European Journal of Internal Medicine xxx (2014) xxx–xxx

Contents lists available at ScienceDirect

European Journal of Internal Medicine

journal homepage: www.elsevier.com/locate/ejim

Original Article

Timing of acute kidney injury — does it matter? A single-centre experience from the United Kingdom

Ching Ling Pang *, Dimitrios Chanouzas, Jyoti Baharani

Heart of England NHS Foundation Trust, United Kingdom

ARTICLE INFO

Article history:
Received 20 January 2014
Received in revised form 23 May 2014
Accepted 4 June 2014
Available online xxxx

Keywords:
Acute kidney injury
Nephrology
Acute medicine

ABSTRACT

Background: Acute kidney injury (AKI) requiring renal replacement therapy (RRT) is associated with high mortality and long-term dependence on RRT. However, there is limited information about the difference in outcome between patients who develop AKI in the community (c-AKI), and those who develop AKI in hospital (h-AKI).
Aim: Identify differences in short- and long-term outcomes between patients admitted with c-AKI and h-AKI who require intermittent haemodialysis, and to identify factors that predict poor outcome.
Design & methods: Single-centre, retrospective analysis of 306 patients with AKI who received intermittent haemodialysis between 2009 and 2011. Follow-up: six months. Primary endpoints: patient and renal survival. Secondary endpoints: time on dialysis, length of hospital stay, and admission to the intensive care unit (ICU).
Results: Survival for patients in the h-AKI group was significantly lower, at 42.9% (compared to 72%). They had a significantly longer length of stay. However, at 6-month follow-up, the survival benefit of the c-AKI group was no longer significant. Patients with h-AKI were more likely to be dialysis independent at discharge and six months although this result did not reach statistical significance. Independent predictors of survival to discharge within the entire group included: renal/post-renal causes of AKI, younger age, pre-existing diabetes, and c-AKI. The only independent predictor for RRT dependence at discharge and six months was pre-existing chronic kidney disease.
Conclusions: h-AKI is associated with high mortality and longer hospital stays during the acute admission. However, h-AKI patients who survive are more likely to be independent of RRT at discharge and follow-up.

1. Introduction

Acute kidney injury (AKI) is a common clinical syndrome affecting patients in the community and in hospital. The incidence of AKI varies according to the definition used but has been reported to be up to 1811 per million population (pmp) per year [1–3]. The multiple aetiologies and risk factors [4] involved mean that it represents a spectrum of renal dysfunction ranging from small rises in serum creatinine [5], to the need for renal replacement therapy (RRT). Acute kidney injury in hospital inpatients is associated with significantly higher mortality rates both in the intensive care unit (ICU) [6] and amongst hospital inpatients [7,8]. It is also associated with longer hospital stays, and increased costs [9]. The associated mortality from AKI depends on the degree of kidney injury, but has been estimated as high as 26.3% for those in RIFLE class F [10]. This figure rises to over 50% for patients requiring RRT, and up to 70% for those requiring treatment in intensive care [7,11,12].

There is a distinction to be made between AKI that develops in the community (community acquired AKI; c-AKI) and AKI that sets in during an inpatient episode (hospital acquired AKI; h-AKI). It is well established that h-AKI is associated with significant morbidity and mortality that cannot be ascribed to comorbid conditions [13]. Despite this, identification of patients who develop AKI post-admission is poor in many centres, with a recent National Confidential Enquiry into Patient Outcome and Death (NCEPOD) study [14] finding that diagnosis was delayed or missed in 43% of admissions. Furthermore, for 20% of these patients, the cause was both predictable and preventable. NCEPOD concluded that the majority of cases had been inadequately assessed on admission for the severity of their illness and pre-existing risk factors, and that referral to nephrology services was delayed or did not happen in 20% of cases.

The use of scoring systems to identify patients with AKI is well validated. Two such scoring systems are: the Acute Dialysis Quality Initiative's (ADQI) RIFLE [15] scoring system, and the Acute Kidney Injury Network [16] (AKIN) scoring system. Direct comparison [17] of these two scoring systems shows that they identify slightly different groups of patients. AKIN scoring identified 9% more Stage 1 patients than RIFLE scoring; and conversely, RIFLE scoring identified 26.9% more patients with AKI than AKIN. Nonetheless, both are independently associated with increased mortality rates [6,10].

Only a handful of studies have examined differences in outcome between c-AKI and h-AKI. Most of these studies were carried out in developing countries with the majority concluding that h-AKI is associated with higher mortality [18–21], although two studies from Brazil and Saudi Arabia found that c-AKI was linked with reduced survival

* Corresponding author. Tel.: +44 7783921024.
E-mail address: c.pang@nhs.net (C.L. Pang).

http://dx.doi.org/10.1016/j.ejim.2014.06.005
0953-6205/

compared to h-AKI [5,22]. A recent North American study showed that patients with c-AKI were more likely to have a shorter length of hospital stay, fewer complications and better overall survival compared to h-AKI [23].

To assess the impact of the timing of acute kidney injury on patient outcome following the NCEPOD report, this study aims to identify and quantify differences in outcomes between patients admitted with c-AKI, and those who develop h-AKI during their hospital stay.

2. Study cohort and methods

2.1. Study cohort and patient selection

This was a single centre, retrospective observational study. Our hospital operates across three sites, all of which have telephone access to a duty nephrologist. Two of the sites have an intensive care unit (ICU) with the capacity to provide continuous haemofiltration (CVVH); but only the main site has the facilities for intermittent haemodialysis (IHD) with a dedicated inpatient & outpatient nephrology presence. Using the renal patient database (PROTON), we identified a total of 306 consecutive patients that were admitted via one of our three hospital sites and received intermittent haemodialysis (IHD) at some point during their admission in the context of AKI between 2009 and 2011. We included patients with AKI on a background of chronic kidney disease (CKD).

Patients were split into two groups: those who already had AKI on admission to hospital (c-AKI), and those in whom AKI developed 48 hours after admission (h-AKI). We identified AKI and differentiated between c-AKI and h-AKI based on the admission creatinine, available creatinine values prior to admission and serial creatinine measurements post-admission according to the AKIN staging system. We did not define AKI based on urine output as this data was not available for c-AKI patients. Data was collected from the renal unit's records, as well as the electronic patient record database (iCare), both of which are continuously updated and include all investigations and blood results performed at all 3 hospital sites, as well as by most GP practices within the trust catchment area.

Data collected comprised basic patient demographics, including: age, gender, ethnicity, modified Charlson comorbidity index, the presence of pre-existing diabetes mellitus, and CKD. The presence of previous CKD was coded based on an eGFR value of <60 ml/min/1.73 m^2 within available blood results prior to hospital admission. Renal function was assumed to be normal if there were no prior blood tests available, and the patient gave no history of pre-existing kidney disease on admission.

The cause of AKI was coded based on clinical information and biopsy results where available. Patients that suffered a pre-renal insult that might have led to clinical sequelae of acute tubular necrosis (ATN) were coded for their initial renal insult in terms of their AKI cause, i.e. pre-renal.

Two primary outcomes were measured: patient survival and renal survival (dialysis independence) at discharge and at 6 months. Secondary outcomes evaluated were: length of hospital stay (LOS), the number of days spent on dialysis, and the rate of admission to a step-up unit (either high-dependency unit (HDU) or ICU).

2.2. Statistics

All statistical analysis was carried out using SPSS. A p-value threshold of <0.05 was deemed statistically significant.

Univariate analysis: Parametric tests (T-test) were used for transformed continuous variables (length of stay and eGFR at discharge). The chi-square test was used for categorical variables. Non-parametric tests (Mann–Whitney U and Spearman's correlation) were used for continuous variables that were not normally distributed.

Multivariate analysis: Variables with p value ≤ 0.1 on univariate analysis were included in the multivariate models. Logistic regression was performed for binary outcome variables. Variables were entered in a single step. Odds ratios with confidence intervals and p values are reported. Linear regression was employed for log transformed continuous outcome variables. Variables were entered in a single step. B values with confidence intervals and p values are reported.

3. Results

3.1. Patient demographics

The characteristics of the study population are shown in Table 1. The mean age of the cohort was 68.2 (+/− 13.1) years. 67% of patients were male. The modified Charlson index was used as a measure of co-morbidity. The majority of patients (62.7%) had a moderate risk score, with an estimated 10-year mortality of 53% or less [24].

Two hundred and fifty (81.7%) patients were admitted with AKI (c-AKI), whilst fifty-six (18.3%) patients developed AKI at least 48 hours after admission (h-AKI) (Table 1). Patients with c-AKI were most likely to present in Stage 1 AKI. By definition, patients in the h-AKI group had normal renal function, or renal function in keeping with their known baseline on admission. Pre-renal causes accounted for the majority of all AKI (70.6%). Renal and post-renal causes accounted for 21.5% and 7.9% of all AKI episodes respectively. The majority of pre-renal causes were multifactorial, and included conditions associated with effective reduced renal perfusion, such as sepsis associated with hypotension and hypovolaemia (Table 2). Most patients were admitted for an acute medical or surgical reason; however, some were admitted for an elective surgical procedure.

Patients with h-AKI were significantly more likely to have sepsis ($p = 0.012$), and a pre-renal cause of AKI ($p = 0.018$). They were also more likely to present at the satellite sites ($p = 0.021$) where no on-site renal services are routinely available. There was no difference in the proportion of patients who had pre-existing diabetes mellitus, or CKD. The Charlson index score was also similar between both groups, indicating a similar co-morbid burden.

3.2. Survival and renal recovery outcomes

On univariate analysis, patients in the h-AKI group had significantly higher mortality rates ($p < 0.001$; Table 3), with just 42.9% surviving to discharge. The initial survival advantage of the c-AKI was short-lived, as no difference in survival was detected amongst the survivors of the two groups at six months post-hospital discharge ($p = 0.772$).

Hospital acquired AKI patients that survived had slightly better renal survival as judged by RRT independence at hospital discharge compared to c-AKI patients (Table 3), although this result did not reach statistical significance ($p = 0.072$). Nevertheless, h-AKI patients that survived to 6 months post-hospital discharge were still more likely to be dialysis-independent compared to c-AKI patients (Table 3), although again, this result did not reach statistical significance ($p = 0.056$). There was no difference in the mean eGFR amongst the RRT-independent patients between the two groups either at discharge or at 6 months.

3.3. Secondary outcome analysis

Patients in the h-AKI group were significantly more likely to have an extended inpatient stay compared to c-AKI ($p < 0.001$; Table 3). On average, their length of stay was twenty-five days longer when compared to the c-AKI group.

There were no significant differences in the length of time spent on haemodialysis; or on the proportion of patients that required admission to an ICU/HDU setting amongst the two groups (Table 3).

Please cite this article as: Pang CL, et al, Timing of acute kidney injury — does it matter? A single-centre experience from the United Kingdom, Eur J Intern Med (2014), http://dx.doi.org/10.1016/j.ejim.2014.06.005