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# Exercise in Chronic Disease: Physiological Research Needed

*Patricia Painter*

Department of Medicine, Division of Renal Diseases and Hypertension, University of Minnesota, Minneapolis, MN, United States

PAINTER, P. Exercise in chronic disease: physiological research needed. *Exerc. Sport Sci. Rev.*, Vol. 36, No. 2, pp. 83–90, 2008. *Regular exercise training may be important for many patients with chronic disease, but research is needed to justify incorporation of exercise into their routine care. Education of health care providers on the importance of exercise is also needed to effectively pursue research and for exercise to be incorporated as a part of the health care plan.* **Key Words:** exercise training, chronic kidney disease, exercise research, renal failure, physical functioning

## INTRODUCTION

Health policy documents, such as the Surgeon General's Report on Physical Activity and Health and Healthy People 2010, are invaluable for promoting the preventive aspects of adopting the behavior of regular physical activity. However, while promoting physical activity for preventive reasons, we must not dismiss the importance of regular physical activity for the 48 million individuals with diagnosed chronic disease.

Many physiological consequences of chronic disease are similar to the physiological consequences observed with physical deconditioning and/or bed rest (1). Patients with various diseases, including cancer, chronic obstructive pulmonary disease, human immunodeficiency virus disease, type 1 diabetes mellitus, and chronic kidney disease (CKD) exhibit impaired cardiac and vascular function; reduced muscle mass, strength/power, and exercise capacity; and increased percentage of body fat. Most people with chronic disease also experience significant fatigue, reductions in physical activity, and poor quality of life. Because most patients with chronic disease become sedentary, it is reasonable to question whether the observed physiological consequences of disease are due to the disease and/or treatment or from physical inactivity.

Physical activity may have differential effects depending on the specific disease, but much more research is needed to identify how regular exercise may be beneficial in chronic disease. This knowledge is critical to promote physical activity as a routine part of clinical practice. This short review will present an approach for developing research that may facilitate and justify implementation of regular physical activity counseling as a routine part of care of patients with chronic disease. Examples will be drawn primarily from literature on CKD.

## CHALLENGES OF EXERCISE IN CHRONIC DISEASE

Although there are good reasons to recommend regular exercise in patient populations, exercise research is not a straightforward endeavor in patients with chronic disease. Research focused on the benefits of regular exercise with patients with chronic diseases faces many challenges. The challenges or factors must be considered in the design, implementation, and interpretation of research. Challenges include both clinical/patient and systemic/environment factors (*i.e.*, priorities within the health care delivery system). The following are major factors that must be considered in implementing exercise research in the chronic disease setting:

1) There is variability in the stage of disease. Foremost, some diseases are progressive, whereas other diseases may stabilize with treatment. Variability in CKD ranges from stage 1, in which there is a reduction in glomerular filtration rate, yet patients are largely asymptomatic to Stage 5, in which some form of renal replacement therapy is required to maintain life (also referred to as end-stage renal disease (ESRD)).

*Address for correspondence:* Patricia Painter, Ph.D., Division of Retinal Diseases and Hypertension, University of Minnesota MMC 1932, 717 Delaware St SE, Suite 353, Minneapolis, MN 55455 (E-mail: tpainter@umn.edu).
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2) There are often multiple comorbidities present that must be considered. In CKD, approximately 45%–50% of patients have type 1 or 2 diabetes mellitus, and many patients have cardiovascular disease. There were few exercise studies that included diabetic patients or those with cardiovascular disease, thus limiting the generalizability of the research findings to only a fraction of the patient population.
3) There are variable treatment regimens, and treatments are continually changing. In CKD, many patients treated with dialysis are on a waiting list for transplantation and, thus, will undergo transplantation when a kidney becomes available. Others may change the type of dialysis treatment, and most will change pharmacological therapies during the course of the disease.
4) Patients may experience a change in clinical status or a setback. Patients treated with dialysis or who are immunosuppressed after transplant are susceptible to infections, which are the main reason for hospitalization. When patients change treatment or clinical status, the intervention may be adjusted or discontinued, and the change is accounted for appropriately.

Moreover, many "systemic" challenges related to the systems of health care delivery and research regulation may be encountered when attempting exercise research in the chronic disease populations. The following are examples of such systemic challenges:

1) The research may be given relatively low priority in the overall treatment scheme. Obviously, routine treatment must take priority over research, but this fact can be disconcerting to the research staff because routine treatment may delay or set the exercise interventions off schedule.
2) There may be a lack of interest or support for the exercise research on the part of the health care providers. Most often, the lack of interest is due to time restraints. To garner support from the health care staff, research staff should do all they can to be sure their work does not interfere with the health care staff and to educate the staff as to the importance of the research for the overall health and well-being of the patients.
3) There may be variable interest for exercise research on the part of patients. The patients may not have experience with healthy lifestyles nor understand exercise to be a part of their treatment regimen. In contrast, other patients may be very interested in the opportunity to do something to improve the symptoms that occur with chronic diseases.
4) In the age of the Health Insurance Portability and Accountability Act of 1996, it may be difficult for researchers to gain access to patients for research studies. Becoming an integrated part of the treatment team may be important for the researcher to reduce the significant burden of subject recruitment.

In summary, exercise research in chronic disease is not a straightforward venture because of many challenges. It is critical to involve the health care providers, so they can provide access to patients and encourage patient participation in the research process. However, despite challenges to doing the research needed to document the benefits of exercise, there are many reasons to justify the use of exercise in patients with chronic disease, both in terms of physical functioning and clinical implications.

## JUSTIFICATION FOR EXERCISE IN CHRONIC DISEASE

There are many clinically relevant reasons to recommend exercise for patients with chronic disease. 1) Exercise training will attenuate the physical deconditioning that patients typically experience upon diagnosis. 2) Exercise training may optimize functioning when used as adjunctive therapy to standard pharmacological or surgical treatments. 3) Exercise training may reduce secondary cardiovascular risk factors and attenuate other clinical consequences of the disease and/or treatment. 4) Improving physical functioning will optimize quality of life/well-being and possibly improve overall outcomes. Research to document the impact of regular exercise on each of the stated clinically relevant reasons is needed for exercise to become integrated as a routine part of treatment. The following are approaches in the development of a program of study that may provide the required justification for exercise in patients with chronic disease.

### Documentation of Exercise Capacity and Limitations to Exercise

Exercise will not be considered important unless there is documentation of deficits in physical functioning. The first published documentation of low functioning in a CKD patient treated with hemodialysis was in 1977 (20). There are now over 45 publications documenting low levels of exercise capacity in hemodialysis patients as measured by $\dot{V}O_{2peak}$ or physical performance testing (2,12). Patients treated with hemodialysis have $\dot{V}O_{2peak}$ that average approximately 50%–60% of age-predicted values (2,10). Figure 1 shows the average $\dot{V}O_{2peak}$ from 14 early studies, in which patients were not treated with human recombinant erythropoietin (rHuEPO) for their anemia.

It is also important to document the mechanisms for the deficit or the physiological factors particular to the pathophysiology that limit exercise capacity. Figure 2 is a

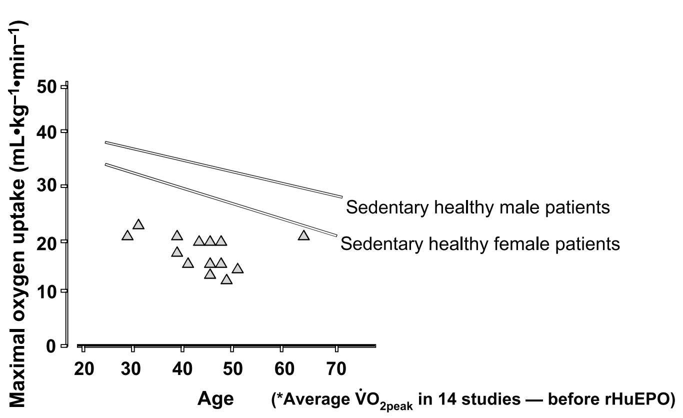


**Figure 1.** Levels of $\dot{V}O_{2peak}$ in hemodialysis patients compared with sedentary normals. Values are average values from 14 studies before the availability of human recombinant erythropoietin (rHuEPO). (Individual references can be found in (2), (4), and (12).)

simplified diagram of oxygen transport from the atmosphere to the working muscle and several physiological determinants of each step. The right side of the diagram shows several basic pathophysiological conditions present with stage 5 CKD (ESRD — in which renal replacement therapy is required) that may affect oxygen transport. Integrating the understanding of oxygen transport factors and regulation during exercise with the pathophysiology of a given disease provides a model for designing research that will target interventions to specific physiological limitations.

For instance, in patients with CKD, it is possible to measure cardiac output through the dialysis access site. The components of the Fick equation have been measured in hemodialysis patients at peak exercise and, compared with normal responses, these patients have low cardiac output primarily because of an attenuated heart rate response (with essentially normal stroke volume) (Fig. 3). The patients also had an attenuated arterial-venous oxygen (a-v$O_2$) difference (Fig. 4, anemic bar). Because these patients were anemic (primarily because of the lack of renal production of erythropoietin by the kidney), the low a-v$O_2$ difference seemed to be due to low arterial content (Fig. 4, anemic bar) because it seemed that these patients were able to extract oxygen to quite low venous levels. Thus, correction of the anemia with rHuEPO may be expected to increase the a-v$O_2$ difference and thus $\dot{V}O_{2peak}$ (10).

In fact, when rHuEPO became available and hematocrit was successfully treated, it was expected that exercise capacity would likewise increase. Five research groups measured $\dot{V}O_{2peak}$ as a part of the early studies of rHuEPO treatment in dialysis patients (see (10) for specific studies). In these studies, the hematocrit target was 33% (not normalized). $\dot{V}O_{2peak}$ increased with increasing hematocrit, but the $\dot{V}O_2$ response was less than what had been shown in studies of hematocrit manipulation in normal healthy individuals. Figure 5 is a summary of six studies that manipulated (increased or decreased) hemoglobin with red cell infusion or through phlebotomy in normal healthy subjects. Also presented in Figure 5 is the $\dot{V}O_2$ response to changes in hemoglobin in the original five dialysis studies. The $\dot{V}O_{2peak}$ response to increasing hematocrit in dialysis patients was clearly blunted (10).

J. Stray-Gunderson *et al.* (unpublished manuscript/observation, 1997) used rHuEPO to gradually increase hematocrit in hemodialysis patients and measured the determinants of $\dot{V}O_2$. Figure 4 indicates that, as arterial oxygen content increased with rHuEPO treatment from the anemic condition, there was a parallel increase in venous oxygen content with no increase in a-v$O_2$ difference. This suggests a fixed limitation in skeletal muscle oxygen extraction. Although the patients improved with elevated hematocrit, medical treatment was not sufficient. The lack of expected improvement and the documentation of no change in a-v$O_2$ difference suggest that the limitation in $\dot{V}O_{2peak}$ may be, in part, due to impaired skeletal muscle function. The impaired skeletal muscle function may be improved with exercise training.

## Documentation of Exercise Training Effectiveness

It is well documented that exercise training improves exercise capacity in patients treated with hemodialysis. In a meta-analysis of exercise training in patients receiving maintenance hemodialysis, Cheema and Singh (2) report 29 trials, including 9 uncontrolled trials, 7 controlled trials, and 13 randomized controlled trials. Although a few trials reported no significant improvement in $\dot{V}O_{2peak}$, most reported significant improvement with aerobic exercise between 17% and 23% (2,4,11,12).

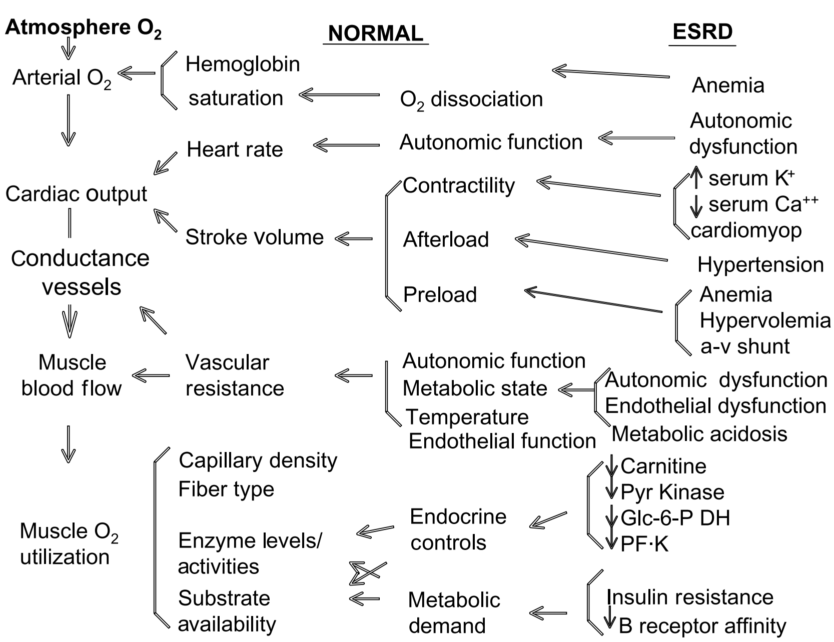


**Figure 2.** Model of oxygen transport from the atmosphere to the working muscles and some of the basic controls of each step in normals. On the right are basic pathophysiological consequences of end-stage renal disease (ESRD) (chronic kidney disease (CKD) stage 5) that may impact oxygen transport and thus limit exercise capacity. This model could be used for any chronic disease condition to identify possible physiological limitations and to target interventions to specific systems.

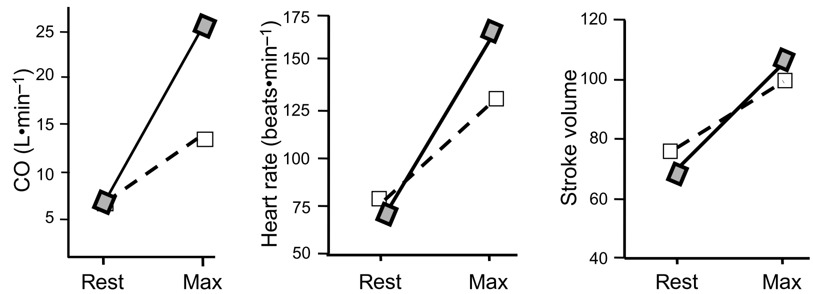


**Figure 3.** Determinants of the Fick equation of oxygen uptake at rest and maximal exercise (max). Reference values (*filled square*) are presented to compare the responses in patients with chronic kidney disease (CKD) treated with hemodialysis (*open square*).

Interestingly, those studies that included a combination of strengthening and aerobic training reported changes in $\dot{V}O_{2peak}$ from 41% to 48%. The training responses are similar in patients with anemia (before availability of rHuEPO) and those treated with rHuEPO for anemia (4). Thus, there may also be other systemic limitations to $\dot{V}O_{2peak}$ because of the disease and/or treatment in these patients (as suggested in Fig. 2).

The measurement of $\dot{V}O_{2peak}$ may not always be the most appropriate measure of physical functioning, especially in older patients who experience frailty, significant concomitant comorbidities, and debilitation. In these patients, other measures of physical functioning are used, such as muscle strength, 6-min walk distance, sit-to-stand-to-sit test time, and gait speed. These measures of physical functioning improve with exercise training (2,11,15).

It is important to note that the natural course of functioning in a given population with chronic disease may be deterioration. Thus, if improvement is not observed or is minimal, it may be because of the natural course of functioning. In such cases, the maintenance of functioning or slight improvements is considered a positive result when the expectation would be deterioration in functioning. This concept was well demonstrated in the data from the Renal Exercise Demonstration Project (15), where all performance-based measures deteriorated in the experimental group that received no intervention but increased slightly or remained stable in the intervention group (15). Thus, the comparison of the change over time in the intervention and usual-care groups were significantly different; even a minimal improvement in the intervention group was a positive outcome.

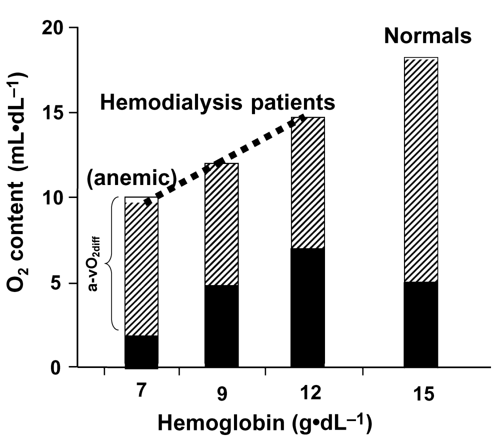


**Figure 4.** Blood oxygen content at peak exercise in hemodialysis patients. The *top line* of each *bar* is arterial oxygen content ($CaO_2$) and the *lower bar* (at the bottom of the *striped box*) is mixed venous content ($CvO_2$). The striped box is the arterial-venous oxygen difference ($a\text{-}vO_{2diff}$). The bars on the left are from hemodialysis patients who were initially anemic, then treated with rHuEPO to increase arterial oxygen content. Reference values at max exercise are presented for comparison. Data for hemodialysis patients come from unpublished data from J.R. Thompson and J. Stray-Gunderson.

## CLINICAL BENEFITS OF EXERCISE TRAINING

In addition to the improvements in exercise capacity or physical functioning, the impact of exercise interventions on clinical conditions is equally important. For example, exercise training in patients with ESRD has been documented to improve cardiac functioning (left ventricular (LV) mass index, ejection fraction, cardiac output index, and stroke volume index) and heart rate variability (2). Muscle structure and neuromuscular control also improved after 6 months of combined aerobic and resistance training. Specifically, increased cross-sectional area of Type I and II muscle fibers, near normalized ratio of Types I to II fibers, improved capillarity and mitochrondia density. These observed exercise-induced skeletal muscle changes are important in patients with a chronic disease because many of the patients experience sarcopenia. Nerve condition also improved. Blood pressure control is improved with aerobic exercise with lower antihypertensive medication requirements (2,11). Several authors report improved fasting glucose and insulin concentrations, with apparent improvement in insulin sensitivity, and others report improved lipid profiles (increased high-density lipoprotein cholesterol and reduced very low density lipoprotein and plasma triglyceride) (2,11). These exercise-induced changes are important benefits that positively affect the secondary cardiovascular comorbidity in this population.

Likewise, quality of life, specifically the "physical domains" are improved with exercise training. The Short-Form 36 (SF-36) health status questionnaire is used as the assessment tool for the quality-of-life measurement in dialysis patients. The benefits in quality of life are most notable in those with the lowest baseline levels (14). Thus, if the benefits in physical functioning are not an adequate justification for implementing exercise, there are important benefits in clinical concerns and in quality of life that may be

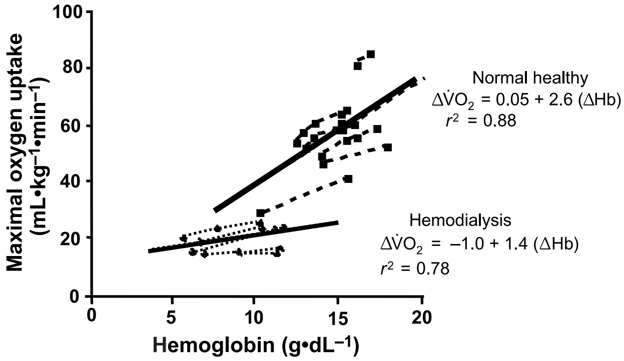


**Figure 5.** Changes in peak $\dot{V}O_2$ responses in healthy individuals (ν) and patients on hemodialysis (σ) with manipulation of hematocrit. Hb indicates hemoglobin.

gained from the incorporation of exercise in the population with chronic disease.

## EFFECTS OF EXERCISE AS AN ADJUNCTIVE THERAPY TO STANDARD CLINICAL INTERVENTIONS

Exercise training may be an important adjunct therapy to standard medical or surgical interventions because it may either improve the therapy or optimize exercise capacity with the treatment. There is evidence that clearance of solutes during the hemodialysis treatment is improved when cycling exercise is used during the treatment. Vaithilingam *et al.* (19) reported statistically greater weekly phosphate removal in 12 patients who exercised during the dialysis treatment compared with those who did not exercise. The phosphate removal with exercise was similar to increasing dialysis time by 1 h per session. Kong *et al.* (7) studied 11 patients who were on paired dialysis session: one with exercise and the other as a control. The rebound of urea, creatinine (an indication of urea clearance), and potassium were reduced significantly with the exercise treatment. The rebound of urea dropped from 12.4% to 10.9%; creatinine, from 21.2% to 17.2%; and potassium, from 62% to 44%. The authors concluded that the improvement in dialysis adequacy with exercise training was equivalent to extending the length of the hemodialysis treatment by 30 min. The mechanism of these increases in clearance with exercise is thought to be increased skeletal muscle blood flow, which exposes more tissue to the dialysis process.

The hypothesis that exercise training will enhance the effects of improved hematocrit on exercise capacity by improving muscle function was tested as a part of a study by Painter *et al.* (13) to determine the effects of normalization of hematocrit with rHuEPO. Patients were randomized into two hematocrit groups (30%–33%, which is standard care) and 40%–42% (experimental group). A second randomization was done within each of these hematocrit groups, to exercise and no exercise. The exercise groups in both hematocrit groups improved $\dot{V}O_{2peak}$, whereas normalizing hematocrit had no effect on $\dot{V}O_{2peak}$. The findings clearly indicate that exercise training maximizes the effect of rHuEPO treatment, regardless of hematocrit target level.

Surgical intervention in ESRD with kidney transplant may also remove some of the pathological factors that limit $\dot{V}O_{2peak}$. It has been documented that $\dot{V}O_{2peak}$ in dialysis patients is significantly improved (although not necessarily normalized) with successful renal transplantation. Two studies report significant increases in $\dot{V}O_{2peak}$ soon (8 and 12 wk, respectively) after successful kidney transplant, in which the uremic state was removed (Fig. 6 — represented by the dotted line between the closed triangles to open squares) (9). Although transplantation improves exercise capacity, it does not completely restore exercise capacity. In an uncontrolled trial of patients, 3 yr after transplant, who underwent strenuous training for the transplant games, there was a 28% improvement in $\dot{V}O_{2peak}$ (Fig. 6, closed square). A cross-sectional study of participants at the 1998 U.S. Transplant Games revealed $\dot{V}O_{2peak}$ levels that averaged 110% above age-predicted reference values (9) (single closed circle). In a randomized controlled trial of exercise over the first year after transplant, $\dot{V}O_{2peak}$ increased an average of 26% (intent-to-treat analysis) (Fig. 6, open square to closed diamond), whereas the usual-care group did not improve over baseline testing and had levels similar to exercise-trained dialysis patients (16). Thus, there is robust evidence that exercise training after transplant maximizes exercise capacity and optimizes the effects of transplantation on physical functioning.

Nandrolone decanoate (an anabolic steroid) is sometimes used in dialysis patients with severe muscle wasting. A randomized clinical trial in hemodialysis patients (four groups: nandrolone only, resistance exercise only, resistance exercise plus nandrolone decanoate, and controls) demonstrated that, despite increased lean mass, there was minimal improvement in quadriceps muscle strength in the group that received the drug alone (5), whereas resistance exercise alone and the nandrolone–plus–resistance exercise groups showed significant gains in muscle strength, with minimal change in lean mass (Fig. 7). Thus, it is clear that the exercise intervention optimized the results of the pharmacological intervention in terms of functional outcomes.

## EFFECTS OF EXERCISE ON PATIENT OUTCOMES

Overall patient outcomes seem to be the driving force in medical treatment. If exercise has a positive impact on overall outcomes such as morbidity, hospitalizations, or mortality, then there is a greater chance of it becoming a part of the routine care. Outcome studies are costly and often difficult, especially in patients with chronic conditions because continuous and/or long-term exercise training may not be possible because of the challenges in exercise research mentioned previously. Until those studies can be done, epidemiological evidence is informative. The United States Renal Data System is a very large database that includes clinical data and outcomes of all patients with CKD started on dialysis in the United States. Over a period of 2 yr, a question of physical activity participation was included in the survey (Morbidity and Mortality Survey). These data were analyzed by O'Hare *et al.* (8) to dichotomize patients into sedentary (never or almost never participate in physical

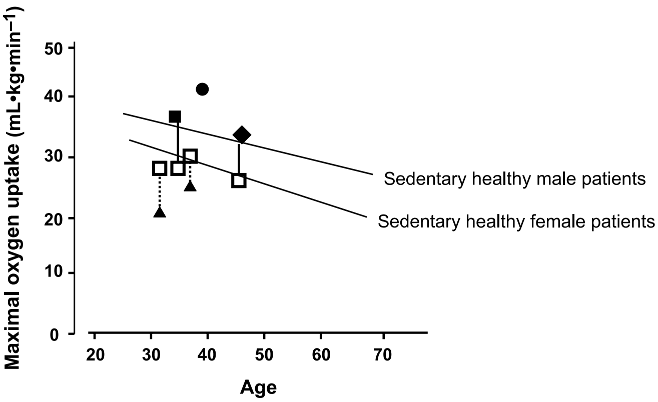


**Figure 6.** $\dot{V}O_{2peak}$ in patients treated with renal transplantation compared with sedentary reference values (9). σ = before transplant; π = after transplant with no exercise training; the change from σ to ρ is from before transplantation to after transplantation without exercise training intervention (2 studies); ρ to ν is change from preexercise to postexercise training study (average, 3 yr after transplant); λ is the average of a cross-sectional study of transplant athletes (average, 8 yr after transplant; ρ to υ is the change in the exercise group of a 1-yr randomized clinical trial (14)).

activity during leisure time) and nonsedentary (participation in some physical activity during leisure time). Of the 2264 patients who reported physical activity data, 35% were categorized as sedentary. Eleven percent of the sedentary patients died over the 1-yr follow-up period compared with 5% of the nonsedentary patients ($P < 0.001$). The patients classified as sedentary at the time of initiation of dialysis showed a 62% greater risk of mortality over 1 yr compared with nonsedentary patients with adjustment for other variables associated with survival in these patients (perception of general health, cardiac disease, peripheral vascular disease, creatinine, hematocrit, dialysis modality, education level, male sex, diabetes, and phosphorous level). Stack *et al.* (18) also analyzed these data and showed similar results. Specifically, patients who reported more frequent exercise (*i.e.*, up to four to five times per week) had improved survival.

In addition to the value of physical activity in predicting outcomes, physical functioning as measured by $\dot{V}O_{2peak}$ and self-reported functioning (SF-36) also are predictive of outcomes. The self-reported physical functioning scale and the overall physical composite scale on the SF-36 health status survey are independent predictors of hospitalization and death in studies with large numbers of patients (up to 16,000 patients followed over 2 yr) (6). Similar results using $\dot{V}O_{2peak}$ were reported by Sietsema *et al.* (17), which found $\dot{V}O_{2peak}$ to be the strongest independent predictor of death ($P = 0.009$) in 175 hemodialysis patients who were followed over a 3.5-yr period. Although the definitive outcomes trial (*i.e.*, a randomized controlled trial of exercise training on morbidity and mortality) has not been done, there is strong epidemiological data that suggest that interventions to increase physical activity and/or physical functioning may be important to optimize outcomes in patients treated with hemodialysis.

Because the medical community is focused on interventions that improve overall patient outcomes — specifically hospitalization/institutionalization, morbidity, and death — documenting that low levels of physical activity and physical functioning are significant predictors of outcomes will justify interventions to increase physical activity and improve physical functioning.

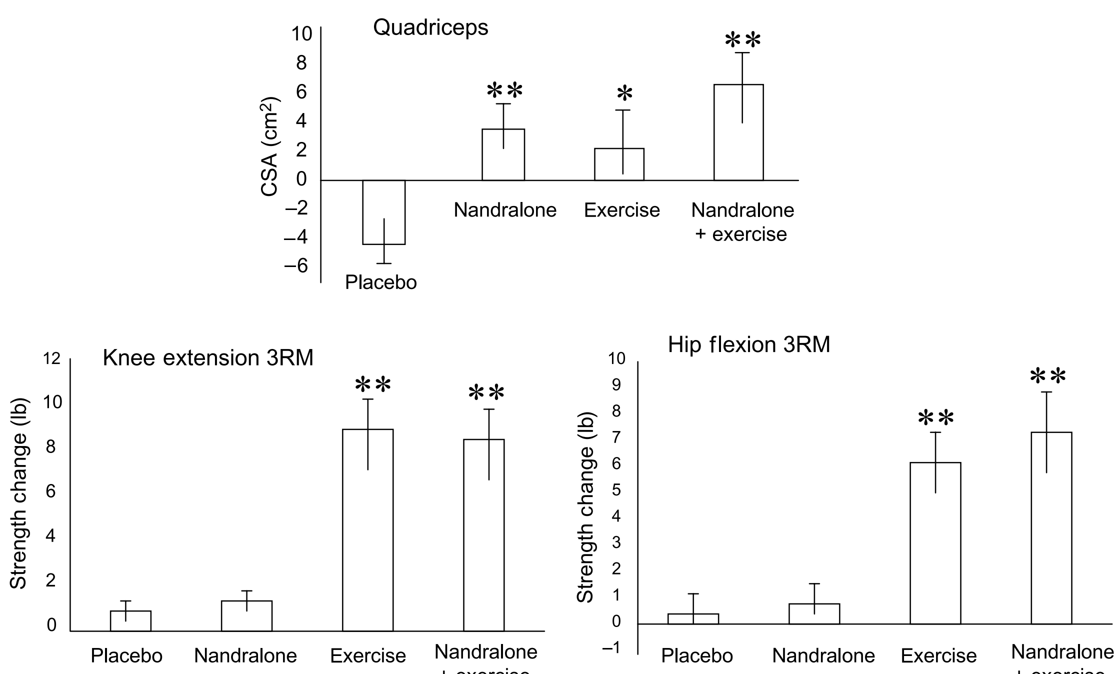


**Figure 7.** Results from a randomized clinical trial of nandrolone decanoate plus resistance exercise training in hemodialysis patients (5). Upper panel is quadriceps cross-sectional area (CSA) in the 4 groups; lower panels are strength changes in the knee extension (3RM) and hip flexion (3RM) in the 4 groups. *$P < 0.01$; **$P < 0.001$ compared with placebo. Figure created by Kirsten Johansen; not previously published. Used with permission.

### There is a Need to Determine Appropriate Outcome Measures

The implementation of exercise programs as a part of the routine care and development of research in chronic disease will require the identification of evaluation measures for research outcomes and for tracking progress in clinical programs. The "gold standard" measure of exercise capacity (*e.g.*, $\dot{V}O_{2peak}$) may not be the most appropriate measure in some patient groups. In CKD, patients are older (>60% are older than 65 yr), have significant muscle weakness and often orthopedic limitations, have transportation limitations in getting to a center where $\dot{V}O_2$ can be measured, and exhibit clinical factors that may limit their performance and interpretation of a graded exercise test (*e.g.*, hypertension and electrocardiographic abnormalities). Considering all these factors, other types of tests such as standardized physical performance (*i.e.*, 6-min walk, shuttle walk, gait speed, get-up-and-go test, and sit-to-stand test) may be more appropriate. Patients with CKD treated with hemodialysis achieve less than 65% of age-predicted values on these tests, and they are documented to be sensitive to change resulting from physical activity interventions (16).

Interpretation of test results from exercise interventions in chronic disease populations may need to be reconsidered. Usually, if an intervention group shows minimal or no change in exercise capacity, then the interpretation would be that the intervention was unsuccessful. However, if the natural course of the disease is for exercise capacity to deteriorate over time, then maintenance of physical functioning is a positive result. This was well demonstrated in the data from the Renal Exercise Demonstration Project (15), where all performance-based measures deteriorated in the group that received no intervention but increased slightly or remained stable in the intervention group. Thus, the comparison of the change over time in the intervention and usual-care groups were significantly different; even a minimal improvement in the intervention group was a positive outcome.

### Considering the Delivery of Exercise Training

Although the cardiopulmonary rehabilitation program model of $3\text{-d}\cdot\text{wk}^{-1}$ exercise at an outpatient center has worked well for the cardiac and pulmonary populations, this model may not be feasible for other patient groups. For patients who are elderly and have significant comorbidity and/or treatment time burden, coming in to a supervised exercise center may not be practical. Many patients will have transportation issues and time constraints. For example, patients treated with hemodialysis have to go to the dialysis clinic three times per week for treatments of 3–4 h in duration. Travel and setup procedures can extend that time to 5–6 h. It is therefore understandable that adherence to a standard outpatient cardiac rehabilitation program on non-dialysis days is low. Thus, creative approaches of delivery of exercise are needed. Use of a cycle ergometer during the dialysis treatment is feasible and results in good adherence and positive benefits.

Implementation of such programs within the patient care setting requires a close working relationship with the dialysis clinic staff, and it is usually necessary to address the corporate policies of the providers to develop new interventions. Independent home exercise with encouragement from the care providers and regular follow-up and support from exercise professionals may also be feasible. Home exercise has been shown to result in positive benefits in hemodialysis patients and in transplant recipients (12,16).

## SUMMARY

The numbers of people with diagnosed chronic disease is steadily growing. Surgical procedures and medical therapies are constantly improving, so these patients are living with chronic disease for much longer than ever before. Many of the known physiological benefits of exercise can be realized by patients with chronic disease, and exercise training may have a positive impact on clinical concerns and overall quality of life and well-being. Involvement of exercise professionals in the care of these patients is long overdue; however, integration of exercise counseling and encouragement into the routine care requires research and education of the health care providers. Exercise professionals must reach out and work closely with those health care providers to determine the most effective and practical way to include exercise research and/or interventions into the routine care. As we gain the research knowledge and clinical experience, practice guidelines can be developed for exercise in the various populations with chronic disease, and it may eventually become routine practice and covered by third-party payers. The ultimate goal is common to the health care providers and patients: to optimize physical functioning, quality of life, and overall medical and surgical outcomes.

### References


1. Bloomfield, S.A., and E.F. Coyle. Bed rest, detraining and retention of training-induced adaptations. In: *Resource Manual for Guidelines for Exercise Testing and Prescription* (2nd edition), J.L. Durstine, P.L. Painter, J.L. Roitman, and L.D. Zwiren (Eds.). Philadelphia: Lea and Febiger, 1993. pp. 115–128.
2. Cheema, B.S., and M.A. Singh. Exercise training in patients receiving maintenance hemodialysis: a systematic review of clinical trials. *Am. J. Nephrol.* 25:352–364, 2005.
3. Cheema, B.S., B.C. Smith, and M.A. Singh. A rationale for intradialytic exercise training as standard clinical practice in ESRD. *Am. J. Kidney Dis.* 45:912–916, 2005.
4. Johansen, K.L. Exercise in the end-stage renal disease population. *J. Am. Soc. Nephrol.* 18:1845–1854, 2007.
5. Johansen, K.L., P.L. Painter, G.K. Sakkas, P. Gordon, J. Doyle, and T. Shubert. Effects of resistance exercise training and nandrolone decanoate on body composition and muscle function among patients who receive hemodialysis: A randomized, controlled trial. *J. Am. Soc. Nephrol.* 17:2307–2314, 2006.
6. Knight, E.L., N. Ofsthun, M. Teng, J.M. Lazarus, and G.C. Curhan. The Association between mental health, physical function and hemodialysis mortality. *Kidney Int.* 63:1843–1851, 2003.
7. Kong, C.H., J.E. Tattersal, R.N. Greenwood, and K. Farrington. The effect of exercise during hemodialysis on solute removal. *Nephrol. Dial. Transplant.* 14:2927–2931, 1999.
8. O'Hare, A.M., K. Tawney, P. Bacchetti, and K.L. Johansen. Decreased survival among sedentary patients undergoing dialysis: results from the dialysis morbidity and mortality study wave 2. *Am. J. Kidney Dis.* 41:447–454, 2003.
9. Painter, P. Exercise following organ transplantation: a critical part of the routine post transplant care. *Ann. Transplant.* 10:28–30, 2005.
10. Painter, P. The importance of exercise training in rehabilitation of patients with end stage renal disease. *Am. J. Kidney Dis.* 24(1 Suppl. 1):S2–S9, 1994.

11. Painter, P. Physical functioning in end-stage renal disease patients: update 2005. *Hemodial. Int.* 9:218–235, 2005.
12. Painter, P., and K.L. Johanson. Improving physical functioning: time to become a part of the routine care. *Am. J. Kidney Dis.* 48:167–170, 2006.
13. Painter, P., G. Moore, L. Carlson, S. Paul, J. Myll, W. Phillips, and W. Haskell. 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
14. Painter, P., L. Carlson, S. Carey, S.M. Paul, and J. Myll. Low functioning patients improve with exercise training. *Am. J. Kidney Dis.* 36:600–608, 2000.
15. Painter, P., L. Carlson, S. Carey, S.M. Paul, and J. Myll. Physical functioning and health related quality of life changes with exercise training in hemodialysis patients. *Am. J. Kidney Dis.* 35:482–492, 2000.
16. Painter, P.L., L. Hector, K. Ray, L. Lynes, S. Dibble, S.M. Paul, S.L. Tomlanovich, and N.L. Ascher. A randomized trial of exercise training after renal transplantation. *Transplantation.* 74:42–48, 2002.
17. Sietsema, K.E., A. Amato, S.G. Adler, and E.P. Brass. Exercise capacity as a predictor of survival among ambulatory patients with end stage renal disease. *Kidney Int.* 65:719–724, 2004.
18. Stack, A.G., D.A. Molony, T. Rives, J. Tyson, and B.V. Murthy. Association of physical activity with mortality in the US dialysis population. *Am. J. Kidney Dis.* 45:690–701, 2005.
19. Vaithilingam, I., K.R. Polkinghorne, R.C. Atkins, and P.G. Kerr. Time and exercise improve phosphate removal in hemodialysis patients. *Am. J. Kidney Dis.* 43:85–89, 2004.
20. Jette, M., G. Posen, and C. Cararelli. Effects of an exercise program in a patient undergoing hemodialysis treatment. *J. Sports Medicine.* 17: 181–184, 1977.