How safe is renal replacement therapy? A national study of mortality and adverse events contributing to the death of renal replacement therapy recipients

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ABSTRACT

Background. Patients receiving treatment with renal replacement therapy (RRT) have high mortality, and ensuring patient safety in this population is difficult. We aimed to estimate the incidence and nature of medical adverse events contributing to the death of patients being treated with RRT.

Methods. This population registry-based retrospective case review study included all patients being treated with RRT for established renal failure in Scotland and who died between 1 January 2008 and 30 June 2011. Deaths were reviewed by consultant nephrologists using a structured questionnaire to identify factors contributing to death occurring in both the inpatient and outpatient setting. Reviewers were able to use any information source deemed relevant, including paper and electronic clinical records, mortality and morbidity meetings and procurator fiscal (Scottish coroner) investigations. Deaths occurring in 2008 and 2009 where avoidable factors were identified that may have or did lead to death of a patient were subject to further review and root cause analysis, in order to identify recurrent themes.
Results. Of 1551 deaths in the study period, 1357 were reviewed (87.5%). Cumulative RRT exposure in the cohort was 2.78 million person-days. RRT complications were the primary cause of death in 28 (2.1%). Health-care-associated infection had contributed to 9.6% of all deaths. In 3.5% of deaths, factors were identified which may have or did contribute to death. These were both organizational and human error related and were largely due to five main causes: management of hyperkalaemia, prescribing, out of hours care, infection and haemodialysis vascular access.

Conclusions. Adverse events contributing to death in RRT recipients mainly relate to the everyday management of common medical problems and not the technical aspects of RRT. Efforts to avoid harm in this population should address these ubiquitous causes of harm.

Keywords: dialysis, mortality, RRT, safety, transplantation

INTRODUCTION

Medical care for patients receiving renal replacement therapy (RRT) is complex and technology dependent; a high burden of comorbidity [1], polypharmacy [2] and the physiological consequences of established renal failure (ERF) mean that RRT patients are potentially vulnerable to medical error. Providing safe care for this population therefore provides some unique challenges beyond the generic patient safety issues common to all health-care settings. Previous reports of patient safety issues in RRT have focused on complications arising from the technical and medical device aspects of RRT [3, 4], drug-related adverse events [5] and dialysis-associated infection [6]. Whilst these reports have led to changes in clinical practice, such as the removal of aluminium from dialysis water supplies and the development of disconnect peritoneal dialysis devices, the overall incidence and nature of adverse events contributing to mortality remain unknown. Mortality rates in the RRT population are very high compared with the general population: a patient with diabetes aged 45–64 when starting RRT has a life expectancy of only 3.3 years [7]. It is not known what proportion of these deaths might be preventable through better care, nor to what extent medical error contributes to the high risk of death in this population.

We studied the deaths of all adults who died over a 42-month period whilst receiving RRT for ERF in Scotland and assessed the frequency with which adverse events caused or contributed to death. By identifying the types of adverse events, we aimed to identify opportunities for quality improvement in RRT patient care and the avoidance of preventable harm.

METHODS

All adult patients dying between 1 January 2008 and 30 June 2011 whilst receiving RRT for ERF in Scotland were included in the Scottish Mortality Audit of Renal Replacement Therapy (SMARRT), a Scottish Renal Registry (SRR) audit instigated to investigate apparent centre-based variation in RRT outcomes [7]. Deaths were identified through the SRR, which has full participation from all nine adult renal units in Scotland and 100% coverage of the Scottish population (5.2 million people). The methods used to collect data for the SRR are described on the SRR website [8]. Patients receiving RRT for acute kidney injury were excluded. Patients who stopped RRT but did not recover renal function (e.g. where RRT was withdrawn and end-of-life care commenced) were included, as were people dying within 90 days of commencing RRT for ERF. Where a patient started RRT and then died before the 91st day or if they recovered before the 91st day but then died within the next 90 days, their nephrologist was asked to decide whether they had been treated for acute or ERF. Only those with ERF are included in this cohort.

Primary cause of death was classified by ERA-EDTA codes and then organized into six main groups: cardiovascular, infection, RRT complications, malignancy, withdrawal of RRT and other [8]. The data routinely collected by the SRR were augmented by data collected by consultant nephrologists in each of the nine renal units following notification of death, using clinical case notes, renal unit electronic patient records and other sources such as morbidity and mortality meetings and critical incident reviews. Data were either entered directly onto the SRR database via a secure connection or were recorded on a purpose-designed paper form for later entry to the SRR. The augmented data included information about the location and primary cause of death, comorbidity and a structured assessment of factors contributing to death. This assessment required both the identification of concerns arising in the management of the patient and an assessment of the probability of whether these concerns had contributed to the subsequent death. Concerns were classified using a five-point scale used in previous mortality audits [9]. Any concerns in the period before death were eligible for consideration, including those occurring in the outpatient setting. A check of data completion was circulated regularly by the investigators to ensure data collection was as complete as possible. Consistency in the opinion-based items of the data set was evaluated by estimating between-observer variation in the observed prevalence rate of adverse events.

Deaths occurring in 2008–09 that had been identified as being in the two categories of highest concern (i.e. where there were areas of concern that either may have, or did, lead to the death of a patient) were subject to further independent case record review. Four nephrologists (K.D., W.M., G.S. and J.F.) and one nephrology trainee (B.B.) reviewed the paper case records and any relevant supplemental information resulting from the initial case review in order to identify factors contributing to the death. The factors emerging from these reviews were synthesized into common themes and classified into: (i) organizational/institutional factors—those relating to the organization or structure of care, (ii) environmental/technical—factors relating to the work environment or medical devices and (iii) human factors—patient or staff characteristics and behaviours. The case reviews did not replace other investigations into the patient’s death, such as critical incident reviews, mortality and morbidity meetings and procurator
fiscal (Scottish coroner) investigations. Where available, information from these other investigations were included in the case reviews.

STATISTICAL ANALYSIS

Numeric results are stated with the denominator and are expressed as a percentage and continuous variables as medians (IQR). Confidence intervals for proportions were estimated using the Wilson score with continuity correction. Confidence intervals for incidence rates were estimated using the exact method for the Poisson distribution and assumed that any cause of death data were missing completely-at-random. Pearson’s \( \chi^2 \) test was used in hypothesis tests for proportions, with a significance level of 0.05. All analyses were carried out in SPSS v17.

RESULTS

During the study period, 5923 adults with ERF were treated with RRT in Scotland and 1551 died. SMARTT data were collected for 87%, and core SRR data were available for 100%. The demographic profile of the patients who died is shown in Table 1. Total RRT exposure in the cohort was 2.78 million days, and the median years of RRT before death per patient was 3.3. Most (80.3%) were receiving haemodialysis prior to death, of whom 47% were using a central venous catheter for haemodialysis access. The most frequent primary cause of death group was cardiovascular, but 28 (2.1%) of deaths occurred as a direct result of an RRT complication and 202 (14.9%) as a consequence of withdrawal of RRT. The most frequent cause of death attributed to an RRT complication in haemodialysis patients was hyperkalaemia [Table 2]. One ‘accident-related to treatment’ was a dialysis-associated fall, and there were no instances of dialysis equipment failure as a primary cause of death. The population incidence of death due to these RRT complications was 1.35 deaths/1000 RRT patients/year (95% CI 0.94–1.95).

Factors contributing to death (but not necessarily the primary cause of death) identified by the nephrologist reviewing each death are shown in Table 3. Health-care-associated infection contributed to 9.6% of all deaths, and failure or infection of vascular access contributed to 10.8% of deaths of haemodialysis patients. Transplant complications had contributed to 37.6% of deaths among patients with a kidney transplant. The high rate of complications in this group largely related to the risks inherent of long-term immunosuppressant medication such as malignancy and susceptibility to infection.

In 47 (3.5%) of deaths in the whole cohort and in 38 (4.0%) of inpatient deaths, areas of concern were identified that either may have or did contribute to the death of the patient. There was a significant variation between assessors in the proportion of patients being classified in these two highest categories (\( \chi^2 P = 0.001 \)), ranging from 0 to 8%. The results of the peer review and root cause analysis of 22 of these deaths (those occurring in 2008 and 2009) are summarized in Table 4. Five main factors contributing to death emerged during the case reviews: hyperkalaemia recognition and management, prescribing errors and complications, out of hours care, prevention and management of infection and vascular access-related issues. Some deaths involved more than one of these factors, and five did not clearly involve any of these factors. Hyperkalaemia-related deaths were partly found to be due to organizational factors, such as the planned admission of a post-operative RRT patient to an inappropriate ward and lack of timely access to emergency haemodialysis. However, human factors were also found to be important, in particular regarding the recognition and appropriate management of hyperkalaemia and poor communication of urgent treatment decisions. Medication issues concerned over-sedation secondary to inappropriate dosing of opioids and the failure to recognize anti-platelet therapy-related bleeding risks. Out of hours care was a factor in several cases where inadequate management of RRT-related complications had occurred without referral to or involvement of more senior clinicians. Infection factors related to delayed recognition and treatment of sepsis and inadequate management of dialysis-related infections (vascular access-related sepsicaemia and peritoneal dialysis-related peritonitis). Haemodialysis vascular access was identified as a factor in two cases and both instances...
related to the creation or maintenance of arteriovenous fistulae. One death occurred as a result of a fall, which, although was thought to be partly dialysis related, had also been attributed to the design of patient-handling equipment.

**CONCLUSIONS**

This is the first study to describe systematically the epidemiology of adverse events causing or contributing to the death of RRT patients. In this national, population-based cohort, direct complications of RRT were responsible for 2.1% of deaths, and in 3.5% of deaths, areas of concern were identified that may have or did lead to the death of a patient. The areas of concern largely fell into five main categories: recognition and management of hyperkalaemia, safe prescribing, out of hours care, the prevention and management of infection and haemodialysis vascular access. These factors were both organizational and human in nature, and no deaths were considered to be directly attributable to the failure or misuse of RRT-related medical devices. These findings suggest that errors are not a common cause of avoidable mortality in the RRT population and that efforts to improve the safety of RRT should focus not just on the technical aspects of RRT, but also consider the many other potential sources of harm in this complex group of patients.

Recent years have seen an increasing focus on patient safety across all areas of health care, partly in response to the publication of landmark reports on this issue in both the USA [10] and the UK [11]. Among general hospital inpatients, the prevalence of preventable death has been estimated to be in the range of 4.1–6.0% [12–14]. Although the definition differs somewhat, the most analogous figure estimated in our study (inpatient deaths where concerns were identified that may have or did contribute to death) was 4.0%, which is in line with these previous estimates. It is difficult to know if the slightly lower estimate in our study is a real difference, or just reflects differences in methodology and definitions. As far as we are aware, there are no previous published estimates of
preventable death in the RRT population, and studies concerning patient safety in this population have largely focused on medical device-related harm [15], novel adverse drug reactions [5, 16], dialysis water purification [4] and blood-borne infections [6]. Strategies to improve patient safety in dialysis units have emphasized the importance of effective communication, falls prevention, reducing medication error, correct dialysis equipment preparation and infection control [17]. In our cohort, no cases of harm due to failure or misuse of RRT-related equipment were documented. This study demonstrates that the five main factors identified in the review of the most serious adverse events largely concern aspects of the everyday care of RRT patients and not the more technical aspects of dialysis or kidney transplantation. This is consistent with studies of adverse safety events in the pre-dialysis chronic kidney disease population, where the commonest causes of harm are from infection, falls, electrolyte/metabolic disturbance and medication error [18]. Patients with CKD are at increased risk of a whole range of adverse events compared with the general hospital population, not just those directly related to CKD itself [19]. Strategies to prevent harm to RRT patients therefore involve all health professionals who care for RRT patients, not just nephrology specialists and those working in dialysis units.

The proportion of deaths attributable directly to RRT complications estimated in this study is small, although the size of the estimate is obviously dependent on what is classified as a RRT complication. For example, dialysis access-related sepsicaemia was not included in this category, and was instead included in the infection group. We were unable to specifically classify instances of sepsicaemia as either access related or non-access related, but analyses from the same cohort demonstrate significantly (adjusted OR 6.9) higher risk of death from sepsicaemia in patients using tunnelled central venous catheters [20]. Hyperkalaemia and other electrolyte disturbances have been implicated as a contributing cause of the high rate of sudden cardiac death in the RRT population [21] (9.2% in our cohort), but were only classified as such here where there was evidence to support death from this cause. Within the CKD population, episodes of hyperkalaemia are associated with markedly increased risk of death (OR 8.0 for CKD Stage 5 patients with severe hyperkalaemia), and patients with Stage 5 CKD are at highest risk of hyperkalaemia [22]. The true contribution of hyperkalaemia, and other electrolyte disturbances, to RRT-related mortality, therefore, may be higher than the estimate in this study. Our study also demonstrates that hyperkalaemia-related mortality may be caused not just by its occurrence, but also by errors in how it is managed and treated. These errors were both organizational and human factors related, and imply that efforts to prevent avoidable hyperkalaemia-related mortality are warranted. In particular, clear protocols concerning how, where and by whom patients at high risk of hyperkalaemia should be managed might avoid otherwise preventable deaths. In addition this study suggests that failure to recognize the signs and symptoms of hyperkalaemia is contributing to avoidable mortality. Professional guidelines on the management of hyperkalaemia have recently been published in the UK for the first time [23], and this may provide a useful opportunity to improve the awareness, understanding and management of this condition.

The only previous published report of safety lapses in a dialysis cohort was a retrospective cohort study of 41 dialysis patients admitted to a surgical service [24]. Multiple lapses of care were identified in 78% of the cohort, relating to provision of appropriate meals, dose adjustments during prescribing and the administration of IV fluids. As with this study, inappropriate dosing of strong opioids was identified as a common error. Medication errors have previously been identified as one of the most common safety events in dialysis units, particularly during transition between care settings or clinical teams [17]. Medication errors have also been found to be common in patients with other stages of CKD, largely as a consequence of failing to adjust correctly for reduced drug clearance and the prescription of nephrotoxic medications [25]. More broadly, studies of patient safety lapses in other patient populations have identified medication errors as a frequent source of harm, with an incidence of adverse events due to medication errors of 2.3% in hospitalized patients [26]. A number of approaches to reducing medication-related harms have been developed [27, 28] and our study suggests that a particular focus on the safe and effective use of opioids in patients with ERF is warranted.

Health-care-associated infection is one of the most significant sources of iatrogenic harm [29], and, in our study, was identified as contributing to the deaths of 9.6% of patients. However, only a minority of these deaths had been identified as being of high concern, which suggests that episodes of health-care-associated infection were in many instances not felt to have been avoidable or the result of medical error. Infection in the RRT population is a complex problem: it is both common (the prevalence of sepsicaemia in dialysis patients is over 100 times that of the general population [30]) and multifactorial, associated with high rates of hospitalization, dialysis-specific infection risks [31] and immunocompromise as a consequence of renal impairment, comorbidity and immunosuppressive therapy [32]. In addition, experience suggests that infection in RRT patients, although the direct cause of death in only a minority, frequently contributes to a multifactorial decline in health status in the period before death. Identifying what proportion of infections in this population is avoidable is, therefore, difficult. However, interventions in other complex, high-risk populations have led to large reductions in health-care-associated infection [33] and suggest that there may be a significant opportunity to reduce infection-related deaths in the RRT population through strategies such as care bundles and minimizing the use of central venous catheters.

This was a mortality-based study; we, therefore, have no data concerning patient safety incidents in patients who did not die, nor those which occurred in earlier time points in the treatment history of patients who then went on to die during the study period. Whilst there are likely to be common themes, the nature and prevalence of non-fatal medical errors may be different to those that result in death. Data were drawn from a single country and it is possible that they do not translate to other health settings or populations. Some of the data included in this study are based on the opinions of individuals. There was evidence of inter-observer variation, as evidenced...
by differences between assessors in the proportion of patients where major concerns were identified, and thus the accuracy of the estimate of the proportion of deaths on RRT that are of major concern is difficult to quantify. Kappa statistics were not estimated because of the difficulties of achieving equal information between observers: in many instances, the assessments concerning factors contributing to death were made using information from sources other than the paper case record, such as electronic care records, team meetings and personal communication with members of the care team. Previous studies using retrospective case record review have also found inconsistency between assessors even when using validated tools [13, 34], and the development of review methodologies that allow objective assessments to be made of the types of complex information available outside the written case record would improve the accuracy of future studies. Future studies might also usefully focus on quantifying and classifying the non-fatal adverse events in the RRT population, since research on this population is lacking.

**SUMMARY**

In the great majority of deaths among RRT patients, no concerns were identified regarding their medical care prior to death, suggesting that the proportion of deaths on RRT that are preventable due to elimination of human error, organizational and environmental factors is small. As has been pointed out in other patient populations, one of the implications of this finding is that mortality is not likely to be a sensitive indicator of the quality of care [35]. Our study also shows that the majority of adverse events contributing to mortality in the RRT population occur away from the haemodialysis machine and should be the concern of not only nephrology specialists, but also any health professionals involved in the management of RRT patients. They largely result from common encountered problems, such as hyperkalaemia, healthcare-associated infection, poor communication, medication error and out of hours working. Quality improvement initiatives to improve the safety of RRT should focus on these ubiquitous causes of patient harm.

**AUTHORS’ CONTRIBUTIONS**

B.B. analysed the data and wrote the first draft of the manuscript. J.B. carried out statistical analysis of the registry data set. C.D., A.D., K.D., J.G.F., A.I., I.K., B.M., K.S. G.A.S., J.P.T. and W.M. were involved in data collection, case review and editing further drafts of the manuscript. WM is the guarantor.

**ETHICS**

Data were collected through the SRR, which is authorized by the Scottish Government. Further ethical approval was not sought.

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**CONFLICT OF INTEREST STATEMENT**

We declare no conflicts of interest. The results have not been published, in full or in part, in any other publication.

(See related article by Pippias and Tomson. Patient safety in chronic kidney disease: time for nephrologists to take action. Nephrol Dial Transplant 2014; 29: 473–475.)

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Greater omentum folding in the open surgical placement of peritoneal dialysis catheters: a randomized controlled study and systemic review

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ABSTRACT

Background. Mechanical catheter dysfunction caused by omentum entrapment remains a major complication of peritoneal dialysis (PD) therapy. The purpose of this study was to determine the outcomes of omentum folding at the time of primary open catheter insertion.

Methods. From March 2008 to December 2012, a total of 67 PD subjects were enrolled in the study and randomly assigned to...