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Letter to the Editor

The Role of Implantable Cardioverter-Defibrillators in Prevention of Sudden Cardiac Arrest in Chronic Kidney Disease

Mortality of dialysis patients is high, in the first year of hemodialysis, all-cause mortality was reported to be 421 deaths per 1,000 patient years after the second month of treatment, decreasing to 193 after one year of therapy. In the same way cardiovascular mortality was reported to peaked at 163 deaths per 1,000 patient years two months after treatment beginning, then to decrease to 79 after 12 months [6]. SCA is reported to be the most frequent cause of death in 24.3 of incident and 26.5% of prevalent dialysis patients recorded in the United States Renal Data System [7].

SCA rate of uremic patients is higher than the rate recorded in subjects with any recognizable cardiac disease and general population (62 vs 5.98 vs 1.89/1,000 patient-year respectively) [8].

Being SCA the most common cause of death in hemodialysis patients, Pun et al. investigated which factors improved survival after arrest, in their study from 2002 to 2005 evaluated 729 patients who suffered a SCA of whom 310 (42.5%) survived 24 hours, and 80 (11%) survived 6 months. Interestingly cardiovascular comorbidities, diabetes, hemoglobin, and dialysis adequacy, did not predict survival, on the contrary presence of indwelling catheter, and medications such as beta blockers (BBL), calcium-channel blockers (CCB), and angiotensin-converting enzyme inhibitors (ACEI) and angiotensin receptor blockers (ARB) remained significantly associated with survival (BBL odds ratio [OR] 0.32 [95% confidence interval (CI) 0.17 to 0.61]; CCB OR 0.42 [95% CI 0.23 to 0.76]; ACEI/ARB OR 0.51 [95% CI 0.28 to 0.95]). Moreover prescription of BBL at the time of the event was the only predictive variable of survival at 24 hours [9].

Karnik, et al., studied 400 SCA between October 1998 and June 1999, out of 5,744,708 hemodialysis session, corresponding to a SCA rate of 7 per 100,000 hemodialysis sessions. Peak in frequency of SCA was more frequent on Monday, patients were more likely to have been treated with potassium dialysate between 0 or 1.0 mmol/L, were older (66.3±12.9 vs. 60.2±15.4

Letter to the Editor

Sudden cardiac arrest (SCA) is defined as sudden, unexpected loss of heart function, breathing and consciousness, resulting from an electrical disturbance in the heart stopping its action and blood flow, and cardiovascular diseases are the major risk factors for SCA. It has been reported that more than 20% of all deaths in patients with advanced chronic kidney disease is due to arrhythmias and SCA [1].

SCA is a malignant condition that could happen out-of-hospital or in-hospital. A metanalysis published in 2010 evaluating more than 140,000 patients, showed that in patients suffering an out-of-hospital SCA survival to hospital admission was 23.8% and survival to hospital discharge 7.6% [2].

Cooper, et al., analyzed more than 2,000 adult in-hospital cardiopulmonary resuscitation (CPR) attempts in a 1200-bed general hospital in UK in order to provide survival rates and associated factors from a 10-year study. Immediate survival rate following CPR was 38.6%, 24.7% at 24 h, 15.9% at discharge, and 11.3% at 12 months. There were very low survival rates for pulse-less electrical activity and asystole compared to ventricular fibrillation, and survival rates were higher in patients aged less than 60 years [3].

Cardiovascular diseases are a frequent complication of renal dysfunction and chronic kidney disease (CKD) and myocardial infarction and stroke have been reported to be risk factors for in-hospital mortality in these patients [4,5].

years), more likely to have diabetes (61.8 vs. 46.8%), and more likely to be dialyzed with a catheter as vascular access (34.1 vs. 27.8%) than the general hemodialysis population. Thirty-seven percent of subjects who had SCA had been admitted to hospital within the past 30 days, and 16% showed a decline in systolic pressure of 30 mm Hg or more before the event. Sixty percent of patients died within 48 hours of the arrest, including 13% while in the dialysis unit [10].

Bleyer, et al., evaluated the data from the United States Renal Data System (USRDS) in order to determine the day of death for United States hemodialysis and peritoneal dialysis patients from 1977 through 1997, and found that in hemodialysis patients, Monday and Tuesday were the most common days during which sudden and cardiac death happened [11].

Davis, et al., studied retrospectively the outcome of SCAs attended by Emergency Medical Services (EMS) staff during a period of 14 years. During the study period 102 SCAs occurred around the time of dialysis, 10 before, 72 during, and 20 after hemodialysis. Ventricular fibrillation or tachycardia was demonstrated in 72 cases. Of those who survived transportation to a hospital, survival to discharge was 24% with 15% survival at 1 year. Considering non-survivors 38% died in the dialysis facility, 18% died in the emergency department and 43% after hospital admission [12].

On the other hand treatment of SCA appears to be underutilized in patients with renal dysfunction, as shown by Moss, et al. who followed-up 221 dialysis patients who had a SCA. They found that only 74 (34%) had cardio-pulmonary resuscitation, only 6 out of 74 (8%) subjects survived to hospital discharge, and 2 out of 74 (3%) were still alive at 6 months after cardio-pulmonary resuscitation. Twenty-one (78%) of the 27 successfully resuscitated dialysis patients died after a few days. The study underlined that 95% of the deceased patients were on mechanical ventilation in an intensive care unit at the time of death [13].

Increased risk of SCA does not involve only patients with severe renal failure but also those with mild or moderate CKD, in fact reduction in glomerular filtration rate by 10 ml/min increases SCA risk by 11% [14], and decreasing renal function independently predict substantially increased risks of death and hospitalization in subjects with heart failure, being the risk directly proportional to CKD stage [15].

In 2003 Peberdy, et al., published the results on more than 14,000 in-hospital SCA recorded between January 2000 and June 2002 in 207 US hospitals included in the National Registry of Cardiopulmonary Resuscitation (NRCPR). Renal insufficiency was described as pre-existing condition in 29% and dialysis was an intervention reported in 3% of cases [16].

In 2010, Larkin using data from the same registry analyzed a cohort of more than 49,000 adults, and found that renal insufficiency or dialysis was reported in 32.5% of cases and the latter condition was independently associated with in-hospital mortality [17].

Moreover after a SCA surviving patients suffer consequences such as post-cardiac arrest syndrome (PCAS) due to anoxic brain injury, arrest-related myocardial dysfunction, and systemic ischemia/reperfusion response [18]. PCAS could also cause acute renal failure. Yanta et al., analyzed retrospectively 311 adult patients aged 58 years, admitted to an intensive care unit after successful resuscitation from out-of-hospital SCA, and found that 32 (10.3%) developed acute renal failure, of whom 13 (40.6%) were treated by renal replacement therapy, and 27 (8.7%) developed acute kidney injury. Development of renal failure was not associated with survival to hospital discharge [19].

All these data demonstrate that SCA and renal dysfunction are strongly related at every stage of the disease, CKD is a risk factor for SCA and SCA is an important cause of death in these population, suggesting a role for implantable cardioverter-defibrillator (ICD).

On the other hand impact of ICD implantation on survival of patients with renal dysfunction is still a matter of debate, on the other hand data suggest that the benefit decreases with worsening renal dysfunction [20].

CKD has been reported to be a clinical relevant predictor of mortality in patients undergoing ICD implantation for primary prevention purpose [21].

Goldenberg and colleagues performed a retrospective analysis of the outcome associated with renal dysfunction in patients enrolled in the Multicenter Automatic Defibrillator Implantation Trial-II, showing that decline in renal function by 10 ml/min/1.73m², increased the risk of SCA and all-cause mortality by 17 and 16%, respectively. ICD was clearly associated with a survival benefit in patients with GFR \geq 35 ml/min/1.73 m², on the other hand ICD had no benefit if GFR < 35 ml/min/1.73 m² [22].

Sakhuja, et al., conducted a meta-analysis in order to evaluate the effectiveness of ICD therapy in patients receiving dialysis, and found that despite having ICDs, uremic patients had a 2.7-fold higher mortality. Moreover they compared subjects receiving dialysis and those with CKD but not receiving dialysis, and did not find significant difference in mortality [23].

A considerable percentage of subjects affected by CKD have multiple comorbid conditions and poor functional capacity, suggesting a low expectation of survival with a good functional status. These data could suggest contraindication to ICD implantation. Herzog et al., evaluated survival of dialysis patients after SCA and the impact of ICD implantation, and found that only 7.6% of dialysis patients who survived after SCA received the device [24]. On the other hand Voigt, et al., analyzed the utilization of ICD in survivors of SCA in United States from 1996 to 2001 and found that only 30.7% of subjects were implanted before discharge [25].

Due to the close relationship between SCA and advanced renal dysfunction, dialysis units should be organized following

recommendations suggested by Surana, et al. [8], i.e. basic life support training of dialysis staff, presence of crash carts in place and availability of defibrillation.

On the other hand Lehrich et al., evaluated the effectiveness of automated external defibrillators (AED) use in outpatient dialysis clinics analyzing a cohort of 43,200 hemodialysis patients from 2002 to 2005 and recorded 729 in-center SCAs, and found that unfortunately AED presence was not associated with better outcome [26].

Makki, et al., performed a meta-analysis assessing the effect of ICD on all-cause mortality in CKD patients at high risk of sudden cardiac death and the effect of CKD on all-cause mortality in patients who already had an ICD for primary or secondary prevention purposes. Authors concluded that CKD was associated with greater risk of death, on the other hand, ICD implantation reduced mortality in CKD patients at high risk of SCA [27].

Hess, et al., evaluated more than 47,000 patients enrolled in the National Cardiovascular Data Registry ICD registry assessing the rate of death after primary prevention ICD placement between January 1, 2006, and December 31, 2007, according to CKD stage. They found that subjects with CKD were older, less commonly men, more often white, and more frequently had comorbid illness and that risk of death after ICD placement was proportional to CKD severity. Factors associated with increased risk of death included CKD severity, age >65 years, heart failure symptoms, diabetes mellitus, lung disease, serum sodium <140 mmol/L, atrial fibrillation or flutter, and a lower ejection fraction. They concluded that in patients with CKD, several factors could influence clinical decision making on primary prevention ICD candidacy [28].

These data were confirmed by Kiuchi et al., who demonstrated higher risk of anti-tachycardia therapy pacing in patients with left ventricular dysfunction, ICD and worsening renal dysfunction [29].

Moreover in order to create an advanced cardiac life support (ACLS) protocol suitable for patients with advanced renal dysfunction and identification of specific features that could be treatable by emergency physicians, the creation of an international database based on several reports and including different management of SCA in this population is desirable. Acute correction of metabolic acidosis could represent a very important factor in patients undergoing ACLS [30].

Management of CKD patients at risk for of rhythm disturbances is complex, due to fact that patients with CKD have higher burden of comorbidities. Drawing any conclusion on the best cost/effectiveness strategy to avoid SCA is difficult, probably patients need to be stratified on the basis of age and general clinical conditions and renal dysfunction per se, before prescribing any cardiac implantable electronic device. Further studies in this particular population are needed, requiring collaboration between cardiologists, nephrologists and other specialists.

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