32. Kidney disease (chronic) and kidney transplant

Author

Susanne Heiwe, PT, PhD, the Physiotherapy Clinic, Karolinska University Hospital and Department of Medicine and Department of Clinical Sciences, Karolinska Institutet, Stockholm, Sweden

Summary

Chronic kidney failure is a toxic syndrome caused by a deteriorating kidney function to excrete waste products, regulate the salt-water and acid-base balance and secrete endocrine hormones. Chronic kidney failure leads to progressive fatigue and a gradually decreased physical work capacity concurrently with the deterioration of kidney function. Without physical exercise, the maximum physical work capacity and muscle strength are reduced by up to 50 per cent compared with the normal expected value once the patient commences regular dialysis treatment. However, this reduction in capacity can be prevented and the patient can maintain normal muscle function plus physical and functional ability if a regular physical exercise programme is started pre-uraemia. Patients with chronic kidney failure have the same ability as healthy people of the same age to improve their muscle function and increase their physical and functional ability regardless of how far the disease has progressed. Physical exercise is an important part of the treatment of chronic kidney failure. Recommended physical activities include walking, cycling and strength training.

Training method	Example	Intensity	Frequency (times/week)	Duration
Aerobic fitness training	Walking Interval training on ergometer bike	70% of VO_2 max* RPE** 14/20	3	60 min.
Strength training	Sequence training Individual training with wrist weights for resistance.	80% of 1 RM***	3	1–2 sets of 8–10 repetitions (reps)
Muscular endurance training	Sequence training Individual training with wrist weights for resistance.	50% of 1 RM	3	Max. number of reps 13–15 acc. to Borg's RPE scale.
Functional training (i.e. walking, balance and coordination training)	Walking for example on a treadmill or balance ma.t Knee bends. Walking up and down stairs. Standing up from sitting.		3	Max. walking duration and max. reps of other exercises. 13–15 acc. to Borg's RPE scale

* VO_2 max = maximum oxygen uptake capacity.
** RPE = Borg's Ratings of Perceived Exertion, RPE scale (41).
*** RM = Repetition Maximum. 1 RM corresponds to the maximum weight that can be lifted through the entire exercise movement one time.

Definition

Chronic kidney failure is a global health problem. Consequences of chronic kidney failure include the loss of kidney function and cardiovascular disease. Chronic kidney disease can either be defined as kidney damage or a glomerular filtration rate (GFR) of less than 60 ml/min/1.73 m^2 for a minimum period of three months and diagnosed without knowledge of its cause. There are five stages of chronic kidney disease:

1. GFR ≥ 90 Kidney damage with normal or increased kidney function
2. GFR 60–89 Kidney damage with a slight decrease in kidney function
3. GFR 30–59 Average kidney function
4. GFR 15–29 Serious decrease in kidney function
5. GFR < 15 Kidney failure

Prevalence/Incidence

At the end of year 1999, the prevalence or the number of patients in active uraemia treatment in Sweden was 693 for every million people with an annual incidence of 120 new patients for every million people. The average age of patients who start treatment is 66 years, i.e. most patients being treated for uraemia today are pensioners (1).

Cause

The most common causes of chronic kidney disease is chronic glomerulonephritis (30%) followed by diabetes mellitus (18%), hereditary polycystic kidney disease (13%), chronic pyelonephritis (10%) and nephrosclerosis (9%). As for the remaining 20 per cent, the cause cannot be determined (1).

Risk factors

- Hypertension with unsatisfactory blood pressure control.
- Diabetes Types 1 and 2 with proteinuria and unsatisfactorily controlled blood pressure and blood glucose levels.

Pathophysiology

Chronic kidney disease leads to an irreversible loss of the glomerular filtration rate (GFR) and toxic syndrome caused by the kidney's failing ability to excrete waste products, regulate the salt-water and acid-base balance and secrete endocrine hormones. The majority of patients with chronic kidney disease have cardiovascular complications. Around 70 per cent of all patients have left ventricular hypertrophy at the start of dialysis and the risk of a dialysis patient dying due to cardiovascular complications, independent of age, is the same as for an average 80-year old (2, 3).

Symptoms

Patients with chronic kidney disease experience a change in taste sensations accompanied by a dry mouth, thirst and a metallic taste in the mouth. These symptoms together with nausea, abdominal bloating and diarrhoea often lead to a loss of appetite and weight loss (4, 5). Uraemia is in itself a catabolic condition with a reduced ability to excrete nitrogenous waste products, i.e. breakdown products of proteins. This in turn leads to a lower intake of proteins and energy which together with metabolic acidosis leads to muscle degradation and muscle atrophy (6, 7). As a result, patients develop anaemia with further fatigue and weakness. Salt and water retention and the impact it has on the renin-angiotensin system leads to hypertension and cardiovascular complications. Displacements in the calcium phosphate vitamin D parathyroid hormone axis cause decalcification of the skeleton with the added risk of calcification of soft tissue. Untreated uraemia generally leads to fatigue, increased fragility, sleep disorders, itchiness, leg cramps, weight loss, muscle hypotrophy and a reduced physical ability (8, 9).

Diagnostics

The initial diagnosis involves assessing the electrolyte status with serum creatinine and serum urea followed by a GFR determination using iohexol or Chrom EDTA clearance.

Current treatment principles

Pre-uremic stage – GFR < 25 ml/min

At this stage of the disease, the prime objective is to slow down the uraemia progression and alleviate uremic symptoms in addition to preparing the patient for dialysis and/or kidney transplant. The basis of slowing down the uraemia progression is a blood pressure control which should give a systolic blood pressure of < 140 mm Hg and a diastolic blood pressure of < 90 mm Hg. A good metabolic control is also important for persons with diabetes. A reduced dietary protein intake has an alleviating effect on uremic symptoms and is also likely to affect the uraemia progression although there is a lack of documented, clear-cut scientific evidence to support this. Renal anaemia is treated with erythropoietin and iron supplements while hypocalcaemia and vitamin D deficiency are treated with lime substitution and active vitamin D. Hyperphosphatemia is treated with phosphate binding medication. Patients with metabolic acidosis are prescribed sodium bicarbonate tablets. During the pre-uraemia stage, the patient is prepared for the necessity of regular dialysis treatments and informed about the two types of dialysis available, i.e. haemodialysis and peritoneal dialysis and if required, the possibility of a kidney transplant. Patients are also required to undergo a minor operation to gain entry/give access to the bloodstream so that dialysis can be performed.

Haemodialysis – GRF about 5–10 ml/min

Access to the patient's bloodstream is attained by way of an arteriovenous fistula which involves stitching together an artery and a vein in the arm to create a large quick flowing and thick walled artery that can cope with the insertion of two needles three times a week. Using a dialysis machine, the blood is then pumped into a dialysis filter that cleans it. The treatment can either take place at a specialist dialysis ward or at home once the patient has been trained to use a self-test haemodialysis machine.

Peritoneal dialysis – GRF about 5–10 ml/min

Access to the patient's bloodstream is attained in the form of a small catheter inserted into the abdominal cavity below the navel. Here, the richly vascular peritoneum is used as dialysis membrane. Four times a day and night, the cavity of the abdomen is filled with around two litres of a glucose solution with a balanced saline content. The solution remains in the cavity of the abdomen for approximately six hours, absorbing waste products and excess fluids before being drained through the catheter. This method is called Continuous Ambulatory Peritoneal Dialysis (CAPD). Alternatively, a machine can be used to pump smaller volumes of fluids in and out of the abdomen cavity of the patient in short cycles during the night when the patient is sleeping for a maximum period of 9–10 hours. This method is called Continuous Cyclic Peritoneal Dialysis (CCPD). Peritoneal dialysis can be managed by the patient at home.

Kidney transplant
A kidney transplant can be performed using a kidney from a close relative or, if this option is not available to the patient, from a recently deceased person. In the latter case, the patient is put on a waiting list for a so-called necro kidney.

Effects of physical activity

Exercise response

A number of studies have shown that persons with chronic kidney disease who are either in the pre-uraemia stage (10–13) or undergoing dialysis treatment (14–19) have the same relative ability to improve their aerobic fitness, muscle strength and endurance as healthy individuals of the same age. However, chronic disease patients need to exercise regularly to counter the decline in their aerobic fitness (20), muscle strength and endurance (21), which will otherwise occur because of the strong catabolic effects of kidney failure.

Natural progression with no exercise

The natural progression of chronic kidney failure is a gradual decline in aerobic capacity during the pre-uraemia stage to around 50 to 60 per cent of the capacity normally seen in a person of the same age and gender undergoing dialysis treatment (22, 23). The most significant etiological factors of this decline is renal anaemia and muscle weakness (23). Today, renal anaemia is treated with erythropoietin and muscle fatigue with physical exercise.

A lack of physical exercise can lead to the individual not being able lead an active and social life. This may result in deteriorating health-related quality of life and an increasing need for the society's involvement. Adults suffering with chronic kidney disease are also at greater risk for cardiovascular diseases, a risk that increases with inactivity. Excessively degraded physical strength could also result in delayed medical acceptance for a kidney transplant, as the individual in question may not be deemed able to cope with the side-effects of medical treatment.

The level of physical activity spontaneously increases following a successful kidney transplant, but will not return to normal without physical exercise (24, 25).

Acute effects

Patients with chronic kidney disease may suffer from high blood pressure, fluid retention and hyperkalaemia. All of these conditions may worsen due to a lack of physical exercise. Exercise in itself may increase the level of serum potassium due, for example, to exercise induced acidosis (26).

Long-term effects

Firstly, physical exercise increases the maximum working capacity (10–19), muscle strength and muscle endurance (10, 13, 16, 19). Patients in the pre-uraemia stage usually manage to normalise their working capacity, muscle strength and endurance after three months of regular exercise, while patients undergoing dialysis treatment usually see a significant improvement after three to six months of regular exercise. Patients in the pre-uraemia stage or undergoing dialysis treatment can increase their functional ability through exercise (13, 18, 27). Physical exercise will also lead to a decline in depressive symptoms and an enhanced self-esteem and quality of life (28, 29). Moreover, physical exercise has a favourable influence on a number of cardiovascular risk factors in patients with chronic kidney disease, resulting in improved blood pressure and lipid control (30) and increased insulin sensitivity (31) as well as an increased heart-rate variability, vagal activity and a lower frequency of cardiac arrhythmia (32, 33).

Following a successful kidney transplant, physical exercise may result in nearly normal physical capacity (34, 35). Muscle strength training has proven to result in improved muscular strength in adult kidney transplant recipients (36, 37).

So as to reduce the risk of cardiovascular disease, physical exercise should be combined with lifestyle changes, such as an improved diet (38).

Indications

Primary prevention

No human studies indicate that physical exercise has a direct, primary preventive influence on the onset of chronic kidney failure.

Secondary prevention

No human studies indicate that physical exercise prolongs or combats uraemia progression. Nevertheless, an indirect secondary preventive effect on uraemia progression should not be ruled out, bearing in mind the favourable influence that physical exercise has on the blood pressure control of patients with high blood pressure and on the blood glucose control of patients with diabetes.

Prescription

Muscle fatigue is the most restrictive factor for the majority of patients. Hence, exercise should initially emphasize muscle strength and endurance training plus balance and coordination training to be complemented with fitness training at a later stage. See Table 1 for a description of various forms of exercise, intensity, duration and frequency.

Table 1. Description of various forms of exercise.

Training method	Example	Intensity	Frequency (times/week)	Duration
Aerobic fitness training	Walking Interval training on ergometer bike	70% of VO_2 max* RPE** 14/20	3	60 min.
Strength training	Sequence training Individual training with wrist weights for resistance.	80% of 1 RM***	3	1–2 sets of 8–10 repetitions (reps)
Muscular endurance training	Sequence training Individual training with wrist weights for resistance.	50% of 1 RM	3	Max. number of reps 13–15 acc. to Borg's RPE scale.
Functional training (i.e. walking, balance and coordination training)	Walking for example on a treadmill or balance mat. Knee bends. Walking up and down stairs. Standing up from sitting.		3	Max. walking duration and max. reps of other exercises, 13–15 acc. to Borg's RPE scale.

* VO_2 max = maximum oxygen uptake capacity.
** RPE = Borg's Ratings of Perceived Exertion, RPE scale (41).
*** RM = Repetition Maximum. 1 RM corresponds to the maximum weight that can be lifted through the entire exercise movement one time.

Special considerations in connection with chronic kidney failure

For all patients

- In view of the high prevalence of cardiovascular diseases, the patient must have a stable heart status, well-controlled blood pressured and not suffer from excessive fluid retention.
- Patients with chronic kidney failure can easily develop tendinitis (inflammation of tendon/tendon bone attachment). Subsequently, it is important to incorporate a long warming up and cooling down period as well as flexibility and stretching exercises in the exercise programme. In addition, the intensity and duration of the exercise programme should increase in stages.
- Patients with a polycystic kidney disease should not perform exercises that involve jumping about or lead to added abdominal pressure due to the risk of mechanical damage to the kidney.

Patients undergoing haemodialysis treatment

- Blood pressure must not be taken using the arm with the arteriovenous fistula or graft as the blood vessels could be damaged if the blood flow is blocked.
- Patients with a central dialysis catheter, most often positioned on the neck or chest, should avoid lifting their arms above their head and avoid neck movements as the catheter may be detached and damaged.

Patients undergoing peritoneal dialysis treatment

- The dialysis fluid must be drained from the abdominal cavity before exercise. If dialysis fluid remains in the abdominal cavity, the patient is at risk of having a hernia and/or damage his/her pelvic floor muscles. Furthermore, it renders it more difficult to exercise with the correct intensity and duration.

Functional tests/need for health checks

- All patients with chronic kidney failure should be referred to a specialist physiotherapist by the attending practitioner for functional tests and physical training.
- The attending practitioner should determine whether or not referring a patient for an exercise test is necessary from a medical viewpoint before the patient starts a training programme. An exercise test is sometimes suggested prior to the start of a training programme to optimise exercise dose and intensity.
- The attending physiotherapist will provide information and encourage the patient to exercise and will also put together an individual exercise programme or try to get the patient involved in a group exercise. Regular functional tests are also carried out.
- The attending practitioner monitors the patient's clinical status and regular laboratory test results.

Table 2 illustrates clinical test methods for the assessment of physical and functional ability and evaluation of exercise response.

Table 2. Test methods for the assessment of physical and functional ability and evaluation of exercise response.

Physical capacity	A standardised symptom-limited exercise test on an ergometer bicycle (39) for the purpose of assessing patient complaints of tired legs, breathlessness and possible chest pains in accordance with the Borg CR10 scale (40). The patient's level of exertion is also measured in accordance with the Borg RPE scale (41).
Muscle strength	One repetition maximum (1RM) (42).
Dynamic muscular endurance	Maximum number of muscle contractions with a load equivalent to 50% of 1 RM and a fixed frequency (13). "Standing heel-rise test" (43).
Static muscular endurance	The total time in seconds that the patient manages to maintain an isometric muscle contraction such as a fully extended knee with a load equivalent to 50% of 1 RM (13).
Functional capacity	A 6-minute walking test (44, 45) for the purpose of assessing patient complaints of tired legs, breathlessness and possible chest pains in accordance with the Borg CR10 scale (40). The patient's level of exertion before and after the test is also measured in accordance with the Borg RPE scale (41). Timed Up & Go (46).

Interactions with drug therapy

Beta blockers
To-date, studies have not shown that beta blockers have a negative effect on the ability to improve fitness. Patients with chronic kidney failure often show symptoms of autonomic neuropathy with a lower maximum pulse during maximum exertion than other healthy individuals of the same age and gender not treated with beta blockers.

ACE inhibitors/AII antagonists
An increasing number of people with chronic kidney disease are treated with these preparations partly as an anti-hypertensive therapy and partly to delay the uraemia progression in patients with diabetes and chronic glomerulonephritis. Patients in the pre-uraemia stage of chronic kidney disease who are treated with these preparations are often sensitive to dehydration with a risk of hypertension and must be extra cautious and drink plenty of fluids during exercise to compensate for the loss of fluid from sweating.

Erythropoietin
Patients with chronic kidney failure receive a substitute treatment of erythropoietin, i.e. they are treated with erythropoietin to compensate for their own inadequate production of erythropoietin. A lower target haemoglobin concentration is a condition if the patient should have the strength to accomplish adequate training and obtain the desired exercise response.

Essential amino acids (Aminess N)
Patients in the pre-uraemia stage are treated with a protein-reduced diet, which could result in a deficiency of essential amino acids. In order to maximise the response of the skeletal muscles to exercise, patients should be prescribed supplements of essential amino acids.

Sodium bicarbonate

Untreated metabolic acidosis leads to an increased frequency of leg cramps and muscle catabolism that are likely to have a negative effect on the response of the skeletal muscles to exercise. Therefore, the patients should be fully compensated for the metabolic acidosis and prescribed a supplement of sodium bicarbonate tables.

Calcium tablets and active vitamin D

Hypocalcaemia and hyperparathyroidism lead to a higher frequency of muscle skeletal symptoms. Calcium tablets and active vitamin D should then be used to obtain calcium homeostasis.

Contraindications

Absolute

- Acute infection
- Uncontrolled hypertension (systolic blood pressure > 180 mm Hg and/or diastolic blood pressure > 105 mm Hg).
- Unstable angina.
- Severe cardiac arrhythmia.
- Uncontrolled diabetes.
- Hyperkalaemia.

Relative

- Weight gain of more than 5 per cent of the estimated 'dry weight' between haemodialysis treatments.
- Expressed anaemia and arteriosclerotic cardiovascular disease.

Risks

To-date, no patient has had a serious incident during or after exercise. However, all exercise should be carried out in accordance with the guidelines above under the supervision of a specialist physiotherapist and on the recommendations of a doctor.

References

1. Schön S. Svenskt register för aktiv uremivård 2001 [The Swedish Registry for Active Treatment of Uremia 2001]. The Nephrology Clinic, KSS, SE 541 85 Skövde (srau.kss@vgregion.se).
2. Foley RN, Parfrey PS, Kent GM, Harnett JD, Murray DC, Barre PE. Long-term evolution of cardiomyopathy in dialysis patients. Kidney Int 1998 Nov;54:1720-5.
3. Foley RN, Parfrey PS, Sarnak MJ. Epidemiology of cardiovascular disease in chronic renal disease. J Am Soc Nephrol 1998 Dec;9:S16-23.
4. Fernström A, Hylander B, Rössner S. Taste acuity in patients with chronic renal failure. Clin Nephrol 1966;45:169-74.
5. Klang B, Björvell H, Clyne N. Quality of life in predialytic uremic patients. Quality of Life Research 1996;5:109-16.
6. Guarnieri G, Toigo G, Situlin R, et al. Muscle biopsi studies in chronically uremic patients. Evidence for malnutrition. Kidney Int 1983;24:187S-93S.
7. Williams B, Hattersley J, Hayward F, Walls J. Metabolic acidosis and skeletal muscle adaptation to low protein diets in chronic renal failure. Kidn Int 1991;40:779-86.
8. Klang B, Clyne N. Well-being and functional ability in uremic patients before and after having started dialysis treatment. Scand J of Caring Sciences 1997;11:159-66.
9. Moreno F, Lopez Gomez JM, Sanz-Guajardo D, Jofre R, Valderrabano F. Quality of life in dialysis patients. A Spanish multicentre study. Nephrol Dial Transpl 1996:11:125-9.
10. Clyne N, Ekholm J, Jogestrand T, Lins LE, Pehrsson SK. Effects of exercise training in predialytic uremic patients. Nephron 1991;59:84-9.
11. Eidemak I, Haaber AB, Feldt-Rasmussen B, Kanstrup IL, Strandgaard S. Exercise training and the progression of chronic renal failure. Nephron 1997;75:36-40.
12. Boyce M, Robergs R, Avasthi P, Roldan A, Foster A, Montner A, et al. Exercise training by individuals with predialysis renal failure. Cardiorespiratory endurance, hypertension and renal function. Am J Kidn Dis 1997;30:180-92.
13. Heiwe S, Tollbäck A, Clyne N. Twelve weeks of exercise training increases muscle function and walking capacity in elderly predialysis patients and healthy subjects. Nephron 2001;1:48-56.
14. Goldberg AP, Geltman EM, Hagberg JM, Gavin JR 3rd, Delmez JA, Carney RM, et al. Therapeutic benefits of exercise training for hemodialysis patients. Kidney International 1983;24:303S-9.
15. Painter PL, Nelson-Worel JN, Hill MM, Thornbery DR, Shelp WR, Harrington AR, et al. Effects of exercise training during hemodialysis. Nephron 1986;43:87-92.
16. Kouidi E, Albani M, Natsis K, Megalopoulos A, Gigis P, Guiba-Tziampiri O, et al. The effects of exercise training on muscle atrophy in hemodialysis patients. Nephrol Dial Transpl 1998:13:685-99.

17. Krause R, Abel HH, Bennhold I, Koepchen HP. Long-term cardiovascular and metabolic adaptation to bedside ergometer training in hemodialysis patients. In Doll-Tepper G, Dahms C, Doll B, v Sezam H, red. Adapted physical activity. Heidelberg: Springer-Verlag; 1990. pp. 299-304.
18. Koufaki P, Mercer TH, Naish PF. Effects of exercise training on aerobic and functional capacity of patients with end-stage renal disease. Clinical Physiology and Functional Imaging 2002;22:115-24.
19. Ota S, Takahashi K, Suzuki H, Nishimura S, Makino H, Ota Z, et al. Exercise rehabilitation for elderly patients on chronic hemodialysis. Geriatric Nephrology and Urology 1996;5:157-65.
20. Clyne N, Jogestrand T, Lins L-E, Pehrsson SK. Progressive decline in renal function induces a gradual decrease in total hemoglobin and exercise capacity. Nephron 1994;67:322-6.
21. Kettner-Melsheimer A, Weiss M, Huber W. Physical work capacity in chronic renal disease. Int J Artif Organs 1987;10:23-30.
22. Painter P, Messer-Rehak D, Hanson P, Zimmerman SW, Glass NR. Exercise capacity in hemodialysis, CAPD and renal transplant patients. Nephron 1986;42:47-51.
23. Clyne N, Jogestrand T, Lins LE, Pehrsson SK, Ekelund LG. Factors limiting physical working capacity in predialytic uraemic patients. Acta Med Scand 1987;222:183-90.
24. Nielens H, Lejeune TM, Lalaoui A, Squifflet JP, Pirson Y, Goffin E. Increase of physical activity level after successful renal transplantation. A 5-year follow-up study. Nephrol Dial Transplant 2001 Jan;16:134-40.
25. Painter P. Exercise for patients with chronic disease. Physician responsibility. Curr Sports Med Rep 2003 Jun;2:173-80.
26. Daul AE, Völker K, Hering D, Schäfers RF, Philipp T. Exercise-induced changes in serum potassium in patients with chronic renal failure. J Amer Soc Nephrol 1996;7:1348.
27. Mercer TH, Naish PF, Gleeson NP, Crawford C. Low volume exercise rehabilitation improves functional capacity and self-reported functional status of dialysis patients. American Journal of Physical Medicine and Rehabilitation 2002;81:162-7.
28. Carney RM, McKevitt PM, Goldberg AP, Hagberg J, Delmez JA, Harter HR. Psychological effects of exercise training in hemodialysis patients. Nephron 1983;33:179-81.
29. Kouidi E, Iacovides A, Iordanidis P, Vassiliou S, Deligiannis A, Ierodiakonou C, et al. Exercise renal rehabilitation program (ERRP). Psychosocial effects. Nephron 1997;77:2:152-8.
30. Goldberg AP, Geltman EM, Gavin Jr 3d, Carney RM, Hagberg JM, Delmez JA, et al. Exercise training reduces coronary risk and effectively rehabilitates hemodialysis patients. Nephron 1986;42:311-6.
31. Eidemak I, Feldt-Rasmussen B, Kanstrup IL, Nielsen SL, Schmitz O, Strandgaard S. Insulin resistance and hyperinsulinaemia in mild to moderate progressive chronic renal failure and its association with aerobic work capacity. Diabetologia 1995;38:565-72.

32. Deligiannis A, Kouidi E, Tourkantonis A. The effects of physical training on heart rate variability in hemodialysis patients. Am J Cardiol 1999;84:197-202.
33. Deligiannis A, Kouidi E, Tassoulas E, Gigis P, Tourkantonis A, Coats A. Cardiac response to physical training in hemodialysis patients. An echocardiographic study at rest and during exercise. Int J Cardiol 1999;70:253-66.
34. Painter C, Monestier M, Bonin B, Bona CA. Functional and molecular studies of V genes expressed in autoantibodies. Immunol Rev 1986 Dec;94:75-98.
35. Warburton DE, Sheel AW, Hodges AN, Stewart IB, Yoshida EM, Levy RD, et al. Effects of upper extremity exercise training on peak aerobic and anaerobic fitness in patients after transplantation. Am J Cardiol 2004 Apr 1;93:939-43.
36. Horber FF, Hoopeler H, Scheidegger JR, Grünig BE, Howald H, Frey FJ. Impact of physical training on the ultrastructure of midthigh muscle in normal subjects and in patients treated with glucocorticoids. J Clin Invest 1987 Apr;79:1181-90.
37. LaPier TK. Glucocorticoid-induced muscle atrophy. The role of exercise in treatment and prevention. Review. J Cardiopulm Rehabil 1997 Mar-Apr;17:76-84.
38. Painter P. Exercise for patients with chronic disease. Physician responsibility. Curr Sports Med Rep 2003 Jun;2:173-80.
39. Åström H, Jonsson B. Design of exercise tests with special reference to heart patients. Br Heart J 1976;38:289-96.
40. Borg G. Perceived exertion as an indicator of somatic stress. Scand J Rehab Med 1970;2-3:92-8.
41. Borg G. A category scale with ratio properties for intermodal and interindividual comparisons. In Geissler HG, Petzolds P, red. Psychophysical judgement and the process of perception. Berlin: VEB Deutscher Verlag der Wissenschaften; 1982.
42. McDonaugh M, Davies C. Adaptive response of mammalian skeletal muscle to exercise with high loads. Eur J Appl Physiol 1984;52:139-55.
43. Lunsford BR, Perry J. The standing heel-rise test for the ankle plantar flexion. Criterion for normal. Phys Ther 1995;75:694-8.
44. Guyatt G, Sullivan M, Thompson P, et al. The 6-minute walk: a new measure of exercise capacity in patients with chronic heart failure. Can Med Assoc J 1985;132:919-23.
45. Guyatt G, Thompson P, Berman L, Sullivan M, Townsend M, Jones N, et al. How should we measure function in patients with chronic heart and lung disease? J Chronic Dis 1985;38:517-24.
46. Podsiadlo D, Richardson S. The "Timed Up and Go". A test of basic functional mobility for frail elderly persons. J Am Geriatr Soc 1991;39:142-8, 517-2.