SUDDEN CARDIAC DEATH

How to reduce sudden cardiac death in patients with renal failure

Mihály K de Bie,1 Maurits S Buiten,1 Ton J Rabelink,2 J Wouter Jukema1

Prevention of sudden cardiac death (SCD) is an important target for improving survival in various patient groups and many prevention options have been evaluated. In the past decade several trials have documented beneficial effects for implantable cardioverter-defibrillator (ICD) implantation in patients surviving out-of-hospital cardiac arrest (secondary prevention) and in patients with diminished left ventricular function (primary prevention).1 However, within these patient groups a variety of comorbidities is present which might influence the benefit conferred by prophylactic ICD implantation. One of these comorbidities is chronic kidney disease (CKD), a condition that is highly prevalent among patients with a current ICD indication. CKD is of particular interest since this condition is associated with a substantial risk for non-arrhythmic death and this might negatively influence the beneficial effects of prophylactic ICD implantation. Accordingly this raises the question whether ICD implantation in these patients is appropriate for prevention of SCD or whether other more conservative treatment strategies are preferred with regard to safety and cost effectiveness.

MECHANISMS OF SCD IN CKD

The mechanisms that underlie SCD in patients with CKD are complex and many factors have been associated with increasing the risk for SCD. Beside coronary artery disease (CAD), present in 80% of the patients dying from SCD, many other factors are believed to contribute to the development of SCD in patients with CKD which also might form therapeutic targets for preventing SCD in these patients. The key factors in the development of SCD, including CAD, will be discussed below and are summarised in table 1.

Ischaemic heart disease

CAD is highly prevalent among patients with CKD and is more severe compared to patients without CKD.2 In patients starting dialysis the prevalence of significant CAD is believed to be around 40%.2 However, recent studies evaluating the presence of significant CAD in dialysis patients indicate that this is probably an underestimation of the actual incidence of CAD. Multiple studies have documented that even in asymptomatic dialysis patients without a previous history of CAD, the prevalence of CAD was around 30–40%, indicating that the actual prevalence of CAD in this patient group is around 60%.2

Like in the general population, the presence of CAD is highly associated with the development of SCD in patients with end stage renal disease (ESRD). In addition, in patients with CAD it has been documented that the risk for SCD is related to the severity of CKD; every 10 ml/min decrease in estimated glomerular filtration rate (eGFR) was associated with a 10% increase in risk for SCD. Dialysis patients with CAD were especially at risk for SCD, with a sixfold increased risk for SCD compared to patients with an eGFR >60 ml/min.2

Left ventricular hypertrophy and myocardial fibrosis

Already in the early stages of CKD many patients start to develop left ventricular hypertrophy (LVH) and myocardial fibrosis. The prevalence of these conditions increases with worsening of CKD and increases to over 75% in patients with moderate to severe renal impairment.5,6

The processes involved in the development of LVH and myocardial fibrosis in patients with CKD can be roughly divided into: (1) preload related factors such as hypervolaemia and anaemia; (2) afterload related factors such as systemic arterial resistance, elevated blood pressure, and large vessel compliance; and (3) neither preload nor afterload related factors such as, for example, activation of pathways related to the parathyroid hormone–vitamin D–phosphate axis, oxidative stress, and microinflammation.6

The development of LVH and myocardial fibrosis results in a decreased myocardial capillary density, diastolic dysfunction, and systolic dysfunction. Furthermore, it leads to disturbances in intraventricular conduction. These phenomena predispose to an increase in electric excitability and ventricular arrhythmias.6 This is underlined by the fact that the development and especially worsening of LVH is associated with an increased risk for mortality and in particular with SCD.3

Vascular calcification

Vascular calcification in the general population mostly occurs in the intima of the vessel wall. In patients with CKD, however, media calcification also occurs. Whereas intima calcification—a consequence of inflammation and calcification of atherosclerotic plaques—leads to luminal narrowing of the vessel, medial calcification leads to stiffening of the vessel and thereby reduced vascular compliance, resulting in vascular stiffness. Multiple modifiable and non-modifiable risk factors have been established for vascular calcification in...
Table 1 Mechanisms associated with sudden cardiac death in patients with chronic kidney disease

<table>
<thead>
<tr>
<th>Mechanism</th>
<th>Description</th>
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<tbody>
<tr>
<td>Ischaemic heart disease</td>
<td>Present in 80% of patients dying suddenly in the general population. Highly prevalent and more severe in patients with chronic kidney disease (CKD) and end stage renal disease (ESRD). Most important predictor of sudden cardiac death (SCD) in patients with ESRD. In patients with coronary artery disease, severity of CKD is associated with the occurrence of SCD.</td>
</tr>
<tr>
<td>Left ventricular hypertrophy (LVH) and myocardial fibrosis</td>
<td>Develops in the early stages of CKD and prevalence increases with severity of CKD. Results in phenomena which predispose to electric excitability and ventricular arrhythmias (ie, decreased myocardial capillary density, diastolic and systolic dysfunction) Development of LVH—especially worsening of LVH—are associated with increased risk for SCD.</td>
</tr>
<tr>
<td>Vascular calcification</td>
<td>Intima calcification leads to luminal narrowing resulting in ischaemia Media calcification leads to a reduced vascular compliance resulting in vascular stiffening. Coronary calcification has been associated with higher spatial QRS-T angles, an important marker for SCD.</td>
</tr>
<tr>
<td>Sympathetic over activation</td>
<td>Important mechanism for cardiovascular complications In dialysis patients norepinephrine predicts survival and cardiovascular events Damaged kidneys trigger sympathetic overactivation.</td>
</tr>
<tr>
<td>Dialysis treatment</td>
<td>Timely relation between occurrence of SCD and dialysis treatment Significant decline in incidence of SCD after renal transplantation. Probably rapid fluid and electrolyte shifts play an important role.</td>
</tr>
<tr>
<td>Other risk factors</td>
<td>These include age, diabetes mellitus, malnutrition, inflammation, electrolyte abnormalities and the use of vascular access catheters.</td>
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patients with CKD, with phosphorus topping the list of risk factors. Vascular stiffening in patients with ESRD has been associated with an increase in all cause and cardiovascular mortality. Although the actual relation of vascular calcification with SCD is not clear, recently a strong relation between coronary artery calcification and an increased spatial QRS-T angle was demonstrated. The latter parameter is an important marker for SCD in various patient groups.

### Sympathetic overactivity

Increased sympathetic activity is recognised as an important mechanism for cardiovascular complications. Additionally, in dialysis patients it has been demonstrated that plasma norepinephrine—a marker for sympathetic activity—is an independent predictor of survival and cardiovascular events. Sustained over-activation of the sympathetic nervous system is highly prevalent among patients with CKD, and this condition already develops early in the course of CKD. Probably the damaged kidneys themselves are the trigger for this overactivity since it has been demonstrated that the augmented sympathetic drive subsides after bilateral nephrectomy.

### Dialysis treatment

In dialysis patients, next to the factors mentioned above, probably the treatment itself is an important risk factor for developing SCD. For example, it has been reported that, in patients receiving haemodialysis treatment, the time at which SCD occurs is treatment related. The incidence of SCD is significantly higher in the first 12 h of a dialysis session and also particularly 60–72 h after the start of a dialysis session (figure 1). Furthermore, the incidence of SCD declines significantly in patients after renal transplantation, which also underlines this hypothesis. The rapid fluid and electrolyte shifts that occur during this treatment are important elements in the risk for SCD in this patient group.

### Other risk factors

Many other factors have also been identified as risk factors for developing SCD. These include older age, history of diabetes mellitus, malnutrition, increased inflammation, and electrolyte abnormalities. Also the use of catheters for vascular access has been associated with a higher risk for developing SCD.

### PREVENTION STRATEGIES

Concerning the prevention of SCD in patients with renal failure, various treatment strategies have been evaluated. Most of them interact with one of the risk factors mentioned previously. In the following section the most important treatment strategies will be discussed with regard to their merits (see tables 2 and 3 also).

### Medical interventions

Several medical interventions have been investigated including β-blockers, statins, and erythropoietin therapy.

**β-blockers**

β-blockers interfere with the deleterious actions of the sympathetic nervous system and thereby may improve cardiovascular outcomes in this patient group, especially since it has been documented that sympathetic overactivity is commonly seen in these patients. In patients with CKD who are not on dialysis, limited data exist concerning the beneficial effects of β-blockers in preventing SCD. However, a post hoc analysis of the BIP (Bezafibrate Infarction Prevention) study that has been recently conducted demonstrated that the use of β-blockers was associated with a reduction in acute myocardial infarction or SCD rates in patients with CKD.

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*Figure 1 Incidence of sudden cardiac death and its relation to timing of the dialysis therapy. Reproduced from Bleyer et al, with permission of Nature Publishing Group.*
The beneficial effect of β-blocker treatment in dialysis patients has been more extensively evaluated. Observational data have shown beneficial effects, but a survival benefit has only been demonstrated so far in a prospective randomised controlled trial involving a small subset of dialysis patients. More prospective trials regarding the potential beneficial effects are therefore warranted in order to define the value of this treatment in dialysis patients.

**Table 2** Strategies to reduce sudden cardiac death in patients with chronic kidney disease

<table>
<thead>
<tr>
<th>Medical treatment</th>
<th>Description</th>
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<tbody>
<tr>
<td>β-blockers</td>
<td>A recent study demonstrated a reduction in acute myocardial infarction or sudden cardiac death rates</td>
</tr>
<tr>
<td>Statins</td>
<td>Statins are associated with improved cardiovascular outcomes in patients with chronic kidney disease (CKD)</td>
</tr>
<tr>
<td>Erythropoietin</td>
<td>Recent large trials failed to show a positive result in patients with CKD not on dialysis</td>
</tr>
<tr>
<td>ACE inhibitors/angiotensin receptor blockers</td>
<td>Multiple reports regarding beneficial effects on cardiovascular and renal end points.</td>
</tr>
<tr>
<td>Revascularisation</td>
<td>Based on the results of the COURAGE trial, it should be concluded that prophylactic revascularisation is not beneficial on top of optimal medical treatment in patients with stable angina.</td>
</tr>
<tr>
<td>Implantable cardioverter-defibrillator (ICD)</td>
<td>According to the current guidelines, ICD implantation is recommended in patients with CKD not on dialysis, who meet current criteria for prophylactic ICD implantation.</td>
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The presence of other comorbidities such as atrial fibrillation, wide QRS, older age and severe heart failure negatively influences the possible benefit of ICD implantation in these patients.

**Table 3** Strategies to reduce sudden cardiac death in dialysis patients

<table>
<thead>
<tr>
<th>Medical treatment</th>
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<tbody>
<tr>
<td>β-blockers</td>
<td>One prospective trial demonstrated a beneficial effect in a subset of dialysis patients</td>
</tr>
<tr>
<td>Statins</td>
<td>Two recent large trials failed to demonstrate a benefit for statins in dialysis patients</td>
</tr>
<tr>
<td>Erythropoietin</td>
<td>There is no evidence to correct anaemia above a haemoglobin value of 7.2 mmol/l</td>
</tr>
<tr>
<td>ACE inhibitors/angiotensin receptor blockers (ARBs)</td>
<td>ARB significantly reduced cardiovascular end points in a small study. Another study failed to show positive results for ACE inhibitor, probably due to lack of power.</td>
</tr>
<tr>
<td>Changing dialysis modality</td>
<td>Several alterations have been investigated; however, no beneficial effects with regard to cardiovascular mortality have been reported so far.</td>
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<tr>
<td></td>
<td>There are, however, promising results for increasing dialysis frequency, which might prove beneficial in the future.</td>
</tr>
<tr>
<td>Revascularisation</td>
<td>Revascularisation improves outcome in patients with documented coronary artery disease</td>
</tr>
<tr>
<td></td>
<td>No difference in all-cause mortality or SCD between optimally revascularised dialysis patients and the general dialysis population.</td>
</tr>
<tr>
<td>Implantable cardioverter-defibrillator (ICD)</td>
<td>For both primary and secondary prevention indications survival improvement has been reported.</td>
</tr>
<tr>
<td></td>
<td>Mortality in ICD recipients on dialysis is much higher compared with those not on dialysis, which influences cost effectiveness.</td>
</tr>
</tbody>
</table>

ACE inhibitors and angiotensin type II receptor blockers

Beneficial effects have been reported for both ACE inhibitors and angiotensin type II receptor blockers (ARBs) with regard to cardiovascular and renal end points in various patient populations. In patients with CKD, it was reported in the RENAL (Reduction of Endpoints in NIDDM with the Angiotensin II Antagonist Losartan) trial that the use of an ARB significantly reduced the incidence of the primary composite end point of doubling of serum creatinine concentration, onset of ESRD or death. In dialysis patients, it has also been reported that the ARB candesartan significantly reduced cardiovascular events. On the other hand, another prospective trial in dialysis patients,
evaluating the ACE inhibitor fosinopril, failed to show positive results.\textsuperscript{w25} The latter study was probably underpowered, however.

Whether ACE inhibitors and ARBs reduce SCD in patients with renal failure is not clear. However, in an observational study, it was reported that in dialysis patients who survived a cardiac arrest, ACE inhibitor and/or ARB use was associated with a significant reduced risk of SCD and that there was also a positive correlation between drug dose and survival.\textsuperscript{w26} Future trials should elucidate further the role of ACE inhibitors and/or ARBs in preventing SCD.

**Revascularisation**

Although the presence of CAD is associated with SCD, the recent COURAGE (Clinical Outcomes Utilising Revascularisation and Aggressive Drug Evaluation) trial demonstrated that in patients with stable CAD, percutaneous coronary intervention (PCI) did not reduce the risk of death, myocardial infarction or other major cardiovascular events when added to optimal medical treatment. Therefore, prophylactic revascularisation probably cannot be considered a preventive treatment strategy in patients with CKD.\textsuperscript{13}

Since the COURAGE trial excluded any patients with a serious coexisting illness, in dialysis patients these results might be different. As mentioned, CAD is highly prevalent among dialysis patients. Therefore, it is hypothesised that optimal revascularisation would significantly reduce the incidence of SCD in dialysis patients, especially since it has been reported that dialysis patients with documented significant CAD benefit from revascularisation compared to patients who receive conservative treatment.\textsuperscript{w27} However, a recent study reported that all-cause and arrhythmic mortality in optimally revascularised dialysis patients was not lower than that for the entire dialysis patient population. In this large observational study, the 2 year incidence of all-cause mortality in the entire dialysis population was 40% and the probability of SCD was 14%. This was comparable to the 2 year all-cause mortality of 45% and an incidence of SCD of 14% in optimally revascularised patients. These data do not suggest that revascularisation is not efficacious; rather it can be concluded that a substantial hazard for SCD remains despite optimal revascularisation. Therefore, targeting the non-ischaemic contributors is also warranted in order to reduce SCD.\textsuperscript{14}

**Changing dialysis modality**

Given the suggested relationship between dialysis therapy and SCD itself, altering dialysis therapy might therefore be beneficial in reducing SCD. Recently, several dialysis therapy related factors have been identified, which were associated with an increased risk for SCD (for example, increased ultrafiltration volume and exposure to low potassium dialysate), thereby providing potentially useful methods for altering dialysis treatment.\textsuperscript{w28} Various modifications have been prospectively investigated including increasing dialysis frequency, increasing dialysis dose, and haemodialfiltration. However, no beneficial effects have been reported with regard to reducing (cardiovascular) mortality so far.\textsuperscript{6} Nevertheless, promising results with regard to surrogate end points (such as left ventricular mass) have been reported with an increased frequency of (nocturnal) haemodialysis.\textsuperscript{w29, w30}

**Prophylactic ICD implantation in CKD patients not on dialysis**

Since most ICD trials have not excluded patients solely on the basis on their renal function, current guideline recommendations are also applicable for patients with CKD and even for dialysis patients with a relatively good projected survival.\textsuperscript{1} Based on these recommendations it would be wrong to withhold prophylactic ICD implantation in these patients. Nevertheless, the decision to prevent SCD in CKD patients with prophylactic ICD implantation should be considered challenging, given the particular nature of this patient group.

On the one hand multiple observational studies indicate that renal function is an independent predictor for the incidence of appropriate ICD therapies in both primary and secondary prevention patients.\textsuperscript{w31} Nevertheless, it has also been reported that the presence of renal impairment is a strong predictor of mortality in ICD recipients,\textsuperscript{w32} thereby potentially negatively influencing the survival benefit conferred by appropriate ICD therapies. This was documented in a sub-analysis of the MADIT II trial, for example, which showed that in patients with severe CKD there was no survival benefit in the treatment arm of the study. In patients with mild to moderate CKD the potential benefit of ICD treatment depended on the presence of other risk factors (atrial fibrillation, age $>$70 years, New York Heart Association functional class $>$II, QRS $>$120 ms). Pending on the number of these other risk factors present, the beneficial effect of prophylactic ICD implantation is diminished. It should be noted that in this sub-analysis the survival benefit conferred by prophylactic ICD implantation also disappeared when none of these risk factors—including the presence of CKD—was present\textsuperscript{17} (figure 2).

Considering the higher risk for SCD and/or appropriate ICD therapies in patients with CKD on the one hand, and the higher mortality risk, especially in the presence of other comorbidities, on the other, it could be concluded that the decision for prophylactic ICD implantation should be patient tailored. This warrants more studies investigating the (cost) effectiveness of ICDs in this patient population in order to improve current guidelines. Probably the decision for prophylactic ICD implantation in patients with CKD will depend on the presence and severity of other comorbidities.

**Prophylactic ICD implantation in dialysis patients with an indication according to current guidelines**

As previously mentioned, almost all ICD trials that have been completed so far excluded dialysis patients with severe CKD. On the one hand, these results might be different. As mentioned, CAD is highly prevalent among dialysis patients. Therefore, it is hypothesised that optimal revascularisation would significantly reduce the incidence of SCD in dialysis patients, especially since it has been reported that dialysis patients with documented significant CAD benefit from revascularisation compared to patients who receive conservative treatment. However, a recent study reported that all-cause and arrhythmic mortality in optimally revascularised dialysis patients was not lower than that for the entire dialysis patient population. In this large observational study, the 2 year incidence of all-cause mortality in the entire dialysis population was 40% and the probability of SCD was 14%. This was comparable to the 2 year all-cause mortality of 45% and an incidence of SCD of 14% in optimally revascularised patients. These data do not suggest that revascularisation is not efficacious; rather it can be concluded that a substantial hazard for SCD remains despite optimal revascularisation. Therefore, targeting the non-ischaemic contributors is also warranted in order to reduce SCD. Given the suggested relationship between dialysis therapy and SCD itself, altering dialysis therapy might therefore be beneficial in reducing SCD. Recently, several dialysis therapy related factors have been identified, which were associated with an increased risk for SCD (for example, increased ultrafiltration volume and exposure to low potassium dialysate), thereby providing potentially useful methods for altering dialysis treatment. Various modifications have been prospectively investigated including increasing dialysis frequency, increasing dialysis dose, and haemodialfiltration. However, no beneficial effects have been reported with regard to reducing (cardiovascular) mortality so far. Nevertheless, promising results with regard to surrogate end points (such as left ventricular mass) have been reported with an increased frequency of (nocturnal) haemodialysis.

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patients or did not publish sub-analyses. Therefore, there is little current knowledge regarding the potential benefit of prophylactic ICD treatment in dialysis patients. Nevertheless, several observational studies have indicated that a selected group of dialysis patients may benefit from this prevention strategy, since dialysis therapy is a strong predictor for appropriate ICD therapies. In addition, a large observational study including dialysis patients who survived cardiac arrest demonstrated that prophylactic ICD implantation was associated with a 42% reduction in mortality risk. With regard to primary prevention using prophylactic ICD implantation, a significant survival benefit was also recently demonstrated in a small cohort of dialysis patients. Another small observational study in primary prevention patients did not confirm these findings, however.

Despite the suggested survival improvement, mortality in dialysis patients receiving prophylactic ICD treatment, according to the current guidelines, is significantly higher compared with patients not on dialysis, thereby putting the potential survival benefit in perspective. Therefore, regardless of the impressive relative mortality risk reductions, the absolute survival gain conferred by ICDs might be much lower in dialysis patients, negatively influencing the cost effectiveness of prophylactic ICD treatment. Hence, the cost effectiveness of prophylactic ICD implantation in dialysis patients with an ICD indication deserves more attention in order to establish its role in the prevention of SCD.

Prophylactic ICD implantation in dialysis patients with no current indication for prophylactic ICD implantation

As mentioned above, the rate of SCD in dialysis patients is significantly higher when compared with the general population. The estimated annual incidence of SCD in these patients of 6.9% underscores the importance of preventing sudden cardiac death in this patient group. Of particular interest is the finding that over 70% of the dialysis patients dying suddenly have normal left ventricular function or mild-moderate dysfunction, indicating that factors other than ejection fraction also play an important role in the development of SCD in this patient group. Despite having a preserved ejection fraction, the actual incidence of SCD in these patients with 5-year incidence rates of up to 25% would still be classified as high in a non-dialysis population. Currently, there are no data on prophylactic ICDs in these patients. However, given this high incidence of SCD, prophylactic ICD implantation might confer a substantial survival benefit in these patients. The currently ongoing ICD2 trial will evaluate the potential benefit of prophylactic ICD implantation in dialysis patients in whom there is no current indication for ICD implantation. This pilot study will randomise 200 patients to a treatment and a control arm to test whether prophylactic ICD implantation will reduce the incidence of SCD. In addition, an extensive pre-randomisation screening protocol is being conducted in all participants in order to establish potential predictors for SCD and/or appropriate ICD therapies. This study will also focus on other issues such as safety and cost effectiveness.

SAFETY OF ICD TREATMENT IN PATIENTS WITH RENAL FAILURE

Several issues have been raised with regard to the safety of ICD treatment in patients with renal failure. For example, it has been established that an impaired renal function (eGFR <60 ml/min/m²) is associated with a 4.6-fold increased risk for the development of cardiac device infections. Cardiac device infections can be serious and potentially life threatening. In addition to the increased morbidity and mortality resulting from cardiac device infections, there are also the associated substantial costs which have a negative effect on the cost/benefit ratio of prophylactic ICD implantation.

Also, with regard to in-hospital complications, it has been reported that the incidence of these complications is significantly higher in patients with chronic kidney disease because of their higher risk for developing cardiac device infections, in hospital complications occur more frequently in patients with end stage renal disease, and ICD implantation might increase the incidence of vascular access thrombosis, especially when the device is implanted at the ipsilateral side.

**Box 1 Safety of implantable cardioverter-defibrillator (ICD) treatment in patients with renal failure**

- Patients with chronic kidney disease have a significantly higher risk for developing cardiac device infections.
- In hospital complications occur more frequently in patients with end stage renal disease.
- ICD implantation might increase the incidence of vascular access thrombosis, especially when the device is implanted at the ipsilateral side.
Sudden cardiac death in patients with renal failure: key points

- Patients with renal failure are at increased risk for sudden cardiac death (SCD) on the one hand, but are also at increased risk for non-arrhythmic mortality on the other, making the potential benefit of this treatment less clear.
- The mechanism of SCD in patients with renal failure is complex and, in addition to coronary artery disease, many other factors are also believed to play an important role.
- Several treatment strategies have been investigated with regard to preventing SCD in chronic kidney disease (CKD) and dialysis patients, with differing, mostly disappointing, results.
- Most importantly, in patients with CKD, β-blockers and statins are associated with positive outcomes. In dialysis patients, promising results have been reported for β-blocker treatment and increasing dialysis frequency.
- Current guidelines also recommend prophylactic implantable cardioverter-defibrillator (ICD) implantation in patients with CKD and even in dialysis patients with good projected survival.
- In CKD patients the potential benefit of ICD implantation probably depends on the presence and severity of other comorbidities.
- In dialysis patients the benefits of ICD implantation are less clear, since most trials have excluded these patients.
- Despite observational studies demonstrating a potential benefit in dialysis patients, the mortality rate remains substantial in these patients.
- Of particular interest are dialysis patients who do not meet current ICD implantation criteria.

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with ESRD presenting for ICD implantation compared with patients without ESRD.26,38

Finally, a specific complication in dialysis patients which deserves special attention is the incidence of vascular access thrombosis. In a recent study evaluating the incidence of complications in patients with and without ESRD, it was documented that vascular access thrombosis occurred in 50% of the patients in whom the device was implanted ipsilateral to the dialysis access vein and in 19% of the patients in whom the device was implanted contralateral to the dialysis access vein.20

It should be noted that dialysis access stenosis also frequently occurs in patients with no implanted ICD. Nevertheless this complication is of importance and warrants further investigation. Given the lower incidence of vascular access stenosis, the ICD should be implanted contralateral to the dialysis access side when possible (box 1).

CONCLUSIONS

In patients at risk for SCD, the presence of CKD increases the risk of SCD compared to patients without CKD. However, in addition to this increased risk for SCD there is also an increased risk of death in these patients from causes other than arrhythmia. Current guidelines recommend ICD implantation for various patient groups at high risk for SCD irrespective of the presence of CKD (and even ESRD, if life expectancy is over 1 year). Conversely, the beneficial effects conferred by ICD implantation vary within patients with CKD and probably depend on the presence of other comorbidities. More research is warranted in order to establish which patients with CKD actually benefit from ICD treatment, and in which patients conservative treatment would be more appropriate. For dialysis patients—a patient group at particularly high risk for both SCD and all-cause mortality—with an indication for ICD implantation, beneficial effects have been reported for both primary and secondary prevention. However, given their high all-cause mortality rates, the limited gain in survival negatively offsets the cost effectiveness of this therapy, and therefore this important aspect should be evaluated in future research.

Of interest are dialysis patients with no current indication for ICD implantation. These patients have preserved ejection fraction, and overall survival in these patients is much better compared to dialysis patients with heart failure. Nevertheless, a high risk for SCD remains in these patients. Given the better ratio between SCD and all-cause mortality, prophylactic ICD implantation might improve survival in these patients. The beneficial effects of ICD implantation in dialysis patients with preserved ejection fraction are currently being investigated.

Competing interests In compliance with EBAC/EACCME guidelines, all authors participating in Education in Heart have disclosed potential conflicts of interest that might cause a bias in the article. The authors have no competing interests.

Contributors MKdeB and MB prepared the draft of the manuscript; TR and JWJ revised the draft version and gave final approval of the final version.

Provenance and peer review Commissioned; internally peer reviewed.

REFERENCES

Chapter 9 of this annual report by the USRDS provides important data regarding the incidence of SCD in patients with CKD and furthermore provides various relevant subanalyses.


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9. One of the few randomised controlled trials in dialysis patients that showed a mortality reduction (using treatment with carvedilol).


11. A randomised trial in diabetic dialysis patients evaluating atorvastatin, which failed to show a reduction in cardiovascular death and other cardiovascular end points.


16. This study demonstrated that impaired renal function, and especially impaired renal function requiring dialysis, predicted the time to first appropriate ICD shock.


18. Important sub-analysis of the MADIT-II landmark study reporting the influence of several risk factors, including moderate and severe renal failure, on the benefit of prophylactic ICD implantation.


20. Important study demonstrating a 42% mortality reduction in dialysis patients undergoing prophylactic ICD implantation after surviving cardiac arrest.


22. Rationale and design of a randomised controlled study in dialysis patients that will evaluate prophylactic ICD implantation in dialysis patients with preserved ejection fraction.