15. Sabharwal S, Wilson H. Orthogeriatrics in the management of frail older patients with a fragility fracture. Osteoporos Int 2015; 26: 2387–99.

16. Zeltzer J, Mitchell RJ, Toson B, Harris IA, Ahmad L, Close J. Orthogeriatric services associated with lower 30-day mortality for older patients who undergo surgery for hip fracture. Med J Aust 2014; 201: 409–11.

17. Vestergaard P, Rejnmark L, Mosekilde L. Increased mortality in patients with a hip fracture-effect of pre-morbid conditions and post-fracture complications. Osteoporos Int 2007; 18: 1583–93.

18. Simunovic N, Devereaux PJ, Sprague S *et al.* Effect of early surgery after hip fracture on mortality and complications: systematic review and meta-analysis. CMAJ 2010; 182: 1609–16.

19. Marcantonio ER, Flacker JM, Wright RJ, Resnick NM. Reducing delirium after hip fracture: a randomized trial. J Am Geriatr Soc 2001; 49: 516–22.

20. Huntjens KMB, van Geel TCM, Geusens PP *et al.* Impact of guideline implementation by a fracture nurse on subsequent fractures and mortality in patients presenting with non-vertebral fractures. Injury 2011; 42: S39–43.

21. Huntjens KM, van Geel TA, van den Bergh JP *et al.* Fracture liaison service: impact on subsequent nonvertebral fracture incidence and mortality. J Bone Joint Surg Am 2014; 96: e29.

22. Lawrence TM, Wenn R, Boulton CT, Moran CG. Age-specific incidence of first and second fractures of the hip. J Bone Joint Surg Br 2010; 92: 258–61.

23. Chapurlat RD, Bauer DC, Nevitt M, Stone K, Cummings SR. Incidence and risk factors for a second hip fracture in elderly women. The Study of Osteoporotic Fractures. Osteoporos Int 2003; 14: 130–6.

24. Li L, Roddam A, Gitlin M *et al.* Persistence with osteoporosis medications among postmenopausal women in the UK General Practice Research Database. Menopause 2012; 19: 33–40.

25. Curtis JR, Arora T, Matthews RS *et al.* Is withholding osteoporosis medication after fracture sometimes rational? A comparison of the risk for second fracture versus death. J Am Med Dir Assoc 2010; 11: 584–91.

26. Gibson-Smith D, Klop C, Elders PJM *et al.* The risk of major and any (non-hip) fragility fracture after hip fracture in the United Kingdom: 2000–2010. Osteoporos Int 2014; 25: 2555–63.

27. Dell R, Greene D, Schelkun SR, Williams K. Osteoporosis disease management: the role of the orthopaedic surgeon. J Bone Joint Surg Am 2008; 90(Suppl 4): 188–94.

28. McLellan AR, Wolowacz SE, Zimovetz EA *et al.* Fracture liaison services for the evaluation and management of patients with osteoporotic fracture: a cost-effectiveness evaluation based on data collected over 8 years of service provision. Osteoporos Int 2011; 22: 2083–98.

29. Majumdar SR, Beaupre LA, Harley CH *et al.* Use of a case manager to improve osteoporosis treatment after hip fracture —results of a randomized controlled trial. Arch Intern Med 2007; 167: 2110–5.

30. Lih A, Nandapalan H, Kim M *et al.* Targeted intervention reduces refracture rates in patients with incident non-vertebral osteoporotic fractures: a 4-year prospective controlled study. Osteoporos Int 2011; 22: 849–58.

Safety and tolerability of Tilt Testing and Carotid Sinus Massage in the octogenarians

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Abstract

Objective: to evaluate the safety and tolerability of Tilt Testing (TT) and Carotid Sinus Massage (CSM) in octogenarians with unexplained syncope.

Methods: patients consecutively referred for transient loss of consciousness to the 'Syncope Units' of three hospitals were enrolled. TT and CSM were performed according to the European Society of Cardiology guidelines on syncope. Complications were evaluated in each group. An early interruption of TT was defined as 'intolerance' and considered as a non-diagnostic response.

Results: one thousand four hundred and one patients were enrolled (mean age 72 ± 16 years, male 40.8%). Six hundred and ninety-four patients (49.5%) were 80 years old or older (mean age 83 ± 3 years) and 707 (50.5%) were younger (mean age 60 ± 17 years). Complications after TT occurred in 4.5% of older patients and in 2.1% of the younger ones ($P = 0.01$). All complications were 'minor/moderate', as prolonged hypotension, observed in $\sim$3% of patients $\geq$80 years. Major complications such as sustained ventricular tachycardia, ventricular fibrillation, asystole requiring cardiac massage, transient ischaemic attack, stroke and death were not observed in any patient. The presence of orthostatic hypotension and the mean number of syncopal episodes were predictors of TT complications. Intolerance was reported in 2.4% of older patients and 1% of the younger ones ($P = 0.08$), mainly due to orthostatic intolerance. No complications occurred after CSM.

Conclusions: TT and CSM appear to be safe and well tolerated in octogenarians, who should not be excluded by age from the diagnostic work-up of syncope.

Introduction

Syncope is common in older people [1], with a dramatic age gradient peaking in adults over 70 years, for whom the diagnostic assessment can be complex. In the first instance, an accurate history may not be available from the patient and a witness account is also not infrequently unavailable [2]. Moreover, a prodrome may be absent or, if present, it is often of mild intensity, of short duration and poorly specific or atypical [3]. Finally, older patients frequently experience retrograde amnesia and are unable to recall loss of consciousness [4]. Therefore, Tilt Testing (TT) and Carotid Sinus Massage (CSM) represent important objective diagnostic tests in older patients with syncope. It has been previously demonstrated in a number of small cohort studies that TT and CSM are safe and well tolerated in the elderly [5–10], but there are no large-scale reports about their safety in octogenarians, which will be highly relevant given the projected global increase in the number of these patients. The aim of the present study is to assess TT and CSM safety and tolerability in octogenarians and to identify predictors of complications.

Methods

This is a prospective study carried out in 1,401 patients consecutively referred for investigation of transient loss of consciousness to the 'Syncope Unit' of three different hospitals (Modena, Florence and Dublin). All were investigated as per the European Society of Cardiology (ESC) guidelines on syncope [11], which initial assessment included detailed history, physical examination, 12-lead electrocardiogram (ECG), orthostatic blood pressure (BP) measurements; all patients underwent TT and CSM, because of unexplained syncope after initial evaluation.

The medical assessment included details of co-morbidities (diabetes, hypertension, varicose veins, heart disease), medications (in particular antiarrhythmic, anticonvulsant and hypotensive drugs) and characteristics of the spontaneous episodes (number, prodrome, injuries, predisposing factors and situations). Angiotensin-converting enzyme inhibitors (ACEi), angiotensin receptor blockers (ARB), β-blockers, α-receptor blockers, α-receptor agonists, calcium channel blockers, nitrates, diuretics, benzodiazepines and antidepressants were considered as drugs with definite or potential hypotensive effect. Left and right bundle branch block, anterior or posterior fascicular block, first-degree atrio-ventricular block and bifascicular block were considered as pathological ECG findings. TT and CSM were performed when the cardiological investigation was negative. Orthostatic hypotension was defined as a decrease in systolic BP $\geq$20 mmHg and in diastolic BP $\geq$10 mmHg during 3-min active stand.

TT was performed according to the Italian Protocol [12], previously validated in older patients [6]. After 5 min of supine rest, patients in fasting state and after having taken the usual therapy were tilted up to 60° on a tilt table with foot-plate support. If syncope did not occur within 20 min, the test was potentiated with the administration of sublingual nitroglycerine (GNT) (400 µg Natispray), and the observation was prolonged for additional 15 min. Neurally mediated syncope was defined according to the VASIS classification (Vasovagal Syncope International Study) [13]. A slow and progressive decrease in BP, generally without (or only mild) increase in heart rate, leading to the development of symptoms was defined as 'disautonomic response'. An 'exaggerated response' was defined as a gradual development of symptoms (milder than spontaneous ones) associated with a slow (>5 min) decrease in BP, generally with an increase in heart rate, during the pharmacological phase [14]. To reduce the diurnal autonomic variability, TT was performed between 8:30 and 10:30 am, in a quiet environment, dim lighted and temperate. Severe aortic or mitral valve stenosis and myocardial infarction in the 8 weeks before were contra-indications to TT.

CSM was performed according to the 'Method of symptoms' [15]. Transient ischaemic attack or stroke in the 3 months before, or critical carotid artery stenosis at Doppler

ultrasonography, performed in the presence of carotid bruits, was contraindications to the CSM [16].

TT and CSM were performed under continuous ECG and systemic beat-to-beat BP monitoring. BP was continuously monitored with an appropriate size finger cuff, and the hand was supported with a sling to keep the finger at the heart level.

A written informed consent to perform the neuroautonomic evaluation and to participate in a research study was obtained from each patient.

Complications during TT and CSM were prospectively recorded in all patients. Potential complications of TT and CSM were predefined and classified as follows: minor/moderate: prolonged hypotension (with or without fluid administration), prolonged bradycardia requiring atropine administration, atrial fibrillation (AF) or other supraventricular tachyarrhythmias, non-sustained ventricular tachycardia (nsVT), and major: prolonged asystole requiring cardiac massage, sustained VT (sVT), ventricular fibrillation (VF), transient ischaemic attack (TIA), stroke, death. Minor signs/symptoms not secondary to the vasovagal reaction were also recorded. An early interruption of TT, due to difficulty in maintaining the tilt position, anxiety, poor compliance or symptoms not related to changes in BP or HR, was defined as 'intolerance' and considered as a non-diagnostic response. Causes of intolerance were recorded in both the age groups.

Declaration of sources of funding

Statistical analysis

All analyses were performed using Statistica version 8.0 (StatSoft Italia, Padova, Italy) and SPSS version 12.2 (SPSS Inc., Chicago, IL, USA). The χ^2 test was used to compare dichotomous variables between groups, and the Student t-test for unpaired data was used to compare continuous data with normal distribution. The data are reported as the mean ± standard deviation or as a percentage. Moreover, a multivariate analysis of predictors of different diagnoses and complications was performed by multiple logistic regression. The hazard ratio (HR) was provided with its 95% confidence interval (CI). $P < 0.05$ was considered to be statistically significant. The study population was divided by age in two groups (<80 and ≥80 years old).

Results

Study population

One thousand four hundred and one consecutive patients were enrolled; the mean age was 72 ± 16.8 years (age range 15–95;

median age 79 years; inter-quartile range 67–83); 694 patients (49.5%) were aged ≥80 (mean age 83.6 ± 3.1 years) and 707 patients (50.5%) were younger (mean age 60.7 ± 17.1 years). The characteristics of the population are listed in Table 1.

Older patients had higher co-morbidity rate. Younger patients reported a higher number of syncopal episodes (4.8 ± 6.9 versus 3.7 ± 5.2, $P = 0.002$), whereas unexplained falls were more frequent in older patients (32.6 versus 12%, $P < 0.0001$). Orthostatic hypotension was present in 458 patients (32.7%), with a higher prevalence in older patients (46.7 versus 18.9%, $P < 0.0001$). The 59.6% of the patients was taking anti-hypertensive drugs, (73.5% of older patients versus 46% of the younger ones, $P < 0.0001$).

TT and CSM responses

The neuroautonomic evaluation was positive in 852 patients (60.8%), with a similar positivity rate in the two groups (59.7% in younger and 62% in older patients, $P = 0.4$).

TT was positive in 692 patients (49.4%, respectively, 46.3% in the older and 52.5% in the younger group, $P = 0.02$). The cardio-inhibitory and the mixed response (both cardio-inhibitory and vasodepressive) were more common in younger patients, whereas vasodepressive and dysautonomic responses were more frequent in older patients (data not shown). An exaggerated response was observed in 61 patients (4.4%), with a similar rate in the two groups (4% in younger versus 4.8% in older patients, $P = 0.5$). At multivariate analysis, a positive response to TT was associated with the presence of prodromes (HR 0.88, CI 0.83–0.94, $P = 0.0001$) and syncope related to predisposing conditions (HR 0.92, CI 0.88–0.98, $P = 0.009$), whereas pacemaker (HR 0.91, CI 0.87–0.97, $P = 0.003$) and chronic therapy with nitrates (HR 1.10, CI 1.04–1.17, $P = 0.002$) were associated with a lower TT positivity rate.

CSM was positive in 147 patients (10.5%), without differences in the two groups (9.6% in younger and 11.4% in older patients, $P = 0.3$). Ninety-five patients (64.6%) had cardio-inhibitory Carotid Sinus Syndrome (CSS), 33 had vasodepressive CSS (22.5%) and 19 had mixed CSS (12.9%), with a similar distribution in the two groups. Carotid Sinus Hypersensitivity (CSH) was present in 107 patients (7.6%): among these, 55 were older (7.9%) and 52 were younger (7.4%), $P = 0.7$. At multivariate analysis, advanced age (HR 1.07, CI 1.01–1.14, $P = 0.003$) and male sex (HR 1.14, CI 1.07–1.20; $P = 0.04$) were predictors of positive response.

Complications during CSM and TT

No minor/moderate or major complications occurred during or after the CSM.

Complications after TT were observed in 46 patients (3.3%) and were more prevalent in the older group: 15 younger patients (2.1%) and 31 older patients (4.5%, $P = 0.01$) showed complications. Complications are reported in Table 2.

The prevalence of minor/moderate complications was higher in the older group: 15 younger patients (2.1%) and 30 older patients (4.3%) ($P = 0.01$) showed minor/moderate

Table 1. Characteristics of the population

	All patients (n = 1,401)	Age < 80 years (n = 707)	Age ≥ 80 years (n = 694)	P-value
Mean age (years ± SD)	72.0 ± 16.8	60.7 ± 17.1	83.6 ± 3.1	<0.0001
Number of syncope (mean ± SD)	4.3 ± 6.1	4.8 ± 6.9	3.7 ± 5.2	0.002
Male/Female (n)	571/830	331/376	240/454	<0.0001
Hypertension, n (%)	846 (60.4)	325 (45.9)	521 (75.1)	<0.0001
Diabetes, n (%)	207 (14.8)	91 (12.9)	116 (16.7)	0.04
History of falls, n (%)	311 (22.2)	85 (12.0)	226 (32.6)	<0.0001
Orthostatic hypotension, n (%)	458 (32.7)	134 (18.9)	324 (46.7)	<0.0001
Heart disease, n (%)	324 (23.1)	115 (16.3)	209 (30.1)	<0.0001
Varicose veins, n (%)	443 (31.6)	140 (19.8)	303 (43.7)	<0.0001
Presyncope, n (%)	480 (34.3)	268 (37.9)	212 (30.6)	0.004
Prodromes, n (%)	885 (63.2)	510 (72.1)	375 (54.0)	<0.0001
Situational syncope, n (%)	429 (30.6)	245 (34.7)	184 (26.5)	0.001
Injuries, n (%)	560 (40.0)	237 (33.5)	323 (46.5)	<0.0001
Hypotensive drugs, n (%)	835 (59.6)	325 (46.0)	510 (73.5)	<0.0001
ACEi/ARB, n (%)	636 (45.4)	244 (34.5)	392 (56.5)	<0.0001
β-blockers, n (%)	195 (13.9)	75 (10.6)	120 (17.3)	0.0003
Calcium channel antagonists, n (%)	220 (15.7)	84 (11.9)	136 (19.6)	<0.0001
Alpha-receptor blockers, n (%)	121 (8.6)	38 (5.4)	83 (12.0)	<0.0001
Alpha-receptor agonists, n (%)	12 (0.9)	6 (0.9)	6 (0.9)	0.9
Nitrates, n (%)	99 (7.1)	31 (4.4)	68 (9.8)	<0.0001
Diuretics, n (%)	336 (24.0)	116 (16.4)	220 (31.7)	<0.0001
Antiarrhythmic, n (%)	80 (5.7)	35 (4.9)	45 (6.5)	0.2
Antiepileptics, n (%)	73 (5.2)	39 (5.5)	34 (4.9)	0.6
Antidepressants, n (%)	268 (19.1)	98 (13.9)	170 (24.5)	<0.0001
Benzodiazepines, n (%)	186 (13.3)	77 (10.9)	109 (15.7)	0.008
Pathologic ECG, n (%)	400 (28.6)	134 (18.9)	266 (38.3)	<0.0001
Left bundle branch block, n (%)	52 (3.7)	16 (2.3)	36 (5.2)	0.004
Right bundle branch block, n (%)	87 (6.2)	37 (5.2)	50 (7.2)	0.1
Anterior fascicular block, n (%)	89 (6.4)	28 (4.0)	61 (8.8)	0.0002
First-degree AV block, n (%)	100 (7.1)	30 (4.2)	70 (10.1)	<0.0001
Bifascicular block, n (%)	55 (3.9)	19 (2.7)	36 (5.2)	0.02
Pacemaker, n (%)	60 (4.3)	21 (3.0)	39 (5.6)	0.01

SD, standard deviation; ACEi, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blockers; ECG, electrocardiogram; AV, atrio-ventricular.

complications. Only prolonged hypotension requiring fluid administration was more prevalent in the older group (2.2 versus 0%, $P = 0.02$). The prevalence of prolonged bradycardia requiring atropine administration, AF and nsVT was very low and similar in the two groups.

Minor signs/symptoms were present in 10 patients aged <80 (1.4%) and in 8 patients aged ≥80 (1.2%, $P = 0.95$); they included nausea and/or vomiting requiring anti-emetic drugs in 10 patients, flushing in one patient, persistent bradycardia that did not require atropine or pacing in two patients, frequent ventricular extrasystoles in three patients, short self-limiting atrial tachycardia in one patient and chest pain, without pathological ECG findings, in one patient.

A 87-year-old patient developed a self-limited expressive dysphasia, which was considered as a transient ischaemic event and recorded among major complications. Three patients (0.2%) were referred to the Emergency Department because of AF (two patients), chest pain (not associated with pathologic ECG findings), with no differences between the two age groups (0.3% in younger patients versus 0.1% in the older ones, $P = 0.612$).

Patients with complications had a higher mean age (77.2 ± 12.1 versus 71.8 ± 16.9 years, $P = 0.03$) and showed more frequent venous incompetence (47.8 versus 31.1%, $P = 0.02$) and orthostatic hypotension (50 versus 32.1%, $P = 0.01$); moreover, they reported a higher number of syncopal episodes (7.1 ± 8.2 versus 4.2 ± 6.0, $P = 0.001$), anterior fascicular block (17.4 versus 6%, $P = 0.002$) and bi-fascicular block (10.9 versus 3.7%, $P = 0.01$) (Table 3).

At multivariate analysis, the mean number of syncopal episodes (HR 1.10, CI 1.04–1.16, $P = 0.01$) and the presence of orthostatic hypotension (HR 1.06, CI 1.01–1.13, $P = 0.03$) were predictors of TT complications, whereas the age was not related to the occurrence of complications.

Intolerance to TT was observed in 24 patients (1.7%), including 17 older patients (2.4%) and 7 younger subjects (1%, $P = 0.08$).

Discussion

The main finding of this study is that major complications such as sVT, VF, TIA, stroke and death were not observed in patients ≥80 years during TT and CSM. Only prolonged hypotension, requiring fluid administration in most cases, was more frequent in patients aged 80 or older, even if in a low percentage of cases (∼3%).

Table 2. Tilt testing complications

	All patients ($n = 1,401$)	Age < 80 years ($n = 707$)	Age ≥ 80 years ($n = 694$)	*P*-value
Minor/moderate complications, *n* (%)	45 (3.3)	15 (2.1)	30 (4.5)	0.01
Minor signs/symptoms, *n* (%)	18 (1.4)	10 (1.4)	8 (1.3)	0.952
Prolonged hypotension, *n* (%)	6 (0.4)	2 (0.3)	4 (0.6)	0.968
Prolonged hypotension requiring fluid administration, *n* (%)	15 (1.1)	0 (0.0)	15 (2.2)	0.020
Prolonged bradycardia requiring atropine administration, *n* (%)	2 (0.1)	1 (0.1)	1 (0.1)	0.985
AF, *n* (%)	3 (0.2)	2 (0.3)	1 (0.1)	0.859
nsVT, *n* (%)	1 (0.07)	0 (0.0)	1 (0.1)	0.963
Major complications, *n* (%)	1 (0.07)	0 (0.0)	1 (0.1)	0.963
sVT, *n* (%)	0 (0.0)	0 (0.0)	0 (0.0)	–
VF, *n* (%)	0 (0.0)	0 (0.0)	0 (0.0)	–
Prolonged asystole requiring cardiac massage, *n* (%)	0 (0.0)	0 (0.0)	0 (0.0)	–
TIA, *n* (%)	1 (0.07)	0 (0.0)	1 (0.1)	0.963
Stroke, *n* (%)	0 (0.0)	0 (0.0)	0 (0.0)	–
Death, *n* (%)	0 (0.0)	0 (0.0)	0 (0.0)	–

AF, atrial fibrillation; nsVT, non-sustained ventricular tachycardia; sVT, sustained ventricular tachycardia; VF, ventricular fibrillation; TIA, transient ischaemic attack.

The present study demonstrates that TT and CSM are safe and well-tolerated in octogenarians in a large sample of patients evaluated for suspected syncope according to the protocol proposed by the ESC guidelines on syncope [11].

TT was positive in 49.4% of patients. TT positivity rate was higher in younger patients (52.5 versus 46.3%, $P = 0.02$), as shown in a recent meta-analysis [17], whereas venous incompetence and orthostatic hypotension were more frequent in older patients, suggesting a tendency to orthostatic rather than vasovagal syncope with advancing age; orthostatic hypotension is indeed the first cause of syncope in older patients [7]. The vasodepressive response was the most frequent in the entire sample (58.5%) and more common in older patients, whereas the cardio-inhibitory response was more frequent in the younger ones, according to previous studies [14, 18, 19]. This difference may be due to an age-related decline in the vagal drive to the heart or to reduced susceptibility of the parasympathetic receptors [20]. Multivariate analysis showed that TT positivity was related to a positive history for predisposing factors or conditions and prodromes; chronic therapy with nitrates was associated with a lower TT positivity rate, maybe because the drug tolerance induced by nitrates could interfere with the nitroglycerine administered during the test, reducing or nullifying its effects [21].

CSM was positive in 147 patients (10.5%), showing a cardio-inhibitory response in the 64.6% of the cases. Our incidence of CSS was similar to what previously found in the general population and in older people [7, 22].

Complications related to TT occurred rarely (3.3% of the patients), more frequently in older patients (4.5 versus 2.1%, $P = 0.01$); one of the complications was major (transient dysphasia in a 87-year-old patient), whereas the majority of complications was minor/moderate, consisting mainly in prolonged hypotension. Prolonged hypotension could be an expression of sympathetic dysfunction; in this regard, orthostatic hypotension and a high number of syncopal episodes were predictors of complications.

Gieroba *et al.* [10] previously evaluated the safety of TT in patients aged 60 and older, including a large number of patients with cardiovascular and cerebrovascular co-morbidities. The study population was divided by age in two groups (<75 and ≥75 years old) and 1,969 procedures were performed; of these, 1,495 (76%) were unprovoked TT and 474 (24%) were GNT-provoked TT (GNT 800 μg). The results of the study showed that TT is safe in patients aged 75 and older.

According to the Literature, cardiac arrhythmias are rarely reported after CSM [8, 23–25], and the incidence of neurological complications is low (0.17–0.45%) [15, 16, 26]. In our population, no complications occurred after the '10 s procedure', indicating that this test can be safely performed in octogenarians, as well as the '5 s procedure' evaluated by Walsh *et al.* [8] in a large population of elderly. In our research, all the patients were evaluated for carotid stenosis through the auscultation of the carotid arteries and a vessels ultrasound in case of carotid bruit. Since no neurological complications occurred, our study confirms that this protocol is safe, in accordance to Richardson *et al.* [27].

Intolerance was observed only in 24 patients (1.7%), with a similar rate in the two age groups (2.4 versus 1%, $P = 0.08$). The early interruption of the test was mainly due to orthostatic intolerance (inability to maintain the upright position), as reported by Paling *et al.* in a smaller population [9]. Some authors believe that shortened protocols may improve tolerability, particularly in older patients who are unable to tolerate prolonged upright posture due to physical frailty or medical problems (back pain, neurologic deficits, etc.). Macedo *et al.* [28] and Parry *et al.* [29] have analysed protocols without the passive phase, which proved to be not inferior to conventional TT and unprovoked TT, respectively. Bartoletti *et al.* [30] previously evaluated a similar protocol with a 5-min passive phase reporting a lower positivity rate; therefore, more studies are needed to assess the role of shortened protocols in frail patients.

Limitations

The specificity of TT has not been adequately investigated in patients ≥80 years; therefore, its diagnostic value in this age

Table 3. Characteristics of the patients with and without Tilt Testing complications

	Patients with TT complications (*n* = 46)	Patients without TT complications (*n* = 1,355)	*P*-value
Mean age (years ± SD)	77.2 ± 12.1	71.8 ± 16.9	0.03
Number of syncope (mean ± SD)	7.1 ± 8.2	4.2 ± 6.0	0.001
Male/Female	22/24	549/806	0.3
Hypertension, *n* (%)	29 (63.0)	817 (60.3)	0.7
Diabetes, *n* (%)	7 (15.2)	200 (14.8)	0.9
History of falls, *n* (%)	7 (15.2)	304 (22.4)	0.2
Orthostatic hypotension, *n* (%)	23 (50.0)	435 (32.1)	0.01
Heart disease, *n* (%)	8 (17.4)	316 (23.3)	0.3
Varicose veins, *n* (%)	22 (47.8)	421 (31.1)	0.02
Presyncope, *n* (%)	13 (28.3)	467 (34.5)	0.4
Prodromes, *n* (%)	30 (65.2)	855 (63.1)	0.8
Situational syncope, *n* (%)	17 (36.9)	412 (30.4)	0.5
Injuries, *n* (%)	23 (50.0)	537 (39.6)	0.2
Hypotensive drugs, *n* (%)	27 (58.7)	808 (59.6)	0.9
ACEi/ARB, *n* (%)	19 (41.3)	617 (45.5)	0.8
β-blockers, *n* (%)	6 (13.0)	189 (13.9)	0.9
Calcium channel antagonists, *n* (%)	6 (13.0)	214 (15.8)	0.6
α-receptor blockers, *n* (%)	5 (10.9)	116 (8.6)	0.6
α-receptor agonists, *n* (%)	0 (0.0)	12 (0.9)	0.5
Nitrates, *n* (%)	1 (2.2)	98 (7.2)	0.2
Diuretics, *n* (%)	12 (29.1)	324 (23.1)	0.7
Anti-arrhythmics, *n* (%)	1 (2.2)	79 (5.8)	0.3
Anti-epileptics, *n* (%)	3 (6.5)	70 (5.2)	0.7
Anti-depressants, *n* (%)	6 (13.0)	262 (19.3)	0.3
Benzodiazepine, *n* (%)	6 (13.0)	180 (13.3)	0.9
Pathologic ECG, *n* (%)	18 (39.1)	382 (28.2)	0.1
Left branch block, *n* (%)	1 (2.2)	51 (3.8)	0.6
Right branch block, *n* (%)	6 (13.0)	81 (6.0)	0.05
Anterior fascicular block, *n* (%)	8 (17.4)	81 (6.0)	0.002
First-degree atrio-ventricular block, *n* (%)	5 (10.9)	95 (7.0)	0.3
Bifascicular block, *n* (%)	5 (10.9)	50 (3.7)	0.01
Pacemaker, *n* (%)	1 (2.2)	59 (4.4)	0.5

TT, Tilt Testing; SD, standard deviation; ACEi, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blockers; ECG, electrocardiogram.

group is not very clear. However, the main purpose of this study was to investigate the safety of TT in octogenarians.

Conclusions

In conclusion, the results of the present study demonstrate, in a large sample of patients, that TT and CSM are safe and well tolerated in octogenarians, who should not be excluded by age from this diagnostic work-up.

Key points

- Our research demonstrates that TT and CSM can be safely performed in a large sample of patients aged 80 and older.
- Orthostatic hypotension is a predictor of complications, whereas advanced age is not related to any.
- No previous large studies have evaluated safety and tolerability of TT and CSM in the octogenarians.

Conflicts of interest

None declared.

References

1. Savage DD, Corwin L, McGee DL *et al*. Epidemiologic features of isolated syncope: the Framingham Study. Stroke 1985; 16: 626–9.
2. Shaw FE, Kenny RA. The overlap between syncope and falls in the elderly. Postgrad Med J 1997; 73: 635–9.
3. Del Rosso A, Alboni P, Brignole M *et al*. Relation of clinical presentation of syncope to the age of patients. Am J Cardiol 2005; 96: 1431–5.
4. Parry SW, Steen IN, Baptist M *et al*. Amnesia for loss of consciousness in carotid sinus syndrome: implications for presentation with falls. J Am Coll Cardiol 2005; 45: 1840–3.
5. Parry SW, Kenny RA. The role of tilt table testing in neurocardiovascular instability in older adults. Eur Heart J 2001; 22: 370–2.
6. Del Rosso A, Ungar A, Bartoli P *et al*. Usefulness and safety of shortened head-up tilt testing potentiated with sublingual glyceryl trinitrate in older patients with recurrent unexplained syncope. J Am Geriatr Soc 2002; 50: 1324–8.
7. Ungar A, Mussi C, Del Rosso A *et al*. Diagnosis and characteristics of syncope in older patients referred to geriatric departments. J Am Geriatr Soc 2006; 54: 1531–6.
8. Walsh T, Clinch D, Costelloe A *et al*. Carotid sinus massage—how safe is it? Age Ageing 2006; 35: 518–20.

9. Paling D, Vilches-Moraga A, Akram Q *et al.* Carotid sinus syndrome is common in very elderly patients undergoing tilt table testing and carotid sinus massage because of syncope or unexplained falls. Aging Clin Exp Res 2011; 23: 304–8.

10. Gieroba ZJ, Newton JL, Parry SW *et al.* Unprovoked and glyceryl trinitrate–provoked head-up tilt table test is safe in older people: a review of 10 years' experience. J Am Geriatr Soc 2004; 52: 1913–5.

11. Moya A, Sutton R, Ammirati F *et al.* Guidelines for the diagnosis and management of syncope (version 2009). The Task Force for the Diagnosis and Management of Syncope of the European Society of Cardiology (ESC). Eur Heart J 2009; 30: 2631–71.

12. Bartoletti A, Alboni P, Ammirati F *et al.* The Italian Protocol: a simplified head-up tilt testing potentiated with oral nitroglycerin to assess patients with unexplained syncope. Europace 2000; 2: 339–42.

13. Sutton R, Petersen M, Brignole M *et al.* Proposed classification for tilt induced vasovagal Syncope. Eur J Cardiac Pacing Electrophysiol 1992; 3: 180–3.

14. Raviele A, Menozzi C, Brignole M *et al.* Value of head-up tilt testing potentiated with sublingual nitroglycerin to assess the origin of unexplained syncope. Am J Cardiol 1995; 76: 267–72.

15. Puggioni E, Guiducci V, Brignole M *et al.* Results and complications of the carotid sinus massage performed according to the 'methods of symptoms'. Am J Cardiol 2002; 89: 599–601.

16. Davies AG, Kenny RA. Frequency of neurologic complications following carotid sinus massage. Am J Cardiol 1998; 81: 1256–7.

17. Forleo C, Guida P, Iacoviello M *et al.* Head-up tilt testing for diagnosing vasovagal syncope: a meta-analysis. Int J Cardiol 2013; 168: 27–35.

18. Kapoor WN, Brant N. Evaluation of syncope by upright tilt testing with isoproterenol. A nonspecific test. Ann Intern Med 1992; 116: 358–63.

19. Del Rosso A, Bartoli P, Bartoletti A *et al.* Shortened head-up tilt testing potentiated with sublingual nitroglycerin in patients with unexplained syncope. Am Heart J 1998; 135: 564–70.

20. Pfeifer MA, Weinberg CR, Cook D *et al.* Differential changes of autonomic nervous system function with age in man. Am J Med 1983; 75: 249–58.

21. Rafanelli M, Morrione A, Del Rosso A *et al.* Chronic nitrate therapy reduces positivity rate of tilt testing potentiated with sublingual nitroglycerin in patients with unexplained syncope. Eur J Intern Med 2013; 24: e67–8.

22. Brignole M, Menozzi C, Bartoletti A *et al.* A new management of syncope: prospective systematic guidelines-based evaluation of patients referred urgently to general hospitals. Eur Heart J 2006; 27: 76–82.

23. Deepak SM, Jenkins NP, Davidson NC *et al.* Ventricular fibrillation induced by carotid sinus massage without preceding bradycardia. Europace 2005; 7: 638–40.

24. Carey BJ. Atrial fibrillation precipitated by carotid sinus massage in a patient with unexplained syncope. Ir J Med Sci 2006; 175: 72–3.

25. Manolis AG, Giotopoulou A, Koutouzis M *et al.* Atrial fibrillation induced by carotid sinus massage. Int J Cardiol 2007; 114: e103–4.

26. Munro NC, McIntosh S, Lawson J *et al.* Incidence of complications after carotid sinus massage in older patients with syncope. J Am Geriatr Soc 1994; 42: 1248–51.

27. Richardson DA, Shaw FE, Bexton R *et al.* Presence of a carotid bruit in adults with unexplained or recurrent falls: implication for carotid sinus massage. Age Ageing 2002; 31: 379–84.

28. Macedo PG, Asirvatham SJ, Maia L *et al.* Comparison of a shortened isosorbide dinitrate-potentiated head-up tilt testing with the conventional protocol: tolerance and diagnostic accuracy. Pacing Clin Electrophysiol 2012; 35: 1005–11.

29. Parry SW, Gray JC, Newton JL *et al.* 'Front-loaded' head-up tilt table testing: validation of a rapid first line nitrate-provoked tilt protocol for the diagnosis of vasovagal syncope. Age Ageing 2008; 37: 411–5.

30. Bartoletti A, Gaggioli G, Menozzi C *et al.* Head-up tilt testing potentiated with oral nitroglycerin: a randomized trial of the contribution of a drug-free phase and a nitroglycerin phase in the diagnosis of neurally mediated syncope. Europace 1999; 1: 183–6.