Aging, physical fitness and endothelial function: are all ultracentenarians marathon runners?

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ABSTRACT
This comment focuses on the background and implications of a study published in this issue of Clinical Science by Franzoni and colleagues showing that physical training improves nitric oxide availability and microvascular distensibility not only in young, but also in elderly, individuals. The main features of the study as well as its potential limitations will be also highlighted.

This issue of Clinical Science includes an intriguing study by Franzoni et al. [1] aimed at assessing, in a consistent number of healthy subjects with an age ranging from 22 to 75 years, the relationships between age, physical training and endothelial function. This has been done by measuring circulating blood levels of nitrite and nitrate and by assessing endothelial function in the microcirculation in individuals classified according to their age and physical fitness status as young sedentaries, young athletes, old sedentaries and old athletes. The unique methodological feature of the study is represented by the laser Doppler evaluation of the blood flow patterns in the skin circulation. This has been done in the resting control state and during local heating and ischaemia in order to obtain more direct information on the effects of aging and physical exercise on vascular function at the level of the microcirculation.

Two main antecedents to this study by Franzoni et al. [1] deserve to be highlighted. First, aging is a process well known for being accompanied by a variety of cardiovascular alterations, which include increased left ventricular mass, diminished distensibility and compliance of large- and medium-size arteries, loss of renal function, decreased baroreceptor activity, decreased sympathetic activation, reduction in insulin sensitivity and impaired endothelial function [2–8]. All of these alterations are likely to be involved in the pathogenesis of hypertension of the elderly as well as in the coronary and cerebrovascular alterations which are responsible for the increased risk of myocardial and cerebral infarction characterizing aged individuals [6,7]. Secondly, physical training triggers a number of favourable cardiovascular effects, including sympathetic deactivation, increased baroreceptor activity and insulin sensitivity and an improvement in endothelial function [9–12]. Taken together, these findings represent the rationale of the study by Franzoni et al. [1], which has indeed been designed to determine whether major cardiovascular alterations characterizing the aging process, such as endothelial dysfunction and reduced arterial distensibility, can be favourably affected by physical exercise.

The results of the study by Franzoni et al. [1] are of interest, since they show that in trained young and old individuals physical fitness improves vascular nitric oxide (NO) availability and the vasodilatory properties of the microcirculation. These findings have two major implications. First, they suggest that the age-dependent alteration of endothelial function is a phenomenon widespread to the whole circulation affecting not only large- and medium-size arteries [4], but also small arterial vessels and microcirculation as well. Secondly, the data by Franzoni et al. [1] indicate that the above-mentioned endothelial vascular alterations are not irreversible, but that they can be favourably affected by physical exercise, pointing towards their dependency on an aetiological factor of functional, rather than of structural, nature. This is in line with the observation that regular physical exercise improves endothelium-dependent vasodilation at the level of the large arteries and restores vascular NO availability [13].

Key words: aging, endothelial function, nitric oxide (NO), physical exercise.
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Two further comments deserve to be made. The study by Franzoni et al. [1], although showing a significant, albeit modest, correlation between the levels of NO and the magnitude of the microvascular changes induced by physical exercise, does not allow the clarification of whether the improvement in endothelial function is the main and unique mechanism responsible for the amelioration of the vascular function seen in their study or whether other factors might participate. A likely candidate is the sympathetic nervous system, given the evidence that adrenergic cardiovascular drive (i) is increased by the aging process [5,8], (ii) undergoes a substantial inhibition during prolonged physical training [14], and (iii) may modulate endothelial function both in physiological and pathological states [15,16]. The possible participation of adrenergic neural factors is strengthened further by the observation that in man systemic infusion of \( N^G \)-monomethyl-L-arginine (L-NMMA) inhibits NO synthase and concomitantly exerts sympatho-excitatory effects [17]. Finally, it should be kept in mind, that a ‘chronic’ regular aerobic training programme does not necessarily exert only favourable effects on cardiovascular function. This is because prolonged physical exercise has been shown to favour the development of left ventricular hypertrophy by exposing the heart to a pressure and volume overload [18,19]. Although regarded as a ‘physiological’ process, cardiac hypertrophy accompanying prolonged physical exercise cannot be considered as an innocent phenomenon, given the evidence of its participation in the genesis of life-threatening cardiac arrhythmias frequently detected in the ‘physically’ trained heart [20]. This may explain why longevity and physical fitness do not necessarily go hand-in-hand.

REFERENCES


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