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Cardiorespiratory capacity in children and adolescents on maintenance haemodialysis

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Abstract

Background. Paediatric patients on maintenance haemodialysis (HD) often report their own physical fitness to be hampered. Their physical endurance capacity is known to be significantly lower than that of healthy controls. However, physical endurance was up to now only examined on non-HD days. We were interested in the effect of HD on the cardiorespiratory capacity of children and adolescents on maintenance HD.

Methods. We therefore examined the endurance capacity by cardiopulmonary exercise testing on a cycle ergospirometer, before and after HD in 14 patients (9 male, 5 female; mean age: 15.1 ± 3.0 years; mean period on HD: 16.3 ± 11.5 months).

Results. The feasible time spent on the cycle ergospirometer was significantly reduced after dialysis (8.6 ± 3.2 versus 6.4

± 2.5 min, $P < 0.001$), also the maximal workload was decreased (95 ± 36 W to 74 ± 29 W, $P < 0.003$). The starting and recovery heart rates were higher after than before dialysis. The peak oxygen uptake (VO_2 peak, VO_2 peak/kg) was reduced from 1.644 ± 600 to 1.422 ± 450 mL/min ($P < 0.02$) and from 35 ± 7 to 31 ± 5 mL/min/kg ($P < 0.03$), respectively. The respiratory exchange ratio as well as the lactate values showed significant differences in varied workload levels ($P < 0.05$).

Conclusions. Paediatric patients on maintenance HD in general have a significantly lower exercise capacity compared to a healthy age-matched population, which is expressed much more after dialysis.

Keywords: cardiopulmonary exercise testing; cardiorespiratory capacity; children and adolescents; ergospirometry; haemodialysis

Introduction

Physical activity is considered essential for optimal health, development, socialization and the well-being of children. Children with end-stage renal disease, however, are often restricted from participation in exercise activities, especially children on haemodialysis (HD). Consequently, they show a reduced exercise capacity. Paediatric patients on HD often also report their own physical fitness to be hampered. Only a small number of studies ($n = 8$) have been undertaken in paediatric patients, but exercise capacity was only examined between HD sessions and not on the day of HD [1–8]. The studies concentrated on long-term effects of erythropoietin (EPO) treatment, on physical fitness, health-related quality of life or overall endurance capacity of paediatric dialysis patients [1–8].

In a retrospective literature analysis, a total of 212 children and adolescents (127 boys and 85 girls) aged 6–20 years with chronic kidney disease (CKD) and 66 healthy children (41 boys, 25 girls) were examined. The studies of Bonzel *et al.* [1], Eijssermans *et al.* [2] and Zanconato *et al.* [3] reported impaired values in children and adolescents with CKD for aerobic and anaerobic exercise capacity, as well as for peak work in watts (W_{max}), ventilatory anaerobic threshold (VAT), peak oxygen uptake (VO_{2max}) and peak carbon dioxide production (VCO_{2max}). Eijssermans *et al.* [2] found additional defects in gross motor skills but satisfying values for health-related quality of life. Also, the results showed that children and adolescents with CKD may profit from EPO treatment with increased aerobic exercise capacity and stabilized VO_{2max} , VAT, haemoglobin and oxygen pulse, but also with increased haematocrit and heart rate [4, 5]. Nevertheless, those values remained lower in paediatric dialysis patients than in healthy children [6]. Zanconato *et al.* [3] argued that the reduced work capacity of children and adolescents with CKD is probably due to their low haemoglobin levels and that it may be improved by correcting the anaemia.

In summary, the results point to a considerable overall reduction of endurance capacity in paediatric dialysis patients. The exercise capacity was, however, measured on days without dialysis and therefore does not give any information about a possible negative effect of the HD session *per se* on the exercise capacity. Hence, we now aimed to determine metabolic and physiological parameters of exercise capacity of children and adolescents with CKD before and after HD.

Materials and methods

Fourteen patients requiring chronic maintenance HD were examined. The mean age of the nine boys and five girls was 15.1 ± 3.0 years. Their mean height was 154 ± 16 cm and mean weight 47 ± 11 kg. The calculated mean body mass index (BMI) was low with 19 ± 2 kg/m². The mean period of HD before testing added up to 16.3 ± 11.5 months. Clinical characteristics are shown in Table 1.

Our study was a single-group experiment with a pre- to post-test design to test the exercise capacity of children and adolescents before and after dialysis with a cardiopulmonary exercise test using a cycle ergospirometer. The tests were performed on the short dialysis interval on Wednesdays and Fridays.

The first analysis was performed immediately prior to dialysis. In order to avoid physical overexertion, the second test followed in the same week on another day, immediately after dialysis. The cardiopulmonary exercise

test was performed by ergospirometry with workload levels increasing every minute, according to Godfrey [11]. The subjects started with a watts setting corresponding to half their weight in kilogram. The workload was increased by 10 W/min until subjective exhaustion. The following parameters were measured: time in minutes, number of levels, work in watts, heart rate [initial heart rate, heart rate during the test, peak heart rate and recovery heart rate after 4 min] as well as respiratory parameters (VO_{2peak} , $VO_{2peak/kg}$, respiratory exchange ratio (RER)). Lactate values and perceived exertion according to BORG [12] complemented the measured parameters.

The study was approved by the local Ethics Committee and subjects were considered enrolled after they and/or their parents had signed the informed consent form. The descriptive analysis encompassed calculation of mean values, standard deviations, minima and maxima. The statistical significance of changes in end points from pre- to post-test was assessed with a two-sided Wilcoxon rank-sum test for paired data, with P-values ≤ 0.05 considered significant.

Results

The data obtained showed that the exercise capacity of all subjects was significantly decreased in comparison to the values before dialysis (Table 2). The absolute time of the feasible ergospirometry testing was reduced from 8.6 ± 3.2 min before to 6.4 ± 2.5 min after dialysis ($P < 0.001$), the maximal workload decreased from 95 ± 36 W to 74 ± 29 W ($P < 0.003$) and the absolute levels of workload from 8.5 ± 3.2 to 6.5 ± 2.4 ($P < 0.003$) (see Figure 1). Also, an increase in heart rate was observed, with a mean initial value of 90 ± 15 beats/min before and 108 ± 19 beats/min after dialysis ($P < 0.001$, Figure 1). The heart rate at the different workload levels differed significantly for the first eight levels of cardiopulmonary exercise testing, with values after dialysis being consistently higher at each level ($P < 0.05$, Figure 2). The recovery heart rate 4 min after exercise was significantly higher after (121 ± 25 beats/min) than before dialysis (106 ± 16 beats/min, $P < 0.004$). The peak heart rate of each subject during the test was not significantly different at both dates. The initial blood pressure after dialysis ($103.5 \pm 19.6/72.6 \pm 12.1$ mmHg) showed no significant changes compared to the one before ($109.4 \pm 14.6/72.4 \pm 14.7$ mmHg, $P = ns$).

The peak oxygen uptake was significantly different at the two points of time. After dialysis, VO_{2peak} and $VO_{2peak/kg}$ decreased significantly from 1.644 ± 600 mL/min to 1.422 ± 450 mL/min ($P < 0.02$) and accordingly from 35 ± 7 mL/min/kg to 31 ± 5 mL/min/kg ($P < 0.03$, Figure 1). VO_2 and VCO_2 , however, did not vary before and after dialysis on each workload level. The RER differed during the first four workload levels ($P < 0.05$), whereas the mean measured peak RER, being 1.07 ± 0.15 before and 1.06 ± 0.11 after dialysis, was not different, thus indicating that maximum respiratory capacity was reached at both points of time (Figure 3). Mean peak lactate concentrations were 4.1 ± 1.5 mmol/L prior to dialysis and 4.4 ± 2.8 mmol/L after dialysis ($P = ns$). In contrast to that, significantly higher lactate concentrations were observed after dialysis before exercise, as well as at workload levels two, three, seven and eight ($P < 0.05$, Figure 4). The perceived exertion according to BORG [12] was not different, with mean values of 16 ± 3.3 before and 16.4 ± 1.8 after dialysis indicating a very high perceived exertion.

Table 1. Clinical characteristics of patients included in the study; ADS, attention deficit disorder; ASS, Aspirin; HUS, haemolytic uremic syndrome; SLE, Systemic lupus erythematoses

Patient No	Sex	Age (years)	Medication	Comorbidities	Months on dialysis	Kt/V
1	M	9	Vitamin supplement Alfacalcidol Calecalciferol Sodium hydrocarbonate Sevelamer ASS Ramipril EPO Iron Somatropin	Arterial hypertension Renal osteopathy Renal anaemia Renal microsomia Obesity	21	1.61
2	M	16	Vitamin supplement Folic acid Iron Alfacalcidol Sodium hydrocarbonate Calcium carbonate ASS Tacrolimus Amlodipin EPO Somatropin	Arterial hypertension Renal osteopathy Renal anaemia Renal microsomia Hyperparathyroidism Hypocalcaemia	16	1.37
3	M	16	Vitamin supplement Alfacalcidol Sodium hydrocarbonate Sevelamer ASS EPO Iron Somatropin	Arterial hypertension Renal osteopathy Renal anaemia Renal microsomia	43	1.64
4	W	8	Vitamin supplement Alfacalcidol Sodium hydrocarbonate Amlodipin Losartan Ramipril Atenolol Calciumcarbonat EPO Iron Vitamin supplement Somatropin	Arterial hypertension Renal osteopathy Renal anaemia	14	2.67
5	W	17	Vitamin supplement Alfacalcidol Sodium hydrocarbonate ASS Amlodipin Calciumacetat L-thyroxin Valproat EPO Iron Somatropin	Arterial hypertension Renal osteopathy Renal anaemia Hypothyreosis Epileptic seizures Atrygryposis multiplex congenital mental retardation	13	2.18
6	W	19	Vitamin supplement Alfacalcidol Sodium hydrocarbonate Esomeprazol ASS Estradiol/dydrogesteron Atenolol Calciumcarbonat Prednisolon Mycophenolate mofetil EPO Iron Somatropin	Arterial hypertension Renal osteopathy Renal anaemia Microsomia SLE Osteochondrosis disecans	30	2.30

Continued

Table 1. *Continued*

Patient No	Sex	Age (years)	Medication	Comorbidities	Months on dialysis	Kt/V
7	M	16	Calcium Alfacalcidol ASS Amlodipin Olmesartan Sodium hydrocarbonate EPO Iron Somatropin	Arterial hypertension Renal osteopathy Renal anaemia Microsomia	7	1.34
8	W	15	Vitamin supplement Alfacalcidol Sodium hydrocarbonate ASS Amlodipin Metoprolol Calciumcarbonat EPO Iron Somatropin	Arterial hypertension Renal osteopathy Renal anaemia Renal microsomia Enuresis (secondary) ADS Atypical HUS	1	1.64
9	M	15	Vitamin supplement Zinc Calcitriol Sodium hydrocarbonate Pantozol ASS Ramipril Calecalciferol Calciumacetat EPO Iron Somatropin	Arterial hypertension Renal osteopathy Renal anaemia	19	2.91
10	W	16	Vitamin supplement Calcitriol Sodium hydrocarbonate Pantozol Calecalciferol Tacrolimus Sevelamer Amoxicillin EPO Iron Somatropin	Pulmonary stenosis (minimally) Renal osteopathy Renal anaemia	25	1.76
11	M	17	Vitamin supplement Alfacalcidol Sodium hydrocarbonate Ramipril Amlodipin Metoprolol Doxazosin Calecalciferol Calciumcarbonat Sevelamer ASS EPO Iron	Arterial hypertension Renal osteopathy Renal anaemia	4	1.82
12	M	16	Vitamin supplement Alfacalcidol Sodium hydrocarbonate Hydrogenphosphate Glycerophosphat natrium Calecalciferol Magnesium Prednisolon Tacrolimus Cotrimomaxzol Atenolol EPO Iron	Arterial hypertension Renal osteopathy Anemia Thrombocytopaenia Microsomia Splenomegaly	8	2.76

Continued

Table 1. Continued

Patient No	Sex	Age (years)	Medication	Comorbidities	Months on dialysis	Kt/V
13	M	16	Vitamin supplement Alfacalcidol Sodium hydrocarbonate Pantozol Ramipril Amlodipin Colecalciferol Calciumcarbonate EPO Iron	Arterial hypertension Renal osteopathy Renal anaemia	5	1.79
14	M	16	Vitamin supplement Folic acid Alfacalcidol Sodium hydrocarbonate Pantozol ASS Colecalciferol Calciumacetat Prednisolon Tacrolimus EPO Iron	Prune Belly syndrome Ileostoma Renal anaemia Renal osteopathy Mental retardation	22	1.7

Table 2. Results of cardiopulmonary exercise testing on cycle ergometer, before and after HD^a

(N = 14)	BD, X ± SD	AD, X ± SD	P
Time (min)	8.59 ± 3.18	6.43 ± 2.47	<0.001***
Highest workload achieved (W)	94.64 ± 35.82	74.29 ± 28.98	<0.003**
Initial heart rate (beats/min)	90.00 ± 15.16	107.79 ± 18.94	<0.001***
Peak heart rate (beats/min)	155.29 ± 25.30	160.21 ± 28.87	<0.089
Heart rate after 4 min rest (beats/min)	105.71 ± 16.17	120.71 ± 25.11	<0.004**
VO ₂ peak (mL/min)	1644.00 ± 600.66	1422.43 ± 450.41	<0.019*
VO ₂ peak/kg (mL/min/kg)	34.69 ± 7.37	30.81 ± 5.02	<0.033*
Maximum RER	1.07 ± 0.15	1.06 ± 0.11	<0.777
Maximum lactate (mmol/L)	4.12 ± 1.52	4.39 ± 2.76	<1.000
Maximum perceived exertion	16.00 ± 3.33	16.43 ± 1.83	<0.382
Initial blood pressure (mmHg)	109.36 ± 14.60/ 72.36 ± 14.65	103.50 ± 19.62/ 72.57 ± 12.08	<0.388/0.972
Blood pressure after 4 min rest (mmHg)	114.00 ± 14.59/ 71.86 ± 12.32	115.08 ± 18.68/ 72.31 ± 11.03	<0.814/0.753
Haemoglobin (g/dL)	11.50 ± 2.26	13.02 ± 2.79	<0.002**
Haematocrit (%)	35.35 ± 6.71	38.71 ± 8.38	<0.010**

*P < 0.05

**P < 0.01

***P < 0.001.

^aBD, before dialysis; AD, after dialysis; N, sample size.

Haemoglobin and haematocrit levels were higher after than before dialysis, with an increase of haemoglobin from 11.50 ± 2.26 g/dL to 13.02 ± 2.79 g/dL (P < 0.002) and of haematocrit from 35.35 ± 6.71% to 38.71 ± 8.38% (P < 0.01).

Discussion

Our data obtained before HD, showing a reduced overall exercise capacity of the paediatric dialysis patients, confirm the previous results found in the literature. The data corre-

spond well with those obtained by other authors examining children with chronic kidney failure [1, 3, 6].

The difference in exercise capacity between children and adolescents requiring dialysis and their healthy peers is extremely apparent. Compared to the exercise capacity of healthy children and adolescents, the exercise capacity of our patients with a mean age of 15.1 ± 3.0 years was even lower than that of healthy 10-year-olds [9, 10, 14]. Standard values of the maximal workload capacity for healthy children published by Hebestreit *et al.* [15] are 3.0–3.5 W/kg for boys and 2.5–3.0 W/kg for girls. Similar values are presented by Hollmann *et al.* [16], who report

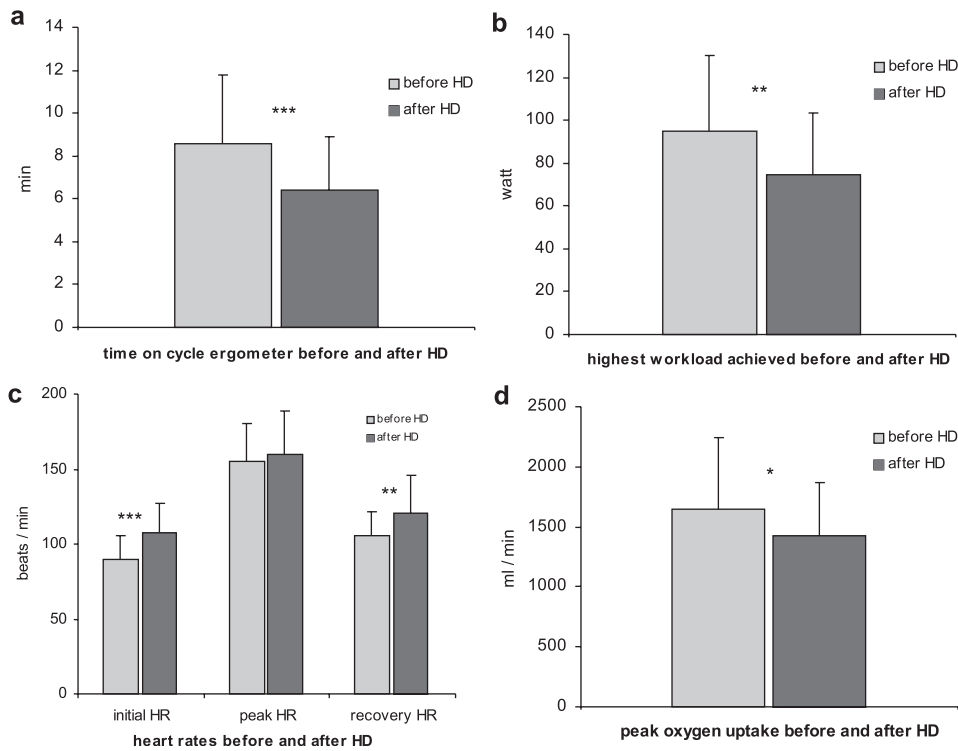


Fig. 1. Results of cardiopulmonary exercise testing on cycle ergometer before and after HD. (a) Shows overall time spent on cycle ergometer, (b) shows highest workload achieved before and after HD (in watts). (c) and (d) demonstrate the lower exercise capacity by a higher heart rate (HR) and a lower peak oxygen uptake after HD. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$ before versus after HD ($N = 14$). The error bars indicate the standard errors of the mean.

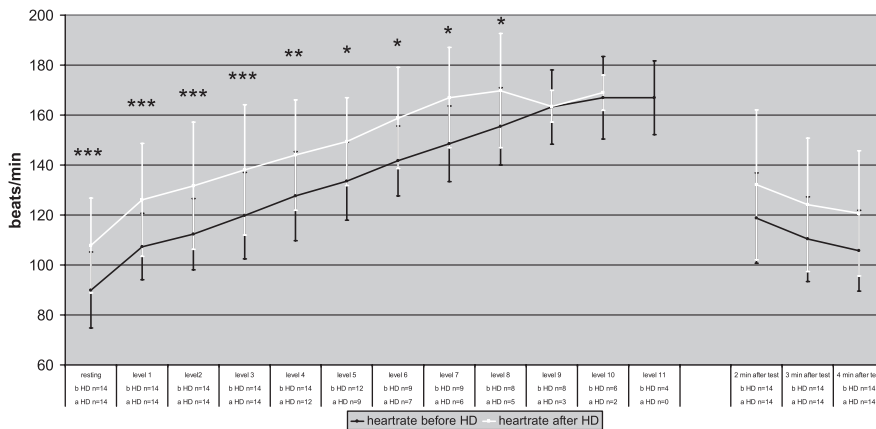


Fig. 2. Progression of heart rate during exercise. The subjects reached different maximal workload levels; number of patients at each level (n) is shown. (b HD) = before HD and (a HD) = after HD. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$ before versus after HD. In Level 9, after HD, a decrease of heart rate at Level 9 is due to the great standard deviation and the reduced subjects number.

3.4–3.6 W/kg for boys and 2.9–3.3 W/kg for girls. The female participants in our study reached a maximal workload of 1.7 ± 0.5 W/kg before and 1.5 ± 0.4 W/kg after dialysis. For the boys, a maximal workload of 2.2 ± 0.4 W/kg before and 1.7 ± 0.4 W/kg after dialysis could be detected. These data show a highly reduced exercise capacity of paediatric dialysis patients, so that even the male participants did not reach the normative values for girls.

Also, a comparison of maximal oxygen uptake relative to body weight in a sample of 6- to 7-year-old children with values obtained in our study gives evidence that the paediatric dialysis patients definitively have a lower exercise

capacity [13]. Mean standard values for the maximal oxygen uptake reported for boys range from 45–55 mL/kg/min to 49–51 mL/kg/min and for girls from 35–45 mL/kg/min to 42–45 mL/kg/min [15, 16]. The male participants in our study achieved a peak oxygen uptake of 38 ± 5 mL/kg/min before and 32 ± 5 mL/kg/min after dialysis session. In girls, peak oxygen uptake was 28 ± 7 mL/kg/min before and 28 ± 3 mL/kg/min after dialysis. Hence, children requiring HD are far behind their healthy peers in terms of exercise capacity.

We, however, for the first time also measured the exercise capacity before and after dialysis. Admittedly, we were

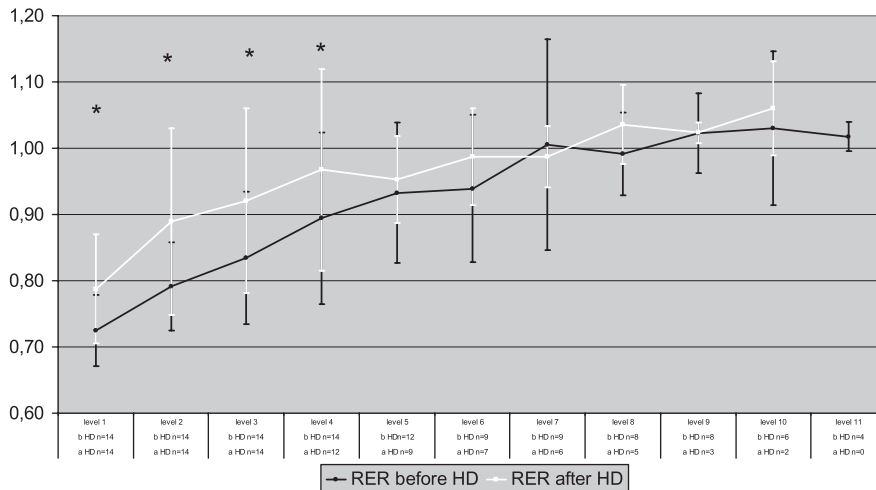


Fig. 3. RER during exercise. The subjects reached different maximal workload levels; number of patients at each level (*n*) is shown. (b HD) = before HD and (a HD) = after HD. **P* < 0.05, ***P* < 0.01, ****P* < 0.001 before versus after HD. The intermittent decrease of the RER develops because of the steadily minimized subjects on the levels as well as the great standard deviation.

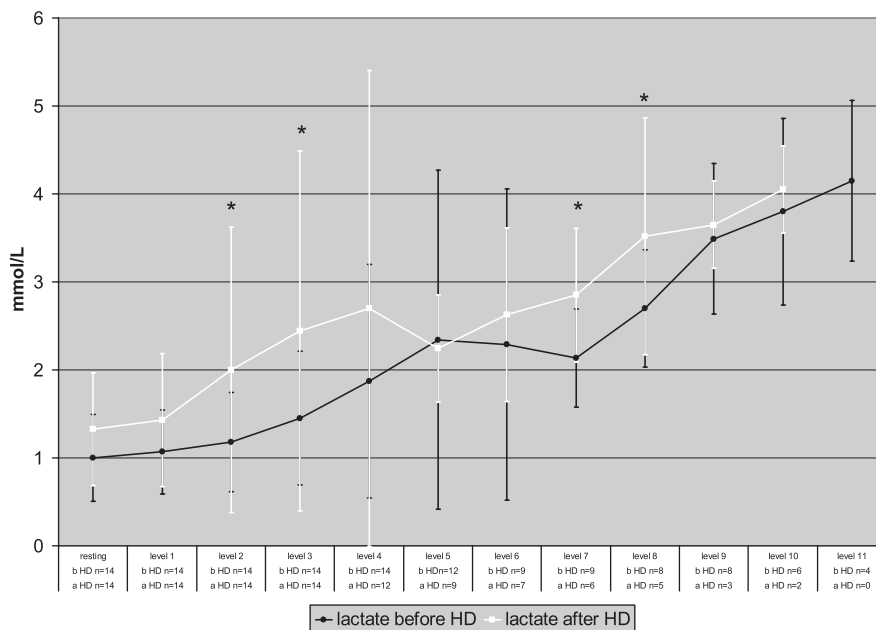


Fig. 4. Lactate during exercise. The subjects reached different maximal workload levels; number of patients at each level (*n*) is shown. (b HD) = before HD and (a HD) = after HD. **P* < 0.05, ***P* < 0.01, ****P* < 0.001 before versus after HD. The decreased lactate value at Level 5 after dialysis and at Level 6 and 7 before HD was based on the great standard deviation and a lower subject number.

not surprised about the negative data obtained: work performed in terms of time and watts decreased significantly after dialysis, with constant cardiac workload. During dialysis, a massive exchange and a rapid reduction of blood volume occur. Hence, a major load appears for the circulation and the haematocrit increases after dialysis. Accordingly, a lower blood pressure and a significantly increased heart rate after dialysis were seen at resting as well as on each workload level. Significant changes of heart rate were detected until workload level eight. Further statistical significance could not be calculated since the sample of patients remaining was too small. The decrease of heart rate on level nine (see Figure 2) can be explained by the lower number of subjects remaining. The participants started with

worse initial cardiovascular conditions after HD, also underlined by the impaired recovery of the cardiovascular system after completion of the test. Because of the systemic strain imposed by HD, the capacity of the patient's cardiovascular system is lower after than before dialysis.

In contrast to the peak respiratory parameters, the respiratory parameters on each level did not show any negative effect of dialysis on performance. Maximal oxygen uptake per kilogram body weight corresponded to values obtained in previous studies [7]. The lack of a significant difference here before and after dialysis supports the thesis that oxygen uptake changes with long-term training but not due to prior short-term stress, here HD [17]. The measured RER indicated that the maximum respiratory capacity was

reached before and after dialysis. The mean values corresponded well with those obtained by Weaver *et al.* [7]. The results after dialysis showed that maximum respiratory capacity was reached earlier and at lower workloads than before dialysis. This confirmed that HD causes a decrease in exercise capacity.

The lactate values showed significant differences on varied workload levels with higher lactate concentrations after dialysis (Figure 4), whereas the mean peak lactate level was not significantly different. As presented in Figure 4, the standard deviation of the lactate values after dialysis was very high especially in Levels 2–4. These values might be due to the different fitness levels of the participants and their main condition. Furthermore, the use of lactate in this heterogenic group is limited to evaluate exercise capacity since the subjects present a disordered acid–base metabolism and receive sodium bicarbonate as medication. Moreover, reduced lactate values in children and adolescents compared to adults can be explained by lower testosterone levels as well as reduced muscular enzyme activity [18].

The decreased exercise capacity after dialysis is therefore not due to a lack of oxygen in the muscle. Abortion of the exercise test was not caused by reaching the maximal muscular capacity but by reaching the maximal respiratory capacity. These results, however, can also be based on the test protocol, with an increase of 10 W workload per minute until subjective exhaustion. In contrast to the original Godfrey protocol, at which the exercise test of children taller than 150 cm starts with 20 W and is raised every minute by 20 W, we modified the test protocol and adapted it to the children's and adolescent's weight [11]. Since the subjects had a low BMI with $19 \pm 2 \text{ kg/m}^2$, they started with a load half of their body weight and an increase of 10 W/min. As children and especially paediatric patients with chronic diseases possess a limited exercise capacity, the starting load was reduced accordingly to their steric habit and increased slightly every minute [15].

In summary, the present study shows that the exercise capacity of paediatric patients with CKD requiring dialysis is far behind their average age-matched healthy peers. On top of that, HD itself leads to a subsequent impairment of exercise capacity just after the procedure. Further studies concerning the exercise capacity of children and adolescents with CKD are desirable and necessary. These studies should focus more on the direct effects of HD on the exercise capacity of paediatric patients. Interventions targeted on physical inactivity of patients could lead to further insights into ways to counter the reduction of exercise capacity. The reduced exercise capacity after HD should therefore be a focus of profound examination. This is the first study to look at the exercise capacity of children on the actual days of HD. However, we were not able to examine how long the reduced exercise capacity persists after dialysis. A reduced exercise capacity in adult dialysis patients was found in several studies on non-HD days or before dialysis sessions [19, 20]. This would support the theory that quality of life is definitively diminished not only directly after the dialysis session but also in between. Although it is problematic to adjust paediatric data to the situation in adults, one can nevertheless speculate that the exercise capacity of adults

would also be hampered even more after the dialysis session. Clearly, further studies are needed. Also, designing specific training programs me during HD to increase the exercise capacity would be an essential target for new interventional studies.

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Conflict of interest statement. None declared.

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