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REVIEW

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Acute kidney injury in elderly intensive care patients: a review

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Abstract The elderly are at high risk for acute kidney injury (AKI). With the aging of the population, the demand for intensive care unit (ICU) admission from older patients will continue to rise, and this clinical entity will likely become increasingly common. In this article we review the relevant literature, discuss the age-related changes that render older people prone to AKI development, and examine the most frequent etiologies for renal impairment in these patients. We also consider the difficulties in achieving an early diagnosis in the elderly ICU patient, the particularities related to AKI treatment in this age group, and the data available on differences in renal recovery and mortality between the young and the old with renal injury. More importantly, we highlight the methods for prevention of AKI development or worsening in the elderly critically ill patient.

Keywords Elderly · Aging · Acute kidney injury · Acute renal failure · Intensive care · Critical illness

Introduction

Increasing attention has been focused on the rising prevalence of elderly patients in the intensive care unit (ICU) [1–3]. This interest in the elderly is warranted by the fact that this segment of the population is rapidly growing [4].

Despite "elderly" being one of the most frequently used terms in the medical literature when referring to older individuals, there is no universally accepted definition or cut-off age. Indeed, whether in intensive care or in other fields, authors have used various ages ranging anywhere from ≥60 years to ≥80 years when referring to these patients. In this review, we have chosen to include articles that refer to older or elderly patients, regardless of whether this indicates patients in their sixties, seventies, eighties or nineties.

What is the incidence of acute kidney injury in the elderly intensive care patient?

Fifty-five percent of all American ICU beds-days are occupied by patients aged ≥65 years [5]. In a multicenter study of 120,123 adult ICU admissions of more than 24 h duration, Australian New Zealand Intensive Care Society Adult Patient (ANCIZS) database researchers determined

that 13% were aged ≥80 years and that the admission rate for this age group increased by 5.6% per year during the period between 2000 and 2005 [6].

Acute kidney injury (AKI) is a common and important occurrence in the ICU [7], and most studies support the statement that the elderly patient is at the highest risk for AKI. The BEST Kidney collaborators, in a prospective multicenter study on 29,269 critically ill patients with a median age of 67 years, determined that 5.7% of the patients developed severe AKI. [8]. Moreover, in a prospective cohort study on risk factors and outcomes of AKI in the ICU as evaluated by the SOFA score, de Mendoça et al. determined that 24.7% of 1,411 patients developed AKI. The median age was significantly higher in the AKI group, and age >65 years was an independent risk factor for the development of AKI [9]. In a longitudinal cohort analysis on 381 critically ill octogenarians, 40% of patients admitted after 1996 developed AKI, as compared to 4% in the time period before 1978 [10]. In their recent study comparing the RIFLE and AKIN classifications, Joannidis et al. analyzed 16,784 patients during the initial 48 h of their ICU stay and determined that the incidence of AKI ranged between 28.5 and 35.5%. The mean age of the patients was 63 years, with 25% aged >75 years [11].

What are the factors contributing to AKI development in the elderly (Fig. 1)?

The aging kidney

In the absence of a specific disease, the kidney undergoes age-dependent structural and functional alterations leading to a significant decrease in renal mass, functioning nephron numbers, and baseline kidney function [12]. In 1937, Wald reported on kidney weights from 414 autopsies [13]. A 19% decline in male and 9% decline in female kidney weight were found when individuals aged 70–79 years were compared with those aged 20–29 years [13]. The loss of renal mass is primarily cortical, with relative sparing of the medulla [14]. The number of functioning glomeruli declines roughly in proportion with the changes in renal weight, whereas the size of the remaining glomeruli increases [15]. The incidence of sclerotic glomeruli rises with advancing age, increasing from less than 5% of the total glomeruli at the age of 40 years to 10–30% by the eighth decade of life [16]. With renal senescence, there is a variable decrease in glomerular filtration rate (GFR). However, the rate of decline varies according to measurement criteria, gender, race, genetic influence and, most importantly, the presence of interacting medical conditions that can impact renal function [17]. When possible, longitudinal studies offer the best method of assessing specific age-related changes on renal function [18]. Rowe et al. as well as investigators at the Gerontology Research Center used both cross-sectional and serial, prospective (longitudinal) analyses on a large group of active men [18, 19]. These studies demonstrated a highly significant reduction in creatinine clearance (Ccr) with age, beginning at age 34 years and accelerating after age 65 years (an approximate 1 ml/min per 1.73 m^2 per year decline in GFR occurring after age 50 years). However, this relationship is not predictable nor an inevitable consequence of aging, as 35% of elderly subjects had a stable Ccr over a 20-year period [18].

When interpreting these studies, one must consider that older studies often used the Cockroft–Gault formula to estimate GFR in study cohorts, while more recent ones use the Modification of Diet in Renal Disease (MDRD) Study Group formula, thus rendering questionable their comparability. Moreover, both approaches may underestimate GFR under certain conditions and thus overestimate CKD in elderly populations.

Effective renal blood flow (RBF) decreases up to 10% per decade of life [20]. Fliser et al. compared renal hemodynamics before and after an amino acid infusion, a technique which is used to assess the functional integrity or reserve of the kidney, in healthy, normotensive younger and older patients. These researchers demonstrated that the increase in RBF in the elderly was markedly impaired, with a higher renal vascular resistance [21]. The rise in renal vascular resistance may in part be related to reduced NO production in the elderly. GFR therefore seems to be preserved to some extent through an increased filtration fraction and renal vasoconstriction [20].

Renal sympathetic-mediated vasoconstriction appears to be exaggerated in the aging kidney, and there is a poor response to vasodilatory mediators, such as atrial natriuretic peptide and prostacyclin [22]. Furthermore, the aging renal vasculature appears to exhibit exaggerated angiotensin-II mediated vasoconstriction [23].

These changes in renal hemodynamics likely lead to an increased risk for AKI. Several studies have demonstrated that in combination with dehydration, a disturbance in autoregulatory defense mechanisms that would normally preserve GFR and RBF (such as increased renal vascular resistance) can in the elderly kidney lead to ischemia and AKI due to drastic falls in RBF [21, 24].

A change in sodium homeostasis results in an impaired ability to concentrate urine and increases the risk of volume depletion in the elderly [25, 26]. Mulkerrin and colleagues even observed a decreased response to dopamine and atrial natriuretic peptide in the elderly [27, 28]. In addition, there is a decrease in the capacity for drug excretion in these patients, the kidney being the main route of elimination for many drugs and their active metabolites [25].

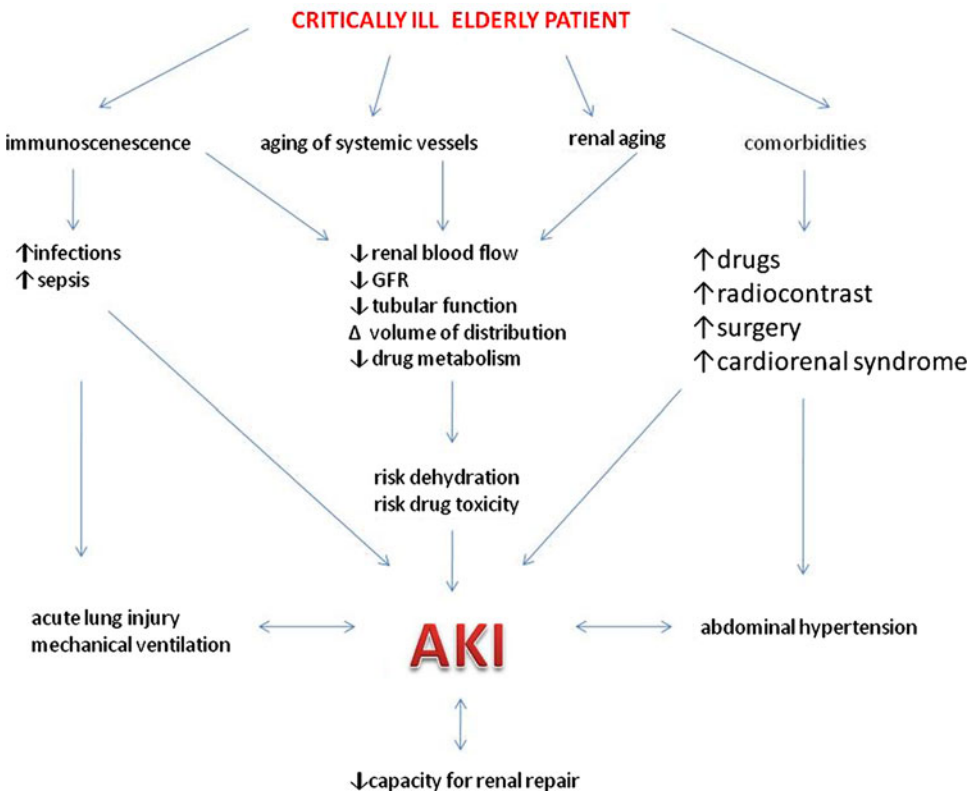

Fig. 1 Factors contributing to the development of acute kidney injury (*AKI*) in the elderly. *GFR* Glomerular filtration rate

The burst of cellular proliferation usually seen in response to acute damage seems to decline with age [29]. Moreover, basal rates of cellular apoptosis increase with age, both under baseline conditions as well as in response to injury. Changes in potential progenitor and immune cell functions are also seen [29]. Growth factors play a critical role in regulating cellular proliferation, migration, and apoptosis, and their expression is upregulated in response to injury. The expression of many of these growth factors decreases with aging, and their respective receptor transduction pathways are often downregulated [30].

Several morphological changes have been well described in the elderly [31]. A decrease in the number and size of tubules, an increase in interstitial collagen deposition, and fibrosis are usually observed [25, 31]. Renal vascular changes similar to those seen in systemic vessels are also frequently noted. Fibro-intimal hyperplasia and hyaline arteriolosclerosis are frequent as well as compensatory hypertrophy of the medullary glomeruli, which then develop hyperfiltration injury, followed by segmental and then by global glomerulosclerosis [25, 31]. A reduction in the total amount of viable glomeruli is frequent [25, 31]. It should be highlighted that these changes are also a feature of hypertension and of many conditions often seen in the elderly; consequently, it is difficult to assess the independent contribution of aging to these alterations [20].

Comorbidities

The incidence of comorbidities dramatically increases with age [32]. Obstruction is a common and usually reversible form of AKI that must not go unrecognized. The dramatic effect of prostatic disease on the incidence of AKI in patients aged 80–89 years is demonstrated in the study by Feest et al. [33] where 35% of the incidence of AKI was accounted for by prostatic disease. With the high prevalence of cardiovascular disease in the elderly, cardiorenal syndrome is increasingly recognized as a cause of AKI in this age group [34]. Furthermore, elderly patients are more likely to have chronic kidney disease (CKD), which greatly increases the risk of AKI. In many cases, these comorbid conditions lead to reduced GFR and reduced renal functional reserve or renal hemodynamic alterations that increase the susceptibility to injurious stimuli [35]. In the presence of hypotension, these structural and functional alterations may lead to dramatic decreases in renal perfusion and ischemic injury.

Drug toxicity

Due to the high prevalence of comorbidities and increased exposure to various medications, older patients are more often victims of iatrogenic complications [36]. Moreover, the physiologic changes associated with aging predispose

the elderly to drug toxicity [36]. Lean body mass decreases in the elderly with respect to adipose tissue, causing alterations in volume of distribution [25]. Water-soluble drugs, such as aminoglycosides, therefore attain higher blood concentrations [25]. A decreased GFR often goes unnoticed when clinicians are focused on only looking at serum creatinine values, which in the elderly may result in an overestimate of the GFR and, ultimately, to overdosage. In this regard, Gill et al. [37] analyzed the use of commonly used regression equations to estimate GFR in the elderly and demonstrated discordant estimations of GFR in >60% of elderly subjects using either the MDRD or Cockroft–Gault equations. Changes in tubular function render the elderly vulnerable to dehydration by a decrease in the capacity to concentrate urine. The use of diuretics in this context may further heighten the levels and toxicity of several drugs. The presence of increased renal vasoconstrictor substances seems to be implicated in the susceptibility to nephrotoxins with aging [29]. For example, the frequently seen nephrotoxicity of nonsteroidal anti-inflammatory drugs (NSAIDS) in the elderly is explained by their higher predisposition for volume depletion and by the inhibition of renal vasodilatatory prostaglandins, which exacerbates the imbalance between vasoconstrictors and vasodialators [38].

Radiocontrast agents

Several large studies have revealed an increased risk of contrast-induced nephropathy (CIN) in the elderly. However, other factors, such as baseline creatinine, diabetes, cardiac failure, emergent procedure, and female sex, confer a considerably higher risk than age [39]. Sidhu and his collaborators prospectively enrolled 13,127 consecutive patients undergoing coronarography who were not on dialysis and stratified them by age. Rates of postcatheterization CIN were significantly higher in the ≥80-year-old group (18.7 vs. 15.0%, $p = 0.048$) [40]. A very recent retrospective study assessed the risk of CIN in 1,071 older trauma patients (>55 years) undergoing computed tomography (CT) ([41]. The group receiving contrast media did not have a higher incidence of AKI.

Surgery

The reported incidence AKI varies between 7 and 31%, depending on patient population, specific surgery, and definition used [42]. In a prospective multicenter study on myocardial revascularization by Mangano and colleagues [43], multi-variable analysis identified advanced age as an independent preoperative predictor of renal dysfunction. More recent studies have confirmed that advanced age is an independent risk factor for complications, including AKI. [44].

Several issues related to the perioperative period confer an increased risk of AKI in the elderly [45, 46]. Intraoperative and postoperative factors can lead to decreased renal perfusion, such as decreased cardiac output and vasodilatation from volatile anesthetics, bleeding, infection, and insensible fluid losses. Renal hypoperfusion may also be related to renal emboli as well as to vascular compression or disruption. Moreover, intra-abdominal hypertension may occur at anytime throughout the perioperative period and can alter kidney function dramatically. The age-related changes described earlier likely confer an increased risk of injury to the elderly patient facing these various insults. Additionally, during this critical period patients are often subjected to several nephrotoxins to which the elderly are particularly susceptible.

Sepsis

Septic AKI has recently emerged as a separate entity, for it is associated with increased mortality and may be characterized by a distinct pathophysiology [47]. Elderly patients are more prone to the development of infection. Coupled with the aforementioned changes in renal function and structure with aging, this may increase the risk of septic AKI. However, this matter has not been specifically studied in an elderly population. Using the database from the BEST Kidney study, Bagshaw et al. discovered that sepsis accounted for 47.5% of all patients with AKI. They also noted a statistically significant difference in age between both groups, with septic AKI patients being older, although this was not considered clinically significant by the authors [48].

What are the common causes of AKI development in the elderly ICU patient?

AKI in the elderly is most often multifactorial, especially in the ICU setting [48] (Table 1). In a prospective, multicenter study on the causes and outcomes of AKI in the elderly, Pascual and Liaño [49] found that most cases were caused by obstruction, acute tubular necrosis, and "pre-renal causes", which are often cardiac failure, dehydration, bleeding, or hypotension in the elderly critically ill. These findings were supported by Akposso et al. [10] in their cohort analysis on AKI in critically ill octogenarians. Older studies, in contrast, found that drug-related toxicity is most commonly involved in this age group [50]. As mentioned, large ICU-based studies report sepsis as a frequent cause; it may be involved in half of all AKI cases. CIN is also a frequent cause, particularly in acutely ill hospitalized patients at risk for undergoing diverse procedures. Renal vascular causes, especially atheroembolic

Table 1 Most common causes of acute kidney injury in the elderly intensive care unit patient

Multifactorial	Causes
Hypoperfusion	Hypotension of any cause
	Hypovolemia
	Bleeding
	Cardiac failure
	Drugs: diuretics, hypotensors
Sepsis	
Drug toxicity	NSAIDs
	Aminoglycosides and other antimicrobials
Obstructive	Prostate hypertrophy
	Pelvic tumors
Renal vascular disease	Atheroembolic renal disease
	Renal artery thromboembolism or dissection
Acute interstitial nephritis	Drugs
	Infection
Rapidly progressive glomerulonephritis	
Myeloma nephropathy	

ICU intensive care unit; *NSAIDs* nonsteroidal anti-inflammatory drugs

disease, are also most commonly seen in elderly patients [51]. Moreover, rapidly progressive glomerulonephritis, acute interstitial nephritis, and myeloma nephropathy are not uncommon in the older patient and need to be considered in the appropriate clinical context [52].

Is the diagnosis of AKI different in the elderly?

Serum creatinine (SC) is currently the most validated and clinically used marker for decreased GFR. The clinical experience with SC is extensive, and it correlates well with mortality in acute settings [11]. SC does, however, have some important limitations, particularly in elderly and critically ill patients.

SC levels depend on creatinine generation, volume of distribution, and renal elimination. The levels may therefore vary widely in all patients depending on a large number of non-renal factors. This is especially true in the elderly as a result of diminished daily production rate of creatinine due to decreased muscle mass [20]. In addition, because of renal reserve, even in the elderly, up to 50% of renal function may be lost before the SC begins to rise. These changes may lead to a significant delay in AKI recognition, implementation of prophylactic measures, and treatment in the elderly.

The problems associated with absolute SC levels for AKI diagnosis are even more manifest in the critically ill elderly. Indeed, commonly used regression equations for the determination of GFR have not been validated in this population [37]. Thus, caution needs to be exercised in using these equations to determine GFR. Furthermore, changes in SC may lag behind changes (decline or recovery) in the GFR by several days [53]. Moreover, besides the presence of important variations in volume of distribution, SC levels in critically ill patients may also be influenced by other factors, such as muscle trauma, fever, immobilization, advanced liver disease, and decreased muscle mass [54]. In addition, these patients are frequently in a non-steady state condition, and it has been shown that changes in the GFR are poorly reflected by daily changes in serum creatinine concentrations in AKI [54]. Interestingly, in a prospective observational study on 28 recently admitted critically ill patients with normal SC and no instability, Hoste et al. noted that SC had a low sensitivity for the detection of renal dysfunction. In fact, a significant number of patients had a decreased GFR despite having a normal SC [55].

Although these shortcomings can render absolute values of SC less reliable, following the changes in SC levels remains a very useful and usually dependable method for diagnosing AKI.

By including small rises of SC in their criteria, the aim of the RIFLE and AKIN classifications is to diagnose AKI at an earlier stage [11]. Despite the limitations inherent to these consensus definitions of AKI, it should be stressed that they have been well validated in several large studies involving patients with a mean age >60 years; therefore, there is good evidence that this classification scheme functions well in the elderly population [11].

Biomarkers have shown promise for the early diagnosis of AKI in various critically ill populations [56]. Cystatin C is the only novel biomarker specifically studied in the elderly. It is an early marker of renal dysfunction and predicts cardiovascular events and mortality in this age group [57]. Most large ICU-based studies on biomarkers have included elderly patients. Indeed, in three recent studies assessing urinary interleukin-18 [58] and neutrophil gelatinase-associated lipocalin (NGAL) [59] in general ICU patients and urinary kidney injury molecule-1, *N*-acetyl-D-glucosaminidase, and NGAL in post-cardiac surgery patients [60], the mean age was 50, 55, and 68 years, respectively.

Can AKI development in the elderly ICU patient be prevented?

The mainstay of AKI management is prevention. Once AKI is established in an elderly patient, implementation of strategies aimed at avoiding further damage is crucial (Table 2).

These measures are valid for all critically ill patients; no specific recommendations apply solely to the elderly.

The optimal blood pressure (BP) target for the prevention of AKI is not clear. In their recommendations for the prevention of AKI in the ICU, the working group for

Table 2 Prevention of AKI in the elderly ICU patient

Hemodynamics	Initiate appropriate monitoring
	Optimize preload, cardiac systolic or diastolic function, and vascular tone
Volume repletion	Be attentive to signs of hypovolemia
	Ensure early guided volume repletion
	Limit use of diuretics and laxatives
Exogenous nephrotoxins	Limit use of all nephrotoxic drugs, in particular NSAIDs and aminoglycosides
	Avoid polypharmacy when possible
	Avoid combining diuretics with nephrotoxic drugs
	Adjust dose according to GFR
	Do not base drug dosing decisions on absolute creatinine levels
	Measure drug levels
Contrast medium	Avoid contrast medium, or at least delay contrast use if patient at risk
	Always use lowest possible quantity of contrast
	Use hypo or iso-osmolar and non-ionic contrast
	Adequate volume repletion (e.g.: NaCl O.9%)
	Bicarbonate infusion possibly beneficial
	N-acetylcysteine use possibly beneficial
Infection and sepsis	Low index of suspicion for early diagnosis
	Diagnose/treat sepsis-related intravascular volume depletion, vasoplegia, and cardioplegia
	Early and appropriate antibiotic initiation
	Early guided volume repletion, avoid high molecular weight hydroxyethylstarch
Perioperative optimization	Differ surgery in at-risk patients if possible
	Initiate appropriate monitoring (hemodynamic, intra-abdominal pressure)
	Early and guided optimization of volume status and hemodynamics,
	Limit exposure to nephrotoxins
Abdominal pressure	Measure intra abdominal pressure in all patients at risk
	Avoid over-resuscitation with fluids
	Low tidal volume strategy, limit plateau pressure.
Mechanical ventilation	Low tidal volume strategy, limit plateau pressure.
	Weaning and extubation as early as possible

nephrology of the European Society of Intensive Care Medicine (ESICM) recommended maintaining mean arterial pressure (MAP) between 60 and 65 mmHg [61]. These recommendations as well as the surviving sepsis guidelines specify in their discussion that target MAP may have to be individually tailored for those at higher risk. Indeed, some studies suggest that higher BP targets may be beneficial in certain patients. A retrospective observational study on hospitalized patients with no documented hypotension [systolic BP (SBP) < 90mmHg] compared patients who developed nosocomial AKI, defined by the RIFLE criteria, to a group who did not [62] and found that relative hypotension was more frequent in patients who developed AKI. A decrease in SBP relative to the premorbid value was a significant independent predictor of the development of severe AKI. These patients were older, with a mean age of 78 and 71 years in both groups.

Bellomo et al. [63] recently reviewed the use of vasopressors and its relation to AKI in the treatment of patients with systemic vasodilatation and normal cardiac output after adequate volume resuscitation. Contrary to common belief, systemic vasopressors do not seem to cause intra-renal vasoconstriction, nor is there any indication that they can induce or aggravate AKI in this context. Instead, well-designed animal studies show that norepinephrine at clinically relevant doses induces renal vasodilatation and increases RBF, most probably through increased systemic BP and decreased renal sympathetic tone [64].

The preferred vasopressor for vasodilatatory shock states is open to debate. Conclusions drawn from prospective observational studies are conflicting [65–68]. Conversely, Random controlled trials comparing vasopressors in septic shock treatment were all unable to demonstrate any notable difference in mortality [69–73].

The landmark study by Rivers et al. found that guided hemodynamic optimization within the first 6 h of septic shock identification in the emergency room significantly decreased hospital mortality [74]. Although some subsequent studies have confirmed that early-goal directed therapy may improve outcomes, this study has led to much debate as its patients may not be representative of most septic patients, and the central venous pressure goal is criticized because estimates of intravascular volume based on any given level of filling pressure do not reliably predict a patient's response to fluid administration [75]. Even though there is no consensus on which hemodynamic goals to use, it is clear that all critically ill patients should be identified and treated as quickly as possible and that early volume administration should ideally be guided, as rapid and large volume loads may lead to fluid overload, which has been found to be deleterious in AKI [75].

There is currently no agreement on which fluid should be used for resuscitation, and the mainstay for correction of extracellular volume depletion remains isotonic crystalloids [61]. However, the increased chloride load may result in hyperchloremic acidosis and associated renal vasoconstriction as well as altered perfusion of other organs [61]. Two small random controlled trials compared intraoperative use of 6% hydroxyethylstarch (HES) in a balanced electrolyte and glucose solution versus HES in 0.9% sodium chloride in elderly patients undergoing major surgery [76] and cardiac surgery [77]. The researchers found that the use of balanced intravenous solutions resulted in better gastric mucosal perfusion, prevented the development of hyperchloremic metabolic acidosis, and was associated with beneficial effects on acid–base status, inflammation, endothelial activation, and kidney integrity [76, 77]. The working group for nephrology of the ESICM state that colloids should be avoided in the resuscitation of septic shock patients, as they may increase the risk of AKI development in this population [61]. However, the working group also mentions that adverse effects on renal function may be restricted to higher-molecular-weight HES.

Does treatment differ in the elderly?

No particular therapies exist for the elderly; however, evidence supports the concept that renal replacement therapy (RRT) is efficient, safe, and well tolerated in these patients [78]. The clinician must be particularly attentive to drug dosing and interactions in patients with advanced age, especially during extracorporeal treatment. This group of patients is also particularly prone to increased hemodynamic instability, bleeding, and neurological complications due to changes in osmolarity and serum electrolytes [79]. This susceptibility in the elderly is due to increased autonomic dysfunction, decreased cardiac reserve, heightened vulnerability to the development of delirium and sensorium changes as well as to the presence of comorbidities and various pharmacologic treatments. Continuous renal replacement therapy (CRRT) has not been specifically studied in the elderly [80]. Although it is more costly, and may be associated with a higher risk of bleeding due to continuous anticoagulation, its slow osmolality shifts may offer some benefits in the elderly, such as a more stable hemodynamic profile and a lower risk of mild disequilibrium syndrome [80].

Do the elderly have worse outcomes?

Existing outcome data on ICU patients requiring dialysis vary widely, with reported mortality ranging from 31 to 80%. In published reports not focusing on renal injury, conflicting data exist when it comes to the short- and long-term survival of elderly ICU patients because of differences between studies in terms of the definition of advanced age, treatment intensity, severity of illness, and length of follow-up and because some studies report ICU mortality while others report hospital outcomes. [5, 81, 82]. Hospital mortality may more accurately represent reality in the elderly, as ICU mortality data can be biased by patient selection. Certainly, several frail elderly patients may have care withdrawn or may be refused access to high-intensity treatments [81]. Some studies report an increased mortality risk in elderly critically ill patients with AKI. The BEST Kidney study showed that advanced age was independently associated with increased hospital mortality [8]. Bagshaw et al. [83] also found an association between advanced age and higher 1-year mortality in ICU patients with severe AKI. Conversely, other well-conducted studies found no difference in mortality attributable to older age; however, these are limited by their retrospective nature and relatively small patient numbers [49]. One of these retrospective studies on 82 patients requiring dialysis after cardiac surgery found that patients aged $\geq$70 years had hospital mortality equal to that of younger patients [84]. Not surprisingly, they also found multiple organ failure (MOF) to be an independent risk factor for increased mortality. In fact, clinical characteristics and outcomes of patients with MOF and AKI requiring RRT are very different from those of CKD patients who develop AKI with dialysis initiation in the ICU. Patients with MOF often have a higher acute severity of illness and short-term mortality, but lower long-term mortality because of less comorbid illness. Indeed, several studies on long-term outcomes of hospital survivors of MOF and AKI treated with CRRT have documented a surprisingly low post-discharge mortality rate and an acceptable self-perceived quality of life [85, 86]. On the contrary, CKD patients who acutely decompensate and require RRT have a lower severity of illness during the AKI episode, shorter ICU/hospital stays, and lower short-term mortality. However, as documented in a study on elderly patients by Ali et al. [87], CKD patients who develop AKI are older and have a higher burden of comorbid illness, which increases their risk for non-recovery of renal function, chronic dialysis, and long-term mortality. These findings have all been recently confirmed in a study on the impact of CKD on AKI outcomes in critically ill patients [88].

Studies on the differences in renal recovery between the young and the old report conflicting data. Schmitt and colleagues conducted a meta-analysis in an attempt to clarify this matter. Studies assessing renal recovery were stratified based on age $\geq$65 or <65 years. Overall, the elderly had significantly worse recovery rates [89]. These results are limited by significant heterogeneity. Indeed, Schiffl and his collaborators came to different conclusions

[90]. From a cohort of 425 ICU patients with AKI, they followed 226 survivors who required RRT for 5 years after hospital discharge. Of these, 57% had a complete recovery of renal function, 43% had a partial recovery, and none of the patients were dependent on RRT. Patients with complete or partial recovery did not differ significantly in mean age. However, the particularly good renal outcome in the elderly noted in this report may be partially explained by the fact that none of the included patients had pre-existing renal disease [90]. Wald et al. [91] recently published a retrospective matched cohort study in which they studied 3,769 cases of hospitalized patients with AKI requiring dialysis and compared them to 13,530 controls without AKI or dialysis during their index hospitalization. Overall, they found that an episode of AKI and dialysis was associated with an almost two-fold higher risk of chronic dialysis, but not increased mortality. Subgroups of patients $\geq$65 years of age and $<$65 years were compared; the older group had a higher risk of chronic dialysis. More importantly, it is evident from the Kaplan–Meier curves that the risk of chronic dialysis and death persists for many years post-discharge. A long-term follow up study by Schiffl and Fischer reported similar observations [90]. These studies highlight the need for long-term follow-up of renal function in these patients.

Ethical perspective

Intensive care unit use is in generally considered to be cost-effective when mixed patient populations are studied [92]. Moreover, some studies have found that older age is associated with lower hospital and ICU costs, independently of hospital mortality, resuscitation status, and discharge location. However, these favorable outcomes may be due to selection bias. Indeed, in a prospective study of 180 octogenarians triaged for ICU, Garouste-Orgeas et al. [81] found that 73% were refused admission. A recent review on mortality in elderly ICU patients concluded that, after adjustment for disease severity, mortality rates are higher in elderly patients than in younger populations [93]. Their long-term prognosis depends mostly on functional status, not on initial disease severity [93, 94]. In fact, a recent prospective study on a cohort of previously healthy elderly ICU patients documented a high mortality rate which increased with age and was mostly related to pre-morbid quality of life [95]. Clearly, chronological age alone is unable to measure the ability of individuals to benefit from a treatment, and should not be the sole criterion used when deciding upon therapeutic intensity. The decision to start RRT in an elderly critically ill patient must therefore be approached in a case-by-case manner [92]. End-of-life wishes are difficult to predict, vary greatly between patients, and can change during the course of an illness. Therefore, although ICU treatment can be cost effective in the elderly [96], one must also consider their risk for poorer functional outcomes and loss of quality of life [92].

Conclusion

Hospitalizations for acute care in the elderly are escalating, and ICUs are facing an increasing demand for care from older individuals. Elderly patients are at the highest risk for AKI because of age-related changes in kidney function, multiple comorbidities, and frequent exposure to iatrogenic insults. Early diagnosis is a challenge, since SC levels are less reliable in this population. Strategies for preventing AKI development or worsening are crucial. Older critically ill patients are at risk for poor functional outcomes. The decision to begin RRT in older patients should be taken in a case-by-case manner, as several ethical issues must be taken into consideration.

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