Intensive Care Med (2014) 40:114–116
DOI 10.1007/s00134-013-3147-x

EDITORIAL

Katerina Rusinova
Bertrand Guidet

"Are you sure it's about 'age'?"

Received: 23 October 2013
Accepted: 24 October 2013
Published online: 12 November 2013

The title is a rephrasing of a line in the James Bond movie *Skyfall*, where Bond asks Silva: "Are you sure it's about 'M'?"

This editorial refers to the article available at doi: 10.1007/s00134-013-3121-7.

K. Rusinova (✉)
Department of Anesthesia and Intensive Care,
Institute for Medical Humanities, Charles University in Prague,
General University Hospital, Prague, Czech Republic
e-mail: katerina.rusinova@vfn.cz

B. Guidet
Department of Intensive Care, Hôpital Saint Antoine,
75012 Paris, France
e-mail: bertrand.guidet@sat.aphp.fr

Ninety-seven percent of elderly patients (over 85 years) treated in the ICU for circulatory failure die within 12 months of the life-threatening episode. The ICU survival rate is 33 % and about 23 % of patients are discharged from hospital, but only 8 % are alive at 6 months and only 3 % at 1 year.

One cannot help but feel uncomfortable and discouraged after reading the results of a secondary analysis of data from a large trial comparing the effects of dopamine and noradrenaline on ICU outcomes by Biston et al. [1], in this issue of *Intensive Care Medicine*.

What are the implications of taking into consideration the very uncertain prognosis associated with elderly patients treated in the ICU for circulatory failure? What is the appropriate clinical algorithm and how should a physician respond the next time a call comes in from an emergency department about an 85-year-old patient in shock?

Researcher vs. attending physician bias and potential conflict of interest

When a study finds a 3 % survival and 97 % mortality rate, then the 3 % are often associated with an 'opportunity for improvement' and the 97 % is presented as a 'challenge.' Although it is an acceptable and motivating proposition for a researcher, the same terms 'opportunity' and 'challenge' can be viewed as unrealistic and misleading expressions relative to the real world of clinical decision-making and complex and unique patient–physician relationships.

Available evidence

Several studies have confirmed the very poor long-term prognosis of elderly patients admitted to the ICU [2–9] (Table 1). Importantly, factors such as an atypical presentation with delayed diagnosis and treatment, suboptimal management (because guidelines are not tailored for an elderly population), lower physiologic reserve, immuno-senescence coupled with an inadequate immune response, more frequent and earlier treatment limitations, and finally inadequate discharge policies (location, timing) may account for or at least contribute to excess mortality. Moreover, up to 50 % of ICU survivors, of all ages, suffer from post-intensive care syndrome (PICS), which is defined as substantial comorbidities (including new or worsening impairments of physical, cognitive, and mental health that adversely impact quality

Table 1 Mortality rates in elderly patients admitted to ICU for sepsis and/or shock

References	Age (years)	Follow-up	Mortality (%)	Patient characteristics
Nasa (2011)	>80	ICU	79	Severe sepsis/septic shock
Tomassini (2011)	>75	In-hospital	55	Cardiogenic shock
Vosylius (2005)	>75	In-hospital	62	Shock
Biston [1]	75–84	1 year	84	Circulatory failure
	>85	1 year	97	Circulatory failure
Lim (2009)	>75	1 year	52	Cardiogenic shock
Tabah (2010)	>80	1 year	67	Septic shock and multiple organ failure
Chelluri (1993)	≥75	1 year	76	Circulatory failure

of life) that can persist for months or even years after hospital discharge [10].

As we move the goal post for measuring outcomes from short-term, simple mortality data to long-term, qualitative results, the luster associated with the short-term success of recent years has now started to tarnish. Data about quality of life, recovery of functional status, cognitive impairment [11], and burden on families and society are equally or maybe even more important and influential. Accurate prediction of long-term prognosis, mainly related to underlying disease and baseline nutritional and functional status, requires a significant expansion of detailed geriatric data.

Evidence from other medical fields

The lens of ICU-centered research is only one way of looking at this problem. Another way is to look for evidence in other medical fields like cardiology, neurology or hematology, which have had to face similar ethical issues. Is there an age restriction for percutaneous coronary intervention (PCI) in ST-elevation myocardial infarction (STEMI) or recombinant tissue plasminogen activator (rtPA) administration in stroke management? Is there an unambiguous age limit to allogeneic stem cell transplantation?

Contrary to previous stroke management guidelines, where the age of 80 was explicitly mentioned as a relative contraindication to rtPA administration, current recommendations do not state any age restriction [12]. A similar formulation (i.e., without age restriction) can be found in the current recommendations for PCI in STEMI management in the elderly [13]. Even the oldest age group can benefit from these interventions. There is a growing body of evidence supporting the use of allogeneic stem cell transplantation in older patients; this evidence is prompting physicians to say, "There should be no upper age limit for hematopoietic stem cell transplantation" [14].

However, "significant comorbidities" still represent a relative contraindication for PCI in STEMI [13]. "Clear and honest information provided to the patient/family about the potential risks and benefits from treatment" is mentioned in eligibility checklist for rtPA for acute ischemic stroke [12]. These issues of awareness of risks/rewards along with a genuine dialogue between physicians and patients and families are becoming a priority and outweigh the impact of age in clinical decision-making.

The patients' and doctors' perspective: "Large left middle cerebral artery stroke is a fate worse than death"

Individual perceptions regarding quality of life changes considerably during aging and the subtitle for this section, which comes from a recent survey among neurologists [15], nicely indicates to what extent physician beliefs and value judgments can impact their decision-making process.

When younger people face a severe disease, they often take an attitude that involves a "struggle against the disease" (an attitude that is also shared by a large number of younger health-care professionals). Elderly patients, on the other hand, are often more nuanced and reflective and adopt a "live and cope with a handicap" attitude. The notion of what is and what is not an "acceptable" handicap may vary greatly in the elderly population and cannot be generalized.

We can be sure that it is NOT only about 'age'

Just as cost constraints are an omnipresent feature of medicine today [16], so uncertainty (about a prognosis and expected long-term outcome) will remain an omnipresent feature of medical decision-making. Despite the presence of better data and evidence, this uncertainty will not disappear from clinical practice.

However, better insight into which patient subgroups are most likely to experience substantial benefits from ICU interventions, plus better insight into the trajectory of ICU survivors after discharge, as well as patient wishes

and personal values would allow us to realistically evaluate the overall context of the patient's health and make the best possible decisions. These issues should be discussed within the health-care system and society at large.

Acknowledgments The authors wish to thank Tom Secrest for editing the English version of the manuscript.

Conflicts of interest The authors declare no conflicts of interest.

References

1. Biston P, Aldecoa C, Devriendt J et al (2013) Outcome of elderly patients with circulatory failure. Intensive Care Med
2. de Rooij SE, Govers A, Korevaar JC, Abu-Hanna A, Levi M, de Jonge E (2006) Short-term and long-term mortality in very elderly patients admitted to an intensive care unit. Intensive Care Med 32:1039–1044
3. Roch A, Wiramus S, Pauly V et al (2011) Long-term outcome in medical patients aged 80 or over following admission to an intensive care unit. Crit Care 15:R36
4. Boumendil A, Angus DC, Guitonneau AL et al (2012) Variability of intensive care admission decisions for the very elderly. Plos One 7:1–11
5. Mahul P, Perrot D, Tempelhoff G, Gaussorgues P, Jospe R, Ducreux JC, Dumont A, Motin J, Auboyer C, Robert D (1991) Short- and long-term prognosis, functional outcome following ICU for elderly. Intensive care Med 17:7–10
6. Fuchs L, Chronaki CE, Park S, Novack V, Baumfeld Y, Scott D, McLennan S, Talmor D, Celi L (2012) ICU admission characteristics and mortality rates among elderly and very elderly patients. Intensive Care Med 10:1654–1661
7. Sacanella E, Perez-Castejon JM, Nicolas JM, Masanes F, Navarro M, Castro P, Lopez-Soto A (2009) Mortality in healthy elderly patients after ICU admission. Intensive Care Med 35:550–555
8. Sprung CL, Danis M, Iapichino G, Artigas A, Kesecioglu J, Moreno R, Lippert A, Curtis JR, Meale P, Cohen SL, Levy MM, Truog RD (2013) Triage of intensive care patients: identifying agreement and controversy. Intensive Care Med 39:1916–1924
9. Philippart F, Vesin A, Bruel C, Kpodji A, Durand-Gasselin B, Garçon P, Levy-Soussan M, Jagot JL, Calvo-Verjat N, Timsit JF, Misset B, Garrouste-Orgeas M (2013) The ETHICA study (part I): elderly's thoughts about intensive care unit admission for life-sustaining treatments. Intensive Care Med 39:1565–1573
10. Unroe M, Kahn JM, Carson SS et al (2010) One-year trajectories of care and resource utilization for recipients of prolonged mechanical ventilation: a cohort study. Ann Intern Med 153:167–175
11. Iwashyna TJ, Ely EW, Smith DM, Langa KM (2010) Long-term cognitive impairment and functional disability among survivors of severe sepsis. JAMA 304:1787–1794
12. Jauch EC, Saver JL, Adams Jr HP, Bruno A et al (2013) Guidelines for the early management of patients with acute ischemic stroke. Stroke 44:870–948
13. Task force on the management of ST-segment elevation acute myocardial infarction of the European Society of Cardiology, Steg PG et al (2012) ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. Eur Heart J 33:2569–2619
14. Popplewell LL, Forman SJ (2002) Is there an upper age limit for bone marrow transplantation? Bone Marrow Transplant 29:277–284
15. Shamy MC, Jaigobin CS (2013) The complexities of acute stroke decision-making: a survey of neurologists. Neurology 13:1130–1133
16. Evans T, Nava S, Vazquez Mata G (2011) Critical care rationing: international comparisons. Chest 140:1618–1624

Intensive Care Med (2014) 40:50–56
DOI 10.1007/s00134-013-3121-7

ORIGINAL

Outcome of elderly patients with circulatory failure

Patrick Biston
Cesar Aldecoa
Jacques Devriendt
Christian Madl
Didier Chochrad
Jean-Louis Vincent
Daniel De Backer

Received: 23 June 2013
Accepted: 17 September 2013
Published online: 17 October 2013

Take-home message: In patients with circulatory failure age is an independent factor associated with a poor outcome. At 1 year, most patients aged 85 year or older were dead.

Electronic supplementary material
The online version of this article (doi:10.1007/s00134-013-3121-7) contains supplementary material, which is available to authorized users.

P. Biston
Department of Intensive Care, CHU Charleroi, Université Libre de Bruxelles, Charleroi, Belgium

C. Aldecoa
Department of Intensive Care, Rio Hortega University Hospital, Universidad de Valladolid, Valladolid, Spain

J. Devriendt
Department of Intensive Care, CHU Brugmann, Université Libre de Bruxelles, Brussels, Belgium

C. Madl
Department of Intensive Care, Medical University of Vienna, Vienna, Austria

D. Chochrad
Department of Intensive Care, Centre Hospitalier Etterbeek Ixelles, Brussels, Belgium

J.-L. Vincent · D. De Backer (✉)
Department of Intensive Care, Erasme University Hospital, Université Libre de Bruxelles, Route de Lennik 808, 1070 Brussels, Belgium
e-mail: ddebacke@ulb.ac.be
Tel.: +32-25-553380
Fax: +32-25-554698

Abstract *Purpose:* The proportion of elderly patients admitted to the ICU is increasing. Mortality rates are known to increase with age but the impact of age on outcomes after circulatory shock has not been well defined. *Methods:* We performed a secondary analysis of data from a large randomized trial comparing the effects of dopamine and norepinephrine on outcome in the ICU. Patients were separated into not old (<75 years), old (75–84 years), and very old (≥85 years). *Results:* Of the 1,679 patients included in the initial trial, 1,651 had sufficient age data available: 1,157 (70 %) were not old, 410 (25 %) were old, and 84 (5 %) were very old. There were minor differences among the age groups in the APACHE II score calculated without the age component (not old, 17 ± 9; old, 18 ± 9; very old, 19 ± 9; $p = 0.047$), but SOFA scores were similar (not old, 9 ± 4; old, 9 ± 3; very old, 9 ± 3; $p = 0.76$). Mortality rates were higher in old and very old patients at 28 days, at hospital discharge, and after 6 and 12 months. Most very old patients were dead at 6 (92 %) and 12 months (97 %). Mortality rates increased with age in all types of shock. Using multivariable analysis, the risk of death was higher in very old patients as compared to not old (adjusted OR 0.33, 95 % CI 0.2–0.56, $p < 0.001$). *Conclusions:* Ageing is independently associated with higher mortality rates in patients with circulatory failure, whatever the etiology. By 1 year after admission, most patients 85 years of age and older were dead.

Keywords ICU · Old patients · Shock · Vasopressors

Introduction

As a consequence of changing demographics, more old and frail patients are admitted to the intensive care unit (ICU) than previously [1]. The outcome of old (>75 years) and very old (≥85 years) patients admitted to the ICU is usually poorer for any diagnosis compared to younger patients [1–4]. These differences have been

described in specific populations, such as sepsis [5] or need for mechanical ventilation [6]. Older patients admitted to the ICU have high short-term mortality and long-term disability [7]. Nevertheless, although survival rates are lower in this population than in younger individuals, they are sufficiently high to justify ICU admission without generalized restriction of care [8]. In addition, long-term outcomes and quality of life of survivors are good enough to suggest that older patients may benefit from ICU admission [9] especially with the poor performance of the prognostic models in predicting mortality in old patients [10].

Circulatory failure is associated with a cascade of events that leads to a major increase in the risk of death in the general population [11]. Data regarding circulatory shock in elderly patients are scarce. In a large Austrian series of 17,126 patients older than 80 years, shock was present in only 3 % of ICU admissions [1]. Moreover, the few data that are available are conflicting. In patients with cardiogenic shock complicating myocardial infarction, Tomassini et al. [12] observed that age older than 75 years was associated with a 1.8 increased risk of death, whereas Lim et al. [13] failed to observe significant differences in 1-year survival. Many factors can contribute to these discrepancies, including associated comorbidities and the relatively small size of these studies. In other types of shock, and especially in septic shock, no data are available. The uncertain benefit of ICU care in this population increases the risk of a priori therapeutic limitations but also of futile interventions. It is thus important to better define the outcome of elderly patients with acute circulatory failure.

Older patients are frequently excluded from clinical trials [14, 15], but they are commonly treated in the ICU. Ageing is associated with important modifications in physiology [15] and pharmacokinetics. In addition, older patients may be more susceptible to adverse drug events [16] than younger patients. In the SOAP II clinical trial, which compared dopamine and norepinephrine in shock states [17] in 1,679 patients, age was not an exclusion criterion and many patients were older than 75 years. We used data from this trial to assess the influence of age on mortality in patients with circulatory shock [18]. We hypothesized that advanced age would be an independent factor associated with outcome. We also explored a possible interaction between age and the effect of the different vasopressor agents. The results were presented in part at ESICM LIVES 2011 [18].

Patients and methods

The overall study design has been published elsewhere [17]. The ethics committee at each participating center approved the trial, and all patients or relatives gave informed consent. Briefly, between 19 December 2003 and 6 October 2007, all adult patients in whom a vasopressor agent was required for the treatment of shock were included in eight participating centers. Shock was defined as a mean arterial pressure (MAP) less than 70 mmHg or a systolic blood pressure less than 100 mmHg despite adequate fluid administration [at least 1,000 ml of crystalloids or 500 ml of colloids unless there was an increase in the central venous pressure (CVP)] associated with signs of tissue hypoperfusion, such as altered mental state, mottled skin, urine output of less than 0.5 ml per kilogram of body weight for 1 h, or a serum lactate level of greater than 2 mEq/l. If hypotension recurred within the 28-day follow-up, the trial-drug solution was resumed first and an open-label solution of norepinephrine was added if needed. Patients were included only once in the trial.

Patients were excluded if they were younger than 18 years of age; had already received a vasopressor agent (dopamine, norepinephrine, epinephrine, phenylephrine, or vasopressin) for more than 4 h during the current episode of shock; had a serious arrhythmia, such as rapid atrial fibrillation (>160 beats per minute) or ventricular tachycardia; or had been declared brain-dead. Of the 2011 patients screened, 1,679 patients were included. All patients were followed to day 28; hospital mortality was available for 1,629 patients (98.7 %), data on 6-month outcome for 1,516 patients (91.8 %), and data on 12-month outcome for 1,346 patients (81.5 %). Organ support-free days were computed as days alive without organ support up to day 28. Shock was separated into septic, cardiogenic, and other types of shock (including hypovolemic and anaphylactic).

To evaluate severity at baseline, we computed at the time of inclusion the Acute Physiology and Chronic Health Evaluation II (APACHE II) score [19] with and without the age component and also the Sequential Organ Failure Assessment (SOFA) score [20].

Statistical analysis

Statistical analyses were performed using IBM® SPSS® Statistics 19 for Windows. Age data were available in 1,651 patients so this represents the population included in the present analysis. To assess the influence of age on outcome, patients were retrospectively divided into not old (<75 years), old (75–84 years old), and very old (≥85 years). To account for imbalances in the numbers of subjects across the age groups, some analyses were repeated after dividing patients into quartiles of ages. The primary outcome was 28-day mortality and the secondary outcomes were ICU, hospital, 6-month, and 1-year mortality rates. The Kolmogorov–Smirnov test was used, and histograms and normal-quantile plots were examined to verify the normality assumption of continuous variables.

Difference testing among age groups was performed using analysis of variance, Kruskal–Wallis, Student's *t* test, Mann–Whitney test, χ^2 test, or Fisher exact test, as appropriate. The Bonferroni correction was made for multiple comparisons. Cumulative mortality throughout the first 28 days after randomization was characterized with the use of Kaplan–Meier curves, with the log-rank test used for the comparison between the age groups. Logistic regression analysis with primary outcome as the dependent variable was performed to determine the unadjusted mortality risk by age. To remove bias of confounding variables for the association between age and mortality, the propensity score of each age class was estimated using ordinal logistic regression. The variables introduced in the propensity score were identified by univariable regression and retained after treatment of colinearity. After checking that balance on all covariates that were used in the propensity model had been achieved, we introduced the propensity score into the logistic regression model [21, 22].

Data are presented as mean ± SD or count (percentage), unless stated otherwise. All tests were two-sided and a p value less than 0.05 was considered statistically significant.

Results

The main demographic data are summarized in Table 1. Of the 1,651 patients included, 1,157 (70.0 %) were not old (<75 years), 410 (25 %) were old (75–84 years), and 84 (5 %) were very old (≥85 years). Old and very old patients had a higher incidence of diabetes, cardiopathy, chronic respiratory failure, and neurologic problems than not old patients, but were less likely to be immunosuppressed or to have cirrhosis or cancer. The presence of chronic renal failure was similar in the three age groups. Overall, disease severity was comparable in the three groups: although the APACHE II score was lower in the younger patients, increasing from 21 ± 9 in not old to 24 ± 9 in old and 25 ± 9 in very old patients ($p < 0.001$), this difference was blunted when age points were deleted from the score (17 ± 9 in not old, 18 ± 9 in old, and 19 ± 9 in very old, $p = 0.047$). SOFA scores were similar in the three groups.

The incidence of septic shock was comparable in the three age groups, but cardiogenic shock was more frequent and other types of shock less frequent in old and very old patients than in not old patients ($p < 0.001$). Very old patients were more frequently admitted for medical conditions.

On admission, more than 80 % of patients were being treated with mechanical ventilation (including 3 % with non-invasive mechanical ventilation) and 7 % with renal replacement therapy, with no differences according to age group (Table 2). Per protocol, all patients were treated with vasopressor agents. The doses of vasopressor agents on the first day of therapy were similar in the three groups, but dobutamine doses were higher in old and very old patients ($p = 0.013$). Similar observations were made for maximal doses of adrenergic agents ($p < 0.01$ for

Table 1 Main demographic data in the three patient groups

	Not old (<75 years) $n = 1{,}157$	Old (75–84 years) $n = 410$	Very old (≥85 years) $n = 84$	p value
SOFA score	9 ± 3	9 ± 3	9.0 ± 3	0.76
Male	684 (60)	219 (53)	38 (46)	0.002
APACHE II	21 ± 9	24 ± 9	25 ± 9	<0.001
APACHE II score (without age)	17 ± 9	18 ± 9	19 ± 9	0.047
Septic shock	728 (63)	248 (61)	52 (62)	0.68
Cardiogenic shock	165 (14)	85 (20)	28 (33)	<0.001
Other types of shock	264 (23)	77 (19)	4 (5)	<0.001
Emergency surgery	199 (17)	47 (12)	5(6)	<0.001
Scheduled surgery	225 (19)	85 (21)	14 (17)	<0.001
Medical admission	733 (63)	278 (68)	65 (77)	<0.001
Shock on ICU admission	975 (83)	324 (79)	67 (80)	0.49
Cancer	266 (23)	76 (19)	14 (16)	<0.001
Diabetes	336 (29)	144 (35)	32 (38)	0.045
Cardiopathy	506 (43)	272 (66)	62 (74)	<0.001
Chronic respiratory failure	328 (28)	164 (40)	30 (36)	<0.001
Immunosuppression	293 (25)	62 (15)	8 (10)	<0.001
Chronic renal failure	218 (19)	88 (21)	18 (21)	0.14
Neurologic problem	198 (17)	104 (25)	26 (31)	<0.0001
Cirrhosis	162 (14)	16 (4)	3 (4)	<0.001

Values are expressed as mean ± SD for continuous data or number (%). p values are given by χ^2 test for dichotomic and one-way analysis of variance (ANOVA) for continuous variables

Table 2 Therapeutic interventions and complications by study group

	Not old (<75 years) $n = 1,157$	Old (75–84 years) $n = 410$	Very old (≥85 years) $n = 84$	p value
Mechanical ventilation	925 (80)	328 (87)	66 (79)	0.078
Renal support	91 (8)	30 (7)	2 (2)	0.078
No therapeutic limitation				
At admission	940 (81)	344 (83)	65 (77)	0.455
At time of death	593 (51)	169 (41)	31 (36)	<0.001
Cause of death				
Shock	221 (20)	99 (24)	22 (26)	0.79
Withdrawal	248 (21)	111 (27)	23 (27)	0.90
Anoxic lesions	55 (5)	16 (4)	2 (2)	0.16
Dobutamine support	163 (14)	101 (24)	21 (25)	<0.001
Myocardial infarction	21 (2)	16 (4)	6 (7)	<0.001
Cardiac arrhythmia[a]	194 (17)	91 (22)	22 (26)	<0.001

Values are expressed as number (%). p values are given by χ^2 test

[a] More than 85 % of arrhythmias were supraventricular in each group

maximal dose of dobutamine). Very old patients had fewer organ support-free days than not old patients (Electronic Supplementary Material Table S1) but these differences were driven by differences in mortality. In survivors, there were no differences among groups in organ support-free days but ICU length of stay was significantly shorter in the very old (Electronic Supplementary Material Table S1).

Mortality rates at 28 days (Fig. 1), at hospital discharge, and at 6 and 12 months (Table 3) increased with age. Most of the very old patients were dead at 6 (92 %) or 12 months (97 %). The two patients alive at 1 year had no organ dysfunction other than shock during their ICU stay, had regained autonomy, and were still alive 3 years after the event. Mortality rates increased with age also when patients were grouped by quartiles of ages and according to the type of shock (Electronic Supplementary Material Table S2 and Fig. S1). Of note, the Kaplan–Meier survival curves separated very early on, with a rapid decrease in survival already evident at 48 h after randomization in the very old patients (Fig. 2).

The percentages of patients with decisions to limit therapy on admission were similar in the three groups (Table 2). However, at the time of death only 36 % of the very old patients remained on full treatment code (versus 51 % for the not old and 41 % for the old patients, $p < 0.001$). Interestingly, the causes of death were similar in the three groups, although myocardial infarction and cardiac arrhythmias were more commonly diagnosed in the oldest patients.

To remove bias of confounding variables for the association between age and mortality, the propensity score of each age class was estimated using ordinal logistic regression (Table 4). The following variables were retained after treatment of colinearity: gender, type of shock, and type of admission. After adjustment for a potential covariate, very old patients still had a significantly increased mortality as compared to not old (adjusted OR 0.33, 95 % CI 0.2–0.56, $p < 0.001$).

There was no significant interaction between age and vasopressor agent on outcome ($p = 0.193$).

Discussion

This study is the first to report on the outcomes of elderly patients in a large population of patients with circulatory failure. Mortality rates increased substantially with age, regardless of the type of shock, raising serious ethical questions about ICU admission in these patients. In particular, patients 85 years of age and older had 28-day mortality rates of 75 % and only exceptionally survived to 1 year (2 %). Our study also provides important information on the epidemiology of shock (outcome, type of shock, organ support) in old and very old patients.

As expected, old and especially very old patients more often had cardiogenic shock than younger patients. Interestingly this increase in the incidence of cardiogenic shock mirrored a marked decrease in hypovolemic and obstructive types of shock, because the incidence of septic shock was similar in the three groups. The prevalence of female patients also increased with age [1], although it is difficult to define to what extent this contributed to the difference in outcome. Although some epidemiologic studies have suggested that females may have less access to care and a higher risk of death for certain diseases [23], after admission, sex does not seem to be a major prognostic factor [24].

The persistent association between age and hospital mortality after adjustment for comorbidities is in accordance with some reports not focusing on patients with circulatory failure [25], but, as expected, the survival rate of patients in circulatory failure was far lower than that of

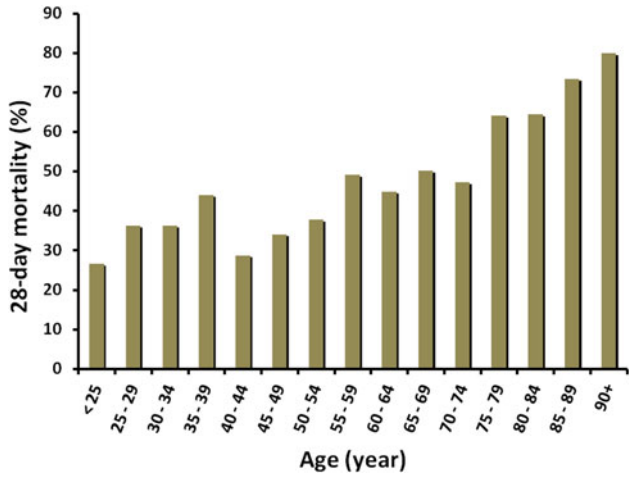

Fig. 1 Twenty-eight day mortality as a function of age

Table 3 Survival rate as a function of time after inclusion in the three age groups

	Not old (<75 years) $n = 1,157$	Old (75–84 years) $n = 410$	Very old (≥85 years) $n = 84$	p value
ICU discharge	667 (58)	164 (40)	28 (33)	<0.001
28 days	649 (56)	146 (36)	21 (25)	<0.001
Hospital discharge	546 (48)	121 (30)	19 (23)	<0.001
6-month survival	439 (41)	80 (21)	6 (8)	<0.001
12-month survival	311 (34)	57 (16)	2 (3)	<0.001

Unadjusted values, expressed as n (%). p values are given by unadjusted χ^2

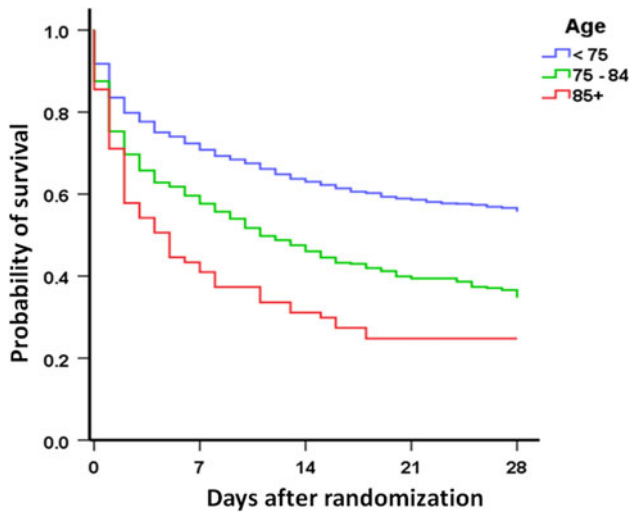

Fig. 2 Kaplan–Meier curves for 28-day survival. p value by log-rank test <0.001

Table 4 Multivariable analysis using logistic regression analysis to assess differences in mortality rate between the different age groups

	Unadjusted		Adjusted	
	OR (95 % CI)	p value	OR (95 % CI)	p value
≥85 (very old)	Reference			
<75 (not old)	0.26 (0.16–0.44)	<0.001	0.33 (0.2–0.56)	<0.001
75–84 (old)	0.61 (0.36–1.04)	0.07	0.7 (0.4–1.2)	0.2

Data are expressed as odds ratio (OR) with 95 % confidence interval (CI). The following variables were retained after treatment of colinearity to construct the propensity score: gender, type of shock, and type of admission

general ICU patients. However, other studies have reported no association between age and survival in the ICU [26–29]. Small sample sizes and patient selection may contribute to these differences.

The very poor late survival is challenging. At 1 year, only 2 of the 84 very old patients treated with vasopressors were still alive. In contrast to our expectations, these were not patients who developed complications after elective surgery but rather patients admitted with septic shock. Of note too, these patients suffered from urinary sepsis, which is known to be associated with better outcomes than sepsis from other sources [30] and had isolated circulatory failure. This suggests that ICU admission for shock is beneficial for few very old patients, and perhaps of most value for those with minimal associated comorbidities or organ dysfunction.

Our study has some limitations. First although our database was large, the number of very old patients was limited. Nevertheless, this is one of the largest series of patients with circulatory failure older than 85 years. Second, we did not calculate specific geriatric assessment scores, such as the Katz [31], SHERPA [32], or Charlson [33] indexes, which are frequently used in geriatric populations to describe patient state at admission and evaluate the risk associated with both chronic and acute pathology. Third, physicians and families may be more prone to limit care in these very old patients than in younger patients, and this may contribute to the poor prognosis. However, there were no differences in limitation of care at admission according to age. In addition, the proportion of patients in each age group included after shock development in the ICU was similar. During initial shock therapy, all patient groups received a similar intensity of therapy with vasopressor agents administered at similar doses and similar use of mechanical ventilation or renal replacement therapy; dobutamine was even used more frequently in very old patients. Nevertheless, the increased incidence of limitations in therapy at the time of death and the early time at which death occurred in old patients suggest that physicians and/or their families rapidly realized the futility of continuing care when evolution was not rapidly favorable.

One may suggest that the patients included in this trial were highly selected, because they were taking part in an

interventional trial. This is probably not the case, because our interventional trial was characterized by a low exclusion rate. Nevertheless, we cannot exclude that many of the old patients may have been denied institution of vasopressor agents and were, therefore, not even screened. If anything, however, this strengthens our findings, because old patients in shock who were deemed to have the best chance of a favorable outcome nevertheless had very low survival rates.

Our findings have strong ethical implications, because there is an increasing demand for ICU admission of older patients [34–36]. This trend is costly, and the financial constraints must be taken into account. Very elderly patients and their families should be informed of the relatively poor prognosis when these patients present with circulatory failure requiring vasopressor agents, with very few patients alive at 1 year. Patients who did survive had good quality of life a few years after the event, which supports the concept of the ICU test [37], but realistic expectations of limited chances of middle-term survival must be kept in mind. The data from the ICE-CUBE database [7, 38] suggest that admission of very old patients to the ICU is indeed associated with a higher mortality.

Our observations also have important implications for research. Patients older than 75 years are sometimes excluded from interventional trials [39]. In our trial, we observed no interaction between age and vasopressor agent, suggesting that the results of the trial also applied to the elderly patients. This observation also implies that the results of the trial were not biased by inclusion of old patients.

In conclusion, this large database of patients with circulatory failure highlights the poor outcomes of elderly patients with circulatory shock: ageing was independently associated with increased mortality and long-term survival was infrequent.

Conflicts of interest None related to this study.

References

1. Ihra GC, Lehberger J, Hochrieser H, Bauer P, Schumtz R, Metnitz B, Metniz P (2012) Development of demographics and outcome of very old critically ill patients admitted to intensive care units. Intensive Care Med 38:620–626
2. Roch A, Wiramus S, Pauly V, Forel JM, Guervilly C, Gainnier M, Papazian L (2011) Long-term outcome in medical patients aged 80 or over following admission to an intensive care unit. Crit Care 15:R36
3. Fuchs L, Chronaki CE, Park S, Novack V, Baumfeld Y, Scott D, McLennan S et al (2012) ICU admission characteristics and mortality rates among elderly and very elderly patients. Intensive Care Med 38:1654–1661
4. Lerolle N, Trinquart L, Bornstain C, Tadié JM, Imbert A, Diehl JL, Fagon JY, Guérot E (2010) Increased intensity of treatment and decreased mortality in elderly patients in an intensive care unit over a decade. Crit Care Med 38:59–64
5. Nasa P, Juneja D, Singh O, Dang R, Arora V (2011) Severe sepsis and its impact on outcome in elderly and very elderly patients admitted in intensive care unit. J Intensive Care Med 27:179–183
6. Barnato AE, Albert SM, Angus DC, Lave JR, Degenholtz HB (2011) Disability among elderly survivors of mechanical ventilation. Am J Respir Crit Care Med 183:1037–1042
7. Nguyen Y-L, Angus DC, Boumendil A, Guidet B (2011) The challenge of admitting the very elderly to intensive care. Ann Intensive Care 1:29
8. de Rooij SEJ, Govers AC, Korevaar JC, Giesbers AW, Levi M, de Jonge E (2008) Cognitive, functional, and quality-of-life outcomes of patients aged 80 and older who survived at least 1 year after planned or unplanned surgery or medical intensive care treatment. J Am Geriatr Soc 56:816–822
9. Sprung CL, Artigas A, Kesecioglu J, Pezzi A, Wiis J, Pirracchio R, Baras M, Edbrooke DL, Pesenti A, Bakker J, Hargreaves C, Gurman G, Cohen SL, Lippert A, Payen D, Corbella D, Iapichino G (2012) The Eldicus prospective, observational study of triage decision making in European intensive care units. Part II: intensive care benefit for the elderly. Crit Care Med 40:132–138
10. Minne L, Ludikhuize J, de Jonge E, de Rooij S, Abu-Hanna A (2011) Prognostic models for predicting mortality in elderly ICU patients: a systematic review. Intensive Care Med 37:1258–1268
11. Sakr Y, Reinhart K, Vincent J, Sprung CL, Moreno R, Ranieri VM, De Backer D, Payen D (2006) Does dopamine administration in shock influence outcome? Results of the sepsis occurrence in acutely Ill patients (SOAP) study. Crit Care Med 34:589–597
12. Tomassini F, Gagnor A, Migliardi A, Tizzani E, Infantino V, Giolitto S, Conte MR, Lanza GA, Gnavi R, Varbella F (2011) Cardiogenic shock complicating acute myocardial infarction in the elderly: predictors of long-term survival. Catheter Cardiovasc Interv 78:505–511
13. Lim HS, Andrianopoulos N, Yan BP, Lim CC, Brennan AL, Reid CM, Freeman M, Charter K, Black A, New G, Ajani AE, Duffy SJ, Melbourne Interventional Group (2009) Survival of elderly patients undergoing percutaneous coronary intervention for acute myocardial infarction complicated by cardiogenic shock. JACC Cardiovasc Interv 2:146–152
14. Gurwitz JH, Goldberg RJ (2011) Age-based exclusions from cardiovascular clinical trials: implications for elderly individuals (and for all of us): comment on "the persistent exclusion of older patients from ongoing clinical trials regarding heart failure". Arch Intern Med 171:557–558
15. Marik PE (2006) Management of the critically ill geriatric patient. Crit Care Med 34:S176–S182
16. Corsonello A, Pranno L, Garasto S, Fabietti P, Bustacchini S, Lattanzio F (2009) Potentially inappropriate medication in elderly hospitalized patients. Drugs Aging 26(Suppl 1): 31–39

17. De Backer D, Biston P, Devriendt J, Madl C, Chochrad D, Aldecoa C, Brasseur A, Defrance P, Gottignies P, Vincent JL, SOAPII Investigators (2010) Comparison of dopamine and norepinephrine in the treatment of shock. N Engl J Med 362:779–789
18. Biston P, Aldecoa C, Devriendt J, Vincent JL, De Backer D (2011) Outcome of elderly patients with circulatory failure. Intensive Care Med 37(1(S)):186 (abstract)
19. Wong DT, Knaus WA (1991) Predicting outcome in critical care: the current status of the APACHE prognostic scoring system. Can J Anaesth 38:374–383
20. Vincent JL, Moreno R, Takala J, Willatts S, De Mendonça A, Bruining H, Reinhart CK, Suter PM, Thijs LG (1996) The SOFA (Sepsis-related organ failure assessment) score to describe organ dysfunction/failure. On behalf of the Working Group on Sepsis-Related Problems of the European Society of Intensive Care Medicine. Intensive Care Med 22:707–711
21. Rubin DB (1997) Estimating causal effects from large data sets using propensity scores. Ann Intern Med 127:757–763
22. Rubin DB (2008) For objective causal inference, design trumps analysis. Ann Appl Stat 2:808–840
23. Collins SD, Ahmad S, Waksman R (2010) Percutaneous revascularization in women with coronary artery disease: we've come so far, yet have so far to go. Nutr Metab Cardiovasc Dis 20:436–444
24. Nachtigall I, Tafelski S, Rothbart A, Kaufner L, Schmidt M, Tamarkin A, Kartachov M, Zebedies D, Trefzer T, Wernecke KD, Spies C (2011) Gender-related outcome difference is related to course of sepsis on mixed ICUs: a prospective, observational clinical study. Crit Care 15:R151
25. Nathanson BH, Higgins TL, Brennan MJ, Kramer A, Stark M, Teres D (2011) Do elderly patients fare well in the ICU? Chest 139:825–831
26. Rodríguez-Regañón I, Colomer I, Frutos-Vivar F, Manzarbeitia J, Rodríguez-Mañas L, Esteban A (2006) Outcome of older critically ill patients: a matched cohort study. Gerontology 52:169–173
27. Wu AW, Rubin HR, Rosen MJ (1990) Are elderly people less responsive to intensive care? J Am Geriatr Soc 38:621–627
28. Fedullo AJ, Swinburne AJ (1983) Relationship of patient ages to cost and survival in a medical ICU. Crit Care Med 11:155–159
29. Chelluri L, Pinsky MR, Donahoe MP, Grenvik A (1993) Long-term outcome of critically ill elderly patients requiring intensive care. JAMA 269:3119–3123
30. Vincent JL, Rello J, Marshall J, Silva E, Anzueto A, Martin CD, Moreno R, Lipman J, Gomersall C, Sakr Y, Reinhart K, EPIC II Group of Investigators (2009) International study of the prevalence and outcomes of infection in intensive care units. JAMA 302:2323–2329
31. Katz S, Down TD, Cash HR, Grotz RC (1970) Progress in the development of the index of ADL. Gerontologist 10:20–30
32. Cornette P, Swine C, Malhomme B, Gillet JB, Meert P, D'Hoore W (2006) Early evaluation of the risk of functional decline following hospitalization of older patients: development of a predictive tool. Eur J Publ Health 16:203–208
33. Charlson ME, Pompei P, Ales KL, MacKenzie CR (1987) A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chron Dis 40:373–383
34. Bagshaw SM, Webb SA, Delaney A, George C, Pilcher D, Hart GK, Bellomo R (2009) Very old patients admitted to intensive care in Australia and New Zealand: a multi-centre cohort analysis. Crit Care 13:R45
35. Wunsch H, Angus DC, Harrison DA, Collange O, Fowler R, Hoste EA, de Keizer NF, Kersten A, Linde-Zwirble WT, Sandiumenge A, Rowan KM (2008) Variation in critical care services across North America and Western Europe. Crit Care Med 36:2787–2793
36. Blot S, Cankurtaran M, Petrovic M, Vandijck D, Lizy C, Decruyenaere J, Danneels C, Vandewoude K, Piette A, Vershraegen G, Van Den Noortgate N, Peleman R, Vogelaers D (2009) Epidemiology and outcome of nosocomial bloodstream infection in elderly critically ill patients: a comparison between middle-aged, old, and very old patients. Crit Care Med 37:1634–1641
37. Curtis JR, Vincent JL (2010) Ethics and end-of-life care for adults in the intensive care unit. Lancet 376(9749):1347–1353. doi: 10.1016/S0140-6736(10)60143-2
38. Boumendil A, Latouche A, Guidet B for the ICE-CUB Study Group (2011) On the benefit of intensive care for very old patients. Arch Intern Med 171:1116–1117
39. Cherubini A, Oristrell J, Pla X, Ruggiero C, Ferretti R, Diestre G, Clarfield AM, Crome P, Hertogh C, Lesauskaite V, Prada GI, Szczerbinska K, Topinkova E, Sinclair-Cohen J, Edbrooke D, Mills GH (2011) The persistent exclusion of older patients from ongoing clinical trials regarding heart failure. Arch Intern Med 171:550–556