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Does the interference phenomenon affect strength development during same-session combined rehabilitation program in hemodialysis patients?

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Abstract

Introduction: This study aimed to assess if an interference effect could blunt the neuromuscular gains induced by a same-session combined rehabilitation in hemodialysis (HD) patients.

Methods: Patients exercised twice a week, for 16 weeks, over their HD sessions. They were either always trained with resistance and endurance exercises (continuous training, "CONT") or alternatively with 1 week of resistance alternated with 1 week of endurance (discontinuous training, "DISC"). Adherence and workload were continuously recorded. Short Physical Performance Battery (SPPB) score, one-leg balance test, and handgrip and quadriceps strength were evaluated before and after training intervention.

Results: Adherence to both programs was high (>90%). SPPB score had significantly improved (CONT: +1.5 point, DISC: +1.2 pt, $p < 0.001$), like one-leg balance test (CONT: +3.7 s, DISC: +5.5 s, $p < 0.05$), handgrip strength of exercised (CONT: +5.5 kg, DISC: +5.6 kg, $p < 0.001$) and of nonexercised arm (CONT: +4.4 kg, DISC: +2.8 kg, $p < 0.01$) as well as maximal quadriceps strength (+22 N·m for dominant and +29 N·m for nondominant leg in both groups, $p < 0.001$) bearing no difference between the trainings.

Conclusion: Same-session combined training does not induce an interference effect in HD patients and temporal separation of exercises does not optimize strength gains. These practical data may be relevant for clinicians and practitioners to alternate endurance and resistance exercises.

1 | INTRODUCTION

End-stage renal disease (ESRD) patients undergoing hemodialysis (HD) are most of the time sedentary, with less than 5,000 footsteps a day.¹ Moreover, ESRD is frequently associated with comorbidities (sarcopenia, diabetes mellitus, hypertension) also contributing to an extremely low daily level of activity associated to a low physical

performance.² Whereas physical activity is defined by any bodily movement produced by the contraction of skeletal muscle that increases energy expenditure above a basal level, exercise is a form of physical activity that is planned, structured, repetitive, and performed with the goal of improving health or fitness.³ Lack of physical activity leads to a muscular remodeling decreasing muscle endurance and strength and tolerance to exercise.⁴ Decrease in muscular mass not

only impedes mobility and increases risk of falling but also favors intramuscular fat infiltration, promoting insulin resistance, metabolic syndrome, and associated systemic consequences.⁵

Numerous studies have demonstrated that physical function is a strong survival predictor and also correlates with a decrease in hospitalization frequency in ESRD patients.⁶ Increasing physical activity considerably reduces mortality.^{3,7,8} Even low-intensity practice was associated with improved lipid profile, insulin sensitivity, and tensional control reducing all-causes cardiovascular events risk.⁹ Exercise during HD procedure was shown not only to be feasible and safe^{10,11} but also beneficial to the global physical function.^{12–14}

Exercise can be qualified of either endurance (aerobic) or resistance (mainly anaerobic): Endurance training corresponds to a low to moderate-intensity exercise performed during a long period of time, whereas resistance exercise implies moderate- to high-intensity contractions during a short period of time. When these contraction modalities are chronically practiced, adaptation of muscle tissue is specific to each regimen. Recently, Scapini et al.¹⁵ concluded that training combining endurance and resistance exercises was the most effective method to improve aerobic aptitudes and arterial blood pressure in adult ESRD patients. From these observations, combined training offering both endurance and strength exercises is the optimal rehabilitation to struggle against HD patients deconditioning.^{11,16,17}

However, when the two modalities are used in the same session in young or old healthy subjects, adaptation mechanisms of each regimen seem to compete with the other.¹⁸ This “interference” effect inside the muscle, identified early in the 1980s,¹⁹ can blunt its full adaptive response and may limit the potential neuromuscular gains.^{17,20,21} To our knowledge, interference effect has not been studied in HD patients following a combined rehabilitation program. Thus, we aimed to investigate whether same-session combined exercise training could blunt the strength gains induced by a combined exercise training regimen proposing to alternate resistance and endurance sessions. We hypothesized that temporal separation of exercises leads to neuromuscular improvements resulting in an optimization of muscle function and strength.

2 | SUBJECTS, MATERIAL, AND METHODS

2.1 | Study protocol and design

This study was designed as longitudinal with measurements before and after exercise intervention in order to compare the efficiency of a 16-week same-session combined exercise training (continuous program, “CONT”) on one hand and a 16-week combined exercise training alternating resistance and endurance sessions on the other hand (discontinuous program, “DISC”) on physical function of HD patients. The study procedures complied with the Declaration of Helsinki on human experimentation and were approved by local ethics committee (IRB-MTP_2020_08_202000560).

2.2 | Participants

A total of 20 HD patients aged from 18 to 85 years old were recruited and provided written informed consent. Inclusion criteria were as follows: HD vintage > 3 months, stable in HD, with no recent hospitalization; life expectancy > 6 months, with medical intradialytic exercise prescription. Exclusion criteria were as follows: contraindication or inability to perform exercise; unstable ischemic or valvular cardiomyopathy, peripheral obliterative arteriopathy > stage III, dysfunctional knee or hip prosthesis, severe respiratory insufficiency, body mass index (BMI) > 35, cardiac pacemaker, pregnancy, and patient under guardianship. Randomization was performed, and participants were sex, age-matched and display similar SPPB scores at baseline when allocated in “continuous” (CONT) or “discontinuous” (DISC) group.

2.3 | Training procedures

All the patients continued their usual HD procedure and had exercise intervention for 30 min during all their three weekly dialysis sessions. Exercising was supervised by physiotherapists and took place during the first 2 h of dialysis using elastic bands and therapy weights for resistance exercising and a bed-adapted cycle ergometer for endurance exercising (Bed Bike, Lemco). The distance virtually traveled is recognized as a motivational factor²² and was used as a target to achieve. Resistance level, speed, and kilometer count were recorded. Ergometer difficulty level was individually adapted to correspond to a 4- (moderate intensity) on the 10-point Borg Rating Perceived Exertion (RPE) scale. The fistula arm remained immobile, and elastic bands resistance and therapy weights (Cuff[®] Therapy weights, Fabrication Enterprises Inc.) were individually chosen to allow for 15–25 repetitions in the same set. Elastic band resistance was light or medium at the beginning, whereas only medium and high resistances were used at the end of the program. Weights ranged from 0.5 to 3 kg, and weights used during the first month were lighter than 2 kg for all the patients. At the beginning, patients performed only one set of each exercise, and number of sets was progressively increased to three before increasing elastic band resistance and weights.

2.4 | Adherence to the protocol

The number of exercise sessions performed was recorded for each participant. All dialysis procedures were associated with exercise during the 16-week protocol, as a total of 48 sessions scheduled. The adherence was calculated as the percentage of effectively carried out sessions.

2.5 | Primary and secondary outcomes

Short Physical Performance Battery (SPPB) allows to assess lower limb function and patients risk of disability.^{23,24} SPPB shows good

reliability with an intraclass correlation coefficient (ICC) of 0.94 and a minimal detectable change score at a 90% confidence interval (MDC₉₀) of 1.7 points.²⁵ SPPB score was chosen as primary outcome as the test was routinely used to evaluate physical function in the HD center. Muscle rehabilitation should improve SPPB score by 2 points with a common standard deviation (SD) of 1.5 points. With a power of 80% and an alpha risk of 5%, nine subjects per program were necessary. Assuming 10% missing data in SPPB, we proposed to include in this study 20 subjects, that is, 10 in each program. SPPB score was assessed before dialysis for all the patients on the same dialysis day, avoiding the first HD session, for pre-post-comparisons. Secondary outcomes included handgrip strength evaluated with a dynamometer, quadriceps contraction force in isometric condition, and one-leg balance test.

2.6 | Maximal grip strength

Handgrip strength evaluation shows good reliability with an ICC of 0.96 for the dominant arm and of 0.95 for the nondominant side and a MDC₉₀ of 3.4 kg for both arms.²⁶ Handgrip testing was performed at the beginning of the program, then every 4 weeks and at the end of the protocol for all the patients. The measurements pre- and post-training were made for each arm, whereas intermediary tests were only performed on the non-fistula arm.

2.7 | Maximal voluntary isometric contraction force

Before and after the training program, maximal voluntary isometric contraction force (MVC) was measured during knee extension with a handheld dynamometer (Microfet2, Hoggan Health), according to the method previously published.²⁷ Briefly, the hand-held dynamometer was fixed behind the subject and linked to the leg by an inelastic-strapped placed 2 cm proximal of the external malleolus. MVC of quadriceps was measured seated, hanging legs, without dorsal support with the knee held at 90° from extension, and arms crossed in front of chest. Three repetitions were done and the maximal value recorded. MVC are taken before and after training programs for CONT and DISC groups.

2.8 | One-leg balance test

To perform the one-leg balance test, patients had to maintain their balance standing on one leg as long as they could with their eyes open. All patients wore shoes and were allowed to freely move their arms. The test lasted no longer than 30 s and was ended before with the time recorded if the patient touched the floor with the second foot. In older adults, one-leg balance test displays an ICC of 0.86 and a MDC₉₅ of 24.1 s.²⁸

2.9 | Sample size calculation

Means of continuous measurement in two samples were compared, and sample size calculation was performed using the T statistic and noncentrality parameter on the website developed by Clinical & Translational Science Institute (UCSF, <https://sample-size.net/>). Considering a type I error rate of 0.05, a type II error rate of 0.2, an effect size of 1.6, and a SD of the outcome in the population of 1, the calculated sample size is 16 distributed equally in two groups. By considering 20% nonadherent patients, 20 patients were enrolled in the study.

2.10 | Statistical analysis

Statistical analyses were performed using StatView®. Each quantitative parameter was presented as mean ± SD. Descriptive analyses were carried out for patients' characteristics and exercise parameters. When appropriate, a repeated measure analysis of variance (ANOVA), a Friedman ANOVA, or a pairwise Wilcoxon test was performed. A result was considered as significant when *p* value was lower than *0.05, **0.01, and ***0.001.

3 | RESULTS

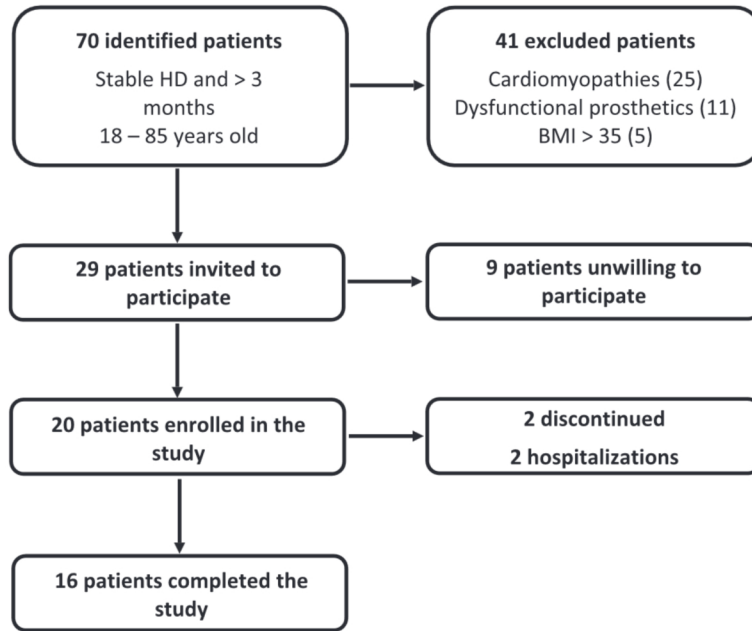
3.1 | Participants

Of the 70 patients screened for eligibility, 41 did not meet inclusion criteria. Among eligible patients, nine declined to participate. A total of 20 patients were included and 16 completed the study (CONT, *n* = 8; DISC, *n* = 8) (Table 1). Baseline characteristics are shown in Table 2. Briefly, mean age was 53.5 ± 20.2 years in the CONT group and 54.8 ± 15.9 years in the DISC group. Mean SPPB score was 9.0 ± 2.7 in the CONT group and 8.4 ± 3.3 in the DISC group.

3.2 | Adherence to training program and workload

Exercise parameters are shown in Table 3. Adherence was high (>90% of planned sessions) in both groups and tended to be higher in the CONT group (*p* = 0.07). Global exercises duration were similar and only temporal repartition of exercises differed between programs. However, virtual kilometers traveled were higher in the CONT group than in the DISC group (350.1 ± 108 km vs. 266.3 ± 153.7 km), but this difference was not statistically significant (*p* = 0.1). Resistance level of the cycle ergometer did not differ between groups (CONT: 3.6 ± 0.5 vs. DISC: 3.5 ± 0.9). Workload of resistance exercises was also similar regarding the mean weight lifted by the patients at the end of the exercise program (1.9 ± 0.9 kg in both groups).

TABLE 1 Flowchart of patient inclusion



3.3 | Physical function

Primary outcome for this study was the SPPB score shown on Figure 1A. CONT and DISC groups were constituted with similar SPPB scores at the beginning of the study, and tests were performed by the same examiner before and after training program. Mean SPPB reached 10.4 ± 1.8 points in the CONT group and 9.6 ± 2.7 points in the DISC group after training program and was statistically different from baseline (+1.5 point in CONT group and +1.2 point in DISC group; $p < 0.001$). No difference was found between trainings probably due to high range of values in each group. However, before training program, the range of values was larger than after, as the lowest score was 3, whereas it was 5 at the end of the study.

Balance score was not statistically different from baseline at the end of the protocol (data not shown). Nevertheless, walking speed was significantly improved after training program in both groups (Figure 1B, $p < 0.01$). Walking speed increased from 0.72 ± 0.23 to 0.89 ± 0.26 m/s in the CONT group and from 0.75 ± 0.34 to 0.88 ± 0.29 m/s in the DISC group. In the same way, the time taken to

perform five sit-to-stands was significantly reduced at the end of the study, corresponding to a mean gain of 12.5% and 15.3%, in the CONT and DISC groups, respectively (Figure 1C, $p < 0.01$). Time recorded decreased from 15.7 ± 5.3 to 13.7 ± 4.6 s in the CONT group and from 18.4 ± 8.1 to 15.6 ± 6.6 s in the DISC group. No training-type effect was found for these two parameters.

3.4 | One-leg balance

Results of one-leg balance tests are depicted on Figure 2A,B. Balance on left leg raised from 17.4 ± 12.5 to 19.7 ± 14 s in the CONT group and from 21.8 ± 10.3 to 28.7 ± 2.2 s in the DISC group. For right leg, time recorded increased from 16.7 ± 13.2 to 21.9 ± 11.4 s in the CONT group and from 25 ± 8.9 to 29.2 ± 2.3 s in the DISC group. Exercise training significantly improved balance for both legs in each group ($p < 0.05$) corresponding to a gain of 21.7% and 23.5%, in the CONT and DISC groups, respectively. No significant difference between training programs was found, although there was a slight

TABLE 2 Baseline characteristics of study participants

	All (n = 20)	Continuous training (n = 10)	Discontinuous training (n = 10)
Age	54.2 ± 17.7	53.5 ± 20.2	54.8 ± 15.9
Sex (male)	9	5	4
Time on HD (years)	3.7 ± 2.1	4.1 ± 3.9	3.3 ± 2.1
Cause of ESRD			
Diabetes	1	1	0
Glomerulonephritis	9	3	6
Hypertension	2	1	1
Polycystic kidney disease	1	1	0
Reflux/urological	3	2	1
Other	1	1	0
Unknown	3	1	2
BMI	25.4 ± 3.1	25.4 ± 3.7	25.4 ± 4.9
Diabetes	3	2	1
Hypertension	15	7	8
β blocker	5	3	2
Coronary artery disease	1	1	0
Heart failure	3	2	1
Charlson Comorbidity Index	4.7 ± 2.1	4.6 ± 2.3	4.8 ± 2.0
SPPB score	8.7 ± 2.2	9.0 ± 2.7	8.4 ± 3.3

Abbreviations: BMI, body mass index; ESRD, end-stage renal disease; HD, hemodialysis; SPPB, Short Physical Performance Battery.

TABLE 3 Exercise parameters of each training program

	Continuous training (n = 8)	Discontinuous training (n = 8)
Adherence (%)	98.3 ± 3.1	94.3 ± 8.9
Kilometers traveled	350.1 ± 158.0	266.3 ± 153.7
Cycling resistance level	3.6 ± 0.5	3.5 ± 0.9
Mean weight lifted (kg)	1.9 ± 0.9	1.9 ± 0.9

tendency for higher improvements in the DISC group compared with CONT group ($p = 0.2$).

3.5 | Handgrip strength

Results of maximal grip strength testing are depicted on Figure 3. Significant improvements were found for the non-fistula arm (Figure 3A, +5.5 and +5.6 kg in the CONT and in the DISC group, respectively) as well as for the fistula arm (Figure 3B, +4.4 and +2.8 kg in the CONT and in the DISC group, respectively).

Handgrip strength follow-up shows that exercise training significantly improved maximal grip force of non-fistula arm all along both training programs (Figure 3C, $p < 0.001$). Whereas only small increases were found after 8 weeks of training in each group, major improvements occurred at the final measure time point. No significant difference was found between groups ($p = 0.34$).

3.6 | Quadriceps isometric contraction force

Quadriceps maximal strength measured in isometric conditions for each leg is presented on Figure 4. Each training program was associated with major leg strength improvements ($p < 0.001$). As shown on Figure 4A, dominant leg maximal extension strength raised from 71.6 ± 37.5 to 94.1 ± 52.6 N-m in the CONT group and from 65.3 ± 30.9 to 87.3 ± 46.1 N-m in the DISC group, corresponding to an increase of 31.3% in the CONT group and of 33.7% in the DISC group. Results of nondominant leg testing depicted on Figure 4B point that strength increased from 58.9 ± 36.5 to 88.3 ± 48.1 N-m in the CONT group and from 47.7 ± 31.7 to 77.4 ± 44.8 N-m in the DISC group, corresponding to a strength improvement of 50.0% and 62.3% respectively in the CONT and in the DISC group. No significant difference was found between groups.

4 | DISCUSSION

The most important findings of this study are (i) that no interference phenomenon was detected as it was observed in healthy subjects and (ii) that combined training is efficient to improve the whole physical function of HD patients regardless of whether this is assessed on same-session combined exercise training or combined exercise training alternating resistance and endurance sessions.

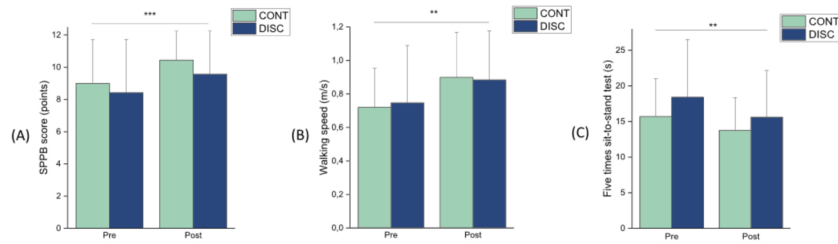


FIGURE 1 Evolution of (A) Short Physical Performance Battery score, (B) walking speed component and (C) five times sit-to-stand component before and after training program for "continuous" (CONT) and "discontinuous" (DISC) groups

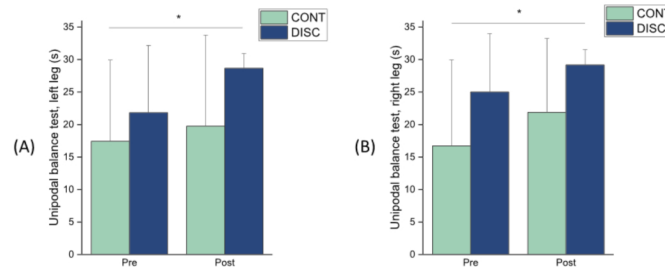


FIGURE 2 Evolution of one-leg balance test of (A) left leg and (B) right leg before and after training program for "continuous" (CONT) and "discontinuous" (DISC) groups

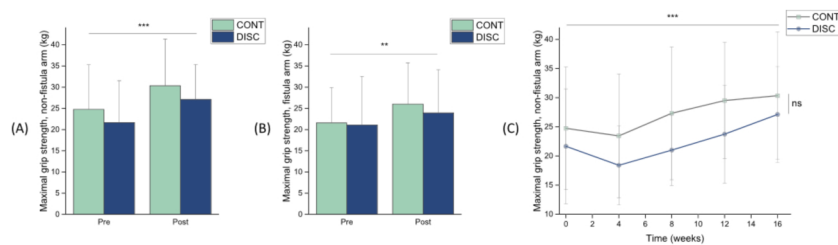


FIGURE 3 Evolution of maximal grip strength of (A) non-fistula and (B) fistula arm before and after training program and (C) non-fistula arm handgrip strength follow-up during training for "continuous" (CONT) and "discontinuous" (DISC) groups

The patients included in this study were young, as the mean age at the induction of HD in France is 63 years.²⁹ They had a relatively high SPPB score at baseline, as the threshold for frailty is under 8.²⁴ Between 3 and 9 on the 12-points score, patient is considered at risk of frailty.²⁴ However, HD patients are known to be weaker and less

active than healthy population of the same age.³⁰ In the study of Bean et al. involving more than 800 patients and where mean age was 74 years old, SPPB was over 10.³¹ Furthermore, physical abilities of ESRD patients rapidly decrease over time³² and are strongly correlated to mortality.³³

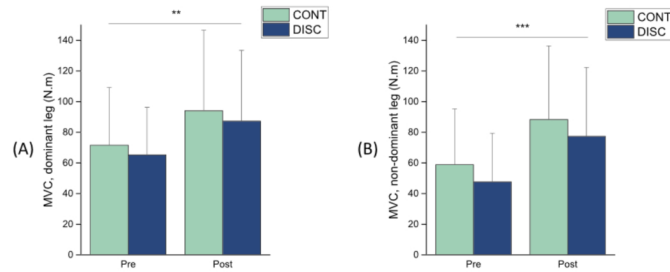


FIGURE 4 Evolution of maximal quadriceps strength of (A) dominant and (B) nondominant leg before and after training program for “continuous” (CONT) and “discontinuous” (DISC) groups

Intradialytic exercise is recognized to be safe and no adverse event occurred during training. Adherence was high in both groups (>90%) and comparable with the findings of Chen et al.³⁴ but higher than in other studies.^{35,36} All the patients clearly expressed their enthusiasm for intradialytic combined exercise practice. Combined training programs are the most efficient to improve functional performances, with higher adherence and acceptability than single-modality trainings.²² As underlined by Mendoza et al., adherence to exercise programs is strongly associated to age and dialysis vintage, age of 41–60 years old and HD vintage between 2 and 5 years favoring high adherence.³⁷ This high adherence in our study might also be explained by the frequency of the trainings: All the dialysis sessions were associated to exercise, and intradialytic training became usual for patients. Furthermore, the same physiotherapist supervised exercising during the program, permitting to develop a confident relationship with patients. Finally, exercise intensity was constantly adapted for each patient so that exercise was never perceived as difficult. Although no significant difference in patients' motivation was highlighted between programs, adherence tended to be higher in the CONT group probably due to exercises diversity and lower duration of an exercise type during the same session.

Workload was relatively high at the end of the protocol, but hardly comparable with other studies, these data were being rarely measured. Nevertheless, workload could be determinant for muscle adaptive response and was equivalent between our groups regarding the weights lifted. Nonetheless, DISC group tended to display a lower kilometer count than the CONT group. This workload difference can be explained by lower rotation speeds compared with CONT group, in part due to the longer duration of exercises in the DISC group. Indeed, rotation speed was not imposed to patients, and like most of the studies about intradialytic exercise, intensity was based on RPE.³⁸ This difference can also be justified by the lower adherence in the DISC group and notably because sessions were mainly missed during endurance weeks.

Limited data are available to compare our SPPB results.²⁵ In the study of Chen et al., patients had a lower SPPB score at baseline compared to our study, but mean age was over 70 years.³⁴ Authors found a 21.1% improvement in SPPB score after their strength training, higher than in our study (+14% in the CONT group and +17% in the DISC group), but their program lasted longer. Our results are in accordance with Thompson et al., who found a mean increase of 1.65 point and where patients' age was comparable.²² SPPB improvement is in part explained by a better walking speed, highly predictive of mobility and daily activities.^{39,40} Our results also indicate a mean reduction of 14% of time recorded during the sit-to-stand test and are in accordance with another study.⁴¹

HD population has an increased fracture frequency and displays a high risk of fall.^{42,43} Thus, effectiveness of combined exercise interventions on balance performance is of clinical importance. Reference value for age-matched healthy population is around 29 s,⁴⁴ confirming that HD patients included here displayed a poor balance. At the end of the program, one-leg balance performance was significantly increased in both groups. These results are hardly comparable with the literature due to lack of studies with similar interventions. The slight tendency for advanced improvements in the DISC group may be due to higher baseline values or to superior effects of alternated programs on balance that remain to be explored.

Muscle leg strength is also linked to the risk of fall, and increasing muscle strength seems to be effective to reduce fall frequency.⁴⁵ Quadriceps strength was converted into joint torque to take account of the lever arm length and groups displayed similar values at baseline. Compared with the data from trials that have used a hand-held dynamometer, patients included in our study displayed similar quadriceps strength of dominant leg at baseline, whereas they were younger.^{27,46} However, patients included in these two other studies were mostly males.^{27,46} The improvements in extension force measured here with a direct assessment method strongly confirm the effectiveness of intradialytic combined training to improve leg strength.

Maximal grip strength is also used in HD patients to detect sarcopenia.⁴⁷ In our study, measurements on the non-fistula arm indicated improvements in both groups (+22.6% in CONT group and +25.2% in the DISC group). To our knowledge, no data exist on grip strength of HD patients following combined training. Other exercise interventions found an increase ranging from 8% to 17%,³⁸ but the nature of exercises was totally different and combined exercise training affect handgrip strength in other pathologies.^{48,49} Two studies with resistance training protocols did not found significant increase in handgrip strength.^{50,51} However, contrarily to these studies, some resistance exercises in our protocol targeted specifically the hand flexors. Of note, dataset was collected at 5 time points in the same conditions and interestingly, improvements occur late. Most of the time, training programs last between 8 and 12 weeks, whereas here, significant difference from baseline is only detectable at 12 weeks for the CONT group and at 16 weeks for the DISC group.

Handgrip strength is known to reflect the general health condition, and an increase in maximal force can be achieved following rehabilitation without adding upper limb training and thus the strength increase found in our study could not be only the result of the specific upper limb training.³⁸ However, the large improvements highlighted here might be explained either by the duration of the training programs and/or the specificity of the exercises performed on the hand flexors. Handgrip strength was also significantly increased in the fistula arm that was not exercised. Strength increase was proved in the contralateral limb after unilateral training of the opposite limb, and this phenomenon is called contralateral strength training effect.^{52,53} Adaptations of fistula arm were certainly lower than in the exercised, non-fistula arm, but unexpectedly reached an amplitude that was functionally significant. Cross-body transfer to the untrained limb usually reaches 52%-80% of the ipsilateral strength increase,^{52,54} patients showing the largest values. To explain the oversized contralateral effect in the CONT group, we analyzed the laterality of the patients. Most of them were right-handed, have the fistula on their nondominant arm, and trained their dominant side, allowing for maximal cross-body transfers.⁵⁵ Only three patients trained their nondominant arm and all were in the DISC group, certainly explaining the smaller strength gains transfers (data not shown).

Although the functional tests used in this study show good reliability and are validated for HD patients, it appears that they are less sensitive to change than direct measurements such as leg extension and handgrip strength.²⁵ Among pre-post-comparisons, SPPB and one-leg balance performance changes were lower than the MDC values previously determined. Despite training groups were randomly constituted with similar patients' profiles, HD population displays a high heterogeneity in physical performance, and sensitivity of functional tests is an issue to clearly establish the efficiency of an intervention. In this way, handgrip strength increase provides relevant information about the efficiency of intervention, as the detected change was largely above the MDC₉₀ determined for HD patients. The determination of minimal detectable change for leg extension strength in HD population might be useful in the future since the

method is reliable, accessible and easy to perform in clinical routine at the bedside of the patients.²⁷

Among the debatable points of this study, we can firstly mention the small number of HD patients included, despite that the inclusion and exclusion criteria were not strict. Nevertheless, high significant differences between the beginning and the end of the training protocol were found, providing strong data for clinical practice. Secondly, although pre-post-tests were separated by 16 weeks, we cannot exclude a learning effect that could have influenced performance changes.⁵⁶ Of note, the patients in this study had a relatively preserved physical function at the inclusion despite a high heterogeneity. Relatively young age (54.2 years) of the patients in this study could improve the efficacy of the protocol notably by a better adherence to the exercise program.³⁷ Concerning the impact of the age on the efficacy of training, several studies have reported that aged people take full advantage of exercise.^{57,58} In a study of Greenwood et al., authors reported an improvement of quality of life on a cohort of 355 HD patients with a median age of 59.3 years.⁵⁹ It is also documented that the benefit of strength training is greatest in frail elderly than elderly.⁶⁰⁻⁶² However, in a retrospective study conducted on older HD patients (>60 years), Imamura et al. found that intradialytic low-intensity resistance training did not improve physical activity and physical function.⁶³ It has been reported that combined exercise training is a valuable strategy for fitness improvement in adults aged over 50 years, but studies concerning participants with a mean age over 80 years are very rare.⁶⁴⁻⁶⁶ Thus, our results required to be extended not only to a larger cohort but also to older HD patients or displaying a more pronounced deconditioning. For the future, studies including biopsy or electromyography will also be required to investigate more precisely muscle structure and function in response to a combined exercise training.

Contrarily to our hypothesis, no interference phenomenon was detected as it was observed in healthy subjects.¹⁷⁻²³ The absence of interference in the present study is undoubtedly related to the intensity of exercises and to the amount of training loads. The interference phenomenon is probably only observable when subjects perform higher training loads. However, we provide here robust and clinically relevant data on efficiency of combined training on the whole spectrum of physical fitness in a relatively young HD population. Intradialytic exercise being efficient and safe, a larger access to physical rehabilitation programs is expected as exercise programs are not yet adopted into standard practice for patients undergoing HD.

5 | CONCLUSION

In summary, our study shows that the interference phenomenon does not seem to affect muscle adaptive response in this rehabilitation context. Combined training programs are associated with a high adherence from HD patients. Whatever the temporal repartition of endurance and resistance exercises, combined trainings improve strength, balance, and endurance of lower limbs of HD patients. Furthermore, practitioners may note that same-session combined training

seems to favor patients' adherence thanks to lower exercises duration and greater diversity. A better adherence can indirectly increase the workload that is clinically determinant for adaptations amplitude.

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CONFLICT OF INTEREST

None declared.

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