ANNEXES TO CHAPTER 3

Clinical Question VI. Are exercises useful for developing arteriovenous fistulae?

Clinical Practice Guidelines (CPG)

Three CPG have been identified that assess dilation exercises (DOQI 2006,[1] ERBP 2007[2], SPANISH 2004[3]). Only the DOQI 2006[1] CPG make recommendations on this type of intervention.

ERBP[1] CPG (Tordoir 2007) From the available veins and arteries, a minimum diameter of the anastomosed vessels (radial artery and cephalic vein) of 2.0 mm is advisable for the creation of a successful arteriovenous fistula (AVF). Venous preservation with additional hand and arm exercises may enhance the quality and the diameters of the arteries and veins for the creation of a fistula.	
DOQI CPG, 2006.[2] These CPG base their clinical recommendations on a number of observational studies and group consensus. Strengthening the forearm by using isometric exercises to increase handgrip strength (e.g., squeezing a rubber ball with or without a tourniquet) may increase blood flow, thereby enhancing vein maturation (Oder 2003), and has been shown to significantly increase forearm vessel size (Leaf 2003) thereby potentially increasing flow through a fistula created using these vessels. The resulting muscle mass increase may also enhance vein diameter. Exercise should be prescribed if there is sufficient time before surgery. **Recommendations:** (A: high impact; B: moderate impact) 1. Patients on haemodialysis with an arteriovenous fistula should do hand and arm exercises. (B)	
Spanish CPG 2004.[3] The effectiveness of exercises on the development of the blood vessel network remains subject to debate. Supporters recommend isometric exercises for the forearm, and intermittent compression of venous return. Both should be carried out in an ongoing basis 3 or 4 times daily. This is one of the recommendations these CPG give for venous preservation: **Recommendations for venous preservation:** Stimulation of muscle/vascular development by using isometric exercises or venous dilatation practices.	
There are very few studies reporting data on the effectiveness of exercise in enhancing AVF maturation or survival. Three observational studies (4-6) have been identified but they only included a small number of patients. The DOQI CPG[1], the only CPG to make a recommendation on this subject, is based on two of these studies. The most recent study presents data which are discordant with the previous studies; the authors themselves say that it was unexpected, but explained by the different exercise plans in each study, the low numbers of participants and the participation in their study of the dominant arm as control group. An RCT with	

a larger number of patients is necessary to obtain conclusive evidence on this intervention.

Jindal 2013.[4] Observational study conducted on 15 adults with CKD and an AVF (GFR < 25 ml/min/1.73 m^2; CV < 2.5 mm) who performed isometric hand-grip and forearm exercises daily for 8 weeks. The exercise plan consisted of 10 series of 20 exercises daily in the arm with the AVF. They were divided into two groups: one doing exercises in the arm for the AVF (EA), and a control group with the other non-exercised arm (NEA). The diameter of the cephalic vein (CV) was measured by ultrasound at baseline and after four and eight weeks of exercise. The primary outcome measure was the mean increase in the diameter of the CV. Secondary endpoints were the number of potential access sites for the AVF, the number of patients with potential sites for creating an AVF and the proportion of subjects who had a successful AVF placement.

Leaf 2003.[5] Observational study conducted in five adult patients with advanced CKD and an AVF [GFR 30.6 ± 5.3 ml / min (mean ± SD)]. All patients were male and mean age was 57 ± 9 years. These patients followed a programme of isometric handgrip and forearm exercises for 6 weeks, repeatedly squeezing squash balls. The diameter of the cephalic vein was measured in both arms: the exercised arm with the AVF and the non-exercised arm that acted as a control group. The measurements were made by Doppler Ultrasound.

Oder 2003.[6] Observational study between August 2000 and January 2002, evaluating 20 adult patients with CKD and an AVF. These patients performed isometric handgrip exercises. Measurements were taken of the diameter of the fistula three times before they squeezed a rubber ball for 5 minutes and three times afterwards. All measurements were made by the same operator by ultrasound. The statistical significance of the difference between the mean diameter before and after the exercise was determined by the paired t test and a $p<0.05$ was defined.

Jindal 2013.[4] The mean diameter of the CV increased in both the EA group and the NEA control from 0.48 to 0.59 mm and 0.71 to 0.81 mm respectively (p=NS). Compared to the baseline value, all the CV diameters had increased significantly after four weeks ($p<0.05$). In the EA group, the mean proximal and distal CV increased from 1.66 to 2.13 mm and 2.22 to 2.81 mm respectively. The number of potential access sites for AVF, increased after four and eight weeks of exercise ($p<0.001$ and p=0.047 respectively). The number of patients with potential sites for creating an AVF increased with respect to baseline after four weeks and eight weeks of exercise (p=0.028 and p=0.082 respectively). A successful AVF was achieved in five of the patients.	**Very low quality**
Leaf 2003.[5] The diameter of the cephalic vein in the exercised arm increased significantly ($p<0.05$) compared to the control arm when measured both in the absence of a tourniquet (048 ± 0.016 versus 0.024 ± 0.023 cm) and with a tourniquet in place (0.056 ± 0.022 versus 028 ± 0.027 cm).	**Very low quality**
Oder 2003.[6] The diameter of the fistula increased in 20 out of 23 patients (87%) after exercise. The mean change in the diameter of the fistula was 0.051 cm or 9.3%, with a corresponding range of -0.02 to 0.153 cm or a change of -3.8% to 25%. This change was statistically significant ($p<0.0001$).	**Very low quality**

Summary of evidence	
Jindal 2013.[4] The performance of isometric hand-grip exercises resulted in an increase in the diameter of the cephalic vein after four weeks, both in the group that performed exercises in the arm for the AVF and in the control group, which did not exercise. The results may be due to systemic side effects of the exercise which may have disproportionally affected the dominant arm. In any event, this is a simple intervention, requiring a minimum amount of resources, and may facilitate creation of AVF in patients previously not considered good candidates for an AVF.	**Very low quality**
Leaf 2003.[5] A simple exercise training programme may lead to a significant increase in the diameter of the cephalic vein, commonly used in the creation of an AVF. An increase in the diameter of the AVF and a consequent increase in blood flow could accelerate maturation of the native arteriovenous fistula, thereby reducing the morbidity associated with vascular access.	**Very low quality**
Oder 2003.[6] Strengthening the forearm by using isometric exercises to increase handgrip strength (e.g., squeezing a rubber ball with or without a tourniquet) may increase the diameter of the AVF and therefore the blood flow.	**Very low quality**
Patients' values and preferences *No relevant studies related to this aspect have been identified.*	
Use of resources and costs *No relevant studies related to this aspect have been identified.*	
Recommendations [Proposal]	
Weak	It is suggested that patients should be advised to perform isometric exercises or that venous dilation practices be applied in patients with chronic kidney disease with an arteriovenous fistula in order to stimulate muscle and vascular development and, consequently, be able to speed up the maturation of the fistula, thereby reducing the morbidity associated with vascular access.

References

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2. Tordoir J, Canaud B, Haage P, Konner K, Basci A, Fouque D, Kooman J, Martin-Malo A, Pedrini L, Pizzarelli F, Tattersall J, Vennegoor M, Wanner C, ter Wee P, Vanholder R. EBPG on Vascular Access. Nephrol Dial Transplant. 2007 May;22 Suppl 2:ii88-117.

3. Rodríguez Hernández JA, González Parra E, Julián Gutiérrez JM, Segarra Medrano A, Almirante B, Martínez MT, Arrieta J, Fernández Rivera C, Galera A, Gallego Beuter J, Górriz JL, Herrero JA, López Menchero R, Ochando A, Pérez Bañasco V, Polo JR, Pueyo J, Ruiz CI, Segura Iglesias R; Sociedad Española de Nefrología. [Vascular access guidelines for hemodialysis]. Nefrologia. 2005;25 Suppl 1:3-97

4. Uy AL, Jindal RM, Herndon TW, Yuan CM, Abbott KC, Hurst FP Impact of isometric handgrip exercises on cephalic vein diameter in non-AVF candidates, a pilot study. J Vasc Access. 2013 Apr-Jun;14(2):157-63..

5. Leaf DA, MacRae HS, Grant E, Kraut J Isometric exercise increases the size of forearm veins in patients with chronic renal failure. Am J Med Sci. 2003 Mar;325(3):115-9

6. Oder TF, Teodorescu V, Uribarri Effect of exercise on the diameter of arteriovenous fistulae in hemodialysis patients. ASAIO J. 2003 Sep-Oct;49(5):554-5.

GRADE TABLES

Date: 2013-10-23
Question: Should isometric handgrip exercises be used for adult CRD patients with AVF?
Bibliography: 1. Uy AL, Jindal RM, Herndon TW, Yuan CM, Abbott KC, Hurst FP Impact of isometric handgrip exercises on cephalic vein diameter in non-AVF candidates, a pilot study. J Vasc Access. 2013 Apr-Jun;14(2):157-63..

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Isometric handgrip exercises (IE)**	**Control(C)**	**Relative (95% CI)**	**Absolute**		
Cephalic vein diameter (follow-up of 4–8 weeks; assessed with: ultrasound)												
1	observational studies	no serious risk of bias	No serious inconsistency	No serious indirectness	serious[1]	none	15	15	0,48 a 0,59 (IE) 0,71 a 0,81 m (C) (p = NS)		⨁⨁◯◯ VERY LOW	

[1]few patients

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Bibliography. Leaf DA, MacRae HS, Grant E, Kraut J Isometric exercise increases the size of forearm veins in patients with chronic renal failure. Am J Med Sci. 2003 Mar;325(3):115-9

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Isometric handgrip exercises (IE)**	**Control(C)**	**Relative (95% CI)**	**Absolute**		
Cephalic vein diameter (6-week follow-up; assessed with: ultrasound)												
1	observational studies	no serious risk of bias	no serious inconsistency	no serious indirectness	Serious [1]	none	5	5	IE 048 + / - 0,016 C 0,024 + / - 0,023 cm) p<0,05		□□□□ VERY LOW	

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Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Isometric handgrip exercises**	**Control**	**Relative (95% CI)**	**Absolute**		
Cephalic vein diameter (mean follow-up of 1 day; measured with: ultrasound)												
1	observational studies	no serious risk of bias	no serious inconsistency	no serious indirectness	Serious[1]	none	20	-	0,51 0 higher (0.02 lower to 0.153 higher) P<0,0001		⨁⨁◯◯ VERY LOW	

[1]few patients