

should be screened for VUR. They also revealed that neurogenic bladder is more prevalent in GJH patients.¹⁰ Based on Gajanan and colleagues' study, it would be important to predict dysfunctional elimination in children born with any syndrome that has GJH.¹¹ According to the previous studies, collagenous proliferation in primary obstructive and refluxing megaureter could be related to dysfunction of the ureteral smooth muscle. Some studies also demonstrated that type III collagen may play a role in the pathophysiology of refluxing megaureters.^{12,13} Changes in the composition of extracellular matrix in the vesicoureteral junction of patients with VUR were also observed previously.

CONFLICT OF INTEREST

None declared.

REFERENCES

- Junnilla JL, Cartwright VW. Chronic musculoskeletal pain in children: part II. Rheumatic causes. *Am Fam Physician*. 2006;74:293-300.
- Simpson MR. Benign joint hypermobility syndrome: evaluation, diagnosis, and management. *J Am Osteopath Assoc*. 2006;106:531-6.
- Seckin U, Tur BS, Yilmaz O, Yagci I, Bodur H, Arasil T. The prevalence of joint hypermobility among high school students. *Rheumatol Int*. 2005;25:260-3.
- Simpson MAJ. Benign joint hypermobility syndrome: evaluation, diagnosis, and management. *JAOA*. 2006;106:531.
- Biro F, Gewanter HL, Baum J. The hypermobility syndrome. *Pediatrics*. 1983;72:701-6.
- De Kort L, Verhulst J, Engelbert R, Uiterwaal C, De Jong T. Lower Urinary Tract Dysfunction in Children With Generalized Hypermobility of Joints. *J Urol*. 2003;170:1971-4.
- Pourmasiri Z, Madani A, Zandi H, Salehpour S, Gorji F, Ahmadzadeh A. The Relationship of Generalized Joint Hypermobility With Vesicoureteral Reflux and Urinary Tract Infection. *Iran J Kidney Dis*. 2014;8:189-93.
- van Eerde AM, Verhoeven VJ, de Jong TP, van de Putte EM, Giltay JC, Engelbert RH. Is joint hypermobility associated with vesico-ureteral reflux? An assessment of 50 patients. *BJU Int*. 2012;109:1243-8.
- Kajbafzadeh A, Sharifi-Rad L, Ladi Seyedian SS, Mozafarpour S, Paydary K. Generalized joint hypermobility and voiding dysfunction in children: is there any relationship? *Eur J Pediatr*. 2014;173:197-201.
- Beiraghdar F, Rostami Z, Panahi Y, Einollahi B, Teimoori M. Vesicourethral Reflux in Pediatrics With Hypermobility Syndrome. *Nephrourol Mon*. 2013;5:924-7.
- Gajanan B, Girish N, Maregowda S, Chandrashekar R. Dysfunctional voiding as a presenting feature of marfan syndrome: a rare case. *UroToday Int J* 2011;4:1-5.
- Medel R Jr, Quesada EM. Ultrastructural characteristics of collagen tissue in normal and congenitally dilated ureter. *Eur Urol*. 1985;11:324-9.
- Lee BR, Silver RI, Partin AW, Epstein JI, Gearhart JP. A quantitative histologic analysis of collagen subtypes: the primary obstructed and refluxing megaureter of childhood. *Urology*. 1998;51:820-3.

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Echocardiography Evaluation and Exercise in Hemodialysis Patients

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See article on page 207

Cardiovascular disease (CVD) is the most common cause of morbidity and mortality in patients with chronic kidney disease (CKD).¹ Hospitalizations of dialysis patients happen frequently and about one-third are from CVD. The annual cardiovascular mortality in dialysis patients is significantly higher

than in the general population and about half of the deaths in dialysis patients are assigned to CVD.¹ Different methods are used for cardiovascular evaluation in patients with CKD. Echocardiography, as a noninvasive and available technique, is the most useful imaging modality for a cardiac assessment.

Echocardiographic measures of left ventricular function and structure abnormality as well as left atrial size have been reported to predict adverse cardiovascular outcomes in patients with CKD.²

Left ventricular hypertrophy (LVH) is common finding in patients with CKD. Chen and colleagues showed that a left atrial diameter larger than 4.7 cm (hazard ratio [HR], 2.14; 95% confidence interval [CI], 1.16 to 3.97; $P = .02$); increased left ventricular mass index (HR, 1.01; 95% CI, 1.00 to 1.01; $P = .003$), and left ventricular ejection fraction less than 55% (HR, 2.01; 95% CI, 1.01 to 3.74; $P = .03$) were independently associated with increased cardiovascular events.² In addition, in patients awaiting kidney transplantation, left atrium diameter ($P = .005$), systolic dysfunction ($P = .007$), and left ventricular mass index ($P = .01$) are independent predictors of cardiovascular mortality and morbidity.³

Left ventricular hypertrophy, alike, is the one of the strongest predictors of the risk of progression to dialysis in patients with nondiabetic CKD, particularly among patients with mild to moderate kidney dysfunction.⁴ Zoccali and coworkers showed that rate of increase in the left ventricular mass index in hemodialysis patients with incident cardiovascular events was significantly higher than in those without such events. This indicated that cardiovascular event-free survival in patients with changes in increased left ventricular mass index below the 25th percentile was significantly higher than in those with changes above the 75th percentile. They showed that 1 g/m² per month increase in left ventricular mass index was associated with a 62% increase in the incident risk of fatal and nonfatal cardiovascular events (HR, 1.62; 95% CI, 1.13 to 2.33; $P = .009$).⁵

Regression of the LVH may have beneficial effects in patient survival. London and colleague showed in 153 patients receiving hemodialysis with a mean duration of 54 months that LVH regression consequence of anemia and hypertension treatment positively affected the survival. They deduced that a partial regression of LVH in patients with CKD had a favorable and independent effect on patients' total and cardiovascular survival.⁶

Left ventricular hypertrophy in patients with CKD is a result of pressure and volume overload. Hence, LVH is more severe in long-term peritoneal dialysis patients than in hemodialysis patients. This

finding is associated with signs of marked volume expansion, hypertension, and hypoalbuminaemia.⁷ Moreover, left ventricular systolic and diastolic function and their echocardiographic parameters are extremely useful prognostic predictors in patients with CKD. In the early stage of CKD, surprisingly, Doppler indexes combined with conventional and tissue Doppler methods could detect the slight changes of diastolic function due to kidney dysfunction.⁸

Recently, tissue Doppler velocity imaging is considered for cardiac function assessment using myocardial tissue velocities for isovolumetric contraction, peak systole, early and late diastolic filling, strain rate, mitral annulus displacement, and isovolumetric relaxation time. Using tissue Doppler velocity imaging in hemodialysis and advanced kidney failure patients demonstrate more frequent and more accentuated myocardial dysfunction, which is found less frequently when using conventional echocardiography.^{9, 10} Tissue Doppler velocity imaging also determined interruption of contractility and contraction in hypertrophied left ventricle, which could not be recognized by conventional echocardiography.¹⁰ Diastolic dysfunction is associated with increased systolic blood pressure and increased levels of parathyroid hormone.¹⁰ Tissue Doppler velocity imaging showed improvement of cardiac function after hemodialysis in patients with CKD.⁹ Improved systolic function is indicated by increases in isovolumetric contraction velocity, peak systole velocity, and strain rate.⁹

Many of advantages of exercise in general population are related to cardiovascular risk factors reduction, improvement of hypertension, diabetes and dyslipidemia control, and quality of life changes.¹¹ In patients with CKD, likewise, several randomized controlled trials showed a cardioprotective effect of exercise training.¹² However, observational studies showed a significant inverse association between physical function, aerobic capacity, and sedentary behavior and mortality in patients with CKD.^{13,14} Dialysis patients have impaired muscular exercise capacity, and moderate exercise training can improve their physical function, skeletal muscle quality, aerobic capacity psychological status, and quality of life.¹⁵⁻¹⁷

Wilund and coworkers showed in a randomized study of 17 hemodialysis patients that after 4

months of intradialytic exercise training (cycling), performance on the shuttle walk test increased by 17% and epicardial fat thickness was reduced by 11% in the exercise group. Serum thiobarbituric acid reactive substance, a marker of oxidative stress, and serum alkaline phosphatase, a recognized risk factor for vascular calcification, were reduced by 38% and 27% respectively in the exercise group, but did not change in the control group. There was no change in left atrial volume, left ventricular mass, myocardial performance index and serum lipids, or inflammatory markers (C-reactive protein and interleukin-6) in the either of the groups.¹⁸

In the current issue of the *Iranian Journal of Kidney Diseases*, Momeni and associates have shown that intradialysis exercise significantly increases left ventricular ejection fraction and decreases systolic pulmonary artery pressure and right ventricular size. These finding may explain some exercise benefit in patients CKD.¹⁹ Exercise training may alleviate some indexes of risk of sudden cardiac death in hemodialysis patients.¹⁶ Exercise training can reduce emotional distress and concomitantly improve heart rate variability.²⁰ Intradialysis exercise improves dialysate urea removal.²¹ In addition, regular exercise during hemodialysis can contribute to a 38% reduction in antihypertensive medication.²²

In summary, cardiac evaluation and effect of exercise training on cardiovascular system by echocardiography, particularly tissue Doppler velocity imaging, can provide additional useful information in patients with CKD.

CONFLICT OF INTEREST

None declared.

REFERENCES

1. Go AS, Chertow GM, Fan D, McCulloch CE, Hsu CY. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. *New Engl J Med*. 2004;351:1296-305.
2. Chen SC, Chang JM, Liu WC, et al. Echocardiographic parameters are independently associated with increased cardiovascular events in patients with chronic kidney disease. *Nephrol Dial Transplant*. 2012;27:1064-70.
3. Rocha SG, Chitalia N, Gregson H, Kaski JC, Sharma R, Banerjee D. Echocardiographic abnormalities in patients on kidney transplant waiting list. *J Nephrol*. 2012;25:1119.
4. Paoletti E, Bellino D, Gallina AM, Amidone M, Cassottana P, Cannella G. Is left ventricular hypertrophy a powerful predictor of progression to dialysis in chronic kidney disease? *Nephrol Dial Transplant*. 2011;26:670-7.
5. Zoccali C, Benedetto FA, Mallamaci F, et al. Left ventricular mass monitoring in the follow-up of dialysis patients: prognostic value of left ventricular hypertrophy progression. *Kidney Int*. 2004;65:1492-8.
6. London GM, Pannier B, Guerin AP, et al. Alterations of left ventricular hypertrophy in and survival of patients receiving hemodialysis: follow-up of an interventional study. *J Am Soc Nephrol*. 2001;12:2759-67.
7. Enia G, Mallamaci F, Benedetto FA, et al. Long-term CAPD patients are volume expanded and display more severe left ventricular hypertrophy than haemodialysis patients. *Nephrol Dial Transplant*. 2001;16:1459-64.
8. Otsuka T, Suzuki M, Yoshikawa H, Sugi K. Left ventricular diastolic dysfunction in the early stage of chronic kidney disease. *J Cardiol*. 2009;54:199-204.
9. Hayashi SY, Brodin LA, Alvestrand A, et al. Improvement of cardiac function after haemodialysis. Quantitative evaluation by colour tissue velocity imaging. *Nephrol Dial Transplant*. 2004;19:1497-506.
10. Hayashi SY, Rohani M, Lindholm B, et al. Left ventricular function in patients with chronic kidney disease evaluated by colour tissue Doppler velocity imaging. *Nephrol Dial Transplant*. 2006;21:125-32.
11. Sato Y, Nagasaki M, Nakai N, Fushimi T. Physical exercise improves glucose metabolism in lifestyle-related diseases. *Experiment Biol Med*. 2003;228:1208-12.
12. Bronas UG. Exercise training and reduction of cardiovascular disease risk factors in patients with chronic kidney disease. *Adv Chronic Kidney Dis*. 2009;16:449-58.
13. 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.
14. 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.
15. Ouzouni S, Kouidi E, Sioulis A, Grekas D, Deligiannis A. Effects of intradialytic exercise training on health-related quality of life indices in haemodialysis patients. *Clin Rehab*. 2009;23:53-63.
16. Kouidi EJ, Grekas DM, Deligiannis AP. Effects of exercise training on noninvasive cardiac measures in patients undergoing long-term hemodialysis: a randomized controlled trial. *Am J Kidney Dis*. 2009;54:511-21.
17. Cheema B, Abas H, Smith B, et al. Progressive exercise for anabolism in kidney disease (PEAK): a randomized, controlled trial of resistance training during hemodialysis. *J Am Soc Nephrol*. 2007;18:1594-601.
18. Wilund KR, Tomayko EJ, Wu PT, et al. Intradialytic exercise training reduces oxidative stress and epicardial fat: a pilot study. *Nephrol Dial Transplant*. 2010;25:2695-701.
19. Momeni A, Nematollahi A, Nasr M. Effect of intradialytic exercise on echocardiographic findings in hemodialysis patients. *Iran J Kidney Dis*. 2014;8:207-11.
20. Kouidi E, Karagiannis V, Grekas D, et al. Depression, heart rate variability, and exercise training in dialysis patients. *Eur J Cardiovasc Prevent Rehab*. 2010;17:160-7.

21. Parsons T, Toffelmire E, King-VanVlack C. The effect of an exercise program during hemodialysis on dialysis efficacy, blood pressure and quality of life in end-stage renal disease (ESRD) patients. *Clin Nephrol.* 2004;61:261-74.
22. Miller BW, Cress CL, Johnson ME, Nichols DH, Schnitzler MA. Exercise during hemodialysis decreases the use of antihypertensive medications. *Am J Kidney Dis.* 2002;39:828-33.

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Factors Associated With Survival of Kidney Allografts

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See article on page 225

Kidney transplantation is generally accepted as the best way for renal replacement therapy in patients with end-stage renal disease.¹⁻⁵ Kidney transplant recipients could have a relatively high quality of life compared with maintenance hemodialysis.^{6,7} Despite the successful kidney transplant surgeries, rejection rate has still a high percentage in these patients; about 10% of them experience rejection within the first year.⁸ Knowing the high rate of complications and risk factors affecting kidney allograft survival, most of which are predictable and preventable, this issue has become increasingly important. Long-term kidney allograft survival has not paralleled improvements made in the past three decades in short-term survival. As mentioned in the literature, factors that may be related to short- and long-term survival are diverse and various.⁹ A main question to be answered about outcomes in kidney transplantation is which factors are associated with short- and long-term graft survival. Accumulating evidence supports that some of the accepted risk factors can be prolonged pretransplant dialysis time, pretransplant and posttransplant hypertension, the use of expanded criteria donors, higher serum levels of creatinine at the time of the first discharge, racial and ethnic differences that are related to the level of health services, underlying disease (diabetes mellitus), body mass index, age of recipients, donor type, proteinuria, sex of recipient and donor, and infections.^{2-6,10-15}

In the current issue of the *Iranian Journal of Kidney*

Diseases, Mirzaee and colleagues present an effective cure model analysis for improve short- and long-term survival rates of kidney allograft. They used a mixture of cure models to assess the short- and the long-term survival rate.¹⁶ They concluded that pretransplant hypertension, body mass index, a serum creatinine level of 1.6 mg/dL and greater upon discharge from the hospital, and donor age and sex were the risk factors affecting the survival of the kidney allograft. These time-dependent survival factors could be improved by controlling effective variables. Since the long-term kidney allograft survival remains an elusive goal, many studies are being conducted in this field, in order to help these patients to have a better life.¹⁷⁻¹⁹

The association of many factors such as female sex, black race, older donor age, deceased donor source, delayed graft function, and acute rejection with the duration of allograft survival formed the basis of study conducted by Gilland colleagues on the relationship between glomerular filtration rate changes and long-term kidney allograft survival.²⁰ They explained that strategies for improving long-term kidney allograft survival that increase baseline allograft function could be more effective than strategies to slow the decline in glomerular filtration rate.

Donor age is a known risk factor for chronic allograft failure in kidney transplant recipients.²¹ For determining the interaction between the donor age and risk of allograft failure, a study was conducted by Meier-Kriesche and colleagues,