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ORIGINAL ARTICLE

Exercise during Hemodialysis in Patients with Chronic Kidney Failure

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Abstract

BACKGROUND Patients with kidney failure undergoing hemodialysis experience physical deconditioning and multimorbidity. Exercise interventions may mitigate this outcome, but their clinical role is unclear.

METHODS This multicenter, cluster randomized controlled trial evaluated combined endurance and resistance exercise training during hemodialysis versus usual care in chronic kidney failure. It assessed physical functioning, quality of life, hospitalizations, and overall survival. The primary outcome was the change in the 60-second sit-to-stand test (STS60) between baseline and 12 months.

RESULTS A total of 1211 patients underwent randomization, 917 (65.9±14.4 years; 38.9% female) of whom were included in the full analysis (exercise intervention, n=446; usual care, n=471). At 12 months, the STS60 repetitions improved from 16.2±7.6 to 19.2±9.1 in the exercise group but declined from 16.2±7.1 to 14.7±7.9 in the usual care group (group difference, 3.85 repetitions; 95% confidence interval [CI], 2.22 to 5.48; P<0.0001). The timed up-and-go test (–1.1 seconds; 95% CI, –1.9 to –0.3) and the 6-minute walk test (37.5 m; 95% CI, 14.7 to 60.4) also differed in the exercise group versus usual care group. The physical summary score and vitality subscale of the quality of life questionnaire (i.e., the 36-item Short Form Health Survey) differed in the exercise group versus usual care group, but the other subscales did not change. Adverse events during dialysis sessions were similar in both groups. Median days spent in the hospital annually were 2 in the exercise group and 5 in the usual care group. Mortality and dialysis-specific adverse events were not affected.

CONCLUSIONS Twelve months of intradialytic exercise in patients with kidney failure significantly improved the STS60 compared with usual care. (Funded by the Innovation Fund, Federal Joint Committee; ClinicalTrials.gov number, NCT03885102.)

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Introduction

Hemodialysis is the primary therapeutic option for patients with end-stage kidney failure, and an estimated 558,060 patients regularly undergo dialysis in the United States.[1] The health economic burden of these patients is very high, and the annual dialysis cost per patient in the United States is approximately $40,000.[2] A majority of patients with kidney failure have multiple comorbidities that are associated with increased morbidity and mortality, including diabetes and cardiovascular disease.[3,4] Moreover, patients with kidney failure undergoing hemodialysis experience severe physical deconditioning, which — coupled with a high prevalence of frailty — results in a vicious cycle of deterioration and reduced quality of life.[3,5-7]

Exercise training in a supervised and structured setting has the advantage of using the time available during routine hemodialysis sessions to attenuate the decline in physical function. Although results from previous studies have been promising,[8-10] prior trials of exercise during hemodialysis have been limited by small sample sizes and short program duration.[11] It therefore remains unclear whether long-term intradialytic exercise training is safe, feasible, and would result in clinically relevant improvements in patients with various kidney disease etiologies, a broad age spectrum, and multiple comorbidities.[12]

We conducted the DiaTT (Dialysis Training Therapy) trial, a multicenter, cluster randomized controlled trial of 12-month intradialytic exercises combining endurance and resistance exercise training. The study assessed physical functioning, quality of life, safety during hemodialysis, hospitalizations, and mortality.[13] We hypothesized that the exercise intervention would improve the 60-second sit-to-stand test (STS60) after 12 months, and other measures of exercise performance, compared with usual care.

Methods

TRIAL DESIGN AND OVERSIGHT

Based on a pilot study,[14] DiaTT was a multicenter, interventional, cluster randomized controlled trial. Details on the study design have been published previously.[13] Briefly, after screening according to predefined inclusion criteria, 24 dialysis centers from one nonprofit kidney care provider (Kuratorium für Dialyse und Nierentransplantation e.V.; Board of Trustees for Dialysis and Kidney Transplantation, Neu-Isenburg, Germany) were included. Subsequently, all hemodialysis patients treated at these centers were assessed for eligibility. Eligibility criteria included age ≥18 years, ambulatory hemodialysis for >4 weeks, no planned peritoneal dialysis or live kidney transplantation, or absolute contraindication to exercise according to the patient's dialysis physician. Full eligibility criteria are provided in the clinical trial protocol (Appendix 1 in the Supplementary Appendix).[13] All patients provided written informed consent. Dialysis centers were cluster-randomized in blocks of two to the exercise group or usual care group (1:1). During the subsequent 3 months, exercise equipment was installed in the intervention centers, and personnel were hired and trained in all centers.

The organizational structure of the study is described in Figure S1. The study protocol was approved by the ethics committee of the coordinating center at the Medical Faculty of the Technical University of Munich and by each regional ethics committee for all participating dialysis centers. An independent monitoring committee evaluated patient safety. The authors vouch for the accuracy and completeness of the data and analyses and for the fidelity of the trial to the protocol. The trial is registered as NCT03885102 at ClinicalTrials.gov.

INTERVENTIONS

Routine dialysis care was continued in both groups. The exercise intervention group received intradialytic exercise three times per week consisting of supervised endurance and resistance exercise that started during the first 2 hours of hemodialysis and lasted for 60 minutes (30 minutes duration for each mode of exercise). Endurance exercise was performed on a bed-cycle ergometer in a semi-recumbent position in a dialysis chair or bed (MOTOmed letto2, RECK-Technik GmbH & Co KG Medizintechnik, Betzenweiler, Germany) (Fig. S2). Ergometers were programmed individually to maintain a target heart rate and adjust resistance accordingly. In very frail subjects or individuals with leg amputations, motor-supported ergometry training could be performed. Resistance exercises, individualized to patients' disabilities, were performed in bed (in a recumbent position) with elastic bands, exercise balls, and dumbbells using the nondialysis shunt arm (eight exercises, two 1-minute sets each with intensity of 12–13 ["somewhat hard"] on the Borg Rating of Perceived Exertion scale) under the guidance and supervision of the trainers. The intensity of all exercises was

progressively increased, assessed every 3 months, and adapted accordingly. Exercise therapists (background in sports science, physical therapy, or similar) received a formal weekend introductory course to the DiaTT training program. They also had access to and received feedback from experienced trainers throughout the study. Health literacy counseling focusing on the general benefits of exercise, including instructions on specific intradialytic exercises, was performed during exercise sessions.

Due to quarantine regulations during the SARS-CoV-2 pandemic, study personnel were temporarily prohibited from entering the dialysis units (details are provided in the study protocol amendment, Appendix 2). During this time, to preserve exercise improvements, a substitute exercise program was provided, which patients could perform at home. Trainers offered encouragement with videos, brochures, and telephone consultancy, and they collected information on exercise adherence on a weekly basis until intradialytic exercise training could continue.

TRIAL OUTCOMES

The primary outcome was the change in the STS60 between baseline and 12 months. Secondary outcomes included: changes in the STS60 between baseline and 3, 6, and 9 months; and changes between baseline and 3, 6, 9, and 12 months for the timed up-and-go (TUG) test, 6-minute walk test (6MWT), and grip strength test.[4,15,16] These were assessed after the long (72-hour) interval in the dialysis units before treatment. Quality of life assessments using the 36-item Short Form Health Survey (SF-36) questionnaire were conducted at the same quarterly intervals. Further secondary outcomes included a yearly total number of hospital admissions, days spent in the hospital, three-point major adverse cardiac events (MACEs [a composite of cardiovascular death, nonfatal stroke, or nonfatal myocardial infarction]), and overall survival.[13]

STATISTICAL ANALYSIS

The statistical analysis plan was published previously[13] and is provided in Appendix 3. The sample size calculation[13] (α=5%, power of 80%) resulted in 897 patients; adding 20% for mortality resulted in 1100 patients being included in the trial. Centers were randomized until this number of participants was reached. Efficacy analyses were performed according to the intention-to-treat principle in the modified full analysis set, including patients who attended the baseline examination and for whom at least one postbaseline visit was documented. The per-protocol population was a subset of the full analysis set, defined as patients who received a minimum of 33% of the initially planned exercise training sessions.

The primary analysis was conducted in the full analysis set with a linear mixed-effects regression model (randomized treatment, baseline STS60, stratification factor region, time points, and time-by-treatment interaction as independent variables). Treatment effect estimates are presented with two-sided 95% confidence intervals (CIs). For patients who died during the trial, which would lead to missing values for the outcome STS60, the "worst possible value" (i.e., 0 repetitions) was inserted. In addition, several sensitivity analyses were conducted (Supplement 1, Table S3). The analysis of secondary efficacy end points was performed with the same type of mixed-effects regression model. Overall survival rates were estimated by using the Kaplan–Meier method. In case of competing events, cumulative incidence rates were calculated.

Statistical calculations were performed by using SAS version 9.4 (SAS Institute, Inc., Cary, NC). No multiplicity adjustments for the secondary and exploratory end points were defined. Therefore, only point estimates and 95% CIs are provided. The CIs have not been adjusted for multiple comparisons and should not be used to infer definitive treatment effects.

Results

TRIAL POPULATION AND BASELINE CHARACTERISTICS

Randomization was stopped at 21 centers when a minimum of 1100 patients had been recruited. Within these dialysis units, 2118 patients were actively receiving hemodialysis. Of these, 1211 (57.2%) agreed to participate in the study and met the inclusion criteria (Fig. 1). Ten dialysis units (578 patients) were randomized to intervention and 11 units (633 patients) to usual care. During a 3-month installation period in all centers to allow for the hiring of local trainers and installing exercise equipment, 193 patients died or dropped out. Of 505 patients in the usual care group and 513 in the training group, 34 and 67 patients, respectively, were excluded from the full analysis set because they had no follow-up examination. Of the remaining patients, 100 patients in the usual care group and 125 in the intervention group withdrew their consent, changed centers, showed lack of compliance, experienced medical events, underwent

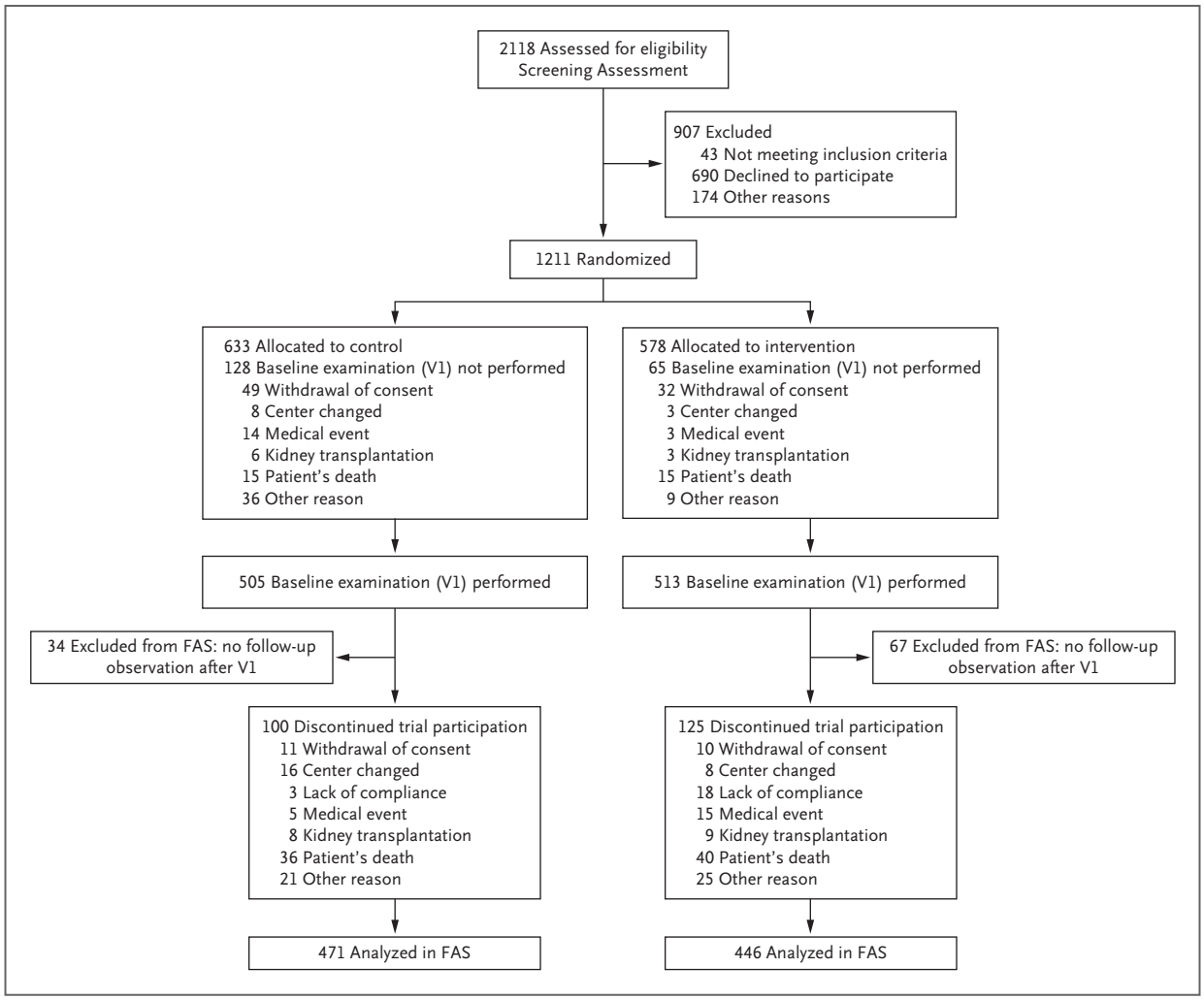

Figure 1. Screening, Randomization, and FAS.

In the dialysis centers that had agreed to participate in the trial and met inclusion criteria, all patients were screened to be included into the trial. When a minimum of 1100 patients fulfilled inclusion criteria and were not excluded, center recruitment was stopped. This led to 21 dialysis centers (1211 patients), of which 10 (578 patients) were randomized to the exercise intervention group and 11 (633 patients) to the usual care group. This was followed by a 3-month "installation period" at all centers to allow for the hiring and training of local exercise therapists and the installation of exercise equipment. A total of 100 patients in the usual care group and 125 patients in the intervention group dropped out of the study. Three patients (one in the usual care group and two in the intervention group) died shortly after visit 5 (V5) but were classified as having died within the study period. The final study population consisted of 446 patients in the intervention group and 471 patients in the usual care group. FAS denotes full analysis set; and V, visit.

kidney transplantation, or died. Overall, at 12 months, 78.8% (371 of 471) of the patients in the control group and 72.0% (321 of 446) in the intervention group were still in the study and remained in the full analysis set (446 patients in the intervention group and 471 patients in the usual care group).

Baseline clinical and physiological data are presented in Table 1. The mean (±SD) age was 65.9±14.4 years, and 38.9% of participants were female. Diastolic blood pressure values (usual care, 134.3±16.3 mm Hg; intervention, 133.9±17.1 mm Hg) and body-mass index (usual care, 28.0 ± 6.3 kg/m^2; intervention, 27.1±5.6 kg/m^2) were comparable in both groups. The causes of kidney failure and distribution of comorbidities were also similar between the two groups. Among all patients, 4.5% had lower extremity amputation, 13.7% were receiving long-term nursing care at home, 3.7% lived in a skilled nursing facility, and 11.1%

Table 1. Baseline characteristics of patients in each group.*		
Characteristic	**Usual Care (n=471)**	**Intervention (n=446)**
Age, yr		
18–64	192 (40.8)	186 (41.7)
65–84	247 (52.4)	239 (53.6)
≥85	32 (6.8)	21 (4.7)
Underlying renal disease		
Hypertensive/vascular nephropathy	130 (27.6)	96 (21.5)
Diabetic nephropathy	95 (20.2)	80 (17.9)
Glomerular nephropathy	100 (21.2)	83 (18.6)
Other or unclear kidney disease†	146 (31.9)	187 (41.9)
Comorbidities‡		
Coronary disease	151 (32.1)	154 (34.5)
Heart failure (NYHA functional class II or higher)§	106 (22.5)	155 (34.8)
Other cardiac disease¶	168 (35.7)	193 (43.3)
Peripheral vascular disease	84 (17.8)	83 (18.6)
Cerebrovascular disease	49 (10.4)	58 (13.0)
Diabetes mellitus	151 (32.1)	131 (29.4)
Impaired physical mobility‖	82 (17.4)	64 (14.3)
Lower extremity amputation	19 (4.0)	22 (4.9)
Dialysis data		
Time since first dialysis, yr	3.8 (0.2–39.9)	4.1 (0.2–42.6)
Dialysis session time, min	261.4±21.5	260.6±17.8
Transport to dialysis by ambulance	43 (9.1)	59 (13.2)
Medication		
Patients with ≥7 medications/d**	405 (86.0)	363 (81.6)
No. of pills/d††	16.5±7.0	17.1±9.4

* Values are presented as n (%), median (interquartile range), or mean (±SD). NYHA denotes New York Heart Association.
† Additional categories ("other") of underlying renal disease were cystic, interstitial, systemic, and hereditary/congenital kidney disease.
‡ Categories of conditions with at least "moderate" severity and with significance for patient prognosis or daily functioning
§ Most of the patients had NYHA functional class II heart failure.
¶ Conditions included atrial fibrillation or other arrhythmias, valvular heart disease, and others aside from coronary disease and heart failure.
‖ Defined as severe arthrosis or use of wheelchair such as for orthopedic reasons or amputations.
** Active ingredients in combination products were counted as separate medications.
†† Medications applied as sprays, ointments, or liquids were not counted. Pills containing more than one active ingredient were counted as one pill.

were not able to use public transport or taxi and were brought to dialysis by ambulance. Most patients were taking multiple medications.

Representativeness of the DiaTT study cohort was assessed by comparing the cohort with nonparticipating patients from the same health insurance companies (917 patients of the full analysis set were compared with 18,337 dialysis patients not participating in the DiaTT trial) according to baseline data, including age, sex, grade of care, and three major comorbidities (diabetes, chronic ischemic heart disease, and chronic heart failure). These data (Supplement 2, Table S4) show a reasonable agreement between the general dialysis cohort and the DiaTT cohort. The only difference was observed in the comorbidity of diabetes, which was 12.5% lower in the DiaTT cohort and 5.7% less in ischemic heart disease. All other parameters, including the grade of care classification, were very similar between groups.

FOLLOW-UP AND TRIAL OUTCOMES

When accounting for clinical events or other reasons for discontinuation of the trial, 78.8% (n=371/n=471) of the patients in the control group and 72.0% (n=321/n=446) in the intervention group remained in the study. For the

primary end point, 39 (8.3%) patients in the control group and 32 (7.2%) patients in the intervention group had reasons not to perform STS60 such as balance difficulties and medical or orthopedic reasons. Overall, 9.8% in the control group and 6.3% in the intervention group were not assessed at 12 months for the primary end point STS60 because of absence from the dialysis unit due to unspecified reasons (e.g., vacation, appointments, or other that could not be specified) on the 2 days when the examination team was present.

In the intervention group, patients participated in a mean of 44.5±22.7 intradialytic exercise sessions. This accounts for 88.1% of exercise sessions that were offered when trainers were present at dialysis centers. This intradialytic training was disrupted because of the SARS-CoV-2 pandemic for 17.4±7.6 weeks depending on centers and state hygiene regulations (range, 11–32 weeks). To compensate for this disruption, a daily home-based training was developed and initiated. Patients trained at home for 5.6±6.1 weeks (range, 0–25 weeks) with a mean total of 19.7±24.1 exercise training days during lockdown periods. Shortly before the first lockdown, in early 2020, we anticipated that the study may have to be terminated, and we, therefore, conducted interim study visits, where feasible, in those centers that were likely to miss the next scheduled visit. No center missed visit 1. One control center missed visit 5 (30 patients at visit 1, 18 patients remaining at visit 4). For visits 2, 3, and 4, the number of centers where the respective regularly scheduled visit could not be done was as follows: intervention centers visit 2 (1 center), visit 3 (1 center), and visit 4 (3 centers); control centers visit 2 (3 centers), visit 3 (2 centers), and visit 4 (4 centers). Values for all patients in these centers were counted as missing unless they had died, in which case a value of 0 was inserted for the primary analysis. The results of the interim visits were used both in the primary analysis and in the sensitivity analyses.

The repetitions performed in the STS60 test improved significantly over 12 months in the intervention group from 16.2±7.6 to 19.2±9.1, but they declined in the usual care group from 16.2±7.1 to 14.7±7.9. The adjusted group difference at 12 months was 3.85 repetitions (95% CI, 2.22 to 5.48; P<0.0001) (Table 2) in the primary analysis. When deceased patients were treated as "missing" instead of inserting a value of 0, the adjusted group difference was 4.48 (95% CI, 2.98 to 5.98; P<0.0001). The data for all other preplanned sensitivity analyses are shown in Table S3.

For the secondary physical performance outcomes, including the TUG (–1.1 seconds; 95% CI, –1.9 to –0.3) and 6MWT (37.5 m; 95% CI, 14.7 to 60.4), there were differences compared with usual care. The grip strength test did not differ between groups over 12 months (Table 2).

Quality of life as assessed by using the SF-36 (Table S1) differed in the Physical Health Component Summary score (mean difference [control minus training] at 12 months –1.86; 95% CI, –3.72 to –0.0). The difference between groups was calculated as changes from baseline to 12 months. The Mental Health Component Summary score[17] did not differ. The SF-36 subscale changes differed for the vitality subscale after 12 months (–6.01; 95% CI, –9.39 to –2.63); all other subscales remained unchanged.

The estimated overall survival rates over 12 months were 90% (95% CI, 87 to 93) in the intervention group and 92% (95% CI, 89 to 94) in the usual care group (Table 3). Cumulative incidence rates for three-point MACEs were 6.9% (95% CI, 4.7 to 9.8) in the intervention group and 3.9% (95% CI, 2.3 to 6.0) in the usual care group. Incidence rates of sudden cardiac death were also not different (Table S2a).

Hospitalizations and serious adverse events are shown in Table 3. Mean hospitalizations per patient were 1.1±1.5 versus 1.3±1.6 in the exercise training group and the usual care group, respectively (P = 0.024); the diagnoses leading to hospitalization are presented in Table S2b. The time spent in the hospital was 10.8±18.9 days per year (median, 2 days; range, 0 to 139 days) in the intervention group and 12.8±20.9 days (median, 5 days; range, 0 to 140 days) in the usual care group (P = 0.036 for both comparisons). Adverse events leading to discontinuation of dialysis occurred in 16% of patients and were not different between groups.

Discussion

The DiaTT trial sought to determine if an exercise training program for ambulatory dialysis units, in which even very weak and frail patients would be able to participate, might improve physical functioning outcomes. We found that using the time on dialysis for combined endurance and strength training significantly improved the primary end point, the change in the STS60, which measures how well patients can rise from a sitting to a standing position (an ability relevant for independent living),[18] compared with

Table 2. Trial outcomes: physical functioning tests.*

Time Point	Usual Care	Intervention	Adjusted Difference† (95% CI)	P Value
Sixty-second sit-to-stand test, repetitions				
At baseline	16.2±7.1	16.2±7.6		
	n=448	n=410		
At 3 months	16.3±7.0	17.4±7.7	1.53	
	n=244	n=319	(–0.10 to 3.17)	
At 6 months	16.9±7.5	17.5±8.5	1.48	
	n=276	n=285	(–0.15 to 3.11)	
At 9 months	16.7±7.7	18.8±9.1	2.72	
	n=177	n=186	(1.06 to 4.37)	
At 12 months‡	14.7±7.9	19.2±9.1	3.85	<0.0001
	n=286	n=261	(2.22 to 5.48)	
Timed-up-and-go test, seconds				
At baseline	12.6±7.4	12.9±8.2		
	n=426	n=389		
At 3 months	12.2±6.5	12.7±8.3	0.01	
	n=239	n=297	(–0.79 to 0.80)	
At 6 months	11.8±6.3	12.3±8.8	–1.11	
	n=265	n=277	(–1.91 to –0.31)	
At 9 months	12.1±7.7	12.9±9.4	–0.37	
	n=167	n=141	(–1.30 to 0.57)	
At 12 months	12.2±5.9	11.9±9.3	–1.11	
	n=266	n=248	(–1.93 to –0.29)	
Six-minute-walk test, m				
At baseline	282.5±156.1	293.0±145.7		
	n=410	n=381		
At 3 months	294.6±159.9	314.1±140.8	13.72	
	n=227	n=282	(–8.98 to 36.42)	
At 6 months	289.6±156.7	299.4±142.8	30.16	
	n=136	n=177	(5.42 to 54.89)	
At 9 months	278.0±163.1	311.4±146.7	37.09	
	n=103	n=55	(8.32 to 65.86)	
At 12 months	287.8±159.3	336.9±173.0	37.54	
	n=244	n=234	(14.69 to 60.38)	
Grip strength test, kg				
At baseline	25.7±10.9	25.1±10.9		
	n=462	n=438		
At 3 months	25.7±11.3	25.9±10.6	–0.60	
	n=273	n=282	(–2.89 to 1.70)	
At 6 months	24.8±11.5	24.8±10.5	1.13	
	n=229	n=209	(–1.19 to 3.45)	
At 9 months	26.0±10.3	26.5±10.5	0.95	
	n=163	n=147	(–1.42 to 3.33)	
At 12 months	25.4±10.9	26.0±10.6	0.50	
	n=325	n=289	(–1.78 to 2.78)	

* Values are mean±SD and number of patients assessed at the respective visit.

† Determined in a mixed linear regression model including baseline physical function test, region, group, and time × group interaction.

‡ Primary end point.

Table 3. AEs and SAEs over 12 Months.*

Medical Events	Usual Care (n=471)	Intervention (n=446)	Significance
Total no. of AEs	2782	2331	
Patients with ≥1 AE	373 (79.2)	338 (75.8)	
Incidence of AE†			
Muscle cramps	204 (43.3)	182 (40.8)	
Leading to discontinuation of dialysis	37 (7.9)	33 (7.4)	
Hypotension	258 (54.8)	241 (54.0)	
Leading to discontinuation of dialysis	29 (6.2)	35 (7.8)	
Severe hypotension‡	2 (0.4)	2 (0.4)	
Needle dislocation	128 (27.2)	111 (24.9)	
Leading to discontinuation of dialysis	10 (2.1)	7 (1.6)	
SAE, total hospitalizations — n	620	510	
Hospitalizations per patient	1.32±1.62	1.14±1.53	P=0.024
Hospitalizations per patient — median (IQR)§	1 (0–12)	1 (0–8)	
Patients with ≥1 hospitalization	281/471 (59.7)	237/446 (53.1)	
Days in the hospital per patient	12.8±20.9	10.8±18.9	P=0.036
Days in the hospital per patient — median (IQR)§	5 (0–140)	2 (0–139)	P=0.036
SAE, deaths¶ — n	36	40	

* Values are presented as n (%) or mean (±SD) unless indicated otherwise. Serious adverse events (SAEs) were defined as hospitalization or death. AEs denotes adverse events; and IQR, interquartile range.

† AEs per patient; a patient with repeated AEs was only counted once.

‡ Significant impairment by the event (e.g., patients can no longer perform usual activities or life is at risk from the event).

§ "0" means patient not hospitalized.

¶ Three patients (one in the usual care group and two in the intervention group) died shortly after visit 5 but were classified as having died within the study period.

usual care. Moreover, improvements were found for other parameters of physical functioning, such as the TUG, assessing leg strength in combination with coordination, and in the distance walked during the 6MWT, a measure of aerobic endurance capacity. The latter improved on average by 37.5 m, which is seen as clinically important in chronic disease,[19,20] and is similar to improvements made by exercise training after acute heart failure decompensation.[16] These effects were associated with changes on the SF-36 vitality subscale and the Physical Health Component Summary score that seem to favor exercise. It remains uncertain whether this relationship is a direct result of improved physical functioning or an indirect effect due to positive motivation by supervised training in groups, or both. These improvements were associated with a median 3-day reduction in the time spent in the hospital and a lower frequency of hospitalizations over 12 months with the exercise program compared with usual care.

The exercise intervention was not associated with excess adverse events and did not interfere with routine dialysis care. Complications during hemodialysis and mortality did not differ significantly between groups (Table 3).

Patients with kidney failure who are receiving hemodialysis are less physically active due to time spent inactive on dialysis (generally 4 to 5 hours thrice weekly). Moreover, comorbidities may further limit physical activity. Beyond that, impairment of kidney function has been shown to be directly related to distinct pathophysiology, including microangiopathy, characterized by a combination of dysfunctional angiogenesis, rarefaction of the vascular bed, and endothelial dysfunction.[21,22] In addition, chronic kidney disease has been shown to impair protein metabolism, mitochondrial mass, and satellite cell activation, and to induce muscle wasting.[23] Regular combined resistance and endurance training have been shown to improve vascular and skeletal muscle function,[24,25] even on a molecular level.[23,26]

Home-based training has been proposed as an alternative to intradialytic exercise training, but results have only been obtained from shorter interventions and in smaller and select cohorts.[11,27] One larger study involving patients who were able to walk assessed a 6-month home-based walking program and observed improvement in functional status and reduced risk of hospitalization.[28] Here we have

included patients with a wide spectrum of comorbidities and advanced age, including frail patients who have been excluded from other exercise trials.

The results of the primary analysis were obtained despite the disruptive conditions created by the SARS-CoV-2 pandemic. Because trainers were not allowed into the dialysis units during lockdown, a home-based training program was developed but could only be introduced after several weeks in some centers; in others, multiple lockdown periods followed each other. As a result, regular thrice-weekly intradialytic training was interrupted for between 11 and 32 weeks. Nonetheless, a clear benefit of this exercise program was shown.

Generalizability of study results to the broader dialysis population in Germany was an important aspect of the DiaTT study design. Comparison with insurance claims data indicated that the patients recruited to DiaTT appear to be similar to patients treated in Germany (Supplement 2, Table S4). However, our study was conducted in a population with a very low representation of non-White patients, which limits generalizability to a broader population of patients treated with hemodialysis (Supplement 2, Table S5). It remains speculative — although likely — that the establishment of a training program with characteristics similar to DiaTT will have similar effects in other populations with diverse racial and ethnic backgrounds. In a population of predominantly African-American patients with less severe chronic kidney disease, the AWARD (Aerobics, Weights, and Renal Disease) trial recently reported promising results with a similar intervention compared with DiaTT.[29] However, to the best of our knowledge, data in patients on hemodialysis are lacking.

Our randomized exercise intervention trial showed that, in a real-world dialysis setting including 57.2% of all dialysis patients from centers involved, with a large age spectrum and representative variety of underlying kidney failure entities and comorbidities, combined endurance and resistance intradialytic exercise training over 12 months improved physical function, reduced hospital days, and was feasible and safe.

Disclosures

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