Influence of exercise training mode on arterial diameter; a systematic review and meta-analysis.

Objectives: To examine whether differences in arterial diameter exist between athletes participating in endurance, resistance or mixed exercise training.

Design: A systematic review with meta-analysis.

Methods: Random effects meta-analyses of the weighted mean difference in aortic, carotid, brachial and femoral arterial diameters, height and body mass were conducted on data from 16 peer-reviewed studies indexed on PubMed, MEDLINE, SCOPUS and Sport Discus. Effect sizes were calculated as the standardised difference in means (δ), and used to compare endurance (n=163), resistance (n=192), and mixed trained athletes (n=360), with controls (n=440).

Results: Compared to controls, endurance athletes displayed the greatest difference in diameter in the brachial artery (δ=1.84, 95% CI: 0.59, 3.09, P<0.01), whereas for mixed athletes, the greatest difference in diameter occurred in the femoral artery (δ=3.65, 95% CI: 2.21, 5.10, p<0.01), despite there being no differences in height or body mass between these groups. Resistance athletes had a significantly greater body mass (p=0.047) and aortic diameter (δ=1.81, 95% CI: 1.58, 2.05, p<0.01) than controls, however differences in other vessels could not be determined through meta-analysis due to insufficient data.

Conclusions: Our results provide evidence for localised arterial differences, which occur more extensively in peripheral vessels (brachial and femoral). Chronically, vascular remodelling may occur as a result of the specific haemodynamic conditions within each vessel, which likely differs depending on the mode of exercise. In the future, empirical research is needed to understand the effect of resistance training on chronic vascular remodelling, as this is not well documented.

Key words: Exercise adaptation, artery, structure, remodelling.

Introduction

Chronic vascular remodelling, including changes in arterial wall thickness,[1] diameter [2] and wall-to-lumen ratio,[3] in response to exercise training has been widely debated. Whilst the majority of research supports differences in arterial diameter in athletes compared to sedentary or recreationally active controls, [1-9] it remains unclear whether the mode of exercise training (endurance, resistance or mixed) plays a role in these differences. This may be due, in part, to the examination of different arteries and the wide range of sports studied. Previously, both blood flow and shear stress patterns have been shown to vary depending on exercise modality,[10] and chronic vascular remodelling has been suggested as a mechanism to reduce exercise-specific shear stress.[7] Structural properties, such as the distribution of collagen and elastin, differs significantly between central and peripheral arteries[11] such that arteries located distally to the heart are stiffer than those located more proximal.[12] Therefore it is conceivable that arterial remodelling in response to chronic exercise training may differ in each vascular bed; occurring more extensively in peripheral arteries and specifically in response to the blood flow and shear stress patterns to which each vessel is exposed during exercise.

The current disparity in results makes it difficult to ascertain whether arterial remodelling occurs regionally in response to a specific type of exercise stimulus or whether remodelling occurs consistently in all vascular beds. Longitudinal studies that have examined arterial diameter following a period of resistance exercise training have reported increases in brachial,[3,6] carotid and femoral [13] diameter, yet others report no change.[3,14] Studies of endurance athletes have also reported larger carotid and femoral diameters compared to controls,[2,15] and conflict exists in relation to brachial [3,16,17] and aortic diameters.[2,15] Assimilating all available data, and grouping current studies according to the mode of exercise, would yield the large sample sizes needed to draw high powered statistical conclusions about the existence of differences in arterial diameter between athletes engaged with endurance, resistance and mixed training. A meta-analysis of such data would also help in evaluating the current state of research, providing future direction for empirical studies and determining whether the mode of exercise training is a potential moderator of arterial adaptation.

Methods

Literature search strategy. A literature search for peer-reviewed publications published before June 2013, and examining the arterial adaptations to exercise training was conducted using the PubMed, MEDLINE, SCOPUS and Sport Discus databases. The keywords and phrases used in the online search were *aortic root, artery, arterial, athletes, diameter, exercise, structure, training,* and *vascular remodelling.* In addition to the online search, reference lists from recently published experimental studies, review papers and meta-analyses were manually examined to locate any other relevant studies not identified as a result of the online search. If articles were unavailable, or presented insufficient data, authors were contacted by email and asked to supply relevant information.

Study Selection. To be included in the current meta-analysis, studies had to meet the following criteria: **(1)** be written in the English-language; **(2)** present data for absolute arterial diameter; **(3)** include male participants only, to prevent any influence of the menstrual cycle as a potential confounding variable;[18] **(4)** have a mean age of the study cohort between 18-40 years to avoid age as a co-factor; **(5)** recruit homogenous groups of athletes involved in either endurance (exercise comprised of a high dynamic component, >70% $\dot{V}O_{2max}$), resistance (exercise comprised of a high static component, >50% maximum voluntary contraction), or mixed training (exercise comprised of both a high dynamic component, >70% $\dot{V}O_{2max}$ and a high static component, >50% maximum voluntary contraction) as previously defined by Mitchell et al.;[19] **(6)** include an age-matched untrained control group in the original study, and **(7)** participants to have no history of illness or current cardiovascular disease in the study groups. Review papers and experimental cohorts of athletes belonging to different sporting classifications were excluded. Two longitudinal studies[13,14] were excluded from the meta-analysis to prevent incorrect assessments of the variance of the summary effect being produced by including a repetitive sample.

Review Process. One investigator (JB) performed database searches and cross referencing, subsequently removing duplicate studies and screening abstracts for appropriateness. The search process highlighted 146 potential studies which could have been included in the meta-analysis. Based on abstract screening, 84 studies were excluded for failing to conform to the inclusion criteria. The remaining 62 studies were independently assessed by two reviewers (JB, JE), with discrepancies resolved by consensus. If any studies presented closely related data, the paper published first was selected for inclusion in the meta-analysis. In four cases, data were reported graphically and after contacting the authors, raw data were obtained from one of these four studies[20] resulting in exclusion of the remaining three.[5,21,22] The search and filtration processes are illustrated in figure 1.

A total of 16 studies were entered into the final meta-analysis for arterial diameter,[1,20,23-36] resulting in an overall sample of 1155 men (see table 1). Participants were categorised into one of four groups, depending on the mode of exercise training undertaken (endurance, resistance, mixed and control). For all 16 studies included in the meta-analysis, the control group were described either as sedentary or recreationally active however none of the controls were participating in more than 3 hours of physical activity per week. Data were subdivided further by anatomical location of four large arteries (carotid, brachial, femoral, and aorta), provided that at least two studies were available for each artery, as previously recommended.[37] Other parameters, such as intima-media thickness, flow-mediated dilation and wall to lumen ratio, and other vessels, including popliteal, subclavian and tibial arteries were considered at initial screening but too few papers reported these data to undertake a meaningful analysis.

Data Extraction. Data related to the mode of training (endurance, resistance and mixed) and the artery under investigation (aorta, brachial, carotid and femoral) were coded discretely for each study. Continuous data for arterial diameter, height and body mass were recorded as group mean ± SD for each study and transferred into a spreadsheet along with sample sizes for both the trained and control groups (Excel 2010, Microsoft Corporation, Redmond, WA).

Statistical Analysis. A random effects meta-analysis model was applied to pooled diameter data for all athletes. Relative weights, calculated as the inverse of the overall study error, were assigned to the mean change for each study on the basis of sample size and between participants' standard error such that studies with a larger sample size and smaller standard error were assigned more weight than studies with a smaller sample size and larger standard error. A Q test and I^2 statistic were employed to assess study-to-study heterogeneity. Statistically significant Q tests ($p<0.05$) and an I^2 statistic >50% were explored further by subgroup analysis based on mode of training and arterial vessel. Meta-regression for each vessel (aorta, brachial, carotid and femoral) within each exercise group (endurance, resistance and mixed) would have allowed for assessment of body size as a potential covariate of arterial diameter; however, insufficient data prevented meaningful application of this technique. Therefore, to address the issue of body size, a random effects meta-analysis model was used to identify any differences in height or body mass between athletes and controls.

Effect sizes were calculated as the standardised difference in means (δ) and differences between subgroups were examined using the 95% CI of each summary mean difference, with alpha set at 0.05. The presence of publication bias was investigated using a funnel plot of standard error and standardised difference in means, in conjunction with Egger's regression intercept test, which provided a quantitative assessment of publication bias.[38] All statistical analyses were carried out with Comprehensive Meta-analysis software version 2.0 (Biostat, Englewood, NJ).

Results

Arterial Diameter. Egger's regression test did not achieve statistical significance for diameter ($p=0.55$), suggesting no presence of publication bias. A significant Q statistic of 121.8 ($p<0.01$) and an I^2 statistic of 87.7 indicated that heterogeneity between the 16 studies was great enough to apply sub-group analysis for the identification of potential moderators. Sub-group analysis revealed that both endurance and mixed athletes had significantly larger brachial and femoral arterial diameters compared to controls (see figure 2). In comparison to the control group, the greatest difference between arterial diameters was seen in the brachial artery for endurance athletes (δ=1.84, 95% CI: 0.59, 3.09, p<0.01) and the femoral artery for mixed athletes (δ=3.65, 95% CI: 2.21, 5.10, p<0.01). In addition, mixed athletes displayed a significantly larger carotid artery diameter compared to controls (δ=1.244 95% CI: 0.28, 2.21, p<0.05), and whilst there was a trend towards a bigger carotid artery diameter in endurance athletes, this was not significant (p=0.09). Data for resistance trained individuals revealed a significantly larger diameter for the aorta, compared to controls (δ=1.81, 95% CI: 1.58, 2.05, p<0.01), however the impact of resistance exercise on brachial, carotid and femoral arterial remodelling could not be determined through the current meta-analysis due to insufficient data. Neither endurance nor mixed athletes displayed bigger aortic diameters compared to controls (p=0.28 and p=0.32 respectively).

Height and Mass. There were no differences in height between endurance, resistance or mixed athletes and controls (p=0.253; p=0.124 and p=0.864, respectively). Similarly, there was no difference in body mass between controls and endurance (p=0.381) or mixed athletes (p=0.692). In contrast, resistance athletes had a significantly greater body mass compared to controls (p=0.047).

Discussion

The purpose of this meta-analysis was to investigate if the mode of exercise training is associated with region-specific differences in arterial diameter. Our meta-analysis of 715 athletes and 440 controls suggests that adaptations in arterial diameter vary significantly between those completing different modes of exercise training, and may also be specific to individual vessels providing support for localised differences in arterial diameter, following chronic exposure to an exercise stimulus. This is in agreement with recent findings[6,9,39-40] including Spence et al.,[3] who found significant changes in femoral artery diameter following six months of endurance exercise, whereas six months of resistance training led to increases in brachial artery diameter. The same authors reported no changes in carotid diameter, irrespective of the mode of exercise undertaken.[3] In contrast, our results provide support for differences in carotid diameter associated with different modes of exercise training.

The impact of resistance exercise on brachial, carotid and femoral arterial remodelling could not be determined through the current meta-analysis. Of the few studies that have reported arterial diameters for resistance trained athletes the results are conflicting,[6,27,31] highlighting the need for further research in this area. Our meta-analysis did however demonstrate that resistance trained athletes were the only group to display a significantly greater aortic diameter. Aortic remodelling as a result of resistance training remains controversial [4,41] and whilst it is understood that the aorta is subjected to high haemodynamic loads during resistance exercise, other factors such as body size may play a role in structural differences. Training load, volume and intensity may also play a key role in localised vascular adaption, but further research is needed to fully understand the influence of these training variables.

Influence of blood pressure and flow patterns on arterial diameter

One explanation for localised remodelling of the arteries may be linked to the specificity of exercise-induced blood flow patterns.[42] Different modalities of lower limb exercise have been shown to cause variation in brachial artery blood flow responses and shear stress patterns.[10] Additionally, during the cardiac cycle blood pressure (BP) fluctuates rapidly and produces stretch on the arterial wall, which is augmented during exercise.[43] Resistance exercise increases shear stress, and is associated with intermittent post contraction increases in blood flow, under a high BP,[44] compared to a continuous increase in blood flow under relatively low BP with endurance exercise.[45] These differences in BP patterns may affect the stretch produced on the arterial wall resulting in changes in arterial diameter which are specific to the exercise stimulus received.

It could also be speculated that localised changes in arterial diameter are augmented by the presence of ischemic muscle contractions, which are believed to occur during continuous force generation above 40% MVC.[7] Ischemic contractions cause large changes in retrograde blood flow with the concomitant development of muscle tension, and in antegrade flow as the redirected volume of blood is released during the subsequent muscle relaxation phase.[46] Greater changes in flow pulsatility associated with ischemic muscle contractions may act as a more powerful stimulus for increasing shear stress and the associated release of endothelial-derived nitric oxide,[47] causing bigger changes in arterial size. Thus exercise that produces ischemia in specific vascular beds may be expected to stimulate greater vascular adaptation in those beds when compared to the vessels with less ischemia. Whilst ischemic muscle contractions occur naturally during force generation at 40% MVC, recently the use of tourniquet cuffs to restrict blood flow during resistance exercise has been used to promote increases in muscle strength and size at much lower intensities than conventional strength training.[48,49] This may have important implications in a clinical or rehabilitation setting, particularly as blood flow restricted resistance exercise at low intensities provides a stimulus sufficient to cause changes in arterial diameter.[50]

Influence of body size on arterial diameter

A recent study concluded that significant relationships exist between brachial arterial diameter and measures of whole body, lean mass and regional mass but not fat mass or height.[51] If differences in body size and composition or changes in anthropometric characteristics occur simultaneously with modifications in arterial diameter, allometric scaling techniques have been suggested to ensure data are comparable within and between populations.[51] Despite there being insufficient data for successful and meaningful application of meta-regression to assess the influence of body size on each artery for each mode of exercise training in the present study, we were able to use meta-analysis to identify the presence of any differences in body size between the groups. Height did not vary significantly between athletes and controls, which suggests that, in support of previous research,[51] there is no relationship between arterial diameter and height. In contrast, resistance athletes did display a significantly larger body mass than controls, and subsequently the larger absolute aortic diameters reported may not exist if the data were normalised using appropriate scaling indices.[52] There were no differences in body mass in endurance or mixed athletes compared to controls. However, our results did illustrate significantly larger brachial and femoral diameters in these athletes, suggesting that differences in arterial structure are independent of body size.

Influence of diameter on arterial function

The relationship between structural and functional adaptation of the artery would suggest that our findings may have implications for some measures of arterial function, such as flow-mediated dilation (FMD), for which the principal determinant is baseline diameter.[53] Recent research has illustrated an inverse relationship between arterial diameter and FMD.[39] Indeed, up to 64% of the variability in FMD values can be explained by variability in baseline diameter.[54] This meta-analysis has shown variations in arterial diameter depending on the mode of exercise, but insufficient data were available to investigate the effect of these structural changes on FMD. Additionally, it is not known how changes in arterial diameter associated with different modes of exercise training might affect BP, blood flow or arterial stiffness. Changes in arterial diameter appear to improve the efficiency of blood flow but maintain blood flow velocity and shear stress acting on the vessel.[5] Reductions in resting BP of 3-4mmHg have been reported as a result of chronic exercise,[45,55,56] irrespective of the mode, although it is not clear whether these reductions are related to changes in arterial diameter. Similarly, disparity in previous findings makes it difficult to ascertain whether changes in diameter and arterial stiffness are interrelated.[14,57] A greater understanding of the relationship between changes in diameter, blood pressure, blood flow and arterial stiffness, and the interaction with different modes of exercise training may help to identify underlying mechanisms responsible for arterial remodelling.

Clinical implications

Regular exercise has previously been shown to reduce both primary and secondary vascular events.[58] The beneficial effects of exercise on traditional cardiovascular risk factors are thought to account for approximately half of the risk reduction associated with exercise and suggestions have been made that direct effects of exercise on the vessel wall may account for some of the remaining risk factor gap.[59]

Exercise training in older subjects has shown remodelling of conduit arteries, leading to decreased wall thickness, and increased lumen diameters, with consequent decrease in wall-to-lumen ratio.[59] The results of this meta-analysis provide support for increased lumen diameters in athletes who have undertaken endurance, resistance or mixed exercise training, and these differences appear to be vessel dependent. It is well known that peripheral arteries are subject to wall thickening, plaque formation and atherosclerosis.[43] Our findings suggest that these peripheral arteries are likely to be the most responsive to exercise training, with the largest femoral vessels observed in athletes engaged in mixed training and the largest brachial vessels in endurance athletes. It is possible therefore, that different modes of training could be prescribed for different stages of vascular disease, however further work is required.

Limitations

This systematic review was limited by the small number of available studies which met our inclusion criteria. Previous studies have examined participants with a wide variation in age, however due to the known influence of age on arterial structure we chose to only examine athletes aged 18-40 years. We therefore acknowledge that our findings can only be applied to this younger population. Similarly, due to a lack of reporting or differentiation in previous studies, we have not examined the potential confounding influence of BP or sex on arterial diameter in athletes. Future studies should report data for males and females separately to ensure that the effect of sex can be assessed, particularly for female athletes where there is currently a lack of available data. The search and filtration process was unblended and limited to English-language studies, which may introduce selection bias. It should also be noted that the capacity of Egger’s regression test to detect bias is limited in meta-analyses based on a low number of small trials; therefore, the results should be interpreted with caution. Similarly not all of the sixteen studies included in the meta-analysis reported on the reliability of their data, making it difficult to determine the quality of diameter measurements. We acknowledge that different methods of diameter assessment exist, ranging from single point calliper measures to advanced automated edge detection software and this variability in practice may have influenced our findings. Future studies should employ the most valid techniques[60] and report the reliability of their measurements.

Whilst athletes were grouped using a classification of sports,[19] it is unlikely that training occurs exclusively using the mode of exercise in which they compete. However, without detailed information about training programmes, it is difficult to establish conclusively that the differences presented are related solely to the training modality. Therefore, we recommend that future studies provide details about the level of experience, training intensity and volume of their participants. Finally the use of appropriate scaling techniques should be adopted, to remove the possible influence of body size and composition.

Future directions

Research is still needed to systematically document arterial changes in response to specific training stimuli, especially resistance training. The use of appropriate scaling indices should be considered when interpreting vascular data and making comparisons within and between different populations. Finally the interaction between cardiac and vascular adaptation is a key area for future research and may help to identify the mechanisms responsible for the structural arterial changes associated with exercise.

Conclusion

Our analysis supports that differences in arterial diameter are related to the specific mode of exercise training. Additionally localised differences in arterial diameter exist for each mode of exercise, which appear to be greater in peripheral vessels (brachial and femoral). This may be associated with the specific haemodynamic conditions within each vessel during exercise. Empirical research investigating arterial remodelling in response to resistance exercise is lacking and requires further investigation.

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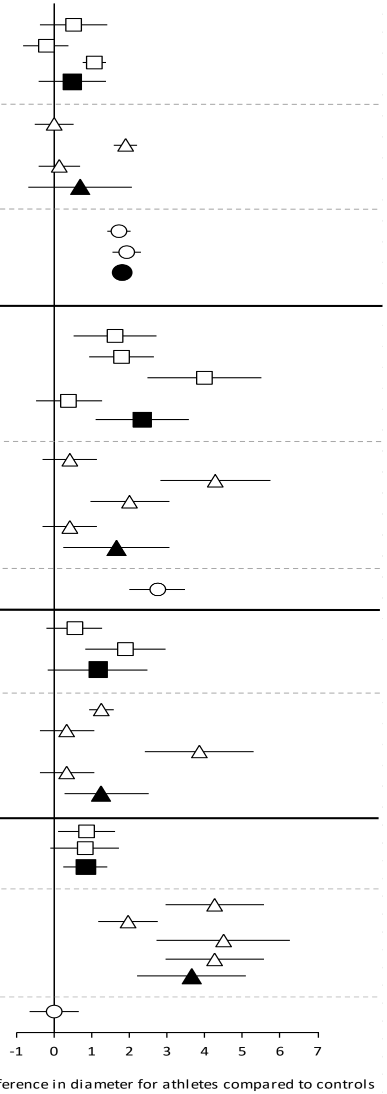
Table 1. Forest plot of the studies included in the meta-analyses of arterial diameter, grouped by exercise mode and by vessel.

Author	Year	Exercise Training Modality	Vessel	Standardized difference in means (δ)	95% CI: Lower Limit	95% CI: Upper Limit	p-Value	Forest Plot
Carlsson *et al.*	2011	ET: Cross-country skiing	Aorta	0.52	-0.37	1.41	0.25	
Dzudie *et al.*	2007	ET: Handball	Aorta	-0.22	-0.82	0.39	0.48	
Spataro	1985	ET: Football, Basketball, Long distance running;	Aorta	1.07	0.77	1.37	0.00	
META-ANALYSIS				0.48	-0.40	1.36	0.28	
Florescu *et al.*	2010	MT: Cycling, Triathlon	Aorta	0.00	-0.51	0.51	1.00	
Spataro	1985	MT: Cycling, Rowing, Canoeing;	Aorta	1.90	1.60	2.20	0.00	
Weiling *et al.*	1981	MT: Rowing	Aorta	0.14	-0.40	0.67	0.62	
META-ANALYSIS				0.69	-0.67	2.05	0.32	
Babaee Bigi & Aslani	2007	RT: Unspecified	Aorta	1.73	1.42	2.04	0.00	
Spataro	1985	RT: Weightlifting, Bodybuilding, Bobsleigh	Aorta	1.94	1.56	2.31	0.00	
META-ANALYSIS				1.81	1.58	2.05	0.00	
Rognmo *et al.*	2008	ET: Cross-country Skiing, Orienteering running, Biathlon Skiing	Brachial	1.61	0.50	2.72	0.00	
Rowley *et al.*	2011	ET; Squash	Brachial	1.79	0.92	2.65	0.00	
Walther *et al.*	2008	ET: Swimming	Brachial	4.00	2.48	5.52	0.00	
Wimer & Baldi	2012	ET: Running	Brachial	0.39	0.45	1.28	0.39	
META-ANALYSIS				1.84	0.59	3.09	0.00	
Kool *et al.*	1992	MT: Cycling	Brachial	0.42	-0.31	1.14	0.26	
Naylor *et al.*	2006	MT: Rowing	Brachial	4.28	2.83	5.73	0.00	
Walther *et al.*	2008	MT: Cycling	Brachial	2.00	0.95	3.05	0.00	
Wijnen *et al.*	1991	MT: Cycling	Brachial	0.42	-0.31	1.14	0.26	
META-ANALYSIS				1.66	0.25	3.07	0.02	
Karagounis	2009	RT: Judo	Brachial	2.74	1.99	3.48	0.00	
Rowley *et al.*	2011	ET; Squash	Carotid	0.54	-0.21	1.28	0.16	
Walther *et al.*	2008	ET; Swimming	Carotid	1.90	0.84	2.95	0.00	
META-ANALYSIS				1.16	-0.16	2.49	0.09	
Abergel *et al.*	1998	MT; Cycling	Carotid	1.25	0.91	1.59	0.00	
Kool *et al.*	1992	MT: Cycling	Carotid	0.33	-0.39	1.05	0.37	
Walther *et al.*	2008	MT: Cycling	Carotid	3.86	2.41	5.30	0.00	
Wijnen *et al.*	1991	MT: Cycling	Carotid	0.33	-0.39	1.05	0.37	
META-ANALYSIS				1.24	0.28	2.21	0.01	
Rowley *et al.*	2011	ET; Squash	Femoral	0.86	0.09	1.62	0.03	
Walther *et al.*	2008	ET: Swimming	Femoral	0.82	-0.10	1.73	0.08	
META-ANALYSIS				0.84	0.25	1.43	0.01	
Kool *et al.*	1992	MT: Cycling	Femoral	4.26	2.97	5.56	0.00	
Schmidt-Trucksass *et al.*	2003	MT: Cycling, Triathlon	Femoral	1.96	1.16	2.76	0.00	
Walther *et al.*	2008	MT: Cycling	Femoral	4.50	2.72	6.28	0.00	
Wijnen *et al.*	1991	MT: Cycling	Femoral	4.26	2.97	5.56	0.00	
META-ANALYSIS				3.65	2.12	5.10	0.00	
Schmidt-Trucksass *et al.*	2003	RT:Weightlifting	Femoral	0.00	-0.67	0.67	1.00	



ET = Endurance Trained (*Squares*); MT = Mixed Trained *(Triangles)*; RT = Resistance Trained *(Circles); Results of published studies are shown in White; Meta-analysis results are shown in black.*

Figure 1: Flow diagram illustrating the literature search process and disposition of articles screened for inclusion.

Figure 2: Difference in diameter of arteries compared to controls for endurance athletes (*white*), resistance athletes (*cross-hatchings*) and mixed athletes (*black*). * p<0.05, ** p<0.01, significant difference from control group.