Introduction

A statement released by the American Heart Association (Thompson, et al., 2003) reported that aerobic exercise of moderate intensity performed for 30 minutes or more per day (relevant to relative intensity of 40-60 % of maximal oxygen uptake, or absolute intensity of 4-6 METs: correspondence to relative intensity should vary according to age (physical fitness)) should be conducted on most, and preferably all, days of the week in order to prevent arteriosclerotic cardiovascular diseases and that medical services and healthcare experts should personally engage in an active lifestyles to familiarize themselves with the issues involved in maintaining lifelong physical activity and to set a positive example for patients and the public. In Japan in recent times, the top three causes of death for both males and females are cancer, cardiac diseases and cerebrovascular diseases. Among them, both ischemic heart diseases and cerebrovascular diseases are attributable to arteriosclerosis and combined they are the leading cause of death in Japan. In addition, stroke due to cerebrovascular diseases is the major event that causes elderly people to become bedridden. Thus, it is presumed that there would be a positive influence on health maintenance and enhancement for middle-aged and elderly people in Japan if the occurrence of arteriosclerotic cardiovascular and cerebrovascular diseases is restricted by actively pursuing the goals set out in the statement made by the American Heart Association.

Arteriosclerosis is classified as arteriolar arteriosclerosis due to the degeneration of arteriole
walls caused by aging, hypertension and diabetes, atherosclerosis due to subintimal deposition of atheromas in large or medium-sized arteries and medial arteriosclerosis that occurs mainly in large artery media as age-related change. The effect of aerobic exercise on the prevention of atherosclerotic disease has been proved by many epidemiological and experimental studies (Thompson, et al., 2003). In fact, a strong quantitative correlation is observed between habitual physical activity level and the risk of several chronic diseases, including coronary artery disease and coronary risk factors, such as hypertension, and non-insulin-dependent diabetes mellitus, demonstrating a graded relationship of increasing risks of the diseases with decreasing levels of the physical activity. Several prospective studies suggested that a decline in physical activity level precedes the development of arteriosclerotic diseases and that the decline is not induced by the disease. Furthermore, the fact that regular exercise is effective in reducing the risk of developing arteriosclerotic diseases has been reported as well as the biological mechanism (i.e., beneficial effects on atherosclerotic risk factor, myocardial function, coronary artery size and vasodilatory capacity, vascular tone, fibrinolysis, platelet function, and vulnerability to ventricular fibrillation) in many intervention and experimental studies. A plausible and consistent relationship between physical activity and its preventive effect on arteriosclerosis has been observed and consequently it is estimated that there should be a causal relationship between them.

This paper will discuss the effect of exercise and physical activity on the decline in arterial distensibility, which is closely related to medial arteriosclerosis of large sized arteries, mainly based on the results of our study, which targeted middle-aged and elderly people. The term ‘arterial distensibility’ is used as a generic term for the physical value including arterial wall distensibility, volume distensibility of tubular structure arteries and arterial compliance. Arterial wall distensibility (D) is the physical volume corresponding to the proportion between stress and strain per unit of length or unit of area of the arterial wall. In contrast, arterial compliance (C) corresponds to the proportion (ΔV/ΔP) between the increase (ΔP) in intra-arterial pressure (P) and the increase (ΔV) in arterial volume (V). Therefore, there is the relation of D = C/V between the arterial distensibility and arterial compliance.

2. The effects of exercise and physical activity on the age-related decrease of arterial distensibility

2.1. Age-related change in artery and systolic hypertension

Hypertension is the leading risk factor for stroke and ischemic heart disease caused by arteriosclerosis. In general, systolic blood pressure increases with age, while diastolic blood pressure decreases (Franklin, et al., 1997). Consequently, systolic hypertension with associated pulse pressure increase is frequently observed in middle-aged and elderly people. Systolic hypertension, which was at one time underestimated as an aging phenomenon, is never innocent to the human body. An increase in systolic blood pressure and pulse pressure is known to be an independent risk factor for stroke and ischemic heart disease (Beneton A, et al., 1997). The occurrence rates of stroke and ischemic heart disease rise more clearly in patients with even moderate systolic hypertension compared to normotensive people (Sagie A, et al., 1993), while it has been shown that a decline in systolic blood pressure lowers the occurrence rates of stroke and ischemic heart disease considerably (Asia Pacific Cohort Studies Collaboration, 2003).

The major reason for the increase in systolic blood pressure and pulse pressure with aging is that the buffering function of blood pressure and the bloodstream declines due to the decrease in arterial compliance caused by lesser extensibility with age-related changes in the wall of the large artery (the central artery), such as the aorta (Nichols and O’Rourke, 1998). That is, when the total systemic arterial compliance decreases, as indicated in the formula C =ΔV/ΔP, arterial inner pressure rises in a condition of a fixed cardiac output. In addition, since the function of collecting blood ejected from the left ventricle by extending the artery wall is restricted, blood pressure drops causing a decrease in bloodstream to peripheral vessels during the left ventricular diastole after a rapid rise occurs in blood pressure during the left ventricular systole. The contribution rate of the proximal aorta (ascending aorta and aortic arch) in systemic arterial compliance is about 60 % (Stergiopulos, et al., 1998) and the contribution rate of the central artery may become larger than this as the descending, abdominal and carotid arteries are included. In terms of the
In some recent studies, it has been observed that systemic arterial compliance decreases with aging (Figure 1 A), and that a decrease in systemic arterial compliance raises systolic blood pressure (Figure 1 B). In some recent studies, it has been elucidated that the decline itself in central artery distensibility can be an independent risk factor for cardiovascular diseases in hypertension patients as well as systolic hypertension (Blacher, et al., 1999, Laurent, et al., 2001).

### 2.2. Arterial distensibility and aerobic exercise capacity

Since an increase in systolic blood pressure due to the decline in arterial distensibility augments the burden on heart (afterload), and the decline in diastolic blood pressure lessens the amount of blood flowing into the cardiac muscle, cardiac functions are suppressed (Urshel, et al., 1968). The decline in arterial distensibility with aging lessens the cardiac function during exercise in particular, which might cause a decline in physical fitness (aerobic exercise capacity) (Nichols and O'Rourke, 1998). In fact, it has been suggested that there exists significant correlation between the peak oxygen uptake or maximal oxygen uptake and arterial distensibility in a wide range of age groups from youth to middle-aged and elderly people by Vaitkevicius, et al. (1993), in youth by Cameron and Dart (1994) and in middle-aged and elderly people by Tanaka, et al. (2000). Moreover, Cameron, et al. observed significant positive correlation between systemic arterial compliance and duration of incremental exercise in middle-aged and elderly people. However, all of these studies investigated the relationship between maximum exercise capability and arterial distensibility. It is presumed that whole body endurance (aerobic) capacity in submaximal exercise is more meaningful than maximal physical capacity to daily vital functions in the majority of middle-aged and elderly people. Thus we have examined the relationship between aerobic capacity and systemic arterial compliance in middle-aged and elderly people during submaximal exercise, and clarified that aerobic capacity (oxygen uptake at the ventilatory threshold level) is low in middle-aged and elderly people as the value of systemic arterial compliance declines (Figure 2: Otsuki, et al., 2003), which means that the decline in distensibility of the central artery is one of the factors to restrict vital function in the every day lives of middle-aged and elderly people.

### 2.3. Arterial distensibility, exercise and physical activity

the relationship between systemic arterial compliance and aerobic exercise capacity

Figure 2

The relationship between systemic arterial compliance and daily physical activity

Figure 3

A causal correlation. However, it is known that arterial distensibility increases through aerobic exercise training, according to some longitudinal studies (Cameron and Dart, 1994, Tanaka, et al, 2000, Kakiyama, et al., 2001, Ohtsuki, et al., 2003, Kakiyama, et al., 2005). In contrast, carotid artery distensibility decreases in people who continue high-resistance training (Miyachi, et al., 2003) and is reported to decrease due to high-resistance training (Miyachi, et al., 2004).

In our examination using multivariate analysis with arterial distensibility, age, daily physical activity level, or risk factors for arteriosclerosis including hyperlipemia as variables (Kakiyama, et al., 1998b, Tanabe, et al., 2003a, 2004), it is indicated that physical activity volume can have the effect of decreasing systolic blood pressure significantly by restricting the decline in artery distensibility with aging. In addition, when examining the relationship between physical activity volume and systemic arterial compliance in middle-aged and elderly people, including those with a higher level of daily physical activity (such as belonging to a "walking circle"), it is suggested that systemic arterial compliance is higher for those for whom the amount of physical activity is larger (Figure 3, in submitting). In Figure 3, the relationship between physical activity volume and systemic arterial compliance is shown by a logarithm regression curve, as the effect of physical activity volume seems to be nonlinear and has an upper threshold. That is, although systemic arterial compliance increases linearly when the amount of physical activity is low, the effect plateaus when the amount of physical activity exceeds 200-300 kcal per day and appears not to increase any more. The American College of Sports Medicine (Pate, et al., 1995) recommends a physical activity level of 200 kcal per day in order to improve physical fitness and to prevent disease. In the studies of Paffenbarger, et al. (1978, 1986), it was indicated that although people with a physical activity level of more than 2000 kcal per week live longer than those whose level was under 500 kcal per week, the heart attack occurrence rate is the lowest for those with a physical activity level of 2000-3000 kcal per week. It was also indicated that the rate of risk becomes rather higher when the physical activity level is more than 4000 kcal per week. Therefore, it is not necessarily true that more physical activity will lead to health benefits. Aerobic exercise of around 200-300 kcal per day is enough for middle-aged and elderly people. Even if they do more than that, an effect matching the amount of increase cannot be expected.

Exercise intensity (energy consumption per unit of time) can influence the effects of exercise, as well as total energy consumption. It has been elucidated that aerobic exercise training with above moderate
intensity increases arterial distensibility (Cameron and Dart, 1994, Tanaka, et al., 2000). The American Heart Association suggests exercise of 4-6 METs for 30 minutes per day as moderate intensity exercise (Thompson, et al., 2003). The American College of Sports Medicine recommends a similar figure (exercise of 3-6 METs) as moderate intensity exercise (Pate, et al., 1995). It is desirable for middle-aged and elderly people to do effective lower intensity exercise that can be performed safely and easily. Thus, we defined moderate intensity exercise that can be performed safely and easily by middle-aged and elderly people as 3-5 METs and compared the effects of different durations of low intensity (under 3 METs), moderate intensity and high intensity (above 6 METs) exercise on arterial distensibility through multivariate analysis by using cross-sectoral data. A significant effect on arterial distensibility was not observed in lower intensity exercise, while a significant effect was observed in middle intensity exercise and it has been suggested that the effect is independent of the total amount of activity and the amount of high intensity activity. A significant effect was observed even during exercise of 3-4 METs intensity, particularly in elderly people (Figure 4). Blair, et al. (1989) studied the relationship between aerobic capacity and death rate and indicated that there is an upper threshold in the effect of physical activity on the decline in death rate and that continuous moderate intensity exercise for about 30 minutes per day is enough to maintain necessary physical fitness. Thus, it is presumed that exercise for the improvement of health should not necessarily be performed at high intensity.

In our longitudinal examination, the effect of comparatively light intensity exercise on arterial distensibility was also acknowledged. Central arterial distensibility and aerobic capacity increased and systolic blood pressure declined in middle-aged and elderly people six months after starting twice-weekly sports lessons that involved light intensity aerobic training and muscular strength training (Kakiyama, et al., 2001). Moreover, both systemic arterial compliance and aerobic capacity (the amount of oxygen consumption at the ventilatory threshold) increased significantly and systolic blood pressure declined in middle-aged and elderly people who performed aerobic exercise (30 minutes per day, 5 times per week) at 80% of the ventilatory threshold using a bicycle ergometer, 12 weeks after starting the exercise (Otsuki, et al., 2003). Thus, it was indicated that aerobic training of light-to-middle intensity improves arterial distensibility and aerobic capacity in a relatively short time. In contrast, significant alteration was not observed in arterial compliance and ventilatory threshold in a study targeting elderly people 70 years of age and older (Otsuki, et al., 2005). Therefore, it is assumed that the effect of exercise on arterial distensibility becomes less with aging. However, as shown in Figure 5 (which covers subjects from 60 to 77 years of age collectively), systemic arterial compliance and ventilatory threshold

![Figure 4](image_url)

**Figure 4** Effect of moderate-intensity (3-4 METs) physical activity on systemic arterial compliance in the elderly (65 yrs <)

![Figure 5](image_url)

**Figure 5** Effect of aerobic training on systemic arterial compliance in the elderly
arterial compliance and systolic blood pressure returned to the previous level one year later following a decrease in physical activity volume (Figure 6). Moreover, arterial distensibility that increased during an eight-week aerobic training programme returned to the former level in the fourth week after stopping training in an intervention experiment for younger people (Kakiyama, et al., 2005). This means that it is necessary to build up a habit of physical activity or continue aerobic exercise training in order to maintain the improved arterial distensibility level. The fact that a positive effect on health can be achieved by adopting a more active lifestyle, even after reaching middle or elderly age, has been reported as in the study of Paffenbarger, et al. (1993).

2.4. Presumptive mechanism of effects of aerobic exercise on arterial distensibility

The decline in arterial distensibility with aging is considered to be caused by the age-related progress of organic change, including the alteration and decrease in elastic fibers that are the main elastic component of arterial wall media and the increase in collagen fibers (Nichols and O’Rourke, 1998). The decline in aorta distensibility was restrained as the age-related alteration of elastic fibers was restrained due to exercise in an experiment using young rats (Matsuda, et al., 1988, 1989, 1993). However, the effect of exercise on the alteration of elastic fibers was not apparent in older rats (Nasaka, et al., 2003) and for humans that live longer and whose degree of age-related organic change is large there seems to be less possibility of restoring elastic fibers through exercise training over a comparatively short term, from several months to half a year. As mentioned above, the increase in arterial distensibility disappeared after a short period due to cessation of exercise training in our study of middle-aged/elderly people and young people (Kakiyama, et al., 2005). Therefore, it is assumed that some different factors, apart from organic changes to the arterial wall, may be related to the effect emerging in the short-term exercise. Smooth muscle in arterial wall media controls artery diameter by changing tension, through contraction and relaxation, and the tension of smooth muscle also affects the hardness of the arterial wall. Smooth muscle tension is controlled by autonomic nervous activity and by a vasoactive substance (e.g. nitric oxide and endothelin-1).
produced by endothelial cells. The increase in sympathetic activity mainly causes contraction of smooth muscle, while nitric oxide causes it to relax and endothelin-1 to contract. Since endurance exercise training suppress sympathetic nervous system activity at rest (Jennings, et al., 1997), it is undeniable that there is a possibility for central artery sympathetic activity to suppress as well. Exercise training is also known to affect arterial endothelial function (Walther, et al., 2004) so that it is possible for these functional factors to be involved in the alteration mechanism of arterial wall distensibility during short-term exercise. It has been reported that endothelium-dependent or -independent vasodilation of the brachial artery increases in middle-aged and elderly people who continue aerobic exercise of high intensity (Rywik, et al., 1999), and a significant correlation is observed between physical activity volume and endothelin-dependent vasodilation of the brachial artery in middle-aged and elderly postmenopausal women (McKechie, et al., 2001). In an animal experiment, mRNA of nitric oxide synthase and protein expression was observed to advance in aortic tissues due to aerobic exercise training (Delp and Laughlin, 1997). The result of our experiment, where older rats were made to exercise (Figure 7), indicates age-related decrease in nitric oxide synthase function, as nitric oxide synthase gene and protein expression in aortic endothelium was less in older rats compared to young rats, while the synthase function improved during 8 weeks of aerobic training (Tanabe, et al., 2003b). In addition, nitrite/nitrate concentration in the blood increased in middle-aged and elderly people after 12 weeks of aerobic training (Maeda, et al., 2004) and endothelin-1 concentration in the blood declined (Maeda, et al., 2003). Nitrite/nitrate in the blood returned to the level it had been before training was begun when exercise was intermitted (Maeda, et al., 2004). These results elucidate a part of an exercise effect mechanism and show the basis for improving the effect of exercise on the age-related decrease in arterial wall distensibility at the same time. It is also undeniable that there are possibilities for the stimulus of short-term exercise to affect cross-links of collagen fibers which are a strong limiting factor of arterial wall distensibility along with elastic fibers (Tanaka, et al., 2000) and to increase arterial wall distensibility by promoting the new formation of elastic fibers rich in elasticity.

3. Conclusion

Both the results of previous studies and of our own study lead to the following conclusion. That is, in order to prevent further hardening of arteries, to decrease the risk of lifestyle related diseases and to maintain and enhance vital functions in middle-aged and elderly people, it is desirable: 1) to increase the activity mass (energy consumption) of aerobic exercise, aiming for 200-300 kcal per day; 2) to do
more than 30 minutes of middle intensity exercise per day as part of that exercise; and 3) to ensure continuation of this appropriate amount of physical activity and exercise.

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References


Prevention of Arteriosclerosis