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Long-term prognosis after acute kidney injury requiring renal replacement therapy

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Abstract

Background. Data on the long-term survival and renal function of patients with acute kidney injury (AKI) treated with continuous renal replacement therapy are scarce.

Methods. We investigated the 3-year survival and need for chronic dialysis in critically ill patients, who had survived an episode of AKI requiring continuous renal replacement therapy.

Results. A total of 206 ICU patients with AKI were randomized in a trial comparing haemofiltration versus haemodiafiltration. Of these, 95 (46%) survived at 90 days. Post-discharge information relating to 3-year survival and renal function was successfully obtained in 89 (94%) of the patients. Of the 89 patients studied, chronic kidney disease (CKD) was present in 32 subjects from the onset, and CKD developed *de novo* in 25 patients following AKI. End-stage renal disease (ESRD) developed in 9 patients (of whom 8 had pre-existing CKD) and 29 patients died. Three-year survival was 67% overall; the mortality at 3 years was 50% for those with pre-existing kidney disease, and 71 and 82% for those with *de novo* and without CKD, respectively.

Conclusion. After an episode of AKI necessitating a continuous renal replacement therapy, rapid progression to ESKD is commonly observed in patients with pre-existing chronic renal impairment. Medical care with an emphasis on nephroprotection is necessary in these patients.

Keywords: acute kidney injury; continuous renal replacement therapy; long-term survival

Introduction

Acute kidney injury (AKI) affects as many as 30% of patients admitted in intensive care units (ICU) [1]. The aetiology in 90% of ICU-related AKI is acute tubular necrosis (ATN), occurring most commonly in the context of multiple-organ failure. Due to recent improvements in intensive care techniques, the in-hospital mortality rate of patients with AKI requiring dialysis has declined over the past 20 years from 41 to 28% [2]. However, many patients who have an episode of ICU-related AKI nowadays are elderly and have severe co-morbidities and in this context, the incidence of AKI has been increasing over the past decades [2–4]. Data on their long-term survival are scarce and often conflicting. Before 1980, $<10\%$ of patients with ATN ended in end-stage renal failure [5]. At 1-year follow-up, only 1% of the patients surviving an episode of ICU-related AKI requiring renal replacement therapy (RRT) were found to have an ongoing requirement for RRT [6]. No prognostic factor for end-stage renal failure could be identified in this study. Longer follow-up of this cohort was

recently published and at 5 years, 5% of the patients still alive needed maintenance dialysis [7]. The longest follow-up (10 years) of 187 patients with AKI showed that 71% of those with chronic renal dysfunction prior to the episode of AKI ($n = 100$) died within the follow-up but only 2 patients needed dialysis in this cohort [8]. Other authors are less optimistic, reporting a chronic dialysis rate up to 20% in survivors of ATN [9]. In this study, we investigated the 3-year survival and need for chronic dialysis in critically ill patients who had both taken part in a randomized controlled trial comparing different doses of RRT, and were still alive 90 days after their episode of AKI [10].

Patients and methods

Between October 2000 and December 2003, 206 ICU patients with AKI were included in a controlled randomized trial comparing haemofiltration and haemodiafiltration [10]. Details of this study were already published. Data on 3-year survival and level of renal function prior to and after AKI were obtained in those who survived >90 days by referring to the Geneva population registry or their medical records (hospital or private physician). Normal renal function prior to the episode of AKI was determined by an estimated GFR (eGFR) ≥60 ml/min according to the MDRD study equation [11]. Only serum creatinine values measured 1 month prior to AKI were considered as valid when calculating the eGFR to determine the renal function prior to AKI. Patients without premorbid creatinine but who had at discharge an eGFR ≥60 ml/min were considered to have no CKD prior to AKI. Non-return to baseline values was diagnosed as incomplete recovery. An eGFR ≤ 60 ml/min prior to AKI was defined as prior CKD and at hospital discharge or at 90 days post-AKI as *de novo* CKD. End-stage kidney disease (ESKD) was defined as CKD requiring maintenance dialysis.

Statistical analysis

The chi-square and *t*-tests were used to compare demographic and baseline characteristics of 3-year survivors and non-survivors. Significant *P*-values were <0.05.

A Kaplan–Meyer analysis was used to determine 3-year survival among patients without CKD and those with known or *de novo* CKD.

Results

Of the 206 patients who took part in the randomized trial, 95 were still alive at 90 days after implementation of RRT. Three-year data on survival and level of renal function were obtained in 89 (94%) patients. Six patients were transferred to other countries and were lost to follow-up. Premorbid creatinine values were obtained in 71 patients. Baseline demographic and clinical characteristics of 3-year survivors and non-survivors are listed in Table 1. At discharge, complete recovery (within ± 10% baseline eGFR or discharge eGFR >60 ml/min) was present in 32 out of 89 patients, dialysis dependence was present in 4 patients and the remainder had partial recovery. The 32 patients with full recovery at discharge had a steady renal function during follow-up.

Patients with de novo CKD after AKI

During the 3-year follow-up, of the 25 patients who developed CKD after AKI, 1 became dependent on dialysis, 5 improved their eGFR, 13 decreased their eGFR and 6 had a steady eGFR.

Table 1. Clinical and laboratory characteristics of patients at 3-year survival (except for serum creatinine)

	Survivors ($n = 60$)	Non-survivors ($n = 29$)
Age (year)	58 ± 16	68 ± 11†
Male gender (%)	50	66
Diabetes (%)	18	21
Diagnosis of AKI (trauma/surgical/medical)	6/9/45	1/12/16†
Apache II score	23 ± 8	18 ± 6††
Sepsis (%)	60	41.4
RRT duration (day)	3 (2–5)	4 (2–5)
Serum creatinine prior to AKI		
Mean, median, (range) (μmol/l)	118, 98 (40–302)	141,119 (54–350)
eGFR prior to AKI (ml/min)	52 (14)	47 (14)
CKD prior to ARF (%)	27	55††
Serum creatinine at discharge or 90 days		
Mean, median, (range) (μmol/l)	144, 100 (52–1060)	161, 135 (39–378)
eGFR at discharge or 90 days (ml/min)	46 (17)	40 (20)
CKD at discharge or 90 days (%)	55	79
Last serum creatinine prior to death or at 3 years		
Mean, median, (range) (μmol/l)	121, 88 (54–535)	196, 154 (53–546)††
eGFR prior to death or at 3 years (ml/min)	47 (17)	30 (19)
CKD prior to death or at 3 years (%)	57	79†

Data are given as mean ± SD or median and IQR.
†$P < 0.05$, ††$P < 0.01$.
BUN: blood urea nitrogen.

Patients with CKD prior to AKI

Among the 32 patients with CKD prior to AKI, 4 had an increase in eGFR, 10 had a decrease, 8 ended in ESKD and the remainder had a stable renal function during the follow-up.

At discharge, eight patients were classified with stage V (NKF/DOQI classification), of whom one improved during follow-up (stage IV CKD). Fifteen were classified with stage IV CKD of whom 2 improved during follow-up (stage III CKD), 8 remained stage IV and 5 ended in stage V. Among the 26 classified at discharge with stage III CKD, 1 improved his renal function during follow-up (stage II CKD), 9 worsened their renal function (2 stage V CKD and 7 stage IV) and 16 remained stage III. Among the 40 classified at discharge with ≤stage II CKD, 28 remained stable and 12 worsened their renal function during follow-up (2 stage V CKD, 1 stage IV, 9 stage III).

Survival

Overall survival in patients with AKI requiring continuous RRT (CRRT) dropped from 46% ($n = 95/206$) at 90 days to 30% ($n = 60/201$) at 3 years.

Overall 3-year survival in the 89 survivors at 90 days was 67%. Among those who died within these 3 years, 79% had

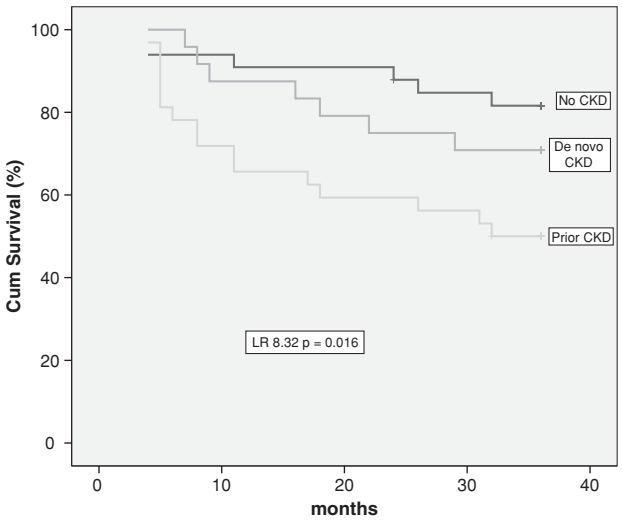

Fig. 1. Kaplan–Meyer analysis of 3-year survival rates in patients without (no CKD prior to AKI) and with prior (prior CKD to AKI) or *de novo* CKD after AKI.

CKD either prior to AKI (55%) or *de novo* developing after AKI (24%), whereas only 55% of survivors had CKD (27% prior to AKI and 28% *de novo* developing after AKI). Three-year survival was 50, 71 and 82% in 90-day survivors with prior, *de novo* and without CKD (log-rank test = 8.32, $P = 0.016$), respectively (Figure 1).

Discussion

In our study of critically ill patients with AKI, those who survived 90 days had a yearly mortality of almost 6%/year during the following 3 years. This rate is more than 10-fold higher than the annual mortality observed in the general population of Geneva residents aged 61–70 (0.8% mortality for the years 2004–2006; Office Cantonal de la Statistique, Geneva). Overall 3-year mortality in the 206 patients originally enrolled in our trial was 70%. These results are in accordance with those previously published. A recent prospective cohort study with 425 patients treated for ATN with RRT mentioned 53 and 35% survival at discharge and at 1-year follow-up, respectively [6]. In the studies with a long follow-up period, 5-year mortality in Finnish patients requiring RRT was reported to be between 50 and 70% [12,13]. A retrospective survey of 301 German ICU patients with severe AKI found a 5-year survival of only 50% amongst discharged patients [14].

Mortality increased in our patients with CKD, with the highest rate observed in those with known CKD prior to AKI, and our results confirm CKD as an important risk factor for death in the general population [15].

It is often accepted that the outcome of AKI is binary: death or survival without the need of RRT, principally because AKI is commonly held to recover in the vast majority of survivors. In a recently published analysis of an international cohort encompassing 1218 patients treated with CRRT, 14% were still dialysis dependent at hospital discharge [16]. Patients who are, however, dialysis free at 90 days post-AKI generally remain so at 1 year, as suggested by the recently reported 1 and 5% incidences of ESKD at 1 and 5 years in patients with ATN requiring RRT [5,7]. In this prospective study, nearly half of the survivors were, however, discharged with moderate-to-severe CKD and none of these patients were known to have CKD prior to the onset of AKI. More discouraging results have, however, also been reported, with prevalence of ESKD ranging from 10 to 16.2% in studies with a long follow-up [9,14,17]. A large retrospective cohort study of 2202 patients treated by RRT (86% by CRRT and 15% by intermittent haemodialysis), of whom 1102 survived 90 days post-AKI, showed a long-term 11.9% incidence of ESKD [14]. Information on post-discharge renal function of 301 German ICU long-term survivors was obtained in 130 patients [14]. CKD was present in 41% of the patients and 10% required maintenance dialysis. The results of our study support these data as the 3-year incidence of ESKD among our survivors was 10%. Notably, our patients with previous CKD had a 25% incidence of ESKD at 3 years. In addition, the prevalence of CKD was elevated with nearly one in two patients with no known CKD prior to AKI progressing to CKD within 3 years.

Our study has some limitations. Though prospective, this observational study relies on a limited sample of patients and lacks statistical power to determine which factors are predictive of long-term survival and the need of RRT.

Our population also had a high prevalence of patients with previous CKD and results may not be extrapolated to other world populations, particularly outside the western hemisphere.

Data were not collected on other co-morbidities such as neoplasia or cardiovascular disorders, nor was the presence or absence of a nephrological follow-up recorded.

Despite its shortcomings, this observational study confirms that after an episode of AKI necessitating CRRT, rapid progression to ESKD is only exceptionally observed in patients with normal renal function prior to the acute renal injury, although one in two patients will progress to CKD. These results will, however, need to be confirmed by a larger prospective study analysing long-term outcomes in these patients. We, however, recommend that patients who develop CKD after AKI should be considered at risk of progressing to ESKD. In this regard, they should receive medical care with an emphasis on nephroprotection, for example detection and treatment of hypertension, coronary heart disease, calcium and phosphate metabolism disturbances and anaemia. Also of note, patients with pre-existing CKD prior to the episode of AKI are at high risk of progressing rapidly to ESKD following an episode of AKI; 25% of our patients with previous CKD developed end-stage renal disease within 3 years after AKI. Pre-dialysis care with preparation for RRT is therefore recommended for these patients.

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Conflict of interest statement. None declared.

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