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REVIEW

Caring for critically ill oldest old patients: a clinical review

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

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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

✉ Nicola Vargas
nicolavargas@tin.it

[1] Geriatric and Intensive Geriatric Care Ward, Azienda Ospedaliera di Rilievo Nazionale e di Alta Specialità "San Giuseppe Moscati", via Contrada Amoretta, 83100 Avellino, Italy

[2] Medicine Ward, Medicine Department, "San Giuseppe Moscati" Hospital, via Gramsci, 81031 Aversa, CE, Italy

[3] 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

[4] Department of Clinical Disease and Internal Medicine, Federico II University of Naples, via Pansini, 80121 Naples, Italy

[5] Department of Neuroscience and Reproductive and Odontostomatological Sciences, University Federico II, Via Pansini, 89121 Naples, Italy

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

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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 retrospectives 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.

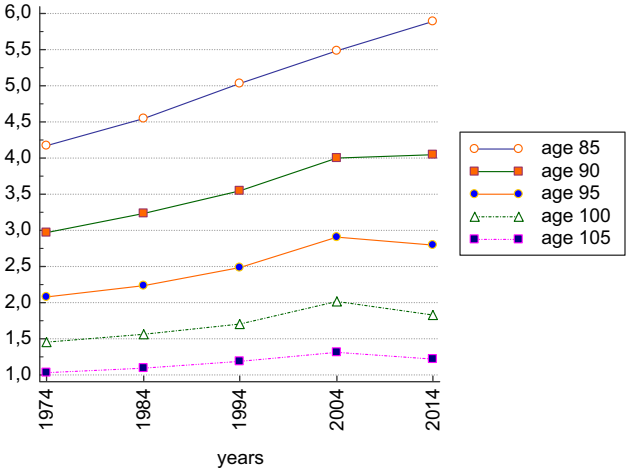

Fig. 1 Life expectancy Italian oldest old 1974–2014

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 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 directived 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

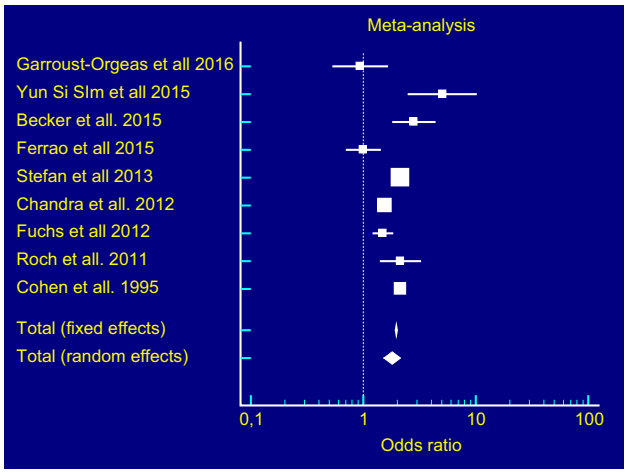

Fig. 2 Odds ratio risk for oldest old patients undergoing to mechanical ventilation in overall oldest old ICU population

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_2O 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 VT 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-open-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 ≥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 ≥ 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 ≥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 ≥ 80 years. In patients with hemodynamic instability aged ≥ 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 ≥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 Kidko AKI guidelines [100] noted that patients with life-threatening indications such as hyperkaliemia, 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 Kidko 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 4th 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.

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Compliance with ethical standards

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

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