

## Caring for critically ill oldest old patients: a clinical review

Nicola Vargas<sup>1</sup> · Loredana Tibullo<sup>2</sup> · Emanuela Landi<sup>1</sup> · Giovanni Carifi<sup>1</sup> ·  
Alfonso Pirone<sup>3</sup> · Antonio Pippo<sup>1</sup> · Immacolata Alviggi<sup>1</sup> · Renato Tizzano<sup>1</sup> ·  
Elisa Salsano<sup>4</sup> · Francesco Di Grezia<sup>1</sup> · Maria Vargas<sup>5</sup>

Received: 23 June 2016 / Accepted: 29 September 2016 / Published online: 19 October 2016  
© Springer International Publishing Switzerland 2016

**Abstract** Despite technological advances, the mortality rate for critically ill oldest old patients remains high. The intensive caring should be able to combine technology and a deep humanity considering that the patients are living the last part of their lives. In addition to the traditional goals of ICU of reducing morbidity and mortality, of maintaining organ functions and restoring health, caring for seriously oldest old patients should take into account their end-of-life preferences, the advance or proxy directives if available, the prognosis, the communication, their life expectancy and the impact of multimorbidity. The aim of this review was to focus on all these aspects with an emphasis on some intensive procedures such as mechanical ventilation, non-invasive mechanical ventilation, cardiopulmonary resuscitation, renal replacement therapy, hemodynamic support,

evaluation of delirium and malnutrition in this heterogeneous frail ICU population.

**Keywords** Oldest old · Critical care · Intensive geriatric care

### Introduction

According to an international convention, oldest old definition identifies a demographic group of people aged 85 and over [1]. Over the past decades, the oldest olds were the most rapidly expanding segment of the population in developed countries [2] thanks to the mortality rate reduction [3], the improvements in economic and social conditions and to the ongoing medical advances [4]. However, the oldest old age group represents only a small proportion of the total population, and in clinical studies it is often considered as a part of a wider age group as that of 65 and over, 75 and over [5] or 80 and over [6]. People aged 85 and over cannot be considered a homogeneous population. They may experience multiple chronic conditions simultaneously as well as some specific and non-communicable diseases as memory loss, urinary incontinence, depression and falls or immobility which are the major causes of disability and health problems [7]. The prevalence of multimorbidity increases in the subjects aged more than 80 up to 78 % [8]. The multimorbidity is associated with a higher mortality [9], to the disability and to a higher health care utilization [10]. Oldest old people are frailer, often ill and more dependent than younger old people. These characteristics influence strongly the decision for the intensive care unit (ICU) admission. The advanced age, the comorbidity, the disability, the burden of chronic conditions, the life expectancy are all factors that

✉ Nicola Vargas  
nicolavargas@tin.it

<sup>1</sup> Geriatric and Intensive Geriatric Care Ward, Azienda Ospedaliera di Rilievo Nazionale e di Alta Specialità “San Giuseppe Moscati”, via Contrada Amoretta, 83100 Avellino, Italy

<sup>2</sup> Medicine Ward, Medicine Department, “San Giuseppe Moscati” Hospital, via Gramsci, 81031 Aversa, CE, Italy

<sup>3</sup> Clinical Nutrition and Dietology Unit, Medicine Department, Azienda Ospedaliera di Rilievo Nazionale e di alta Specialità “San Giuseppe Moscati”, via Contrada Amoretta, 83100 Avellino, Italy

<sup>4</sup> Department of Clinical Disease and Internal Medicine, Federico II University of Naples, via Pansini, 80121 Naples, Italy

<sup>5</sup> Department of Neuroscience and Reproductive and Odontostomatological Sciences, University Federico II, Via Pansini, 89121 Naples, Italy

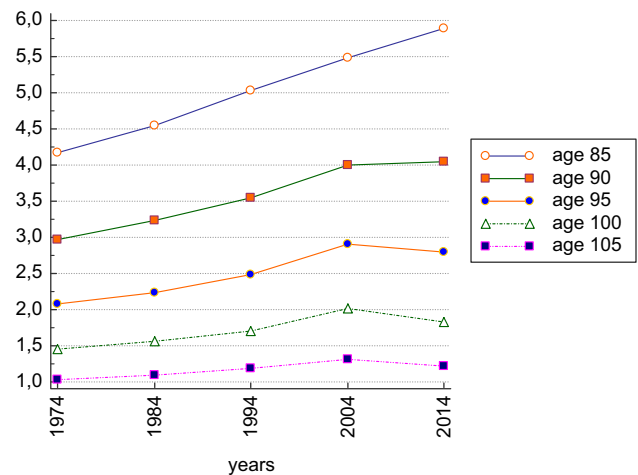
the physicians considered to be clinically relevant on the older critically ill patients' outcome [11]. Currently many clinical trials, national and international surveys, do not provide sufficient data for evidence-based caring for critically ill oldest old patients. The majority of the investigations are retrospective studies, and their data are not homogeneous. The tendency for very old patients to receive less intensive treatment [12] represents an evident bias in reporting data practice. The selection process from emergency room to the ICU admission renders the oldest old patients in these studies poor representatives of the entire population of critically ill older patients [13]. The aim of this review is to focus on some significant factors which influence the caring for critically ill oldest old patients in daily practice.

### The life expectancy evaluation

Taking into account in everyday practice life expectancy, especially of the older patient, it is essential to identify those patients with longer life expectancy, because potentially these patients will more likely benefit from aggressive treatment versus those that are more vulnerable to adverse outcome [14]. The awareness of life expectancy allows to understand more appropriately the preferences of the patients and the possible outcome; furthermore the age must not be the most important factor to decide the ICU admission of the older patients [15]. In 2010 in the USA, life expectancy at the age of 65 rose to 19.1 and the average time to live for a person turning 85 was 6.5 years. Life expectancy by age and all races and origin was 4.6 at the age of 90, 3.5 at the age of 95 and 2.3 years at the age of 100 [16]. Similar trends have been observed in almost all developed nations. The Italian resident population aged more than 85, on January 1, 2015 was 1,930,039 for an amount of 3.18 % of the total resident population. In Italy, life expectancy for oldest old increased over the last 40 years (Fig. 1). Currently those people aged 85 are expected to live 91 years for male and 92.1 for female, while those aged 90 are expected to live, respectively, 94.2 years and 94.8 years. At the age of 95, life expectancy is 97.9 for male and 98.1 for female, while at the age of 100, it is 102 for male and 102.1 for female. At the age of 105, life expectancy is 106.2 [17].

### Oldest old end-of-life treatment preferences

During a severe acute illness, the oldest old patients, even when they are competent, are often unable to express their wishes [18]. The severity of the patients' conditions, poor level of education and male gender are the predictors for a



**Fig. 1** Life expectancy Italian oldest old 1974–2014

passive role in the doctor–patient relationship [19]. Older patients often prefer to defer the decision about intensive cares to others. They frequently prefer that the physicians have the greater input in decision-making process [20, 21]. The self-reported preferences for treatments are influenced mostly by their personal values, religion and by experiences with illnesses [22]. Fried et al. [23] showed that the burden of treatment and its outcomes were strong determinants of older seriously ill patients' preferences. For example, in case of low burden treatment with the outcomes of severe cognitive and/or functional impairment, the majority of older patients would have chosen not to receive the therapy. On the other hand in the case of high burden of treatment with the return to their current health, the majority of them accepted the treatment. Although in this study, the patients had advanced stages of illness, the perception of their life expectancy suggested that they did not consider themselves to be close to death. Furthermore, over the time, seriously ill older patients retain great diversity in their willingness to endure burdensome therapy or risk of severe disability to avoid death [24]. Other determinant on the critically ill older patients' preferences is the awareness of medical practice. Recently Wilson et al. [25] showed that the use of a video depicting cardiopulmonary resuscitation and explaining resuscitation preference options was considered helpful in decision making by patients and surrogates. Independent IADL and ADL older patients were interviewed after the viewing of some videos which described the use of noninvasive mechanical ventilation (NIV), invasive mechanical ventilation and renal replacement therapy (RRT) after a period of IMV. These patients, after this viewing, showed great reluctance to accept life-sustaining treatments, especially IMV and RRT. Retaining their quality of life was the determinant associated with this choice [26].

## Legal issues and advance directives

The decision making for critically oldest old patients is often dependent on the context, and it is made by an agreement between family and clinicians. Furthermore the decision for the life-sustaining treatment and ICU admission is often made when the clinic condition suddenly gets worse and/or the patient is unconscious. The informed consent process still applies unreservedly to older patients. Old age and frailty should be not considered factors which may inhibit ones' decisional capability. In this context, physicians deal with three different situations on a daily basis: (1) patients with good cognitive functioning; (2) patients with various degrees of cognitive impairment; and (3) patients with a legal guardian [27]. In the first case, physicians should give information and recall consent by removing communication barriers (sensorial deficits, low education level, different language, presence of pain and mood disorders, impaired ability to communicate, limited independency, illiterate conditions) for a competent decision. This is the case of critically ill older patients considered competent and capable of choice [28]. In the second case, if there are depression and mild cognitive impairment or early dementia, psychiatric consultation should be taken into account, although these conditions do not preclude the patient's ability to make a competent decision [29]. The assessment of competency should include a clinical and diagnostic interview, a neuropsychological testing and a functional ability assessment [30]. In the third case, the tutor or legal guardian has the duty to sign the informed consent form. If a patient is incompetent, the need for an appropriate surrogate decision maker will be required. The legal procedures of surrogate decision-making process include advanced directives, legal guardians and family members in a hierarchy that varies from state to state. In many nations, the decisional power is given to the relatives, the proxy and to the surrogate (Table 1). In Italy, there are no specific legal regulations about the role of formal advanced directives in medical treatment, as well as the right of a person to designate a proxy for medical decisions. The Italian law, January 9, 2004, n. 6 stated that no decision-making right is acknowledged to family members unless they are legal delegates [31]. The adoption of advanced directives was the first formal response to many critical deficits which made the medical care of dying patients painful [32], expensive [33, 34], and emotionally burdensome to both patients and their families [35]; the comfort care preferences were subverted [36]. In the case of emergency care or any life-saving treatment, Italian law does not require patient consent to undergo treatment. It must be

documented in the medical records by the physician that the procedure used was urgent and essential [27].

## Ventilatory strategy in critically ill oldest old patients

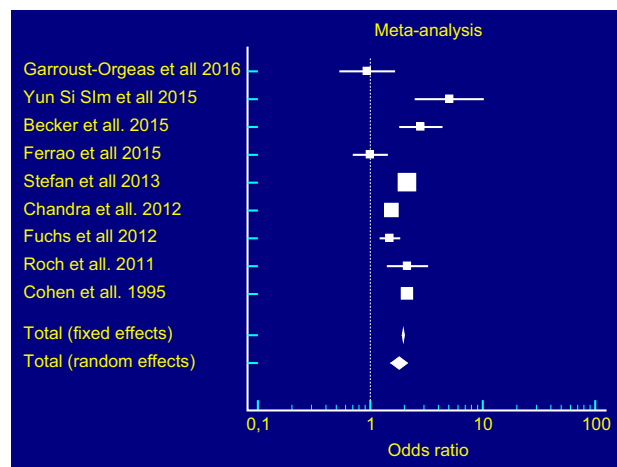
### Mechanical ventilation (MV)

In an emergency scenario, if a severe respiratory failure threatening the oldest old patient's life functions occurs, beyond the advanced or proxy directives, informed consent to intubation is not required. It is, however, essential to inform the patient (and family members) about his/her serious illness, about the need of MV and about the admission to ICU. In the clinical practice, many physicians are reluctant to use MV and ICU admission in oldest old patients even when the criteria are appropriate [37]. The MV use decreased significantly with advanced age even after adjustment for DNR (do not resuscitate) status [38]. There are some main reasons behind this practice. The first reason concerns the poor prognosis and the subsequent belief that MV and ICU care could be deleterious. Secondly this practice may not actually be what the patient or the family wants [39]. Other physicians consider the MV a questionable option in some daily (do not intubate) DNI-related clinical scenarios, for example in an oldest old patient, bedridden, dependent in daily activity, with multimorbidity and with acute respiratory failure [40]. The impact of age on survival after intensive care has been known for a long time. Cohen et al. [41] in 1995 assessed the dramatic impact of age on outcome from mechanical ventilation using a population of 41,848 patients from statewide database. For the patients aged between 85 and 89 ( $n = 3145$ ), the mortality rate was 67 % and for the patients aged 90 or more ( $n = 1812$ ) the mortality rate reached to 75 %. The mortality rate for oldest old patients admitted to ICU who did not receive mechanical ventilation was 22 and 26 %, respectively. The inverse relationship between survival and age with the lower survival rate for patients aged between 85 and 89 and 90 or more undergoing mechanical ventilation (38 percent and 30 percent, respectively) was assessed by Kurek in 1998 [42]. Mortality in older patients has been the subject of numerous investigations. Figure 2 showed clearly that mechanical ventilation is a strong predictive factor of mortality in very seriously ill oldest old patients [41, 43–50]. In a multicenter, prospective cohort study [51] including patients with the average age of 85 ( $n:1671$ ), one third of very old patients died in hospital ( $n 289$ ) while receiving mechanical ventilation, vasopressors or dialysis. In this

**Table 1** Summary about legislation in different country for incompetent patients

	Incompetent patients	Advance directive of treatment
Austria	Decisional power of a relative	Validity of living will and power of attorney
Belgium	Decisional power of a relative	Validity of living will and power of attorney
Bulgaria	Decisional power of the closest relative	No legal availability of living will and power of attorney
Denmark	Decisional power of the closest relative or friend	Validity of living will and power of attorney
Finland	Consultative role of relatives	Still debating
France	Consultative role of relatives	Consultative role
Germany	Validity of designed surrogate. In lack of this consultative role of relatives	Validity of living will and power of attorney
Hungary	Decisional power to proxy	Validity of living will and power of attorney
Italy	No possibility for patients to appoint a surrogate. Only a judge may appoint a support administrator	No legal availability of living will and power of attorney
The Netherland	Consultative role of relatives	Validity of living will and power of attorney
Norway	Consultative role of proxy	Still debating
Spain	Decisional power of a relative	Validity of living will and power of attorney
Switzerland	Decisional power of a surrogate	Validity of living will and power of attorney
Turkey	Still debating	Still debating
UK	Decisional power of a surrogate	Validity of living will and power of attorney
USA	Decisional power of a surrogate	Validity of living will and power of attorney

study, the presence of frailty or advanced directed had little impact on limiting use of sustaining treatments or shortening the time from admission to death. The relationship between mechanical ventilation and low or intense associated treatment, using, respectively, noninvasive ventilation or invasive ventilation with low or high end expiratory support (PEEP) plus vasopressors agents was recently studied by Peigne et al. [52]. Hospital mortality significantly increased with age in all treatment groups and patients with age >80 years showed higher mortality rate independently of intense treatment group. Some authors reported that age had no influence on mortality rate between the younger and the older age group. They found that the only factor showing a significant influence on older patient outcome was the reason for mechanical ventilation, ventilatory versus hypoxemic respiratory failure [53]. A randomized, controlled trial conducted by Ely et al. in 2002 [54] examined age as independent risk factor in recovery and ICU discharge after acute respiratory distress syndrome (ARDS). The 28-day survival was greater in the group of younger patients (<70 years of age) than in older patients. Older age was a strong predictor of in-hospital death. The main finding in this study was that older survivor had greater difficulty achieving liberation from the ventilator and being discharged from the ICU. Mortality rate in patients with ARDS increased with age reaching 60 percent for patients aged 85 or older [55]. The ARDSNet trial [56] showed that the gold standard treatment was a  $V_T$  of 6 ml/Kg calculated on the basis of predicted body

**Fig. 2** Odds ratio risk for oldest old patients undergoing to mechanical ventilation in overall oldest old ICU population

weight and using volume controlled ventilation. The authors stated that high frequency ventilation was the ideal way of ventilating patients with ARDS such as a higher level of PEEP, the prone position and the recruitment maneuvers. Sutherasan et al. [57] showed that in patients at risk of ARDS but without previously noninjured lung, the implementation of protective ventilator strategies, consisting of  $V_T$  of 6 ml/kg, PEEP of 6–12 cm H<sub>2</sub>O and recruitment maneuvers can decrease the development of ARDS, pulmonary infection and atelectasis but not mortality. Eachempati et al. [58] observed that for the older patients of a “pure” ARDS population, the use of a low  $V_T$  strategy

failed to show a marked benefit. The benefit of prolonged mechanical ventilation (for more than 29 days) showed a mortality rate in older patients of 45 % percent while in the younger patients was of 30 % [59]. Prolonged mechanical ventilation was considered one of the most important factors for tracheostomy rate. Age-adjusted incidence of tracheostomy increased by 106 %, rising disproportionately to mechanical ventilation use [60]. Although tracheostomy is a safe surgical procedure in the oldest old patients, the rate of the postoperative mortality was high. The rate reached 75 % within three postoperative months and to 93, 8 within the first year [61]. Tracheotomies are routinely performed for severely ill and elderly patients with respiratory failure. However, mortality rate was high after tracheotomy both in ICU and after discharge [62].

### **Noninvasive mechanical ventilation (NIMV) in oldest old patients**

The choice of noninvasive mechanical ventilation (NIMV) aims to avoid complications in fragile and older patients [12]. Indications for NIMV treatment in older patients did not differ from the younger patients. NIMV, within both the ICU and the ward environment, has reduced intubation rate and mortality in COPD patients with decompensated respiratory acidosis following immediate medical therapy, as shown in RCTs and in many systematic reviews [63]. Age does not imply a poorer response. Chandra in his study [64] reported data about NIMV outcome in acute exacerbations of chronic obstructive pulmonary disease during years 1998–2008. In this study, 12,499 oldest old patients were treated initially with NIV, and 24,359 were initially treated with invasive mechanical ventilation (IMV). The mortality rate was higher in IMV group ( $n: 9167 = 37.7\%$ ) than in NIMV group ( $n: 1220 = 9.7\%$ ). A small proportion of oldest old patients transitioned from NIMV to IMV ( $n: 664$ ) with an increased mortality rate ( $n: 79 = 12\%$ ). In the study by Shortgen et al. [65], very old patients managed using NIMV have an overall satisfactory 6-month survival and functional status, except for endotracheal intubation after NIMV failure. Segrelles et al. [66] compared the results in older patients with those obtained in younger patient group. There were no differences in terms of in-hospital mortality between the two groups. However, this population was more frequently readmitted within 6–12 months after hospital discharge than the younger. In oldest old population, NIMV can be considered as a good alternative for treating respiratory acidosis even for those with a do not intubate order (DNI), defined by the unfavorable balance for intubation expressed by the emergency department physician (on the basis of advanced age and bad clinical status) and consultation with patients and his/her relatives, with a satisfactory long-term

survival, especially when they continue NIMV at home [67]. Refusing ICU admission is common among older patients, especially for those with acute respiratory failure and cancer. The prognosis was influenced by the underlying cause of respiratory failure, efficiency of cough and mental status and by initial selection of patients [68]. Furthermore, the use of NIV as a palliative treatment for respiratory failure and dyspnea has become increasingly common [69]. NIMV could be worthwhile for older patients where invasive ventilation is not considered as an option, either because invasive ventilation is against the patient's wish or because NIMV is considered the limit as a part of end-life-decision. In this context the results in the Bulow's study [70] a 25 % of survival rate to hospital discharge and a 10 % after 5-year among older DNI patients were significant. Palliative NIMV is regularly performed in the ICU as in the medical wards and the emergency department. In the study by Vargas and colleagues [71], very old patients with DNI order were studied. They treated these patients with NIMV in a half-geriatric ward with trained physicians and nurses. After 12 h of NIMV in the geriatric ward, 75 % of these patients were significantly improved. Hospital mortality was related to admission diagnosis and was especially high in case of active end-stage-cancer or hypoxiemic respiratory failure.

### **Hemodynamic support in oldest old patients**

Evidence about hemodynamic support in the clinical setting of critically ill oldest old patients with shock is based mainly on few data because of lack of longitudinal and randomized trials. The incidence of shock in patients older than 80 years admitted to ICU is about 3 % [72]. Data about incidence and outcome of cardiac shock (CS) in oldest old patients are conflicting. Shah et al [73] showed a high incidence of cardiogenic shock in patients aged >85 years (33 %) with ST elevation myocardial infarction. In these patients, the mortality rate was of 54 %. Skoinick et al. [74] in a population of 5557 patients aged  $\geq 90$  years with acute coronary syndrome showed an incidence of CS of 3.1 versus 3.5 % of patients aged 75–89 years. The mortality rate was of 12 %. Biston et al. [75] performed a secondary analysis of data from a large randomized trial on outcome of ICU patients treated with vasopressors. They received vasopressors doses similar to the younger groups except for dobutamine doses which were higher than the other groups. Most of the oldest old patients were dead after 6 (92 %) or 12 months (97 %). The two patients alive after 1 year had no organ dysfunction except for shock during their ICU stay; they had regained autonomy and were still alive 3 years after the event. In the study by Biston et al., the 26 % of patients presented cardiac

arrhythmia and 6 % myocardial infarction. Samuels et al. [76] demonstrate that the hospital mortality correlates with the number and doses of inotropic support. The mortality risk increased from 7.5 % in patients with one inotrope/vasopressor at moderate dose to 80 % using three inotropes at high dose. Inotropes and vasopressors, increasing contractility and afterload, increase the myocardial oxygen consumption. However, in oldest old patients with shock the therapies to improve tissue perfusion may be arrhythmogenic, especially in those presenting a history of coronary artery disease [77]. Patients with acute heart failure syndromes and end-stage heart failure can now be stabilized emergently with the use of mechanical circulatory support devices and extracorporeal life support. Technologies as intra-aortic balloon counterpulsation (IABP), percutaneous and surgically implanted ventricular assist devices, extracorporeal membrane oxygenation, and renal replacement therapies have become a major focus of the ICU and require a multidisciplinary approach [78]. The most important RRTs on IABP use in acute myocardial infarction (AMI) and CS [79, 80] did not consider the oldest old population. They considered patients with an age >75 year, and there was no survival benefit at 12 months of follow-up. A meta-analysis by Sjauw et al. [81] showed that IABP increased bleeding and stroke in AMI CS patients. Furthermore, Stretch et al. [82] showed an increased use of short-term mechanical circulatory support devices in patients aged  $\geq 80$  years from 6.2 % (in 2004–2007) to 11.9 % (in 2008–2011). They found that IABP use before mechanical devices support was a predictor of mortality and increased costs. Preoperative need for IABP is a strong predictor of risk mortality in oldest old patients undergoing surgical procedures. Bridges et al. [83] retrospectively reviewed data of 662,033 patients from the society of thoracic surgeon national database who underwent cardiac surgical procedures. Five patients were more than 100 years old, 1092 patients aged between 90 and 99 years, 59,976 patients were between 80 and 89 years and 621,360 patients were between 50 and 79. The use of IABP, renal failure, peripheral vascular disease and cerebrovascular disease were major risk factors for surgical mortality. For coronary artery bypass grafting (CABG) patients, the surgical mortality was 11.8 % for patients aged >90 years of age, 7.1 % 80–89 years, and 2.8 % for those 50–79 years. In the past decades, the use of Extracorporeal Membrane Oxygenation (ECMO) has grown rapidly. Aso et al. [84] showed that patients aged  $\geq 80$  years (567) treated with ECMO for CS had a mortality rate of 81.7 %. The impella ventricular support system is a family of percutaneous heart pumps (impella 2.5, impella CP, impella 5.0 and impella RP). In clinical practice, the impella catheters are used as support in patients with hemodynamic instability. The most important trials about

impella catheters in elective and urgent high risk percutaneous coronary interventions (PCI), PROTECT I and II [85, 86] excluded patients with age  $\geq 80$  years. In patients with hemodynamic instability aged  $\geq 80$  years, Pershad et al. [67] concluded that the impella circulatory support is reasonable and feasible in selected octogenarians population with similar outcome of younger selected patients. Seyfarth et al. [87] published the results from ISAR-Shock and compared the hemodynamic effects of the impella 2.5 with IABP. They showed that the impella 2.5 provided more hemodynamic improvement compared with IABP for cardiogenic shock patients. Further investigations are necessary to evaluate this positive outcome in older and oldest old patients.

### Renal replacement therapy in the oldest old patient

The epidemiology of AKI and renal replacement therapy (RRT) in oldest old patients is still undefined because of various clinical setting. AKI requiring RRT is a common complication in critically ill patients. The number of very old patients experienced acute on chronic kidney disease (CKD) who started dialysis in the ICU as well as end-stage renal disease (ESRD) has been grown over these past decades. The overall incidence of AKI in ICU patients ranges from 20 to 50 % with less incidence in elective surgical patients and higher incidence in septic patients. The incidence of contrast-induced AKI is less (11.5–19 % of all admissions) than seen in the ICU population [88]. Kurella et al. [89] showed that dialysis initiation among octogenarians and nonagenarians increased dramatically over the past decades translating to a near doubling of the number of patients with incident AKI aged >80 years. The number of octogenarians and nonagenarians starting dialysis increased from 7054 patients in 1996 to 13,577 patients in 2003, consisting in an average annual increase of 9.8 %, dialysis initiation. In 2010, the United States Renal data system report showed a high growth rate (16 %) of dialysis in oldest old population [90]. In oldest old patients, initiation of dialysis has a negative effect on independent living. Jassal et al. [91] showed at the time of dialysis the majority of patients were living at home with no assistance for the activities of daily living. Within the first 6 months after dialysis more than 30 % of patients had functional loss requiring community or private-caregiver support or transfer to nursing home. The critically ill oldest old patients who received dialysis vasopressors and/or mechanical ventilation had significant decline in functional status. The 20 % of them were transferred to long-term care facility [52]. Guerra et al. [92] found a strong association between the age of critically ill patients and

subsequent diagnoses of dementia. The oldest survivors (age >85) had a cumulative incidence of dementia of 33 % over three years. RRT for acute renal failure was a time-dependent risk factor that increased risks only after six months of follow-up. The dialysis Morbidity and Mortality Study Wave II study [93] reported the maximal prevalence of frailty in the oldest old age patients (78.8 % of those who were older than 80 years). The frailty was defined by the presence of weight loss, weakness, low physical activity and exhaustion. Tamura et al. [94] found that the survival in patients  $\geq 80$  years of age, with ESRD and starting hemodialysis was 46 % after 1 year. In this study, the mean survival rate was of 24.9 months in patients aged between 65 and 79 years, 15.6 % months in those aged between 80 and 84, 11.6 months for those aged between 85 and 89 and 8.4 months in those aged 90 years and older. Lamping et al. [95] found that 12-month survival rate of elderly patients on dialysis was lower in patients aged over 80 years (54 %) versus patients aged between 75 and 79 years (69 %) and versus patients aged between 70 and 74 years (80 %). Despite this lower survival rate, the authors found that comorbidity was a more important determinant of outcome than age. Nordio et al. [96] showed that impact of age on excess mortality risk was very relevant on survival of patients treated by long-term dialysis. Five-year relative survival showed for older patients 26 deaths/100 patient-year versus 14 deaths/100 patient-year of patients aged between 65 and 75 years. Joly et al. [97] analyzed the characteristics of octogenarians treated with dialysis or conservative therapy. During the 12-year observation period, the 68.7 % patients died. The median survival rate was 28.9 months in patients undergoing dialysis, compared with 8.9 months in patients treated conservatively with substantial prolongation of life of the patients on dialysis. In contrast with these data, Akposso et al. colleagues [98] showed that patients older than 80 years with AKI have mortality rate similar to younger adult patients. In patients over 80 years old, the mortality was less severe than expected, and these patients could benefit from the renal replacement therapy (RRT) of modern intensive care medicine. The conventional criteria to initiate dialysis are: dyselectrolytemia; refractory metabolic acidosis, fluid overload, uremic bleeding and uremic encephalopathy [99]. The Kidco AKI guidelines [100] noted that patients with life-threatening indications such as hyperkalemia, severe acidosis or diuretic-resistant fluid overload should be dialyzed emergently. In the absence of these fatal events, there is a limited and controversial evidence about the right moment to initiate RRT in critically ill patients. In this context, the Kidco guidelines stated that there are no definitive conclusions about time of initiation of RRT (early vs. late). However, the decision to initiate dialysis depends on the judgment of the clinicians.

Several nonrandomized studies have reported improving outcomes associated with earlier RRT. Bouman et al. [101] in critically ill patients with oliguric acute renal failure reported that survival at 28 days and recovery of renal function were not improved by high ultrafiltration volumes or early initiation of hemofiltration. Recently two RCTs studied the time of initiation RRT (early vs. late RRT) with conflicting conclusion [102, 103]. The trial ELAIN randomized 231 predominantly postsurgical patients. The median difference among those receiving RRT was 21 h. This study included oldest old patients. Early RRT resulted in a 15.4 % reduction in 90-day mortality compared with delayed RRT. There was no difference in dialysis dependence beyond 90 days. The AKIKI trial was a multicenter trial that compared two strategies for starting RRT in 620 mixed critically ill patients with AKI who were receiving mechanical ventilation and/or vasoactive drugs. The mean age was lower than that in the ELAIN Trial. No difference in 60-day mortality was found. For oldest old critically ill patients, the evaluation of the time of initiation of RRT, in daily practice, requires a multidisciplinary approach involving the patient and relatives. Although dialysis undoubtedly prolonged survival in patients with ESRD, it is imperative that clinicians actively discuss and consider nonaggressive renal care in addition to RRT. Physicians should be responsible for offering care that promotes the best quality of life and not necessarily the longest duration [104]. Among survived critically ill patients requiring RRT, failure to recover kidney function, progression to end-stage kidney disease (ESKD) leading to dialysis dependence remain a significant medical and economic issue [105]. In a systematic review [106] intermittent renal replacement therapy (IRRT), used as an initial modality of RRT, was associated with a 1.7 times greater risk for dialysis dependence when compared with continuous renal replacement therapy (CRRT).

### **Cardiac arrest and cardiopulmonary resuscitation (CPR) in oldest old patients**

Cardiac arrests in adults are often due to ventricular fibrillation (VF) or pulseless ventricular tachycardia (VT), which are associated with better outcomes than asystole or pulseless electrical activity (PEA) [107]. Ventricular fibrillation and pulseless electrical activity were the most common cardiac arrest rhythms in elderly patients as well as a diagnosis of heart failure, myocardial infarction, or renal insufficiency. In the study by Chan et al. [108], the risk adjusted rate of 1-year survival was 63.7 % among patients aged between 65 and 74, as compared with 58.6 % among patients aged between 75 and 84 and 49.7 % among patients aged 85 or older. The survival rate was

significantly lower in oldest old population and among patients with moderate or severe neurologic disabilities at discharge. An epidemiologic study of in-hospital CPR in the elderly by Ehlenbach et al. [109] analyzed 65,530 patients aged between 85 and 89 and 34,039 patients aged 90 and over. The mortality rate for the group aged between 85 and 89 was 85 % and 9895 survived to hospital discharge (15.1 %). In the second group, 4156 patients (12.2 %) survived to hospital discharge. The authors argued that the associations of oldest old patients and higher burden of chronic illness with poorer survival were not surprising. The finding that residence in a skilled nursing facility before admission provides that chronic illness affects outcomes after CPR. The variables associated with failure to discharge in patients who undergo to CPR were dementia, sepsis on the day before resuscitation, increase levels of serum creatinine, cancer, coronary artery disease and location of resuscitation [110]. Funada et al. [111] studied the neurological outcome and survival of large database of elderly patients with out-hospital cardiac arrest. The cohort of oldest old patients included 136 392 patients aged between 85 and 94 and 23 577 patients aged >95. One month survival outcome was 0.59 % (803/132,292) among patients aged between 85 and 94 and 0.27 % (63/23,577) among patients aged >95. Compared to patients aged between 75 and 84 those aged between 85 and 94 and >95 had significantly worse outcomes. The authors found that annual trend in 1-month survival with favorable neurological outcome by age, witness status, first documented rhythm and etiology demonstrated in all subgroups an improvement in outcomes. Furthermore, 1-month survival with favorable outcomes did not improve among patients in the oldest old age group or for those who had unwitnessed out-hospital cardiac arrest. Postcardiac arrest brain injury is a syndrome resulting from a critical reduction in blood flow or oxygen and nutrient supply. Common clinical features include coma and vegetative status, seizures and myoclonus. [112]. Targeted temperature management (TTM) is an essential element of postresuscitation care for global ischemic brain injury. The 2015 Cardiopulmonary resuscitation (CPR) guidelines recommend that comatose (i.e. lack of meaningful response to verbal commands) adult patients with return of spontaneous circulation (ROSC) have TTM (induced hypothermia) as a beneficial and effective treatment (class I) [113]. This guideline recommends selecting and maintaining a constant temperature between 32 and 36 °C. Data about the use of TTM in oldest old comatose cardiac arrest survivors seems to show that age is considered an independent predictor of TTM underutilization. A descriptive analysis of TTM application from 130,582 completed records of the Cardiac Arrest Registry to Enhance Survival (CARES) found that treatment rates significantly decreased from age

75–84 [114]. Bosson et al. [115] in a retrospective study showed that TTM was associated with improved neurologic outcome in the elderly population. Busch et al. [116] showed in advanced-age postarrest survivors group a favorable outcome and highlight the need for more ad hoc clinical trials.

### **Delirium and cognitive impairment in oldest old seriously ill patients**

Delirium is a syndrome characterized by sudden severe confusion and rapid changes in brain function, inattention and disorganized thinking or altered level of consciousness. The Diagnostic and Statistical Manual of Mental disorders 4<sup>th</sup> Edition (DSM-IV) includes four items for diagnosing delirium: disturbance of consciousness, change in cognition, development over a short period, and fluctuation [117]. The development of delirium in older critically ill patients is due to a dynamic and complex process associated with numerous risk factors such as advanced age, medical comorbidity, preexisting mental impairment, neurological diagnoses, observational and occult metabolic abnormalities, withdrawal from chronic psychoactive medications, sleep deprivation, sedatives [118]. Dementia is an important predisposing risk factor during and after the ICU recovery [119]. On the other hand, intensive care survivors had significantly more cognitive problems than those who did not suffer from delirium. Delirium was considered an independent predictor of worse score on neuropsychological testing and associated with worse global cognition at 3 and 12 months [120, 121]. Cognitive impairment, mainly problems with memory and names until 18 months after discharge, seems to be correlated with the duration of delirium during ICU recovery [122]. In patients survived after mechanical ventilation evaluated at 12 months, the duration of delirium was associated with worse scores on activities of daily living and impaired perception of motor sensory function [123]. Clinical evaluation of delirium is difficult in the setting of unstable and intubated patients. The incidence ranges from 19 % [124] to 89 % [125]. A recent meta-analysis about the outcome of delirium in critically ill patients concluded that nearly a third of patients admitted (30 %) to an intensive care unit develop delirium and these patients are at increased risk of dying during admission, longer stays in hospital and cognitive impairment after discharge [126]. The clinical practice guidelines for the management of pain, agitation and delirium in adult patients in ICU [127] stated that there are no evidences that treatment with haloperidol reduces the duration of delirium as opposed to atypical antipsychotics. In the event of delirium unrelated to alcohol or benzodiazepine withdrawal, this guideline suggests the



continuous IV of dexmedetomidine rather than benzodiazepine infusions, and it does not recommend the administration of rivastigmine. The prevention recommends to identify delirium risk factors (dementia, high severity illness, coma, benzodiazepine administration, ETOH abuse) to mobilize and exercise patients early, to promote sleep, to restart baseline psychiatric medicines if indicated and to avoid benzodiazepine use.

### Nutrition in critically oldest old patients

The impossibility to adequately feeding and anorexia for critically ill patients in ICU could range from few days to various months. In older patients, this context often overlaps with preexisting malnutrition. Older people are at an increased risk of inadequate diet and malnutrition, and the rise in the older population will put more patients at risk. Inadequate diet and malnutrition are associated with a decline in functional status, impaired muscle function, decreased bone mass, immune dysfunction, anemia, reduced cognitive function, poor wound healing, delay in recovering from surgery, and higher hospital and readmission rates and mortality [128]. In the ICU context, the accurate evaluation of energy requirements and the assessment of daily caloric intake to avoid undernutrition and overfeeding are difficult. The main vital signs as for example heart rate, respiratory rate, temperature, urine output, fluid balance, presence of sepsis can change from one day to another with repercussions on energy expenditure. The European Society of Parenteral and Enteral nutrition (ESPEN) guidelines [129] recommend using, as gold standard, the indirect calorimetry (IC) but states that if unavailable the caloric estimation could be based on body weight or calculated with mathematical formulas. Numerous studies showed that in mechanically ventilated patients an optimal nutritional therapy is associated with a decrease in mortality. Wells et al. [130] found a decrease in 28-day mortality by 50 % when energy and protein targets are reached. Increased intakes of energy and protein appear to be associated with improved clinical outcomes in critically ill patients, particularly when BMI is <25 or >or =35. In oldest old critically patients, when possible, enteral nutrition is mandatory for preserving intestinal function. A meta-analysis demonstrated reduced mortality when enteral nutrition was initiated early in critically ill patients [131] as well as the late initiation of parenteral nutrition was associated with faster recovery and fewer complications, as compared with early initiation [132]. Furthermore clinical practice guidelines recommend enteral nutrition as the preferred route for caloric support with early initiation when possible [133].

### Conclusion

The aging of global population requires a special attention for the critically oldest old patients. Despite technological advances, mortality for critically ill oldest old patients remains high. The intensive caring should be able to combine technology and a deep humanity considering that the patients are living the last part of their lives. Their clinical management should take into account the patient's preference and the capability to avoid the medical futility respecting the patients' quality of life and their dying process with dignity. In selected oldest old patients as in the case of patients with hypercapnic acute respiratory failure or with the necessity of comfort measures only, NIMV should be preferred to IMV. Identification of the patients at risk of malnutrition as well as of those at risk of delirium should be the hallmark of intensive caring. The CPR scenario requires a correct evaluation of the possible negative outcome. Although RRT could be safe in oldest, old is associated with high risk of morbidity and mortality. The Italian legal issues require further evaluations, especially about the lack of decisional power of proxy, surrogates and relatives. Heterogeneity of oldest old patients population need a broader geriatric assessment and the need of the adequate evaluation of the burden of comorbidities and critically ill disease on prognosis. Further investigations are necessary to develop a better therapeutic strategy for oldest old critically ill patient-centered.

**Acknowledgments** We wish to thank Dr. Palmira Martino Teacher of English Language for kindly reviewing the English of the manuscript.

### Compliance with ethical standards

**Conflict of interest** The authors have no financial or other kind of personal conflicts with this paper.

**Statement of human and animal rights** This article does not contain any studies with human participants or animals performed by any of the authors.

**Informed consent** For this type of study formal consent is not required.

### References

1. Schoenmaeckers R (2004) Active ageing in europe Volume 2 demographic characteristics of the oldest old. Population Studies Series 47, Council of Europe Publishing : Strasbourg
2. National Research Council (US) Panel on a research agenda and new data for an aging world. Preparing for an aging world: the case for cross-national research. Washington (DC): National Academies Press (US); 2001. 2, Our Aging World. <http://www.ncbi.nlm.nih.gov/books/NBK98375/>

3. Kannisto V (1996) Development of oldest old mortality 1950–1990. Evidence from 28 developed countries. *Population Studies*, 50:143–144
4. Riley J (2001) *Rising life expectancy: a global history*. Cambridge Univ. Press, Cambridge
5. Tomassini C (2005) The demographic characteristics of the oldest old in the United Kingdom. *Popul Trends Summer* 120:15–22
6. UN (2014) Characteristics of the older population. In: UN, *World population ageing 2013*, UN. doi:[10.18356/448b609b-en](https://doi.org/10.18356/448b609b-en)
7. Andersen-Ranberg K, Petersen I, Robine J-M et al (2005) Who are the oldest-old? In: Börsch-Supan A, Brugiavini A, Jürges H, Mackenbach J, Siegrist J, Weber G (eds) *Health, ageing and retirement in Europe: first results from the survey of health, ageing and retirement in Europe*. Mannheim Research Institute for the Economics of Aging, s. 35–40 6 s
8. van den Akker M, Buntinx F, Metsemakers JFM et al (1998) Multimorbidity in general practice: prevalence, incidence, and determinants of co-occurring chronic and recurrent diseases. *J Clin Epidemiol* 51:367–375
9. Gijzen R, Hoeymans N, F Schellevis et al (2001) Causes and consequences of comorbidity: are view. *J Clin Epidemiol* 54:661–674
10. Marengoni A, Angleman S, Melis R et al (2011) Aging with multimorbidity: a systematic review of the literature. *Ageing Res Rev* 10:430–439
11. Garrouste-Orgeas M, Timsit JF, Montuclard L et al (2006) Decision-making process, outcome, and 1-year quality of life of octogenarians referred for intensive care unit admission. *Intensive Care Med* 32:1045–1051
12. Boumendil A, Aegerter P, Guidet B et al (2005) Treatment intensity and outcome of patients aged 80 and older in intensive care units: a multicenter matched-cohort study. *J Am Geriatr Soc* 53:88–93
13. Girard TD, Ely EW (2008) Changing demographics in the intensive care unit in Irwin and Rippe's. In: *Intensive care medicine*. Sixth Edition. Wolters Kluwer; Lippincott Williams & Wilkins
14. Korc-Grodzicki B, Holmes HM, Shahrokni A (2015) A Geriatric assessment for oncologists. *Cancer Biol Med* 12:261–274
15. Nuckton TJ, List ND (1995) Age as a factor in critical care admissions. *Arch Intern Med* 155:1087–1092
16. Arias E (2015) United States life tables. *Natl Vital Stat Rep* 64:1–63
17. Italy, resident population by year, sex and age. <http://demo.istat.it/pop2015/index.html>. Accessed 18 June 2016
18. Conti M, Merlani P, Ricou B (2012) Prognosis and quality of life of elderly patients after intensive care. *Swiss Med Wkly* 142:w13671. doi:[10.4414/smw.2012.13671](https://doi.org/10.4414/smw.2012.13671)
19. Benbassat J, Pilpel D, Tidhar M (1998) Patients' preferences for participation in clinical decision making: a review of published surveys. *Behav Med* 24:81–88
20. Cicirelli VG (1997) Relationship of psychosocial and background variables to older adults' end-of-life decisions. *Psychol Aging* 12:72–83
21. Henderson A, Shum D (2003) Decision-making preferences towards surgical intervention in a Hong Kong Chinese population. *Int Nurs Rev* 50:95–100
22. Cohen-Mansfield J, Droge JA, Billig N (1992) Factors influencing hospital patients' preferences in the utilization of life-sustaining treatments. *Gerontologist* 32:89–95
23. Fried T, Bradley E, Towle V et al (2002) Understanding the treatment preferences of seriously ill patients. *N Engl J Med* 346:1061–1066
24. Fried T, Van Ness P, Byers A et al (2007) Changes in preferences for life-sustaining treatment among older persons with advanced illness. *J Gen Intern Med* 22:495–501
25. Wilson ME, Krupa A, Hinds RF et al (2015) A video to improve patient and surrogate understanding of cardiopulmonary resuscitation choices in the ICU: a randomized controlled trial. *Crit Care Med* 43:621–629. doi:[10.1097/CCM.0000000000000749](https://doi.org/10.1097/CCM.0000000000000749)
26. Philippart F, Vesin A, Bruel C et al (2013) The ETHICA study (part I): orderly's thoughts about intensive care unit admission for life-sustaining treatments. *Intens Care Med* 39:1565–1573
27. Giampieri M (2012) Communication and informed consent in elderly people. *Minerva Anestesiol* 78:236–242
28. Kapp MB (2010) Legal issues arising in the process of determining decisional capacity in older persons. *Care Manag J* 11:101–107
29. Appelbaum Paul S (2007) Assessment of patients' competence to consent to treatment. *N Engl J Med* 357:1834–1840
30. Berg JW, Appelbaum PS, Grisso T (1996) Constructing competence: formulating standards of legal competence to make medical decisions. *Rutgers Law Rev* 48:345–371
31. Italian law January 9, 2004 n 6. <http://www.camera.it/parlam/leggi/040061.htm>. Accessed 21 June 2016
32. The SUPPORT Principal Investigators (1995) A controlled trial to improve care for seriously ill hospitalized patients: the study to understand prognoses and preferences for outcomes and risks of treatments (SUPPORT). *JAMA* 274:1591–1598
33. Lubitz J, Riley GF (1993) Trends in medicare payments in the last year of life. *N Engl J Med* 328:1092–1096
34. Scitovsky AA (1994) The high cost of dying, revisited. *Milbank Q* 72:561–591
35. Guidelines for the Appropriate Use of Do-Not-Resuscitate Orders (1991) Council on ethical and judicial affairs. *JAMA* 265:1868–1871
36. Somogyi-Zalud E, Zhong Z, Hamel MB et al (2002) The use of life-sustaining treatments in hospitalized persons aged 80 and older. *J Am Geriatr Soc* 50:930–934
37. Garrouste-Orgeas M, Boumendil A, Pateron D et al (2009) Selection of intensive care unit admission criteria for patients aged 80 years and over and compliance of emergency and intensive care unit physicians with the selected criteria: an observational, multicenter, prospective study. *Crit Care Med* 37:2919–2928
38. Esteban A, Anzueto A, Frutos-Vivar F et al (2004) Outcome of older patients receiving mechanical ventilation. *Intensive Care Med* 30:639–646
39. Nguyen Y-L, Angus DC, Boumendil A et al (2011) The challenge of admitting the very elderly to intensive care. *Ann Intensive Care* 1:29. doi:[10.1186/2110-5820-1-29](https://doi.org/10.1186/2110-5820-1-29)
40. Scala R, Esquinas A (2012) Non invasive mechanical ventilation for very old patients with limitations of care: is the ICU the most appropriate setting? *Crit Care* 16:429. doi:[10.1186/cc11352](https://doi.org/10.1186/cc11352)
41. Cohen IL, Lambrinos J (1995) Investigating the impact of age on outcome of mechanical ventilation using a population of 41,848 patients from a statewide database. *Chest* 107:1673–1680
42. Kurek CJ, Dewar D, Lambrinos J et al (1998) Clinical and economic outcome of mechanically ventilated patients in New York State during 1993 analysis of 10,473 cases under DRG 475. *Chest* 114:214–222
43. 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. doi:[10.1186/cc9984](https://doi.org/10.1186/cc9984)
44. Fuchs L, Chronaki CE, Park S et al (2012) ICU admission characteristics and mortality rates among elderly and very elderly patients. *Intensive Care Med* 38:1654–1661
45. Chandra D, Stamm JA, Taylor B et al (2012) Outcomes of noninvasive ventilation for acute exacerbations of obstructive pulmonary disease in the United States, 1998–2008. *Am J Respir Crit Care Med* 185:152–159

46. Stefan MS, Shieh MS, Pekow PS et al (2013) Epidemiology and outcomes of acute respiratory failure in the United States, 2001 to 2009: a national survey. *J Hosp Med* 8:76–82
47. Ferrão C, Quintaneiro C, Camila C et al (2015) Evaluation of long-term outcomes of very old patients admitted to intensive care: survival, functional status, quality of life, and quality-adjusted life-years. *J Crit Care*. doi:10.1016/j.jcrc.2015.05.005
48. Becker S, Müller J, de Heer G et al (2015) Clinical characteristics and outcome of very elderly patients  $\geq 90$  years in intensive care: a retrospective observational study. *Ann Intensive Care* 5:53. doi:10.1186/s13613-015-0097-1e1
49. Sim YS, Jung H, Shin TR et al (2015) Mortality and Outcomes in very elderly patients 90 years of age or older admitted to the ICU. *Respir Care* 60:347–355
50. Garrouste-Orgeas M, Ruckly S, Grégoire C et al (2016) Treatment intensity and outcome of nonagerians selected for admission in ICUs: a multicenter study of the Outcomerea Research Group. *Ann Intensive Care* 6:31. doi:10.1186/s13613-016-0133-9
51. Heyland D, Cook D, Bagshaw SM et al (2015) The very elderly admitted to ICU: a quality finish? *Crit Care Med* 43:1352–1360. doi:10.1097/CCM.0000000000001024
52. Peigne V, Somme D, Guérot E et al (2016) Treatment intensity, age and outcome in medical ICU patients: results of a French administrative database. *Ann Intensive Care* 6:7. doi:10.1186/s13613-016-0107-y
53. Pesau B, Falger S, E Berger et al (1992) Influence of age on outcome of mechanically ventilated patients in an intensive care unit. *Crit Care* 20:489–492
54. Wesley Ely E, Wheeler AP, Thompson T et al (2002) Recovery Rate and prognosis in older persons who develop acute lung injury and the respiratory distress syndrome. *Ann Intern Med* 136:25–36
55. Rubenfeld GD, Caldwell E, Peabody E et al (2005) Incidence and outcomes of acute lung injury. *N Engl J Med* 353:1685–1693
56. (2000) Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. The Acute Respiratory Distress Syndrome Network. *N Engl J Med* 342:1301–1308
57. Sutherasan Y, Vargas M, Pelosi P (2014) Protective mechanical ventilation in the non-injured lung: review and meta-analysis. *Crit Care* 18:211. doi:10.1186/cc13778
58. Eachempati SR, Hydo LJ, Shou J et al (2007) Outcomes of acute respiratory distress syndrome (ARDS) in elderly patients. *J Trauma* 63:344–350
59. Gracey DR, Naessens JM, Krishan I et al (1992) Hospital and posthospital survival in patients mechanically ventilated for more than 29 days. *Chest* 101:211–214
60. Mehta AB, Syeda SN, Bajpayee L et al (2015) Trends in tracheostomy for mechanically ventilated patients in the United States, 1993–2012. *Am J Respir Crit Care Med* 192:446–454
61. Baskin JZ, Panagopoulos G, Parks C, Komisar A (2004) A Clinical outcomes for the elderly patient receiving a tracheotomy. *Head Neck* 26:71–75
62. Drendel M, Primov-Fever A, Talmi YP et al (2009) Outcome of tracheostomy in patients over 85 years old (oldest old patients). *Otolaryngol Head Neck Surg* 140:395–397
63. Royal College of Physicians, British Thoracic Society, Intensive Care Society Chronic obstructive pulmonary disease: non-invasive ventilation with bi-phasic positive airways pressure in the management of patients with acute type 2 respiratory failure (2008) Concise Guidance to Good Practice series, No 11. London RCP. <http://www.rcplondon.ac.uk/pubs/brochure.aspx?e=258>
64. Chandra D, Stamm JA, Taylor B et al (2012) Outcomes of NIV for acute exacerbations of COPD in the United States, 1998–2008. *Am J Respir Crit Care Med* 185:152–159
65. Schortgen F, Follin A, Piccari L et al (2012) Results of non-invasive ventilation in very old patients. *Ann Intensive Care* 2:5. doi:10.1186/2110-5820-2-5
66. Segrelles Calvo G, Zamora García E, Girón Moreno R et al (2012) Non-invasive ventilation in an elderly population admitted to a respiratory monitoring unit: causes, complications and one-year evolution. *Arch Bronconeumol* 48:349–354. doi:10.1016/j.arbres.2012.05.001
67. Scarpazza P, Incorvaia C, Amboni P et al (2011) Long term survival in elderly patients with a do not intubate order treated with non invasive mechanical ventilation. *Int J Chron Obstruct Pulmon Dis* 6:253–257. doi:10.2147/COPD.S18501
68. Salturk C, Karakurt Z, Takir HB (2015) NIMV in older patients in noninvasive mechanical ventilation: theory, equipment, and clinical application By Antonio M. Esquinas 2015. Springer Edition
69. Piroddi IM, Barlaschini C, Esquinas A et al (2016) Non invasive mechanical ventilation in elderly patients: a narrative review. *Geriatr Gerontol Int*. doi:10.1111/ggi.12810
70. Bülow HH, Thorsager B (2009) Non-invasive ventilation in do-not-intubate patients: five-year follow-up on a two-year prospective, consecutive cohort study. *Acta Anaesthesiol Scand* 53:1153–1157. doi:10.1111/j.1399-6576.2009.02034.x
71. Vargas N, Vargas M, Galluccio V et al (2014) Non-invasive ventilation for very old patients with limitations to respiratory care in half-open geriatric ward: experience on a consecutive cohort of patients. *Aging Clin Exp Res* 26:615–623
72. Ihra GC, Lehberger J, Hochrieser H et al (2012) Development of demographics and outcome of very old critically ill patients admitted to intensive care units. *Intensive Care Med* 38:626
73. Shah P, Najafi AH, Panza JA et al (2009) Outcomes and quality of life in patients  $\geq 85$  years of age with ST-elevation myocardial infarction. *Am J Cardiol* 103:170–174
74. Skolnick AH, Alexander KP, Chen AY et al (2007) Characteristics, management, and outcomes of 5,557 patients age  $\geq 90$  years with acute coronary syndromes: results From the CRUSADE initiative. *J Am Coll Cardiol* 49:1790–1797. doi:10.1016/j.jacc.2007.01.066
75. Biston P, Aldecoa C, Devriendt J et al (2014) Outcome of elderly patients with circulatory failure. *Intensive Care Med* 40:50–56. doi:10.1007/s00134-013-3121-7
76. Samuels LE, Kufman MS, Thomas MP et al (1999) Pharmacological criteria for ventricular assist device insertion following postcardiotomy shock: experience with Abiomed BSV system. *J Card Surg* 14:288–293
77. Nasa P, Juneja D, Singh O (2012) Severe sepsis and septic shock in the elderly: an overview. *World J Crit Care Med* 1:23–30. doi:10.5492/wjccm.v1.i1.23
78. Morrow DA, Fang JC, Fintel DJ et al (2012) Transformation of the cardiovascular intensive care unit and the emerging need for new medical staffing and training models: a scientific statement from the American Heart Association. *Circulation* 126:1408–1428
79. Thiele H, Zeymer U, Neumann FJ et al (2012) Intraaortic balloon support for myocardial infarction with cardiogenic shock. *N Engl J Med* 367:1287–1296. doi:10.1056/NEJMoa1208410
80. Thiele H, Zeymer U, Neumann FJ et al (2013) Intra-aortic balloon counterpulsation in acute myocardial infarction complicated by cardiogenic shock (IABP-SHOCK II): final 12 months results of a randomised, open label trial. *Lancet* 382:1638–1645
81. Sjaw KD, Engstrom AE, Vis MM (2009) A systematic review and meta-analysis of intraortic balloon pump therapy in ST

- elevation myocardial infarction: should we change the guidelines'. *Eur Heart J* 30:459–468
82. Stretch R, Sauer C, Yuh D et al (2014) National trends in the utilization of short-term mechanical circulatory support. *J Am Coll Cardiol* 64:1407–1415
  83. Bridges CR, Edwards FH, Peterson ED et al (2003) Cardiac surgery in nonagenarians and centenarians. *J Am College Surg* 197:347–356
  84. Aso S, Matsui H, Fushimi K et al (2016) In-hospital mortality and successful weaning from venoarterial extracorporeal membrane oxygenation: analysis of 5263 patients using a national inpatient database in Japan. *Crit Care* 20:80. doi:10.1186/s13054-016-1261-1
  85. Dixon SR, Henriques JP, Mauri L et al (2009) A prospective feasibility trial investigating the use of the impella 2.5 system in patients undergoing high risk percutaneous coronary intervention (the PROTECT I trial): initial U.S. experience. *JACC Cardiovasc Interv* 2:91–96
  86. O'Neill WW, Kleiman NS, Moses J et al (2012) A prospective, randomized clinical trial of hemodynamic support with Impella 2.5 versus intra-aortic balloon pump in patients undergoing high risk percutaneous coronary intervention: the PROTECT II study. *Circulation* 126:1717–1727
  87. Seyfarth M, Sibbing D, Bauer I et al (2008) A randomized clinical trial to evaluate the safety and efficacy of a percutaneous left ventricular assist device versus intra-aortic balloon pumping for treatment of cardiogenic shock caused by myocardial infarction. *J Am Coll Cardiol* 52:1584–1588. doi:10.1016/j.jacc.2008.05.065
  88. Case J, Khan S, Khalid R et al (2013) Epidemiology of acute kidney injury in the intensive care unit. *Crit Care Res Pract* 2013:479730. doi:10.1155/2013/479730
  89. Kurella M, Covinsky KE, Collins AJ et al (2007) Octogenarians and nonagenarians starting dialysis in the United States. *Ann Intern Med* 146:177–183
  90. US Renal Data System Report (2010) <https://www.usrds.org/atlas10.aspx>
  91. Jassal SV, Karoboyas A, Comment LA et al (2016) Functional dependence and mortality in the international dialysis outcomes and practice patterns study (DOPPS). *Am J Kidney Dis* 67:283–292. doi:10.1053/j.ajkd.2015.09.024
  92. Guerra C, Linde-Zwirble WT, Wunsch H (2012) Risk factors for dementia after critical illness in elderly medicare beneficiaries. *Crit Care* 16:R233. doi:10.1186/cc11901
  93. (1997) The USRDS Dialysis Morbidity and Mortality Study: Wave 2. United States Renal Data System. *Am J Kidney Dis* 30(2 Suppl 1):S67–85
  94. Tamura MK (2009) Incidence, management, and outcomes of end-stage renal disease in the elderly. *Curr Opin Nephrol Hypertens* 18:252–257. doi:10.1097/MNH.0b013e328326f3ac
  95. Lamping DL, Constantinovici N, Roderick P et al (2000) Clinical outcomes, quality of life, and costs in the North Thames Dialysis Study of elderly people on dialysis: a prospective cohort study. *Lancet* 356:1543–1550
  96. Nordio M, Limido A, Maggiore U et al (2012) Survival in patients treated by long-term dialysis compared with the general population. *Am J Kidney Dis* 59:819–828. doi:10.1053/j.ajkd.2011.12.023
  97. Joly D, Anglicheau D, Alberti C (2003) Epidemiology and outcomes: octogenarians reaching end-stage renal disease: cohort study of decision-making and clinical outcomes. *JASN* 14:1012–1021. doi:10.1097/01.ASN.0000054493.04151.80
  98. Akposso K, Hertig A, Couprie R (2000) Flahaut A Acute renal failure in patients over 80 years old: 25-years' experience. *Intensive Care Med* 26:400–406
  99. Pannu N, Gibney RN (2005) Renal replacement therapy in the intensive care unit. *Ther Clin Risk Manag* 1:141–150
  100. KDIGO Clinical Practice Guideline for Acute Kidney Injury. <http://www.kdigo.org/Clinical>
  101. Bouman CS, Oudemans-Van Straaten HM, Tijssen JG et al (2002) Effects of early high-volume continuous venovenous hemofiltration on survival and recovery of renal function in intensive care patients with acute renal failure: a prospective, randomized trial. *Crit Care Med* 30:2205–2211
  102. Zarbock A, Kellum JA, Schmidt C et al (2016) Effect of early vs delayed initiation of renal replacement therapy on mortality in critically ill patients with acute kidney injury: the ELAIN randomized clinical trial. *JAMA* 315:2190–2199. doi:10.1001/jama.2016.5828
  103. Gaudry S, Hajage D, Schortge F et al (2016) Initiation strategies for renal-replacement therapy in the intensive care unit. *N Engl J Med* 375:122–133. doi:10.1056/NEJMoa1603017
  104. Jassal SV, Watson D (2009) Dialysis in late life: benefit or burden. *CJASN* 12:2008–2012. doi:10.2215/CJN.04610709
  105. Ethgen O, Schneider AG, Bagshaw SM et al (2014) Economics of dialysis dependence following renal replacement therapy for critically ill acute kidney injury patients. *Nephrol Dial Transplant*. doi:10.1093/ndt/gfu314
  106. Schneider AG, Bellomo R, Bagshaw SM et al (2013) Choice of renal replacement therapy modality and dialysis dependence after acute kidney injury: a systematic review and meta-analysis. *Intensive Care Med* 39:987–997. doi:10.1007/s00134-013-2864-5
  107. Nadkarni VM, Larkin GL, Peberdy MA et al (2006) National registry of cardiopulmonary resuscitation investigators first documented rhythm and clinical outcome from in-hospital cardiac arrest among children and adults. *JAMA* 295:50–57
  108. Chan Paul S, Nallamothu Brahmajee K, Harlan M et al (2013) Long-term outcomes in elderly survivors of in-hospital cardiac arrest. *N Engl J Med* 368:1019–1026. doi:10.1056/NEJMoa1200657
  109. Ehlenbach WJ, Barnato AE, Curtis JR et al (2009) Epidemiologic Study of in-hospital cardiopulmonary resuscitation in the elderly. *N Engl J Med* 361:22–31
  110. Ebell MH, Becker LA, Barry HC et al (1998) Survival after in-hospital cardiopulmonary resuscitation a meta-analysis. *J Gen Intern Med* 13:805–816
  111. Funada A, Goto Y, Maeda T et al (2016) Improved survival with favorable neurological outcome in elderly individuals with out-of-hospital cardiac arrest in Japan—a nationwide observational cohort. *Circ J* 80:1153–1162. doi:10.1253/circj.CJ-15-1285
  112. Kuroda Y (2016) Neurocritical care update. *J Intensive Care* 4:49. doi:10.1186/s40560-016-0141-8
  113. Neumar RW, Shuster M, Callaway CW et al (2015) American heart association guidelines update for cardiopulmonary resuscitation and emergency cardiovascular care. *Circulation* 132:S315–S367
  114. McNally B, Kellermann A, Crouch A et al (2009) Cardiac arrest registry to enhance survival (CARES)
  115. Bosson NE, Kaji AH, Koenig WJ, Niemann JT (2016) Effect of therapeutic hypothermia on survival and neurologic outcome in the elderly. *Ther Hypothermia Temp Manag* 6:71–5. doi:10.1089/ther.2015.0030
  116. Busch M (2011) Søreide Should advanced age be a limiting factor in providing therapeutic hypothermia to cardiac arrest survivors? A single-center observational study. *Ther Hypothermia Temp Manag* 1:29–32. doi:10.1089/ther.2010.0006
  117. Diagnostic and statistical manual of mental disorders, 4th ed. text rev: DSMIV-TR. Arlington, VA: American Psychiatric Association, 2011

118. Reade MC, Finfer S (2014) Sedation and delirium in the intensive care unit. *N Engl J Med* 370:444–454. doi:[10.1056/NEJMr1208705](https://doi.org/10.1056/NEJMr1208705)
119. Mc Nicoll L, Pisani MA, Y Zhang et al (2003) Delirium in the intensive care unit: occurrence and clinical course in older patients. *J Am Geriatr Soc* 51:591–598
120. Girard TD, Jackson JC, Pandharipande PP et al (2010) Delirium as predictor of long term cognitive impairment in survivors of critical illness. *Crit Care Med* 87:1513–1520
121. Pandharipande PP, Girard TD, Jackson JF et al (2013) Long term cognitive impairment after critical illness. *N Engl J Med* 369:1306–1316
122. van den Boogaard M, Schoonhoven L, Evers AW et al (2012) Delirium in critically ill patients: impact on long-term health related quality of life and cognitive functioning. *Crit Care Med* 40:112–118
123. Brummel NE, Jackson JC, Pandharipande PP et al (2014) Delirium in the ICU and subsequent long term disability among survivors of mechanical ventilation. *Crit Care Med* 42:369–377
124. Bergeron N, Dubois MJ, Dumont M et al (2001) Intensive care delirium screening checklist: evaluation of a new screening tool. *Intensive Care Med* 27:859–864
125. Ely E, Girard TD, Shintani AK et al (2007) Apolipoprotein E4 polymorphism as a genetic predisposition to delirium in critically ill patients. *Crit Care Med* 35:112–117
126. Salluh JIF, Wang H, Schneider EB et al (2015) Outcome of delirium in critically ill patients: a systematic review and meta-analysis. *BMJ* 350:25–38
127. Barr J, Fraser GL, Puntillo K et al (2013) Clinical practice guidelines for the management of pain, agitation, and delirium in adult patients in the intensive care unit. *Crit Care Med* 41:263–306
128. Ahmed T, Haboubi N (2010) Assessment and management of nutrition in older people and its importance to health. *Clin Interv Aging* 5:207–216
129. Sobotka L, Schneider SM, Berner YN et al (2009) ESPEN guidelines on parenteral nutrition: geriatrics. *Clin Nutr* 28:461–466
130. Weijs PJ, Stapel SN, de Groot SD et al (2012) Optimal protein energy nutrition decreases mortality mechanically ventilated, critically ill patients: a prospective observational cohort study. *JPEN J Parenter Enteral Nutr* 36:60–68. doi:[10.1177/0148607111415109](https://doi.org/10.1177/0148607111415109)
131. Doig GS, Heighes PT, Simpson F et al (2009) Early enteral nutrition, provided within 24 h of injury or intensive care unit admission, significantly reduces mortality in critically ill patients: a meta-analysis of randomised controlled trials. *Intensive Care Med* 35:2018–2027
132. Casaer MP, Mesotten D, Hermans G et al (2011) Early versus late parenteral nutrition in critically ill adults. *N Engl J Med* 365:506–517
133. McClave SA, Martindale RG, Vanek VW et al (2009) Guidelines for the provision and assessment of nutrition support therapy in the adult critically ill patient: society of critical care medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (ASPEN). *JPEN J Parenter Enteral Nutr* 33:277–315