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EFFECT OF PREOPERATIVE ISOMETRIC EXERCISES ON CEPHALIC VEIN DIAMETER IN AV FISTULA PATIENTS

Plastic Surgery

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ABSTRACT

Purpose: Incidence rate of arteriovenous fistula (AVF) is not very high. AVF formation is often not attempted due to small cephalic vein (CV) diameter. We hypothesized that forearm CV diameter can increase by isometric handgrip exercises and gave better results for AVF formation in AVF patients.

Methods: All patients with (eGFR<25mL/min/1.73m2; CV<2.5mm) and without prior vascular access were selected. They did regular handgrip exercises in the preferred excercised arm (EA), with the nonexercised arm (NEA) as control. CV diameter was measured at baseline, by ultrasound at four and eight weeks. The primary endpoint was the mean increase in CV diameter. Secondary endpoints were mean CV diameter increase from baseline, increased proportion of potential AVF sites and successful AVF placement.

Results: A total of 60 patients were selected and 51 finished the study. Mean CV diameter increased in both the EA and NEA by 0.46-0.75 and 0.45-0.60 mm, respectively. Compared to baseline, all CV diameters increased significantly (P<.05) after four weeks. In the EA, mean distal and proximal CV increased from 1.68 to 2.43 mm and from 2.27 to 2.87 mm, respectively. The changes noted in the NEA were not significant. There were also significant increases in the number of sites and patients eligible for AVF formation. 16 patients had successful AVF placement.

Conclusions: Isometric handgrip exercises resulted in significant CV diameter increases after eight weeks, in the EA group and potentially allows for AVF formation in those not previously deemed patients.

KEYWORDS

Arteriovenous fistula, Chronic kidney disease, End stage renal disease, Hemodialysis, Isometric exercise, Vascular access, Vein mapping

INTRODUCTION

End-stage renal disease (ESRD) management is one of the costly treatment associated with high patient morbidity. The cost of arteriovenous grafts (AVG) and central venous catheters (CVC) are higher than arteriovenous fistulas (AVF) (1), and AVF have been associated with improved patient outcomes (2-4). Few patients are not good candidates for AVF formation. For example, the prevalence of AVF is lower in women, obese, geriatric patients and patient with peripheral vascular disease (8).Some of the women and the obese patients have smaller and insufficient vein diameter is the most common vascular barrier for AVF formation (7). Measurement of vessel diameter with pre-operative duplex ultrasound has been found to associate with peri-operative findings and maximizes the number of AVFs formation and their success. (9-10). Vein diameters < 2.5 mm on vein mapping have been associated with primary AVF failure (11), and most surgeons will choose AVG placement in this scenario. We hypothesized that small vein diameter may be a modifiable risk factor for primary AVF failure. Prior studies suggest that an increase in vein diameter is possible with an exercise (12,13,15). The actual mechanism is not known, but is supposed to involve increased arterial flow, endothelium dependent vasodilatation and flow-induced adaptation (12).

The aim of this study was to look for effect of exercise intervention on diameter of veins and placement of AVF in patients who were not AVF patients because of small vein diameter.

MATERIALS AND METHODS

Study design and population

We conducted a prospective study to assess the effects of isometric handgrip exercises on cephalic vein diameters < 2.5 mm. Patients were selected from civil hospital ahmedabad, civil hospital surat and M K Shah Medical college & Research Center, Ahmadabad. Both men and women of age 18 and older were selected if they had a diagnosis of CKD Stage IV or V (eGFR < 20 or < 25 L/min/1.73m2 with diabetes) and had a distal forearm cephalic vein < 2.5 mm in diameter in one or both arms. Vein mapping was done as a pre dialysis routine. Exclusion criteria included prior vascular access surgery, positive Allen test or clinically poor arterial flow or severe calcifications. Other exclusion criteria included ESRD, physical or mental disability limiting access placement or ability to perform exercises and medical contraindi cations for vascular access surgery. Written and informed consent was taken from all patients.

Exercise regimen

Patients were asked to perform isometric forearm strengthening exercises in their preferred access arm. The non-exercised arm served as a control. During the first visit, patients were provided with a squeeze ball. Patients were asked to perform 10 sets of 20 isometric handgrip exercises daily in the study arm for a total of 8 weeks. Each set consisted of 20 contractions per minute with each contraction held for approximately three seconds for a total of 5 minutes per set. Patients were instructed to perform each set with at least 5 minutes rest in between sets. This regimen was chosen in an effort to maximize adherence because of its simplicity. Isometric handgrip exercises were performed and patients were asked to record the number of exercises performed daily on an exercise log.

Study procedures

Follow up of patients was at 0, 4 and 8 weeks. Telephonic verification of patients' exercise were taken at two and six weeks. Patients were asked to demonstrate the handgrip exercises at every visit and submit the self-reported exercise log. They also submitted a blood pressure log and reported any adverse effects. Venous diameter measurements were obtained at redetermined anatomic locations in both arms based on 1.0 cm below the antecubital fossa (proximal) and 1.0 cm above the ulnar process (distal). The cephalic vein within each forearm was examined and measured by Doppler applying tourniquet at the upper arm. Anterior/posterior and transverse measurements of bilateral cephalic veins obtained at each arm. The radiologist was blinded to the intervention arm and to the study week number in order to avoid bias. We measured subject adherence objectively by the self-reported exercise logs.

Outcomes

Our null hypothesis is that isometric hand exercises have no effect on vein diameter in patients with CKD. The primary endpoint was the mean change in venous diameter between the control (non-exercised) arm and the study (exercised) arm at 0 and 4 weeks, and 0 and 8 weeks. Secondary endpoints were the proportion of patients that achieved at least one cephalic venous diameter > 2.5 mm, the proportion of potential forearm access sites with at least one cephalic venous diameter > 2.5 mm, and the proportion of patients that had a successful AVF placement.

Statistical analysis

Mean change in venous diameter between the exercised and non-exercised arm at 0 and 4 weeks, and 0 and 8 weeks was the primary endpoint. The Student's *t* test was used to compare mean changes in vein diameter from baseline of both the groups at weeks 4 and 8. Secondary endpoints were mean change in vein diameter from baseline (paired *t* test), and a comparison of proportions of patients and access sites for AVF with vein diameter ≥ 2.5 mm at 4 and 8 weeks ($\chi 2$ or mid-p exact test). The proportion of patients with successful AVF placement, and a comparison of high risk subgroups (male sex, age < 70, tobacco use, and diabetes mellitus, body mass index < 30, GFR ≥20), were evaluated in this study.

RESULTS

Sixty patients were enrolled in the study. Five patients were excluded because their all forearm veins were > 2.5 mm in diameter. Four patients dropped out after selection and did not finish the exercise regimen. Baseline characteristics of the 51 patients who finished the study are listed in Table I. There were 19 female and 32 male. The mean age was 52.7 years old with a mean eGFR of 21 mL/min/1.73m^2. 30 patients who had a history of tobacco abuse, 15 with a history of DM and 10 patients who were obese. The non exercised arm was typically the dominant arm, which would account for the larger baseline venous diameter (Tab. I).

Table I - Baseline Demographic And Clinical Information On 51 Patients Who Completed The Study

Baseline variable	N(%) or Mean ± SE
Age (years)	52.7 ± 4.3
Male sex	32 (62.7%)
MDRD eGFR (mL/min/1.73m^2)	21.5 ± 1.3
Body Mass Index > 30	10 (19.6%)
Diabetes Mellitus	15 (29.0%)
Tobacco Use	30 (58.82)
Meds (Aspirin)	36 (70.58%)
Meds (Clopidogrel)	3 (5.88%)
Diameter (mm) of distal (forearm) cephalic vein (NEA)	1.53 ± 0.18
Diameter (mm) of distal (forearm) cephalic distal vein (EA)	1.68 ± 0.16
Diameter (mm) of proximal (forearm) cephalic vein (NEA)	2.21 ± 0.24
Diameter (mm) of proximal (forearm) cephalic vein (EA)	2.27 ± 0.22

EA = exercised arm; NEA = non-exercised arm; SE = standard error of the mean.

Regarding subject adherence, 55 patients submitted exercise logs, and 51 patients submitted logs for the entire eight week period.

For the primary outcome, there was statistically significant difference in the change in venous diameter in exercised arm at eight week (Tab. II). There were positive venous diameter increases (range 0.45 to 0.75 mm) in the exercised arm. For evaluation of subgroup outcomes, we assessed the impact of certain demographic variables (male sex, age < 70, tobacco use, and diabetes mellitus, body mass index < 30, GFR ≥20) on the primary outcome, but found no significant interactions.

Table II - Comparison Of Mean Change In Cephalic Forearm Vein Diameter Between Exercised And Control Arms

Variable	Exercised Arm	Control Arm	p
	Mean Change ± SE	Mean Change ± SE	
Distal Cephalic Vein 0 weeks to 4 weeks (mm)	0.46 ± 0.16	0.35 ± 0.20	0.259
Distal Cephalic Vein 0 weeks to 8 weeks (mm)	0.75 ± 0.20	0.40 ± 0.15	0.003
Proximal Cephalic Vein 0 weeks to 4 weeks (mm)	0.45 ± 0.25	0.31 ± 0.20	0.226
Proximal Cephalic Vein 0 weeks to 8 weeks (mm)	0.60 ± 0.32	0.36 ± 0.20	0.004
SE = standard error of the mean.			

When compared to baseline, there was a significant increase in cephalic vein diameter from 1.68 ± 0.16 mm to 2.43 ± 0.19 mm at eighth weeks for the exercised arm (Tab. III). To assess subgroup outcomes, we assessed the impact of certain demographic variables (male sex, age < 70, tobacco use, and diabetes mellitus, body mass index < 30, GFR ≥20) on this secondary outcome. Among male, there was a statistically significant increase in distal venous diameter at fourth weeks also (P=.006) and a trend towards increase in proximal venous diameter at eight weeks (P=.059). No interactions were noted for the other subgroups.

Table III - Changes In Forearm Cephalic Venous Diameter (mm, By Duplex Ultrasound) At Four And Eight Weeks Compared To Baseline

Vein diameter (mm)	N	Pre Mean ± SE	Post Mean ± SE	P
Exercised Arm (EA)				
Distal; 0 to 4 weeks	51	1.68 ± 0.16	2.14 ± 0.15	.012
Distal; 0 to 8 weeks	51	1.68 ± 0.16	2.43 ± 0.19	.004
Proximal; 0 to 4 weeks	51	2.27 ± 0.22	2.72 ± 0.26	.021
Proximal; 0 to 8 weeks	51	2.27 ± 0.22	2.87 ± 0.31	.009
Non-exercised Arm (NEA)				
Distal; 0 to 4 weeks	51	1.53 ± 0.18	1.88 ± 0.22	.018
Distal; 0 to 8 weeks	51	1.53 ± 0.18	1.93 ± 0.22	.029
Proximal; 0 to 4 weeks	51	2.21 ± 0.24	2.52 ± 0.23	.014
Proximal; 0 to 8 weeks	51	2.21 ± 0.24	2.57 ± 0.25	.028

EA = exercised arm; NEA = non-exercised arm; SE = standard error of the mean.

Table IV shows how the number of potential AVF access sites and the number of patients with potential AVF access sites changed over the course of the study. At baseline, there were 32 sites with vein diameter ≥2.5 mm, and this sites increased to 59 (p=.047) and 72 (*P*<.001), after four and eight weeks of exercise, respectively. Among patients, there were 10 and 13 exercised and non exercised arms that may have been eligible for an AVF based on at least one potential access site with vein diameter of 2.5 mm. After four weeks of exercise, the number increased to 25 (*P*=.187) and 18 (*P*=.980) study and control arms, respectively. After eighth weeks of exercise, the number increased to 30 (*P*=.039) and 20 (*P*=.074) study and control arms, respectively.

Table IV - Numbers Of Access Sites And Patients With Vein Diameter ≥ 2.5 Mm After Four And Eight Weeks Of Exercise

	Baseline	Week 4	P	Week 8	P
Study					
# sites ≥ 2.5mm	14/102	31/104	.079	40/104	.003
# patients ≥ 2.5mm	10/51	25/51	.187	30/51	.039
Control					
# sites ≥ 2.5mm	18/102	28/102	.304	32/102	.025
# patients ≥ 2.5mm	13/51	18/51	.980	20/51	.074
Total					
# sites ≥ 2.5mm	32/102	59/102	.047	72/102	<.00
# patients ≥ 2.5mm	23/51	43/51	.261	50/51	.004

Legend: Comparisons are between 0 and 4 weeks and 0 and 8 weeks. Total number of patients = 51. Each arm for each subject had two potential venous sites: distal and proximal forearm cephalic vein. Thus the number of potential sites in either the EA or NEA is two times the number of patients, and the total number of potential sites is four times the total number of patients.

A total of 25 patients have had a dialysis access placed with an AVF. Of the 25 AVF that were placed, 16 AVFs are currently being used successfully for dialysis. The remainder of the patients are still pre dialysis, and none of the patients have required additional interventions to maintain patency.

DISCUSSION

We disproved our null hypothesis because the difference in vein diameter change was significantly greater in the exercised arm. There were 32 male (62.7%) and the mean age of patients was 52.7 years. 30 patients who had a history of tobacco abuse, 15 with a history of DM and 10 patients who were obese.

When compared with baseline, there were significant increases noted in vein diameter after eight weeks of exercise in distal forearm cephalic veins for the exercised arms. The mean change in cephalic vein diameter at 8 week in distal and proximal forearm was statistically significant.

While not all of the means in our study crossed the 2.5 mm threshold, the increases were significant. These results validate the findings of prior studies performed in slightly different patient populations. These studies showed the following significant increases in cephalic vein diameters after similar exercise regimens (2.8 mm mean increase after six weeks [12]; 0.21 mm mean increase after eight weeks [13]; 0.6 mm median increase (0.4 - 1.2 interquartile range) after four weeks [15]). Uy et al study demonstrated positive increase in cephalic vein diameter in both exercised and control group. [16]

There was a significant increase in the number of patients and vein sites potentially eligible for AVF formation over time (Tab. IV), and several of the patients eventually had an AVF placed. At the time of document preparation, there are 25 patients who have had an AVF placed and 16 of these are using the AVF successfully for dialysis.

Limitations

Our s patients had DM, which may not be representative of the general CKD/ESRD population. Regarding exercise adherence, there was variability with respect to subject completion of the self-reported logs.

Our study did not assess changes in arterial diameter, arterial flow, resistive indices, or central vein patency, which are also important components of assessing a potential AVF candidate. Sonography is highly operator dependent and patients were assessed by different radiologist due to multi institutional study so examiner assessment variability. Inter-assessment variability between vein measurements is possible as are vein diameter changes related to temperature or volume status.

Based on vascular duplex imaging and comorbidities, some patients are deemed AVG patients and await access placement until closer to commencing dialysis. Female sex, older age, obesity and diabetes are known associations for poor AVF suitability and outcomes. For these patients, we would propose a trial of isometric forearm exercises in an attempt to increase vein diameter, which could alter their candidacy for AVF. In our study four weeks of isometric handgrip exercises results in a significant increase in vein diameter in patients with advanced CKD and several of the patients underwent successful AVF placement. This intervention is simple, inexpensive, and may facilitate AVF placement in patients previously deemed poor patients for AVF.

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