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The Implication of Hand Exercises on Arteriovenous Fistula Maturation Process: A Systematic Review

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Abstract— **Background:** Renal failure is one of the most common diseases and might develop to the end-stage level in which need to have hemodialysis to survive. Generally, Arteriovenous Fistula (AVF) created for hemodialysis access and its maturity depends on several factors, including hand exercise. This study aims to evaluate the implications of hand exercises in the process of AVF maturation in patients with chronic kidney failure. **Methods:** Performing literature search using Pubmed, The Cochrane, and Google Scholar databases were done from 2015 to 2019. All case series, cohort studies, and clinical trials were considered if they met inclusion criteria. **Result:** From 603 studies, five studies were met inclusion criteria. Four studies showed hand exercises with different protocols from each study. The outcome parameter was varied throughout all the studies. Hand exercise has believed to have a potential effect on AVF maturation. Through ultrasonographic value, diverse findings in the outcome such as arterial and vein diameter and increasing of blood flow measured. One study had assessed clinical maturation in AVF as one of the outcomes of the study. Nevertheless, one study showed no significant effect of hand exercise in ultrasonographic maturation. **Conclusion:** Hand exercises with different types of exercises can make changes in AVF maturation parameters. However, it needs further accessible evidence study with the same exercise protocol and evaluation so that the effect of the protocol on AVF maturation can be drawn.

Keywords: Hand Exercise, Arteriovenous Fistula, Chronic Kidney Failure

1. Introduction

Renal failure is defined as abnormalities of kidney structure or function, present for ≥3 months, with implications for health. Approximately 20 million people in the United States might develop into End-Stage Kidney Disease (ESRD). It is a state of progressive loss of kidney function ultimately resulting in the need for renal replacement therapy such as dialysis. Based on the characteristics of durability, improved access survival, low rate of complication, and cost-effectiveness, AVF is a preferred type of vascular access for hemodialysis. The role of vascular surgeons' in AVF creation is to attain a strong structure and easy access which can be used for hemodialysis. Not only to create, but knowledge of maintaining the vascular access from dysfunction is needed. Vascular access dysfunction represents a significant proportion of the morbidity affecting hemodialysis patients with its attendant health care-related expenditure. Numerous studies have examined the clinical predictors of failure of AVF maturation. Statistically, the data showed that age over 65 years, female sex, obesity, diabetes, forearm, extensive vascular disease, heart disease, and surgeon-specific factors were the most vital clinical predictors of delay or failure in the process of vascular access maturation. Besides those factors, hand exercise has been studied in several studies to evaluate its usefulness. Hand exercise might be one of the practicable efforts to achieve maturation which contributed to post-operative strategy in post AVF creation patients. However, scarce scientific evidence of hand exercise effectiveness is still limited. This study aims to study the implications of hand exercises in the process of AVF maturation in patients with chronic kidney failure.

2. Methods

Search strategy

The authors performed a literature search using Pubmed, The Cochrane, and Google Scholar. The following search strategies were used on each database: ((upper extremity exercise) or (hand exercise) and (arteriovenous fistula maturation) and (systematic review)). The study aims to obtain the most

recent articles. Therefore, the authors restricted the search to studies from 2015 until 2019. Regarding the language, the search was restricted to articles published in English. Abstracts were reviewed online and suitable full-text articles were downloaded for data extraction. Two independent reviewers identified the titles and abstracts of potentially relevant studies. Disagreement was discussed and resolved with a third reviewer if necessary. Additional publications were identified from the reference list of the determined study.

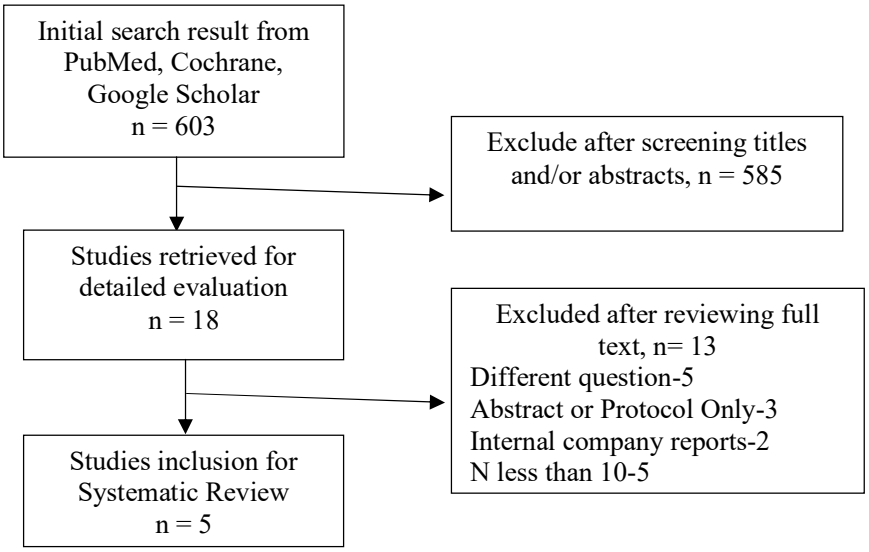

Figure 1. Flow diagram of search results and selection of studies

Inclusion and Exclusion Criteria

Bibliographies of the retrieved articles were hand-searched for additional potentially relevant studies. A multistage assessment was used to determine of articles would qualify for the analysis. Authors were review only in the abstract at the initial phase. Publication including patients presented chronic renal individuals in stage V, older than 18 years of age and both males and females who were undertaking hand exercises for arteriovenous fistula maturation and had undergone doppler ultrasounds or radiological exams to define the anatomy of arteries and veins. Studies that presented hand exercises using rubber rings and elastic bands and manual pressure with isometric exercises using a squeeze ball were considered eligible methods. Animal studies and studies with the population in unstable hemodynamics were excluded.

Data Extraction

The following data were independently abstracted by authors: study design, population, intervention, length of follow-up and outcome.

3. Results

Analysis of studies

In total, 604 articles were identified using the search strategies mentioned above. 585 abstracts were rejected due to discrepancy in title and abstracts, leaving 17 articles for closer scrutiny. 17 articles were read, ten articles were excluded due to exclusion criteria. Five full-text articles have met the eligibility for assessment, three articles were randomized controlled trials (RCTs), and two other articles were quasi-experimental and pilot longitudinal studies with a follow-up of 30 days. One article was designed to evaluate the effect of hand exercises before or pre-surgery arteriovenous fistula creation to reach arteriovenous fistula maturation.

Participants

From five studies, there were 310 participants in total with stage 4 or 5 chronic kidney disease been observed in researches and all were out-patient clinic patients simply put all the participants were considered hemodynamically stable. Participants' mean age range between 45,8 to 67 years old. The characteristic of participants is shown in table 1. The characteristics of participants in the studies varied greatly, but in three studies, hypertension was one of the most common commodities found in participants, and in other studies only mentioned diabetes mellitus that could be found in the participants. Dyslipidemia was also mentioned as one of the most found in participants in one study. The number of male participants dominated in the seven studies reviewed by the authors.

The studies were heterogeneous concerning the type of hand exercises, duration of the exercises, variation in every exercise, and length of follow-up. Given the heterogeneity among studies and weakness in study methodology, we could not analyze them. Instead, we qualitatively reviewed the pertinent results of each study. The Jadad score ranged from 1 to 5 (maximum score for the scale=5) for the RCT. Unfortunately, there is no scale in common use to assess non-RCTs therefore we can’t analyze them.

Tabel 1. Study designs and Characteristic

Author	Trial Type	Control Group	(n)	Groups	Drop Out, Loss to Follow-Up	Number Analyzed	Study Length	Age (mean) years old	Male (%)	Female (%)	Setting	Jadad Score (max= 5)
Fontsere et al (2016)	RCT, single blinded	NE	85	HE: 38	16 (13 loss to follow-up, 3 drop out)	69	4 weeks	66,8	70,0	30,0	Post surgery	3
Barbosa et al (2018)	RCT, double blinded	HE wo/ BFR	26	HE w/ BFR: 12	4 (Loss to follow-up)	26	8 weeks	61,33	69,23	30,77	Pre surgery	3
Distefano et al (2019)	Pilot Longitudinal study	-	17	HE: 17	NR	17	4 weeks	67	88,23	11,77	Pre surgery	-
Mo et al (2019)	RCT, single blinded	Different exercise	86	HE:38	8 (Loss to follow-up)	78	12 weeks	54,33	64,10	35,90	Post surgery	3
Poetra et al (2019)	Quasi Experimental	NE	14	HE: 7	NR	14	5 weeks	45,86	71,42	28,58	Post surgery	-
RCT= Randomized Control Trial, NE = No Exercise, HE= Hand exercise w/= with, wo/= without, BFR= blood flow restriction												

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Tabel 2. Intervention and Outcome

Studies	Intervention	Length of study	Outcome	Results
Fontsere et al (2016)	Experimental group: 1. Elbow Flexion-Extension (2 sets of 10 repetitions every day for 1 month) 2. Wrist Flexion-Extension (2 sets of 10 repetitions every day for 1 month) 3. Hand open-close (2 sets of 25 repetitions every day for 1 month). Control group: No exercise	4 weeks	-Clinical maturation (easily palpable vein with straight superficial segment length more than 10cm, good palpable thrill, sufficient diameter). -Ultrasonography maturation (Draining vein diameter ≥5mm, Skin-vein distant <6mm, Brachial blood flow rate ≥500mL/min).	-Clinical maturation (94.7% vs. 80.6%, p = 0.069) -Ultrasonographic maturation (81.6% vs. 74.2%, p = 0.459). -Ultrasonographic maturation of distal AVF (p=0,331) -ultrasonographic maturation of proximal AVF (p=0,342) -Clinical maturation in distal anastomose (p=0.019) -Clinical maturation in proximal anastomose (p=0,609)
Barbosa et al (2018)	Experimental group: - Inflating tensiometer placed on the nondominant upper arm with artery occlusion was 50% of the systolic blood pressure obtained during and maintained during 3 exercises. Control group: Without BFR - Both groups, receiving same exercise program. consist of 3 exercises. Tennis ball, 6 sets of	8 weeks	- Doppler Ultrasound (cephalic vein diameter, cephalic vein distensibility, radial artery diameter, radial artery flow peak and mean flow velocity) - Handgrip strength - Forearm circumference	*(2cm)* -Cephalic vein diameter (p=0,411) -Cephalic vein distensibility (p=0,803) -Radial Artery diameter (p=0,074) - Systolic peak flow (p=0,279) *(10cm)* -Cephalic vein diameter (p=0,340) -Cephalic vein distensibility (p=0,422) - Radial artery diameter (p=0,139) - Systolic peak flow (p=0,150) *(20cm)* -Cephalic vein diameter (p=0,226)

	10 squeezes. more 5 squeezes were added each week. Dumbbells, 3 sets of 10 x with 1 kg in the 1st two weeks, 2 kg in the 2nd two weeks, 3 kg in the last 4 weeks of observation. Handgrip, 40% of 1 repetition maximum 3 sets of 20 x/min.			-Cephalic vein distensibility (p=0,699) - Radial artery diameter (20cm) (p=0,724) - Systolic peak flow (p=0,341)
Distefano et al (2019)	Squezee polyurethane foam ball 7mm in diameter, 3x/day in 1min for 30 days	4 weeks	-Doppler ultrasound (radial artery diameter, brachial artery diameter)	Radial artery (p<0,001) Brachial artery (p< 0,001)
Mo et al (2019)	Experimental group: Hold 6-pound of Dumbbells (4 sessions per day on non-dialysis day for 5 minutes per sessions at 30 times per minute for 3 months). Control: Handgrip squeezing with rubber balls for 3 months.	12 weeks	-Doppler ultrasound (Drainage vein (DV) blood flow and diameter, AVF proximal artery blood flow, Brachial artery blood flow).	Experimental group: -DV (p=0.001) -DV diameter (p=<0.001) -Proximal artery blood flow (p=0.004) -Brachial artery blood flow (p=0.024)
Poetra et al (2019)	Experimental group: Hand exercise using hand gripper (3 sets of 10 squeezes each at 1minute interval, 2 times in the morning and 2 times in afternoon for 5 weeks). Control: No exercise.	5 weeks	-Forearm circumference -Handgrip strength -Doppler ultrasound (Cephalic vein diameter, Blood flow volume, Blood flow velocity). -Effect size (ES) of exercise to forearm circumference, blood flow volume, and cephalic vein diameter	-Forearm circumference (p<0.001) -Cephalic vein diameter (p=0.046) -Blood flow volume (p=0.035) -ES exercise to forearm = 0.4 -ES exercise to blood flow volume = 0.53 -ES exercise to cephalic vein diameter = 0.84

Effect of Intervention

The definition of AVF maturation in some studies is not all revealed. However, several studies reported AVF maturation can be evaluated clinically and ultrasonographically with doppler ultrasound. Based on the authority of Fontsere et al, clinical maturation is described as a palpable vein with a superficial stratification length of more than 10 cm, good palpable thrill, sufficient diameter. Meanwhile, achieving the ultrasonography maturation is by measuring a draining vein with a diameter of ≥ 5mm, a skin-vein distance of <6 mm, with a blood flow rate of ≥ 500mL / min. All these studies used different types of hand exercises. The variation of the duration of the hand exercise and the number of portions of hand exercise which were given to participants also greatly varied.

Hand Exercises and Its Effect to Artery and Vein Diameter and Blood flow

Three articles studied the effect of hand exercises in experimental groups with control groups. Although types of exercise, number of exercise portions, and length of follow-up were different in these studies, they had a significant impact on venous dilation as in Poetra et al, which stated that handgrip training alone increased the diameter of the cephalic vein ($p = 0.046$). Likewise, in Tapia et al study with isometric exercise in the experimental group, venous dilation was evaluated by ultrasonography after 4 weeks of hand exercise. However, in the Fontsere et al study which had elbow flexion, wrist flexion, and hand open-close training methods within 4 weeks, clinical maturation was significant only at the distal anastomosis ($p=0.019$) but not in doppler ultrasonography (DUS) maturation ($p=0.459$). Patients with chronic kidney disease frequently have impaired endothelial function, according to several studies. There is a correlation between the diameter of the artery and the success rate of the AVF construction. The study conducted by Distefano in 2019 stating that there is a correlation between the diameter of the artery and the success rate of the AVF construction. The study observed for four weeks in 17 patients with ESRD candidates to AVF creation by squeezing a polyurethane ball for 3x per day in 10min. There was a significant increase in the diameter of the radial artery and brachial artery ($p<0.001$). One study compared the effects of one type of exercise with other exercises conducted by Mo et al. By comparing the efficacy of a dumbbell in the experimental group and handgrip squeezing in the control group, observed for 12 weeks and found a significant increase in draining vein ($p=0.001$) in the experimental group.

Two studies provide exercise intervention in the population before AVF creation. Barbosa et al study in 2018 used blood flow restriction with a sphygmomanometer placed on a non-dominant arm with a large cuff of 50% of its systolic blood while doing hand exercise as a form of intervention in the experimental group then compared to the control group. Three studies have a significant value of blood flow after doing exercises.

4. Discussion

Arteriovenous fistula (AVF) is the best method to achieve vascular access in a patient with end-stage kidney disease who undergoes chronic hemodialysis (Rodriguez et al., 2007). AVF is made by surgery and but it needs a period of time to can be used directly. The access must be mature in advance. According to KDOQI (Kidney Disease Outcomes Quality Initiative), AVF is considered mature by using ultrasonography if the blood flow is ≥600ml/min, vein diameter ≥6mm, and ≤0.6cm depth from the skin (KDOQI 2006). Moreover, maturation can also be determined by clinical examination, as a straight superficial vein with good palpable thrill with 96% sensitivity and 68% specificity (Basile et al, 2005) (Ferring et al, 2014). To hastening the duration of AVF maturation process, several studies suggested having a hand exercise after surgery. In our study, we found four studies that stated that hand exercises may contribute to changes in the parameter of maturation such as vein diameter, arterial diameter, and increase blood flow measuring by ultrasound and clinical maturation. Each study has a different exercise protocol due to the limitation of the standard procedure yet. Therefore, the outcome can be varied. Some studies mentioned the exercise caused increased blood flow intermittently, which make increase shear stress of vascular endothelial cell. The increasing shear stress gives a signal to the endothelial cell to express a gene that results in nitric oxide production which can make a dilation of the vessel wall (Russ et al., 2003) (Tingken et al., 2010). Changes in vessel diameter will also result in resistance and flow changes. The bigger the vessel size, the flow will increase and can also cause remodeling in arterial, fistula, and venous site (Lehoux et al., 2002) (Corpataux et al., 2002).

One study by Barbosa et al was adding a restriction to increase the diameter of artery and vein so that the maturation period becomes faster. The mechanism is believed due to turbulent flow throughout the vessel which enhanced shear tear, followed by increasing nitric oxide produced by endothelial cell resulting in increased diameter (Pyke KE & Tschakovsky ME. 2005). But there no significant differentiation between restriction and without restriction in arteria or vein diameter in both studies.

5. Conclusion

Hand exercises with different types of exercises may positively contribute to a change in AVF maturation parameter. To attain a more definite conclusion of the efficacy of the study of hand exercise will need further study with the same exercise protocol.

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