS OF MORTALITY

Univariate correlations of baseline patient characteristics with in-hospital mortality are presented in Table 1. Older age, deterioration in functional, mental and cognitive capacity, pressure sores and the presence of a permanent urinary catheter were each significantly correlated with in-hospital mortality, in contrast to gender, place of residency and mode of feeding. Atrial fibrillation and past or present malignant diseases were the only two co-morbid conditions significantly correlated with in-hospital mortality. Chronic drug therapy with statins (HMG-CoA reductase inhibitors) or acetylsalicylic acid was associated with reduced risk of dying while in hospital. Lower blood albumin levels, elevated creatinine and urea, as well as elevated leukocyte and neutrophil levels were all risk factors for in-hospital death [Table 2]. Admission due to an acute infectious disease, as well as the need for inotropic therapy and occurrence of diarrhea with positive fecal *Clostridium difficile* toxin were strongly correlated with in-hospital mortality ( $P < 0.0001$  each). However, compared to an acute infectious disease, the presence of acute coronary

**Table 2.** Hospitalization characteristics, and univariate correlation with in-hospital mortality\*

Variable	All patients (n=333)	Discharged alive (n=259)	In-hospital mortality (n=74)	P value
No. of hospital admissions	1.44 $\pm$ 0.9	1.43 $\pm$ 0.9	1.5 $\pm$ 0.9	0.552
No. of hospitalization days in 2006	9.1 $\pm$ 8.2	8.9 $\pm$ 7.9	9.9 $\pm$ 9.5	0.359
<b>Mean laboratory values on admission</b>				
Albumin (g/dl)	3.22 $\pm$ 0.55	3.31 $\pm$ 0.47	2.91 $\pm$ 0.61	$< 0.0001$
Sodium (mEq/L)	137 $\pm$ 7.2	136.6 $\pm$ 6.8	139.1 $\pm$ 8.4	0.013
Hemoglobin (g/dl)	11.4 $\pm$ 1.8	11.6 $\pm$ 1.9	11.2 $\pm$ 1.9	0.097
MCV ( $\mu\text{m}^3$ )	85.9 $\pm$ 6.9	85.5 $\pm$ 7.2	87.4 $\pm$ 6.7	0.054
Creatinine (mg/dl)	1.57 $\pm$ 1.1	1.4 $\pm$ 1	1.8 $\pm$ 0.9	0.005
Urea (mg/dl)	78.1 $\pm$ 46.8	70.5 $\pm$ 43.2	94.1 $\pm$ 48.7	$< 0.0001$
Leukocyte count ( $\times 10^3/\text{mm}^3$ )	13.41 $\pm$ 20.3	10.9 $\pm$ 4.9	16.5 $\pm$ 13.7	$< 0.0001$
Neutrophils (%)	78.8 $\pm$ 11.1	78 $\pm$ 11.2	83.5 $\pm$ 9.3	$< 0.0001$
Lymphocyte count ( $\times 10^3/\text{mm}^3$ )	1.2 $\pm$ 0.60	1.3 $\pm$ 0.6	1.1 $\pm$ 0.7	0.067
Acute coronary syndrome	68 (20.4%)	47	21	0.054
Acute infectious disease	200 (60%)	139	61	$< 0.0001$
Inotropic therapy	15 (4.5%)	1	14	$< 0.0001$
Pseudomembranous colitis	11 (3.3%)	3	8	$< 0.0001$

\* Data are presented as mean  $\pm$  SD for laboratory values, number of admissions and hospitalization days. The remaining variables are presented as number (percentage). MCV = mean corpuscular volume.

disease showed only a positive trend with in-hospital mortality in univariate analysis ( $P = 0.054$ ) [Table 2]. The number of hospital admissions in one year and the total number of hospitalization days were not found to be positively correlated with in-hospital mortality. Predictors of in-hospital mortality were examined by a multivariate logistic regression model [Table 3]. Of the patient baseline variables, the presence of pressure sores (OR 2.7, 95% CI 1.4–5.2), malignant disease and atrial fibrillation in the past or present (OR 3.3, 95% CI 1.7–6.2; OR 2.1, 95% CI 1.1–3.8, respectively), and older age (OR 1.16, 95% CI 1.06–1.29) significantly increased the risk of dying in the hospital. From the hospitalization characteristics, acute infectious disease (OR 2.8, 95% CI 1.4–5.8) and particularly positive fecal *Clostridium difficile* toxin (OR 7.2, 95% CI 1.7–31) were the significant predictors of in-hospital mortality in multivariate analysis [Table 3]. From the 259 patients discharged alive from the hospital, 145 (56%) died during the post-discharge follow-up period. The parameters independently associated with post-discharge mortality in multivariate analysis were older age (hazard ratio 1.08, 95% CI 1.03–1.13,  $P = 0.003$ ), deteriorating mental capability (HR 1.26, 95% CI 1.06–1.50,  $P = 0.009$ ), non-spontaneous urination (HR 1.56, 95% CI 1.14–2.13,  $P = 0.005$ ), elevated white blood cell count and urea levels (HR 1.02, 95% CI 1.01–1.02,  $P < 0.0001$ ; HR 1.005, 95% CI 1.002–1.007,  $P = 0.001$ , respectively), the presence of atrial fibrillation (HR 1.59, 95% CI 1.18–2.14,  $P = 0.003$ ), and the need for inotropic drug therapy (HR 2.34, 95% CI 1.17–4.67,  $P = 0.016$ ). Higher albumin levels were associated with reduced post-discharge mortality (HR 0.42, 95% CI 0.31–0.57,  $P < 0.0001$ ). Some of these predictive factors for post-discharge death are presented by survival curves in Figure 1. As observed in the univariate analysis of in-hospital mortality patterns, post-discharge mortality analysis also indicates that an acute infectious disease (and not acute coronary syndrome) was significantly correlated with mortality [Figure 1].

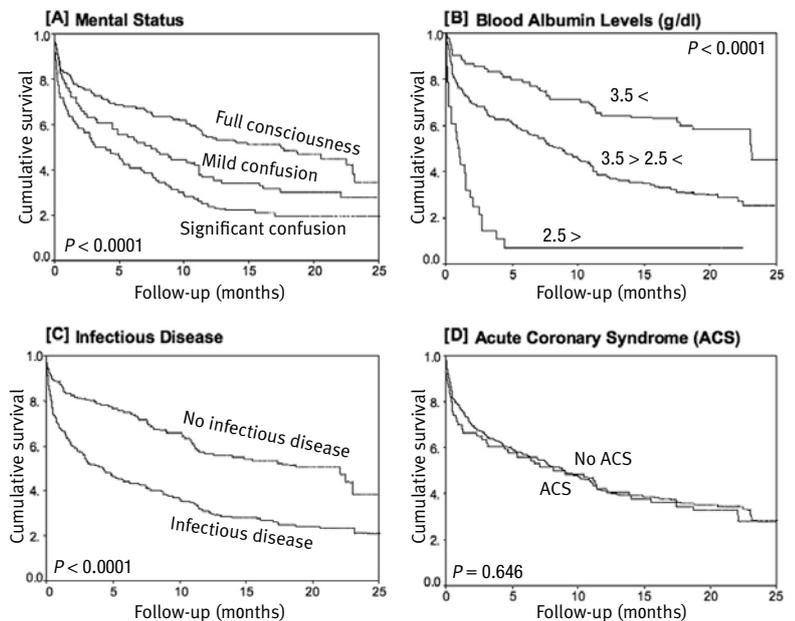
**DISCUSSION**

The population of hospitalized nonagenarians in internal medicine departments is rapidly increasing. The sociodemographic analysis of our study cohort shows that despite their advanced age, almost half of the patients were living in their own homes before hospitalization and were evaluated as functionally independent with normal or mildly impaired mental and cognitive abilities. Functional, mental and cognitive abilities, in addition to urination and feeding status and the presence of pressure sores, were strongly correlated with in-hospital mortality. In addition, mental capability and

**Table 3.** Multivariate logistic regression model for prediction of in-hospital mortality

Variable	$\chi^2$ score	Adjusted odds ratios (95% confidence limits)	P value
<b>Pre-hospitalization parameters</b>			
Age	10.45	1.16 1.06–1.29	0.001
Pressure sores	22.75	2.72 1.43–5.22	< 0.0001
Malignant disease	13.1	3.27 1.72–6.23	0.0003
Atrial fibrillation	5.40	2.05 1.11–3.79	0.002
<b>Hospitalization parameters</b>			
Acute infectious disease	7.61	2.84 1.39–5.81	0.006
<i>Clostridium difficile</i> toxin	13.86	7.24 1.70–30.84	0.0002

**Figure 1.** Cumulative survival rates 2 years post-discharge, related to patients and hospitalization characteristics



permanent urinary catheter were significant predictors of post-discharge death. A decline in functional and cognitive status has been reported as a significant risk factor for mortality in several studies. The NonaSantfeliu Study, evaluating one year mortality patterns in nonagenarian populations, reported similarly that a decline in functional and cognitive status was associated with increased one year mortality rates in univariate but not multivariate analysis [14]. The Danish 1905 cohort survey found that a high disability level and poor physical and cognitive performance of nonagenarians predicts mortality within 15 months of follow-up [4]. It should be emphasized that these studies were community population-based studies and did not evaluate hospitalized patients as did the current study. The findings of Yust-Katz et

OR = odds ratio  
HR = hazards ratio

al. [15] in nonagenarians hospitalized in a geriatric hospital showed similar results, namely, that the main prognostic factors were continence and functional state prior to admission. Overall, these data underscore the importance of evaluating the functional capabilities of elderly patients at admission in order to assess outcomes of hospitalization and predictors of death and, accordingly, to provide adequate in-hospital care that will reduce risk factors for disability and death.

The major co-morbidities in the current study were cardiovascular diseases. Interestingly, a high prevalence of atrial fibrillation (32%) was demonstrated, as compared to a lower prevalence of about 10% reported in octogenarians [16]. Moreover, in univariate and multivariate analyses the diagnosis of atrial fibrillation was significantly associated with in- and out-of-hospital mortality, possibly related in part to the high rate of cardiovascular diseases with advancing age. Hypertension was the most prevalent co-morbid diagnosis. Four classes of antihypertensive drugs were used, each by 24%–39% of the patients, indicating utilization of several antihypertensive drugs by each patient. In the present study, hypertension was not significantly associated with increased in-hospital and post-discharge mortality. Blood pressure levels are known in the literature to be related to the risk of stroke and death, especially from cardiovascular diseases. However, evidence that treating very old patients with antihypertensive drugs is beneficial is inconclusive, and several studies previously showed reduced survival rates after lowering blood pressure in the very old despite decreasing the risk of stroke and cardiovascular disease [17,18]. The recent HYVET trial addressed this issue and demonstrated that treating hypertension in patients above the age of 80 in order to achieve a target blood pressure of 150/80 mmHg is indeed beneficial and is associated with reduced risk of death from any cause [19].

Regarding chronic drug therapy, univariate analysis showed that statins and acetylsalicylic acid were the only drugs in our study associated with reduced in-hospital mortality. These two drugs are widely utilized for primary and secondary prevention of cardiovascular events and are associated with reduced mortality and morbidity in a variety of endpoints. A recent meta-analysis of 51,351 older individuals showed that statin therapy reduced all causes of mortality by 15% (95% CI 7%–22%) [20]. In light of the under-utilization of these drugs in the very old, partially due to concerns of adverse reactions in the elderly and their reduced life expectancy, future studies should be conducted to establish the efficacy and safety of these drugs in the very old population and to evaluate their use.

Our study demonstrates that several laboratory values on admission to hospital are significantly associated with mortality. Advanced renal failure, leukocytosis, neutrophilia and hypoalbuminemia were all risk factors for in-hospital death in univariate analysis, and predictors for post-discharge mor-

tality in Cox regression survival analysis. Reduced albumin levels indicate low nutritional status and frailty in the elderly population and hence are a risk factor for death when this population is hospitalized. In this regard, Sonnenblick and co-researchers [12] demonstrated that low albumin levels were related to in-hospital mortality in a cohort of elderly patients admitted to an internal medicine department, and Iwata et al. [21] showed hypoalbuminemia to be predictive of post-discharge mortality (HR 2.16, 95% CI 1.13–4.14) in a cohort of patients discharged from an acute care setting of a general hospital and followed for one year after discharge.

Acute infectious disease was the leading cause of hospitalization in our study. The presence of an infectious disease was significantly correlated with in-hospital and post-discharge mortality. In these patients, the need for inotropic drug therapy and the presence of fecal *Clostridium difficile* toxin were strong predictors of death. Mortality rates from *Clostridium difficile*-associated diseases have increased in recent years, and severe cases are becoming more common. In the United States, of *Clostridium difficile*-related deaths, 75% occurred in people above age 75, and 37% above age 85 [22]. This trend may be due to the emergence of virulent strains of the bacterial toxins, the wider use of antimicrobial medications, and longer hospital stays for the elderly. In contrast to infectious diseases, acute coronary syndromes were not related to in-hospital or post-discharge mortality in this study – despite the fact that age is known to be a powerful predictor for adverse events after acute coronary syndromes, and that the odds for in-hospital death increase by 70% for each 10 year increase in age in patients with acute coronary events [23,24]. Moreover, since acute coronary events may also occur in the setting of other acute illnesses, we would expect it to be correlated with adverse hospitalization outcomes. The fact that most of the patients with acute coronary syndrome in the present study were defined only as having had non-ST-elevation myocardial infarctions (73%) and did not require interventional therapy may have contributed to the lower mortality rates from acute coronary syndromes. Higher risk patients may have been hospitalized in cardiac intensive care units.

Our work has several limitations. The study participants were from a single medical institution. The data on co-morbidities and drug treatment were retrieved from patient files and therefore might not be detailed or accurate. Further prospectively designed studies will allow utilization of comprehensive geriatric assessment tools.

In conclusion, our study emphasizes the rising significance of hospitalized nonagenarians in the daily practice of internal medicine departments and clarifies sociodemographic and hospitalization characteristics associated with adverse events in a representative cohort of hospitalized nonagenarians. We have shown that the main predictors for in-hospital death

of nonagenarians are pressure sores, older age, atrial fibrillation, malignant disease, and admission due to an acute infection, especially *Clostridium difficile*-associated diseases. In addition, mental decline, permanent urinary catheter, leukocytosis, renal failure and hypoalbuminemia predicted post-discharge mortality. A comprehensive assessment of the elderly at admission and identification of the above risk factors will help determine in-hospital management, discharge planning and rehabilitation programs.

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