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ORIGINAL ARTICLE

Impact of age and blood pressure on the lower arterial pressure limit for maintenance of consciousness during passive upright posture in healthy vasovagal fainters: preliminary observations☆

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Abstract Maintenance of consciousness importantly depends on systemic arterial blood pressure (BP) remaining above the lower pressure limit for cerebrovascular autoregulation. This study evaluated the impact of age and baseline arterial blood pressure (BP) on the BP recorded at onset of syncope in otherwise healthy individuals undergoing passive head-up tilt (HUT) testing for suspected vasovagal syncope. Since hypertension is thought to shift the lower autoregulation point to higher values, and since older healthy patients tend to have higher BP than younger individuals, we hypothesized that even among healthy individuals HUT-induced syncope would occur at higher BP in older compared with younger subjects. Three groups of otherwise healthy individuals who had positive HUT were identified: Group 1: <25 years, $n = 17$; Group 2: 25–59 years, $n = 18$; and Group 3: ≥ 60 years, $n = 7$. As expected, baseline arterial systolic blood pressure of patients ≥ 60 years (162 ± 37 mmHg) was significantly higher than in the other two groups (Group 1: <25 years, 116 ± 15 mmHg; Group 2: 25–59 years, 128 ± 12 mmHg). Further, the ≥ 60 age group tolerated upright posture for a longer period before syncope than did younger patients. However, despite a trend for BP at syncope to increase with age, differences were small (Group 3: ≥ 60 years, 61 ± 15 mmHg, Group 2: 25–59 years, 58 ± 6 mmHg, and Group 1: 54 ± 16 mmHg) and were not statistically

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significant. Thus, in generally healthy individuals, age and baseline BP has only a minor effect on the lower limit of BP necessary for maintenance of consciousness. On the other hand, higher baseline BP provides older individuals a greater blood pressure 'reserve' for maintenance of consciousness compared with younger subjects.
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Introduction

Maintenance of consciousness importantly depends on maintaining systemic arterial pressure at a value greater than the lower limit of cerebrovascular blood flow autoregulation [1—5]. In this regard, previous studies suggest that disease related factors (particularly hypertension) shift the lower limit of cerebral autoregulation upward to higher blood pressure levels [2—5]. Based on these observations, we hypothesized that since ageing tends to be associated with higher baseline arterial blood pressures, the lower limit of cerebral autoregulation would be higher in generally healthy older individuals than in younger subjects. To assess this hypothesis, we evaluated the impact of age and baseline arterial blood pressure (BP) on the arterial pressure recorded at onset of syncope in otherwise healthy individuals undergoing head-up tilt (HUT) testing for suspected vasovagal syncope. We expected that syncope induced during head-up tilt-table testing (HUT) would occur at higher systemic arterial pressures in older individuals, and that this effect would have an impact on orthostatic tolerance of various age groups.

Methods

The study population comprised only apparently healthy patients who developed head-up tilt (HUT) induced syncope during diagnostic testing for evaluation of syncope of unknown origin, and in whom an intra-arterial line was used to document blood pressure during testing. In each case the medical history suggested a neurally mediated vasovagal faint as the cause of syncope, but head-up tilt testing was recommended in an attempt to substantiate the diagnosis. All patients were free of structural heart (including left ventricular hypertrophy) or cardiovascular disease as assessed by medical history, physical examination, electrocardiogram and echocardiogram. None of these patients was considered hypertensive prior to this evaluation.

All data and end-points were collected prospectively in patients undergoing tilt-table testing. However, in order to insure a relatively healthy study population, patients were excluded from this analysis if they were taking any cardiac or antihypertensive medications on a long-term basis, apart from aspirin. In particular, care was taken to exclude patients with diastolic hypertension (defined as a resting diastolic pressure >90 mmHg in the absence of medications) or significant systolic hypertension (>165 mmHg in the absence of medications), diabetes mellitus, suspected primary autonomic dysfunction, or suspected orthostatic syncope.

Written informed consent was obtained of all patients prior to commencing HUT, using an investigational review board/ethics committee approved document. All cardioactive medications were withheld for approximately 48 h prior to study. In brief, the HUT protocol comprised an equilibration period in the supine position of 20—30 min following placement of intra-vascular cannulae, after which patients were tilted to 70 degrees head-up position [6,7]. The study was terminated at the point at which loss of consciousness occurred or at onset of intolerable pre-syncopal symptoms associated with systemic hypotension with or without overt bradycardia. Patients were returned to the supine position at test termination.

Systolic blood pressure (BP) and heart rate (HR) were measured continuously throughout the study. For purposes of analysis five time points during upright posture were selected: (1) 0%, baseline upright position, (2) 25% of time to syncope, (3) 50% of time to syncope, (4) 75% of time to syncope, and (5) 100%, at the onset of the syncopal event. Percent time of HUT was used instead of absolute clock time in order to permit patient-to-patient comparison, since individual patients became syncopal at different time points during the period of upright posture.

The tip of the fluid-filled intra-arterial cannula system (placed via percutaneous access to the femoral artery) was positioned at approximately the level of the renal arteries. This introduced a potential consistent (across all patients) measurement error due to vertical displacement between the renal arteries and the carotid arteries. This error was minimized by placement of the pressure transducer at approximately shoulder level with the patient in the upright position.

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Data analysis

All data are reported as mean ± standard deviation (SD). The study population was divided into three age groups: Group 1: <25 years ($n = 17$), Group 2: 25–59 years ($n = 18$), and Group 3: ≥60 years ($n = 7$). To account for multiple measurements, ANOVA was used to determine significant differences between the groups. A P value <0.05 was considered to be statistically significant.

Results

Data from 43 patients (11 males and 32 females) were evaluated. Patient age ranged from 13 years to 82 years.

Baseline blood pressure

In the baseline upright position, approximately one minute after assumption of upright posture, the mean arterial systolic blood pressure of patients ≥60 years was 162±37 mmHg. This value was significantly higher than were comparable measurements in either patients 25–59 years, 128±12 mmHg ($P = 0.0312$), or patients <25 years, 116±15 mmHg ($P = 0.0063$). Diastolic pressures did not differ across groups.

During the initial course of exposure to upright posture (i.e., at 25% and 50% of HUT duration), patients ≥60 years (Group 3) maintained an arterial systolic blood pressure significantly greater than that recorded in younger patients (Fig. 1). Subsequently, however, as pressures fell toward values associated with syncope, differences tended to vanish.

Arterial systolic blood pressure at syncope

At syncope (i.e., 100% HUT duration) there was a trend toward higher arterial pressure values in patients who had the higher baseline arterial pressures, but differences were not statistically significant (see Fig. 2). Similarly, age-related differences were small and not statistically significant (Group 3, ≥60 years, 61±15 mmHg; Group 2, 25–59 years, 58±6 mmHg; and Group 1, 54±16 mmHg) (Fig. 3, lower panel). However, age-related difference in blood pressure 'reserve' (Fig. 3, upper panel) was more clear, and appeared to increase with increasing age (Mann–Whitney U test: Group 1 vs Group 2, P = NS; Group 1 vs Group 3, $P = 0.0008$; Group 2 vs Group 3, $P = 0.0085$).

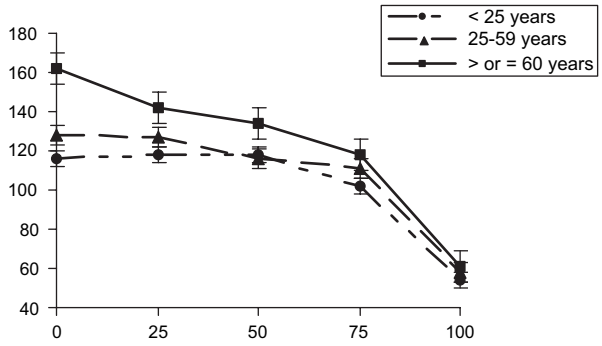


Figure 1 Graph depicting the mean systolic BP for each of the three patient age groups vs the % time to syncope (0% represents baseline upright of HUT and 100% time represents syncope). The systolic BP of patients in the ≥60 age group was significantly (P<0.05) greater than that of the two younger groups at 0%, 25% of HUT and at 50% of time to syncope compared to patients, <25 years. At syncope, the mean systolic BP of the three groups was not significantly different, although there was a trend for older patients to faint at higher pressures than did younger patients (see Table 1).

Heart rate

Mean heart rates, and heart rate changes during HUT did not differ significantly in the three groups (Fig. 3). Heart rates tended to rise from tilt initiation to 75% of HUT duration. Not unexpectedly, the greatest decline in HR was seen between 75% of HUT duration and syncope onset (100% HUT duration) in all groups.

HUT duration

The duration of HUT prior to onset of syncope tended to increase with age (Table 1). Thus, on average the healthy ≥60 age group tolerated upright posture longer than did healthy younger patients (duration 26±18 min, vs Group 1 10±2 min and Group 3 15±3 min, both $P = 0.003$).

Discussion

This study examined heart rate and blood pressure responses to HUT in apparently healthy individuals of various ages who were suspected of having a diagnosis of vasovagal syncope. Not unexpectedly, otherwise healthy patients ≥60 years of age had a mean baseline arterial systolic pressure higher than was present in younger individuals. It was expected, based upon previous reports [2–5,8–11], that this age-related tendency would translate into

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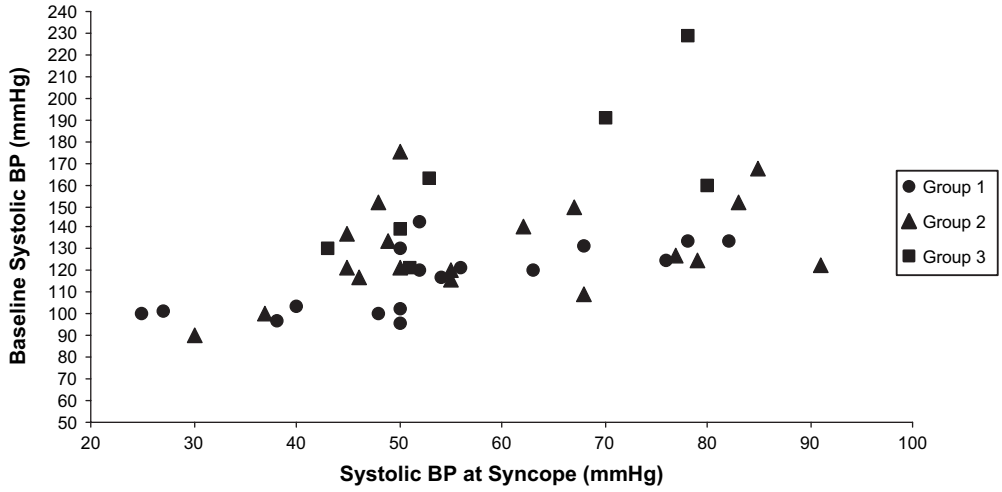


Figure 2 Graph depicting the relationship between baseline systolic blood pressure (ordinate) plotted against the systolic blood pressure at syncope for each patient (abcissa). Patients with higher baseline systolic blood pressures tended to become syncopal at higher systolic blood pressures (i.e., the approximate lower limit of blood flow autoregulation). However, the apparent relationship was not statistically significant.

a higher value for the lower blood pressure limit for maintenance of consciousness (i.e., lower limit of cerebral blood flow autoregulation). In fact, a trend in this direction was observed albeit of relatively small magnitude. Thus, given a higher baseline blood pressure without a substantial upward shift of the lower limit of cerebral blood flow regulation, the healthy older vasovagal fainter appears to exhibit a greater blood pressure 'reserve' for maintenance of consciousness than does the younger fainter. This finding accounts for the observation that older patients tolerate longer periods of passive upright posture before onset of syncope than do younger individuals.

Age-related orthostatic tolerance

Apart from the 'autoregulatory' aspects of the cerebrovascular bed, arterial baroreceptor effects (i.e., modulation of heart rate and vascular resistance), and renal and hormonal influences, play important roles in long-term stabilization of cerebral blood flow [10—12]. Transient failure of protective mechanisms, or the intervention of factors such as drugs, dehydration or haemorrhage, which reduce systemic pressure below the autoregulatory range, may provoke a syncopal episode. These risks are generally considered to be greater in older patients [12,13] for several reasons. First, older individuals are more often exposed to culprit drugs (e.g., diuretics, vasodilators), and are more often subject to disease states, which increase likelihood of fainting. Second, ageing alone has been associated with diminution of cerebral blood flow [8,9,13], and thereby decreases the safety factor for cerebral nutrient flow. Finally, conditions commonly found in older patients, particularly hypertension, have been reported to shift the lower limit of cerebrovascular autoregulation to higher pressures. On the other hand, numerous reports have evaluated the effects of age on orthostatic tolerance [14—19], and while a consensus has not been achieved, several suggest that older relatively healthy patients are somewhat more tolerant of passive orthostatic stress than are younger individuals [14—16].

In a study of older individuals using HUT, Fitzpatrick et al. [15] observed that among 27 control subjects, only 7.4% exhibited positive tests, a value far less than the 15—20% commonly reported in younger age groups. A similar finding was noted by Grubb et al. [14] in evaluation of the elderly. Among older 'control' patients, none had a positive tilt response. Similarly, Bloomfield et al. [17] evaluated 352 HUT outcomes, 133 of which were patients >65 years. They found that positive HUT occurred more frequently in younger patients, with $>50\%$ of tests being positive in patients ≤ 65 years, compared with 37% in those >65 years.

Lipsitz et al. [16] also compared orthostatic tolerance (60 degrees for 15 min) in elderly and young volunteers. In this study mean arterial pressure actually tended to increase to a greater extent in the elderly, whereas heart rate increments were less. Forearm vascular flow and resistance changes

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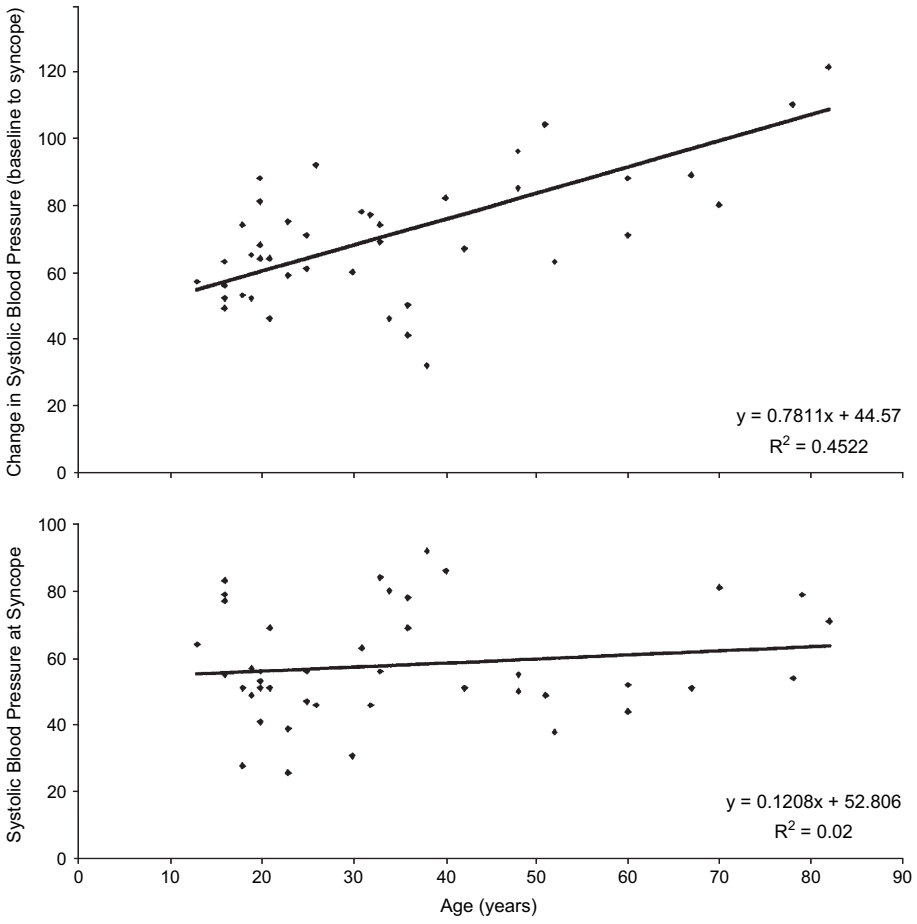


Figure 3 Figure illustrating the relationship between age (years, lower panel) and both systolic blood pressure at syncope (lower panel), and change in systolic blood pressure from baseline to syncope (upper panel). Increasing age did not substantially alter BP at syncope, but did appear to be associated with an increasing difference between baseline BP and BP at syncope (the 'reserve'). See text for discussion.

did not appear to differ with age. In terms of susceptibility to syncope, among 22 elderly subjects (83 ± 6 years), six had a history of unexplained syncope despite previous evaluation. However, only one of these six patients had a positive tilt test. Of the remaining 16 asymptomatic individuals, none had a positive test. By contrast, four of nine younger patients had positive responses during the same protocol; two of the four positive tests occurred in individuals with a previous history of unexplained syncope.

Based on these reports, it seems reasonable to conclude that generally healthy elderly patients exhibit greater passive orthostatic tolerance than do younger individuals. Our findings suggest that the basis for this finding is in large measure the tendency for otherwise healthy older individuals to exhibit higher baseline blood pressures, with relatively small upward shift of the lower limit of cerebral blood flow regulation. The result is a greater arterial pressure 'reserve' for maintenance of consciousness.

Table 1 Arterial systolic blood pressure during HUT by age group (mmHg)

	Baseline upright	25%	50%	75%	Syncope	HUT duration (min)
<25 years	116 ± 4*	118 ± 4*	118 ± 3*	102 ± 6	54 ± 4	10 ± 2*
25–59 years	128 ± 4*	127 ± 5*	116 ± 4	111 ± 5	58 ± 6	15 ± 3*
≥60 years	162 ± 14	142 ± 12	134 ± 14	118 ± 12	61 ± 6	26 ± 7

*$P = 0.03$ compared to patients ≥60 years.

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Limitations

Interpretation of the findings in this study is limited by the fact that the number of patients $\geq$60 years was small, the blood pressure range studied was limited, and determination of the time point at which syncope occurs is always imprecise. These factors were an inevitable consequence of both the inclusion of only a relatively healthy cohort (albeit with an element of moderate isolated systolic hypertension), and the need to avoid excessively prolonged periods of hypotension in severely symptomatic near-syncopal patients. A further limitation relates to the precision with which estimation of the blood pressure value at the time of syncope. In this regard, an intra-arterial catheter provided reliable pressure records. Consequently, the greatest potential error lay in the timing of the end-point (i.e., the precise moment of syncope). However, for the most part pressure changes occur slowly at that point in the study, thereby minimizing the impact of any error associated with timing of the end-point.

Conclusions

In relatively healthy patients undergoing evaluation for presumed vasovagal syncope, the lower limit of systemic pressure at which consciousness is maintained appears to increase with age. However, this effect is relatively minor compared with the increase in baseline upright blood pressure. As a result, there is a relatively larger difference between systemic pressures at baseline and at syncope in older patients, than is observed in younger subjects. This greater difference (i.e., the cerebral consciousness blood pressure 'reserve') may account for the greater than expected tolerance to passive upright posture observed in healthy older subjects compared to the young.

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