Circulatory Functions to Maintain Physical Activity of Daily Life in Elderly People

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To maintain physical fitness to perform daily physical activity in the elderly, the circulatory function to perform exercise should be preserved. However, it declines with age and impairs endurance exercise performance in sedentary people. Based upon the concept that exercise capacity should be estimated as ability to continue exercise without serious circulatory stress, a new testing protocol was proposed. It consisted of determining the load for initiation of steeper blood pressure elevation during graded exercise (BP_critical). BP_critical decreased with advancing age in sedentary adult people. The decline in BP_critical was not related to age-associated change in muscle mass, and was considered to be determined by the changes with age in muscle metabolism and peripheral circulation. To continue exercise, oxygen supply is a key factor and blood flow is a major determinant. When the exercising muscle mass was small or the exercise intensity was low, the blood supply to the exercising limb did not differ in older people compared to younger people. In contrast, the vasodilatory response to exercise or to vasodilatory substance was impaired in sedentary older people with concomitant change in vascular structure such as thickening of intima-media thickness, widening of vessel diameter, etc. These age-associated declines in peripheral circulation and vessel structure are prevented by regular exercise, allowing circulatory function to be preserved in the elderly.

Keywords: limb blood flow, blood pressure, regular exercise, vessel structure, vasodilatory capacity

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1. Introduction

Daily physical activity puts stress on the cardiovascular system, such as blood pressure elevation, heart rate increase, peripheral vessel constriction, etc. The magnitude of stress depends on the physical activity of the person (the intensity/duration of exercise, muscle mass recruited in the activity, posture changes, etc.) on one hand, and on the cardiovascular function of the person on the other. As such, improving cardiovascular function will contribute to maintaining or increasing physical fitness to perform daily physical activity. The purpose of this review, therefore, was to discuss the circulatory function to perform prolonged work from the view point of maintaining physical activity of daily life in ordinary elderly people with respect to peripheral circulation and vascular structure.

2. Cardiovascular responses to daily life

As a basis for considering cardiovascular capacity required for performing physical activity of daily life, knowledge has been accumulated on the cardiovascular response to daily life using heart rate and blood pressure as indices (Cavelaars, et al., 2004, Green & Madigan 2002, Tsai, et al., 2003, Van Egeren 1991).

As already accepted, the heart rate increases linearly related to the increase in exercise intensity. Blood pressure has been another parameter for mobility frequently used in the study of daily physical activity (Cavelaars, et al., 2002, 2004, Green & Madigan 2002, Tsai, et al., 2003, Van Egeren 1991). Van Egeren (1991) showed that it was a reliable parameter for mobility, based upon a study of body motion and blood pressure performed simultaneously.
for 24h in 82 healthy normotensive employees with sedentary jobs. He found a significant relationship between pressure and motility and concluded that skeletal motor outflow affects the regulation of blood pressure in the normal circumstances of everyday life. An example of blood pressure variation during 24 hours is shown in Figure 1 (Mancia, et al., 2003).

The absolute values of heart rate and blood pressure change depending on the physical activity level performed during the day and the physical fitness level of the subject. In addition to the absolute values, Mancia, et al., (2003) demonstrated the importance of the ramp slope of changes. In Figure 1, systolic blood pressure (SBP) and heart rate changes in normotensive and hypertensive subjects are illustrated. In their study, the SBP ramp was estimated by computing the slope of the regression line between the SBP values included in the ramp and time. The analysis was conducted for three or more consecutive beats characterized by a progressive increase or reduction. Their finding was that the ramp slope was steeper in hypertensive subjects than in normotensive subjects. This is significantly important because hypertensive people are characterized not only by a higher absolute blood pressure but by steeper blood pressure changes.

3. Blood pressure elevation as an indicator of exercise performance capacity

There have been several discussions concerning whether responses to standardized laboratory mental and physical challenges accurately reflect blood pressure variability during routine daily activities. Commonly used laboratory tests can give some information about the behavior of blood pressure in daily life (Floras, et al., 1987).

Recently Kagaya, et al., (2001) have developed a new laboratory test using blood pressure to estimate exercise performance capacity for people including elderly people. Figure 2A shows the testing protocol. Exercise was performed in a supine position after a 3-min resting condition. The exercise comprised an incremental 30-s static handgrip exercise and was discontinued after the blood pressure began to increase steeply.

Blood pressure was measured at the end of each load and was plotted against the load (Figure 2B). The load for initiation of steeper blood pressure (in most cases SBP was used) elevation (BP_{critical}) was determined as an intersection point of two regression lines; for lower loads and higher loads.

Using this protocol, BP_{critical} was measured for males and females including elderly people. Figure 3 illustrates the results from eighty-seven women, ranging in age from 50 to 83 years old (Kagaya, et al., 2001). Mean BP_{critical} calculated for each age group decreased significantly from 10.8±0.7 kgw for 50s to 8.8±0.4 kgw for 60s (p<0.05), and to 6.6 ±0.5kgw for 70s (p<0.01). The decline of BP_{critical} depends partly on reduction of daily physical activity, because a significant correlation coefficient of 0.356 (P<0.01) was obtained between number of steps/day and BP_{critical}, though only 13% of the variance could be explained by daily physical activity.

Muscle endurance performance or muscle work capacity has been assessed by the force decline rate or endurance time to maintain a given relative force (Bemben, et al., 1996, Kagaya & Ikai 1971, Petrofsky & Lind, 1975, Start & Graham 1964), and no age-associated change was observed in muscular endurance if exercise performance was estimated.
Concerning factors for age-related reduction in BP\textsubscript{critical}, the most provable candidate would be a decline of muscle strength or muscle mass, because previous literature (Start & Graham 1964) indicated that absolute muscle endurance was affected by muscle strength. However, Muraoka, et al. (2001) reported that no significant correlation coefficients were found between BP\textsubscript{critical}, muscle thickness (muscle volume), and grip strength in elderly women. They demonstrated that forearm muscle thickness did not decrease significantly in elderly women, whereas BP\textsubscript{critical} decreased with age. These results suggested that the decline of muscle strength or muscle mass might be excluded from the major determinants of age-associated reduction of BP\textsubscript{critical} though it is interesting to note that muscle strength had a close relationship to BP elevation when exercise intensity exceeded BP\textsubscript{critical} (Muraoka, et al., 2001).

There were several findings that suggested that the steeper blood pressure elevation at higher intensity would be due to activation of a metabo-receptor-mediated reflex from the exercising muscle. During static exercise, intra-muscular pressure increased with increasing exercise intensity (Sejersted, et al., 1984), and active muscle blood flow did not increase (Kagaya & Homma, 1997b) despite an augmented oxygen requirement, which resulted in miss-matching between oxygen supply and demand. Thus muscle-sympathetic nerve activity (MSNA) began to increase at higher intensity in tandem with intracellular pH (Victor, et al., 1988, Bousehl, et al., 1998). Therefore, BP\textsubscript{critical} will reflect a nonlinear change in the metabolic and circulatory condition of

**Figure 2** Exercise protocol (A) and determination of critical load for steeper blood pressure elevation (BP\textsubscript{critical})(B). (Kagaya, et al., 2001)
A:Exercise comprised an incremental 30-s static handgrip exercise separated by 30-s recovery. The initial load was 1kg and 2kg for females and 2.5kg for males, respectively. Thereafter the load was increased by 2kg for females, and 2.5kg for males every 60s until the blood pressure began to increase markedly.
B:BP\textsubscript{critical} was determined as an intersection point of two regression lines using SBP.
SBP: Systolic blood pressure, MBP: Mean blood pressure, DBP: Diastolic blood pressure
BP\textsubscript{critical}:Critical load for steeper blood pressure elevation

**Figure 3** Age-dependent changes in load at BP\textsubscript{critical} in females (Kagaya et al. 2001).
50s: subjects aged in range 50-59 years old
60s: subjects aged in range 60-69 years old
70s: subjects aged in range 70-83 years old.
*, **: p<0.05, p<0.01 vs 50s
###: p<0.01 vs 60s
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This is an important reason why high BP_{critical} is recommended for elderly people to maintain daily physical activity. Physiological changes in peripheral circulation and vasculature are discussed below.

4. Vasodilatory capacity of peripheral vessels as a major determinant of regional muscle work capacity

The effects of regular exercise on respiratory and cardiovascular function have been well established. They include the improvement of maximal oxygen uptake, cardiac output, aerobic metabolism in the muscle, etc. Furthermore, an increase in energy consumption contributes to prevention of obesity. Among these favorable effects of regular exercise, an improvement of endurance exercise performance capacity of limb muscles is expected (Kagaya & Ikai 1971, Martin, et al., 1991).

To improve muscle endurance capacity, the amount of blood flow to exercising muscles is the most important determinant, because it predominantly regulates the transport of oxygen to exercising muscles (Ikai & Taguchi 1969, Palmieri, et al., 2005).

This section deals with age-associated change in 1) blood flow to the exercising limb, and 2) vessel structure and function.

4.1. Effects of ageing on limb blood flow and vasodilatation

Basal whole-limb blood flow and vascular conductance declined progressively across the adult age-range in both healthy men (Dinenno, et al., 1999, 2001, Proctor, et al., 2003) and women (Moreau, et al., 2003). In contrast, vascular resistance increased with age (Dinenno, et al., 1999, Proctor, et al., 2003). Interestingly, in postmenopausal women, leg blood flow was 23% lower compared with premenopausal women, whereas only 13% lower in women using hormone replacement (Figure 4).

Next, vasodilatory capacity was discussed as a key factor to support prolonged exercise or adaptability to various stresses. This capacity has been evaluated using exercise alone or arterial occlusion immediately after exercise (Kagaya 1994, Martin, et al., 1991, Poole, et al., 2003, Sinoway, et al., 1986, 1987, Snell, et al., 1987), flow-mediated dilatation (Eskurza, et al., 2004), or by infusion of a vasodilator substance (Eskurza, et al., 2004, DeSouza, et al., 2000, Taddei,

![Figure 4](image-url)

**Figure 4** Differences in femoral artery blood flow, vascular conductance and vascular resistance in premenopausal, and treated and untreated postmenopausal women (Moreau, et al., 2003)

Resting femoral artery blood flow (A), femoral vascular conductance (B) and femoral vascular resistance (C) in premenopausal women (Pre) and in postmenopausal women using hormone replacement therapy (Post HRT) and not using HRT (Post No-HRT). *P < 0.001 vs. Pre; †P < 0.05 vs. Post, No-HRT.

exercising muscles.

Taken together, the age-associated decline in BP_{critical} will be related to changes in muscle metabolism and peripheral circulation with age.
et al., 2001). Some studies indicated that peak blood flow (Kagaya & Homma, 1997a, Jasperse et al., 1994) or blood flow during submaximal exercise (Proctor, et al., 2003b, Poole, et al., 2003) did not differ in the elderly compared to a young control group. However, vascular conductance decreased significantly in elderly subjects (Kagaya & Homma. 1997a). In contrast, other studies demonstrated that vasodilatory capacity was reduced with age in sedentary (Beere, et al., 1999, DeSouza, et al., 2000, Lawrenson, et al., 2003, Proctor, et al., 1998, 2003a, Taddei, et al., 2001) and active people (Proctor, et al., 1998). As indicated above, leg blood flow was preserved in sedentary old subjects compared with sedentary young subjects when exercise intensity was lower (Poole, et al., 2003) (Figure 6). However, when exercise intensity increased, leg blood flow at a given work intensity was attenuated in older subjects. Similarly, vasodilatation to acetylcholine was different in young and old subjects (DeSouza, et al., 2000). As seen in Figure 7, vasodilatation was inhibited in older people (Taddei, et al., 2001) and flow-mediated vasodilatation (FMD) was also impaired in older sedentary men compared with younger sedentary men (Eskurza, et al., 2004).

Figure 5 Reduction of vascular conductance in brachial artery in elderly women (Kagaya & Homma, 1997a). 20s, 40s, 60s: 20-29 years old, 40-49 years old, 60-69 years old, respectively. ■; Baseline, □; post-exercise. Vascular conductance of 60s was significantly lower compared to 20s (*p<0.05) and 40s (#p<0.05).

Figure 6 Relationship between cycle work rate (WR) and leg blood flow (A), arterial-venous O₂ difference (B), and leg O₂ consumption (O₂; C) in young and old subjects. (Poole, et al., 2003) Significantly different response at submaximal (#)WRs, and at maximal (*) WR in old subjects.

Exercise using small muscle mass.

However, it would be attenuated in older people when maximal or near-maximal vasodilatation is challenged in a situation such as exercise at high intensity or exercise using larger muscle mass, during infusion of vasodilator substance.

A possible physiological mechanism to explain reduced vasodilatory capacity includes augmented muscle sympathetic activity (Moreau, et al., 2003), inhibited response to vasodilatory substances or reduced NO availability (Taddei, et al., 2003), attenuated exercise pressor reflex (Markel, et al., 2003), and increased oxidative stress (Eskurza, et al., 2004) in older people. The finding that the blood flow was lower in postmenopausal women
and hormone replacement therapy prevented this reduction (Moreau, et al., 2003) suggests that hormonal change should be added as one of the candidates to reduce blood flow in older women. These age-associated changes in peripheral circulatory function will induce blood pressure response to graded exercise and result in a decline in BPcritical. Additionally, structural changes in the vessel (Dinenno, et al., 1999, Tanaka, et al., 2002) will influence the vasodilatory capacity, as discussed in the following section.

4.2. Age-associated changes in vessel structure


One of the major modifications of the vessel with advancing age was widening of the arterial diameter and reduction of blood flow velocity at the baseline (Salmasi & Dore 1995, Shimizu, et al., 2000a, 2001, Shimizu & Kagaya 2004) and during exercise (Salmasi & Dore 1995) in the central and peripheral artery. Shimizu & Kagaya (2004) examined 515 healthy women ranging in age from 18-88 years and found in both the carotid and brachial arteries that the diameter became significantly larger over the age of 50 years, whereas mean blood flow velocity in the carotid artery became lower with age (Figure 8). The enlargement became prominent when baseline blood pressure exceeded approximately 170 mmHg (Shimizu, et al., 2000b). Vessel diameter was inversely related to blood flow velocity both in the carotid (p<0.001) and brachial arteries (p<0.01)(Shimizu & Kagaya 2004). This finding suggests that the age-associated enlargement of the vessel will result in reduction of
endothelium-dependent vasodilatation, because of the reduced shear stress due to slower blood velocity in older people.

Additionally, thickening of the arterial wall with advancing age has been reported in the femoral artery (Dinenna, et al., 2000) and carotid artery (Tanaka, et al., 2002). Femoral artery IMT significantly increased in older men (Dinenna, et al., 2000, Tanaka, et al., 2002), both in sedentary and endurance-trained people (Tanaka, et al., 2002) (Figure 9). Although the diameter of the lumen became larger with advancing age (Shimizu & Kagaya 2004), IMT standardized by the diameter of the vessel was still larger in older men. Interestingly, older subjects who showed higher muscle sympathetic nerve activity (MSNA) had a thicker IMT in the femoral artery than those with lower MSNA (Dinenna, et al., 2000). However, direct evidence to show the influence of ageing on the relationship between MSNA and IMT has not been obtained.

These changes in vessel structure would influence arterial stiffness (Tanaka, et al., 2000), and thus would change the vasodilatory capacity and amount of blood flow supplied to the muscles with advancing age.

5. Effects of regular exercise on vasodilatory capacity and vessel structure in elderly

The effects of regular exercise on cardiovascular function in the elderly have been well documented in the literature (Spina 1999, Kallinen, et al., 2002). Furthermore, improved physical fitness due to training was clarified to increase and maintain physical activity in daily life of older adults (Fujita, et al., 2003), which will lead to improvement in quality of life.


Recent cross-sectional studies of trained and untrained or fit and unfit people, or intervention studies, have increased our knowledge on this topic in the elderly. One of the most important findings is that regular exercise will preserve vasodilatory capacity in elderly (Beere, 1999, DeSouza, et al., 2000, Eskurza, et al., 2004, Ho, et al., 1997, Martin, et al., 1991, Tanaka, et al., 2000) in skeletal muscles. Vasodilatory capacity was estimated by measuring maximal hyperemia after ischemic exercise or vasodilation caused by infusion of a vasodilator substance. Using ischemic exercise, Martin, et al., (1991) demonstrated that maximal leg hyperemia in trained older people was significantly higher than in sedentary older people. The studies on vasodilatory response to acetylcholine or ascorbic acid infusion demonstrated that regular exercise prevented the age-associated decline in metabolic vasodilation (DeSouza, et al., 2000) or flow-mediated vasodilation (Eskurza, et al., 2004).

DeSouza, et al., (2000) showed that the vasodilator response to acetylcholine in endurance-trained older men (50-76 years) did not differ from that in young endurance-trained men (Figure 10). They concluded that endothelium-dependent vasodilatation
was well preserved in men who regularly performed aerobic exercise. This conclusion was strongly supported by their additional, longitudinal training study. Middle-aged and older sedentary men (56±2 years) participated in a 3-month exercise training program, which consisted of 42 minutes of aerobic exercise at an intensity of 72% maximal heart rate (HRmax), conducted 5.5 days per week (on the average). After training, forearm blood flow and vascular conductance responding to acetylcholine was augmented (Figure 11).

In line with their study, Beere (1999) reported that older (60-74 years of age) subjects increased the peak and leg blood flow by 50% after three months of aerobic training at 75-90% of their HRmax. Although Olive, et al., (2000) showed that maximal blood flow was activity-dependent and not aging-dependent, the vasodilatory capacity of trained older people was less than that of trained younger people, as reviewed above. The interaction of ageing and physical activity effects on vasodilatory capacity remains to be studied further.

Interestingly the redistribution of blood flow to various organs differed between young and old, and between fit and sedentary subjects (Ho, et al., 1997). The reductions in splanchnic and renal blood flow were attenuated in sedentary older subjects than in younger and older fit subjects. Further study should be performed on this topic.

The mechanism to preserve vasodilatory capacity in elderly people who perform regular exercise has not definitely been determined yet. However,
changes in endothelium function to produce vasoconstrictor and vasodilator substances due to training is included as a possible mechanism (Maeda, et al., 2003, 2004).

In addition, the effect of exercise on vessel structure could not be excluded to explain the preserved vasodilatory capacity in trained elderly people. Tanaka, et al., (2002) clearly demonstrated that regular exercise prevents the increase in IMT of the carotid artery in older men (Figure 9), though the training effect was site-specific (Moreau, et al., 2002). In addition, physically active healthy older people showed a reduced arterial stiffness and an augmented flow-mediated vasodilatation compared to sedentary older people (Eskurza, et al., 2004, Tanaka, et al., 2000). Therefore, it is reasonable to suppose that the vessel property changes due to regular exercise have a significant role in maintaining blood flow during exercise in older people.

6. Summary

To maintain physical fitness to perform daily physical activity in the elderly, the circulatory function to perform exercise should be preserved. The findings on age-associated changes in circulation in sedentary people and effects of regular exercise on the peripheral circulatory function are summarized as follows;

1. A critical load for steeper blood pressure elevation (BP_critical) for increasing exercise loads has been proposed as an indicator of muscle work capacity. Age-associated decline in BP_critical was found in elderly people.
2. When the exercising muscle mass was small or exercise intensity was low, blood supply to the exercising limb did not differ in older people compared to younger people.
3. The vasodilatory capacity in response to exercise or vasodilatory substance was reduced at baseline and during exercise in sedentary older people.
4. Intima-media thickness increased with age in the carotid and femoral arteries of older people, suggesting the reduction of arterial compliance. The widening of the vessel diameter was observed in the brachial and carotid artery, whereas blood flow velocity became slower with age, suggesting that the stimulus to endothelium to produce vasodilatory substance became less.
5. There are several findings to show that regular exercise prevents these age-related declines in circulatory functions. These include preserved limb blood flow in response to exercise.
exercise or vasodilatory substance and reduced intima-media thickness in the artery.

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