International Urology and Nephrology **32:** 559–565, 2001.

Multi-organ renal failure in the elderly

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Abstract. Periodically the question is posed "Why the persistently high mortality in acute renal failure?". By 1986, little progress seemed to have been made in improving outcome and it was stated that once oliguria was resistant to volume replacement and cardiac support, the patient had at best only a 50% chance of surviving. During the period 1960–1985, it can be shown that although outcome was not improving, older and sicker patients were being treated. Reviewing the literature of the past decade, the age and case mix of patients appears stable, but there is no suggestion of improvement in outcome. ARF with sepsis continues to have a mortality of 65 to 80%, and the outcome remains poor in elderly patients with failure of two or more organs. Progress has been slow in Intensive Care Units, and the past 20 years has seen little more than a move away from parenteral towards enteral feeding. Recent advances, however, in ventilatory techniques and the use of supra-physiological doses of glucocorticoids may lead to some improvement in outcome.

Key words: Acute renal failure, Elderly, Epidemiology, Intensive care unit, Multiple organ failure, Outcome, Mortality

Introduction

What can be done for elderly patients with multiple organ renal failure? As the man when asked for directions said, "Well, I wouldn't start from here". I will start by defining what one means by elderly, acute renal failure (ARF), and multiple-organ failure (MOF). Then I will briefly discuss the epidemiology and causes of acute renal failure with particular reference to susceptibility in the elderly. I will consider what is known about outcome, both from the historical perspective and the current state of the art. Have we made any progress in the subject [1]? When auditing and contrasting outcome in critically ill patients one of the most difficult tasks is to compare like with like. Finally, I will consider whether anything can be done to prevent multiorgan renal failure, and discuss outcome and the question "Was it worth it"?

Definitions

Generally *elderly* is considered as over the age of 65. However in many studies, the elderly are not treated as a special group but the entire population is reviewed in age decades. There are many definitions of *acute renal failure*. This review considers patients who require some form of renal replacement therapy (in general terms "dialysis"). In the recent literature, definitions vary greatly regarding the severity of renal insufficiency [2–10] (Table 1), and in two recent epidemiological studies, definitions ranged from a creatinine of greater than 177 μmol/L (2 mg/dl) [2] to greater than 500 μmol/L [5].

Severe ARF is now seen predominantly in ICUs and usually is associated with dysfunction of other organ systems. Critical illness can be defined as "a potentially lethal acute failure of one or more organ systems". As will be seen later the outcome of acute renal failure depends largely on the underlying cause and severity of the disease (number of other organs failing). Severe combined acute respiratory and renal failure (SCARRF) – a variant of MOF which is associated with severe sepsis and massive trauma, provides a clear reference point when defining the MOF syndrome in the ICU [11].

Of the many attempts to measure the severity of illness, the most widely used of these scoring

Table 1. Definitions and demographics of acute renal failure

Reference	Year	Rise in creatinine μmol/l (mg/dl)	ICU admission	Ventilated	Dialysis
Madrid Study *Liano F*	1996	> 177 (2.0)	28%	28%	36%
French Study *Brivet FG*	1996	> 300 (3.5)	100%	57%	58%
Scotland *Khan IH*	1997	> 300			8%
Community Study, UK *Feest TG*	1993	> 500			13%
Leeds, UK *Turney JH*	1990	> 600 or dialysis	—	40%	90%

systems is the Acute Physiological And Chronic Health Evaluation score (APACHE II) [12], which scores 12 physiological measurements on the first day of entry into the ICU. Also a weighting is awarded for age and pre-existing chronic health problems. More recently this system has been amended and the physiological measurements increased to 17 (APACHE III) [13]. Another commonly reported physiological scoring system is the Simplified Acute Physiological Score (SAPS) which scores 12 measurements and is weighted. The number of organs failing can be measured by the Organ System Failure score (OSF). With this and others it is sometimes difficult to define cut-off points, and points that do not depend on therapy. Auditing and comparing outcomes from different periods may be confounded by the increasing age of people being treated and the changing case mix. The APACHE score may not be able to discriminate these various confounding features.

Epidemiology and causes of ARF

Most studies of the incidence of ARF are retrospective reviews of patients admitted to renal units or to ICUs. Feest and his colleagues [5] addressed this question in a prospective review of a regional community of half a million people in South West England over a two-year period. They defined *severe* ARF as a creatinine rising above 500 μmol/L and subsequently falling. They identified 125 such people, or 140 per million population (pmp) each year. Of this group 72% were over the age of 70 years, and prostatic disease accounted for the diagnosis in 25%. 51 pmp were referred to an appropriate specialist although in retrospect 70 pmp were considered suitable for referral. Figure 1 shows the rate of renal failure per age decades in this study, after patients with prostate disease had been excluded; as can be seen the incidence rises exponentially over the age of 70. In another prospective study, the Madrid ARF Study Group [2], recorded episodes of ARF (creatinine >177 μmol/l) in 13 Madrid hospitals prospectively over a nine-month period. Overall incidence was 209 pmp but, in 48% of these cases, renal function was normal on admission.

Risk factors for the elderly

The elderly are at greater risk of ARF [14, 15] because, with increasing age, both anatomical and physiological changes occur in the kidney (Table 2). Also this group has an increased burden of chronic disease such as cardiovascular disease, hypertension, diabetes and prostatic disease. Often they are given drugs that are nephrotoxic in persons with a reduced GFR, and obstructive uropathy is common.

The physiological changes associated with the ageing kidney (Table 2) include not only a progressive fall in GFR, but a progressive fall in renal blood flow which may precede the fall in GFR. Also the elderly have a progressive inability to concentrate urine, conserve salt and water, and the reduced diluting capacity makes older people particularly prone to hyponatraemia [14].

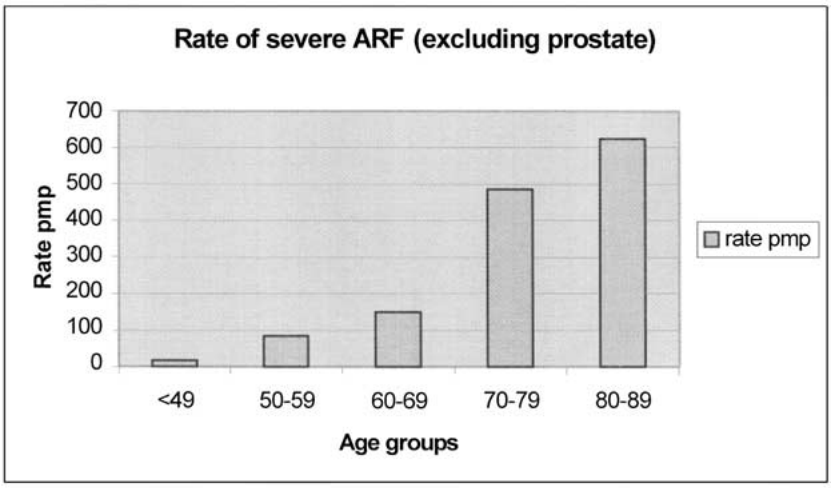

Figure 1. Incidence of severe ARF in adults: results of a community based study. (Feest TG et al., *BMJ 1993: 306; 481–483*).

Table 2. Physiological changes in aging kidney

Progressive decline in:
• Renal blood flow: 50% fall from age 20 → 80
• GFR: falls by –1 ml/min/yr from age 40
• Urinary concentrating ability
• Diluting capacity
• Ability to conserve Na^+, when salt restricted
• Renal acid excretion
• Peripheral renin activity and aldosterone.

Management and outcome

Historical perspective

In 1972, in their paper "Why the persistently high mortality in acute renal failure?" (16), a group from Guy's Hospital addressed one of our great concerns namely that outcome has not improved with time. Fourteen years later Stewart Cameron returned to this subject in an editorial review 'Acute Renal Failure – the continuing challenge' [1]. "In 1986 . . . once oliguria is resistant to volume replacement and cardiac support, the patient has at best only a 50% chance of surviving". He concluded "almost four decades have passed without any real improvement . . . let us hope a 5th decade will not pass in similar disappointment". Thus 14 years further on we can address this question again: "have we made any progress?"

One likely explanation for the outcome not improving is that we now are treating older and more difficult patients. In a large retrospective study from a single centre in Leeds, UK [6], Turney and his colleagues reviewed 1347 patients treated in their unit during the period 1956–1988. They defined *severe* ARF as either a creatinine greater than 600 μmol/L or the need for dialysis. They showed clearly that the populations treated had become progressively older and more complex. They compared two subgroups of this population, who had sepsis and ARF, reviewing 100 patients treated in the 1960s with 100 treated in the 1980s. The mean age rose from 51 to 63 years and patients requiring ventilation rose from 2 to 41%. Nevertheless survival fell from 49 to 37% [17]. A similar study, from the John Hopkins Hospital, compared the period 1977–1979 with 1991–1992 [18]. This was more encouraging because although APACHE scores were similar in both periods, in the second period the patients were older and had more chronic health problems, yet the outcome clearly improved (all survivors: 52% versus 32%) [18]. Thus by 1990, it appeared that, while overall outcome was not improving, the patients were older and the case mix had become more complex.

Current situation

In a large French study of acute renal failure [3] a prospective audit of all patients entering 20 ICUs over a six-month period was carried out. ARF was defined as a rise in creatinine above 300 μmol/L or a 100% rise in creatinine for those with chronic renal insufficiency with previous creatinine of 150–300 μmol/L. During this period they identified 360 patients, who repres-

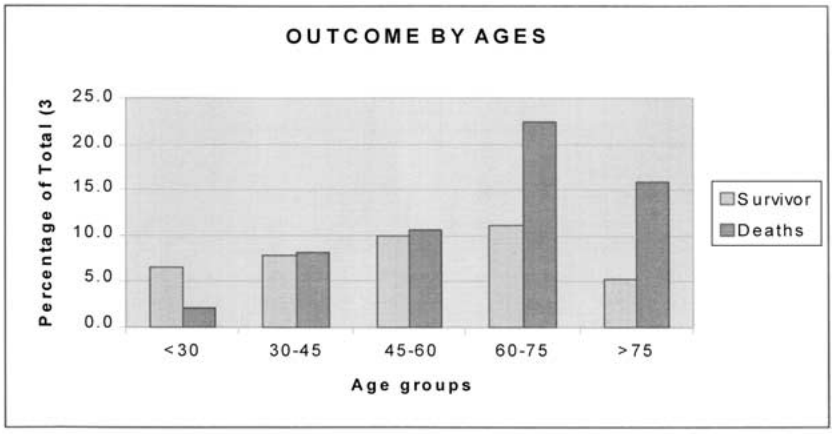

Figure 2. French Study Group on ARF. (Brivet FG et al., *Crit. Care Med 1996: 24; 192–198*).

ented 7% of all ICU admissions. At entry to hospital, 217 patients had renal failure whereas 143 developed ARF later ("delayed ARF"). The overall mortality was 58%. The admission diagnosis was medical in 78%, emergency surgery in 17% and elective surgery in 5%. Of the cases, 17% were judged to be pre-renal, 79% renal and 4% post renal, although often several causes were noted for renal failure; 52% were oliguric, 57% required ventilation, in 48% sepsis was considered to contribute to the ARF, and in 32% hemodynamic instability was a contributing factor. A review of previous health status showed that only 41% were in good health three months earlier, and 39% had one or more pre-existing diseases. The mean APACHE II score for the whole group was 24. Increasing age was identified as a risk factor (Figure 2).

Table 3. French Study Group of ARF
Brivet FG et al., Crit Care Med 1996: 24; 192–198

	Yes	No
Ventilated	73%	49%
Sepsis	73%	45%
Oliguria	70%	46%
Delayed ARF	71%	50%

All mortality = 58%.
Renal failure = 62%.

Table 4. Outcome of combined acute multiple organ and renal failure treated with continuous hemofiltration or hemodiafiltration

	Survivors	Non-survivors
Age	57 yr	60 yr
APACHE II	25	29
Inotropes	45%	96%
Ventilated	71%	86%
Septic shock	44%	67%

Ref [21].

Causes of death and outcome

On reviewing the cause of death in their large group, Turney and his colleagues identified 636 deaths (47% mortality) [19]. The most important factor was the underlying cause of ARF. 67% of deaths were a direct consequence of sepsis that continued from the initial infection. Deaths from secondary complications, for example gastrointestinal hemorrhage, declined with time.

In the French Study Group, the overall mortality was 58%, although in those requiring dialysis it was higher – 62% [3]. Table 3 shows that various factors made survival less likely. Multivariate analysis identified six features as significant risk factors: the two demographic features were age and previous ill health; renal features were the presence of oliguria, occurrence of delayed ARF and sepsis contributing to the cause of ARF; physiological risk factors were a higher APACHE score [3]. In a subanalysis of patients with sepsis, the French Group [20] found an overall mortality of 75% (vs. 45% without sepsis). These patients also were older (62 vs. 58 years).

A recent study that reported outcome and quality of life in survivors, also gave important information on nonsurvivors [21]. Of 250 patients, of whom 66%

Table 5. Outcome in the elderly (> 65 years)

		Nos	Age	Dialysis	Survival
Lameire N 1987	ARF	100	> 65	77%	57%
Bellomo R 1994	ARF	72	> 65	100% CHDF	47%
Klouche K 1995	ARF	68	> 65	60%	37%
Alarabi 1997	ARF after cardiovasc surgery	111	70 (65–80)	100% CAVHD CAVH	58% (38–91%)
Maziak DE 1998	Ruptured AA	88			60%

Table 6. Preventing multiple organ failure

1. Treat underlying condition
2. Fluid resuscitation
3. Timely intubation and ventilation
4. Appropriated antimicrobial therapy
5. Enteral feeding
6. Medical staff hygiene (hand washing)

died, it can be seen in Table 4 that non-survivors were older, had higher APACHE scores and were more likely to be ventilated, given inotropes and be in septic shock. Other reviews of outcome in the elderly with ARF show that the mortality remains at 50–70% [7–10, 22] (Table 5).

What can be done?

The outcome in elderly patients undergoing high-risk procedures, has improved in the last two decades [23]. Even elderly patients admitted to the ICU have hospital survival rates of 60–70% if they have less than two-organ failure or APACHE scores below 25 [24–26]. Unfortunately patients often enter the ICU as emergencies, or following some unforeseen or unexpected surgical complication.

Strategies for preventing multiple-organ failure are shown in Table 6. In essence, these have not changed in the last 30 years, although during this period we have moved away from parenteral feeding towards enteral feeding. Although the importance of hygiene among the medical staff (handwashing) was pointed out 150 years ago, sepsis from this source is still a major factor.

Recent advances in Intensive Care

1. *Acute Respiratory Distress Syndrome (ARDS).* Survival in acute respiratory distress syndrome (ARDS) has improved due to better (pressure controlled) ventilation using lower (6 ml/kg not 12 ml/kg) tidal volumes. Setting the positive end-expiratory pressure (PEEP) around the inflection point (pressure volume curves at the bedside) avoids sheer stresses in alveoli as they open and collapse down with tidal ventilation [27].

Initially nitric oxide in the ventilator improves oxygenation but has not been shown yet to improve outcome [28]. In patients with unresolving ARDS, the use of steroids (2 mg/kg methylprednisolone) daily at about day 7–10, as the patient enters the fibroproliferative phase, improves outcome and reduces mortality [29].

2. *Nutrition*. We have moved away from parenteral nutrition, which was virtually routine in the 1980s. A recent meta-analysis in malnourished patients [30] concluded that such nutrition did not improve survival, but may reduce complications. Conversely there is increasing interest in immune-enhancing enteral nutrition (omega-3 fatty acids, purine nucleotides, arginine, and glutamine). A recent meta-analysis concluded that such supplementation reduces complications, infections and hospital stay, but does not reduce mortality [31].

3. *Steroid supplementation*. Recent studies suggest that supraphysiological doses of hydrocortisone improve the outcome in septic shock (hydrocortisone 100 mg 8 hourly [32], 100 mg followed by 0.18 mg/kg/hr [33]). This may be particularly important for patients on inotropes; here the steroid supplements reduce the time to withdrawl of inotropes.

Long-term outcome

Patients do not always recover renal function and although there is not much data, it seems that between 5 to 15% of survivors remain dialysis dependent [2, 34]. In a review of long-term outcome [21] 85 survivors from a group of 250 with ARF (34%) were contacted by post: 35 (42%) were alive and replied, 17 were known to be dead and 33 did not reply. Of those who replied, 95% felt that their ICU care had been worthwhile, 68% were satisfied with their present life style, but 42% were unable to walk 200 meters. Cost per one-year of survival was estimated at $50,000 [21].

Thus it can be seen that ARF with sepsis continues to have a mortality of 65 to 80%, and the outcome remains poor in elderly patients with failure of two or more organs.

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