Isometric Exercise Increases the Size of Forearm Veins in Patients with Chronic Renal Failure

DAVID A. LEAF, MD, MPH; HOLDEN S-H. MACRAE, PHD; EDWARD GRANT, MD; JEFFREY KRAUT, MD

ABSTRACT: *Objectives:* Delay in maturation or failure of maturation of Cimino-Brescia fistulae contributes to the significant vascular access-related morbidity of chronic hemodialysis patients. Increased size and capacitance of native veins before the formation of vascular access has been considered an important variable in the success rate of native fistulae. We evaluated whether a formal exercise program might alter the size of native veins. *Methods:* The effect of exercise on venous size was evaluated in 5 patients with severe chronic renal failure [glomerular filtration rate, 30.6 ± 5.3 mL/min (mean ± SD)]. Five male patients with a mean age of 57 ± 9 years underwent a 6-week forearm exercise training program, involving nondominant arms, that included isometric hand-grip contractions to 25 to 35% of MVC lasting 40 to 120 seconds and repetitive squeezing of squash and racquet balls. Both the volume and intensity of exercise training was increased weekly based on strength measured by hand-grip dynamometer and on the patients' indicated level of comfort. Cephalic vessel size in both the nondominant (trained) and dominant (control) arms, with and without a tourniquet, were obtained using Doppler ultrasound before and after the 6-week exercise training program. *Results:* The size of the cephalic vein of the exercised arm increased significantly ($P < 0.05$) compared with the control arm when measured in both the absence (048 ± 0.016 versus 0.024 ± 0.023 cm^2) and the presence of a tourniquet (0.056 ± 0.022 versus 028 ± 0.027 cm^2). *Conclusions:* These findings indicate that a simple, incremental resistance, exercise-training program can cause a significant increase in the size of the cephalic vein commonly used in the creation of an arteriovenous fistula. The increase in size and resultant probable increase in blood flow might accelerate the maturation of native arteriovenous fistulae, thereby lessening the morbidity associated with vascular access. **KEY INDEXING TERMS:** Physical exercise; Cimino-Brescia fistula; Hemodialysis; Veins; Renal failure. **[Am J Med Sci 2003;325(3):115–119.]**

Infection, clotting, and failure of vascular access accounts for a large portion of the morbidity experienced by chronic hemodialysis patients.[1] These complications of vascular access are largely confined to artificial arteriovenous grafts,[2–6] which make up more than 65% of the vascular access used in the United States. The artificial arteriovenous graft has become the most frequently created graft for vascular access because the nature of the arterial supply required for successful formation is much less than that necessary for formation of the native Brescia-Cimino fistula, in which the brachial artery is usually joined to the cephalic vein.[7] Moreover, the time required for maturation of the vascular access is substantially less for the artificial graft than for the Brescia-Cimino fistula.

Forearm exercise, such as squeezing of a tennis ball, has commonly been used to accelerate the maturation of the Brescia-Cimino fistula after the access is constructed. Indeed, failure to consistently exercise is often the cause of delayed maturation of the graft. Although low blood flow through the access before construction of the vascular access has been considered an important factor in the successful construction of the graft,[8–10] the effect of physical exercise training has not been evaluated.

Studies by Lind and McNicol[11] have demonstrated transient increases in blood flow with acute exercise. Those investigators measured total forearm blood flow at 5, 10, 15, 20, and 30% of maximum voluntary contraction (MVC) during isometric contractions using a hand-grip protocol. They demonstrated that

From the Divisions of General Medicine (DAL), Nephrology (JK), and Radiology (EG), Greater Los Angeles VA Healthcare System and UCLA School of Medicine, Los Angeles, California; and Department of Sports Medicine (HS-HM), Pepperdine University, Malibu, California.

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Correspondence: David A. Leaf, M.D., M.D.H., 111G, Division of General Medicine, Greater Los Angeles V.A. Healthcare System, 11301 Wilshire Boulevard, Los Angeles, CA 90073 (E-mail: david.leaf@med.va.gov).

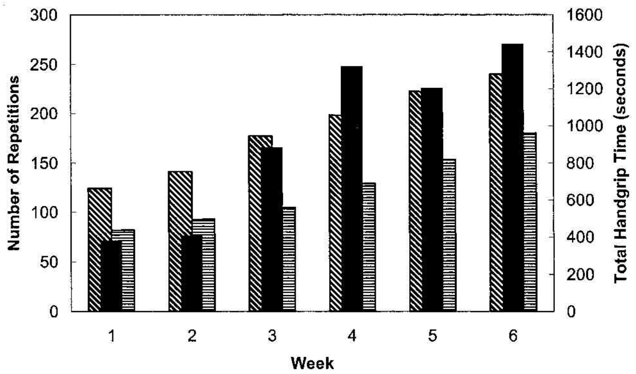

Figure 1. Rate of progression of hand-grip/forearm exercise training for all subjects. Data shown are for the 4 weekly training sessions, which included at least 2 sets of each activity (▧, squashball; ▤, racquetball; ■, hand-grip).

forearm blood flows reached peak values at approximately 20 to 30% of MVC and approached 2400 mL/min at 30% MVC, 2000 mL/min at 20% MVC, and 1500 mL/min at 15% MVC. The isometric contractions in that study were maintained for 5 minutes. A postcontraction reactive hyperemia developed at contraction cessation in which blood flows were elevated above precontraction values for 8 minutes (at 20 and 30% MVC). Thus, acute increases in blood flow at relatively low muscle force were observed during isometric muscle actions. The present study was designed to determine whether persistent and significant alterations in venous capacitance could be produced using a modification of Lind and McNicol's exercise program in which the regimen was tailored specifically for each subject.

Subjects

Patients were selected from the Renal Clinic of the Greater Los Angeles Health Care System. Only patients with a serum creatinine greater than 1.5 mg/dL were considered for inclusion in the study. The protocol was approved by the Institutional Review Board of the Greater Los Angeles Veterans Administration Healthcare System and informed consent was obtained from each participant in accordance with the Helsinki Declaration.

Procedures

Exercise Program. Patients underwent a structured program combining exercise with controlled heating of the nondominant forearm 4 times per week for a total of 6 weeks as depicted in Figure 1. The untrained (dominant) forearm served as a control.

Forearm Heating. A wrap-around heat pad (Kaz Incorporated, Hudson, New Jersey) was used to raise the temperature of the nondominant forearm beginning 10 minutes before exercise and continuing until 10 minutes after exercise was discontinued.[12,13]

Forearm Exercise. The 6-week exercise-training program included isometric hand-grip contractions at 30 to 40% of MVC lasting 80 to 360 seconds and repetitive squeezing of a squash ball and a racquet ball. The volume and intensity of exercise was increased and adjusted weekly based on measurements of hand-grip strength using a dynamometer (Jamar, Clinton, NJ) according to the subject's level of comfort. The rate of adaptation to the training regimen was adjusted by altering the volume (frequency and duration of contraction) and intensity (force production) of training. The exercise program was administered both on site and at home. Briefly, subjects met once per week with an exercise physiologist for hand-grip strength assessment and to undergo the first training session of the week. The remaining 3 exercise sessions were performed at home. For these sessions, the patients followed a detailed program, delineated in written instructions, that was also explained to them by the exercise physiologist. All subjects were contacted by telephone on the remaining training days to confirm that the training had occurred as planned.

On-Site Training Sessions. Subjects conditioned their forearm musculature by squeezing a squash ball and racquetball, and by performing sustained hand-grip contractions with a hand-grip dynamometer. All 3 activities were divided into 2 to 3 sets of each activity, and repetitions of each activity were progressively increased on a weekly basis and adjusted based on each subject's adaptation. The training program and rate of progression of exercise is shown in Figure 1. Squash ball conditioning progressed from 20 to 60 repetitions over the 6-week program at a volume increment of ~11% per week. Racquet ball conditioning progressed from 10 to 45 repetitions, or a volume increment of ~13% per week over the 6-week program. Isometric hand-grip exercise was conducted at 30 to 40% of MVC and was sustained for 80 to 360 seconds per training session over the 6-week program (an increase in time of ~12% per week). Squeezing of the squash and racquet balls was performed slowly, and rest intervals of ~60 to 90 seconds were permitted between each activity and between each set.

Home-Based Training Sessions. Each subject was given a Kaz heating pad, a dynamometer, and detailed written instructions on how to perform the exercise. Patients were encouraged to exercise on the days prescribed (3 at home) and were contacted by the exercise physiologist to determine whether training had occurred as prescribed.

Measurement of Hand Grip Strength. Hand-grip testing was performed on both the dominant and nondominant hand at the beginning of each week (ie, before conducting the first training session). The subjects were given 2 practice trials (one per hand) to familiarize them with the task before the first assessment of hand-grip strength.[14] Subjects performed the hand-grip test in the seated position after the dynamometer had been adjusted to fit the hand being tested. The arm was flexed to 90° at the elbow and held away from the body, and the subjects were encouraged to squeeze the hand-grip of the dynamometer as hard as possible for 2 to 3 seconds. Two trials were performed on each hand (left, then right, and then repeated once more), and the mean score was used to adjust the hand-grip training for that week.

Measurement of Venous Capacitance. Gray-scale images of the cephalic veins for nondominant (exercised) and dominant (control) arms were obtained using a near-field focused, 7-to-12 MHz transducer (Phillips, Bothell, WA). Minimal transducer pressure was applied to minimize distortion of the veins. Cross-sectional area measurements were obtained using available software. Two measurements were obtained for each vein, and the results were averaged. Images were obtained in the area of the distal cephalic vein, at the level of the wrist. Measurements were made with and without application of a tourniquet.All data are presented as mean ± SD. Significant differences were determined using two-way analysis of variance (significance, $P < 0.05$) between measurements of nondominant (exercised) and dominant (control) arms with and without the tourniquet and between tourniquet and nontourniquet measurements in the nondominant forearm measurements before and after exercise training.

Results

Clinical characteristics of the 5 patients are shown in Table 1. All patients were male, reflecting the predominant male population of the Veterans

Table 1. Clinical Characteristics of the Patients at the Time of Entry (n = 5)

Subject	Age (years)	Weight (kg)	Creatinine	Hematocrit	Renal Failure Diagnosis	Medications
1	54	76.8	2.5	0.354	Renal cell cancer	Felodipine Metolazone
2	45	86.4	5.6	0.261	Diabetes mellitus	Insulin Metolazone Diltiazem Metoprolol
3	59	77.3	2.0	0.380	Diabetes mellitus	Insulin Furosemide Fosinopril Isosorbide Simvastatin
4	71	75.0	4.1	0.299	Hypertension	Fosinopril Diltiazem Clonidine Furosemide Metoprolol
5	56	84.6	4.9	0.391	Diabetes mellitus	Glipizide Atenolol Felodipine Simvastatin
Mean ± S.D.	57 ± 9	80.0 ± 5.1	3.8 ± 1.5	0.337 ± 0.53		

Administration. The mean age was 57 ± 9 years. Diabetes mellitus was the underlying cause of the renal disease in 3 patients and hypertension and renal cell cancer in the remaining 2 patients. By physical examination, all patients had no evidence of significant vascular disease. In all patients, the right hand was the dominant hand. Serum creatinine concentration averaged 3.8 ± 1.5 mg/dL and glomerular filtration rate averaged 33.7 ± 5.3 mL/min, indicating the patients had moderate to severe renal failure.

All patients who entered the study completed the 6-week exercise program. The exercise physiologist responsible for each subject confirmed by telephone call, on each day's training session, that the subject had completed the prescribed training.

Table 2 shows the changes in the size of the cephalic veins at the end of the 6 week period in both the exercised and non exercised arm with without application of a tourniquet. As can be seen, vessel size rose 2-fold in the exercised arm by 6 weeks of training both with and without application of a tourniquet (0.056 ± 0.022 versus 0.028 ± 0.027 cm^2) and (048 ± 0.016 versus 0.024 ± 0.023 cm^2), respectively. Two-way analysis of variance comparing these changes with the dominant (control) forearm showed significant ($P < 0.05$) increases in the exercised forearm after exercise training both with and without tourniquet application. No significant differences were noted between tourniquet and nontourniquet measurements in the nondominant forearm measurements before and after exercise training. Figure 2 shows individual changes in cephalic blood vessel size before and after completion of the program. After the program, blood vessel size is increased in a virtually uniform manner, except in subject 1, whose cephalic vein increased by 38% with tourniquet application but not without the tourniquet. It is notable that this subject's underlying medical condition differs from that of the other subjects (ie, renal cell cancer), and his entry cephalic

Table 2. Changes in Cephalic Vein Size after a 6-Week Left-Forearm Exercise Training Program in 5 Predialysis Patients

	Pre-training (mean ± SD)	Post-training (mean ± SD)
Cephalic vein size no tourniquet (cm^2)		
Left	0.024 ± 0.023	0.048 ± 0.016*
Right	0.013 ± .005	0.018 ± 0.011
Cephalic vein size with tourniquet (cm^2)		
Left	0.028 ± 0.027	0.056 ± 0.022*
Right	0.017 ± 0.005	0.025 ± 0.010

** Significant (P < 0.05) pre- to post-training effect by 2-way analysis of variance comparing left (exercised) with right (control) forearm both with and without tourniquet application.*

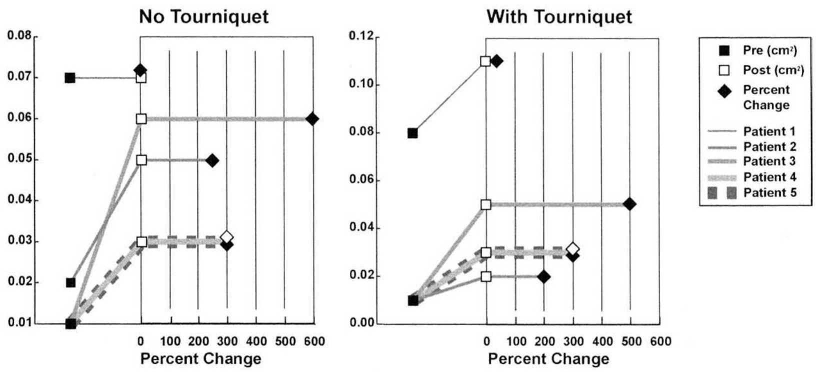

Figure 2. Changes in size of cephalic veins in individual subjects after a 6-week exercise program. The change in vein size varied among all subjects.

blood vessel size was more than 3 times larger than any other subjects.

Conclusions

In the present study, 5 patients with severe renal failure underwent a structured exercise program of 6 weeks' duration. Venous size of the cephalic vein, as estimated by Doppler ultrasound, increased substantially at the end of the exercise period. These data indicate that exercise can lead to a marked sustained increase in venous size. The increase in cephalic vein size could improve the results of vascular access surgery, but this remains to be determined.

Two subjects in this investigation had to reduce the time of performing isometric hand-grip exercise during 1 week of training but were able to perform the prescribed training for the remainder of the program. The data in Figure 1 illustrate the typical training progression for all 5 subjects. The results of the present study demonstrate that a structured forearm exercise program of 6 weeks' duration can produce a significant and sustained increase in the size of the cephalic veins in patients with chronic renal failure. Indeed, on average, the size of the cephalic vein rose 2-fold by completion of the study. Paradoxically, the increase in venous size was unaccompanied by an increase in hand-grip strength. Although unanticipated, the failure to observe any increase in strength could have been related to the type of exercise program because subjects exercised at submaximal levels of work intensity (30 to 40% MVC) and performed low-intensity squeezing of squash and racquetballs, and because the program was of short duration. On the other hand, as shown in Figure 1, the exercise program resulted in continuous improvement in muscular endurance, and circulatory changes are a more direct outcome of increased muscular endurance than strength. Regardless, the primary outcome of this study was not to increase grip strength but to establish an appropriate intensity and volume of training to elicit changes in venous capacitance.

Although the percentage increase in size of the cephalic veins was marked, the absolute change in size was relatively modest. Because volume (ie, blood flow) is related to radius,[3] this change in lumen size represents an even greater potential increase in venous capacitance. This effect was enhanced by the application of a tourniquet. It is not unreasonable to expect that a more prolonged or strenuous exercise program might give rise to a much greater increase in vein size, although this remains to be determined. It is also possible that a ceiling for exercise-induced increase in venous size exists. Subject 1, who began the study with the largest cephalic vein, had the least change after exercise. Further studies will be required to examine this issue.

Access placement for hemodialysis patients is particularly difficult in diabetic or elderly patients who may have impaired arterial perfusion. Three of the 5 patients studied had diabetes mellitus as the underlying cause of renal disease, evidence that patients with diabetes can benefit from an exercise program. None of the patients had clinically evident vascular disease. The presence of significant vascular disease might attenuate the response of the venous system to exercise, but this remains to be determined. Although our study showed a profound effect of exercise training in increasing cephalic vessel size in a relatively small number of subjects, our findings need to be extended to a larger population of patients that includes women.

In summary, our study indicates that a simple unstrenuous exercise program can induce a sustained increment in cephalic vein size. Whether this increment in vein size will reduce maturation time and improve the success rate of fistula formation remains to be determined.

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