Introduction

The aging population, the fastest growing sector of the general population in the Western world, is also rapidly increasing in Taiwan. The proportion of elderly in Taiwan has grown from 6.93% of the total population at the end of 1993 to 8.62% in 2000 and to 9.6% in 2005. If current trends continue, it is predicted to reach 10.44% by the year 2010. Given the demographic shift, we can expect an increasing number of elderly patients with both acute and chronic renal failure. Deaths due to renal disease in the elderly in Taiwan have increased gradually, accounting for 4.30% of all causes of mortality in 2005. A number of factors may contribute to the increased incidence of acute renal failure (ARF) in older individuals. Because of structural and functional alterations, the aging kidney is less able to adapt to rapid hemodynamic changes and changes in salt and water balance. The elderly are also subject to a number of chronic systemic diseases such as hypertension, diabetes mellitus, atherosclerosis, heart disease, and malignancy. Some of these result in direct kidney damage, while others may be superimposed on or complicate pre-existing renal disease. Compared with younger individuals, the elderly consume twice as many medications, some of which are nephrotoxic, and may be more sensitive to them. For example, if there is already a decrease in renal reserve, there is a higher risk of renal failure with diagnostic contrast medium as compared with younger people.

Depending on its severity, ARF may require renal replacement therapy. In patients who are hemodynamically unstable, continuous renal replacement therapy (CRRT) is preferred over intermittent dialysis. Given their frequent comorbidities, the elderly may be at a higher risk of hemodynamic instability and therefore more likely to undergo CRRT. We reviewed the literature dealing with CRRT in the elderly. We searched MEDLINE with the terms “acute renal failure”, “elderly”, “continuous renal replacement therapy”, and “dialysis”. We primarily selected articles published in the last 5 years, but did not exclude commonly referenced and highly regarded

SUMMARY

Elderly individuals are more prone to the development of acute renal failure (ARF) under circumstances of structural and functional changes. When accompanied by multiple organ failure, the elderly are exposed to an excess risk of death. These factors have led ARF to be one of the most important clinical conditions in the elderly. Continuous renal replacement therapy (CRRT) affords better hemodynamic stability than conventional intermittent hemodialysis (IHD), although evidence supporting its superiority over IHD is lacking. Given their frequent comorbidities, the elderly may be at a higher risk of hemodynamic instability and therefore more likely to undergo CRRT. Until evidence is available, we recommend CRRT for ARF in patients whose hemodynamic status makes them unable to tolerate IHD. Clinicians should be familiar with this treatment modality as the need for it will most likely increase. [International Journal of Gerontology 2007; 1(1): 46–51]

Key Words: acute renal failure, continuous renal replacement therapy, dialysis, elderly
older publications. We also searched the reference lists of articles identified by these strategies and selected those judged relevant, including both review articles and book chapters. There was no restriction on the language of publication.

Our review is focused on the causes and prognosis of ARF in the elderly, which are essential to understanding the impact of ARF in these patients. We also review the principles of CRRT in this particular demographic group. Clinicians should be familiar with this treatment modality as the need for it will most likely increase.

Aging and the Kidney

The main characteristic of the aging kidney is a limitation of the adaptive renal response to various threats. This lower renal reserve means that elderly individuals are more prone to develop ARF under high-risk circumstances than younger people. If there is already a pre-existing impairment in renal function, any new insult may further damage the kidneys. Understanding the functional and structural changes in the aging kidney helps explain why this is the case.

Functional changes

The kidney has an autoregulatory function to adapt to low renal perfusion pressures by preserving renal blood flow and glomerular filtration rate (GFR) at relatively constant levels. With increasing age, this function declines. The ability of the elderly kidney to maintain urine concentration, acid-base balance, and normal renin/aldosterone activity is also impaired. Thus, electrolyte disturbances and deterioration of GFR are common in elderly patients admitted to the hospital for a variety of systemic diseases.

Structural changes

As we age, it can be seen microscopically that the nephrons become smaller and macroscopically that there is gross atrophy of the kidney. By about the age of 30 years, some glomeruli are already partially or totally sclerosed. There are additional microscopic changes, including in the tubules, interstitium, and renal vessels. Between the ages of 30 and 90 years, the average renal weight decreases by 20–30%, from 200–270 g to 180–200 g. Because of these age-associated changes, theoretically, even a modest reduction in renal function can seriously threaten an elderly patient.

Incidence of ARF in the Aging Population

The true incidence of ARF is difficult to estimate because more than 30 definitions have been used in various studies. Generally, ARF is defined as a rapid (i.e., over hours to weeks) and usually reversible decline in the GFR. The Acute Dialysis Quality Initiative group has developed a useful classification system and definitions for ARF and acute-on-chronic renal failure. Because the definitions do vary, it must be admitted that published incidence figures may not be exact. However, the relative trend is clear: ARF is considerably more common in the elderly than in younger people. In a 2-year prospective study in England, it was found that individuals above 70 years of age comprised more than 70% of all those with severe ARF. The incidence was 17 per million in those below 50 years of age but 949 per million in those aged 80–89 years. A similar study in Spain found that the incidence of ARF in patients aged above 80 years was 1,129 cases per million.

Causes of ARF in the Elderly

The causes of ARF in the elderly have been extensively discussed and generally fall into 3 major categories: prerenal, intrinsic, and obstructive. In a retrospective series of 381 patients above 80 years of age with ARF reported by Akposso et al., 1% had prerenal, 53.5% had intrinsic, and 22.3% had obstructive causes of ARF. Etiologies of prerenal ARF in this series were primarily extracellular dehydration (59.7%) and heart failure (15.4%). Intrinsic renal failure was attributable to shock (49.1%), nephrotoxic drugs (6%), rhabdomyolysis (9.8%), and multiple myeloma (6.8%). Obstructive renal failure was predominantly caused by prostatic tumors (48.4%) and malignant pelvic tumors such as bladder cancer, ovarian or uterine cancer, and colorectal cancer.

Prognosis of ARF in the Elderly

Among elderly patients, ARF frequently occurs in the setting of critical illness, e.g., medical or surgical complications and multiple organ failure. The mortality in such patients is high, reportedly ranging from 40% to 80%. Various factors have been identified as predictors of mortality in elderly patients with ARF. The worst
prognostic factors identified by Sesso et al.28 and others29–31 are cardiac disease, organ failure, mechanical ventilation, malignancy, oliguria, and requirement for dialysis. However, there is no clear consensus as to whether age per se is an independent risk factor. A study by Druml et al.32 failed to show any relationship between advanced age and outcome of ARF, a finding echoed by other groups4,33. The most recent analysis of prognosis of ARF in the very old (>80 years) showed a slightly but significantly higher mortality than in an age-matched control population without ARF. However, the ARF-specific mortality in the elderly was no worse than the overall ARF-specific mortality in the literature23. Thus, it cannot be concluded that old age is an independent predictor of a poor outcome, and age therefore should not be used as a factor in making therapeutic decisions for ARF when it occurs in the elderly.

Renal Replacement Therapy in the Elderly

In the absence of effective pharmacologic therapy, the management of ARF is primarily supportive with renal replacement therapy as needed. This was first successfully used for a 67-year-old woman with ARF in September 194534. The available modalities include peritoneal dialysis, intermittent hemodialysis (IHD), CRRT, and hybrid renal replacement therapies. The optimal dialytic therapy for ARF in general remains controversial, and there has been little discussion of this question specifically focused on elderly patients with ARF.

Although peritoneal dialysis offers some theoretical advantages, there are several medical and technical reasons for why it is currently less frequently used. Conventional IHD in the elderly is complicated in this population by the prevalence of cardiac and peripheral vascular disease. These factors make older patients particularly susceptible to HD-associated hypotension, among other complications. Hemodynamic instability and the resulting shortened dialysis time limit the effect of the dialytic dose. Hybrid, or sustained low-efficiency, dialysis is an extended dialysis method characterized by slower blood and dialysate flow rates. The term “hybrid” indicates that it combines features of both IHD and CRRT. It can be maintained for prolonged periods, providing excellent detoxification with cardiovascular stability and flexible treatment time35–38. However, these techniques are still largely experimental and are thus beyond the scope of this article.

CRRT affords better hemodynamic stability than conventional IHD39 and is, therefore, particularly attractive for elderly patients with ARF. There are as yet, however, no controlled studies in this population showing definite evidence of benefit. In addition, CRRT may be of benefit in treating nonrenal problems in critically ill patients40–42. It allows continuous removal of large fluid volumes or toxic substances, such as cytokines and chemokines in sepsis, acute respiratory distress syndrome, or burns43. Again, however, it should be pointed out that there is as yet no robust evidence of improved outcomes in these settings. CRRT is also useful in fluid control and management of acid-base and electrolyte imbalances44–46. When IHD is used, time is always a limiting factor, hence the need for relatively high blood and dialysate flow rates, which correlate with the degree of blood purification achieved. CRRT permits the use of slower flow rates and may achieve weekly clearances that are equal or even superior to IHD. These advantages of CRRT must be balanced against its greater cost in terms of equipment and staff time47.

Definitions and Therapeutic Potential of CRRT

In 1977, Kramer et al.48 developed continuous arteriovenous hemofiltration in order to avoid the side effects of IHD. Today, this particular access method is rarely used because it carries its own set of adverse effects49. Additionally, blood flow and ultrafiltration volume are largely dependent on the patient’s mean arterial pressure. These shortcomings have led to several technical modifications. CRRT is now generally performed with a pump50. It may use primarily convective clearance (continuous venovenous hemofiltration) or diffusive clearance (continuous venovenous hemodialysis), or it may involve a combination of these procedures (continuous venovenous hemodiafiltration). Solute removal by diffusion is determined by the molecular weight of the solute, the concentration gradient across the dialysis membrane, and, to a lesser extent, the membrane surface area. Smaller solutes such as urea, creatinine, and electrolytes are cleared largely by diffusion, but as their molecular weight increases, substances are less likely to be removable by diffusion. Convective clearance depends on the ultrafiltration rate and is relatively independent of molecular size. Convection has an advantage over diffusion in being able to clear
middle- or large-molecular weight toxins in patients with sepsis. The particular CRRT modality chosen, then, depends on the substances requiring clearance. Diffusion is more appropriate if small molecules such as urea, uric acid, potassium, and creatinine are the targets, whereas convection is more useful for larger molecules. However, it must be noted that there is not yet enough evidence from clinical trials to determine if these differences at a molecular level actually translate into measurable differences in clinical outcome.

**Timing of CRRT Initiation**

The generally accepted indications for initiation of CRRT in ARF include volume overload unresponsive to fluid restriction and diuretics, hyperkalemia refractory to medical management, metabolic acidosis that is severe or accompanied by volume overload that precludes adequate bicarbonate therapy, overt uremic symptoms (anorexia, nausea, vomiting) or signs (uremic pericarditis, bleeding, encephalopathy), or anuric ARF unresponsive to acute interventions such as reversal of prerenal factors or relief of obstruction. CRRT is also indicated for certain dialyzable intoxications (e.g., lithium, toxic alcohols, salicylate) and for some cases of hypomagnesemia, hyperphosphatemia, or hypercalcemia.

Observational studies have suggested that the precise timing of initiation of CRRT in the elderly may have a profound effect on outcome, although no randomized controlled trials have yet specifically addressed this question. After cardiac surgery, for example, a better outcome has been observed when CRRT is begun early. Since the consequences of complications are likely to be more severe for a critically ill patient, early initiation of therapy to support organ function may improve the outcome by providing an opportunity for the patient to recover from the underlying illness. CRRT in this setting has the primary goal of providing adequate renal support for other organ functions. This requires a change in our traditional approach of waiting for specific metabolic or biochemical abnormalities prior to initiation of dialysis. The broad goals for treating ARF with dialysis, then, are to: (1) maintain fluid and electrolyte, acid-base, and solute homeostasis; (2) prevent further insult to the kidney; (3) promote renal recovery; and (4) permit other supportive measures (e.g., nutrition) that might otherwise be limited in the presence of ARF.

**Intermittent vs. Continuous Therapy: Does it really make a difference?**

In theory, it sounds as if CRRT ought to improve survival in elderly patients with ARF. In fact, however, there is as yet no hard evidence to support the superiority of CRRT over IHD in terms of survival. Studies that have been performed have been limited in scope, of relatively poor quality, or have failed to define subgroups in such a way as to provide a solid basis for choosing 1 method over another. Most of the current evidence comes from observational studies or studies of unselected patients. There have been small studies of specific conditions, e.g., CRRT provided a slightly greater physiologic benefit than IHD in treating 12 patients with cerebral edema and ARF. A distinction should be made between articles that discuss the theoretical benefit of CRRT and those based on rigorous clinical trials. A multicenter, randomized trial involving 161 patients failed to show a benefit for CRRT over IHD, but the authors acknowledged the difficulties in designing a trial that uses clearly defined populations with equivalent treatment doses and associated treatments. Other studies have also failed to show a clear cut benefit for CRRT, but none of these have specifically addressed the value of this treatment in the elderly. Large-scale randomized trials, which will most likely have to be multicenter collaborative efforts, are needed to demonstrate whether the theoretical advantages of CRRT in fact provide a better outcome for elderly patients with ARF.

Until such evidence is available, we recommend CRRT for ARF in patients whose hemodynamic status makes them unable to tolerate IHD. This is likely to be the case for many elderly patients with ARF, particularly in the face of other critical illnesses such as sepsis or multiple organ failure.

**References**

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