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REVIEW

Sudden cardiac death in end stage renal disease: unlocking the mystery

D. Zachariah · P. R. Kalra · Paul R. Roberts

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Abstract Sudden cardiac death (SCD) is a major cause of concern in end stage renal disease (ESRD), contributing to 70 % of cardiovascular mortality and 27 % of all-cause mortality in dialysis patients. Yet its mechanisms and pathogenesis remain largely obscure. This review discusses the potential reasons for an exaggerated risk of SCD in ESRD populations taking into account recent studies and registry data and additionally explores the reasons for the reported recent decline in SCD. The types of arrhythmias typical of the hemodialysis population are yet to be fully characterised and in this paper, we introduce an ongoing implantable loop recorder (ILR) based study in hemodialysis patients—CRASH ILR (Cardio Renal Arrhythmia Study in Haemodialysis patients using Implantable Loop Recorders). The findings of this study will hopefully guide the design and implementation of larger ILR based studies before undertaking larger scale interventional therapeutic trials in this high risk population.

Keywords End stage renal disease (ESRD) · Sudden cardiac death (SCD) · Arrhythmia · Hemodialysis · Implantable loop recorders

D. Zachariah · P. R. Kalra
Portsmouth Hospitals NHS Trust, Portsmouth, UK

D. Zachariah (✉)
Queen Alexandra Hospital, Southwick Hill Road, Cosham, Portsmouth PO6 3LY, UK
e-mail: donahez@hotmail.com

P. R. Kalra
National Heart Lung Institute, Imperial College, London, UK

P. R. Roberts
Southampton University Hospital, Southampton, UK

Introduction

Chronic kidney disease (CKD), even in its intermediate stages, has been shown to adversely impact on cardiovascular (CV) outcomes. Mild renal insufficiency in the Heart outcomes and Prevention evaluation (HoPe) study (serum creatinine level 125–200 μmol/l, n = 980 patients with CV disease) was associated with a 40 % increase in the risk of cardiac death when compared with those who had CV disease and normal kidney function [1]. In the presence of end stage renal disease (ESRD), the risk of CV mortality increases exponentially with sudden cardiac death (SCD) contributing to 70 % of CV mortality and 27 % of all-cause mortality in hemodialysis patients [2]. SCD is defined as an unexpected natural death from a cardiac cause within 1 h of onset of symptoms in a person not known to have a potentially fatal condition [3]. The risk of SCD increases as estimated glomerular filtration (eGFR) falls [4, 5]. In their landmark study of 19,440 CKD patients who underwent cardiac catheterisation, Pun et al. [32] demonstrated the impact of declining eGFR on SCD- this relationship was most striking when eGFR fell <60 ml/min/1.7^2 with a hazard ratio (HR) for each 10 ml/min/1.73 m^2 decline in eGFR of 1.11 (95 % confidence interval (CI) 1.06–1.17, $p < 0.001$) [6].

Following renal transplantation, the general risk of SCD appears to be favourably modified, yet the risk from CV disease remains 3–5 times higher compared to the general population. Although there are no robust SCD mortality data in kidney transplant recipients, a significant number of their deaths are attributed to arrhythmia [7]. It is believed that persistent sympathetic over activity and the use of immunosuppressant drugs may play a role in the CV disease continuum [8].

This review will focus primarily on the cardiac abnormalities linked with SCD in patients with ESRD.

Sudden cardiac death—risk factors and pathogenesis

The potential risk factors for SCD in ESRD have been the subject of cardio renal research in recent years. Shared risk factors for CV disease and ESRD undoubtedly play a role in SCD in the hemodialysis population. Diabetes for example is the etiology of ESRD in 20 % of new dialysis cases [9] and is itself associated with a risk of SCD (nocturnal hypoglycaemia can cause ventricular arrhythmias via QT segment prolongation [10]). Similarly, coronary artery disease (CAD), documented in up to 50 % of post mortem studies of SCD in the general population [11] is found in 40 % of dialysis patients [12]. Coronary artery bypass grafting (CABG) or revascularisation in the hemodialysis population does not appear to remove all risk of CV mortality. In one study, all-cause and arrhythmia-related mortality in dialysis patients treated with coronary revascularisation remained high at 290 and 76 deaths per 1,000 patient years respectively [13], suggesting that the link between the two transcends above isolated myocardial ischemia and its effects.

Factors such as inter-dialytic interval (SCD being most common following a long inter-dialytic period, mode of dialysis (hemodialysis carries greater risk compared to peritoneal dialysis), composition of dialysate fluid and dialysis induced rapid fluid and electrolyte shifts (potassium, magnesium, phosphate and calcium [14]) have all been scrutinised, yet the relative importance of the various pathophysiological mechanisms that drive this phenomenon remain largely mysterious. Endothelial dysfunction, interstitial fibrosis and sympathetic over activity are some of the other factors thought to contribute to the increased risk of SCD in ESRD patients [15–18]. ECG findings such as micro T wave alternans, abnormal ventricular repolarization manifesting as QT prolongation and QT dispersion, secondary to the above, have been linked to SCD.

Hemodialysis induces changes in cardiac structure such as left ventricular (LV) hypertrophy and LV dilatation (documented in 75 and 34 % of patients respectively [19]). Independent associations have been demonstrated even between moderate renal impairment and abnormal left ventricular geometry in the absence of clinical heart failure [20]. This may be partly driven by uremic toxins such as indoxylsuplhate and p-cresylsulphate via activation of renal inflammatory and fibrotic processes seen in CV disease related to renal dysfunction [21]. These novel pathways may offer potential early intervention strategies for pre-dialysis patients by targeting the site of toxin production (colon in this case).

A recent study utilising rat models to understand the pathogenesis of ventricular arrhythmias in CKD has suggested that abnormalities in cardiac ion channel and calcium handling can increase vulnerability to early after depolarization, triggered activity and ventricular arrhythmias. In comparison with normal rats, mRNA levels of TGF-β, microRNA-21, and sodium calcium-exchanger type 1 were up regulated in CKD rats whereas the levels of microRNA-29, L-type calcium channel, sarco/endoplasmic reticulum calcium-ATPase type 2a, Kv1.4, and Kv4.3 were down regulated. Cardiac fibrosis in this setting was mild and not different between groups [22], as such this could represent the mechanism of arrhythmias in CKD prior to the onset of left ventricular wall fibrosis.

Incidence of SCD

Registry data are prone to certain inherent limitations, under reporting being one of them. This has been a concern with SCD as well and in their study, Bleyer et al. reviewed death notification forms from 1995 to 2003 in five US dialysis centres using an accepted definition of SCD. Of the 88 of 228 deaths (39 %) that could have been classified as sudden, only 59 (26 % of total deaths) were classified as sudden [14] with the remaining deaths being classified as per their etiologies—e.g. acute myocardial infarction.

Nonetheless it is encouraging to note that the 2013 annual data report from the US Renal data system [2] (the comprehensive national data system that collects, analyzes, and distributes information about ESRD in the United States) demonstrated a decline in the rate of SCD in haemodialysis patients between 2000 and 2011. The rate of SCD in hemodialysis patients fell from 72 to 49 per 1,000 patient years with the largest absolute decline occurring in those at highest risk (elderly, white race, diabetes). The reduction in SCD was most striking in patients on peritoneal dialysis where the rates fell from 62 to 36 per 1,000 patient years. These figures were much more modest in the incident dialysis population (the first 90 days of therapy, known to be a period of heightened SCD risk) with a significant difference in the incidence of SCD in hemodialysis of 7 versus 2 % in peritoneal dialysis patients, at the end of the first year.

In the light of the above, it is useful to analyse the possible explanations for this reduction in SCD. While the increased use of implantable cardioverter defibrillators (ICD) may play a role, overall they remain under utilised. Two-year mortality in dialysis patients following ICD implant still remains high (53 % following implantation for primary prevention and 58 % after implantation for secondary prevention) [2]. Of note beta blocker usage amongst dialysis patients has certainly increased and appears to contribute to the decline in mortality [2].

A further question that arises is whether SCD is as common as suggested by the US data systems. The recent UK Renal Registry annual report [23] revamped the coding

system for classification of cause of death, differentiating 'Uncertain' and 'Other' causes of death and as a result, there was a substantial reduction in the proportion of patients attributed to uncertain causes of death. Subsequently in the 2011 cohort, cardiac disease was responsible for 23 % of deaths in prevalent dialysis patients, with 'uncertain' and 'other' causes of death contributing to 28 %. It is therefore possible that other catastrophic aetiologies such as intra-cerebral pathology, pulmonary emboli or aneurysms might be contributing to so-called 'SCD'. If this is the case, the beneficial role of a routine ICD would be questionable.

Arrhythmias and dialysis

Whilst some data are available in relation to numbers of presumed SCD in the dialysis population, there is very limited literature evaluating the actual arrhythmic burden in patients with ESRD. Studies have shown the presence of repolarization abnormalities (QT prolongation, QT dispersion and abnormal T wave axis deviation) in the presence of renal impairment [24, 25] (Table 1). Holter monitoring around dialysis sessions have documented a significant burden of high grade ventricular ectopy and even non sustained ventricular arrhythmias [26, 27]. Ventricular ectopy has been extensively analysed and there appears to be no added risk secondary to the burden of ectopic activity. These studies have generally used the Lown classification for ventricular premature beats which does not take into consideration the duration of arrhythmias or additional risk factors. Thus it is plausible that the predictive value of such non-sustained arrhythmias or other ECG abnormalities recorded in the risk assessment of SCD may not have been explored adequately.

While it has been hypothesized that the process of hemodialysis per se is arrhythmogenic, intradialytic cardiac arrest is a relatively rare phenomenon. Studies have demonstrated intra-dialytic abnormal ventricular repolarization (increased QT dispersion [28] and QT prolongation) yet there has been no evidence of a direct relationship between intradialytic arrhythmias and SCD. Pun et al. in their study of 510 witnessed cardiac arrests in 43,200 hemodialysis patients, failed to show any significant risk association with the use of QT-prolonging medications and in fact demonstrated that increased ultrafiltration volumes and electrolyte abnormalities—low Ca dialysate <2.5 mEq/l [odds ratio (OR) 2.00, 95 % CI 1.40–2.90], higher corrected serum Ca (OR 1.10, 95 % CI 1.00–1.30) and increasing serum dialysate Ca gradient (OR 1.40, 95 % CI 1.10–1.80) were associated with increased risk of sudden cardiac arrest [29]. A separate study showed low potassium dialysate of less than 2 meq/l to be implicated in SCD [30]. More recently Genovesi et al. in their study of 122 hemodialysis patients were also unable to show a significant QTc variation between basal/pre-dialysis, intra dialysis and post dialysis. In their multivariate model, while all three measured QTc intervals appeared to have prognostic values for total mortality, only prolonged basal QTc and intra dialytic QTc intervals were significant predictors of SCD [31].

The risk of SCD appears to be most significant immediately before and immediately after the first weekly haemodialysis session [32, 33]. A bimodal distribution of death occurrences, with a 1.7-fold increased death risk occurring in the 12 h period starting with the dialysis procedure and a threefold increased risk of death in the 12 h before HD at the end of the weekend interval was demonstrated by Bleyer et al. [14]. These daily variations seem to be less in patients on peritoneal dialysis or home hemodialysis or even hemodialysis patients receiving more than three sessions per week [34]. It is thus plausible that the bimodal peak in risk of arrhythmias may be driven by two different types of underlying arrhythmic phenomena, such as tachyarrhythmias and bradyarrhythmias. Bradyarrhythmias secondary to conducting system disease or electrolyte abnormalities may prove detrimental either via profound bradycardia or asystole, or via bradycardia induced tachyarrhythmia.

The burden of supraventricular tachyarrhythmias in dialysis patients also remains largely undefined. Atrial ectopics and atrial fibrillation (AF) have been documented in routine ECGs and 24 h ECG recordings, with a recent meta-analysis suggesting AF prevalence of about 12 % [35] in the hemodialysis population. AF appears to be more common in the intra dialytic period [36]. This is important as AF not only increases the risk of stroke 9.8 fold [37] in the hemodialysis population but has also been identified as an independent risk factor for sudden death [38]. Stroke prevention utilising oral anticoagulants in the dialysis population remains controversial, warranting careful consideration of risks and benefits. All of the above therefore call for a better understanding of the burden of AF and paroxysmal AF in hemodialysis patients.

Therapeutic measures to prevent sudden cardiac death

Survival benefits secondary to risk factor modification remain largely unproven. Statins for example have repeatedly been shown to have no benefits on cardiovascular death, non-fatal myocardial infarction, stroke or all-cause mortality in dialysis patients despite appropriately lowering serum cholesterol [39]. This may be explained by CV disease in this population being mediated by low high density lipoproteins, chylomicrons or small dense low

Table 1 ECG parameters in advanced CKD/hemodialysis patients linked to arrhythmias and sudden cardiac death

ECG parameter	References	N	Method of ECG evaluation	Findings
Heart rate				
Heart rate (HR)	Cice et al. [58]	407 ESRD patients	48 h Holter monitoring	HR >85 beats per minute was an independent predictor of global and CV risk (ROC curve and Cox regression analysis $p < 0.001$) in this population free of CVD, LVSD and anti-arrhythmic therapy
Heart rate variability (HRV)	Suzuki et al. [59]	281 HD patients	24 h ECG	Decreased scaling exponent $\alpha(1)$, a non-linear measure of HRV reflecting fractal organisation remained significant after adjusting for clinical risk factors (HR per 0.25 decrement of 1.46, 95 % CI 1.16–1.85) and in a prediction model composed of clinical risk factors, increased the C statistic from 0.84 to 0.87 ($p = 0.03$), with 50.8 % (95 % CI 20.2–83.7) continuous net reclassification improvement for 5-year mortality
HRV	Oikawa et al. [60]	383 HD patients	24 h ECG	Decreased HRV parameters in the time- and frequency-domain were identified as predictors of all-cause and CV death in a Cox univariate and multivariate analysis respectively[HR 0.988 (95 % CI 0.982–0.994) and 0.984 (95 % CI 0.974–0.993)]
HRV	Fukuta et al. [61]	120 chronic HD patients	24 h ECG	HRV measures were significantly reduced in HD patients. During a follow-up period of 26 ± 10 months, 17.5 % patients died (47 % from cardiac causes). Decreases in HRV measures such as triangular index (TI), very-low-frequency (0.0033–0.04 Hz) power, ultra-low-frequency (<0.0033 Hz) power (ULF) and the ratio of low-frequency (0.04–0.15 Hz) power to high-frequency (0.15–0.4 Hz) power had significant predictive value for cardiac death but not for non-cardiac death
QT interval				
QT duration	Thomson et al. [62]	39 dialysis patients	Holter monitoring during dialysis	Frequent nocturnal HD was associated with a decrease in QTc interval for all patients (from 436.5 to 421.3 ms, $p = 0.0187$) and for patients with prolonged QTc at baseline (468.2–438.2 ms, $p = 0.0134$). Dialysis duration predicted a decrease in QTc better than dialysis frequency and prevalence of borderline or prolonged QTc increased in patients who dialysed for less than 4 h per session (12/39–22/39, $p = 0.039$)
QT duration	Genovesi et al. [31]	122 HD patients	Holter recording	44 patients (36.0 %) had a prolonged QTc (450 ms in men and 460 ms in women). Median follow-up was 3.9 years. In multivariate analysis age at recruitment [HR = 1.07, 95 % confidence interval (CI) 1.03–1.11, $p < 0.001$], prolonged QTc (HR = 2.16, 95 % CI 1.20–3.91, $p = 0.011$) and presence of dilated cardiomyopathy (HR = 3.75, 95 % CI 1.01–7.00, $p < 0.001$) were independently associated with total mortality, while only prolonged QTc (HR = 8.33, 95 % CI 1.71–40.48, $p = 0.009$) and increasing LVMI (HR = 1.01, 95 % CI 1.00–1.02, $p = 0.022$) were associated with SCD
QT dispersion (QTd)	Oktavia et al. [63]	61 dialysis patients	12 lead ECG	No correlation between increased QTd and clinical factors assessed (hypertension, pulse pressure, intradialytic hypotension, LVH, old myocardial infarct, diabetes mellitus, and nutritional status). The means of QT interval and QTd increased after HD session (from 382 ± 29 to 444 ± 26 ms, $p < 0.05$; and from 74 ± 21 to 114 ± 53 ms, respectively, $p < 0.05$)
Left ventricular hypertrophy (LVH)				
LVH as per 14 different ECG criteria	Covic et al. [64]	418 dialysis patients	Interval ECGs during dialysis	An independent association between LVH and CV mortality using Novacode method for LVH assessment was demonstrated (HR = 3.04; 95 % CI 1.11–8.28, $p < 0.05$). Patients with persistent ECG changes of LVH had increased risk of CV mortality compared to those with new LVH, LVH regression and no LVH ($p < 0.044$)

Table 1 continued

ECG parameter	References	N	Method of ECG evaluation	Findings
QRS/T				
QRS-to-T angle (TCRT) and T wave morphology dispersion (TMD)	Poulikakoset al. [65]	81 dialysis patients	Holter monitor during dialysis	Patients with major arrhythmic events exhibited extreme TCRT and TMD values and minimal intradialytic changes
QRS/T	De Bie et al. [66]	277 hemodialysis patients	12 lead ECG	An abnormal spatial QRS-T angle ($\geq$130° in men, $\geq$116° in women) was associated with a higher risk of death from all causes (HR 2.33; 95 % CI 1.46–3.70) and SCD (HR 2.99; 95 % CI 1.04–8.60). It was also of incremental prognostic value when added to a risk model consisting of known risk factors
QRS amplitude	Lee et al. [67]	30 dialysis patients	Single 12 lead ECG	QRS amplitude increased by 0.18 $\pm$ 0.30 mV ($p < 0.01$), correlating with increase in average basal septal and lateral systolic velocity on echocardiography and reduction of diastolic filling pressure, median weight loss following dialysis was 1.6 $\pm$ 1.3 kg (95 % CI 1.1–2.1, $p < 0.001$)
	Thomson et al. [68]	39 dialysis patients	12 lead ECG	HD modalities of longer duration were associated with improvements in ECG parameters associated with SCD (greater reduction of T peak to T end duration and less QRS amplitude variation). These improvements preceded changes in Cornell or Sokolow–Lyon electrocardiographic measures of LV mass
T wave morphology				
T-wave residuum (TWR)	Lin et al. [69]	325 HD patients	12 lead ECG	Direct comparison between CV death and non-CV death patients showed that relative TWR predicted CV mortality (0.20 $\pm$ 0.21 vs 0.24 $\pm$ 0.17 %, $p = 0.005$). In a Cox model, relative TWR was an independent predictor of CV (RR = 1.86; $p = 0.013$) and arrhythmia-related mortality (RR = 2.10; $p = 0.012$)

CI confidence interval, *CV* cardiovascular, *CVD* cardiovascular disease, *ESRD* end stage renal disease, *HD* hemodialysis, *HR* hazard ratio, *LV* left ventricular, *LVH* left ventricular hypertrophy, *LVMI* left ventricular mass index, *LVSD* left ventricular systolic dysfunction, *QTc* corrected QT interval, *ROC* receiver operating characteristic, *RR* relative risk, *SCD* sudden cardiac death

density lipoproteins and thus bypassing disease modifying processes mediated by statins.

Similarly erythropoietin stimulating agents, which cost $1.87 billion annually [2] in US dialysis patients have failed to decrease CV mortality and have in fact been associated with an increased risk of stroke in a large randomized controlled trial in diabetic CKD patients [40]. Active vitamin D supplementation, the second largest medical expenditure in dialysis patients, has also not been shown to reduce left ventricular hypertrophy or improve left ventricular diastolic dysfunction in these patients [41]. The EValuation Of Cinacalcet Hydrochloride Therapy to Lower Cardio Vascular Events (EVOLVE) trial evaluating the use of calcimimetics to treat secondary hyperparathyroidism in dialysis patients has not demonstrated a reduction in cardiovascular deaths either [42].

A large observational study by Foley et al. [43] indicates that beta blocker therapy has a robust association with survival in dialysis patients. Beta blockers exert asympatho-inhibitory effect, can decrease the frequency of ventricular arrhythmias, improve heart rate variability and increase baroreflex sensitivity. Sympathetic over activity is particularly linked with the diseased kidney and although beta blocker specific trials in dialysis patients are limited, data suggests they play a positive and beneficial role in the management of CV disease and reduction of mortality in this population. In a recent placebo-controlled trial of 112 HD patients with dilated cardiomyopathy, Cice et al. [44] showed that carvedilol use was linked with a significant reduction (52 vs. 73 %) in mortality. Beta blocker use at the time of a cardiac arrest in HD patients has also been associated with higher survival [45]. It is therefore encouraging to note that 58 % of current HD patients with no cardiac comorbidities are on beta blockers, as compared to 17 % in 1996–1997 [2, 46].

Implantable cardioverter defibrillators

An ICD offers a well-established interventional treatment in the reduction of SCD in patients with poor LV function or failed SCD. While guidelines do not exclude their use in ESRD patients, they remain significantly under-used. The reasons are multifold. Firstly, the evidence behind ICDs is based on trials that largely excluded those with severe CKD. It is unclear whether ventricular arrhythmias are indeed the primary cause for SCD and if so, whether as a result of concurrent electrolyte imbalances, there is a risk of intractable arrhythmias that will not respond to anti-tachycardia pacing or defibrillation. Guidelines recommend that ICDs are implanted only in those with a life expectancy of >1 year. Prognosis in ESRD is poor and the risks of infection, issues with vascular access or bleeding complications make device implantation even less inviting.

Studies have questioned the efficacy of ICDs in preventing SCD in the presence of CKD [47, 48] with conflicting results on overall mortality reduction in dialysis patients [49]. In one study, one-, two-, and three-year unadjusted survival for dialysis patients receiving an ICD after cardiac arrest were 71, 53, and 36 %, respectively, versus 49, 33, and 23 % for matched dialysis patients who did not receive an ICD [50]. Overall mortality in this study of ESRD patients was significantly higher than that reported for non-ESRD patients in the Anti-Arrhythmics versus Implantable Defibrillators (AVID) trial [51] yet the relative benefit from ICD therapy was similar (42 % reduction in overall death risk for ESRD patients versus 38 % reduction in the AVID trial). The risk of death after primary prevention ICD placement also appears to be proportional to CKD severity [52]. This is despite an increased frequency of appropriate ICD shocks documented in this population. Pun et al.'s meta- analysis of data from the Multicenter Automatic Defibrillator Implantation Trial I (MADIT-I), MADIT-II, and the Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT) ($n = 2{,}867$ patients of whom 36.3 % had eGFR <60 ml/min/1.73 m^2) demonstrated that the survival benefit of ICDs in comparison to usual care depends on eGFR and the ICD was associated with survival benefit for patients with eGFR ≥60 ml/min/1.73 m^2 (adjusted HR 0.49, 95 % posterior credible interval 0.24–0.95), but not for patients with eGFR <60 ml/min/1.73 m^2 (adjusted HR 0.80, 95 % posterior credible interval 0.40–1.53) [53]. A recent meta-analysis of seven studies reporting on patients with ESRD having ICDs concluded that those receiving dialysis had a 2.7 times greater mortality compared with those not on dialysis [54].

ESRD patients have longer stays, higher in-hospital mortality and higher rates of device related complications [55], warranting careful consideration of risks vs benefits of device therapy on an individual basis. In their decision model analysis evaluating risks and benefits of ICD implantation in CKD, Amin et al. [47] demonstrated that with stages 1 and 2 CKD, ICD implantation reduces mortality. In more advanced CKD, the benefit was less significant and age-dependent—ICD implantation was favoured at ages <80 years for stage 3, ages <75 years for stage 4 and ages <65 years for stage CKD.

CRASH-ILR (Cardio Renal Arrhythmia Study in Haemodialysis patients using Implantable Loop Recorders)

Whilst one might argue for a randomised control trial of ICD therapy in dialysis patients, the mixed reports cited

above as well as a number of 'negative' results from large scale interventional trials in ESRD might make investigators cautious about embarking on further studies in this population. There is one such study (ICD2 trial) underway, designed to evaluate the efficacy and safety of prophylactic ICD therapy in reducing SCD in 200 dialysis patients aged 55–80 years [56]. Engaging dialysis patients in interventional research is particularly challenging and it becomes essential to identify sub-populations of patients with ESRD who are most likely to benefit from an intervention. Prior to designing a trial aimed at reducing SCD, such as with ICD implantation, it is fundamental to gain an understanding of the true burden of arrhythmias (bradycardia and tachyarrhythmia) in the presence of ESRD. A 12 lead ECG only represents a snapshot of cardiac electrical activity and may be recorded when the patient is asymptomatic or between periods of abnormal arrhythmias. Conventional ambulatory ECG recording is more favourable as it provides data for 1–10 days at a time but again this could be an asymptomatic period. Event monitors require patients to have symptoms, have sufficient warning to activate the monitor and to be able to activate the monitor when symptomatic. All of these limitations would appear to be addressed by the use of implantable loop recorders (ILR) and we propose this as the next logical step in the investigation of SCD in the presence of ESRD. We feel that an enhanced understanding is fundamental to embarking on interventional studies.

We therefore designed a unique study called CRASH-ILR (Cardio Renal Arrhythmia Study in Haemodialysis patients using Implantable Loop Recorders) conducted jointly by cardiologists and renal physicians in a regional dialysis unit. In this pilot study of 30 patients we implant a new generation implantable loop recorder (ILR) (Reveal XT, Medtronic, Inc) in patients who have been on hemodialysis for more than 90 days. Demographics, history of co-morbidities, details of dialysis sessions, electrolyte levels and echocardiographic data including precise left ventricular mass measurements are recorded for each patient. Patients download data from the Reveal XT every time they dialyse (thrice weekly) via a secure mobile phone link. In >5,000 days of continuous ECG recording in pts on HD >22 % had significant events (2 patients demonstrated >3 s pauses requiring pacemaker implantation, one died from SCD and ILR interrogation identified ventricular fibrillation, one required ILR explantation due to infection and died from unrelated SCD several weeks later, one had sudden onset of atrial tachycardia requiring anti arrhythmic drugs). Patient activated recordings were all associated with sinus rhythm [57]. We aim to document >30,000 days of monitoring and thus provide insight into developing and powering a definitive study that utilises ILR technology to identify ESRD patients at high risk for SCD). Data from such a study will underpin a targeted interventional study that has a realistic chance of benefit.

Conclusion

Cardiovascular death is common in ESRD, and it has been suggested that SCD accounts for around 27 % of all-cause mortality in this population. Yet data are unclear and this may represent an overestimation. There is uncertainty regarding the arrhythmic mechanism (i.e. brady or tachy arrhythmias) as ESRD with associated neurohormonal activation and cardiac structural abnormalities serves as the perfect substrate for both of these mechanisms. Studies utilizing implantable loop recorder technology will add to our understanding of the pathophysiology and mechanisms involved in SCD and will guide the design and implementation of a larger study aimed at characterising patients at risk of developing arrhythmias.

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Conflict of interest D. Zachariah has received travel assistance from Medtronic UK. Paul R Kalra has received research grants and travel assistance from Medtronic UK. Paul R Roberts has been paid consultancy fees by Medtronic, Boston scientific and Sorin.

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