

Sudden Death in Peritoneal and Hemodialysis Patients: Is There Any Difference?: Review

Periton Diyalizi ve Hemodiyaliz Hastalarında Ani Ölüm: Bir Fark Var mı?

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ABSTRACT Dialysis patients possess a very high rate of mortality. Cardiovascular diseases are still leading causes of death in this population. Most of deaths occur suddenly. Incidence of sudden death in general population is around 1/1000 person per year and peaks between 45 to 75 years of age. In general population sudden cardiac death occurs mostly in the context of ischemic heart disease. High rates of sudden death in dialysis patients can not be explained on the base of ischemic heart disease alone. There are many additional risk factors in dialysis patient. Also there is concern whether hemodialysis and peritoneal dialysis make any difference in terms of sudden death or not. Sharp fluid and electrolyte changes occur during hemodialysis sessions. Peritoneal dialysis offers more steady volume and electrolyte management. On the other hand peritoneal dialysis process exposes patient to a high burden of glucose. Obesity, dyslipidemia and anemia issues are also somewhat different between peritoneal and hemodialysis patients. Treatment of heart diseases in dialysis patients is also not promising. We review current medical literature for comparison of these two dialysis modalities in terms of sudden death.

Key Words: Death, sudden; peritoneal dialysis; renal dialysis

ÖZET Diyaliz hastalarında mortalite oranı çok yüksektir. Kardiyovasküler hastalıklar en sık ölüm nedenleridir. Ölümler sıklıkla ani ölüm şeklindedir. Ani ölüm insidansı genel popülasyonda 1/1000 civarındadır ve 45 ile 75 yaşları arasında tepe noktasına ulaşır. Genel popülasyondaki ani ölüm olayları çoğunlukla iskemik kalp hastalığı zemininde oluşmaktadır. Diyaliz hastalarındaki yüksek ani ölüm oranları tek başına iskemik kalp hastalığıyla açıklanamamaktadır. Diyaliz hastalarında ek risk faktörleri vardır. Hemodiyaliz ve periton diyalizinin ani ölüm yönünden fark oluşturup oluşturmadıkları konusu da bu çerçevede ilgi çekmektedir. Hemodiyaliz seansları sırasında hızlı sıvı ve elektrolit değişimleri olur. Periton diyalizi daha yavaş bir sıvı ve elektrolit değişimi imkanı vermektedir. Öte yandan periton diyalizi işleminde hastalar çok yüksek glikoz yüküne maruz kalmaktadır. Obezite, dislipidemi ve anemi konularında da hemodiyaliz ve periton diyalizi arasında farklar vardır. Diyaliz hastalarında kalp hastalıklarının tedavisi de yüz güldürücü değildir. Diyaliz modaliteleri arasında, ani ölüm yönünden farklılıkları ortaya koymak amacıyla mevcut tıbbi literatür gözden geçirildi.

Anahtar Kelimeler: Ölüm, ani; periton diyalizi; böbrek diyalizi

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SUDDEN CARDIAC DEATH IN GENERAL POPULATION

Sudden death is generally accepted as a rapid death occurring within an hour after start of symptoms in a previously asymptomatic patient. Incidence is around 1/1000 person per year and peaks between 45 to 75 years of age. In general population, sudden cardiac death (SCD) occurs in

the context of ischemic heart disease in 80% and nonischemic cardiomyopathies in 10-15% of victims. Some other vascular, genetic, neoplastic and inflammatory conditions also lead to SCD. Low ejection fraction is a powerful predictor of SCD. Left ventricular hypertrophy (LVH), prolonged QT interval, QT dispersion, intraventricular conduction abnormalities (QRS duration), premature ventricular contractions and non-sustained ventricular tachycardia in a diseased heart may be markers of sudden death.¹ Triggering event in a vulnerable myocardium can lead fatal arrhythmia. Final common rhythms leading to death are ventricular tachycardia, fibrillation and bradyarrhythmias.²

SUDDEN DEATH IN GENERAL DIALYSIS POPULATION

Heart diseases are leading causes of death in dialysis patients and 60% of cardiac deaths occur as SCD, making 27% of total deaths, although a study reports stroke as most frequent cause of sudden death. Rate of SCD increases as glomerular filtration rate drops and reaches highest level as the patient's renal functions deteriorates to dialysis level. Risk of SCD increases with the time spent on dialysis.³⁻⁵

Coronary heart disease and cardiac ischemia from classical coronary atherosclerosis with plaque rupture are the main cause of sudden death in general population. Contrary to the general population, classical coronary heart disease may not be responsible for the majority of sudden death in dialysis population.⁶ Despite revascularization for obstructive coronary disease in end stage kidney disease (ESKD) patients, the incidence of SCD still remains high.⁷ Yet exact role of ischemic heart disease is not known, since diagnosis of myocardial infarction or injury may not be possible because of deaths occurring outside the hospitals and decreased specificity of cardiac markers of injury in ESKD. In general population decreased systolic function is the greatest risk factor for SCD. It is also common in dialysis patients and is associated with poor prognosis.⁸ On the other hand at initiation of dialysis minority of patients have systolic dysfunction (16%), but the incidence of SCD is still high. Some form of resistance to treatment is also re-

TABLE 1: Comparison of risk factors for sudden cardiac death in peritoneal and hemodialysis patients

	Peritoneal Dialysis	Hemodialysis
High systolic blood pressure	+ ⁵	+ ^{36*}
Low diastolic blood pressure	+ ⁵	?
Diabetes Mellitus	+ ⁴³	+ ³⁴
Level of glycemia	?	+ ³⁴
Ischemic heart disease	+ ⁷	+ ⁷
Systolic dysfunction	+ ^{5,8}	+ ⁸
Left ventricular hypertrophy	+ ⁸	+ ⁸
QT dispersion	+ ⁴¹	+ ⁴²
Atrial fibrillation	?	+ ²⁰
Microvascular injury	?	+ ¹⁰
Decreased baroreflex sensitivity	+ ¹²	+ ¹²
Rapid electrolyte changes	?	+ ¹⁵
Dyskalemia	?	+ ²⁰
Obstructive sleep apnea	?	+ ²⁸
Ultrafiltration volume	?	+ ³⁵
Vitamin D	± ⁴⁶	+ ²⁹

Numbers indicate selected references.

+ Yes; * Only long lasting hypertension; ? No data=May be.

ported.⁹ Additional factors that may render a dialysis patient to relatively vulnerable to SCD and resistant to treatments are sought (Table 1).

SUDDEN DEATH IN HEMODIALYSIS PATIENTS

A study by Nishimura et al. on hemodialysis (HD) patients shows that there may be microvascular injury which is reflected by impaired fatty acid metabolism in apparently normal coronary perfusion state.¹⁰ Microvascular disease is also reported by other researchers.¹¹ Baroreflex sensitivity is another mechanism related to SCD. Baroreflex becomes less sensitive in chronic renal failure and degree of loss of sensitivity is equal in both dialysis modalities.¹² LVH, which is highly prevalent in ESKD patients, rapid fluid and electrolyte changes, autonomic dysfunctions, endothelial dysfunction, interstitial fibrosis, inflammation, malnutrition, high phosphorous levels may contribute to a resistant state to treatment.¹³⁻²¹

QT prolongation and increased QT dispersion, which is defined as the difference of longest and shortest QT intervals on standard electrocardio-

gram, are frequently seen in dialysis patients and related to SCD.^{22,23} QT prolongation may occur during dialysis session and is related to serum calcium level.²⁴ QT prolongation may result from electrical inhomogeneity which may be related to LVH and fibrosis.²⁵ Iron overload is also reported to prolong QT interval.²⁶ In animal model over-expressed angiotensin causes defects in potassium channels, gap junction proteins and electrical remodeling.²⁷ Obstructive sleep apnea is common among dialysis patients and related to SCD. It may affect 21-47% of dialysis patients compared to 2-4% of general population.²⁸ Data from The German Diabetes and Dialysis Study (Die Deutsche Diabetes Dialyze, 4D) study suggests that SCD is increased three-fold in dialysis patients with vitamin D level <25 nmol/L compared to those with vitamin D level >75 nmol/L.²⁹ Non-dialysis patients with vitamin D deficiency have also increased risk of SCD.³⁰ On the other hand injectable vitamin D analogue use is associated with increased SCD.³¹ High levels of P-selectin, a molecule associated with inflammation and atherosclerosis, at initiation of dialysis is associated with sudden SCD among male dialysis patients. Dialysis modality does not affect outcomes.³²

Regional wall motion abnormality seen during HD progresses to fixed systolic dysfunction and this is associated with increased risk of death.³³ In sub-group analysis of 4D study, poor glycemic control in HD patients was strongly associated with SCD in diabetic hemodialysis patients.³⁴ Dyskalemia in hemodialysis patients is associated with SCD.²⁰

Pun et al. reported that exposure to dialysate that has low potassium and calcium levels, increased ultrafiltration volume, low predialysis serum creatinine level are strongly associated with SCD in HD patients.³¹ They have also claimed that history of coronary heart disease, congestive heart failure, diabetes mellitus and hypertension were not significantly associated with SCD. Paoletti et al. also found no relation with SCD and some traditional risk factors including diabetes mellitus and systolic hypertension. A prospective study of 123 patients for 10 years revealed that long lasting hy-

perension was significantly more frequently observed in SCD compared to patients dying from other reasons (129 vs. 53 months).³⁵

SUDDEN DEATH IN PERITONEAL DIALYSIS PATIENTS

Effect of dialysis modality on SCD is subjected to some studies. More steady nature of fluid and electrolyte changes in peritoneal dialysis (PD) can provide some advantage over HD.¹⁵ Despite this overt advantage of peritoneal dialysis, SCD rates are not lower than that of HD. It is reported that, PD patients would have a higher risk of SCD than HD patients after two years of initiation of dialysis.³⁶ There are some reports showing equal, even better survival in PD compared to HD patients, but data on sudden death are not presented.^{37,38}

Data regarding SCD in PD patients are relatively less than that of HD patients. Some of the studies include data from both HD and PD patients, but the data are neither presented separately nor in comparison with each other (Table 1).

Kawaguchi et al. have reported reasons for drop outs among 5391 PD patients.³⁹ They observed 82 deaths, 9.6 % of which were regarded as sudden death. Cerebrovascular accidents, ischemic heart disease and congestive heart failure were responsible from 22%, 14.6% and 8.5% of deaths respectively. Most of the risk factors for SCD are common to PD and HD patients. Malnutrition and hypoalbuminemia are seen in both dialysis modalities, but are more prevalent among PD patients. Paoletti et al. have reported that hypoalbuminemia is associated with SCD significantly, but they did not present data from HD and PD patients separately. QT dispersion is reported to be greater in PD patients.³⁵ However other reports do not confirm this finding.^{40,41}

In one of the few studies performed solely on PD patients, some authors found that left ventricular systolic dysfunction is the most significant predictor of sudden cardiac death, followed by high systolic and low diastolic blood pressure. They have reported that ejection fraction cut off of 48.0% was associated with a specificity of 78.6% and a sensi-

tivity of 57.7% in predicting sudden cardiac death. N-terminal pro-brain natriuretic peptide was more significantly associated with SCD than cardiac troponin. Chow et al. reported that likelihood of SCD increases in PD patients when the patient is male, has diabetes mellitus and blood transfusions.⁴² Glycemic control, indicated by glycated hemoglobin (HbA1c) was associated with all cause mortality both in diabetic and non-diabetic PD patients, but data on SCD were not presented separately.^{43,44}

Effects of Vitamin D level on SCD in PD patients are not determined precisely. Three year follow-up of 230 PD patients resulted in 70 deaths. Of them 18 were as SCD and 12 due to other cardiovascular events. They found that there were no additional effects of low vitamin D status on cardiovascular events in patients with established systolic dysfunction and LVH (Table 1).⁴⁵

PREVENTION OF SCD IN ESKD PATIENTS

For hemodialysis, prevention of large potassium swings may reduce sudden death.¹⁶ But this is not the case in peritoneal dialysis. Studies on other measures to reduce SCD in dialysis patients do not

make distinction between HD and PD patients. So there is no reliable data to compare HD and PD patients.

Carvedilol may increase survival in dialysis patient with dilated cardiomyopathy.⁴⁶ Angiotensin converting inhibitors and angiotensin receptor blockers has been shown to be helpful in some studies.^{47,48} Increased usage of ACE inhibitors and beta-blockers are recommended.⁴⁹

Intracardiac defibrillator (ICD) therapy prevented arrhythmic deaths, but their rate of non-arrhythmic adverse outcomes were high.⁵⁰ ICDs can increase survival in dialysis patients but not to degree of non-dialysis patients.⁵¹ Despite having ICDs, patients receiving dialysis had a 2.7-fold higher mortality compared with those not receiving dialysis. It is also proposed that beta-blockers might be less cardioprotective in this population than in patients not receiving dialysis.⁵² Rate of complications is high and ESKD patients are less responsive to ICD.⁵³ It is not recommended for advanced aged dialysis patients.⁵⁴

Finally, there are no studies suggesting benefit of increasing dialysis dose on SCD.

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