Cardiovascular and Kidney Disease within the Geriatric Population in Developing Countries

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Edited by

Georgi Abraham, Narayan Prasad and Santosh Varughese

Cambridge Scholars Publishing

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FOREWORD

SARBJIT VANITA JASSAL

STAFF NEPHROLOGIST AND PROFESSOR OF MEDICINE,
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> "Despite my being an old gypsy there is a tendency to respectability inherent in old age" Albert Einstein 1879-1955

Care of the older individual embodies the true essence of medicine. Healthcare professionals strive to balance the art of caring with the science of treatment, while keeping the patient and the patient's personal values in the centre. Over my years practicing in the field of Geriatric Nephrology, my patients have taught me to listen to their experience of living with ill health, and to add their knowledge to my understanding of disease and disease pathophysiology. My patients have, on many occasions, reminded me how reduced wellbeing, symptoms and loss of pleasure arise from both the illness as well as therapies I am using to treat disease. So my strong belief is geriatric nephrology care is the patience to listen, to interpret and to care.

The older individual differs from their younger self, through their experiences. They have enjoyed the same pleasures and challenges that you and I enjoy in our current daily routine, but with it, have acquired an experience and understanding we have not yet been given. When their perspective differs from ours, it is important to step back, and hear their opinion. As doctors we may not always know what is best for the *individual*, but rather know how the different therapeutic options available to us may best achieve their desires.

With this in mind, it is truly exciting to see this body of work published. Widely recognized experts from across the whole of India have rallied to contribute. Each chapter synthesizes our understanding of disease, with new information across a wide spectrum of topics spanning urogenital disease through to glomerulopathies. Chapters cover the full kidney

trajectory covering topics that relate to early stages of kidney disease, updates on dialysis and transplant care, as well as cardiovascular disease (including rehabilitation), heart failure and cerebrovascular disease, dosing of drugs, pain management, to the provision of care in the final days of life. This book extends beyond traditional texts that explain pathophysiology and interventions, to incorporate suggestions of how to modify care for those with frailty or age-related change; adjust drug dosing and prescription in relation to age; and includes age-specific guidelines where available. The inclusion of specific chapters on principles of shared decision making, symptom management and palliation, and pain management, is commendable. From my own perspective, inclusion of data on non-disease specific impairments, such as accidental falls, cognitive changes and functional loss, when assessing patients for therapy is a delight!

I have no doubt in recommending this book to our future clinicians, and experts, as well as to those of us currently in the field. It is filled with gems! My heartfelt thanks to all the authors who have contributed to this body of work, and to the Editors who let me share in this work prior to its publication.

PREFACE

GEORGI ABRAHAM
SANTOSH VARUGHESE
NARAYAN PRASAD

We are in the 21st century and with increase in longevity, there is an enormous growth in the geriatric population.

This increase is predominantly seen in populous countries in the South Asian region and to a lesser extent in Sub Saharan Africa. Though there is diversity in culture, ethnicity, food habits, health care provision and socioeconomic status, there is an increasing trend in the incidence of life style diseases such as hypertension, diabetes mellitus, coronary artery disease, obesity, malignancy and kidney disease.

Medical education is a continuous process. As there is a critical knowledge gap regarding the diseases of the geriatric population in developing countries, the editors have thoughtfully crafted out chapters contributed by those who are renowned for their clinical and academic excellence to bridge this gap. These esteemed authors stem from different developing countries as well as developed countries. The chapters in the book are written in simple readable English with figures, graphs and tables that are tailored for developing countries. This book is wide in its scope and is targeted towards medical students, interns, post-graduates general practitioners, physicians and specialists in renal medicine.

We want to thank our spouses – Rene, Reena, and Renu for their continued support in our endeavours.

CHAPTER ONE

ACUTE KIDNEY INJURY IN THE ELDERLY

SANTOSH VARUGHESE
SERENE SARA VARGHESE
SNEHA HARIDAS

An illustrative case

A 75-year-old man with past medical history of diabetes mellitus, hypertension and ischemic heart disease presents to the emergency department with nil urine output for 6 hours following severe diarrhoea. There is fever 400C, tachycardia (heart rate 110/min) and hypotension (Blood pressure 90/60 mmHg). His regular medications include aspirin 75mg, atorvastatin 10mg, glyburide 5mg twice daily along with chlorthalidone 12.5mg and amlodipine 10mg. He has recently been on diclofenac sodium tablets for his backache.

Introduction

Acute kidney injury (AKI) is defined as a sudden decrease in renal function that may be detected by a rise in serum creatinine by at least ≥0.3 mg/dl within 48 hours[1]. This leads to nitrogenous waste product accumulation with dysregulation of electrolytes and often an increase in extracellular volume. In many parts of the world, the fastest growing age group is that aged 60 years and above. AKI in this group thus becomes an important concern for family doctors, community physicians and specialists. Data from the pre-COVID era suggested that about 13.3 million cases of AKI occur each year worldwide, of which an astounding 85% are in low and middle income countries.[2,3] A study from central India suggested that the elderly form 47.15% of the entire AKI cohort[4] while data from a large tertiary teaching centre in south India that specifically

looked at tropical AKI, suggested that 10.1% of patients were older than 65 years of age.[5]

What makes the elderly vulnerable to AKI?

The changes that happen in aging are remarkably similar to those in chronic kidney disease (CKD). Indeed, CKD is considered a state of premature or accelerated aging.[6] With increasing age, there is reduction in renal mass. By the ninth decade the weight may have decreased by a fifth or a quarter of its original adult weight.[1,7,8] This likely results from ischemic changes and sclerosis of the glomeruli, affecting up to half the cortical glomeruli by 70 years.[9,10,11,12] There is an increase in mesangial cells and thickening of glomerular basement membranes. The hemodynamic changes that occur due to aging include impairment in autoregulation,[9] decreased production of vasoactive substances like nitric oxide[14] leading to increase in renal vascular resistance,[15] impaired renal vasodilatation[13] and decrease in renal blood flow and blood flow reserve.[16] Thus, a veritable decline in glomerular filtration rate (GFR) results.[17]

Age related changes of increase in expression of genes promoting senescence[18] and inhibiting cellular proliferation[19] result in reduced tubular cell proliferation.[19] There is thickening of tubular basement membrane, reduction in number and size of tubules and increasing interstitial fibrosis and tubular atrophy. There is increase in oxidative stress accompanied by reduction in the defences against them.[20]

Several of the elderly have subclinical chronic Inflammation is associated with increased disability, decreased muscle strength and increased risk of dying mortality,[21–24] increase in frailty,[25–33] and perhaps increased susceptibility to AKI. Ischemia/reperfusion injury leads to production of CCR2, a chemokine that leads to AKI.[34,35] Injury results in upregulation of TLR4 in the proximal tubular cells and infiltrating leukocytes,[36,37] and communication among leukocytes, proximal tubular cells and endothelial cells.[38]

With increasing age, there is increase in reactive oxygen species (ROS) and advanced glycation end products (AGEs) and reduction in anti-inflammatory AGE receptor AGER1 that is designed to bind and quench excess ROS and AGEs and inactivate the proinflammatory receptor RAGE.[39,40] Animal studies show that in mitochondria of diabetics, RAGE induces both superoxide and ROS.[41] Levels of ROS and functioning

endoplasmic reticulum stress pathway and pre-existing determine the severity of AKI[42] and a decrease in GFR causes a rise in AGE.[40] Modification of diet may alter levels of AGE, AGER1, and ROS in both diabetic and non-diabetic adults. These are potential targets for prevention and management of AKI.[43]

In addition, comorbidities like diabetes mellitus, hypertension, atherosclerosis, ischemic heart disease, etc. occur more often in the older population. Impaired autoregulation leads to reduction in renal perfusion and ischemic damage with decrease in blood pressures.[44] Presence of hypertension and atherosclerotic vascular disease may cause subclinical injury, adding to the age-related glomerular changes.[45] Use of renin angiotensin aldosterone system (RAAS) blockers may heighten the risk of AKI especially when volume depleted.[46] Both percutaneous vascular interventions and cardiac surgery add insult to injury with precipitation of AKI. Prostatic enlargement causing urinary tract obstruction and infection related AKI is also an important risk factor in elderly males.[47]

Epidemiology

The risk of developing AKI appears to increase with increasing age. A United States of America study showed that, for every 1000 patients- in those aged 85 years and above, 46.9 episodes, between 80 and 84 years, 34.2 episodes, between 75 and 79 years, 24.9 years, between 70 and 74 years, 18.1 episodes and in 66-69 years, 13.6 episodes respectively occur.48 Additionally, AKI appears to have a 3 to 8 fold increased risk of occurrence in patients aged more than 60 years; and older the age, the greater is the risk of AKI.[47] While the trend of increase in frequency of AKI with increasing age is seen both in those requiring renal replacement therapy and those who do not, there is more dialysis required, and severe AKI in the elderly in comparison to the younger patients.[49] The mortality is elderly patients with AKI may reach as high as 80%; with the risk of dying at its highest in those requiring renal replacement therapy.[50] Both in-hospital mortality[51] and 1-year mortality are higher in these patients with the recovery of renal function after AKI being more difficult.[52–54]

Etiology

The etiology of AKI in the elderly generally mirrors that of the rest of the population with a greater likelihood of multiple factors contributing to the occurrence of AKI.[55] Similar to the rest of the world, sepsis is at the top of

the list of causes in south Asian elderly patients.[33–35] A study from western India found that in elderly patients, AKI resulting from a combination of drug induced nephrotoxicity and sepsis was the commonest cause.[56]

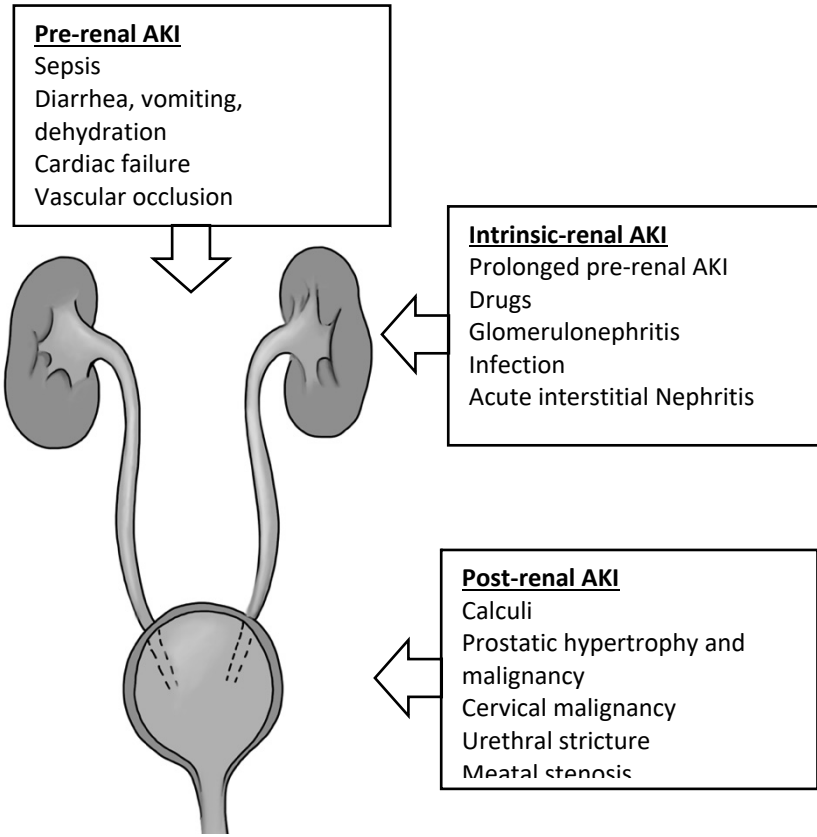

Figure 1 shows the sites of injury in AKI i.e. pre-renal, intrinsic renal and post-renal with a few common etiologies at each site.

Pre-renal AKI may account for about a third of AKI in the elderly.[57] A myriad of causes includes increased propensity to dehydration and decreased intravascular volume[58] from use of diuretics, and left ventricular dysfunction, resulting in decreased renal perfusion.[55] Decrease in the sensation of thirst and lack of physical prowess to assess fluids may result in a volume mismatch between gastro-intestinal fluid loss and oral replacement.[55] Clinical scenarios of both hypernatremia and hypovolemic

hyponatremia have been observed in these patients. The response of renal vasculature to decrease in perfusion may be impaired in patients who are on RAAS blockers, thus increasing likelihood of their developing AKI.
In cases of intrinsic renal AKI, acute tubular necrosis (ATN) is the most common pathological cause.[57,59] The major contributors to development of ATN are sepsis, drugs, (including non-steroidal anti-inflammatory drugs), prolonged intra-vascular depletion, surgical procedures especially cardiac surgeries, contrast induced nephropathy (CIN), predominantly coronary angiogram and interventional procedures, and chemotherapeutic drugs. Elderly patients are at a higher risk of aminoglycoside induced nephrotoxicity.[60]

Cholesterol embolism must be considered as a possible cause when AKI occurs following a vascular intervention. The common risk factors for developing ATN (e.g., diabetes mellitus, pre-existing CKD, hypoalbuminemia, malignancies, generalized atherosclerosis) are more commonly seen in the elderly population.[61]

Reduction in muscle mass with age may lead to an over estimation of creatinine clearance, and inadvertently higher dose of medication with potential nephrotoxicity that may lead to ATN.[63] Age, by itself, is not a risk factor for CIN[64] but the increased prevalence of pre-existing CKD makes CIN an important cause of ATN in hospitalized elderly patients.

Acute neutrophil cytoplasmic antibody (ANCA) vasculitis may cause crescentic glomerulonephritis that may present as AKI. Diagnostic clues include presence of microscopic hematuria with erythrocytic casts and elevated ANCA levels, typically antimyeloperoxidase.[65] Other glomerulonephritides may also less commonly encountered. Renal histology is invariably necessary for confirmation of diagnosis, prognostication (based on degree of glomerulosclerosis, interstitial fibrosis and tubular atrophy) and deciding on treatment with immunosuppressive drugs. The latter is an important consideration since high dose immunosuppressive therapy is associated with increased mortality in elderly patients.[66] Renal biopsy procedure per se does not confer any age related increased risk.[67] The contribution of acute interstitial nephritis (AIN) to the burden of AKI in elderly patients is not known. Eosinophiliuria as a diagnostic finding is neither sensitive nor specific[68] and histological confirmation is required. With commonly used drugs like proton pump inhibitors being implicated, we may see more drug induced AIN with time.[69]

It is sometimes difficult to differentiate between pre-renal and intrinsic renal AKI. Certain parameters that help in the differentiation between the two have been described. They are listed in Table 2.

Approximately 10% of AKI in the elderly is secondary to destructive causes[70,71].Prostatic hypertrophy of carcinoma and stricture of the urethra and imported causes of obstructive AKI in metastatic malignancy of the genital tract is the most common cause amongst females. Anticholinergic drugs may also be a cause of obstruction is likely diagnosed by ultrasound and bladder catheterization may be necessary.

Molecular mechanisms causing AKI in elderly patients

Without attempting to discuss all the molecular mechanisms involved in AKI, an attempt is made to highlight a few facets specifically relevant to the elderly. Stress-induced cellular senescence with increasing age is seen to be associated with AKI.[72] Older kidneys have greater expression of the senescence marker p16 (INK4A) and a greater percentage of glomerular, tubular, and interstitial cells expressing p16 (INK4A) compared to younger ones.[73,74] Other modulators that are implicated in senescence and tubular regeneration after AKI, and potentially its severity and duration shortening of the telomere,[75] Dicer-associated microRNA downregulation,[76] heme oxygenase–regulated autophagy,[77] chordin 1–regulated expression of bone morphogenic protein,[78] and others. It is speculated that in kidneys of elderly, following an episode of AKI, senescent cells may have accelerated cell death or an impaired response to injury[72]. The accelerated cell death may leave fewer tubular epithelial cells that can de-differentiate and proliferate,[79,80] thus hampering recovery of renal function in the elderly.

Some animal studies have shown that peroxisome proliferator – activated preceptor gamma (PPARγ) agonists protect against development of AKI81 but the resultant fluid retention and edema have limited their widespread clinical use, especially in the elderly.[82]

Establishing a diagnosis of AKI

The KDIGO (Kidney Disease: Improving Global Outcomes) criteria for diagnosing AKI and its predecessors AKIN (Acute Kidney Injury Network)[1] and RIFLE ((Risk, Injury, Failure, Loss of kidney function, and End-stage kidney disease), all rely upon changes in estimated glomerular filtration rate (eGFR) or measured levels of serum creatinine. Since these

values reflect changes in current values of serum creatinine rather than GFR, equations are unhelpful in clinical use as they are valid only in a steady state. Though attempts have been made to modify these equations for use in AKI patients, they are yet to be validated and are cumbersome in their present form.[83] Serum levels of creatinine are affected by tubular excretion, volume of distribution,[84] nutritional state and drugs. Sepsis decreases the proteinuria of creatinine and lower serum levels ensue. This makes early diagnosis of AKI difficult.[85] This is why even minute changes in serum creatinine require the clinician to be vigilant for possible development of AKI. Table 3 details the KDIGO AKI diagnostic criteria1 and staging. As per the criteria, AKI is diagnosed if there is any of the following: rise in serum creatinine by ≥ 0.3 mg/dl within 48 hours; to a value ≥ 1.5 times known or presumed baseline, within seven days; or decrease in urine output to at least < 0.5 ml/kg/h for six hours.

On the other hand, it is estimated that nearly a fifth of AKI cases may be over diagnosed because of false–positivity.[86] The variability of serum creatinine contributes to this error and some suggest using an absolute value of rise in creatinine rather than a percentage for making a diagnosis of AKI.[86] A better alternative is use of cystatin C, especially in the elderly, where cystatin C based eGFR predicts mortality better than using creatinine based eGFR.[87,88] Oliguria has better sensitivity and specifically than creatinine, for making a diagnosis of AKI[89]but is obviously limited in use for oliguric AKI alone.

In situations when the diagnosis is in doubt, or when making an accurate diagnosis is imperative, one may consider using molecular markers (see table 4)[62] that have been shown to be useful in establishing an early diagnosis and/or prognosis. In the future, these could potentially replace creatinine as a marker for diagnosis, monitoring and for assessing response to medical intervention.[90] These biomarkers are far from becoming the panacea that is hoped for, with most requiring large multi-centre human studies to confirm their usefulness in AKI. Since these have a short half-life, the biomarker measurement must be done as close to the onset of injury as possible. Figure 2 shows the timelines of their rise and measurement of which detects AKI earlier than the traditional rise in serum creatinine.[91] They are yet to be standardized uniformly and have not shown specific superiority for AKI in the elderly.

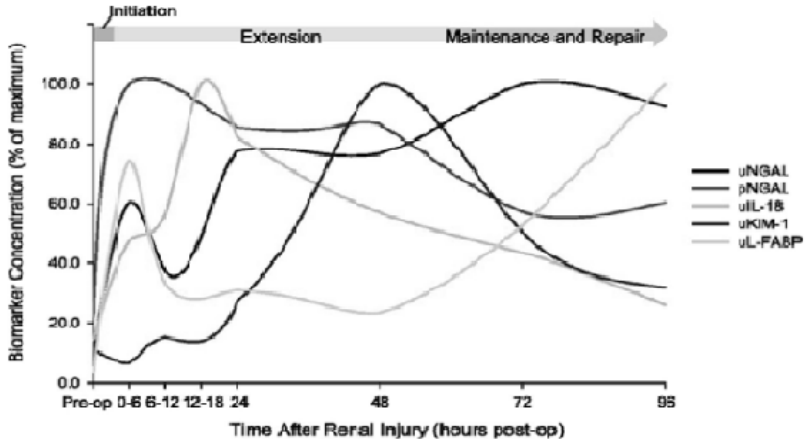

Figure 2: AKI biomarker concentration after renal injury in cardiac surgery patients.

At the present time, clinical session, course of illness – before and during hospitalization, along with serum creatinine and oliguric (where present) form the basis of making a diagnosis of AKI.

Management

Medical management of elderly patients who develop AKI is very complex and the astute clinician will do well to be aware of all the ramifications involved. Even apart from the occurrence of AKI, the elderly are more likely to require hospitalization compared to their younger contemporaries.[93,94] Hospitalization per se increases mortality risk,[95] as well as poses functional disability[93,96] and risk of dementia.

Probably the phrase “primium non nocare” (Latin phrase meaning “first, do no harm”) has never been more apt as in the care of elderly patients with AKI. Medical therapy routinely given to younger patients can potentially do more harm than good for frail elderly patients with AKI.57

Risk assessment and evaluation, early detection and prevention are important factors of medical care of any patient with AKI. The geriatric age specific strategies including Acute Care for Elders (ACE) and Geriatric Evaluation and Management (GEM) have not been tailored to meet the needs of elderly patients with AKI.[62]

For a typical elderly patient who comes to the emergency department with a diagnostic suspicion of AKI, unless there is overt fluid overload with edema and/or orthopnoea, intravenous fluid replenishment is invariably done. While this is often an initial step of treating AKI, the initially administered salt and water invariably adds to the fluid accumulation that takes weeks to resolve completely.[97] This excess fluid is associated with congestion of visceral organs, including the kidney and potentially further AKI,[98] as well as increased mortality.[99,100]

Subclinical accumulation of fluid is often missed in the overall intensive care management. Expansion of volume leads to erroneous GFR estimation.[62] Patient's clinical condition influences the volume distribution among various compartments, fluid volume requirements and ability to tolerate mismatches.[101,102] The balance between intra fluid resuscitations and post resuscitations fluid balance can influence mortality,[62] mandating early fluid restriction or planning on early fluid removal.[103]

Nutritional needs are sometimes relegated to second place since urgent overwhelming medical treatment requirements naturally take precedence. Nutritional status at the time of ICU admission is indelibly associated with mortality.[104] It is estimated that less than 50% of patients in ICU are adequately nourished[105] or receive adequate nutritional supportive therapy. The reasons for the latter are several, including difficulty in assessing nutritional status.[62] Body composition measurements and serum albumin do not correlate well in patients with AKI[106] since they are influenced by inflammation, hypercatabolic state and extracellular fluid volume. Nutritional intervention also does not influence these parameters, making them inappropriate for assessment of response to therapy or follow up[107] The benefit of providing nutritional support to elderly patients with AKI has not been robustly studied. A low protein diet to control uremia has been the traditional pattern; but hypercatabolic AKI can cause loss of 1.08/kg/day of protein each day and protein restriction may worsen malnutrition.[108] When renal replacement therapy (RRT) is instituted, a single session of dialysis can cause the patient can lose up to 1.4gm of amino acids and 5gm/day of protein mandating nutritional supplementation.[109–113] Continuous renal replacement therapy (CRRT) has the advantage of allowing adequate nutritional supplementation without fear of volume overload.[114] However, high protein intake has not been shown to be superior to normal protein intake in patients with AKI, with respect to blood urea nitrogen levels, urine output or survival.[115]

AKI caused by, or worsened by acute coronary syndrome and cardiac failure, called Cardio-Renal syndrome Type I (or acute cardio renal syndrome) influences the prognosis in elderly patients (166 to 168 from 9).[116–118] Therefore, it is mandatory that these patients be managed carefully, especially with regard to fluid balances and potentially nephrotoxic medications. Careful choice of optimal medication, with renal function appropriate dose-adjustment of drugs is often necessary.

It is known that AKI occurring soon after a myocardial infection, increases the risk of a second acute coronary syndrome90,119 requiring clinicians to be ever vigilant. The relationship of the above, with aging, though plausible, is yet to be clearly established.[62]

The overall principles of treatment of AKI in the elderly are similar to the general population. Complications of dyselectrolytemia, metabolic acidosis, uremic encephalopathy and acute pulmonary edema due to fluid over load, may be life threatening,[120] necessitating urgent medical intervention. Issues like timing of initiation of RRT, dosages and choice of modality are hotly debated topics.[121] An added dilemma in providing RRT in the elderly is the balance of 'goals of care' and 'life expectancy' against provision of the "best treatment".[122] Wherever possible, the patient themself must be part of the advanced care planning to accommodate the patient's personal preferences.[123] The relevance of this discussion cannot be overstated, especially in the backdrop of resource-poor settings, like many parts of south Asia or when the patient's medical care expenses need to be paid from his own savings, rather than the government or through medical insurance. A possible option is to offer a time-limited trial of RRT, in addition to appropriate clinical care; and to assess prognosis on a periodic basis and alter the decision on further treatment accordingly.[124]

There has been no study comparing the different modalities of RRT in the elderly with AKI. Peritoneal dialysis (PD) is useful for AKI from a variety of causes including sepsis, diarrhoea, tropical infections, snake bite, following cardiac surgery, hepatorenal syndrome, poisonings, etc.[125–128] The usefulness of PD becomes paramount in resource-poor settings and poor access to hemodialysis facilities. A study from southern India showed that PD may be equivalent to CRRT in critically ill AKI patients with similar outcomes at much lower costs.[129]

Course and Outcome

A. Mortality

Elderly patients with AKI have short-term mortality ranging between 20% and 45%. The mortality rate is higher in hospital–acquired compared to community–acquired AKI,[130] and in intrinsic-renal AKI compared to pre-renal or post-renal AKI.[130] Worldwide, the overall outcome seems to be improving, despite increasing patient comorbidities.[131] Whether this holds true for developing countries as well, is unclear. In keeping with improving survival of patients with AKI as a whole, mortality in elderly patients with AKI has also been reducing.[132]

Unlike their younger counterparts, long-term survival is greatly affected in elderly patients with AKI.[133] However, this increased risk of mortality vary greatly among elderly patients.[134,135] In a study from north-western India, hospital-acquired AKI, sepsis and requirement of dialysis, development of nosocomial infection and critical illness were associated with increased mortality. Of these, nosocomial infection (OR 9.72) and critical illness (OR 9.97) independently predicted increased long-term mortality.[135] It is possible that comorbidities influence variation in mortality between patients.[136] Synergy between these comorbidities makes interpretation of contribution of individual comorbidity difficult.[130]

One study reported no difference in survival in patients who developed AKI after cardiac surgery between those less than 70 years and those older,[137] suggesting that age may not be the lone or most importance factor contributing to long-term mortality after AKI in the elderly.

B. Progression to Chronic Kidney Disease

The last two decades have provided more and more data showing conclusively that Aki is not a completely reversible condition. AKI in a hospitalized patient renders up to 20-fold heightened risk of developing CKDI in the future.[138–140] Meta-analysis of data from studies have shown that patients age 65 years an older have less likelihood of recovery of renal function following an AKI compared to their younger counterparts, (RR 1.28).[52] Reduction in tubular cell proliferation, cell turnover, growth factor expression and capacity to recruit progenitor cells to the sites of injury to affect repair are postulated to be reasons for occurrence of CKD following

AKI in the elderly.[134,141] The risk of progressive CKD is highest in AKI patients who required ICU care.[142]

C. Functional Outcome

An often-neglected area is the assessment of quality of life and functional status after "recovery" of AKI in elderly patients. A study using the SF-36 (a 36 item Short Form Health Survey) suggested that in comparison with the general population, following AKI, the elderly have similar mental health scores but lower physical health summary scores.[143] Long-term quality of life scores were reduced in two of three studies [144,145] while the third reported no difference.[146] Interestingly, even those patients with suboptimal quality of life scores subsequently felt they were as healthy as those who never had the AKI.

Conclusion

With the general increase in longevity, there will be more and more elderly people who develop AKI and require expert medical treatment, including intensive care and RRT. It is, therefore, imperative that family physicians, community physicians, internists, intensivists and nephrologists are all equally adept at taking care of these patients, in perhaps, their hour of greatest need. The elderly have a higher risk for developing AKI, mainly due to sepsis and drugs, but often AKI is secondary to a multi-factorial etiology. AKI may be detected late in the elderly, adding to the risk of an unfavourable outcome. AKI portends an increased mortality, compounded by comorbidities. Hence, an expert multi-disciplinary team must be involved in providing the best care.

Goals of care and prognosis must be discussed with the patient (and / or family members) to make the optimum treatment plan. Mortality (both short and long term) is higher in elderly patients with AKI. In the long-term, they are at higher risk of developing CKD and having a lower quality of life.

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