

Impairment of the Postural Venoarteriolar Reflex in Aged Individuals

MONIKA GNIADÉCKA¹, ROBERT GNIADÉCKI², JØRGEN SERUP^{1,2} and JØRGEN SØNDERGAARD¹

¹Bioengineering and Skin Research Laboratory, Department of Dermatology, Bispebjerg Hospital, Copenhagen, University of Copenhagen and ²Department of Dermatological Research, Leo Pharmaceutical Products, Ballerup, Denmark

The venoarteriolar vasoconstriction reflex plays a major role in the prevention of leg oedema in the upright position in man. We studied the venoarteriolar vasoconstriction reflex with laser Doppler flowmetry in young (21 subjects, age 17–27) and very old (20 subjects, age 75–100) healthy volunteers. In the group of young volunteers, after lowering of the lower extremity 50 cm below the heart level, cutaneous blood flux decreased to 16.6% of the baseline, whereas in the group of old persons the venoarteriolar reflex was impaired and the flux decreased only to 29.2%. The difference between the two groups was statistically significant ($p < 0.001$). These results may explain the increased prevalence of postural oedema in old people. **Key words:** skin blood flow; laser Doppler flowmetry; oedema.

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M. Gniadecka, Laboratory of The Bioengineering and Skin Research Laboratory, Department of Dermatology, University of Copenhagen, Bispebjerg Hospital, Bispebjerg Bakke 23, DK-2400 Copenhagen, Denmark.

A change from the supine to the standing position causes a profound fall in limb blood flow due to constriction of precapillary sphincters in cutaneous, subcutaneous and muscular arterioles (1). Postural vasoconstriction in the human leg is mainly caused by a local sympathetic axon reflex, named the venoarteriolar reflex (VAR) (1, 2). Such a response acts as an oedema prevention mechanism: the increase in precapillary resistance prevents the rise in capillary hydrostatic pressure (1). In this manner excessive capillary filtration is reduced in the dependent position.

Evidence has been presented that loss of VAR contributes significantly to the development of postural oedema. Impairment in VAR has been detected after nifedipine administration (3), in chronic venous insufficiency (4, 5) and in the premenstrual syndrome (6). In these instances enhancement of oedema formation has also been noted.

Due to the fact that by the end of the day ankle oedema is seen frequently in old but only rarely in young individuals, it is believed that age adversely affects mechanisms that prevent postural oedema formation (7). It has also been argued that oedema impairs skin nutrition and metabolism and thus it may have pathophysiological consequences (8). However, the reason for the enhanced oedema formation in old age has not been elucidated. As VAR is the major oedema prevention mechanism in humans, we investigated with laser Doppler flowmetry (LDF) the integrity of VAR in a group of old healthy volunteers. We propose that impairment of VAR contributes to the development of postural oedema.

MATERIAL AND METHODS

Twenty-one young (6 men, 15 women, median age 19, range 17–27) and 20 aged volunteers (6 men, 14 women, median age 85, range 75–100) entered the study after giving their informed consent. Measurements were carried out in the morning in a room where the temperature was 22–23°C, following acclimatisation of the subjects at rest in supine position for approximately 10 min. Blood flux in the skin was recorded using a laser Doppler flowmeter (PF2 Perimed, Stockholm, Sweden). An unheated probe in a standard round plastic holder was placed 10 cm above the medial malleolus and held in this position with double-sided adhesive rings (Beiersdorf, Germany). The processing filter was set at 4 kHz, the time constant at the output amplifier at 0.2 s and the gain at 10x. Skin blood flux traces were recorded initially while the subject remained in the supine position (5 min) and another 5 min following leg lowering 50 cm below the heart level. Our previous investigations showed that after this manoeuvre VAR is reproducibly and selectively activated (5), and it is known that the reflex from baroreceptors is not triggered in these conditions (2). Average values from both measurements ("flux 1" and "flux 2" [mV], respectively) were calculated. The VAR index, which is independent of the initial flux values, was expressed as follows:

$$\frac{\text{flux 1} - \text{flux 2}}{\text{flux 1}} \times 100\%$$

For statistical analysis two-sided Student's *t*-test was used. The test for independent and paired samples was employed as appropriate.

RESULTS

In the supine position the baseline blood flux (flux 1) over the medial malleolus was higher in the aged group than in the young individuals (29.2 ± 2.3 vs. 16.6 ± 2.1 , respectively, $p < 0.001$).

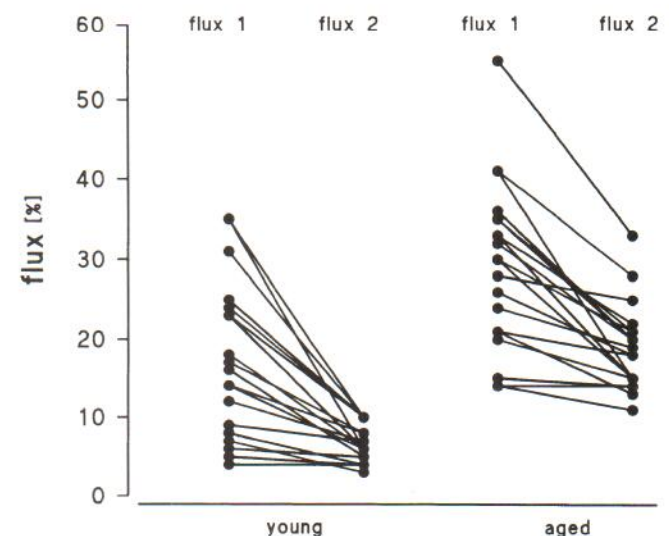


Fig. 1. Venoarteriolar reflex in young and aged group of volunteers. Dots represent blood flux recorded from single persons before (flux 1) and after leg lowering 50 cm below the heart level (flux 2).

After leg lowering a statistically significant ($p < 0.001$) decrease of blood flux was recorded in both groups (Fig. 1). However, the slope of the decrease was stronger in the young group: the VAR index equalled $49.5 \pm 4.8\%$ in the young population and 31.8 ± 3.6 in the aged one. This difference was highly significant, $p = 0.006$. The blood flux after leg lowering (flux 2) was significantly higher in the aged group (18.9 ± 12 vs. 6.7 ± 0.5 , $p < 0.01$).

DISCUSSION

Our results showed that the baseline blood flux was higher and the venoarteriolar reflex impaired in the ankle region of aged individuals.

Flux of the blood is related to the product of average speed and concentration of moving red blood cells in the tissue sample volume. Measurement of flux values with LDF is regarded as a reliable non-invasive method for evaluation of the cutaneous venoarteriolar reflex in humans, and the Perimed laser Doppler equipment used by us has been applied in numerous studies on VAR (e.g. 2–4, 6).

The increased baseline blood flux in cutaneous circulation of aged individuals was an unexpected finding. It is generally believed that tissue perfusion decreases with age, and evidence has been provided that blood supply in aged skin is significantly diminished (7, 9). However, the increased laser Doppler flux does not necessarily represent only the nutritive perfusion. For instance, increased flux has been detected in patients with venous leg ulcers, and it has been suggested that this finding results from the enhancement of flow in arteriovenous anastomoses (5, 10). Alternatively, the increased transparency of the thin senile skin and blood vessel walls might enhance penetration of laser light and possibly increase flux values.

A more intriguing finding was the impairment of VAR in the old population. Evidence exists that vasoconstriction elicited by a variety of stimuli in different vascular beds is less efficient in the elderly. For example, cutaneous vasoconstriction after application of cold to the contralateral limb (11–13) and after an inspiratory gasp (13) is attenuated in aged people. The vasoconstrictor response of the isolated subcutaneous vessels to the agonists of alpha-1 adrenergic receptors and to nerve stimulation also decreases with age (14). VAR is a local neurogenic reflex, mediated by thin C-fibres (1). The impairment of VAR is usually attributed to damage to these neural fibres. This mechanism has been extensively investigated in diabetes. In these patients the degree of VAR impairment has been proposed as a parameter of the severity of autonomic neuropathy (15, 16). In other neuropathic disorders VAR is also impaired (17). It seems likely that the observed impairment of VAR in old individuals may be caused by neurogenic mechanisms.

Impairment of VAR may have pathophysiological consequences. Ineffective counteracting of the increased transcapillary blood pressure in the upright position may promote the development of postural oedema. Oedema impairs skin oxygen consumption (18), probably by a mechanical interference with oxygen diffusion between capillaries and target tissues. Protein-rich oedema fluid is also believed to promote fibrin cuff formation around capillaries and sequester growth factors necessary

for skin growth and repair (19, 20). Experimentally evoked oedema impairs wound healing (21). Bearing in mind the link between upright posture, leg oedema and the development of lipodermatosclerosis and venous leg ulcers (22), it is conceivable that impairment of VAR in the elderly contributes to the development of these diseases.

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