Exercise Performance Falls over Time in Patients with Chronic Kidney Disease Despite Maintenance of Hemoglobin Concentration

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Physical function is limited in patients with kidney disease, although previous studies have been confounded by anemia. What is not clear is how physical performance changes over time as renal function deteriorates. A cohort of 12 patients (10 male, two female; mean ± SD age 49 ± 11 yr) who had stages 3 to 4 chronic kidney disease without previous anemia were examined, and nine were followed for a 2-yr period. Assessments were made of peak oxygen consumption (VO2peak) by cycle ergometry, leg extension strength, and fatigue on an isokinetic dynamometer and thigh muscle cross-sectional area (TMCSA) by computed tomography. At baseline, creatinine clearance was 31 ± 13 ml/min and hemoglobin concentration ([Hb]) was 129 ± 9 g/L. VO2peak was low (1.88 L/min, 82% of predicted), and maximal isometric voluntary contraction was 188 ± 42 Nm, with a TMCSA of 144 ± 27 cm². VO2peak correlated with creatinine clearance corrected for body surface area (r = 0.613, P = 0.034) but not to [Hb]. VO2peak adjusted for patient weight correlated with leg fatigue (r = −0.693, P = 0.012). For those with follow-up tests, there were falls in renal function by 28% (P = 0.007) and VO2peak by 9% (P = 0.03), whereas [Hb] did not change. Leg strength fell across a range of isokinetic speeds (P = 0.04), whereas no change in TMCSA was observed. In conclusion, exercise performance as measured by aerobic (VO2peak) and leg strength tests were reduced in patients with stages 3 to 4 chronic kidney disease. As renal function declined over time, there was a corresponding decline in exercise performance even when [Hb] was maintained.


It is well recognized that patients with chronic kidney disease (CKD) have limited physical function. This has been shown both subjectively in quality-of-life surveys (1) and objectively by measures of exercise such as walking times/distances (2), treadmill (3) and cycle ergometry tests (4–6), and measures of strength (3,6–8). A reduced ability to exercise has significance not only on quality of life but also on morbidity and mortality. Using the Short Form 36 (SF-36) quality-of-life questionnaire, low scores for self-reported physical function in patients who initiated dialysis are independently associated with a higher mortality risk (to a level similar to that of low albumin) (9).

Why exercise performance is limited remains unclear. In patients with CKD, there is an independent association with exercise performance across a wide range of renal function (5) that can be improved significantly after renal transplantation (10). However, despite good kidney function and exercise training programs, the level of exercise performance does not return to expected “normal” values up to 1 yr after transplantation (11). The most significant feature that confounds many of these studies is anemia, which, when treated in both patients with CKD (12) and hemodialysis patients (13–17), has resulted in improved exercise performance. Unfortunately, the absolute rise in hemoglobin (Hb) has not been matched by similar improvements in exercise.

We also previously found impaired potassium (K⁺) regulation during exercise in hemodialysis patients compared with healthy control subjects (18). Because muscle K⁺ disturbances are linked with muscle fatigue (19), this was suggested to contribute to reduced exercise capacity in hemodialysis patients (18). When Hb concentration ([Hb]) was corrected, the change in plasma [K⁺] to work performed (Δ[K⁺]/work) ratio (as a marker of K⁺ regulation during exercise) was inversely related to [Hb] (15). This has not been studied in patients who have CKD and are not on dialysis.

We therefore studied patients who have CKD and have not had a history of anemia to assess the relationships of aerobic exercise performance, muscular strength, and fatigability with renal function and muscle mass. We then followed the cohort for up to 2 yr to examine the relative impact of changes in kidney function and [Hb] with respect to exercise performance. In addition, we studied aerobic performance with respect to K⁺ regulation.

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Materials and Methods
Patients with CKD were recruited from the Royal Melbourne and Western Hospitals (Victoria, Australia) and followed for 2 yr or until they commenced dialysis if renal function deteriorated. The research was carried out under the principles of the Declaration of Helsinki. All patients gave written informed consent after approval from the human research ethics committees of the Royal Melbourne Hospital and Victoria University (Melbourne, Australia).

Inclusion criteria were age between 18 and 70 yr, a calculated creatinine clearance (Cockcroft-Gault) between 15 and 50 ml/min, and Hb ≥120 g/L with satisfactory iron stores. Exclusion criteria were a history of [Hb] <120 g/L at any time, expected to commence dialysis within 12 mo, body mass index >40 kg/m², significant history of left ventricular failure or ischemic heart disease, peripheral vascular or cerebrovascular disease, uncontrolled hypertension, severe hyperparathyroidism, pregnancy, active malignancy, or renal transplant.

Data were collected on patients’ age, gender, and body size. Hematology and biochemistry tests were performed at baseline and every 3 mo during the course of the study. Creatinine clearance was calculated as per Cockcroft and Gault (20). Medications and medical and social history were noted at each exercise test visit.

Tests
The following tests were performed at both baseline and end of study. Cycle ergometry and leg strength tests were performed on different days separated by a minimum of 48 h.

Cycle Ergometry and Peak Oxygen Consumption. All tests were performed on an electronically braked cycle ergometer (Lode Excalibur, Groningen, Netherlands) with seat and handlebar positions kept constant for each patient upon repeated testing. An incremental exercise test was performed according to a protocol of 2 min seated rest followed by cycling with a pedal cadence of 60 to 70 rpm. An initial resistance of 15 W was applied and increased by 15 W each minute until fatigue, defined as the inability to maintain pedal cadence >60 rpm. Expired air was collected via a two-way nonbreathing valve (Hans-Rudolph Co., Kansas City, MO) and a 6-L mixing chamber. Expired volume was measured using a flow transducer (KL Engineering, Sunnydale, CA), and mixed expired oxygen and carbon dioxide were analyzed by rapid responding gas analyzers (model S-3A; Amtek, Pittsburgh, PA). Ventilatory gas data were calculated over 15 s, and VO₂ was calculated (TurboFit, Ventura, CA). Mixed expired air was collected via a 15-L mixing chamber, and then a single breath test was performed according to a protocol of 2 min seated rest followed by cycling with a pedal cadence of 60 to 70 rpm. The venous blood was arterialized by placing the hand in a water bath (45°C) for 10 min before exercise testing and sustained until 10 min after recovery. A 4-ml sample was collected in a plain tube. A 0.5-ml whole-blood aliquot was removed and stored on ice for duplicate measures of [Hb] and hematocrit (Sysmex, K-800, Kobe, Japan). The remaining portion was centrifuged for 3 min at 4500 rpm. The plasma then was analyzed in duplicate for K⁺ (Ciba Corning 865pH/Blood Gas Analyzer; Bayer, Norwood, MA). Fluid shifts were calculated according to changes in [Hb] and hematocrit (23). Change in plasma volume (APV) from baseline allowed the calculation of net K⁺ change at each time point.

Leg Strength and Fatigue Tests. Isometric and dynamic leg strengths were assessed on an isokinetic dynamometer (Cybex Norm 770; Henley HealthCare, Medway, MA). The patients were seated in a chair with the back set at 90 degrees. Straps secured the patient across the chest, hips, and dominant thigh and ankle, with the axis of rotation centered to the femoral condyles, allowing assessment of dominant leg extension. The dynamometer was calibrated before every testing session, and torque data were adjusted for gravity. After a warm-up of 1.5 min, gentle extension and flexion and isometric strength (maximal voluntary contraction [MVC]) was assessed at a 60-degree knee extension, in triplicate. Isokinetic leg strength was performed at speeds of 60, 120, 180, 240, 300, and 360 degrees/s in triplicate through a range of 0 to 90 degrees. Each patient had a familiarization test. Formal tests then were conducted on 3 separate days, with the mean of the three tests recorded.

Muscle fatigue also was assessed on the dynamometer for the dominant leg. The patient performed 30 maximal extensions at an isokinetic speed of 180 degrees/s at a frequency of 0.5 Hz. The fatigue index (FI) was calculated as the percentage of force drop over the 30 repetition using the following formula:

\[
\text{FI}(\%) = \frac{\text{mean of 3 highest values in initial 5}}{\text{mean of 3 highest values in last 5}} \times 100
\]

Each patient had a familiarization test. Formal tests then were conducted on 3 separate days, with the mean of the three tests recorded.

Thigh Muscle Cross-Sectional Area. Thigh muscle cross-sectional area (TMCSA) was measured by computed tomography (CT) scan (16 Channel Scanner, GE Medical Systems, Waukesha, WI). An initial anterior–posterior scout film was taken of the thigh, and then a single transverse image was taken of the dominant leg 20 cm above the medial femoral condyle. Muscle area was calculated as the total area of the muscle compartment minus the femur area.

Statistical Analyses
All data are presented as mean ± SD unless specified. Pearson correlation coefficients are used for baseline data, and a backward stepwise regression analysis model was used for multiple variables where stated. Paired t test was used to compare baseline and end-of-study results. All tests were performed using Sigma Stat software (version 2.03; SPSS Inc., Chicago, IL) with significance taken as \( P < 0.05 \).

Results
Patient Characteristics
Twelve patients were enrolled (10 male, two female). No patients were undertaking any form of regular exercise. Baseline characteristics, cause of renal failure, biochemistry, and hematology are shown in Table 1. Although all patients completed the baseline set of tests, three patients subsequently withdrew. One deteriorated quickly and commenced dialysis 3 mo after baseline testing. One was unable to do further tests because of knee pain, and one withdrew because of poor recovery after major surgery. Therefore, nine patients had follow-up tests, and seven completed a full 2 yr.

For those with follow-up, calculated creatinine clearance fell (35 ± 13 versus 25 ± 11 ml/min; \( P = 0.007 \)). During the same period, [Hb] did not change (131 ± 10 versus 126 ± 11 g/L; \( P = 0.21 \)). There were no other changes from baseline characteristics for patient size and blood biochemistry (data not shown).
Medications varied greatly between patients. β Blockers were used by four patients, angiotensin-converting enzyme inhibitors/angiotensin II receptor blockers were used by 11, calcium channel blockers were used by four, diuretics were used by six, vitamin D was used by four, and insulin was used by one. During the trial, β blocker therapy did not change; 6 patients had alterations in vitamin D therapy and phosphate binders.

Cycle Ergometry and VO$_2$peak
All patients cycled to volitional fatigue, eventually stopping as a result of leg weakness ($n = 8$), shortness of breath ($n = 1$), or both ($n = 3$). Satisfactory test performance was indicated by the mean respiratory exchange ratio (RER) of 1.14 ± 0.05 at peak exercise (Table 2). Heart rate at fatigue was 93 ± 9% of maximum predicted (220 – age bpm for those who were not on β blockers compared with 63 ± 11% for those who were treated with β blockers; $P < 0.001$). There were no adverse events and, in particular, no significant adverse electrocardiogram changes during the tests or in recovery.

Results for VO$_2$peak achieved and predicted, peak work rate, total work achieved, and heart rate for the baseline test are shown in Table 2. Only two patients were able to achieve a VO$_2$peak >100% of predicted. Other than maximum heart rate, the mean respiratory exchange ratio (RER) of 1.14 ± 0.05 at peak exercise (Table 2). Heart rate at fatigue was 93 ± 9% of maximum predicted (220 – age bpm for those who were not on β blockers compared with 63 ± 11% for those who were treated with β blockers; $P < 0.001$). There were no adverse events and, in particular, no significant adverse electrocardiogram changes during the tests or in recovery.

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treatment with a β blocker had no impact on exercise results. From rest to volitional fatigue, plasma volume fell by a mean of 11 ± 5%, and plasma [K⁺] rose (4.97 ± 0.42 versus 6.21 ± 0.51 mmol/L). This represents a rise in plasma [K⁺] of 1.09 ± 0.25 mmol/L when corrected for the change in plasma volume and a corresponding Δ[K⁺]/work ratio of 25.9 ± 10.7 μmol/L per J.

From a reduced baseline VO₂peak, there was a further decline in VO₂peak with follow-up testing over 2 yr, matched by a reduced time to fatigue and total cumulative work performed (Table 3, Figure 1). The tests were comparable in peak RER and reduced time to fatigue and total cumulative work performed. There were no differences between baseline and follow-up tests in the relative decline in plasma volume (−10.5 ± 3.3 versus −9.1 ± 4.5%; P = 0.39) or increase in [K⁺] (1.08 ± 0.18 versus 1.00 ± 0.22 mmol/L; P = 0.36) during exercise.

### Leg Strength and Fatigue Tests

MVC was 188 ± 42 Nm (n = 12) at baseline and for those with follow-up testing did not change over time (Table 3). Dynamic strengths are demonstrated in Figure 2. The follow-up tests found significantly lower peak torque (P < 0.05) for isokinetic speeds of 60, 120, 180, and 240 degrees/s. Across the entire torque-velocity curve, including MVC, there was a main effect for time, with baseline greater than follow-up values (P = 0.04). When torque is expressed relative to weight (Nm/kg), follow-up tests had a lower peak torque (P < 0.05) for isokinetic

### Table 3. Comparative baseline and follow-up tests (n = 9) for cycle ergometry, leg strength and fatigue index, and TMCSA

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Follow-Up</th>
</tr>
</thead>
<tbody>
<tr>
<td>VO₂peak (L/min)</td>
<td>1.83 ± 0.61</td>
<td>1.66 ± 0.58b</td>
</tr>
<tr>
<td>VO₂peak (ml/min per kg)</td>
<td>22.1 ± 4.1</td>
<td>20.1 ± 4.7b</td>
</tr>
<tr>
<td>% Predicted VO₂peak</td>
<td>80 ± 13</td>
<td>73 ± 12</td>
</tr>
<tr>
<td>Time to fatigue (min)</td>
<td>11.5 ± 2.4</td>
<td>10.3 ± 2.6b</td>
</tr>
<tr>
<td>Total cumulative work (kJ)</td>
<td>47.5 ± 24.8</td>
<td>37.6 ± 23.9b</td>
</tr>
<tr>
<td>Peak HR (beats/min)</td>
<td>136 ± 32</td>
<td>127 ± 33</td>
</tr>
<tr>
<td>% Peak HR</td>
<td>80 ± 19</td>
<td>75 ± 18</td>
</tr>
<tr>
<td>RER at fatigue</td>
<td>1.14 ± 0.05</td>
<td>1.10 ± 0.10</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>83 ± 20</td>
<td>84 ± 22</td>
</tr>
<tr>
<td>MVC (Nm)</td>
<td>178 ± 33</td>
<td>172 ± 31</td>
</tr>
<tr>
<td>Isokinetic strength (Nm; degrees/s)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>60</td>
<td>150 ± 34</td>
<td>135 ± 27b</td>
</tr>
<tr>
<td>120</td>
<td>124 ± 33</td>
<td>111 ± 24b</td>
</tr>
<tr>
<td>180</td>
<td>104 ± 28</td>
<td>92 ± 17b</td>
</tr>
<tr>
<td>240</td>
<td>85 ± 24</td>
<td>71 ± 14b</td>
</tr>
<tr>
<td>300</td>
<td>68 ± 21</td>
<td>61 ± 16</td>
</tr>
<tr>
<td>360</td>
<td>61 ± 17</td>
<td>54 ± 17</td>
</tr>
<tr>
<td>FI (%)</td>
<td>21 ± 6</td>
<td>19 ± 6</td>
</tr>
<tr>
<td>TMCSA (cm²)</td>
<td>145 ± 30</td>
<td>146 ± 32</td>
</tr>
</tbody>
</table>

aData are mean ± SD. FI, fatigue index; MVC, maximal voluntary contraction; TMCSA, thigh muscle cross-sectional area.

bP < 0.05.

### Correlations

As with the normal healthy population, a strong linear relationship was seen between VO₂peak and the total work per-
formed \((r = 0.98, P < 0.001; \text{Figure 3})\). Baseline \(\text{VO}_{2\text{peak}}\) had a number of correlates on univariate analysis (Table 4), including creatinine clearance when adjusted for BSA (Figure 4). There was no relationship between \(\text{VO}_{2\text{peak}}\) and [Hb]. The change in creatinine clearance and the change in \(\text{VO}_{2\text{peak}}\) during the study period did not correlate. \(\text{VO}_{2\text{peak}}\) adjusted for weight correlated inversely with the thigh muscle FI \((r = -0.693, P = 0.012; \text{Figure 5})\). Baseline MVC correlated with weight \((r = 0.668, P = 0.0176)\) and height \((r = 0.827, P < 0.001)\) but not TMCSA, [Hb], or renal function \((n = 12)\).

**Discussion**

This study examined patients who had moderate to severe CKD (stages 3 to 4) yet have maintained a near-normal [Hb] without a history of anemia. We found that exercise performance that was measured by \(\text{VO}_{2\text{peak}}\) on a cycle ergometer was significantly below that predicted for healthy, sedentary individuals of the same age and gender (21) and inversely correlated to thigh muscle fatigue. We also found that despite the maintenance of [Hb], \(\text{VO}_{2\text{peak}}\) declined a further 9% as mean creatinine clearance fell by 28%. This was also associated with a decline in muscle strength, despite maintenance of muscle cross-sectional area.

Measured either by peak work rate or \(\text{VO}_2\), numerous exercise studies have demonstrated that patients with CKD underperform compared with predicted performance capabilities (24) or with healthy control subjects (8); however, the relationship between renal function and exercise capacity usually is confounded by the associated anemia that occurs with CKD. Anemia per se is well established as a factor that limits exercise in the normal population (25,26), and a direct relationship between Hb and \(\text{VO}_2\) also has been demonstrated in patients with CKD (5,6). Furthermore, when anemic patients with CKD are treated with erythropoietin to increase [Hb], exercise capacity (12) and \(\text{VO}_{2\text{peak}}\) (27) have been shown to improve, although only modestly compared with the increase in [Hb]. The patients in this study had not previously been anemic, and they maintained a near-normal [Hb] throughout; however, of note is that these patients already had a reduced \(\text{VO}_{2\text{peak}}\) at entry to the study despite the preserved [Hb]. During 2 yr of follow-up, we found a further 9% fall in \(\text{VO}_{2\text{peak}}\) without a change in [Hb], suggesting that, at least in this cohort of patients, factors other than a decline in oxygen-carrying capacity influence the deterioration in exercise performance.

Our findings support a strong relationship between renal function and \(\text{VO}_{2\text{peak}}\) in those with moderate CKD even when [Hb] has been maintained. It seems that at least moderate renal dysfunction is required before this relationship is observed. Previously, Clyne et al. (5) demonstrated a correlation between reduced GFR (<30 ml/min) and maximal exercise capacity when controlled for Hb, and a post hoc analysis of the Heart and Estrogen/Progestin Replacement Study (HERS) found poor subjective physical function correlated with renal function beginning when the GFR fell below 60 ml/min (CKD stage 3) (28). This also is supported by a study of young adults with mild renal impairment (29) and another in the elderly (30), which had similar exercise performances to their control groups.

**Table 4.** Univariate correlations with \(\text{VO}_{2\text{peak}}\) at baseline tests \((n = 12)\)

<table>
<thead>
<tr>
<th>VO(_{2\text{peak}}) (L/min)</th>
<th>(r)</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creatinine clearance corrected for BSA (ml/min per 1.73 m(^2))</td>
<td>0.613</td>
<td>0.034</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>0.730</td>
<td>0.007</td>
</tr>
<tr>
<td>Height (m)</td>
<td>0.719</td>
<td>0.008</td>
</tr>
<tr>
<td>MVC (N)</td>
<td>0.661</td>
<td>0.019</td>
</tr>
<tr>
<td>TMCSA (cm(^2))</td>
<td>0.619</td>
<td>0.032</td>
</tr>
<tr>
<td>[Hb] (g/L)</td>
<td>-0.405</td>
<td>NS</td>
</tr>
</tbody>
</table>

![Figure 3](image-url)  
**Figure 3.** Correlation between \(\text{VO}_{2\text{peak}}\) for incremental cycle ergometry test and total cumulative work performed during the test for 12 patients at baseline. Regression line is shown with 95% confidence intervals \((\text{CI}; r = 0.98, P < 0.001)\).

![Figure 4](image-url)  
**Figure 4.** \(\text{VO}_{2\text{peak}}\) versus creatinine clearance (Cockcroft-Gault, corrected for BSA) for baseline tests. Regression line ± 95% CI \((r = 0.613, P = 0.034; n = 12)\).
One factor that is known to affect aerobic performance is muscular strength. For this cohort of patients, we found a relationship between VO$_{2peak}$ and strength (MVC). This relationship has previously been noted by Diesel et al. (31), who found in hemodialysis patients that strength was a better predictor of exercise capacity than [Hb]. Kettner-Melsheimer et al. (6) earlier had found a marked reduction in isometric leg extension strength in patients with CKD, being only two thirds that of healthy control subjects in men and one quarter in women. The patients in this study exhibited a mean MVC of only 85% of a comparative sedentary control group from our laboratory (unpublished data), a similar reduction to that from the predicted VO$_{2peak}$. Corresponding with the decline in aerobic performance over 2 yr was a fall in muscle strength parameters across the dynamic range of isokinetic strength tests.

The parallel reductions in both VO$_{2peak}$ and muscle strength without a change in [Hb] suggest that intrinsic muscle changes such as enzymatic defects or alterations in fiber type and structure contribute more to poor performances than do limitations in oxygen supply. Underscoring this is our finding that the short isokinetic fatigue test correlated inversely with the longer aerobic VO$_{2peak}$ results. This relationship also is suggested by a study that showed that strength training alone can improve VO$_{2peak}$ (7) even when thigh muscle area does not change (3).

One enzymatic abnormality that potentially could affect exercise performance relates to the regulation of muscle intracellular K$^+$ by the sodium-potassium ATPase. Intracellular K$^+$ is reduced in renal failure (32), and resting muscle membrane potential has been found to change linearly in association with renal function (33). Disturbances in muscle K$^+$ homeostasis also have been linked with muscular fatigue (19). Together with a more recent study demonstrating a relatively higher plasma K$^+$ rise with exercise in hemodialysis patients (18), this suggests that abnormalities in muscle K$^+$ regulation may be a factor that limits exercise performance. Although the patients in this study had a relatively high plasma [K$^+$] before exercise testing (5.0 ± 0.4 mmol/L), we found that the ΔK$^+$/work performed ratio was similar to that in the control subjects reported by Sangkabutra et al. (18), which was significantly lower than that in hemodialysis patients. Between baseline and follow-up tests in this study, however, there was no difference in the [K$^+$] rise with exercise. We also found no correlation between the change in plasma [K$^+$] and renal function, [Hb], or VO$_{2peak}$, suggesting that, in this cohort at least, [K$^+$] increases did not restrict muscle performance and thus incremental exercise. The normal ΔK$^+$/work ratio found here is consistent with findings of McMahon et al. (15) in hemodialysis patients, in whom [Hb] raised from 100 to 140 g/L resulted in a lower ΔK$^+$/work ratio.

Histologic muscle changes that are found in CKD also may influence muscle function. Grossly altered muscle fiber size and fiber type distribution are seen in both patients with CKD (34,35) and hemodialysis patients (36,37). It is interesting that these can be improved not only with exercise training (38,39) but also when [Hb] is increased with erythropoietin treatment (40). In addition to fiber changes, the amount of contractile tissue will have an impact on exercise performance. We used CT scanning for cross-sectional area as a measure of index of muscle size and therefore were unable to determine fat content of the muscle. CT scanning has been validated as a reliable indicator of nutrition in hemodialysis patients (41); however a magnetic resonance scan is more sensitive. Magnetic resonance scanning previously found that the proportion of muscle contractile tissue is reduced in hemodialysis patients compared with healthy control subjects despite similar muscle size (42).

There are limitations to this study. The small sample size highlights the difficulties of enrolling patients with CKD in studies that require a long follow-up and a number of assessments. This was compounded by the relative difficulty of finding nonanemic patients with CKD. Selection bias was an additional potential limitation because the enrolled patients were likely to be healthier and well motivated. This, however, only highlights the very limited exercise capacity of patients with CKD in general as others are likely to have an even poorer performance. Another factor with the potential to limit VO$_{2peak}$ could be the multiple medications that are required by patients with CKD. The most significant is β blocker therapy. Fortunately, this was not translated into a reduced exercise performance in this study. Although the four patients in this study had significantly lower heart rates at fatigue, there was no difference in any other parameter measured either before exercise or at fatigue, including the RER, consistent with previous studies (5).

**Conclusion**

Exercise performance was reduced in CKD stages 3 to 4 even in the absence of anemia. Whether measured by oxygen consumption or leg strength, exercise performance progressively fell as renal function deteriorated. The likely causes are myriad, although, in this study, intrinsic muscle changes that result in reduced muscle strength and fatiguability, and aerobic performance are likely to be dominant. To maintain the well-being and functional capacity of patients with CKD, therefore, attention...
should be directed toward maintaining strength and aerobic fitness as well as focusing on renal function and anemia.

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