Peritoneal Dialysis International, Vol. 35, pp. 388–396
doi: 10.3747/pdi.2014.00278

0896-8608/15 $3.00 + .00

ISPD GUIDELINES/RECOMMENDATIONS

ISPD CARDIOVASCULAR AND METABOLIC GUIDELINES IN ADULT PERITONEAL DIALYSIS PATIENTS PART II – MANAGEMENT OF VARIOUS CARDIOVASCULAR COMPLICATIONS

Angela Yee Moon Wang,[1] K. Scott Brimble,[2] Gillian Brunier,[3] Stephen G. Holt,[4] Vivekanand Jha,[5] David W. Johnson,[6,7] Shin-Wook Kang,[8] Jeroen P. Kooman,[9] Mark Lambie,[10] Chris McIntyre,[11] Rajnish Mehrotra,[12] and Roberto Pecoits-Filho[13]

Department of Medicine,[1] Queen Mary Hospital, University of Hong Kong, Hong Kong; St. Joseph's Healthcare,[2] McMaster University, Hamilton, Ontario, Canada; Lawrence S. Bloomberg Faculty of Nursing,[3] University of Toronto, Toronto, Ontario, Canada; Division of Nephrology,[4] The Royal Melbourne Hospital, University of Melbourne, Melbourne, Australia; George Institute for Global Health India,[5] Postgraduate Institute of Medical Education and Research, Chandigarh, India; University of Queensland at Princess Alexandra Hospital,[6] Brisbane, Australia; Centre for Kidney Disease Research,[7] Translational Research Institute, Brisbane, Australia; Department of Internal Medicine,[8] College of Medicine, Severance Biomedical Science Institute, Yonsei University, Korea; Division of Nephrology,[9] University Hospital Maastricht, Maastricht, The Netherlands; Health Services Research Unit,[10] Institute for Science and Technology in Medicine, Keele University, Keele, Staffordshire, United Kingdom; School of Medicine,[11] University of Nottingham, Royal Derby Hospital Centre, Derby, United Kingdom; Harborview Medical Center,[12] Division of Nephrology/Department of Medicine, University of Washington, Washington, DC, United States; and School of Medicine,[13] Pontifícia Universidade Católica do Paraná, Curitiba, Paraná, Brazil

Cardiovascular mortality has remained high in patients on peritoneal dialysis (PD) due to the high prevalence of various cardiovascular complications including coronary artery disease, left ventricular hypertrophy and dysfunction, heart failure, arrhythmia (especially atrial fibrillation), cerebrovascular disease, and peripheral arterial disease. In addition, nearly a quarter of PD patients develop sudden cardiac death as the terminal life event. Thus, it is essential to identify effective treatment that may lower cardiovascular mortality and improve survival of PD patients. The International Society for Peritoneal Dialysis (ISPD) commissioned a global workgroup in 2012 to formulate a series of recommendation statements regarding lifestyle modification, assessment and management of various cardiovascular risk factors, and management of the various cardiovascular complications to be published in 2 guideline documents. This publication forms the second part of the guideline documents and includes recommendation statements on the management of various cardiovascular complications in adult chronic PD patients. The documents are intended to serve as a global clinical practice guideline for clinicians who look after PD patients. We also define areas where evidence is clearly deficient and make suggestions for future research in each specific area.

***Perit Dial Int* 2015; 35(4):388–396 www.PDIConnect.com**
doi: 10.3747/pdi.2014.00278

KEY WORDS: Coronary artery disease; heart failure; left ventricular hypertrophy; stroke; peripheral artery disease; atrial fibrillation; sudden cardiac death; peritoneal dialysis.

Cardiovascular morbidity and mortality remain high in patients on peritoneal dialysis (PD). An earlier analysis based on the United States Renal Data System indicated that dialysis patients whose condition was complicated by an acute myocardial infarction had high mortality from cardiac causes and poor long-term survival. The poor survival rates after acute myocardial infarction persisted over time in these patients even in the reperfusion era (1). The other key cardiovascular complication in PD patients is left ventricular hypertrophy which has an estimated prevalence ranging from 44% to

Correspondence to: Dr. Angela Yee Moon Wang, Department of Medicine, Queen Mary Hospital, University of Hong Kong, 102 Pok Fu Lam Road, Hong Kong.
aymwang@hkucc.hku.hk
Received 2 March 2015; accepted 15 March 2015.
Supplemental material available at www.pdiconnect.com

over 90% (2,3). Left ventricular hypertrophy predicts an increased risk of mortality and adverse cardiovascular outcomes in PD patients (3). In particular, it is associated with an increased risk of heart failure/circulatory congestion (4). In PD patients, the reported prevalence of heart failure is estimated around 35% and even higher, up to 60% among those whose condition was previously complicated by heart failure (4). Notably, more than half of the PD patients with heart failure have normal ejection fraction, indicating that diastolic dysfunction is an important contributing factor to heart failure in these patients (5). The presence of heart failure is a powerful predictor of adverse clinical outcomes in dialysis patients (4). Data from the United States Renal Data System suggest that heart failure is a very frequent cause of hospitalization in dialysis patients, and the mortality rate after heart failure was 83% at 3 years (6). Furthermore, nearly 25% of all deaths in dialysis patients, including those receiving PD, are sudden cardiac death in nature (7,8), of which the underlying mechanisms remain far from clear. Impaired left ventricular systolic dysfunction is one of the key predictors of sudden cardiac death in PD patients (8). On the other hand, a recent analysis from a large nationwide retrospective cohort from Taiwan showed that PD patients are at increased risk of stroke in comparison with an age- and sex-matched reference cohort, though the risk of hemorrhagic stroke appeared lower compared with hemodialysis patients (9). Peripheral arterial disease is also exceedingly common in PD patients, with a reported prevalence of 28.5% (range, 4.8% – 47%) in PD patients, the majority of whom have subclinical peripheral arterial disease (10). The prevalence of peripheral arterial disease is increasing with the increasing global incidence of diabetes as the cause of end-stage renal disease. Peripheral arterial disease is also a strong predictor of adverse clinical outcomes and mortality (10). Last but not least, atrial fibrillation is an important, and also the most common, abnormal cardiac rhythm in dialysis patients. The exact prevalence in PD has not been determined but, in hemodialysis, it is estimated around 12.5 – 27% and is associated with an increased risk of stroke (11,12).

The current publication forms the second International Society for Peritoneal Dialysis (ISPD) cardiovascular and metabolic guideline document, makes recommendations on assessment and management of coronary artery disease, left ventricular hypertrophy and dysfunction, heart failure, arrhythmia (specifically atrial fibrillation), cerebrovascular disease, peripheral vascular disease and sudden cardiac death. There are altogether 26 guideline statements of which only 5 statements are graded as level 1 or 'strong' recommendations, 18 statements are graded as level 2 or 'weak' recommendations and 3 statements are ungraded. Each guideline statement is provided with a brief rationale paragraph and key references. Full detailed rationale and evidence review tables are provided in the online publication. In addition, the workgroup has defined areas where evidence is clearly deficient and provided a list of suggestions for future research in each specific area.

GUIDELINE 3.1. CORONARY ARTERY DISEASE

3.1.1 We recommend serial measurements of cardiac troponins be used to evaluate acute myocardial infarction and acute coronary syndrome in peritoneal dialysis patients with acute symptoms (chest pain), along with electrocardiographic changes or other clinical evidence suggestive of acute myocardial ischemia. (1B). A rise in troponin level of >20% within 4 – 6 hours with at least 1 value above the 99th percentile should be diagnosed as acute myocardial infarction or acute coronary syndrome. (1C)

RATIONALE: Troponin I (TnI) or Troponin T (TnT) levels are frequently elevated in dialysis patients. Whilst there may be changes in the removal of troponins or fragments by residual renal function or different dialysis modalities, the consensus is that elevated levels represent an increased 'leak' of these markers from myocytes (13). Whilst there are subtle differences between TnI and TnT in renal failure, these are unlikely to be clinically relevant. It is difficult to define a reference range in the normal population, and even more difficult in dialysis patients; thus, a single elevated troponin level without clinical correlates is unlikely to be helpful, apart from indicating an enhanced cardiovascular risk (14). A rise in serial markers, along with appropriate clinical context, is the currently accepted definition of an acute coronary syndrome (15). The difficulty lies in the definition of how much change constitutes a significant change. A 20% serial change is taken as ~3 standard deviation of change and assumes an analytical coefficient of variation of up to 7% (16).

3.1.2 We suggest asymptomatic peritoneal dialysis patients incidentally found to have high cardiac troponins without dynamic changes be considered as having an elevated cardiovascular risk (2B) and may benefit from investigation for underlying cardiac disease such as cardiac hypertrophy, dysfunction, or occult coronary artery disease (ungraded).

RATIONALE: There are limited data on the utility of a single troponin result. There are some data on the utility of troponin in transplant workup, but no good evidence that elevated troponin can be reduced by any intervention, or that intervention improves outcomes. Nevertheless, there may be a rationale for looking at patients with high troponin levels to see whether all cardiovascular risks have been appropriately addressed with interventions that potentially improve outcomes (for example, volume and blood pressure control to improve left ventricular hypertrophy or coronary artery angioplasty/bypass in those with proven coronary artery disease) but the evidence for this in PD is lacking (17).

3.1.3 We recommend a thorough history and physical examination in all patients initiating peritoneal dialysis therapy to identify any significant cardiac conditions including coronary artery disease, recent myocardial

infarction, decompensated heart failure, significant arrhythmias, and severe valvular disease for further specific management. (1D)

RATIONALE: Cardiovascular disease is under-diagnosed and under-treated in patients with chronic kidney disease (CKD), including those on PD (18,19). Identifying treatable disease is desirable. Many cardiovascular disease symptoms and signs may be masked in patients on dialysis (18,19). A good history and physical examination will identify many abnormalities or provide a clue to further workup. Moreover, it is not associated with any adverse effect or additional cost.

3.1.4 We suggest noninvasive stress testing be considered in peritoneal dialysis patients who are kidney transplant candidates without active cardiac conditions and who have 3 or more of the following coronary artery disease risk factors: diabetes mellitus, prior cardiovascular disease, >1 year on dialysis, left ventricular hypertrophy, age >60 years, smoking, hypertension, and dyslipidemia. (2C)

RATIONALE: There is no evidence to suggest that universal screening for coronary artery disease is beneficial. Furthermore, it increases costs and may be harmful (20). Myocardial perfusion studies such as dobutamine stress echocardiography and thallium scintigraphy are useful in identifying patients with significantly increased risk of future myocardial infarction and coronary artery disease in both diabetic and non-diabetic end-stage renal disease patients (21,22). Relevant risk factors for coronary artery disease include diabetes mellitus, prior cardiovascular disease, >1 year on dialysis, left ventricular hypertrophy, age >60 years, smoking, hypertension, and dyslipidemia. The specific number of risk factors that should be used to initiate testing remains to be determined but ≥3 is regarded as a reasonable threshold (19).

3.1.5 We suggest peritoneal dialysis patients with ischemic heart disease be treated with antiplatelet agents. (2D)

RATIONALE: Compared with the general population, dialysis patients with ischemic heart disease are less likely to be put on anti-platelet agents despite their proven benefits (23–25). Therefore, unless there is clear evidence of an increased bleeding risk, all PD patients with ischemic heart disease should receive anti-platelet agents according to current recommendations for the general population.

GUIDELINE 3.2. LEFT VENTRICULAR HYPERTROPHY, DYSFUNCTION, AND HEART FAILURE

3.2.1 We suggest evaluation of left ventricular hypertrophy, dilatation, systolic and diastolic function, as well as cardiac valvular abnormalities including valvular calcification, using echocardiography in peritoneal dialysis patients after initiation of peritoneal dialysis and repeat if change in clinical status. (2C)

RATIONALE: Left ventricular hypertrophy, systolic and diastolic dysfunction, as well as cardiac valvular calcifications, are all highly prevalent in PD patients and predict an increased risk of all-cause and cardiovascular mortality (26). Systolic dysfunction also predicts an increased risk of heart failure and sudden cardiac death in PD patients (4,8).

3.2.2 We suggest peritoneal dialysis patients with significantly impaired systolic function be evaluated for the presence of coronary artery disease. (2C)

RATIONALE: The presence of left ventricular systolic dysfunction or clinically evident heart failure may reflect underlying coronary ischemia.

3.2.3 We suggest peritoneal dialysis patients with left ventricular hypertrophy or heart failure be considered for treatment with an angiotensin converting enzyme inhibitor or angiotensin receptor blocker. (2D)

RATIONALE: Data regarding the use of angiotensin converting enzyme inhibitors (ACEIs) or angiotensin receptor blockers (ARBs) for cardiovascular protection have remained scanty and there are virtually no hard outcome studies in PD patients. One randomized controlled trial (27) reported a non-significant 7% reduction in cardiovascular events after 24 months of treatment with an ACEI in hemodialysis patients compared with placebo in the intention to treat analysis. A secondary per-protocol analysis suggested a trend towards benefit in the composite cardiovascular endpoint with ACEIs. Another small open-labeled randomized trial suggested a reduction in mortality and cardiovascular events with an ARB compared with placebo but patients with background symptomatic cardiac disease were excluded (28). Cice *et al.* reported significant long-term survival and cardiovascular benefits and reduction in hospitalization for heart failure over 3 years by combining an ACEI with an ARB in hemodialysis patients with class II-III heart failure and systolic dysfunction (29). Another recent meta-analysis suggested that left ventricular mass index may regress more with ARB treatment than without in CKD (30). Given the overall very limited evidence, a weak recommendation was drawn in relation to the use of ACEIs or ARBs for cardiovascular disease in PD patients.

3.2.4 We suggest peritoneal dialysis patients with left ventricular hypertrophy, dilated cardiomyopathy, or systolic heart failure be considered for treatment with a beta-blocker. (2C)

RATIONALE: Treatment with a beta blocker significantly improved left ventricular remodeling, systolic function, and functional class of hemodialysis patients with dilated cardiomyopathy compared with placebo (31,32), and improvement was maintained up to 24 months. Subsequent extended follow-up of the same cohort reported a significant survival benefit, fewer cardiovascular deaths, all-cause hospitalizations, fewer

fatal myocardial infarctions, fatal strokes, and hospitalizations for worsening heart failure with carvedilol than with placebo. However, there are so far no randomized trials examining the efficacy of beta-blockers for cardiovascular protection in PD patients.

3.2.5 We suggest peritoneal dialysis patients already receiving an angiotensin converting enzyme inhibitor or angiotensin receptor blocker be considered for treatment with a mineralocorticoid receptor antagonist. (2B)

RATIONALE: Spironolactone has been shown to significantly reduce the progression of left ventricular mass index over a 24-month period and improve the rate of change of ejection fraction at 24 weeks in PD patients compared with controls (33). A recent open-label, randomized controlled trial showed that adding spironolactone to ACEI or ARB significantly lowered the risk of reaching the primary composite endpoint of death from cardiovascular and cerebrovascular events and hospitalizations due to cardiovascular and cerebrovascular events and risk of all-cause deaths in oligoanuric hemodialysis patients (34).

3.2.6 We suggest peritoneal dialysis patients with heart failure and anemia receive treatment for anemia and have target hemoglobin no different from peritoneal dialysis patients without heart failure. (2D)

RATIONALE: Current available evidence does not support correction of anemia as a therapeutic strategy for regressing left ventricular hypertrophy and dilatation or preventing heart failure in PD patients. No randomized controlled trial has examined whether treatment of anemia may improve hard outcomes of PD patients with heart failure.

GUIDELINE 3.3. STROKE

3.3.1 We suggest carotid duplex ultrasonography be performed early in peritoneal dialysis patients with transient ischemic attack or acute thromboembolic stroke to identify the presence of significant carotid artery stenosis. (ungraded)

RATIONALE: There is very limited evidence to guide routine screening for cerebrovascular disease in dialysis patients, including PD patients. Given the lack of evidence, we recommend following the American Heart Association (AHA) guidelines (35) in managing PD patients with transient ischemic attack or stroke. The AHA guidelines recommend that, as part of the diagnostic workup for patients presenting with transient ischemic attack or ischemic stroke, the high-risk, modifiable condition of carotid artery stenosis be excluded as a cause of the ischemic symptoms.

3.3.2 We suggest that peritoneal dialysis patients not be routinely prescribed antiplatelet therapy for primary prevention of cerebrovascular disease. (2C)

RATIONALE: Antithrombotic therapy is recommended by the AHA Guidelines for Primary Prevention of Stroke for those patients considered to be at high cardiovascular risk, but not for those at low risk (36). However, a recent Cochrane review evaluating the effects of antiplatelet therapy on cardiovascular events, mortality, and bleeding in 11,701 patients with CKD and with either stable or no cardiovascular disease found that antiplatelet therapy was associated with uncertain effects on stroke and an increased risk of minor bleeding (37). Given the unclear benefit of antiplatelet therapy for primary stroke prevention and the increased risk of bleeding in patients with CKD, we felt that PD patients should not routinely be prescribed antiplatelet therapy for primary prevention of cerebrovascular disease.

3.3.3 We suggest individualization of warfarin prescription for prevention of stroke in peritoneal dialysis patients with atrial fibrillation in view of an increased risk of bleeding and uncertain effects on cerebrovascular outcomes. (2D)

RATIONALE: Although antithrombotic therapy is recommended by the AHA Guidelines for Primary Prevention of Stroke for patients with atrial fibrillation to prevent stroke (38), all the trials upon which this recommendation was based excluded dialysis patients. A systematic review of 8 studies (including case series, cohort studies, and randomized controlled trials) evaluating warfarin therapy in hemodialysis patients found that the rates of major bleeding episodes for those receiving warfarin were approximately twice the rate expected in hemodialysis patients receiving either no warfarin or subcutaneous heparin (39). Moreover, a systematic review and meta-analysis of 25 studies (including cross sectional and cohort studies) evaluating outcomes of stroke in dialysis patients with atrial fibrillation found that, while atrial fibrillation was associated with almost a 2-fold increased risk of stroke and mortality in these patients compared with dialysis patients without atrial fibrillation, overall, warfarin use did not appear to decrease the risk of the combined outcome of hemorrhagic and ischemic stroke, especially in the larger studies (40). Thus, the risk-to-benefit ratio of warfarin for stroke prevention in dialysis patients, including patients on PD, with atrial fibrillation is uncertain and we feel should be individualized.

3.3.4 We do not recommend the use of novel oral anticoagulants to prevent stroke in atrial fibrillation in peritoneal dialysis patients. (1D)

RATIONALE: While new oral anticoagulants are now available to prevent stroke in patients with atrial fibrillation, all these new oral anticoagulants are mostly cleared by the kidney and are contraindicated in patients with CKD stage 5 on dialysis (41,42). Thus, we do not recommend use of these new oral anticoagulants for stroke prevention in patients on PD with atrial fibrillation.

3.3.5 We suggest caution with administration of thrombolytic therapy to peritoneal dialysis patients with acute ischemic stroke in view of uncertainty regarding whether benefits outweigh risks. (ungraded)

RATIONALE: Current available evidence is insufficient to draw any recommendation in relation to the use of thrombolytic agents as a treatment of acute ischemic stroke in patients on dialysis (43). Thus, a very careful assessment of risks vs benefits must be undertaken before administering intravenous thrombolytics for treatment of acute ischemic stroke in dialysis patients, including patients on PD.

GUIDELINE 3.4. PERIPHERAL ARTERIAL DISEASE

3.4.1 We recommend peritoneal dialysis patients, particularly those with diabetes mellitus, have regular clinical evaluation for peripheral arterial disease (including inquiry of symptoms of intermittent claudication and rest pain, examination of signs for peripheral arterial disease, and palpation of peripheral arterial pulses). (1D)

RATIONALE: Although there are no studies comparing routine clinical evaluation of stage 5 CKD patients for peripheral arterial disease (PAD) vs evaluation only in response to symptoms, the Kidney Disease: Improving Global Outcomes (KDIGO) CKD Guidelines recommend that "adults with CKD be regularly examined for signs of PAD and be considered for usual approaches to therapy (1B)" (44). Given the high prevalence of clinical and subclinical PAD in PD patients, especially among diabetics, and the adverse clinical outcomes associated with PAD, the workgroup felt that a strong recommendation should be given for regular clinical evaluation of PAD in PD patients.

3.4.2 We suggest an ankle-brachial index <0.9 be used to aid the diagnosis of peripheral arterial disease in peritoneal dialysis patients. (2D)

RATIONALE: The most common screening test employed to detect PAD in studies of PD patients was the ankle-brachial index (ABI) using a cut-point of ≤0.9 to define PAD. This threshold has been reported to have a sensitivity of 95% and a specificity of 100% for PAD detection in patients without CKD, although there are no studies examining the sensitivity and specificity of ABI in PD (or hemodialysis or CKD) patients specifically. Using ABI has been recommended for general population screening in at-risk patients by the American College of Cardiology (ACC)/AHA (45,46) or in patients with suspected PAD by the Trans-Atlantic Inter-Society Consensus Document on Management of Peripheral Arterial Disease (TASC II) guidelines (47).

3.4.3 We suggest a toe-brachial index ≤0.6 be used in addition to the ankle-brachial index to aid in the diagnosis of peripheral arterial disease in symptomatic patients in whom the ankle-brachial index is unreliable due to non-compressible vessels (such as when the ankle-brachial index is ≥1.3). (2D)

RATIONALE: In patients with abnormally high ABI values due to non-compressible vessels (for example those with medial arterial calcification), the AHA/ACC and TASC II guidelines recommend measuring the toe-brachial index (TBI) using a cut-point ≤0.6 to define PAD as toe arteries are less likely to be affected by vascular calcification than ankle arteries (45–47). There are only 2 studies of TBI in PD patients, which did not evaluate the sensitivity and specificity of cut-point values and/or the clinical performance of ABI and TBI relative to color Doppler, angiography, or prediction of future limb vascular complications.

3.4.4 We suggest peritoneal dialysis patients with non-critical peripheral arterial disease receive supervised exercise therapy. (2C)

RATIONALE: Exercise therapy has been found in general PAD patient populations with intermittent claudication to have equivalent effectiveness to percutaneous luminal angioplasty in a meta-analysis of 8 randomized controlled trials (48) and to produce significantly improved walking time, pain-free walking distance, and maximum walking distance (but not mortality, amputation, peak exercise calf blood flow or ABI) compared with usual care or placebo in a meta-analysis of 22 trials involving 1,200 participants (49). There are no randomized controlled trials testing the efficacy of exercise therapy in CKD patients with PAD. However, given the overall benefits of exercise in CKD patients, the workgroup felt that a weak recommendation for prescribing supervised exercise therapy in PD patients with non-critical PAD was justified.

3.4.5 We suggest peritoneal dialysis patients with peripheral arterial disease be considered for antiplatelet therapy. (2D)

RATIONALE: In a recent systematic review and meta-analysis (25,37) of 31 randomized controlled trials of 11,701 adult patients with CKD and stable or no cardiovascular disease, antiplatelet therapy was associated with a reduction in myocardial infarction and an increased risk of minor bleeding and uncertain effects on stroke, all-cause mortality, cardiovascular mortality, and major bleeding. None of these studies examined PD patients or the use of anti-platelet therapy as a treatment for PAD. The Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines (50) recommend CKD patients with PAD be treated with antiplatelet agents, as in the general population. However, the KDIGO Cardiovascular update (51) emphasizes that evidence is lacking and that bleeding risks may be increased. Given the current lack of randomized controlled trials and a high degree of uncertainty regarding the risk vs benefit associated with antiplatelet therapy in PD patients with PAD, the workgroup felt a weak recommendation was justified.

3.4.6 We suggest peritoneal dialysis patients with peripheral arterial disease, particularly those with diabetes mellitus, receive multidisciplinary foot care involving regular foot examination, treatment by a podiatrist/chiropodist and education about home foot care (including use of hydrating lotions and appropriate foot wear). (2C)

RATIONALE: Five low quality studies of diabetic CKD patients (including 3 studies exclusively in dialysis patients) have reported reductions in amputations following institution of multidisciplinary preventive foot care programs. The KDIGO CKD Guidelines suggest that "adults with CKD and diabetes are offered regular podiatric assessment (2A)" (44).

GUIDELINE 3.5. ARRHYTHMIA

3.5.1 We recommend all peritoneal dialysis patients undergo a 12-lead electrocardiography at initiation of dialysis and then repeat at least annually to screen for any abnormal electrical activity of the heart including atrial fibrillation. (1C)

RATIONALE: The exact prevalence of atrial fibrillation has not been determined in PD, but in hemodialysis it is estimated around 12.5 – 27% and is much higher than the prevalence rates described for the general population. An even higher prevalence is described when Holter monitoring technique is employed (52,53). The risk of hospitalization due to atrial fibrillation increases linearly with the decrease in glomerular filtration rate (GFR). The mortality rates for dialysis patients with atrial fibrillation were also significantly higher than for control subjects (54). Therefore, regardless of whether atrial fibrillation is an independent risk factor for mortality or represents a risk predictor, we recommend that atrial fibrillation be regularly screened in all PD patients, because it indicates a markedly increased risk for comorbidities and death.

GUIDELINE 3.6. SUDDEN CARDIAC DEATH

3.6.1 We suggest peritoneal dialysis patients with low ejection fraction, high troponin and N-terminal pro-brain natriuretic peptide levels and those who survive a previous tachyarrhythmic cardiac arrest be considered at high risk for sudden cardiac death. (2C)

RATIONALE: Sudden cardiac death (SCD) is common in PD patients, accounting for around 25% of all deaths (55). Heart failure is associated with an increased risk of SCD, and left ventricular systolic dysfunction emerged as the most significant predictor of SCD in a study based on PD patients (5). Cardiac troponin T was associated with SCD independent of echocardiographic parameters but N-terminal pro-brain natriuretic peptide was associated with SCD only in the univariate analysis (8). A retrospective analysis of hemodialysis patients showed that patients who survived an episode of tachyarrhythmic cardiac arrest presented an increased risk of SCD in the future (56).

3.6.2 We suggest beta blockers be considered for primary prevention of sudden cardiac death in high-risk peritoneal dialysis patients. (2D)

RATIONALE: There are currently no randomized controlled trials that examined the effectiveness of various anti-arrhythmic agents in preventing SCD in PD patients, although some studies from CKD and hemodialysis patients suggest beta blockers may be associated with a reduced rate of SCD (57). However, none of the studies examined SCD as the primary endpoint.

3.6.3 We suggest an implantable cardioverter-defibrillator be considered for secondary prevention of sudden cardiac death in peritoneal dialysis patients who survive an episode of cardiac arrest confirmed as being the result of malignant ventricular arrhythmia (except those occurring within first 48 hours post-acute myocardial infarction). (2D)

RATIONALE: Implantable cardioverter-defibrillator devices (ICDs) are the only interventions that appears to robustly reduce SCD in the setting of primary or secondary prevention in the general population (excluding those that occurred immediately post-myocardial infarction) (58). There are so far no randomized controlled trials examining the use of ICDs for primary prevention of SCD in dialysis patients. However, there are observational data from hemodialysis patients showing that the use of ICDs may be associated with an improved survival in survivors of cardiac arrests (59). Putting together the very limited evidence available, the workgroup suggests a weak recommendation statement be drawn regarding the use of ICD in PD patients who survive an episode of cardiac arrest confirmed to be resulting from malignant ventricular arrhythmia.

RESEARCH RECOMMENDATIONS

SECTION 1: Coronary Artery Disease

- The lack of reliable longitudinal data in PD patients means that there are opportunities to perform studies of cardiac biomarkers in PD patients, with specific reference to the influence of residual renal function, PD dose, intra- and inter-individual variation and assay characteristics.
- Can intervention in asymptomatic patients (e.g. coronary artery angioplasty/bypass) alter the longer term troponin level and does this predict a better outcome?
- Establish the prevalence and risk factors for cardiovascular disease amongst patients on PD.
- Compare dobutamine stress echo and thallium scintigraphy for their predictive value for coronary artery disease in PD patients.
- What are the factors that indicate high risk for atherosclerotic coronary artery disease amongst PD patients?
- Does the use of antiplatelet therapy improve cardiovascular outcomes in PD patients with ischemic heart disease?

SECTION 2: LV Hypertrophy, LV Dysfunction, and Heart Failure

- A randomized controlled trial to evaluate the efficacy of ACEI or ARB or its combination vs placebo in improving hard outcomes (namely mortality and cardiovascular events) in PD patients with or without baseline heart failure or other cardiac co-morbidity.
- A randomized controlled trial to evaluate the efficacy of mineralocorticoid receptor antagonist vs placebo in improving hard outcomes (namely mortality and cardiovascular events) in PD patients with or without baseline heart failure or other cardiac co-morbidity.
- A randomized controlled trial to evaluate and compare the various blood pressure targets in relation to hard outcomes in PD patients with and without baseline heart failure.
- A randomized controlled trial to evaluate the efficacy of icodextrin in improving hard outcomes in PD patients with and without baseline heart failure.
- A randomized controlled trial to evaluate the efficacy of oral activated vitamin D in improving hard outcomes in PD patients with and without baseline heart failure.
- A randomized controlled trial to evaluate the efficacy of salt restriction in improving hard outcomes in PD patients with and without baseline heart failure.
- A randomized controlled trial to evaluate the efficacy of cardiac resynchronization therapy in improving hard outcomes in PD patients with heart failure.

SECTION 3: Stroke

- A randomized controlled trial of antiplatelet therapy for the primary prevention of cerebrovascular disease in PD patients.
- A randomized controlled trial of warfarin therapy for prevention of stroke in PD patients with atrial fibrillation.

SECTION 4: Peripheral Arterial Disease

- The diagnostic performance of ABI, TBI and other non-invasive tests for PAD should be formally evaluated in dialysis populations, including PD patients.
- The impact of screening for PAD vs no screening on clinical outcomes in dialysis populations (including PD patients) should be evaluated by a randomized controlled trial.
- A randomized controlled trial of supervised exercise therapy vs usual care to prevent PAD in PD patients.
- A randomized controlled trial of statins vs matching placebo for primary prevention of PAD in PD patients.
- A randomized controlled trial of supervised exercise therapy vs usual care for the treatment of PAD in PD patients.
- A randomized controlled trial of cilostazol vs matching placebo for the treatment of PAD in PD patients.
- A randomized controlled trial of naftidrofuryl oxalate vs matching placebo for the treatment of PAD in PD patients.
- A randomized controlled trial of revascularization vs supportive medical care in PD patients with PAD and critical limb ischemia (primary endpoint – amputation; secondary endpoints including duration of hospitalization, mortality, costs, sepsis).
- A randomized controlled trial of primary revascularization vs primary amputation in PD patients with PAD and critical limb ischemia.

SECTION 5: Arrhythmia

- Prospective analysis of the impact of various cardiac arrhythmia on clinical outcomes of PD patients.
- Defining specific risk factors for various cardiac arrhythmias in the PD population.

SECTION 6: Sudden Cardiac Death

- Cohort studies and randomized controlled trials in the PD population should document SCD as a specific and standardized endpoint.
- A randomized controlled trial of beta blockers for primary prevention of SCD in PD patients is warranted.
- A randomized controlled trial of ICDs in the high-risk group of PD patients is warranted.

SECTION 7: Arterial Stiffness

- A randomized controlled trial of cardiovascular risk modification based on arterial stiffness measurements compared with conventional clinical evaluation in PD patients.

DISCLOSURES

AYMW has received research grants or speaker honoraria from Baxter, Sanofi, Fresenius Kabi and Abbvie. KSB has received research funding from Baxter. SH has received research grants, consultant fees or honoraria from Amgen, Baxter, Gilead, Novartis and Shire. VJ has received research funding and is on the Advisory Board for Baxter. DJ has received consultancy fees from Baxter, Fresenius, Gambro, Amgen, Janssen-Cilag, Roche, Genzyme, Shire, Sigma, Sanofi-Aventis, Boehringer-Ingelheim, Lilley, Merck, Sharpe & Dohme, Bristol-Myers Squibb, and Novartis; speaker honoraria from Baxter, Fresenius, Gambro, Amgen, Janssen-Cilag, Roche, Servier, Shire, Merck, Sharpe & Dohme, Boehringer-Ingelheim, and Bristol Myers Squibb; research grants from Baxter Extramural, Fresenius, Roche Foundation for Anaemia Research (RoFar), Amgen, Janssen-Cilaz, Pfizer, and Abbott; and, travel sponsorships from Baxter, Fresenius, Gambro, Amgen, Janssen-Cilag, Roche, and Shire. JK has received unrestricted research grants from Fresenius FMC Europe, speakers' grants from Baxter healthcare and Fresenius FMC, and consultancy fees from Sanofi. ML has received unrestricted research grant from Baxter. CM has received research grant funding from both Baxter and Fresenius, honorariums from Baxter, Fresenius, Braun, Sanofi, and is an adviser for Astra Zeneca. RM hass received research support and/or honoraria from Baxter Healthcare and DaVita. RP-F has received speaker

honoraria from Baxter, Renal Research Institute, Abbott, AMGEN, Astra Zeneca, research grants from Fresenius Medical Care, Baxter, and a consultancy fee from Novartis, AMGEN, Abbott, Astra Zeneca. GB and S-WK have no conflicts of interest to declare.

ACKNOWLEDGMENTS

We would like to acknowledge the clerical support and assistance provided by Miss Giorgia Manuzi and all the valuable input and comments from Drs. Simon Davies and Martin Wilkie for this guideline work.

REFERENCES

1. Herzog CA, Ma JZ, Collins AJ. Poor long-term survival after acute myocardial infarction among patients on long-term dialysis. *N Engl J Med* 1998; 339:799–805.
2. Stack AG, Saran R. Clinical correlates and mortality impact of left ventricular hypertrophy among new ESRD patients in the United States. *Am J Kidney Dis* 2002; 40:1202–10.
3. Wang AY, Wang M, Woo J Lam CW, Lui SF, Li PK, *et al*. Inflammation, residual kidney function, and cardiac hypertrophy are interrelated and combine adversely to enhance mortality and cardiovascular death risk of peritoneal dialysis patients. *J Am Soc Nephrol* 2004; 15:2186–94.
4. Wang AY, Wang M, Lam CW, Chan IH, Lui SF, Sanderson JE. Heart failure in long-term peritoneal dialysis patients: a 4-year prospective analysis. *Clin J Am Soc Nephrol* 2011; 6:805–12.
5. Wang AY, Wang M, Lam CW, Chan IH, Lui SF, Sanderson JE. Heart failure with preserved or reduced ejection fraction in patients treated with peritoneal dialysis. *Am J Kidney Dis* 2013; 61:975–83.
6. Trespalacios FC, Taylor AJ, Agodoa LY, Bakris GL, Abbott KC. Heart failure as a cause for hospitalization in chronic dialysis patients. *Am J Kidney Dis* 2003; 41:1267–77.
7. Collins AJ, Foley RN, Chavers B, Gilbertson D, Herzog C, Johansen K, *et al*. United States Renal Data System 2011 Annual Data Report: Atlas of chronic kidney disease & end-stage renal disease in the United States. *Am J Kidney Dis* 2012; 59(1 Suppl 1):A7, e1–420.
8. Wang AY, Lam CW, Chan IH, Wang M, Lui SF, Sanderson JE. Sudden cardiac death in end-stage renal disease patients: a 5-year prospective analysis. *Hypertension* 2010; 56:210–6.
9. Wang HH, Hung SY, Sung JM, Hung KY, Wang JD. Risk of stroke in long-term dialysis patients compared with the general population. *Am J Kidney Dis* 2014; 63:604–11.
10. Liu JH, Lin HH, Yang YF, Liu YL, Kuo HL, Wang IK, *et al*. Subclinical peripheral artery disease in patients undergoing peritoneal dialysis: risk factors and outcome. *Perit Dial Int* 2009; 29:64–71.
11. Wizemann V, Tong L, Satayathum S, Disney A, Akiba T, Fissell RB, *et al*. Atrial fibrillation in hemodialysis patients: clinical features and associations with anticoagulant therapy. *Kidney Int* 2010; 77:1098–106.
12. Genovesi S, Vincenti A, Rossi E, Pogliani D, Acquistapace I, Stella A, *et al*. Atrial fibrillation and morbidity and mortality in a cohort of long-term hemodialysis patients. *Am J Kidney Dis* 2008; 51:255–62.
13. Wang AY, Wai-Kei Lam C. The diagnostic utility of cardiac biomarkers in dialysis patients. *Semin Dial* 2012; 25:388–96.
14. Melloni C, Alexander KP, Milford-Beland S, Newby LK, Szczech LA, Crusade Investigators, *et al*. Prognostic value of troponins in patients with non-ST-segment elevation acute coronary syndromes and chronic kidney disease. *Clin Cardiol* 2008; 31:125–9.
15. Newby LK, Jesse RL, Babb JD, Christenson RH, De Fer TM, Diamond GA, *et al*. ACCF 2012 expert consensus document on practical clinical considerations in the interpretation of troponin elevations: a report of the American College of Cardiology Foundation task force on Clinical Expert Consensus Documents. *J Am Coll Cardiol* 2012; 60:2427–63.
16. NACB Writing Group, Wu AH, Jaffe AS, Apple FS, Jesse RL, Francis GL, *et al*. National Academy of Clinical Biochemistry laboratory medicine practice guidelines: use of cardiac troponin and B-type natriuretic peptide or N-terminal proB-type natriuretic peptide for etiologies other than acute coronary syndromes and heart failure. *Clin Chem* 2007; 53:2086–96.
17. Garg R, Singh A, Khaja A, Martin A, Aggarwal K. How does volume status affect BNP and troponin levels as markers of cardiovascular status in peritoneal dialysis? *Congest Heart Fail* 2009; 15:240–4.
18. Gowdak LH, Arantes RL, de Paula FJ, Krieger EM, De Lima JJ. Underuse of American College of Cardiology/American Heart Association Guidelines in hemodialysis patients. *Ren Fail* 2007; 29(5):559–65.
19. Lentine KL, Costa SP, Weir MR, Robb JF, Fleisher LA, American Heart Association Council on the Kidney in Cardiovascular Disease and Council on Peripheral Vascular Disease, *et al*. Cardiac disease evaluation and management among kidney and liver transplantation candidates: a scientific statement from the American Heart Association and the American College of Cardiology. *J Am Coll Cardiol* 2012; 60:434–80.
20. Friedman SE, Palac RT, Zlotnick DM, Chobanian MC, Costa SP. A call to action: variability in guidelines for cardiac evaluation before renal transplantation. *Clin J Am Soc Nephrol* 2011; 6:1185–91.
21. Sharma R, Pellerin D, Gaze DC, Gregson H, Streather CP, Collinson PO, *et al*. Dobutamine stress echocardiography and the resting but not exercise electrocardiograph predict severe coronary artery disease in renal transplant candidates. *Nephrol Dial Transplant* 2005; 20:2207–14.
22. Rabbat CG, Treleaven DJ, Russell JD, Ludwin D, Cook DJ. Prognostic value of myocardial perfusion studies in patients with end-stage renal disease assessed for kidney or kidney-pancreas transplantation: a meta-analysis. *J Am Soc Nephrol* 2003; 14:431–9.
23. Tomaszuk-Kazberuk A, Kozuch M, Malyszko J, Bachorzewska-Gajewska H, Dobrzycki S, Musial WJ. Pharmacologic treatment in dialysis patients hospitalized for cardiovascular reasons: do we follow the guidelines? *Ren Fail* 2013; 35(2):235–42.
24. Dempster DW, Rosenstock JL, Schwimmer JA, Panagopoulos G, DeVita MV, Michelis MF. Underutilization of aspirin in hemodialysis patients for primary and secondary prevention of cardiovascular disease. *Clin Nephrol* 2005; 64(5):371–7.
25. Palmer SC, Di Micco L, Razavian M, Craig JC, Perkovic V, Pellegrini F, *et al*. Antiplatelet agents for chronic kidney disease. *Cochrane Database Syst Rev* 2013; 2:CD008834.
26. Wang AY, Wang M, Lam CW, Chan IH, Zhang Y, Sanderson JE. Left ventricular filling pressure by Doppler echocardiography in patients with end-stage renal disease. *Hypertension* 2008; 52:107–14.
27. Zannad F, Kessler M, Lehert P, Grünfeld JP, Thuilliez C, Leizorovicz A, *et al*. Prevention of cardiovascular events in end-stage renal disease: results of a randomized trial of fosinopril and implications for future studies. *Kidney Int* 2006; 70:1318–24.
28. Takahashi A, Takase H, Toriyama T, Sugiura T, Kurita Y, Ueda R, *et al*. Candesartan, an angiotensin II type-1 receptor blocker, reduces cardiovascular events in patients on chronic haemodialysis—a randomized study. *Nephrol Dial Transplant* 2006; 21:2507–12.
29. Cice G, Di Benedetto A, D'Isa S, D'Andrea A, Marcelli D, Gatti E, *et al*. Effects of telmisartan added to Angiotensin-converting enzyme inhibitors on mortality and morbidity in hemodialysis patients with chronic heart failure a double-blind, placebo-controlled trial. *J Am Coll Cardiol* 2010; 56:1701–8.
30. Yang LY, Ge X, Wang YL, Ma KL, Liu H, Zhang XL, *et al*. Angiotensin receptor blockers reduce left ventricular hypertrophy in dialysis patients: a meta-analysis. *Am J Med Sci* 2013; 345:1–9.
31. Cice G, Ferrara L, Di Benedetto A, Russo PE, Marinelli G, Pavese F, *et al*. Dilated cardiomyopathy in dialysis patients—beneficial effects of carvedilol: a double-blind, placebo-controlled trial. *J Am Coll Cardiol* 2001; 37:407–11.
32. Cice G, Ferrara L, D'Andrea A, D'Isa S, Di Benedetto A, Cittadini A, *et al*. Carvedilol increases two-year survivalin dialysis patients with dilated cardiomyopathy: a prospective, placebo-controlled trial. *J Am Coll Cardiol* 2003; 41:1438–44.
33. Ito Y, Mizuno M, Suzuki Y, Tamai H, Hiramatsu T, Nagoya Spiro Study Group, *et al*. Long-term effects of spironolactone in peritoneal dialysis patients. *J Am Soc Nephrol* 2014; 25:1094–102.
34. Matsumoto Y, Mori Y, Kageyama S, Arihara K, Sugiyama T, Ohmura H, *et al*. Spironolactone reduces cardiovascular and cerebrovascular morbidity and

mortality in hemodialysis patients. *J Am Coll Cardiol* 2014; 63:528–36.
35. Furie KL, Kasner SE, Adams RJ, Albers GW, Bush RL, Fagan SC, *et al*. Guidelines for the prevention of stroke in patients with stroke or transient ischemic attack: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke* 2011; 42:227–76.
36. Goldstein LB, Bushnell CD, Adams RJ, Appel LJ, Braun LT, Chaturvedi S, *et al*. Guidelines for the primary prevention of stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke* 2011; 42:517–84.
37. Palmer SC, DI Micco L, Razavian M, Craig JC, Perkovic V, Pellegrini F, *et al*. Effects of antiplatelet therapy on mortality and cardiovascular and bleeding outcomes in persons with chronic kidney disease: a systematic review and meta-analysis. *Ann Intern Med* 2012; 156:445–59.
38. Furie KL, Goldstein LB, Albers GW, Khatri P, Neyens R, Turakhia MP, *et al*. Oral antithrombotic agents for the prevention of stroke in nonvalvular atrial fibrillation: a science advisory for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke* 2012; 43:3442–53.
39. Elliott MJ, Zimmerman D, Holden RM. Warfarin anticoagulation in hemodialysis patients: a systematic review of bleeding rates. *Am J Kidney Dis* 2007; 50(3):433–40.
40. Zimmerman, D, Sood MM, Rigatto C, Holden RM, Hiremath S, Clase CM. Systematic review and meta-analysis of incidence, prevalence and outcome of atrial fibrillation in patients on dialysis. *Nephrol Dial Transplant* 2012; 27:3816–22.
41. Heidbuchel H, Verhamme P, Alings M, Antz M, Hacke W, Oldgren J, *et al*. EHRA practical guide on the use of new oral anticoagulants in patients with non-valvular atrial fibrillation: executive summary. *Eur Heart J* 2013; 34(27):2094–106.
42. Cove CL, Hylek EM. An updated review of target-specific oral anticoagulants used in stroke prevention in atrial fibrillation, venous thromboembolic disease, and acute coronary syndromes. *J Am Heart Assoc* 2013; 2(5):e000136.
43. Tariq N, Adil MM, Saeed F, Chaudhry SA, Qureshi AI. Outcomes of thrombolytic treatment for acute ischemic stroke in dialysis-dependent patients in the United States. *J Stroke Cerebrovasc Dis* 2013; 22(8):e354–59.
44. KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease: Chapter 4: Other complications of CKD: CVD, medication dosage, patient safety, infections, hospitalizations, and caveats for investigating complications of CKD. *Kidney Int* 2013; 83:91–111.
45. Hirsch AT, Haskal ZJ, Hertzer NR, Bakal CW, Creager MA, Halperin JL, *et al*. ACC/AHA 2005 Practice Guidelines for the management of patients with peripheral arterial disease (lower extremity, renal, mesenteric, and abdominal aortic): a collaborative report from the American Association for Vascular Surgery/Society for Vascular Surgery, Society for Cardiovascular Angiography and Interventions, Society for Vascular Medicine and Biology, Society of Interventional Radiology, and the ACC/AHA Task Force on Practice Guidelines (Writing Committee to Develop Guidelines for the Management of Patients With Peripheral Arterial Disease): endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation; National Heart, Lung, and Blood Institute; Society for Vascular Nursing; TransAtlantic Inter-Society Consensus; and Vascular Disease Foundation. *Circulation* 2006; 113: e463–654.
46. Hirsch AT, Haskal ZJ, Hertzer NR, Bakal CW, Creager MA, Halperin JL, *et al*. ACC/AHA 2005 guidelines for the management of patients with peripheral arterial disease (lower extremity, renal, mesenteric, and abdominal aortic): executive summary. A collaborative report from the American Association for Vascular Surgery/Society for Vascular Surgery, Society for Cardiovascular Angiography and Interventions, Society for Vascular Medicine and Biology, Society of Interventional Radiology, and the ACC/AHA Task Force on Practice Guidelines (Writing Committee to Develop Guidelines for the Management of Patients With Peripheral Arterial Disease) endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation; National Heart, Lung, and Blood Institute; Society for Vascular Nursing; TransAtlantic Inter-Society Consensus; and Vascular Disease Foundation. *J Am Coll Cardiol* 2006; 47:1239–312.
47. Norgren L, Hiatt WR, Dormandy JA, Nehler MR, Harris KA, Fowkes FG, *et al*. Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC II). *Eur J Vasc Endovasc Surg* 2007; 33(Suppl 1):S1–75.
48. Frans FA, Bipat S, Reekers JA, Legemate DA, Koelemay MJ. Systematic review of exercise training or percutaneous transluminal angioplasty for intermittent claudication. *Br J Surg* 2012; 99:16–28.
49. Watson L, Ellis B, Leng GC. Exercise for intermittent claudication. *Cochrane Database Syst Rev* 2008; CD000990.
50. K/DOQI Workgroup *et al*. K/DOQI clinical practice guidelines for cardiovascular disease in dialysis patients. *Am J Kidney Dis* 2005; 45:S1–153.
51. Herzog CA, Asinger RW, Berger AK, Charytan DM, Diez J, Hart RG, *et al*. Cardiovascular disease in chronic kidney disease. A clinical update from Kidney Disease: Improving Global Outcomes (KDIGO). *Kidney Int* 2011; 80:572–86.
52. Abbott KC, Trespalacios FC, Taylor AJ, Agodoa LY. Atrial fibrillation in chronic dialysis patients in the United States: risk factors for hospitalization and mortality. *BMC Nephrol* 2003; 4:1–10.
53. Genovesi S, Pogliani D, Faini A, Valsecchi MG, Riva A, Stefani F, *et al*. Prevalence of atrial fibrillation and associated factors in a population of long-term hemodialysis patients. *Am J Kidney Dis* 2005; 46:897–902.
54. Vazquez E, Sanchez-Perales C, Lozano C, Garcia-Cortes MJ, Borrego F, Guzman M, *et al*. Comparison of prognostic value of atrial fibrillation versus sinus rhythm in patients on long-term hemodialysis. *Am J Cardiol* 2003; 92:868–71.
55. USRDS Annual Data Report. Cardiovascular special studies. [Available online at: http://www. usrds.org/2004/pdf/09_cardio_04.pdf]
56. Pun PH, Lehrich RW, Smith SR, Middleton JP. Predictors of survival after cardiac arrest in outpatient hemodialysis clinics. *Clin J Am Soc Nephrol* 2007; 2:491–500.
57. Tangri N, Shastri S, Tighiouart H, Beck GJ, Cheung AK, Eknoyan G, *et al*. B-blockers for prevention of sudden cardiac death in patients on hemodialysis: a propensity score analysis of the HEMO study. *Am J Kidney Dis* 2011; 58(6):939–45.
58. Greenberg H, Case RB, Moss AJ, Brown MW, Carroll ER, Andrews ML; MADIT-II Investigators. Analysis of mortality events in the Multicenter Automatic Defibrillator Implantation Trial (MADIT-II). *J Am Coll Cardiol* 2004; 43(8):1459–65.
59. Herzog CA, Li S, Weinhandl ED, Strief JW, Collins AJ, Gilbertson DT. Survival of dialysis patients after cardiac arrest and the impact of implantable cardioverter defibrillators. *Kidney Int* 2005; 68(2):818–85.