SPECIAL ARTICLES

A Rationale for Intradialytic Exercise Training as Standard Clinical Practice in ESRD

Birinder Singh Bobby Cheema, MSc, Benjamin Charles Faulknor Smith, BSc, and Maria A. Fiatarone Singh, MD

• The purpose of this article is to present a rationale for intradialytic exercise training in patients with end-stage renal disease based on the empirical evidence to date and determine whether this evidence has translated into enhanced renal rehabilitation practices throughout the world. According to the published literature, intradialytic exercise improves exercise adoption and adherence in this cohort, is performed safely, and is feasible to administer. Moreover, intradialytic exercise can improve solute removal, dialysis adequacy, intradialytic protein synthesis, muscular strength, peak oxygen consumption, nutritional status, and quality of life. Despite these findings, there currently are no policies or position stands regarding exercise prescription for hemodialysis patients in Australia. According to a telephone survey we conducted, intradialytic exercise programs are essentially nonexistent in this country. However, such programs are being implemented successfully as standard clinical practice in dialysis units in Germany, and there is reason to believe that this practice can be expanded throughout the world. At present, additional research is indicated. There is a lack of large-scale, robustly designed, randomized, controlled trials of intradialytic exercise training. Such research is needed to conclusively show the clinical importance of intradialytic exercise for hemodialysis patients, which may influence current standard clinical practice among nephrologists and, as such, improve the health and quality of life of this vulnerable cohort. *Am J Kidney Dis* 45:912-916.

INDEX WORDS: Resistance training; aerobic training; peak oxygen uptake (Vo_{2peak}); dialysis adequacy; survey; Australia; health; quality of life (QOL); standard of care.

THE 2003 REPORT from the Australia and New Zealand Dialysis and Transplant Registry indicates that 12,945 individuals in Australia live with end-stage renal disease (ESRD), and 7,205 of these individuals receive maintenance hemodialysis (HD).[1] Almost 2,000 new patients began HD therapy in Australia in 2002, a 5% increase over the previous year, and this number is projected to continue to increase significantly in the future.[1] According to the US Renal Data System, similar trends are occurring in the United States, where nearly 400,000 individuals currently live with ESRD.[2]

Approximately 91% of patients diagnosed with ESRD will commence HD treatment as renal replacement therapy.[2] Although advances in dialysis techniques and control of comorbid diseases have extended the lifespan of HD patients, these individuals continue to experience significant impairment of quality of life (QOL). The reduced QOL experienced by this cohort may be attributed to: (1) physiological alterations in the internal milieu secondary to ESRD, (2) comorbidities, (3) biological aging, (4) lifestyle restrictions and sedentary behavior imposed by 12 to 18 h/wk of maintenance HD treatment, and (5) loss of psychological and functional health status as a direct consequence of factors 1 through 4. With the increasing incidence of ESRD and increased competition for kidney transplants, greater efforts must be directed toward improving the QOL of patients receiving maintenance HD treatment.

Numerous health-related benefits derived from engaging in appropriately structured exercise regimens have been documented extensively with sedentary adults, frail elderly persons, and individuals with a wide array of chronic illnesses.[3] Accordingly, the efficacy of exercise training for

From the School of Exercise and Sport Science and Faculty of Medicine, University of Sydney, Australia; Hebrew Rehabilitation Center for Aged; and Jean Mayer USDA Human Nutrition Center on Aging, Tufts University, Boston, MA.

Received October 22, 2004; accepted in revised form January 18, 2005.

Originally published online as doi:10.1053/j.ajkd.2005.01.030 on March 3, 2005.

Address reprint requests to Birinder Singh Bobby Cheema, MSc, BHK, PhD Research Student, School of Exercise and Sports Science, The University of Sydney, PO Box 170, Lidcombe, NSW, Australia 2141. E-mail: bche3157@mail.usyd.edu.au

0272-6386/05/4505-0015$30.00/0
doi:10.1053/j.ajkd.2005.01.030

patients with ESRD has been investigated for the past 25 years. The rationale for prescribing exercise in this patient population is extremely strong; however, barriers to regular exercise participation are many, which may explain the persistent sedentary behavior of this cohort. Motivation to exercise has been problematic, particularly when training is performed on nondialysis days.[4]

In an attempt to promote exercise adoption, several investigators have prescribed exercise training during routine HD treatment, time typically devoted to complete idleness or such sedentary pursuits as watching television. An accumulating body of literature suggests that intradialytic exercise is safe, beneficial, feasible to administer, and enhances compliance with exercise training. Therefore, the purpose of our article is 2-fold: (1) to present a rationale for the efficacy of intradialytic exercise training based on the empirical evidence to date, and (2) to determine whether this evidence has translated into enhanced renal rehabilitation practices throughout the world.

A RATIONALE FOR INTRADIALYTIC EXERCISE

Health-Related Adaptations

Painter et al[5] conducted the first clinical trial to prescribe exercise during routine outpatient HD treatment. Fourteen patients performed up to 30 minutes of cycling using adapted cycle ergometers during the second or third hour of HD treatment 3 times/wk for 6 months.[5] Exercising patients significantly improved peak oxygen uptake ($V\text{O}_{2\text{peak}}$) by 23% after the 6-month intervention,[5] an extremely beneficial adaptation given that $V\text{O}_{2\text{peak}}$ in this cohort has been reported to be 155% less than that observed in healthy, sedentary, age-matched individuals ($P < 0.001$).[6] No change in $V\text{O}_{2\text{peak}}$ was reported in the control group.

At least 16 additional reports[7-22] available in the published literature have prescribed intradialytic exercise regimens of sufficient frequency, intensity, duration, and modality to elicit significant beneficial adaptations. Physiological adaptations include holistic (central and peripheral) enhancement of the cardiorespiratory system, improved blood pressure regulation, and reversal of the malnutrition-inflammation complex (Table 1). Functional adaptations include improved muscle strength, exercise capacity, habitual and fastest gait speed, and ability to perform such activities of daily living as sit-to-stand movements (Table 1). Intradialytic exercise also can induce positive psychological adaptations in this cohort by reducing symptoms of anxiety, depression, and fatigue and enhancing various components of QOL, including general health, vitality, and perceptions of physical functioning (Table 1). Clearly, there is evidence to suggest that the benefits of intradialytic exercise can ameliorate the physiological, functional, and psychological impairments commonly induced and/or exacerbated by the ESRD process (Table 1).

Clinical Relevance

Damaging solutes are disproportionately retained in skeletal muscle during HD, and this gradient re-equilibrates after treatment, a process recognized as postdialysis solute rebound. Studies have shown that acute bouts of intradialytic exercise cycling can significantly reduce the postdialysis rebound of urea, creatinine, and potassium, thereby increasing the removal of these 3 solutes through dialysis.[23] Phosphate removal also can increase significantly as a result of intradialytic exercise.[22,24] Kong et al[23] concluded that the improvement in dialysis adequacy is equivalent to extending the length of the HD treatment session by 30 minutes. Mechanisms underlying this enhancement of dialysis adequacy likely include increased blood perfusion between the working muscle and bloodstream, thereby enabling more thorough removal of the damaging solutes through HD treatment.[23] These benefits also may translate into the long-term enhancement of dialysis adequacy (Kt/V),[19] although this hypothesis has not been rigorously investigated in a randomized controlled trial involving exercise training.

Muscle wasting is the most significant predictor of morbidity and mortality in HD patients.[25] HD treatment can significantly decrease protein synthesis directly through the loss of amino acids in dialysate[26] and therefore may be a factor contributing to the prevalent muscle catabolism in this cohort. However, Pupim et al[27] showed that 15 minutes of intradialytic cycling at 40% of maximal heart rate combined with adequate nutritional supplementation significantly increased amino acid uptake and net protein accretion during HD treatment compared with nutritional supplementation alone ($P < 0.05$). Moreover,

Table 1. The Impact of ESRD Can Be Counteracted With Intradialytic Exercise Training

Impact of ESRD	Impact of Intradialytic Exercise
Physiological adaptations	
Reduced VO_{2peak}	Increased VO_{2peak}[5,7,11,17]
Reduced VO_2 at anaerobic threshold	Increased VO_2 at anaerobic threshold[7,11]
Elevated submaximal heart rate	Reduced submaximal heart rate[7,21]
Poor control of blood pressure	Improved control of blood pressure[5,13,18]
Increased use of antihypertensive medications	Decreased use of antihypertensive medications[5,13]
Increased adiposity	Favorable adaptation of body composition[8]
Reduced oxidative metabolism	Increased phosphofructokinase activity[21]
Exacerbated malnutrition-inflammation complex	Reduced C-reactive protein[9,19]/increased albumin[19]
Uremia and elevated solute concentrations	Improved removal of toxins by dialysis[19,22]
Functional adaptations	
Reduced muscular strength	Increased muscular strength[8,12,14]
Reduced exercise capacity	Increased 6-min walk distance[16,20]
Reduced maximal work capacity	Increased maximal vertical work capacity[5]
Functional limitations	Improved habitual and fastest gait speed and sit-to-stand movement time[15,16]
Psychological adaptations	
Increased subjective fatigue symptoms	Reduced subjective fatigue symptoms[20]
Poor perception of physical functioning	Improved perception of physical functioning[14-17]
Poor perception of general health	Improved perception of general health[7,15,16]
Increased anxiety	Reduced anxiety[10]
Poorer mental health	Improved mental health[14]
Greater experience of bodily pain	Reduced experience of bodily pain[15,16]
Reduced vitality	Increased vitality[15]

NOTE. All listed effects of intradialytic exercise training are significant according to trials to date.[5,7-22]

intradialytic exercise resulted in a nearly 4-fold increase in postdialysis growth hormone levels ($P < 0.05$).[27] These adaptations suggest that exercise may ameliorate muscle catabolism by promoting an anabolic milieu, thereby potentially improving the clinical sequelae of sarcopenia, such as muscle weakness, falls, fractures, frailty, insulin resistance, and immune dysfunction, in HD patients.

Adherence

Konstantinidou et al[11] and Kouidi et al[7] investigated exercise adherence rates in HD patients by comparing training protocols performed on nondialysis days and during dialysis. The investigators showed that training on nondialysis days yielded significantly greater cardiorespiratory adaptations[7,11]; however, this result must be interpreted with caution given that training volume was not equal between regimens. Patients engaging in the intradialytic training program significantly improved cardiorespiratory outcomes compared with nonexercising controls.[11] Perhaps more importantly, exercise training on nondialysis days resulted in a greater percentage of subject attrition versus intradialytic training at 6 months (23.8% versus 16.7%, respectively),[11] 1 year (20.8% versus 12.5%, respectively),[7] and 4 years (37.5% versus 21.0%, respectively).[7]

The most common reason for discontinuing exercise on nondialysis days in 5 of 9 patients (55.5%) who withdrew before 4 years was "a lack of motivation."[7] Other commonly cited reasons included "lack of time" and "transportation difficulties."[11] The investigators concluded that it is difficult to persuade patients to maintain exercise programs on nondialysis days.[7,11] Therefore, exercising during HD is often recommended as a more feasible, convenient, and time-effective solution to promote exercise adherence in this cohort.[4,5,7,11]

Safety

No serious exercise-induced adverse events have been reported in the 17 published trials of intradialytic exercise training conducted with

HD patients,[5,7-22] suggesting that in appropriately screened patients, risks of this method of training are low. This is notable in light of the high prevalence of cardiovascular disease, hypertension, and diabetes in this cohort. Large, long-term, randomized, controlled trials are required to confirm this apparent safety.

REHABILITATION PRACTICES IN HD UNITS WORLDWIDE

Despite a strong rationale for the implementation of intradialytic exercise programs, such efforts are not being promoted by Kidney Health Australia. There are no policies or position stands regarding exercise prescription for HD patients in this country, and no discussions currently are ongoing toward this end. According to a telephone survey we conducted of all 145 HD units in Australia, only 3 units (2.1%) offered an exercise program to their patients and only 1 unit (0.68%), as an extension of a recent research study,[22] prescribed exercise at a sufficient dose to induce clinical and physiological adaptations. Thus, intradialytic exercise as standard clinical practice is essentially nonexistent in Australia.

Statistics regarding the worldwide prevalence of intradialytic exercise programs are not available; however, our findings for Australia stand in marked contrast to the standard of care in several other countries.

During the past 20 years, research groups in Germany, Greece, the United States, Sweden, the Czech Republic, Japan, and several other countries have initiated exercise programs for individuals with kidney disease as outpatient training programs or during HD.[28] For example, exercise in the dialysis setting has become part of clinical practice in the Ruhr area of Germany, where approximately 20% of all dialysis patients are involved in intradialytic exercise programs.[4] However, according to these investigators,[4] the number of participating patients could markedly increase if more dialysis units were to establish such training programs. Currently, 50% of units in the Ruhr area are prescribing exercise.[4] In several of these units, participation rates have reached 75%.[4] In a recent survey of 48 nephrologists conducted at the 2003 World Congress on Nephrology in Berlin,[7] 15% reported that intradialytic exercise programs were offered at their dialysis units.[29] The majority of these units were in Germany.[29]

We were unable to find evidence to suggest that intradialytic exercise has become integrated as clinical practice in other countries. Greater financial support from the German Health Care System toward intradialytic exercise programs may be the mechanism responsible for this practice of dialysis units in Germany.[4,29] Support from expert advisory bodies, government-funded health care resources, private advocacy groups, industry, and the health care professional community likely will be required if such practices are to become routine in other countries, such as Australia, as well.

Although research into the efficacy of exercise in patients with ESRD has been ongoing since 1977, there currently is no American College of Sports Medicine position stand regarding exercise prescription for this cohort. By comparison, such position stands exist for overweight/obesity, bone health, type 2 diabetes, hypertension, coronary artery disease, healthy adults, and elderly persons.[30] This disparity may be caused by the limited availability of large-scale, robustly designed, randomized, controlled trials of exercise training in patients with ESRD. Of the 17 reports of intradialytic training we reviewed, only 6 were randomized controlled trials,[7-9,11-12,17] whereas 5 were controlled trials,[5,10,13,15-16] and 6 were uncontrolled trials.[14,18-22] This paucity of hard empirical data may be responsible for the low rates of exercise counseling among nephrologists,[31] the absence of position stands, and the limited involvement of health care service providers in promoting and/or financially supporting exercise programs for patients with ESRD.

Robust long-term clinical trials are needed to identify optimal modalities and doses of exercise for this cohort for a broad range of clinical outcomes, including cardiovascular morbidity and mortality, muscle catabolism, visceral obesity, malnutrition-inflammation complex, insulin sensitivity, depression, endothelial dysfunction, vascular access maturation and efficacy, functional independence, and QOL, among others.

REFERENCES

1. Australia and New Zealand Dialysis and Transplant Registry: ANZDATA Registry, 2003. Available at: http://

www.anzdata.org.au/anzdata/AnzdataReport/download.htm. Accessed: January 7, 2005

2. US Renal Data System: USRDS 2003 Annual Data Report. The National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases. Bethesda, MD, 2003

3. Fiatarone Singh MA: Exercise comes of age: Rationale and recommendations for a geriatric exercise prescription. J Gerontol 57A:M262-M282, 2002

4. Daul A, Schafers R, Daul K, Philipp T: Exercise during hemodialysis. Clin Nephrol 61:S26-S30, 2004 (suppl 1)

5. Painter PL, Nelson-Worel JN, Hill MM, et al: Effects of exercise training during hemodialysis. Nephon 43:87-92, 1986

6. Deligiannis A, Kouidi E, Tassoulas E, et al: Cardiac effects of exercise rehabilitation in hemodialysis patients. Int J Cardiol 70:253-266, 1999

7. Kouidi E, Grekas D, Deligiannis A, Tourkantonis A: Outcomes of long-term exercise training in dialysis patients: Comparison of two training programs. Clin Nephrol 61:S31-S38, 2004 (suppl 1)

8. Cheema B, O'Sullivan A, Chan M, et al: A randomized controlled trial of progressive resistance training during maintenance hemodialysis treatment: The PEAK Study. J Aging Phys Act 12:260, 2004 (abstr)

9. Smith BCF, Cheema BSB, O'Sullivan AJ, et al: Resistance training during hemodialysis reduces C-reactive protein. Results from a randomized controlled trial of Progressive Exercise for Anabolism in Kidney Disease (the PEAK study). J Am Geriatr Soc (in press) (abstr)

10. Moug S, Grant S, Creed G, Boulton Jones M: Exercise during haemodialysis: West of Scotland pilot study. Scott Med J 49:14-17, 2004

11. Konstantinidou E, Koukouvou G, Kouidi E, Deligiannis A, Tourkantonis A: Exercise training in patients with end-stage renal disease on hemodialysis: Comparison of three rehabilitation programs. J Rehabil Med 34:40-45, 2002

12. DePaul V, Moreland J, Eager T, Clase CM: The effectiveness of aerobic and muscle strength training in patients receiving hemodialysis and EPO: A randomized controlled trial. Am J Kidney Dis 40:1219-1229, 2002

13. Miller B, Cress C, Johnson M, Nichols D, Schnitzler M: Exercise during hemodialysis decreases the use of antihypertensive medications. Am J Kidney Dis 39:828-833, 2002

14. Oh-Park M, Fast A, Gopal S, et al: Exercise for the dialyzed: Aerobic and strength training during hemodialysis. Am J Phys Med Rehabil 81:814-821, 2002

15. Painter P, Carlson L, Carey S, Paul S, Myll J: Low-functioning hemodialysis patients improve with exercise training. Am J Kidney Dis 36:600-608, 2000

16. Painter P, Carlson L, Carey S, Paul SM, Myll J: Physical functioning and health-related quality-of-life changes with exercise training in hemodialysis patients. Am J Kidney Dis 35:482-492, 2000

17. Painter P, Moore GE, Carlson L, et al: Effects of exercise training plus normalization of hematocrit on exercise capacity and health-related quality of life. Am J Kidney Dis 39:257-265, 2002

18. Anderson JE, Stewart KJ, Hatchett L: Ambulatory blood pressure (ABP) and pre and post hemodialysis (HD) blood pressure are lower after 3 months of exercise training. J Am Soc Nephrol 12:319A, 2001 (abstr)

19. Zaluska A, Zaluska WT, Bednarek-Skublewska A, Ksiazek A. Nutrition and hydration status improve with exercise training using stationary cycling during hemodialysis (HD) in patients with end-stage renal disease (ESRD). Ann Univ Mariae Curie Sklodowska [Med] 57:342-346, 2002

20. Ridley J, Hoey K, Ballagh-Howes N: The exercise-during-hemodialysis program: Report on a pilot study. CANNT J 9:20-26, 1999

21. Moore GE, Parsons DB, Stray-Gundersen J, Painter PL, Brinker KR, Mitchell JH: Uremic myopathy limits aerobic capacity in hemodialysis patients. Am J Kidney Dis 22:277-287, 1993

22. Vaithilingham I, Polkinghorne K, Atkins R, Kerr P: Time and exercise improve phosphate removal in hemodialysis patients. Am J Kidney Dis 43:85-89, 2004

23. Kong C, Tattersall J, Greenwood R, Farrington K: The effect of exercise during hemodialysis on solute removal. Nephrol Dial Transplant 14:2927-2931, 1999

24. Adorati M: The effect of intradialytic exercise of solute removal. Nephrol Dial Transplant 15:1264, 2000 (comment)

25. Lowrie EG, Huang WH, Lew NL, Liu Y: The relative contribution of measured variables to death risk among hemodialysis patients, in Friedman EA (ed): Death on Hemodialysis. Amsterdam, The Netherlands, Kluwer, 1994, pp 121-141

26. Lim VS, Bier DM, Flanigan MJ, Sum-Ping ST: The effect of hemodialysis on protein metabolism. A leucine kinetic study. J Clin Invest 91:2429-2436, 1993

27. Pupim LB, Flakoll PJ, Levenhagen DK, Ikizler TA: Exercise augments the acute anabolic effects of intradialytic parenteral nutrition in chronic hemodialysis patients. Am J Physiol Endocrinol Metab 286:E589-E597, 2004

28. Krause R, Daul A: Preface. Clin Nephrol 61:S1, 2004 (suppl 1)

29. Krause R: Nephrologists' view of exercise training in chronic kidney disease. Clin Nephrol 61:S2-S4, 2004 (suppl 1)

30. American College of Sports Medicine Position Stands. Available at: http://www.acsm-msse.org/pt/re/msse/positionstandards. Accessed: January 7, 2005

31. Johansen KL, Sakkas GK, Doyle J, Shubert T, Dudley RA: Exercise counseling practices among nephrologists caring for patients on dialysis. Am J Kidney Dis 41:171-178, 2003