Results of carotid sinus massage in a tertiary referral unit—is carotid sinus syndrome still relevant?

MAW PIN TAN1,2, JULIA L. NEWTON1,2, PAM REEVE2, ALAN MURRAY3, TOM J. CHADWICK4, STEVE W. PARRY1,2

1Institute for Ageing and Health, Wolfson Centre, Campus for Ageing and Vitality, Newcastle University, Newcastle upon Tyne NE4 5PL, UK
2Falls and Syncope Service, Royal Victoria Infirmary, Newcastle upon Tyne NE1 4LP, UK
3Regional Medical Physics Department, Freeman Hospital, Newcastle upon Tyne NE7 7DN, UK
4Institute of Health and Society, 21, Claremont Place, Newcastle University, Newcastle upon Tyne NE2 4AA, UK

Address correspondence to: S. W. Parry. Tel: (+44) 191 2825237; Fax: (+44) 191 2825338. E-mail: swparry@hotmail.com

Abstract

Background: carotid sinus hypersensitivity (CSH) is associated with syncope, drop attacks and unexplained falls in older people. However, a recent study has also reported a prevalence of 35% in asymptomatic community-dwelling older people.

Objective: we conducted a retrospective observational study to investigate the haemodynamic and symptom responses of a large cohort of patients undergoing carotid sinus massage (CSM).

Methods: the electronically stored haemodynamic data of 302 consecutive patients, aged 71 ± 11 years, investigated with CSM for unexplained falls and syncope was analysed. Bilateral sequential CSM was performed in the supine and upright positions with continuous electrocardiogram (ECG) and non-invasive beat-to-beat blood pressure monitoring (Taskforce™, CN Systems, Austria). CSH (CSH) was defined by maximal R–R interval ≥ 3 s (cardioinhibitory) and/or a systolic blood pressure drop of ≥ 50 mmHg (vasodepressor).

Results: a total of 74/302 (25%) subjects had CSH, 37 (50%) of which were cardioinhibitory (CI) and 37 (50%) were vasodepressor (VD) subtypes. Subjects with positive CSM were significantly older (75.2 vs 70.2 years, P < 0.001), and more likely to be male (32% vs 19%, P < 0.01). CSH was diagnosed with right-sided CSM alone in 45 (61%) subjects and erect CSM only in 36 (49%) subjects. Symptom reproduction was more likely with the CI than the VD subtypes (82% vs 28%; P < 0.001).

Conclusion: CSH was diagnosed in 25% of patients investigated with CSM at our specialist unit, lower than the prevalence of 39% reported for community-dwelling older individuals. This discrepancy may be explained by selection bias and demographic differences, but raises the possibility of CSH being an age-related epiphenomenon rather than a causal mechanism for syncope, drop attacks and unexplained falls. Our observations have important implications for clinical practice and the development of future research strategies.

Keywords: carotid sinus hypersensitivity, syncope, loss of consciousness, non-accidental falls, elderly

Received 9 January 2009; accepted in revised form 23 April 2009
Is carotid sinus syndrome still relevant?

Carotid sinus syndrome (CSS) is still relevant for the following reasons:

1. **Clinical Relevance:** CSS is associated with symptoms of dizziness, blackouts, and fainting. Recognizing CSS can prevent life-threatening complications.
2. **Prevalence:** CSS is prevalent, with estimates ranging from 13.7% to 56% in community-dwelling individuals over 65 years.
3. **Quality of Life Impacts:** CSS can significantly affect quality of life, impacting daily activities and mobility.
4. **Economic Impact:** Treating CSS can save healthcare resources by preventing hospitalizations and unnecessary medical procedures.

**Methods**

**Subjects**

The haemodynamic profile of consecutive patients investigated with carotid sinus massage for the investigation of unexplained syncope, falls and drop attacks from 1 January 2004 to 31 March 2007 at a specialist tertiary referral unit was systematically reviewed. Prior written consent had been obtained from all patients for their information to be stored in a secure database for future audit and research purposes. Ethical approval had been obtained from the Local Research and Ethics Committee.

**Data Analysis**

Comparisons were made with the independent t-test for continuous variables, while odds ratios (OR) with 95% confidence intervals (CI) were reported for categorical data which were compared with the chi-squared test. The maximal RRI following CSM was non-normally distributed, and hence transformed into HR in beats per minute (b.p.m.) using the equation: HR = 60 (s)/RRI (s). Two-tailed P-values of 0.05 were considered statistically significant. The HR and SBP responses to CSM for individual subjects in the various positions were considered paired data and compared with paired sample t-tests. Consequently, subjects who did not have corresponding pairs, e.g. right supine and left supine if the test was aborted after right supine CSM, were excluded to avoid potential biases. Two-tailed P-values with Bonferroni’s correction of \( P = 0.025 \) were considered statistically significant to allow for the multiple comparisons. Statistical analyses were performed with SPSS® 14.0 for Windows.
Table 1. Characteristics of patients investigated with carotid sinus massage

<table>
<thead>
<tr>
<th></th>
<th>CSM+ (n = 74)</th>
<th>CSM− (n = 228)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years), mean (95% CI)</td>
<td>75.2 (73.2, 77.2)</td>
<td>70.2 (68.6, 71.8)</td>
</tr>
<tr>
<td>Sex, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>43 (58)*</td>
<td>91 (40)</td>
</tr>
<tr>
<td>Female</td>
<td>31 (42)</td>
<td>137 (60)</td>
</tr>
<tr>
<td>Medical history, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>9 (12)</td>
<td>10 (4)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>3 (4)</td>
<td>30 (13)</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>3 (4)</td>
<td>4 (2)</td>
</tr>
<tr>
<td>Ischaemic heart disease</td>
<td>4 (5)</td>
<td>12 (5)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1 (1)</td>
<td>6 (3)</td>
</tr>
<tr>
<td>Dementia</td>
<td>0 (0)</td>
<td>4 (2)</td>
</tr>
<tr>
<td>Depression</td>
<td>0 (0)</td>
<td>19 (8)</td>
</tr>
<tr>
<td>Medications, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Psychoactive medications</td>
<td>17 (23)</td>
<td>65 (29)</td>
</tr>
<tr>
<td>Cardioactive medications</td>
<td>36 (49)</td>
<td>91 (40)</td>
</tr>
<tr>
<td>Heart rate (b.p.m.), mean (95% CI)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RR interval† (s), mean (95% CI)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline heart rate</td>
<td>69.1 (67.4, 70.8)</td>
<td>71.9 (70.8, 72.9)</td>
</tr>
<tr>
<td>Minimal heart rate</td>
<td>28.1 (25.6, 30.6)</td>
<td>55.1 (53.9, 56.3)</td>
</tr>
<tr>
<td>Baseline RRI</td>
<td>0.87 (0.85–0.89)</td>
<td>0.83 (0.82–0.85)</td>
</tr>
<tr>
<td>Maximal RRI</td>
<td>2.13 (1.96–2.34)</td>
<td>1.09 (1.06–1.11)</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg), mean (95% CI)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline SBP</td>
<td>139.0 (136.0, 141.8)</td>
<td>139.0 (137.3, 140.6)</td>
</tr>
<tr>
<td>Maximal SBP drop</td>
<td>61.1 (59.2, 63.0)</td>
<td>25.8 (25.0, 26.5)</td>
</tr>
</tbody>
</table>

*Male Odds Ratio = 2.05 (95% CI = 1.20–3.49).
†Untransformed means and 95% CIs presented.

CSM = carotid sinus massage; CI = confidence interval.

Results

Subjects

Two thousand six hundred and seventy-five new patients were referred to our facility over the 3-year period. Three hundred and two patients, mean age = 71.5 years (range = 38–98 years), were investigated with CSM. Seventy-four (25%) patients had positive responses to CSM in at least one position. Thirty-seven (50%) subjects had CI–CSH, and 37 (50%) had VD–CSH. Of the 37 subjects with CI–CSH, 9 (24%) subjects had an SBP reduction of <50 mmHg and 28 (76%) had an SBP reduction of 50 mmHg or greater. Patients with CSH were significantly older (75.2 vs 70.2 years, \( P < 0.001 \)), and positive responses were more likely in men than women [32% vs 19%, OR = 2.05, 95% CI (1.20–3.49); \( P < 0.01 \)] (Table 1). The increase in the positivity rate of CSM with age is more clearly demonstrated in Figure 1.

Position of CSM

Forty-five (61%) subjects had a positive CSM on the right side, 13 (18%) on the left side and 16 (22%) on both sides. Twenty-two (30%) patients had a positive response to CSM in the supine position, 16 (22%) in both supine and erect positions and 36 (49%) patients had a positive response with CSM in the upright position only. It was possible to have positive haemodynamic responses in more than one position, as even though no further CSM was carried out if the exact original presenting symptoms were reproduced, subjects who had positive haemodynamic responses without symptom reproduction continued to have further CSM until CSM had been performed in all four positions or until their original presenting symptom was reproduced.

The haemodynamic responses to CSM on both right and left carotid sinuses were available for comparison in 282 cases in the supine position and 211 in the erect position (Figure 2). The minimal HR was significantly lower with right-sided CSM compared to left-sided CSM in both supine (mean difference = −4.50, 95% CI = −5.98 to −3.02; \( P < 0.001 \)) and erect postures (mean difference = −5.28, 95% CI = −7.42 to −3.15; \( P < 0.001 \)). The SBP reduction was significantly larger in right-sided CSMs compared to left-sided CSMs in both supine (mean difference = 4.12, 95% CI = 2.56–5.67; \( P = 0.001 \)) and erect postures (mean difference = 4.03, 95% CI = 1.95–6.10; \( P < 0.001 \)). Paired comparisons between supine and erect responses were possible in 229 cases for right-sided CSM and 206 cases in left-sided CSM. The minimal HR post-CSM was significantly higher in the supine posture compared to the erect posture for both right-sided (mean difference = −3.30, 95% CI = −5.25 to −1.35; \( P < 0.001 \)) and left-sided (mean difference = −5.35, 95% CI = −7.27 to −3.43; \( P < 0.001 \)) CSM. SBP responses, however, were significantly smaller with supine posture compared to the erect posture in both right-sided (mean difference = −7.02, 95% CI = −8.95 to −5.10; \( P < 0.001 \)) and left-sided CSM (mean difference = −4.83, 95% CI = −6.51 to −3.15; \( P < 0.001 \)).
Is carotid sinus syndrome still relevant?

Figure 2. (A) Heart rate (b.p.m.) and (B) systolic blood pressure (mmHg) responses according to position of CSM. The clear squares represent the mean values for right to left comparisons, with upward error bars representing standard errors, while the opaque triangles represent the mean values for supine to erect comparisons with downward error bars representing standard errors. Right-sided CSM produced significantly lower minimal heart rate and larger SBP reduction compared to left-sided CSM in both supine ($P < 0.001$) and erect ($P < 0.001$) positions. Supine CSM resulted in lower minimal heart rate, but smaller SBP reduction compared to erect CSM in both right ($P < 0.001$) and left ($P < 0.001$) sides. HR = heart rate; SBP = systolic blood pressure; CSM = carotid sinus massage.

**Symptom response to CSM**

Information on symptom response to CSM was available for 73 of the 74 subjects. Fifty-two (71%) patients developed symptoms during or immediately following CSM. Thirty-two (62%) experienced syncope, 4 (8%) reported symptoms of presyncope, 15 (29%) complained of dizziness and one (2%) reported tingling in the hands. Twenty-one (29%) of the 73 patients were asymptomatic despite a positive CSM according to the diagnostic criteria. Forty-one (56%) subjects had reproduction of original presenting symptoms in response to CSM, 39 (95%) with complete symptom reproduction and 2 (5%) with partial reproduction of symptoms. Thirty-four (92%) subjects with the CI subtypes experienced symptoms with CSM compared to 18 (50%) of subjects with the VD subtype ($OR = 11.33$, 95% CI = 2.94–43.68; $P < 0.001$). Thirty-one (84%) of CICSH subjects but only 10 (28%) of VDCSH subjects had reproduction of presenting symptoms ($OR = 13.43$, 95% CI = 4.30–41.94; $P < 0.001$). No complications were reported in all 1,134 episodes of CSM performed on the 302 individuals.

**Discussion**

Twenty-five per cent of patients investigated with CSM in our tertiary referral unit had CSH. Positive responses to CSM, however, increased with age [5, 7]. Kerr and colleagues [8] recently reported a CSH prevalence of 39% in a sample of 272 community-dwelling elders aged $> 65$ years and 35% in the subgroup without falls, syncope or dizziness. If we considered only patients older than 65 years in our group of subjects, the positivity rate was 30%, still considerably lower than Kerr et al.’s prevalence in asymptomatic elders. Is CSH therefore merely an age-related clinical sign with the historical relationship suggested between CSH and syncope [1] simply signifying the coincidental occurrence of two common conditions within the same individuals? While CSH has been demonstrated in patients presenting with syncope with reproduction of spontaneous symptoms [12, 13], there are no data showing real-time haemodynamic derangements reproducing those seen during laboratory testing. Cardioinhibitory CSH associated with syncope is a Class 1 indication for permanent cardiac pacing for syncope occurring during spontaneous carotid stimulation and Class IIa indication for syncope with no clear provocative event [14]. The recommendations were, however, made on the basis of one randomized controlled study involving 60 subjects, a few other uncontrolled or non-randomized comparative studies [15, 16], and consensus rather than hard evidence (Class C). Since the publication of the above European Society of Cardiology guidelines, a further randomised controlled study also involving 60 subjects has also reported a beneficial effect for cardiac pacing in syncopal individuals with CSH and an otherwise negative work-up [17].

The evidence for the role of CSH in unexplained falls and drop attacks are even less established. CSH was reported as the attributable diagnosis, with either associated symptoms during CSM, or resolution of symptoms after clinical intervention, in 40% of drop attacks [3]. Patients with non-accidental falls presenting to the accident and emergency department were more likely than control subjects to have CSH [2]. However, while an initial randomized-controlled trial comparing cardiac pacing for patients with CICSH presenting with unexplained falls to conservative treatment found that cardiac pacing significantly reduced subsequent
The lower prevalence of CSH in patients investigated at our facility compared to older individuals in a local geographical area may be explained by referral bias and fewer male subjects in our cohort. While Kerr et al. [8] included all community-dwelling elders aged over 65, healthcare providers tended to refer healthier individuals to a syncope unit, and frailer individuals with multiple pathology to a general geriatric unit or day hospital. The investigative strategy adopted by our unit is to first and foremost exclude any primary cardiac pathology, in accordance to current guidelines [10]. Therefore, despite the association between CSH with sinoatrial disorders and ischaemic heart disease [4], patients with a history of heart disease are investigated for cardiac causes, without undergoing CSM. Only 44% of our cohort were male subjects compared to the 57% reported by Kerr et al. [8], CSH was significantly more likely in male subjects in both studies, which will also account for the higher prevalence of CSH in the community study.

Seventy-one per cent of our subjects developed symptoms with CSM and 56% were considered to have reproduction of presenting symptoms. If we diagnosed CSS by reproduction of symptoms, the diagnostic rate of CSS in our unit would be 14%. Defining CSS by symptom reproduction during CSM, so-called method of symptoms [7] will, however, dismiss cases with amnesia for loss of consciousness. Amnesia for loss of consciousness has been documented in 12% of patients presenting with syncope and 95% of patients presenting with unexplained falls, with witnessed syncope during CSM [20]. A more liberal approach of diagnosing CSS if no other attributable cause of unexplained falls or syncope can be found after a systematic approach has also been undertaken [10]. The recently published pacing study by Claesson et al. [17] mentioned earlier supports the more liberal approach to diagnosing CSS.

Symptom reproduction was significantly less likely in patients with pure VDCSH, with only 28% of subjects with VDCSH having reproduction of symptoms compared to 84% of subjects with CICSH. This raises the possibility of different underlying mechanisms for the VD and cardioinhibitory responses. The pathophysiology of CSH is poorly understood, with no clear evidence [21] for the central alpha-adrenoceptor upregulation hypotheses [21, 22]. Indeed, CICSH may be the trigger for the mechanisms contributing to associated symptoms, such as abnormal cerebral autoregulation [23].

Our study also further highlights the right-sided preponderance of CSH, and the importance of upright CSM [24]. Over 60% of our subjects had positive CSM on the right side alone. The magnitude of both HR and blood pressure responses was also significantly higher on the right side. This is assumed to be due to the predominantly right-sided innervation of the sinoatrial node [25]. The right-sided preponderance in positive responses to CSM has been noted previously [9], but had never before been systematically explored in a large sample. In 49% of our subjects, the diagnosis of CSH was only made with erect CSM and would have been missed if only supine CSM was performed. We have previously reported this important clinical observation [24], though CSH was diagnosed with upright CSM only in a smaller proportion (31%) of patients [24].

The mechanism by which the erect posture affects the HR and blood pressure responses to CSM remains unclear. On assumption of the upright posture, plasma volume is displaced towards the lower extremities by force of gravity. In normal subjects, sympathetic drive is increased to produce vasoconstriction and reflex tachycardia in order to maintain mean arterial pressure [26]. Parasympathetic tone is conversely reduced [27]. The cardioinhibitory response to CSM is vagally mediated and can be abolished with atropine [28], while the VD response is probably the result of sympathetic withdrawal [29]. As one would expect, the reduction in parasympathetic tone and enhanced sympathetic tone during the erect posture would account for the smaller HR response to CSM. The SBP drop following CSM, however, appears to be paradoxically exaggerated despite the increased sympathetic tone of the upright posture. This phenomenon may be explained by a reduction in vasoconstrictive ‘reserve’.

**Conclusion**

CSH was present in 25% of patients presenting with syncope, drop attacks and unexplained falls to our specialist falls and syncope facility. This figure appears lower than the prevalence of 35% in asymptomatic community-dwelling older people, raising the possibility that CSH may be an age-related physical sign rather than a causal mechanism of syncope, unexplained falls and drop attacks. In this large series, CSH was more likely in men than women, right-sided than left-sided CSM and erect than supine CSM. Correspondingly, greater HR and SBP reductions occurred during right-sided CSM than left-sided CSM, and a greater SBP but smaller HR response occurred with erect CSM compared to supine CSM. The importance of repeating CSM in the erect position was reinforced, while symptom reproduction was predominantly a feature of CICSH. CSM was remarkably safe with no complications reported in 1,134 episodes of massage. These observations have important implications for the conduct and interpretation of the test, and for the rational planning of future research.

**Key points**

- The positivity rate of carotid sinus massage in a large series of patients investigated at a tertiary referral unit is 25%.
- CSH may be an age-related physical sign, rather than a causal mechanism of syncope, unexplained falls and drop attacks.
- Carotid sinus massage was positive in the erect position only in 49%.
• Symptom reproduction is significantly more likely in the cardioinhibitory subtypes than the VD subtype.

Acknowledgements

Our thanks to Ann Harrison and Dawn Jungerius for providing database support.

Funding

M.P.T. was a recipient of the Royal College of Physicians/Dunhill Medical Trust Joint Research Fellowship. The Newcastle Hospitals Charitable Trusts provided the financial support to design and maintain the database which supported this work. This study was also supported by the National Institute for Health Research Biomedical Research Centre for Ageing which was awarded to the Newcastle upon Tyne Hospitals NHS Trust.

Conflicts of interest

None declared.

References

5. Humm AM, Mathias CJ. Unexplained syncope—is screening for carotid sinus hypersensitivity indicated in all patients aged >40 years? J Neurol Neurosurg Psychiatry 2006; 77: 1267–70.
Gender differences and cognitive aspects on functional outcome after hip fracture—a 2 years’ follow-up of 2,134 patients

BODIL SAMUELSSON1, MARGARETA I. HEDSTRÖM2, SARI PONZER3, ANITA SÖDERQVIST3, EVA SAMNEGÅRD1,4, KARL-GÖRAN THORNGREN5, TOMMY CEDERHOLM6, MARIA SÄÄF7, NILS DALEN1

1Division of Orthopaedics, Department of Clinical Science, Karolinska Institutet, Danderyd Hospital, SE-18288 Stockholm, Sweden
2Department of Clinical Science, Intervention and Technology (Clintec), Karolinska Institutet, Karolinska University Hospital, 14186 Stockholm, Sweden
3Division of Orthopaedics, Department of Clinical Science and Education, Karolinska Institutet, Södersjukhuset SE-1 1883 Stockholm, Sweden
4Department of Orthopaedics, Visby General Hospital, SE-62184 Visby, Sweden
5Department of Orthopedics, Lund University Hospital, SE-22185 Lund, Sweden
6Department of Public Health and Caring Sciences, Clinical Nutrition and Metabolism, Uppsala University, Uppsala Science Park, SE-75185 Uppsala, Sweden
7Department of Medicine, Karolinska University Hospital, Karolinska Institutet, Stockholm, Sweden

Address correspondence to: B. Samuelsson, Sophiahemmet University College, Box 5605, SE-11486 Stockholm, Sweden.
Tel: (+46) 704 176 973; Fax: (+46) 8 10 29 09. Email: bodil.samuelsson@shh.se

Abstract

Background: Hip fractures as well as cognitive dysfunction become increasingly prevalent in growing ageing populations. Hip fractures are approximately three times more common in elderly women.

Objective: We analysed outcome after hip fracture with respect to gender and cognitive function.


Methods: Gender differences in residence, walking ability and activity of daily living (ADL) were analysed at baseline, after 4 and 24 months in patients with and without intact cognitive function.

Results: Women were older, more often living alone and had poorer walking ability (P < 0.001). Cognitive dysfunction was equally common by gender. Women were more often treated with a prosthesis (P < 0.001) and sent to rehabilitation (P < 0.001). In the cognitive dysfunction group, men had more co-morbidity (P < 0.001) and total loss of walking ability (P = 0.03), but more often resided in own homes (P = 0.03). There was no gender difference in ADL.

Conclusion: Men had a higher risk for loss of walking ability and death only in patients with cognitive dysfunction. Cognitive function was the most important factor for returning to own home and regain pre-fracture function.

Keywords: Hip fracture, gender differences, cognitive function, living conditions, walking ability, elderly