





Clinical Kidney Journal, 2021, vol. 14, no. 2, 688-695

doi: 10.1093/ckj/sfz194 Advance Access Publication Date: 5 February 2020 Original Article

ORIGINAL ARTICLE

# Upper limb isometric exercise protocolled programme and arteriovenous fistula maturation process

Irati Tapia González<sup>1,2,3</sup>, Vicent Esteve Simó<sup>1,2</sup>, Sara Ibañez Pallares<sup>1,4</sup>, Fátima Moreno Guzman<sup>2</sup>, Miquel Fulquet Nicolás<sup>2</sup>, Verónica Duarte Gallego<sup>2</sup>, Anna Saurina Solé<sup>2</sup>, Mónica Pou Potau<sup>2</sup>, Montserrat Yeste Campos<sup>4</sup> and Manel Ramírez de Arellano Serna<sup>2</sup>

<sup>1</sup>Funtional Unit Vascular Access, Nephrology Department, Consorci Sanitari Terrassa, Barcelona, Spain, <sup>2</sup>Nephrology Department, Consorci Sanitari Terrassa, Barcelona, Spain, <sup>3</sup>Department of Medicine, Universitat Autónoma de Barcelona, Barcelona, Spain and <sup>4</sup>Vascular Surgery Department, Consorci Sanitari Terrassa, Barcelona, Spain

Correspondence to: Irati Tapia González; E-mail: ITapiaG@cst.cat

### **ABSTRACT**

Introduction. Arteriovenous fistula (AVF) is the gold standard for vascular access (VA) for end-stage chronic kidney disease (CKD) patients. Post-operative exercises may help to improve maturation. Nevertheless, scarce scientific evidence has been reported about their utility to date. Our objective was to assess the effect of a post-operative isometric exercise programme on native VA maturation in patients with stage 5–5D CKD.

Methods. We performed a 24-month prospective study. After surgery, patients were randomized to the isometric exercise group (EG) or control group (CG). An isometric exercise protocolled programme was performed in the EG. The CG received usual care. Demographic data, muscle strength using a hand-grip (HG) dynamometer, main Doppler ultrasound (DUS) measurements, clinical and DUS maturation and VA complications were assessed at 4 and 8 weeks post-operatively.

Results. For 60 sixty patients (30 in the EG), demographic data and HG and DUS measurements at baseline were similar. A significant increase in HG was observed only in the EG at the end of the study ( $20.7 \pm 8.1$  versus  $25.1 \pm 10.3$  kg, P = 0.001). The EG obtained the highest clinical maturation at 4 (CG 33.3% versus EG 70%, P = 0.009) and 8 weeks (CG 33.3% versus EG 76.7%, P = 0.002). Similarly, DUS maturation was better in the EG at 4 (CG 40% versus EG 80%, P = 0.003) and 8 weeks (CG 43.3% versus EG 83.3%, P = 0.003) and remained so in the EG for both distal and proximal VA territories for all these periods.

**Conclusions.** The upper limb isometric exercise protocolled programme improved clinical and DUS maturation in our patients in both the distal and proximal VA territories. Further studies are required to support these results.

Keywords: chronic kidney disease, isometric exercise, maturation, vascular access

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (http://creativecommons.org/licenses/by-nc/4.0/), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited. For commercial re-use, please contact journals.permissions@oup.com

<sup>©</sup> The Author(s) 2020. Published by Oxford University Press on behalf of ERA-EDTA.

### INTRODUCTION

Autologous arteriovenous fistula (AVF) is the preferred choice for vascular access (VA) in patients with chronic kidney disease (CKD) undergoing a haemodialysis (HD) programme [1-5], due to its increased rate of permeability and reduced rates of complications and hospitalizations [6-11]. The maturation process for VA is one of the most important factors affecting the subsequent correct functioning of the VA given that an immature VA leads to more complications and, as a result, can reduce the likelihood of VA survival [12-14].

Both the current guidelines from the Spanish Nephrology Society relating to VA for haemodialysis [5] and the guidelines from the Kidney Disease Outcomes Quality Initiative recommend that patients carry out regular isometric exercises, in both the pre-intervention and post-intervention periods, as preventative measures with respect to the development of AVFs and the occurrence of complications [7, 15].

In recent years, some studies have suggested that isometric physical exercise of the arms can serve as a strategy to accelerate the maturation of AVFs [16-19]. However, the evidence available on the role of physical exercise in the post-operative period for improvement in the maturation or survival of autologous AVFs remains limited.

The aim of our study was to evaluate the effects of a fixed programme of isometric physical exercise on the maturation of autologous AVFs in patients with CKD stages 5-5D.

### **MATERIALS AND METHODS**

Between November 2015 and December 2017, a prospective, randomized, single-centre 24-month study was performed, approved by the ethics committee of our institution and in accordance with the standards of the Declaration of Helsinki, in order to evaluate the effects of an isometric exercise programme carried out in the post-operative period on the maturation of autologous AVFs in patients with CKD stages 5-5D.

The inclusion criteria established were obtaining informed consent, age >18 years, CKD stage 5 or 5D, candidate for autologous AVF for haemodialysis (HD) in upper limbs and preserved capacity for understanding. Patients excluded were those that had a prior autologous AVF in the same arm, were not candidates for autologous AVFs, had suffered a cardiovascular event in the last 3 months, had limited osteoarticular pathology and those that did not give written, informed consent.

# Data on demographics, biochemistry, nutrition and muscle strength

The demographic parameters included age, sex, renal aetiology, Charlson Comorbidity Index and traditional cardiovascular risk factors. Similarly, data on the main nutritional and biochemical parameters were collected.

Muscle strength of the AVF limb was evaluated at the start of the study and at 4 and 8 weeks post-intervention. An adapted mechanical hand-grip dynamometer was used to carry out these measurements. The muscle strength in the arm on which the intervention was carried out, estimated in kilograms, was measured using a pre-published protocol [20-22]. An average was calculated on the basis of three consecutive measurements with a rest interval of 15s between each, carried out by the same investigator in order to avoid any possible bias in measurement.

# Physical examination, ultrasound parameters and maturation criteria

All patients underwent a protocol-based physical examination and universal preoperative ultrasound mapping. The physical examination consisted of a visual assessment of both arms, the venous system was explored by means of venous palpation both with and without a tourniquet and the quality of arterial pulses was determined by means of digital palpation, including the Allen test.

Ultrasound examination was carried out by the Functional Unit Vascular Access team, following the same protocol and using the same ultrasound device: a Sonoline G40 ultrasound system (Siemens Medical Solutions, Mountain View, CA, USA). The ultrasound data analysed in both arms for each patient were the diameters (mm) of the radial artery (RA) and humeral artery (HA), the cephalic vein (CV) diameters in the lower and upper arm, the diameter and depth of the basilic vein (BV), as well as the permeability and continuity of all the vessels. Similarly, peak systolic velocities (PSVs; in cm/s) in the RA and HA, the resistance index (RI) of the RA following the reactive hyperaemia test and the flow through the HA were recorded.

In accordance with the current Clinical Guidelines for Vascular Access of the Spanish Nephrology Society, the nondominant arm was preferentially selected and a distal area chosen for creation of the AVF [5]. All AVFs were created by the same team from the Vascular Surgery section within our institution (with extensive experience in this field) following exhaustive clinical and ultrasound assessment and using similar AVF procedures. The ultrasound measurements considered to be suitable for a distal AVF were CV diameter in the lower arm >2 mm or >2.5 mm with tourniquet, RA diameter >1.5 mm, PSV >50 cm/s and a reactive hyperaemia test with an RI <0.7. Similarly, measurements considered suitable for a proximal AVF were HA diameter >2.5 mm, PSV >50 cm/s, CV diameter at the elbow  $>2.5\,\text{mm}$  and BV diameter  $>2.5\,\text{mm}$  [5]. All of the measurements (pre-operatively and at 4 and 8 weeks) were carried out at the same sites (HA 3 cm from the bifurcation of the artery and veins 3 cm proximal to the arteriovenous anastomosis). The AVF flow was estimated by means of flow in the HA as the method with the best correlation [23, 24]. Local anaesthesia was usually used, except for brachial basilic AVF with superficialization, which was performed under regional blockade. The AVF localization recorded was distal (radiocephalic) and proximal (brachiocephalic or brachiobasilic, with or without superficialization) or both with side-to-end anastomosis.

Clinical and ultrasound maturation were assessed at 4 and 8 weeks post-intervention. The criteria for clinical maturation were established as the presence of a palpable thrill, visible vein and a straight line >10 cm. The ultrasound maturation criteria were depth < 0.6 cm from the skin, outflow vein with a diameter >6 mm and HA flow rate >600 mL/min [5]. Any AVF complications were also recorded (stenosis, thrombosis, haematoma, pseudoaneurysm or VA steal syndrome).

# Allocation to groups and isometric physical exercise protocol

During the post-operative period, patients were randomized using a centralized information technology-based randomization tool and allocated to two study groups: the control group (CG) and the intervention group [exercise group (EG)].

The CG received the standard advice relating to AVF from the nephrology nursing staff. This advice consisted of carrying

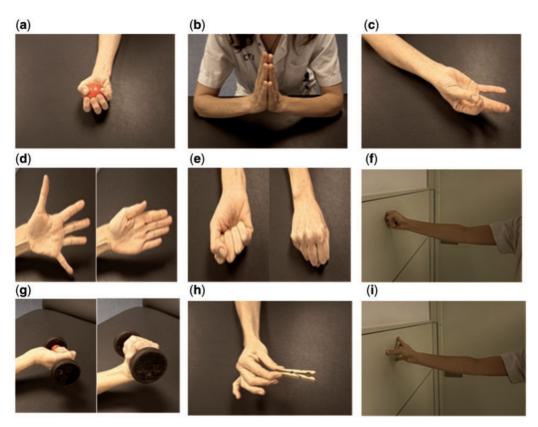


FIGURE 1: Isometric exercises of the distal region: (a) pressure with rubber ball, (b) interpalmar pressure, (c) pressure digital clamp, (d) adduction-abduction, (e) prone cuff supination, (f) pressure cuff, (g) flexoextension with a weight of 1 kg, (h) pressure clamp and (i) interdigital pressure.

out isometric exercises on an outpatient basis (repeated squeezing of a rubber ball and/or lifting weights of 1-2 kg) on the arm that had been subjected to the intervention, after a brief verbal explanation.

The EG carried out a protocol-based programme of physical isometric exercises in the post-operative period agreed upon with the Department of Rehabilitation: the exercises built up as they progressed and were specific for each region and each study period.

Similarly, the patients were provided with a monitoring sheet for the isometric physical exercises in which the type of exercise was set out along with a corresponding image. A table was provided for logging exercises, which was to be filled out when each exercise was completed, as well as a brief explanation for each exercise.

Distal region. During the first study period, five isometric exercises were carried out in the AVF arm for a period of 4 weeks. The exercises, which were to be carried out daily, consisted of squeezing a rubber ball, exerting pressure on the palms of the hand, squeezing with the fingertips, adduction-abduction and pronosupination of the fist.

In the second study period, the exercises scheduled in the first period were repeated with the addition of the following: pressure made with the fist, flexoextension with a weight of 1kg, squeezing fingertips together and squeezing fingers together across their lengths. A table of equivalences was given to patients to make the exercises more suitable to the patients' home environment (e.g. 1kg of rice or lentils). Sets and repetitions of each scheduled exercise were increased progressively every week (Figure 1).

Proximal region. During the first period, four types of isometric exercise were carried out, which consisted of a proximal fingertip squeeze, applying distal finger pressure, pronosupination of the fist with 1 kg and lifting a 1-kg weight. The exercises scheduled for the second period consisted of repeating the exercises from the first period and complementing them with the following exercises: applying finger pressure against a wall and stretching a band. The same number of series and repetitions were carried out as for the distal region (Figure 2).

The level of compliance and adherence to the exercise schedule was only analysed for the EG. Patients were assessed for compliance (yes or no) if they submitted the outpatient monitoring form during follow-up visits.

The level of adherence was quantified on the basis of the boxes filled out on the monitoring sheet, at both 4 and 8 weeks post-intervention. The following ranges were defined: low (1-7 boxes), low-moderate (8-14 boxes), moderate (15-21 boxes) and high (22-28 boxes).

Statistical analysis. Statistical analysis was carried out using the SPSS Statistics software, version 24.0 (IBM, Armonk, NY, USA). Quantitative variables were expressed as mean values and standard deviation (SD). Qualitative variables were expressed as percentages. At the end of the study, quantitative data of the same group were compared using the paired sample Student's t-test, with  $P \le 0.05$  considered statistically significant.

# **RESULTS**

During the study period, 81 VA procedures were carried out at our institution. Fourteen cases of vascular prostheses were

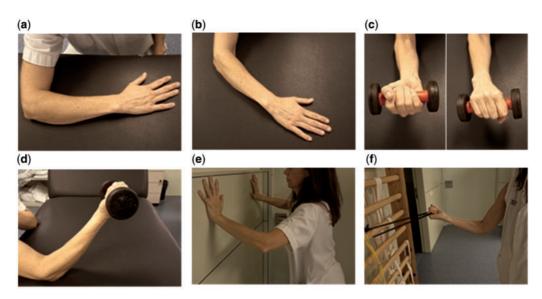


FIGURE 2: Isometric exercises of the proximal region: (a) proximal digital pressure, (b) digital distal pressure, (c) prone supination with 1 kg, (d) weight lifting with 1 kg, (e) digital pressure on wall and (f) stretch with elastic band.

Table 1. Sociodemographic parameters

Parameters	Global	EG $(n = 30)$	CG (n = 30)	P-value	
Age (years)	68.6 ± 13.0	67.3 ± 14.2	69.9 ± 11.9	0.199	
Sex (men), % (n)	71.3 (42)	66.7 (19)	73.3 (22)	0.500	
Charlson Comorbidity Index	$6.9 \pm 2.4$	$6.9 \pm 2.8$	$7.3 \pm 3.1$	0.124	
Hypertension, % (n)	91.7 (55)	86.7 (26)	96.7 (29)	0.177	
Diabetes mellitus, % (n)	46.7 (28)	46.7 (14)	46.7 (14)	0.602	
Dyslipidaemia, % (n)	65 (39)	66.7 (20)	63.3 (19)	0.500	
Smokers, % (n)	31.7 (19)	42.1 (8)	57.9 (11)	0.290	
Ischaemic heart disease, % (n)	26.7 (16)	16.7 (5)	36.7 (11)	0.072	
Handgrip (kg)	22.2	20.7	23.7	0.427	
Localization of arteriovenous fistula					
Distal, % (n)	60 (36)	53.3 (16)	66.7 (20)	0.443	
Left, % (n)	80 (48)	80 (24)	80 (24)	0.443	
Preoperative variables	` ,	, ,	, ,		
Lower arm CV diameter (mm)	$2.6 \pm 0.7$	$2.7 \pm 0.5$	$2.5 \pm 0.7$	0.218	
Upper arm CV diameter (mm)	$3.3 \pm 0.9$	$3.5 \pm 0.6$	$3.2 \pm 1.2$	0.119	
Upper arm BV diameter (mm)	$3.9 \pm 1.2$	$4.1 \pm 1.1$	$3.8 \pm 1.3$	0.259	
Bracial artery flow (mL/min)	$137.7 \pm 35.9$	$142.8 \pm 35.2$	$134.6 \pm 36.6$	0.870	

Results are expressed by mean  $\pm$  SD unless stated otherwise.

excluded. Four patients did not submit the informed consent form. Three patients dropped out during follow-up (one from the CG and two from the EG). Finally, 60 patients were analysed: 30 from the CG and 30 from the EG.

The main sociodemographic factors are shown in Table 1. The VA most frequently applied was the radiocephalic fistula (60%) with localization on the left side (80%). No significant differences were found between the two study groups.

Table 2 shows the biochemical data and nutritional and haematological parameters, with no differences observed in the data across the two groups.

The post-operative ultrasound measurements showed significant increases in the diameter of the outflow vein (EG  $3.3 \pm 0.8$  versus  $6.5 \pm 1.9$  mm, P = 0.013; CG  $2.9 \pm 0.6$  versus  $6.1\pm1.4\,mm,\,P\!=\!0.004)$  and in the HA flow (EG 142.8  $\pm$  35.2 versus  $1647.3 \pm 999.9 \,\text{mL/min}$ , P = 0.001; CG  $134.6 \pm 36.6 \,\text{versus}$  $1270.1 \pm 653.7$  mL/min, P = 0.001) in both groups at the end of the study (Table 3). No significant differences were found for the groups with respect to Doppler ultrasound variables at the end of the study. In relation to muscle strength, an increase was observed only in the EG at the end of the study (20.7  $\pm$  8.1 versus  $25.1 \pm 10.3$  kg, P = 0.001).

Table 4 shows the results relating to clinical and ultrasound maturation for both study periods. Clinical maturation was significantly greater in the EG, both at 4 weeks (CG 33.3% versus EG 70%, P = 0.009) and at 8 weeks (CG 33.3% versus EG 76.7%, P=0.002) post-intervention. Similarly, the ultrasound maturation was significantly greater in the EG both at 4 weeks (CG 40% versus EG 80%, P = 0.003) and at 8 weeks (CG 43.3% versus EG 83.3%, P = 0.003) post-intervention. These significant results from the EG continued to show significance subsequent to analysis for the different regions (distal and proximal) for all of the periods studied. Globally, inadequate vein diameters in 95.5%, flow volumes in 31.8% and depths in 28% of cases were

P < 0.05 indicates statistical significance.

Table 2. Biochemical parameters

Parameters	EG (n = 30)			CG (n = 30)		
	Baseline	End of study	P-value	Baseline	End of study	P-value
Main biochemical data						
Glucose (mg/dL)	$157.2 \pm 51.2$	$153.8 \pm 72.4$	0.845	152.2± 32.1	$154 \pm 33.1$	0.821
Creatinine (mg/dL)	$8.1 \pm 2.3$	$8.2 \pm 3.1$	0.924	$7.8 \pm 2.3$	$7.8 \pm 2.6$	0.985
K (mEq/L)	$5.3 \pm 0.7$	$5.6 \pm 0.8$	0.726	$5.3 \pm 0.9$	$5.2 \pm 1.1$	0.964
Ca (mg/dL)	$8.8 \pm 0.8$	$8.9 \pm 0.2$	0.931	$8.8 \pm 0.4$	$8.9 \pm 0.8$	0.863
P (mg/dL)	$4.4 \pm 1.2$	$4.3 \pm 1.2$	0.866	$4.5 \pm 1.4$	$4.5 \pm 1.3$	0.978
i-PTH (pg/mL)	$189.2 \pm 156.2$	$170.1 \pm 132.6$	0.872	$178.8 \pm 114$	$181.7 \pm 137.9$	0.972
Nutritional parameters						
Albumin (g/dL)	$3.8 \pm 0.3$	$3.9 \pm 0.3$	0.722	$3.8 \pm 0.3$	$3.9 \pm 0.4$	0.813
Pre-albumin (mg/dL)	$35.3 \pm 11.2$	$35.4 \pm 8.8$	0.789	$33.6 \pm 11.1$	$33.1 \pm 9.5$	0.850
Total cholesterol (mg/dL)	$140.1 \pm 54.2$	147.1± 57.1	0.346	$151.2 \pm 32.4$	$148.9 \pm 34.5$	0.721
HDL cholesterol (mg/dL)	$42.6 \pm 11.2$	$40.2 \pm 11.9$	0.597	$42.5 \pm 10.3$	$41.6 \pm 41.6$	0.623
Triglycerides (mg/dL)	$153.9 \pm 83.5$	$156.6 \pm 75.6$	0.724	$159.3 \pm 69.6$	$154.2 \pm 73.4$	0.497
LDL cholesterol (mg/dL)	$66.7 \pm 44.1$	$73.4 \pm 46.8$	0.432	$69.2 \pm 65.6$	$65.7 \pm 30.5$	0.526
Haemogram data						
Haemoglobin (g/dL)	$11.6 \pm 1.5$	$11.7 \pm 1.3$	0.793	$11.8\pm1.4$	$11.6\pm1.1$	0.726
Ferritin (ng/mL)	$434.5 \pm 271.1$	$412 \pm 269.4$	0.820	$396.8 \pm 157.1$	$425.2 \pm 213.4$	0.769

Results are expressed by mean  $\pm$  SD.

Table 3. Muscle strength and ultrasound data

Variables	EG (n = 30)			CG (n = 30)		
	Baseline	End of study	P-value	Baseline	End of study	P-value
Muscle strength data (kg)						
Handgrip	$20.7 \pm 8.1$	$25.1 \pm 10.3$	0.001*	$23.7 \pm 9.2$	$23.9 \pm 9.3$	0.703
Ultrasound data						
Outflow vein diameter (mm)	$3.3 \pm 0.8$	$6.5 \pm 1.9$	0.013*	$2.9 \pm 0.6$	$6.1\pm1.4$	0.004*
Braquial blood flow rate (mL/min)	$142.8 \pm 35.2$	$1647.3 \pm 999.9$	0.001*	$134.6 \pm 36.6$	$1270.1 \pm 653.7$	0.001*

Results are expressed by mean  $\pm$  SD.

Statistical significance is indicated by \*P < 0.05.

Table 4. Clinical and ultrasound maturation rates

Variables	4 weeks			8 weeks		
	EG $(n = 30)$	CG (n = 30)	P-value	EG $(n = 30)$	GG (n = 30)	P-value
Clinical maturation, % (n)	70 (21)	33.3 (10)	0.009*	76.7 (23)	33.3 (10)	0.002*
Ultrasound maturation, % (n)	80 (24)	40 (12)	0.003*	83.3 (25)	43.3 (13)	0.003*
Distal territory, % (n)	, ,	, ,		, ,	` '	
Clinical maturation	60 (12)	40 (8)	0.038*	58.3 (14)	41.7 (10)	0.020*
Ultrasound maturation	64.7 (11)	35.3 (6)	0.023*	63.2 (12)	36.8 (7)	0.019*
Proximal territory, % (n)						
Clinical maturation	64.3 (9)	20 (2)	0.040*	71.4 (10)	20 (2)	0.018*
Ultrasound maturation	85.7 (12)	40 (4)	0.028*	92.9 (13)	60 (6)	0.049*

Statistical significance is indicated by \*P < 0.05.

the main reasons why AVFs did not mature by the end of the study.

The levels of compliance of patients from the EG at 4 and 8 weeks were 70 and 66.7%, respectively. Adherence at 4 weeks was high in 90% of patients and low in 10%. Adherence at 8 weeks was high in only 65% of cases, moderate in 10%, lowmoderate in 5% and low in 20%.

With reference to AVF complications, we only observed an increased percentage of significant stenosis in the CG compared with the EG (24 versus 3%, P = 0.026) at the end of the study. There were no significant differences for the rest of the AVF complications over the course of the study (no aneurysm, one case of pseudoaneurysm in the EG, 27% with haematomas in the CG and 20% in the EG and 6% of

P < 0.05 indicates statistical significance.

K, potassium; Ca, calcium; P, phosphorus; i-PTH, intact parathyroid hormone; HDL, high-density lipoprotein; LDL, low density lipoprotein.

patients with distal hypoperfusion syndrome in the CG and 3% in the EG).

## DISCUSSION

The results obtained in our study demonstrate that the implementation of a protocol of post-operative isometric physical exercise achieved an improvement in the maturation of autologous AVFs for haemodialysis.

An explanation for these findings seems to be that subsequent to carrying out the AVF procedure, there is evidence of a significant increase in laminar blood flow that favours an increase in nitric oxide (NO) and prostacyclins, leading to vasodilation, inhibition of the proliferation and migration of smooth muscle cells and platelet aggregation [16, 25, 26]. Release of peroxynitrite (an important matrix metalloproteinase activator) in combination with the NO allows for a long-term structural adaptation to the modified blood flow and seems to play an important role in vascular remodelling [27, 28]. Exercise promotes vascular remodelling, as evidenced by an increase in capillarity within the active muscle and enlargement of the vessels, which increases the flow capacity to the muscle [26].

The vital importance of the process of AVF maturation is widely known. Adequate AVF maturation leads to its proper functioning, with fewer complications arising and increased AVF survival [29]. In spite of current clinical guidelines for VA for dialysis, isometric exercises were recommended as a strategy to promote maturation of the AVF: the evidence available to date on the role of physical exercise in the postoperative period for the improvement of maturation of autologous AVFs remains very limited.

To date, a few observational studies with several limitations have demonstrated the effects of carrying out different schedules of post-operative physical exercises, namely isometric exercises over short periods of time, on autologous AVFs. These exercises have brought about a number of morphological and haemodynamic changes, assessed by means of ultrasound of the AVF (increased thickness and diameter of the outflow vein and an increase in brachial artery flow), although their direct impacts on AVF maturation have not been evaluated [16, 18, 30-32].

After an exhaustive review of the literature, we found only two randomized controlled studies that have directly evaluated the effects of post-operative physical exercise on the maturation of AVFs [17, 19]. In a group of 50 patients, Salimi et al. [19] observed increased clinical (13 versus 5%) but not ultrasound (22 versus 17%) maturation of autologous AVFs 2 weeks after creation when carrying out isometric exercises exclusively during haemodialysis sessions. Similarly, Fontseré et al. [17] analysed clinical and ultrasound maturation of AVFs in 72 patients after carrying out a post-operative programme of isometric exercises, as compared with 1 month prior to the programme's creation, carried out on an outpatient basis. In this way, the authors were able to conclude that these isometric exercises had increased clinical maturation of AVFs at 1 month from creation and therefore this type of exercise programme should be considered for the maturation process, especially in the distal

In a general sense, our results are virtually identical to those obtained in previously published studies, both in terms of the morphological and haemodynamic changes, as well as in terms of the benefits of maturation of the AVF. However, there are some differences that should be highlighted. In relation to the study by Salimi et al. [19], we found large methodological

differences were evident, both in terms of the shorter study duration (only 2 weeks) as well as the type of exercise performed (exclusively during the HD sessions). We are of the opinion that these two differences alone may explain the greater rate of maturation obtained in our study.

Compared with the study by Fontseré et al. [17], with similar patient numbers, clinical and sociodemographic characteristics (both in the same geographic area) and methodology applied, the results are similar in terms of the rate of autologous AVF maturation in the EG. Unlike the study by Fontseré et al. [17], in our study both clinical and ultrasound maturation were also found to be significant at 4 weeks in the AVF created in the proximal region. It seems likely that the detailed isometric exercise programme used in our study (agreed upon with rehabilitations, with a greater number of repetitions and specific to each region and time period) could justify this difference. In addition, our study provides significant data on both clinical and ultrasound maturation at 8 weeks: the usual point in time when punctures are carried out on mature AVFs in clinical practice. Tracking data and data on completion of these types of physical exercise programmes were also collected, which have not previously been reported in the literature. In this regard, it should be pointed out that the exercise programme was completed correctly by a large number of patients and that adherence within the group of those completing the programme was high in most cases, therefore we found this to be safe since we did not observe any subjects dropping out during the study. We also see the programme to be effective, given the increase in muscle strength and how easy the exercises were to perform on an outpatient basis. One requirement was that of close monitoring in order to avoid patients dropping out.

Interestingly, we observed rates of both clinical and ultrasound maturation that were too low during our measurement controls in the study periods as compared with the literature after the creation of autologous AVFs [11, 33]. The greater average patient age, the lack of significant comorbidities such a ischaemic heart disease and smoking, the more distal location of AVFs performed at our centre in order to preserve vascular structures and the increased rate of stenosis observed in the CG all serve as predictors of poor AVF maturation and could be some of the factors that may be involved in these findings. Other possible factors include the limited information and advice regarding isometric exercises received by patients in the CG, limited to just a brief verbal explanation, and the presumed reduced compliance and adherence in a group without a detailed schedule and no subsequent follow-up (the degree of non-compliance in the EG was >30% at the end of the study). It may be that deleting these fistulas from the subsequent analysis, at the expense of being able to develop late maturation or perform an early intervention in cases of surgical complications (not included in the design of the study), could improve the survival rates in this group. In the same way, carrying out outpatient follow-up in the CG could also reveal some differences, although it would be difficult to carry out reliable patient monitoring in such a group after they had received a brief verbal explanation without a schedule for controlled exercises.

Regarding AVF complications, we did not find any episodes of thrombosis in our study. It is probable that our exhaustive preoperative physical and ultrasound examinations selected the optimal VA sites. Furthermore, the follow-up period could be shortened to detect any episode of thrombosis.

The main points of interest in our study are based on its randomized design, carried out without any source of funding, as well as the comprehensive methodology applied, with the creation of a schedule of approved isometric exercises that are safe and adapted to the location and maturation stage of the AVF created. The exercises are easy for patients to perform on an outpatient basis and offer the possibility of logging and monitoring of compliance in daily clinical practice.

With reference to the limitations of our study, the small sample size should be highlighted, both due to the small number of VA procedures carried out each year at our institution and the specific methodology used. The latter has made it difficult for other nearby hospitals to participate, which would have allowed a greater number of patients to be included.

# CONCLUSION

In conclusion, our study suggests that a post-operative programme of isometric exercises for AVF offers, at both 4 and 8 weeks, greater clinical and ultrasound maturation in the distal and proximal regions of the arms. Pending further studies in the future, we intend to maintain the current recommendations based on carrying out physical exercise during the maturation process with our patients.

## **ACKNOWLEDGEMENTS**

Thanks to Dr Lucía Martínez Carnovale for her valuable cooperation in this study. This study has been carried out within the framework of the PhD programme in medicine at the Universitat Autónoma de Barcelona.

## CONFLICT OF INTEREST STATEMENT

None declared.

# REFERENCES

- 1. Santoro D, Benedetto F, Mondello P et al. Vascular access for hemodialysis: current perspectives. Int J Nephrol Renovasc Dis 2014; 7: 281-294
- 2. Gibson KD, Gillen DL, Caps MT et al. Vascular access survival and incidence of revisions: a comparison of prosthetic grafts, simple autogenous fistulas, and venous transposition fistulas from the United States Renal Data System Dialysis Morbidity and Mortality Study. J Vasc Surg 2001; 34: 694–700
- Allon M, Robbin ML. Increasing arteriovenous fistulas in hemodialysis patients: problems and solutions. Kidney Int 2002; 62: 1109-1124
- 4. Rodríguez Hernández JA, González Parra E, Julián Gutiérrez JM et al. Vascular access guidelines for hemodialysis. Nefrologia 2005; 25(Suppl 1): 3-97
- 5. Ibeas J, Roca-Tey R, Vallespín J et al. Spanish clinical guidelines on vascular access for haemodialysis. Nefrologia 2017; 37(Suppl 1): 1–193
- 6. Kukita K, Ohira S, Amano I et al. 2011 update Japanese Society for Dialysis Therapy Guidelines of Vascular Access Construction and Repair for Chronic Hemodialysis. Ther Apher Dial 2015; 19(Suppl 1): 1-39
- 7. Vascular Access Work Group. Clinical practice guidelines for vascular access. Am J Kidney Dis 2006; 48(Suppl 1): S248-S273
- 8. Ng LJ, Chen F, Pisoni RL et al. Hospitalization risks related to vascular access type among incident US hemodialysis patients. Nephrol Dial Transplant 2011; 26: 3659-3666
- 9. Ethier J, Mendelssohn DC, Elder SJ et al. Vascular access use and outcomes: an international perspective from the

- Dialysis Outcomes and Practice Patterns Study. Nephrol Dial Transplant 2008; 23: 3219-3226
- 10. Kumbar L, Karim J, Besarab A. Surveillance and monitoring of dialysis access. Int J Nephrol 2012; 2012: 649735
- 11. Rooijens PP, Tordoir JH, Stijnen T et al. Radiocephalic wrist arteriovenous fistula for hemodialysis: meta-analysis indicates a high primary failure rate. Eur J Vasc Endovasc Surg 2004; 28: 583-589
- 12. Dhingra RK, Young EW, Hulbert-Shearon TE et al. Type of vascular access and mortality in U.S. hemodialysis patients. Kidney Int 2001; 60: 1443-1451
- 13. Burkhart HM, Cikrit DF. Arteriovenous fistulae for hemodialysis. Semin Vasc Surg 1997; 10: 162-165
- 14. Yap H-Y, Pang S-C, Tan C-S et al. Catheter-related complications and survival among incident hemodialysis patients in Singapore. J Vasc Access 2018; 19: 602-608
- 15. Hemodialysis Adequacy 2006 Work Group. Clinical practice guidelines for hemodialysis adequacy, update 2006. Am J Kidney Dis 2006; 48(Suppl 1): S2-S90
- 16. Oder TF, Teodorescu V, Uribarri J. Effect of exercise on the diameter of arteriovenous fistulae in hemodialysis patients. ASAIO J 2003; 49: 554-555
- 17. Fontseré N, Mestres G, Yugueros X et al. Effect of a postoperative exercise program on arteriovenous fistula maturation: a randomized controlled trial. Hemodial Int 2016; 20: 306-314
- 18. Leaf DA, MacRae H-H, Grant E et al. Isometric exercise increases the size of forearm veins in patients with chronic renal failure. Am J Med Sci 2003; 325: 115-119
- 19. Salimi F, Nassiri GM, Moradi M et al. Assessment of effects of upper extremity exercise with arm tourniquet on maturity of arteriovenous fistula in hemodialysis patients. J Vasc Access 2013; 14: 239-244
- 20. Haidar SG, Kumar D, Bassi RS et al. Average versus maximum grip strength: which is more consistent? J Hand Surg Br 2004; 29: 82-84
- 21. O'Driscoll SW, Horii E, Ness R et al. The relationship between wrist position, grasp size, and grip strength. J Hand Surg Am 1992; 17: 169-177
- 22. Mathiowetz V, Kashman N, Volland G et al. Grip and pinch strength: normative data for adults. Arch Phys Med Rehabil 1985; 66: 69-74
- 23. Wiese P, Nonnast-Daniel B. Colour Doppler ultrasound in dialysis access. Nephrol Dial Transplant 2004; 19: 1956-1963
- 24. Lomonte C, Casucci F, Antonelli M et al. Is there a place for duplex screening of the brachial artery in the maturation of arteriovenous fistulas? Semin Dial 2005; 18: 243-246
- 25. Pol MM. Hand exercise for arteriovenous fistula. Glob Surg 2018; 4: 1-3
- 26. Prior BM, Lloyd PG, Yang HT et al. Exercise-induced vascular remodeling. Exerc Sport Sci Rev 2003; 31: 26-33
- 27. Lehoux S, Castier Y, Tedgui A. Molecular mechanisms of the vascular responses to haemodynamic forces. J Intern Med 2006; 259: 381-392
- 28. Castier Y, Brandes RP, Leseche G et al. p47phox-dependent NADPH oxidase regulates flow-induced vascular remodeling. Circ Res 2005; 97: 533-540
- 29. Malovrh M. Non-matured arteriovenous fistulae for haemodialysis: diagnosis, endovascular and surgical treatment. Bosn J Basic Med Sci 2010; 10(Suppl 1): S13-S17
- 30. Turmel-Rodrigues LA, Bourquelot P, Pengloan J. Hemodialysis arteriovenous fistula maturity: US evaluation. Radiology 2003; 227: 906-907
- 31. Khavanin Zadeh M, Gholipour F, Naderpour Z et al. Relationship between vessel diameter and time to

- maturation of arteriovenous fistula for hemodialysis access. Int J Nephrol 2012; 2012: 942950
- 32. Kong S, Lee KS, Kim J et al. The effect of two different hand exercises on grip strength, forearm circumference, and vascular maturation in patients who underwent arteriovenous fistula surgery. Ann Rehabil Med 2014; 38: 648
- 33. Rooijens PP, Burgmans JP, Yo TI et al. Autogenous radialcephalic or prosthetic brachial-antecubital forearm loop AVF in patients with compromised vessels. A randomized, multicenter study of the patency of primary hemodialysis access. J Vasc Surg 2005; 42: 481-487