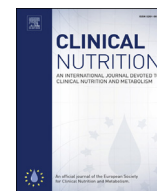




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## Original article

# Characterization of deficits across the spectrum of motor abilities in dialysis patients and the impact of sarcopenic overweight and obesity

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## SUMMARY

**Background & aims:** Physical performance deficits in kidney failure predict mortality and quality of life. We aimed to quantify deficits in multiple motor abilities, investigate associations of lean and fat tissue content with test results and analyzed performance of sarcopenic individuals with adipose tissue excess. **Methods:** Ninety hemodialysis patients and 140 healthy controls performed 6-minute walk test, gait speed measurement, sit-to-stand and time up and go tests, upper extremity handgrip and tapping tests, Stork balance and forward bend flexibility tests. Human Activity Profile questionnaire was used to assess habitual activity. Body composition was measured by bioimpedance analysis.

**Results:** Relative performance deficit of dialysis patients in age, sex, height and comorbidity adjusted estimated marginal means was largest for balance and flexibility (−52 and −33%), followed by lower extremity deficits in sit-to-stand, time up and go and 6-minute walk tests (−29, −19 and −15%, respectively),  $p < 0.05$  for all comparisons. Upper extremity performance was less affected. Lean tissue index associated significantly positively with five and fat tissue index associated significantly negatively with two out of nine tests. Sarcopenic overweight and obese individuals exhibited significant deficits mainly in lower extremity tests with worse composite lower extremity score when compared to other categories of body composition.

**Conclusions:** Patients with hemodialysis treated kidney failure have largest functional deficits in balance, flexibility and lower extremity functions. Lean and fat mass associate oppositely with physical performance measures and individuals at unfavorable extremes of these indices express significantly impaired lower extremity functions.

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Physical performance of people living with kidney failure on renal replacement therapy is an important predictor of morbidity and mortality [1,2]. Various exercise regimens with aerobic, resistance or mixed training may all improve health outcomes such as aerobic capacity, muscular strength, and health-related quality of life [3]. So far, the optimal modality of physical rehabilitation for

dialysis patients has not been defined. A proper insight into the magnitude and nature of deficits across the spectrum of motor abilities in dialysis patients is needed to set goals and define the minimal common demands of an optimized exercise and nutritional rehabilitation program.

A limited number of previous studies have shown that dialysis patients exhibit a reduced habitual physical activity level [4,5], lower 6-minute walk test distance [6], reduced handgrip strength [7], reduced strength of foot dorsiflexion [8], and reduced performance at sit-to-stand or stair climbing tests [5]. However there is a lack of data quantifying and comparing relative deficits of dialysis patients to healthy controls simultaneously at multiple physical abilities such as lower extremity and gait performance, upper extremity performance, balance and flexibility. All these motor abilities are important for every-day functioning and preservation of mobility and it would be valuable to define the abilities with largest deficit demanding emphasis in rehabilitation programs.

**Abbreviations:** AAS, adjusted activity score; BAL, Stork balance test; BMI, body mass index; CI, confidence interval; CRP, C-reactive protein; ESA, erythropoiesis-stimulating agent; FLEX, sitting forward bend test; GLM ANOVA, general linear model analysis of variance; HAP, Human Activity Profile; HD, hemodialysis; HGS, handgrip strength; PTH, parathyroid hormone; SGA, subjective global assessment; SGS, spontaneous gait speed; STS-10, 10 repetition sit-to-stand test; TAP, upper extremity tapping test; TUG, time up and go test; 6MWT, 6-minute walk test.

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Furthermore, a characterization of the impact of unfavorable (but modifiable) body composition phenotype such as lean tissue loss and adipose tissue accumulation may help to identify individuals at risk for future mobility loss and estimate the possible benefit of preventing these changes.

There were three goals of this study. First, we performed simultaneous quantification of physical performance deficits at multiple dimensions of motor abilities: gait performance, lower extremity functional tests, upper extremity performance, balance, flexibility and habitual activity level to see which dimensions suffer greatest deficits in renal failure compared to healthy controls. Second, we analyzed associations of body lean and fat tissue content with performance across all measured physical tests. Third, we hypothesized that muscle loss and adipose tissue gain associate with inferior performance and that specific phenotype combining both these unfavorable body composition changes may suffer from largest motor deficits so we analyzed performance of sarcopenic individuals with adipose tissue excess and compared them to other body composition phenotypes.

## 1. Materials and methods

### 1.1. Study design and participants

This was a cross-sectional case–control study recruiting a sample of prevalent hemodialysis patients from 10 outpatient dialysis units and population based control subjects. Main outcome measures were results of functional performance tests covering a wide spectrum of motor abilities: spontaneous gait speed (SGS), 6-minute walk test (6MWT), 10 repetition sit-to-stand test (STS-10), time up an go test (TUG), handgrip strength (HGS), upper extremity tapping test (TAP), sitting forward bend (FLEX), Stork balance test (BAL) and the result of Human Activity Profile questionnaire (HAP) to assess the level of physical abilities and activities in home environment. Measurements were done in the period from July to December 2014. Subjects were invited to participate if older than 18 years, able to walk with or without additional support and if they voluntarily signed the informed consent for participation. Exclusion criteria were: acute disease in the last 4 weeks before study start, active malignant disease or chronic infection, consequences of cerebrovascular accident, heart failure of NYHA stage 3–4, symptomatic angina pectoris Canadian Cardiovascular Society stage 2–4, chronic obstructive pulmonary disease stages 3 and 4, decompensated liver cirrhosis, symptomatic peripheral arterial obstructive disease, painful degenerative or inflammatory arthropathy with current use of analgesic therapy and symptomatic psychiatric disease. Control subjects were recruited on a convenience basis from a wide range of community settings (work sites, schools, nursing homes, community centers for older adults). They were demanded to have no history of renal disease or serum creatinine below 133  $\mu\text{mol/l}$  (1.5 mg/dl). Same comorbidity criteria as for dialysis patients were applied with them. The study was approved by the Slovenian Medical Ethics Committee (document No. 125/05/14). All participants gave informed consent to inclusion in the study.

### 1.2. Research protocol

The exact methodology and measurements description was given previously [9–11]. In short, physical performance tests were performed in the afternoon hours and for dialysis patients on non-dialysis days (mean time lag from the last dialysis session was  $25 \pm 6$  h). This timing of measurements was deliberately chosen to assure safety for dialysis patients since they have highest degrees of hypervolemia and hyperkalemia immediately prior to dialysis

sessions, there is a known increased risk of sudden death in the hours immediately prior to and the first hours after dialysis procedures [12] and there are increased levels of fatigue on dialysis days [13]. Application of questionnaires assessing demography, clinical information, medical history and HAP Questionnaire were followed by anthropometric measurements (instruments by SiberHegner, Zurich, Switzerland), vital signs recordings and bio-impedance body composition analysis (Body Composition Monitor, Fresenius Medical Care, Bad Homburg, Germany). Here, estimated lean and fat mass in kg were normalized to squared body height in  $\text{m}^2$  to give lean and fat tissue mass indices. Additional medical information on comorbidities and most recent blood test laboratory values were obtained from dialysis centers and attending physicians. Comorbidity was graded by Davies comorbidity score [14]. HAP questionnaire is used to assess the level of physical activity with the result reported as the adjusted activity score (AAS), on a scale of 1–94 points (larger values designate higher level of ability in the every-day life) [11,15,16]. Previously HAP questionnaire was recognized as the best single substitute for quantitative measurement of habitual physical activity in hemodialysis patients [15].

Motor tests were performed in a fixed fatigue-minimizing sequence: SGS, 6MWT, FLEX, HGS, TAP, BAL, TUG, STS-10. SGS was measured on a 4 m distance with the time to travel this distance taken two times to the nearest tenth of second and the average value of velocity reported as outcome. 6MWT was performed on a 30 m track according to the guideline [17] with the traveled distance measured to the nearest meter. FLEX was measured as the ability in cm to bend forward as far as possible in a sitting position with extended upper and lower limbs. The maximal length of reach of the fingertips beyond the feet plane in cm was taken as the result value (maximum value of two attempts, see Supplementary Fig. 1). Jamar hand dynamometer (Sammons Preston, Warrenville, IL, USA) was used to assess HGS engaging both hands three times and the best value of all attempts was taken as a result (in kg units). TAP test counted the number of side-to-side taps with movement of the upper limb mainly in the shoulder joint above a special panel in a sitting position. The maximal achievable number of contacts of the hand with two most lateral panel end-plates residing 1 m apart in 20 s was electronically counted with both limbs separately (see supplementary Fig. 2). The average number of taps of the left and right arm was taken as the result. BAL was measured as per protocol of the standard Stork balance test, reporting the average time (in seconds) of three trials in maintaining the position on one same leg with their hands on the hips and the uninvolvement of the foot against the medial side of the knee of the stance leg. TUG test result was measured as the average time (in seconds) of two attempts to rise from the sitting position, walk around the 3 m distance and return to the sitting position. STS-10 time (in seconds) was measured as the time needed to perform rises from the chair of a standard height to the full leg extension and back to sitting position 10 times in a single attempt.

### 1.3. Statistical analyses

Sample size calculation was first calculated under the predictions of expected  $R^2$  value for multiple regression of the 6MWT distance of 0.4, with 7 predictors in the multivariate model as presented in ref. [9] A minimum of 36 subjects per group was calculated, however the sample size for dialysis patients was targeted to a minimum of 70 participants to allow at least 10 patients in each decade of age from 20 to 80 years of age thus being able to report meaningful representative results of the 6MWT. Sample size for control subjects was planned to contain 140 individuals to satisfy a 2:1 ratio with dialysis patients as the compensation for a convenience sampling method of healthy controls.

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