Cardiac Rehabilitation in Patients with Chronic Kidney Disease

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Key Words

Chronic kidney disease, exercise, anemia

Background

Chronic kidney disease (CKD) is a common problem, with an estimated 2 million affected Canadians, according to the Kidney Foundation of Canada. Cardiovascular disease (CVD) is prevalent in patients with CKD and is the leading cause of death regardless of CKD stage. While dialysis is commonly considered to be the most significant consequence of kidney impairment, patients are much more likely to die a cardiovascular death before requiring renal replacement therapy.[1] In fact, as renal function declines, all-cause and cardiovascular mortality increases exponentially; a possibility that was "significantly higher in lower-risk populations" such as those with a low prevalence of CVD.[2]

It is also estimated that upwards of 40% of patients with established CVD have concomitant CKD.[3] The presence of CKD is associated with a dramatically worse prognosis in those with established coronary artery disease and heart failure, such as an increased risk of death and hospitalization.[3,4] It is estimated that there is a 3-, 7- and >10-fold increase in mortality after myocardial infarction with mild (average glomularal filtration rate [eGRF]), moderate (eGFR 35-50 mL/min) and severe (eGFR) renal dysfunction, respectively.[5] To make matters worse, patients with CKD have worse revascularization outcomes (PCI or CABG) with higher procedural complication rates.[6]

CVD Risk Factors and CKD

The burden of traditional risk factors in CKD is tremendous. Traditional risk factors such as hypertension, dyslipidemia, advanced age, diabetes, smoking and physical inactivity are rampant in the CKD population. Some estimates place the prevalence of hypertension, diabetes and dyslipidemia at over 60% each, which may explain a large part of the increased risk associated with CKD.[1,6-8]

Despite controlling for these standard risk factors, CKD remains a powerful predictor for future cardiovascular events, prompting the American Heart Association to recommend that patients with CKD should be "considered in the highest-risk group."[1] This is likely related to the unique nature of CKD and the disturbed physiology it confers. Overall, traditional risk factors parallel the relationships described in the general population with some important differences. In CKD patients there is a U-shaped mortality curve associated with cholesterol and hypertension levels with an increased risk of death for both extremes of measurement. Furthermore, it has been proposed that CKD represents a "qualitatively and quantitatively" different risk factor exposure. i.e., as CKD is etiologically linked to both diabetes and hypertension, patients with CKD may represent a cohort who have had a more severe and prolonged exposure. Likewise, CKD is associated with more severe hypertension and dyslipidemia. There is also the burden of CKD-associated non-traditional risk factors. Several, such as inflammation (C-reactive protein, interleukin-6, fibrinogen), anemia, oxidative stress, abnormal calcium/phosphate metabolism, and hemodynamic overload, have been associated with increased cardiovascular risk in both the general and CKD population.[1,7]

"…patients with [chronic kidney disease] should be 'considered in the highest-risk group.' "

Multidisciplinary cardiac rehabilitation (CR) programs offer an optimal opportunity to intervene on this cohort. Despite their high-risk status, patients with CKD are less likely to receive aggressive risk factor modification with therapies that are proven to be beneficial in patients with normal renal function. Some studies have found that prescription rates of ASA, beta-blockers, statins, and ACE-inhibitors are inversely related to renal function.[1,3,5,9] However, a Canadian analysis published in 2004 indicates that patients with CKD of all stages do derive benefit from these therapies, often to a similar extent as those with preserved eGFR.[1,3]

Physical Fitness and CKD

Patients with CKD have limited physical function across many subjective and objective domains. Repeatedly, studies have noted deficits in measures of cardiopulmonary fitness (walking distance/time, treadmill, cycle ergometry) and strength when compared to normal controls or predicted performance capabilities. This reduction in exercise capacity has been shown to significantly impair quality of life, and

to be independently associated with a higher morbidity and mortality.[10-13]

To compound these observations, recent research has shown that there is an association between declining exercise performance and creatinine over time, independent of hemoglobin level. A recent study examined patients with moderate renal impairment (eGFR).[14] At baseline, the authors found that exercise performance was significantly lower than that predicted for healthy, sedentary individuals of the same age and gender (VO_2 peak by cycle ergometer 1.88 L/min, 82% predicted). Over two years, oxygen consumption declined as renal function deteriorated (9% decrease in VO_2 peak with a 28% decrease in eGFR). Likewise, leg strength, as measured by isokinetic dynameter, fell with eGFR despite maintenance of thigh muscle cross-sectional area as measured by computer tomography.

The Benefits of Cardiac Rehabilitation

The CKD population is traditionally understudied; however, evidence suggests that structured exercise programs can improve outcomes in this population. Through a combination of flexibility, strengthening and aerobic exercise training, renal rehabilitation programs have been shown to have beneficial effects on physical fitness (aerobic and resistance), psychosocial function, quality of life (sickness impact and symptom scores), cardio-respiratory parameters (including LV systolic function) and renal functional parameters in patients with moderate-severe CKD.[2,10,15,16] They have also demonstrated beneficial effects on blood pressure, lipid parameters, hemoglobin levels and measures of arterial stiffness. However, only two studies to date have specifically examined the effects of a structured CR program on patients with CKD.[17, 18]

The first study, published in 2005, examined a group of patients with and without mild-moderate CKD who completed CR. At baseline, the patients with CKD were older, had a higher risk factor and co-morbidity burden, and had a lower functional capacity and perceived health status. At the end of the CR program, both groups achieved significant improvements in body weight/body mass index, waist circumference, diet, lipid profiles, 6-minute walk distances, self-reported physical activity level and perceived health status. As well, a similar proportion of patients achieved their secondary prevention goals in both groups. It is worth noting that while CKD patients continued to have lower physical component health summary scores and functional capacity than the non-CKD group, their improvement after CR was comparable to the non-CKD group. The authors observed that patients with CKD achieved similar benefits in coronary risk reduction with CR as did patients without CKD.[17]

The second study took the research a step further and examined higher-risk patients (post-bypass) with end-stage renal disease being treated with hemodialysis. They found that the patients who received CR within 6 months post-bypass had a 35% reduced risk in all-cause mortality and a 36% reduced risk of cardiac death compared with dialysis patients who had not received CR.[18]

Barriers to Cardiac Rehabilitation

Despite the observed benefit of CR in CKD, CR programs are highly underutilized. In the previously described study, enrolment in structured CR programs post-bypass was only 10%, less than half the rate for non-dialysis patients.[2] While socio-economic, logistic and patient-related factors do play a role, referral patterns are biased against CR where patients with CKD are often deemed "unsuitable" for ongoing cardiac rehabilitation. This seems to contravene the observation that the CKD population may have the most to gain from a structured CR program given their significant RF and overly severe disease burden.[17]

Special Considerations in this Population

Hemoglobin – Anemia is a well-established risk factor for decreased exercise capacity in the general population. In the CKD population, a direct relationship has been demonstrated between hemoglobin level and exercise capacity. Studies have shown that treatment with erythropoesis-stimulating agents (i.e., erythropoietin) in the CKD population improves exercise capacity and VO_2 peak.[19] As such, every effort should be made to correct the anemia associated with CKD.

Strength training and resistance exercises – Abnormalities in muscle fibre size and distribution are well described and common in the CKD population. It has been suggested that these "intrinsic muscle changes … contribute more to poor performances than do limitations in oxygen supply."[14] Correspondingly, a study from 1997 showed that, similar to the general population, strength training alone can improve VO_2 peak in CKD patients, thus underscoring the importance of resistance activity.[16]

Psychological Stressors and Adjustment

Patients with CKD may have higher stress levels, with concerns related to alteration in social and role responsibilities, dependence and interdependence issues, and uncertainty about the future. Typically, these concerns intensify as patients progress to end-stage renal disease and the need for renal replacement therapy draws nearer. Cardiac rehabilitation provides an opportunity to foster coping skills

and help patients adjust to these stressful changes.

Dietary Counselling

Nutritional counselling plays an important role in CKD patients of all stages. Appropriate and early intervention can maintain a patient's well-being through maintenance of optimal nutrition, preventing or minimizing the metabolic derangements of CKD, and retarding the progression of renal failure.[20]

Conclusion

Patients with CKD represent a high-risk subset of patients who stand to gain significant benefits from a traditional structured multidisciplinary CR program. Outside of the significant gains that can be made from regular structured exercise, CR offers the opportunity to provide comprehensive secondary prevention. The multidisciplinary nature of the program also allows tailored therapy with dietary intervention, psychosocial counselling, life skills and coping skills retraining, as well as pharmacologic intervention as needed.

References:

1. Sarnak MJ, Levey AS, Schoolwerth AC *et al.* Kidney disease as a risk factor for development of cardiovascular disease: a statement from the American Heart Association Councils on Kidney in Cardiovascular Disease, High Blood Pressure Research, Clinical Cardiology, and Epidemiology and Prevention. *Circulation* 2003;108:2154-69.
2. Tonelli M, Wiebe N, Culleton B *et al.* Chronic kidney disease and mortality risk: A systematic review. *J Am Soc Nephrol* 2006;7:2034-47.
3. Ezekowitz JA, McAlister FA, Humphries K *et al.* The impact of renal insufficiency on pharmacotherapy and outcomes in 6427 patients with ischemic cardiomyopathy. *J Am Col Card* 2004;44:1587-92.
4. Hillege HL, Nitsch D, Pfeffer MA *et al.* Renal function as a predictor of outcome in a broad spectrum of patients with heart failure. *Circulation* 2006;113: 671-78.
5. Wright RS, Reeder GS, Herzog CA *et al.* Acute myocardial infarction and renal dysfunction: a high-risk combination. *Ann Intern Med* 2002;37:563-70.
6. Reddan DN, Szczech LA, Tuttle RH *et al.* Chronic kidney disease, mortality, and treatment strategies among patients with clinically significant coronary artery disease. *J Am Soc Nephrol* 2003;4:2373-80.
7. Parfrey PS, Foley RN. The clinical epidemiology of cardiac disease in chronic renal failure. *J Am Soc Nephrol* 1999;10:1606-15.
8. Collins AJ, Kasiske B, Herzog C *et al.* Excerpts from the United States renal data system 2002 annual data report: atlas of end-stage renal disease in the United States. *Am J Kidney Dis* 2003;41:S57-70.
9. Santopinto JJ, Fox KAA, Goldberg RJ *et al.* Creatinine clearance and adverse hospital outcomes in patients with acute coronary syndromes: findings from the global registry of acute coronary events (GRACE). *Heart* 2003;89:1003-08.
10. Fitts SS, Guthrie MR, Blagg CR. Exercise coaching and rehabilitation counseling improve quality of life for predialysis and dialysis patients. *Nephron* 1999;82:115-21.
11. Sietsema KE, Amato A, Adler SG, Brass EP. Exercise capacity as a predictor of survival among ambulatory patients with end-stage renal disease. *Kidney Int* 2004;65:719-24.
12. Stenvinkel P, Barany P, Chung SH, Lindholm B, Heimbürger O. A comparative analysis of nutritional parameters as predictors of outcome in male and female ESRD patients. *Nephrol Dial Transplant* 2002;17:266-74.
13. O'Hare AM, Tawney K, Bacchetti P, Johansen KL. Decreased survival among sedentary patients undergoing dialysis: Results from the dialysis morbidity and mortality study wave 2. *Am J Kidney Dis* 2003;41:447-54.
14. Leikis MJ, McKenna MJ, Petersen AC *et al.* Exercise performance falls over time in patients with chronic kidney disease despite maintenance of hemoglobin concentration. *J Am Soc Nephrol* 2006;1:488-95.
15. van Vilsteren MCBA, de Greef MHG, Huisman RM. The effects of a low-to-moderate intensity pre-conditioning exercise programme linked with exercise counselling for sedentary haemodialysis patients in The Netherlands: results of a randomized clinical trial. *Nephrol Dial Transplant* 2005;20:141-46.
16. Boyce ML, Robergs RA, Avasthi PS *et al.* Exercise training by individuals with predialysis renal failure: Cardiorespiratory endurance, hypertension, and renal function. *Am J Kidney Dis* 1997;30:180-92.
17. Venkataraman R, Sanderson B, Bittner V. Outcomes in patients with chronic kidney disease undergoing cardiac rehabilitation. *Am Heart J* 2005;150:1140-46.
18. Kutner NG, Zhang R, Huang Y, Herzog CA. Cardiac rehabilitation and survival of dialysis patients after coronary bypass. *J Am Soc Nephrol* 2006;17:1175-80.
19. Clyne N, Jogestrand T. Effect of erythropoietin treatment on physical exercise capacity and on renal function in predialytic uremic patients. *Nephron* 1992;60:390-96.
20. Mitch WE. Beneficial responses to modified diets in treating patients with chronic kidney disease. *Kidney International* 2005;67:S133-S135.