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Prevention of sudden cardiac death in patients with chronic kidney disease, focusing on implantable cardioverter defibrillator therapy

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CHAPTER III

How to reduce sudden cardiac death in patients with renal failure

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SUDDEN CARDIAC DEATH IN PATIENTS WITH RENAL FAILURE: KEY POINTS

- Patients with renal failure are at increased risk for SCD on one hand, but also at increased risk for non-arrhythmic mortality, making the potential benefit of this treatment less clear.

- The mechanism of SCD in patients with renal failure is complex and next to CAD many other factors are also believed to play an important role.

- Several treatment strategies have been investigated with regard to preventing SCD in CKD and dialysis patients, with different mostly disappointing, results.

- Most importantly in patients with CKD β-blocker therapy and statins are associated with positive outcomes. In dialysis patients promising results have been reported for β-blocker therapy and increasing dialysis frequency.

- Current guidelines recommend prophylactic ICD implantation also for patients with CKD and even dialysis patients with good projected survival.

- In CKD patients the potential benefit of ICD implantation probably depends on the presence and severity of other co morbidities.

- In dialysis patients the benefits of ICD implantation are less clear, since most trials excluded these patients.

- Despite observational studies demonstrating a potential benefit in dialysis patients, the mortality remains substantial in these patients.

- Of particular interest are dialysis patients who do not meet current ICD implantation criteria.

INTRODUCTION

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 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 patients 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 summarized in table 1.

Ischemic heart disease

Coronary artery disease is highly prevalent among patients with CKD and is more severe compared to patients without CKD.[w1] In patients starting dialysis the prevalence of significant CAD is believed to be around 40%.[w2] 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%.[w3]

Like in the general population the presence of coronary artery disease (CAD) is highly associated with the development of SCD in patients with end stage renal disease (ESRD).[w4] In addition, within patients with CAD it has been documented that the risk for SCD is related to the severity of CKD, for every 10 ml/min decrease in estimated glomerular filtration rate was associated with a 10% increase in risk for SCD. Dialysis patients with CAD

were especially at risk for SCD, compared to patients with estimated glomerular filtration rate (eGFR) >60ml/min there was a 6 fold increased risk for SCD.[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 in patients with moderate to severe renal impairment.[w5]

The processes involved in the development of left ventricular hypertrophy and myocardial fibrosis in patients with CKD can be roughly divided in (1) preload related factors such as hypervolemia and anemia, (2) afterload related such as systemic arterial resistance, elevated blood pressure and large-vessel compliance and (3) not preload or afterload related factors such as for instance activation of pathways related to the PTH-vitamin D-phosphate axis, oxidative stress and microinflammation.[w6]

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 increased in electric excitability and ventricular arrhtyhmias.[w6] This is underlined by the fact that the development of LVH and especially worsening of LVH are associated with an increased mortality risk in particular also for SCD.[3, w7]

Vascular Calcification

Vascular calcification in the general population mostly occurs in the intima of the vessel wall. In patients with CKD however also media calcification occurs. Whereas intima calcifications, a consequence of inflammation and calcification of atherosclerotic plaques, lead to luminal narrowing of the vessel, medial calcifications lead to stiffening of the vessel and thereby reduce vascular compliance and result in vascular stiffness. Multiple modifiable and non-modifiable risk factors have been established for vascular calcification in patients with CKD with phosphorus being at the top of the list of the risk factors.[w8]

Vascular stiffening in patients with end stage renal disease has been associated with an increased all-cause and cardiovascular mortality.[w9] 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.[w10]

Sympathetic over activity

Increased sympathetic activity is recognized 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.[w11] 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.[w12, w13]

Dialysis treatment

In dialysis patients next to the factors mentioned above, probably the treatment itself is an important risk factor for developing SCD. For instance it has been reported for patients receiving hemodialysis treatment that the time at which SCD occurs is treatment related. The incidence of SCD is significantly higher in the first twelve hours from the start of a dialysis session and in particular 60 to 72 hours after the start of a dialysis session. [4] (See figure 1) Furthermore the incidence of SCD declines significantly in patients after renal

Table 1: *Mechanisms associated with SCD in patients with CKD*

Ischemic Heart Disease	• Present in 80% of patients dying suddenly in the general population • Highly prevalent and more severe in patients with CKD and ESRD • Most important predictor of SCD in patients with ESRD • In patients with CAD severity of CKD is associated to the occurrence of SCD
Left Ventricular Hypertrophy and Myocardial fibrosis	• Develops already in the early stages of CKD and prevalence increases with severity of CKD • Results in phenoma which predispose to electric excitability and ventricular arrhythmias. (i.e. decreased myocardial capillary density, diastolic and systolic dysfunction.) • Development of LVH -and especially worsening of LVH- are associated with increased risk for SCD.
Vascular calcification	• Intima calcification leads to luminal narrowing resulting in ischemia • 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.
Sympathetic over activation	• Important mechanism for CV complications. • In dialysis patients norepinphrine predicts survival and CV events • Damaged kidneys themselves trigger sympathetic overactivation
Dialysis treatment	• Timely relation between occurrence SCD and dialysis treatment • Significant decline in incidence of SCD after renal transplantation. • Probably rapid fluid and electrolyte shifts play an important role
Other risk factors	• These include age, diabetes mellitus, malnutrition, inflammation, electrolyte abnormalities and the use of vascular access catheters.

transplantation, which also underlines this hypothesis.[5] The rapid fluid and electrolyte shifts that occur during this treatment are important elements in the risk for SCD in this patient group.[6]

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. [6, w14]

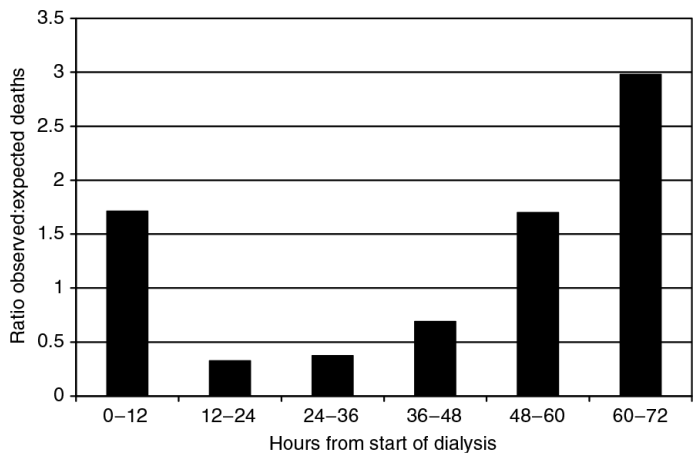

Figure 1: Incidence of sudden cardiac death and its relation to timing of the dialysis therapy
Reproduced from Bleyer et al.[4], with permission of Nature Publishing group

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 before. In the following section the most important treatment strategies will be discussed with regard to their merits. See also tables 2 and 3.

Medical interventions

Several medical interventions have been investigated including β-blocker therapy, statin therapy and erythropoietin therapy:

β-blocker therapy

β-blockers interfere with the deleterious actions of the sympathetic nervous system and

thereby might improve cardiovascular outcomes in this patient group, especially since it has been documented that sympathetic overactivity is commonly seen in this patient group.[w15]
In patients with CKD, that are not on dialysis, limited data exists 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 performed demonstrated that the use of β-blockers was associated with a reduction in acute myocardial infarction or sudden cardiac death rates in patients with CKD.[7]
The beneficial effect of β-blocker therapy in dialysis patients, has been more extensively evaluated. Observational data showed beneficial effects, however so far only in a small subset of dialysis patients a survival benefit has been demonstrated in a prospective randomized controlled trial.[8] More prospective trials regarding the potential beneficial effects are therefore warranted in order to define the value of this therapy in dialysis patients.[9]

Statin therapy

Statins have proven to have significant beneficial effects on cardiovascular endpoints in various patient groups. For patients with CKD, including dialysis, recently it was concluded form the SHARP (Study of Heart and Renal Protection) trial that simvastatine + ezetimibe significantly reduces major atherosclerotic events.[10] Furthermore, the JUPITER (Justification for the Use of Statins in Prevention-an Intervention Trial Evaluating Rosuvastatin) trial showed that Rosuvastatin reduces first cardiovascular events in patients with low-density lipoprotein cholesterol (LDL-C) elevated high sensitivity CRP (hsCRP) and moderate CKD.[w16] Next to these results also a recent meta-analysis reported a 20% risk reduction of cardiovascular mortality in patients with CKD including dialysis patients.[w17]
In dialysis patients it should be noted however, that 2 recent large trials failed to show a reduction in CV-mortality.[11,12] This negative result probably is driven by the fact that the effect of statins on SCD is doubtful since the mechanisms involved are less amenable to cholesterol lowering. The latter is confirmed by the fact that there was no difference in SCD in various dialysis and non-dialysis trials investigating statins. [11, w18]

Erythropoietin (EPO)

It has been suggested that there is a relation between anemia and LVH in CKD patients. Considering the relation between LVH and SCD in this patient group a strong effect of restoring anemia in this patients was suspected.[6] On the other hand, when correcting Hb with erythropoietin, it should be taken in account that this is also associated with an increase in blood pressure, vascular access thrombosis and also an increased number of CV events, counterbalancing potential positive effects.[w19]
Despite the suspected beneficial effects of EPO several large trials in patients with CKD -not on dialysis- failed to show positive results.[w20] In dialysis patients also various trials have explored the effects of EPO. However, currently there is insufficient published literature to

generalize risk or benefits of Hb levels > 7.2 mmol/L (120/g/L),[w21] and therefore only partial anemia correction is nowadays recommended for these patients. [w22]

Angiotensin Converting Enzyme Inhibitors (ACEi) / Angiotensin Type II Receptor Blockers (ARB)

For both ACEis and ARBs beneficial effects have been reported with regard to cardiovascular and renal endpoints in various patient populations. In patients with CKD it was reported in the RENAAL (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 endpoint of doubling of serum creatinin concentration, onset of ESRD or death.[w23] In dialysis patients it has furthermore been reported that the ARB Candesartan significantly reduced cardiovascular events.[w24] On the other hand another prospective trial in dialysis patients evaluating ACEi failed to show positive results.[w25] Probably the latter study however was underpowered.

Whether ACEis and ARBs reduce SCD in patients with renal failure is not clear. However, it has been reported, in an observational study, that in dialysis patients who survived a cardiac arrest, ACEi 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.[w26] Future trials should further elucidate the role of ACEi and/or ARB in preventing SCD.

Revascularization

Although the presence of CAD is associated with SCD, it should be noted that recently the COURAGE (Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation) trial demonstrated that in patients with stable CAD, PCI did not reduce the risk of death, myocardial infarction or other major cardiovascular events when added to optimal medical therapy. Therefore prophylactic revascularization probably can not be considered a preventive treatment strategy in patients with CKD.[13]

Since the latter trial excluded patients with a serious co-existing illness, in dialysis patients these results might be different. As mentioned, CAD is highly prevalent among dialysis patients. Therefore it is hypothesized that optimal revascularization 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 revascularization compared to patients who receive conservative treatment.[w27] However, recently it also has been reported that all-cause and arrhythmic mortality in optimally revascularized dialysis patients was not lower than that for the entire dialysis patient population. In a 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 43% and an incidence of SCD of 14% in optimally revascularized patients. These data do not suggest that revascularization is not efficacious, rather it can be concluded that a

substantial hazard for SCD remains despite optimal revascularization. Therefore targeting the non-ischemic contributors is also warranted in order to reduce SCD.[14]

Changing dialysis modality

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

Prophylactic ICD implantation in CKD patients not on dialysis

Since most ICD trials did not exclude patients solely based 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.[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 with prophylactic ICD implantation should be

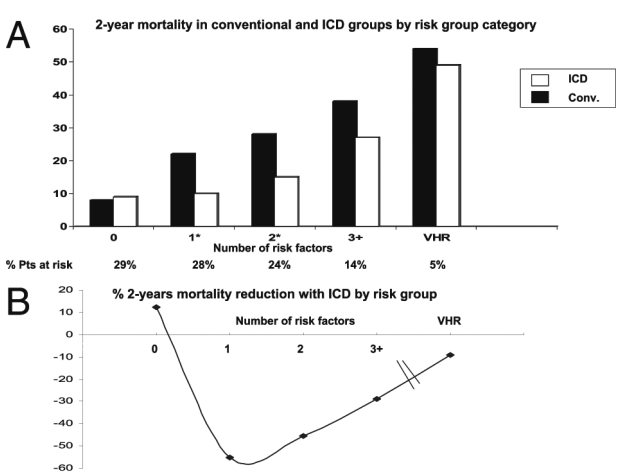

Figure 2: (A) Two year Kaplan-Meier mortality rates in the implantable cardioverterdefibrillator (ICD) and conventional (Conv.) therapy groups of the MADIT II study based on the number of risk factors and for patients with severe kidney disease, considered very high risk (VHR); and (B) the corresponding 2 year mortality rate reduction with an ICD, by risk score and in VHR patients. *p<0.05 for the comparison between the conventional therapy and ICD groups. Reproduced from Goldenberg et al,[17] with permission of Elsevier.

Table 2: *Strategies to reduce SCD in CKD patients*

Medical	
β-*blocker*	• A recent study demonstrated a reduction in acute myocardial infarction or sudden cardiac death rates.
Statins	• Statins are associated with improved cardiovascular outcomes in CKD patients.
Epo	• Recent large trials failed to show a positive result in patients with CKD not on dialysis.
ACEi / ARB	• Multiple reports regarding beneficial effects on cardiovascular and renal endpoints. For instance the RENAAL study showed a reduction in primary endpoint doubling of serum creatinin, onset of ESRD or death.
Revascularization	• Based on the results of the COURAGE trial it should be concluded that prophylactic revascularization is not beneficial on top of optimal medical therapy in patients with stable angina.
ICD	• According to the current guidelines ICD implantation is recommended in patients with CKD –not on dialysis- who meet current criteria for prophylactic ICD implantation. • 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.

considered challenging given the particular nature of this patient group.
On 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.[15, w31] Nevertheless, it has been also reported that the presence of renal impairment is a strong predictor for mortality in ICD recipients,[16, w32] thereby potentially negatively influencing the potential survival benefit conferred by appropriate ICD therapies. This was for instance documented in a sub analysis of the MADIT II trial, 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, NYHA > II, QRS > 120ms). Pending on the number of these other risk factors present the beneficial effect of prophylactic ICD implantation diminished. Of interest 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- were present.[17] Figure 2.
Considering the higher risk for SCD and/or appropriate ICD therapies in patients with CKD on one hand and the higher mortality risk, especially in the presence of other comorbidities, on the other hand, it should be concluded that the decision for prophylactic ICD implantation should be patient tailored. This warrants for more studies investigating

Table 3: *Strategies to reduce SCD in dialysis patients*

Medical	
β-blocker	• One prospective trial demonstrated a beneficial effect in a subset of dialysis patients.
Statins	• 2 recent large trials failed to demonstrate a benefit for statins in dialysis patients.
Epo	• There is no evidence to correct anemia above an Hb of 7.2mmol/L
ACEi / ARB	• ARB significantly reduced CV endpoints in a small study. Another study failed to show positive results for ACEi, probably due to lack of power. • ACEi/ARB use was associated with a reduction of SCD in cardiac arrest survivors.
Changing dialysis modality	• Several alterations have been investigated, however no beneficial effects with regard to CV mortality have been reported so far. • There are however promising results for increasing dialysis frequency, which might prove beneficial in the future.
Revascularization	• In patients with documented CAD revascularization improves outcome. • No difference in all-cause mortality or SCD between optimally revascularized dialysis patients and the general dialysis population.
ICD	• For both primary and secondary prevention indications survival improvement has been reported. • Mortality in ICD recipients on dialysis much higher compared to those not on dialysis, which influences cost-effectiveness. • Prophylactic ICD implantation in dialysis patients who do not meet ICD implantation criteria is currently being investigated

(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 co-morbidities.

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 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, at least a selected group of dialysis patients, might benefit of this prevention strategy, since dialysis therapy is a

strong predictor for appropriate ICD therapies.[15, w31] In addition, a large observational study including dialysis patients who survived cardiac arrest demonstrated that prophylactic ICD implantation was associated with a 42% reduction of mortality risk.[18] With regard to primary prevention using prophylactic ICD implantation also a significant survival benefit was recently demonstrated in a small cohort of dialysis patients, which was even higher, approximately 60%.[w33] It should be noted that another small observational study in primary prevention patients did not confirm these findings.[w34]
Despite the suggested survival improvement, mortality in dialysis patients receiving prophylactic ICD treatment, according to the current guidelines, is significantly higher compared to patients not on dialysis thereby putting the potential survival benefit in perspective.[w35] 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 the rate of SCD in dialysis patients is significantly higher when compared to 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.[5]
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.[w36] Despite having a preserved ejection fraction the actual incidence of SCD in these patients -with 5-year incidences up to 25%[w36] would still be classified as high in a non-dialysis population. Currently there is 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 randomize 200 patients to a treatment and a control arm to test whether prophylactic ICD implantation will reduce the incidence of SCD. Next to that an extensive pre randomization 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.[19]

Safety of ICD treatment in patients with renal failure

Several issues have been raised with regard to the safety of ICD treatment patients with renal failure. For instance it has been established that an impaired renal function (eGFR <60ml/min/m3) is associated with 4.6 fold increased risk for the development of cardiac device infections.[w37] Cardiac device infections are a serious, potentially life threatening, condition. Next to the increased morbidity and mortality cardiac device infections also are also associated with substantial costs thereby negatively influencing the cost-benefit ratio of prophylactic ICD implantation.
Also with regard to in hospital complications is has been reported that the incidence of these complications is significantly higher in patients with ESRD presenting for ICD implantation compared to patients without ESRD.[w38]
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 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 ICD implanted. 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. See table 4.

Table 4: *Safety of ICD treatment in patients with renal failure*

• Patients with CKD have a significantly higher risk for developing cardiac device infections
• In hospital complications occur more frequently in patients with ESRD
• ICD implantation might increase incidence of vascular access thrombosis, especially when the device is implanted at the ipsilateral side.

CONCLUSIONS

In patients at risk for SCD, the presence of CKD increases the risk of SCD compared to patients without CKD. However, next to this increased risk for SCD also an increased risk for death not due to arrhythmia exists in these patients. Current guidelines recommend ICD implantation for various patient groups at high risk for SCD irrespectively 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 co-morbidities. More research is warranted in order to establish which

patients with CKD actually benefit of 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 the limited gain in survival, given their high all-cause mortality, 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.

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