# Chapter 27: Rehabilitation Services for Elderly Dialysis Patients

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Based on recent data, Canadians starting dialysis between the ages of 75 and 79 yr will have an average life expectancy of 3.2 yr.1 In the United States, patients 65 to 79 yr of age starting dialysis have a reported life expectancy of 25 mo.<sup>2</sup> During this time, patients may experience transient or permanent loss of personal independence, which, in turn, has a negative impact on their quality of life and financial situation and a significant impact on health care utilization.3 In general, older patients have complex medical histories and a higher incidence of chronic ailments such as arthritic pain, vision loss, or fatigue. Often patients adapt by walking more slowly or taking more rests and developing fixed routines with little variability or limiting activities. Over time, these symptoms and adaptations have a cumulative effect on functional status, possibly leading to dependency. In the renal literature, prevalent patients on hemodialysis seem to have high levels of functional loss.<sup>4</sup> Preliminary studies show that this is exacerbated by acute hospitalization.5 The impact of a lower functional status may be reduced by offering rehabilitation to dialysis patients. In the nondialysis literature such programs are common and seem to limit the impact of functional disability on patients, their families, and the healthcare system.<sup>6,7</sup> In this chapter, I will review the benefits and concepts of geriatric rehabilitation, the role of the nephrologists, and highlight some common complications.

### WHAT IS GERIATRIC REHABILITATION?

Rehabilitation can be defined as a process by which form and function is restored after injury or illness, such that life can be lived to the fullest capacity compatible with the degree of abilities and disabilities.<sup>8</sup> This definition recognizes two important characteristics of rehabilitation in the older population first that restoration of function is most likely to occur in those with a recent loss of function and, second, that rehabilitation involves a process by which patients both learn new ways to restore function but also methods which help them adapt to the new disability.

Geriatric rehabilitation depends highly on a model of interdisciplinary care. In this model, different team members have both overlapping and complementary skills. Unlike acute care units where the physician often heads the team, rehabilitation teams do not depend on leadership from one particular discipline. Rather, treatment decisions are led by the team member most involved with the patient. Team members include physicians, nurses, social workers, occupational therapists, physiotherapists, speech therapists, psychologists, and pharmacists. Nurses play a key role because they spend the most time with the patient. Through their daily interactions with patients, nurses empower patients to assume self-care and responsibility and evaluate their psychosocial needs. Often nurses help reduce muscle deconditioning by encouraging patients to perform self-care activities outside of their formal therapy sessions. After multiple team members assess the impact of disease on functionality from a variety of perspectives, they identify, through discussion, which of the disciplines is best suited to developing solutions before working in a collaborative manner. As an example, one patient with difficulty walking indoors may work with a physiotherapist to increase muscle strength, whereas another may benefit from occupational therapy sessions to learn to overcome visual limitations.

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	Percent				Percent	
Publication	N Patients With Diabetes	Comorbidity Details	Mean Age (yr)	Average LOS (d)	Discharged Home	Comments
Li (2008) <sup>24</sup>	164 51	CCI = 7.8 ± 2.5	74.5	48.5	68	Majority had a high burden of comorbid diseases. 24% patients required transfer to an acute care institution, of whom 40% did not return to rehab
Forrest (2005) <sup>19</sup>	40 Not reported	Not reported	62.3	12.1	80.0	Prior medically complicated conditions in 8 patients (20%)
Forrest (2004) <sup>18</sup>	34 Not reported	Not reported	68.7	16.0	72.2	Mostly admitted post-procedure. Prior acute hospitalization in 27%
Frank (2002) <sup>20</sup>	5 Not reported	Not reported	76.4	—	20.0	Used Berg Balance Scores and mobility for functional assessment
Garrison (1997) <sup>21</sup>	3 100	100	50.0	18.0-34.0	100.0	Small sample size, postamputation only
Czyrny (1994) <sup>17</sup>	19 Not Reported	Not Reported	59.0	27.0	79.0	Postamputation
Cowen (1995) <sup>16</sup>	28 Not reported	Not reported	61.5	17.5	89.0	Reported converted functional impairment measure

55.2

44.2

n/a

Table 1. Summary of studies evaluating inpatient rehabilitation in dialysis patients

Not reported

4 LOS, length of stay; CCI, Charlson Comorbidity Index.

Greenspun (1986)<sup>22</sup>

# PUBLISHED BENEFITS OF REHABILITATION IN **DIALYSIS CARE**

100

Numerous programs have reported using rehabilitation in their dialysis units. Most develop exercise programs designed to build muscle strength through exercise regimens during dialysis or within the home.9-14 Such programs have been largely successful but are often confounded by high drop-out rates and the high costs of providing staff to supervise the exercises.

Cardiac rehabilitation is recommended for dialysis patients who have recently survived myocardial infarction, had bypass surgery, or those with chronic stable angina. Dialysis patients have been shown to benefit from actively participating in cardiac rehab, with outcome studies showing a 35% reduced risk for cardiac mortality.<sup>15</sup> However, cardiac rehab seems to be underused in dialysis patients, with only 10% of dialysis patients, compared with 23% of the general population, undergoing cardiac rehabilitation after coronary artery bypass graft (CABG) surgery.<sup>15</sup> Reasons behind this apparent paradox have not been clearly identified.

In the older individual, building muscle can be challenging, because patients do not have the strength or capacity to perform strenuous or repetitive exercises. Sensory changes, such as in hearing or vision, or decreases in cognitive function also limit the ability to learn new exercises. Geriatric renal rehabilitation has not been widely formalized and, in many cases, is available only on a case-by-case basis. Published results of outcomes with dialysis rehabilitation are available but often limited by small study size and the inclusion of young patients (<70 yr of age) with few comorbid conditions (Table 1).<sup>16–22</sup> Success rates, as measured by the proportion of patients returning home, vary from 20 to 100%. In the largest and most recent report, approximately 70% of patients<sup>23,24</sup> met their personalized goals and returned home (Figure 1). At the time of admission, patients had a significant burden of comorbidity and high levels of functional dependence. In our unit, dialysis is offered on site on a daily dialysis schedule. Staffing levels have been increased in both the dialysis suite and on the ward to accommodate the higher burden of comorbidity and higher dependency levels.24

scores

Postamputation

# **ISSUES UNIQUE TO REHABILITATION OF ELDERLY DIALYSIS PATIENTS**

### **Comorbidity Burden**

Elderly dialysis patients have a high incidence of comorbidity with recent studies in prevalent hemodialysis patients showing the mean number of medical conditions to be around 10.5  $\pm$ 3.5.25 The high number of comorbid illnesses place a heavy medical burden on the rehabilitation unit staff and the pharmacy. Elderly dialysis patients have a high rate of transfer out to acute care for new or recurrent acute illnesses. Of those who

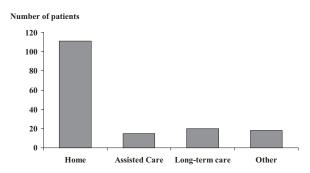


Figure 1. Graph showing discharge disposition of patients admitted to the Toronto Dialysis Geriatric Rehabilitation Program. Patients who did not return to rehabilitation after an acute intercurrent illness or who transferred to palliative care are shown as having been discharged to Other.

are transferred, almost 40% are too unwell to return to rehabilitation.  $^{\rm 24}$ 

### **Dialysis Scheduling**

Short daily dialysis is recommended where possible. It is well tolerated and may lead to improved nutrition and better participation in therapy sessions. Patients report less fatigue and fewer symptoms associated with rapid fluid shifts. Scheduled dialysis and rehabilitation therapy sessions lead to improved outcomes and shorter length of hospital stay.<sup>19</sup>

# **Enforced Immobility During Dialysis**

Patients may benefit from occupational therapy and physiotherapy assessment during the dialysis session. Customized seating aids may improve seating balance while simple physiotherapy exercises may reduce the impact of remaining relatively immobile for longer sessions.

# THE SICK ROLE: THE IMPORTANCE OF ENCOURAGEMENT

Many healthcare workers perceive dialysis patients as being heavily dependent and unable to participate in exercise. In contrast, patients are interested in maintaining their functional independence and taking part in exercise. In a study to identify the barriers to exercise, one important factor identified was that neither nurses nor doctors encourage elderly patients to be active.<sup>26</sup> Studies to see whether changing staff attitudes can alter patient perceptions or activity levels are underway.

# ROLE OF THE NEPHROLOGIST IN DIALYSIS-RELATED GERIATRIC REHABILITATION

The nephrologist role is to work with the team and to take a lead position on identification and referral of patients who may benefit from rehabilitation; customization of the individual medical goals and targets (goals should be adapted to allow the patient to best achieve personal independence and function and yet maintain long-term health); and reduction of polypharmacy and rationalization of medication.

One of the more difficult roles a nephrologist must play is the identification of patients who would benefit from rehabilitation. Few nephrologists are formally trained in rehabilitation medicine, and there is little literature to advise on screening or referral protocols. Nevertheless, it is the nephrologist who follows the chronic predialysis and dialysis patient most closely and who is involved in their long-term care planning. The nephrologist is therefore best placed to identify functional decline and question if rehabilitation would improve functionality. A practical first step is to perform a full geriatric assessment after major events such as dialysis initiation and at set intervals thereafter. Unfortunately, this field is relatively new and it remains unclear whether all patients should be screened, and if so, how often and with what tools. Clearly clinical events such as hospitalization, falls, or a change in social status (*e.g.*, moving home or the death of a spouse or carer) should prompt a functional reassessment by either the primary physician or members of the allied health team.

Nephrologists should also work closely with the rehabilitation team to evaluate and, if necessary, reset health targets for older dialysis patients. Although nephrologists routinely adjust ultrafiltration/target weight and blood sugar targets, some patients may require temporary relaxation in these goals particularly during periods of functional loss. Relaxation of dietary restrictions may allow improved nutrition and allow patients to meet their calorie requirements during a period of repair and recovery. Minor adjustments in volume status can have a significant effect on fatigue. In our experience, debilitated individuals often report or manifest symptoms during their physiotherapy or occupational therapy sessions. Adjustment of target weight based on these observations or symptoms can impact function, with small changes (e.g., an increase or decrease of 200 ml of ultrafiltration) being effective in some cases. (We have maximized this through the use of short daily dialysis regimens.) Some flexibility around blood sugar control may also be helpful for individuals who are prone to labile diabetes. Although tight blood sugar control is always a long-term objective, we have found it necessary to relax blood sugar goals during the initial rehabilitation period. By having a tolerance for a higher mean blood sugar, the patient may feel more able to focus on other aspects of care. Success in these other aspects of personal functioning, empowers them to then address selfcare issues around blood sugar management. Sadly, the need to fulfill benchmark targets may limit the longer-term use of individualized care plans in patients with borderline functional independence.

Nephrologists play a key role in helping to rationalize medications. Many dialysis patients experience polypharmacy. Inpatient rehabilitation care is an ideal setting for discontinuation of medications such as gastric acid suppressants, sedatives, and laxatives, the aim being to reduce unnecessary drugs and minimize drug interactions.

Pain management and detection and treatment of depression are two important aspects of rehabilitation care. Many patients undergoing rehabilitation report chronic pain. Arthritic knees or hands can limit the use of aids and therefore impact both functionality and recovery. The presence of chronic uncontrolled pain may lead to depression and of course *vice versa*, meaning that pain management strategies should include antidepressants if appropriate.

# IDENTIFYING AND MANAGING COMMON PROBLEMS IN DIALYSIS REHABILITATION

# Pain

Pain management is a major issue in ESRD. The topic is large and complex because of the altered metabolism of many drugs, and the reader is encouraged to read further on the topic.<sup>27–29</sup> Key summary principles are discussed below.

Appropriate drugs include acetaminophen  $\pm$  codeine and opiates. Nonsteroidal anti-inflammatory drugs (NSAIDs) can be used in anuric patients with arthritic symptoms. Ideally these should only be used in short courses at low dose because of the lower drug clearance and high risk of gastrointestinal side effects.

Preferred opiates include hydromorphone, fentanyl, and methadone. Morphine, meperidine, and detroporoxyphene should be avoided because of accumulation of the drug. Caution must be exercised with transdermal administration of fentanyl because it seems to have a variable absorption depending on the location of the patch. In addition, absorption may vary depending on the temperature of the skin in that area. (Personal note: We avoid the use of fentanyl in our unit.)

If prescribing opiates, aim to use regular doses of long-acting agents at set times, e.g., twice a day; doses should be supplemented with additional breakthrough medications, particularly initially because the use of breakthrough medications helps determine how much uptitration is needed. Medication doses can be reassessed every 3 to 5 d. The regular dose of a long-acting agent should be increased to be equal to the total average dose of opiate used since the last titration. Therefore, if the patient is taking 3 mg hydromorphone long acting twice daily and is, on average, taking an additional 1-mg breakthrough dose five times a day, one would increase the total long-acting hydromorphone doses to 6 mg twice a day (for a total of 12 mg opiate/24 h) in the hope that pain will be sufficiently well controlled to not require breakthrough drugs. Down titration is best done by a gradual reduction in the opiate doses administered twice daily.

The use of adjuvant therapies such as heat packs, transdermal electrical nerve stimulation therapy, acupuncture, and antidepressants nortriptyline (in preference to amitriptyline) and gabapentin is encouraged.

### **Sleep Disorders**

Sleep disorders and chronic fatigue are common symptoms in dialysis patients. Sleep hygiene programs include regular sleep scheduling, keeping the patient out of bed and the bedroom until bedtime, a snack before bedtime, and instruction on mental imagery or deep breathing relaxation techniques. Sleeping during dialysis, although common, should be discouraged. A patient with a poor sleep pattern may be suffering from concomitant depression, and assessment is advised. If associated with depression, the use of antidepressants with a mildly sedative effect may be beneficial. Mirtazapine is often used because it causes relatively short-term drowsiness (6 to 8 h) and also acts as an appetite stimulant.

# Depression

Depression is common in both dialysis patients and those undergoing rehabilitation. Frail elderly dialysis patients are therefore at particularly high risk, especially around the time of dialysis initiation. Unfortunately, symptoms, such as fatigue or poor sleep and loss of appetite, can be attributed both to dialysis dependency and to depression, and therefore, depression is best detected by having a high index of suspicion. Patients respond well to antidepressants. In our unit, the preference is for the newer agents such as citalopram and sertraline in particular because they have a lower incidence of drug–drug interactions. As mentioned previously, mirtazapine is particularly useful in patients with poor appetite and/or sleep problems. Venlafaxine is our preferred choice for patients with significant anxiety symptoms.

#### **Confusional States**

Cognitive impairment is common in dialysis patients<sup>30</sup> and may significantly impact the success rates with rehabilitation. Associated delirium or agitation is not uncommon and may improve after medication rationalization or treatment of any intercurrent illness. Careful assessment of sensory functions, such as hearing or vision, may be beneficial. Patients with reduced vision or hearing may not be aware of "normal" external stimuli and what may be a simple startle reaction may be misinterpreted as agitation. Agitated patients may respond well to routine. If possible, dialysis scheduling should facilitate dialysis in the same station at the same time each day for vulnerable patients.

### CONCLUSIONS

Widespread development of programs offering rehabilitation to dialysis patients is likely increasingly worthwhile as the average age of the dialysis patients increases. Programs seem effective in minimizing the disability associated with aging and chronic disease. Nephrologists play an important role in identification of patients; setting appropriate medical goals; and managing common problems such as pain control. Specific training in care of the elderly patient may be of benefit to nephrologists.

### TAKE HOME POINTS

- There is a high burden of dependency and disability in the older dialysis population
- Recent onset dependence and disability may be reversed through targeted rehabilitation programs
- Rehabilitation outcomes are improved if nephrologists work in conjunction with rehabilitation specialist teams; important areas for collaboration include identification of appropriate candidates, medical goal adjustment, and pain and medication management
- Scheduled dialysis sessions are associated with better rehabilitation outcomes; short daily dialysis sessions are best tolerated (opinion)

# DISCLOSURES

None.

# REFERENCES

\*Key References

- Jassal SV, Trpeski L, Zhu N, Fenton SSA, Hemmelgarn BR: Changes in survival over the years 1990–1999 for elderly patients initiating dialysis. CMAJ 177: 1033–1038, 2007
- Kurella M, Covinsky KE, Collins AJ, Chertow GM: Octogenarians and nonagenarians starting dialysis in the United States. Ann Intern Med 146: 177–183, 2007
- 3. USRDS Data report. http://www.usrds.org/adr\_2007.htm 2007
- Cook WL, Jassal SV: Functional dependencies among the elderly on hemodialysis. *Kidney Int* 73: 1289–1295, 2008\*
- Lo D, Chiu E, Jassal SV: A prospective pilot study to measure changes in functional status associated with hospitalization in elderly dialysisdependent patients. *Am J Kidney Dis* 52: 956–961, 2008
- Forster A, Young J, Lambley R, Langhorne P: Medical day hospital care for the elderly versus alternative forms of care. Cochrane Database Syst Rev CD: 001730, 2008
- Clark GS, Siebens HC: Rehabilitation of the geriatric patient. In: *Rehabilitation Medicine*, edited by DeLisa JA, Philadelphia, Lippincott, 1993, pp 642–665
- 8. Eisenberg MG: Dictionary of Rehabilitation. New York, Springer, 1995
- Johansen KL, Painter PL, Sakkas GK, Gordon P, Doyle J, Shubert T: 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
- 10. Painter P, Johansen KL: Improving physical functioning: time to be a part of routine care. *Am J Kidney Dis* 48: 167–170, 2006
- Painter P, Carlson L, Carey S, Paul SM, Myll J: Low-functioning hemodialysis patients improve with exercise training. Am J Kidney Dis 36: 600–608, 2000
- Johansen KL, Shubert T, Doyle J, Soher B, Sakkas GK, Kent-Braun JA: Muscle atrophy in patients receiving hemodialysis: effects on muscle strength, muscle quality, and physical function. *Kidney Int* 63: 291– 297, 2003
- Painter P: The importance of exercise training in rehabilitation of patients with end-stage renal disease. Am J Kidney Dis 24: S9, 1994
- 14. Painter P: Why exercise can make a difference. *Nephrol News Issues* 20: 52, 2006

- Kutner NG, Zhang R, Huang Y, Herzog CA: Cardiac rehabilitation and survival of dialysis patients after coronary bypass. J Am Soc Nephrol 17: 1175–1180, 2006
- Cowen TD, Huang CT, Lebow J, DeVivo MJ, Hawkins LN: Functional outcomes after inpatient rehabilitation of patients with end-stage renal disease. Arch Phys Med Rehabil 76: 355–359, 1995
- Czymy JJ, Merrill A: Rehabilitation of amputees with end-stage renal disease. Functional outcome and cost. Am J Phys Med Rehabil 73: 353–357, 1994
- Forrest GP: Inpatient rehabilitation of patients requiring hemodialysis. Arch Phys Med Rehabil 85: 51–53, 2004
- Forrest G, Nagao M, Iqbal A, Kakar R: Inpatient rehabilitation of patients requiring hemodialysis: improving efficiency of care. Arch Phys Med Rehabil 86: 1949–1952, 2005\*
- Frank C, Morton AR: Rehabilitation of geriatric patients on hemodialysis; a case series. *Geriatr Today* 5: 136–139, 2002
- Garrison SJ, Merritt BS: Functional outcome of quadruple amputees with end-stage renal disease. Am J Phys Med Rehabil 76: 226–230, 1997
- Greenspun B, Harmon RL: Rehabilitation of patients with end-stage renal failure after lower extremity amputation. Arch Phys Med Rehabil 67: 336–338, 1986
- Jassal SV, Chiu E, Li M: Geriatric hemodialysis rehabilitation care. Adv Chronic Kidney Dis 15: 115–122, 2008
- Li M, Porter E, Lam R, Jassal SV: Quality improvement through the introduction of interdisciplinary geriatric hemodialysis rehabilitation care. Am J Kidney Dis 50: 90–97, 2007\*
- Cook WL, Jassal SV: Prevalence of falls among seniors maintained on hemodialysis. Int Urol Nephrol 37: 649–652, 2005
- Kontos PC, Miller KL, Brooks D, Jassal SV, Spanjevic L, Devins GM, De Souza MJ, Heck C, Laprade J, Naglie G: Factors influencing exercise participation by older adults requiring chronic hemodialysis: a qualitative study. *Int Urol Nephrol* 39: 1303–1311, 2007
- 27. Arnold RM, Verrico P, Davison SN: Opioid use in renal failure #161. J Palliat Med 10: 1403–1404, 2007
- Davison SN: Pain in hemodialysis patients: prevalence, cause, severity, and management. Am J Kidney Dis 42: 1239–1247, 2003\*
- Davison SN: Chronic pain in end-stage renal disease. Adv Chronic Kidney Dis 12: 326–334, 2005
- Murray AM, Tupper DE, Knopman DS, Gilbertson DT, Pederson SL, Li S, Smith GE, Hochhalter AK, Collins AJ, Kane RL: Cognitive impairment in hemodialysis patients is common. *Neurology* 67: 216–223, 2006

# REVIEW QUESTIONS: REHABILITATION SERVICES FOR ELDERLY DIALYSIS PATIENTS

- 1. A 72-yr-old lady presents with acute chest pain to the emergency room. She has been living independently in her own home for some years without difficulty. She is noted to have chronic kidney disease on initial bloodwork. Over the following few days, her cardiac condition deteriorates. Because of marked fluid overload and her background CKD, she needs to start dialysis emergently. One month after initiating dialysis, she is noted by the dialysis staff to be unsteady on her feet when coming to dialysis. Since discharge, she is known to have had multiple falls at home and is currently complaining of pain in her left shoulder after a fall. She has no fracture but has significant bruising and pain and has limited movements of the arm. Her BP is 160/85 mmHg predialysis and 140/78 mmHg postdialysis. Her medications include a renal vitamin, aspirin 81 mg OD, ramipril 10 mg OD, metoprolol 50 mg po twice daily, atorvastatin 20 mg qHS, lorazepam 10 mg qHS, quinine sulfate 300 mg OD on dialysis days for cramps, allopurinol 100 mg OD, hydroxyzine 25 mg three times daily for itch, omeprazole 20 mg OD, zopiclone 7.5 mg qHS, and acetaminophen 1000 mg QID prn for pain. Which of the following statements is true:
  - a. Her falls are likely only happening on postdialysis days and therefore related to hypotension; the most appropriate action is adjustment of target weight
  - b. The most appropriate first step is to manage her pain by introduction of an opiate on a regular schedule
  - c. The most appropriate first step is to prescribe a walker to help with her unsteadiness
  - d. Her falls are likely multifactorial and, taken together with her unsteadiness and polypharmacy, she may benefit from referral to a rehabilitation specialist for evaluation, and treatment.
- 2. An 85-yr-old hemodialysis patient is referred for rehabilitation after the family notice a decline in his functional status

over the past few months. The rehabilitation team review the literature for clinical evidence about the effectiveness of inpatient geriatric rehabilitation in elderly, dialysis patients. Which of the following statements is true:

- a. Strong, grade A (randomized controlled trial) evidence that rehabilitation is effective in elderly dialysis patients
- b. Some Grade B evidence (from observational studies) that rehabilitation is effective in elderly dialysis patients
- c. No evidence in either direction (either supporting effectiveness or no effectiveness) in elderly dialysis patients
- d. Strong evidence (randomized controlled trial) that rehabilitation is not effective in elderly dialysis patients
- 3. A 68-yr-old man is admitted to an acute medical ward with symptoms consistent with pneumonia. He is seen by the physio as part of the discharge planning process and is noted to be having difficulty walking and transferring because of muscle weakness. His bone mineralization profile shows he has mild secondary hyperparathyroidism with elevated PTH levels. He starts undergoing physiotherapy and rehabilitation with the physio on an adhoc basis. He is a dialysis patient and receives dialysis in the outpatient dialysis suite on Monday, Wednesday, and Friday mornings where possible. He is a pleasant man who is cooperative and readily amenable to changing his dialysis time to later in the afternoon to suit the staff. There is concern that he does not appear to be making any progress in his walking. Which of the following statements is true:
  - a. Rehabilitation provided on an acute medical ward is ineffective
  - b. Changing patients to a fixed dialysis schedule may reduce the length of stay
  - c. Dialysis patients are likely to require twice as long for rehabilitation as nondialysis patients
  - d. The muscle weakness is unlikely to resolve with exercises as it is related to a myopathy associated with secondary hyperparathyroidism