Carotid sinus hypersensitivity—a modifiable risk factor for fractured neck of femur

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Abstract

Background: the potential impact on morbidity, mortality and health care economics makes it important to identify patients at risk of fracture, in particular fractured neck of femur (FNOF). Older patients with carotid sinus hypersensitivity (CSH) are more likely to have unexplained falls and to experience fractures, particularly FNOF. Our objective was to determine the prevalence of CSH in patients with FNOF.

Design: case–controlled prospective series.

Methods: consecutive cases were admissions over 65 years with FNOF. Controls were consecutive patients admitted for elective hip surgery, frail elderly people admitted to hospital medical wards and day-hospital patients. All patients had a clinical assessment of cognitive function, physical abilities and history of previous syncope, falls and dizziness, in addition to repeated carotid sinus massage with continuous heart rate and phasic blood pressure measurement.

Results: heart rate slowing and fall in systolic blood pressure was greater for patients with FNOF than those admitted for elective hip surgery (P < 0.05 and P < 0.001). CSH was present in 36% of the FNOF group, none of the elective surgery group, 13% of the acutely ill controls and 17% of the outpatients. It was more likely to be present in FNOF patients with a previous history of unexplained falls or an unexplained fall causing the index fracture. The heart rate and systolic blood pressure responses to carotid sinus stimulation were reproducible.

Conclusion: older patients with an acute neck of femur fracture who do not give a clear history of an accidental fall or who have had previously unexplained falls are likely to have CSH. CSH may be a modifiable risk factor for older patients at risk of hip fracture.

Keywords: carotid sinus hypersensitivity, falls, fractured neck of femur

Introduction

In the UK the incidence of fractured neck of femur (FNOF) increases with age from 2 per 1000 population at 35–54 years to 5 per 1000 population at 74–84 years. Women over 65 make up 80% of all cases [1–3]. The probability of sustaining a hip fracture before the age of 85 is 12% for women and 5% for men and, if present trends continue, it is predicted that these probabilities will double by the year 2016 [4]. At any one time 20% of orthopaedic beds in the UK are occupied by these patients and mortality rates in elderly patients with a hip fracture are up to 35% [5].

The most common cause of FNOF is a fall, yet only 1% of falls result in FNOF [4]. The increase in hip fractures with age is not fully accounted for by an increase in the number of falls or a decrease in hip bone mass, indicating that other factors increase a person’s susceptibility [6, 7]. An important but often overlooked cause of unexplained falls and syncope in elderly subjects is carotid sinus hypersensitivity (CSH). CSH is diagnosed when carotid sinus massage produces marked bradycardia (cardioinhibitory response—asystole in excess of 3 s) and/or hypotension (vasodepressor response—50 mmHg fall in systolic blood pressure). Symptoms result from cerebral hypoperfusion caused by bradycardia, hypotension or both, and are mediated by exaggerated baroreflex activity [8]. In one series of patients with CSH, 25% had sustained
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a fracture during a symptomatic event, the most common being FNOF [9].

We have determined the prevalence of CSH in a consecutive series of patients with FNOF and reviewed the clinical characteristics of these patients.

Methods

We recruited 55 consecutive patients over 65 years admitted with a FNOF and 35 consecutive patients over 65 years admitted for elective hip surgery (elective hip surgery, control group). Patients were excluded if they had a recent myocardial infarction or a stroke (within 3 months) or had a carotid bruit or a history of ventricular fibrillation or ventricular tachycardia. Five patients with FNOF and two patients admitted for EHS were excluded.

Subjects were studied within 24 h of admission. All had a full clinical assessment including general medical history and examination. The history included details of pre-morbid falls, syncope and dizziness, the frequency and duration of symptomatic episodes, details of associated soft tissue injuries or fractures and factors known to provoke symptoms. Cognitive function (Blessed mental test score [10]) and level of ability to perform common physical activities of daily living (Barthel index [11]) before their index fall were also measured. Cognitive function and the Barthel index were used as markers of frailty. Information was acquired where applicable from carers and other informants.

The clinical assessment was followed by right and left sided supine carotid sinus massage with continuous heart rate (electrocardiograph) and phasic blood pressure (digital photoplethysmography: Finapres) recording before, during and for 2 min after carotid sinus massage. The operator doing carotid sinus massage was blind to the recordings. Carotid sinus massage was performed using a standard technique: longitudinal massage over the carotid sinus, medial to the sternomastoid muscle and level with the upper border of the cricoid cartilage. Carotid sinus massage was carried out for 5 s with a 1 min interval between right and left sides. Carotid sinus massage was repeated, both supine and upright (head-up tilt to 70°, footplate-assisted), before hospital discharge. Orthostatic changes in blood pressure and heart rate were also recorded after 15 min supine and during 2 min of standing before discharge. FNOF patients were reviewed 6 months after hospital discharge; the remaining 42 had a pre-discharge assessment at 15 ± 4 days. Thirty EHS patients had carotid sinus massage on admission (mean age 74 ± 7 years; 18 female). The mean length of stay was 16 ± 6 days and all had pre-discharge assessment at 11 ± 3 days.

Heart rate slowing and fall in systolic blood pressure during carotid sinus massage was more marked for FNOF than EHS patients (P < 0.05 and P < 0.001 respectively) and responses did not differ for the different study days (Figures 1 and 2). CSH was detected in 56% of the FNOF patients (n = 18) but in none of the EHS patients (P < 0.01). Ten patients had cardioinhibitory CSH on admission or before discharge. A response in excess of 3 s was reproducible in four and in excess of 2.5 s in the remaining six (Figure 3). Eight patients had vasodepressor CSH which was reproducible in five; the remaining three patients had died before repeat carotid sinus massage (Figure 4).

FNOF patients were older than EHS patients (P < 0.01) but age did not influence the prevalence of CSH (P = 0.2). FNOF patients had poorer cognitive function (P < 0.01) and were more likely to have previously experienced unexplained falls (P < 0.01). There was no difference in either the ability to perform...
Within the FNOF group, those with documented CSH had more marked cognitive impairment ($P < 0.05$), were more likely to have a history of previous unexplained falls ($P < 0.05$) and to have had an unexplained fall precipitating the index fracture ($P < 0.01$) than those with no evidence of CSH (Table 2).

Acutely ill and outpatient controls were the same age and had cognitive and physical function scores similar to those of FNOF patients (Table 1). Significantly fewer patients in these groups had CSH: 13% of the acutely ill controls and 17% of the outpatient controls (acutely ill versus FNOF, $P < 0.05$; outpatient control versus FNOF, $P < 0.08$). Overall heart rate and systolic blood pressure responses during carotid sinus massage did not differ from those of FNOF patients. When acutely ill and outpatient controls were compared with EHS patients, the overall heart rate response to carotid sinus massage was slower and the systolic blood pressure response greater (Figures 5 and 6). Similarly, the prevalence of CSH was higher for acutely ill and outpatient controls than EHS patients ($P < 0.02$ and $P < 0.04$ respectively). In acutely ill and outpatient controls with CSH neither the frequency of symptoms of dizziness, syncope or falls, nor the degree of cognitive impairment or daily activities (Barthel index) or for previous symptoms of syncope or dizziness (Table 1).

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physical frailty differed from those in whom the response was normal, but numbers were small. FNOF, acutely ill and outpatient controls were more likely to have ischaemic heart disease and/or cerebrovascular disease (P < 0.01) than EHS patients, but there was no difference in the use of cardiovascular medication.

Six months after discharge, 30 FNOF patients were available for review. Of the remainder, six had died, four refused to attend and two were lost to follow-up. Of the 10 patients with previously documented CSH, eight had a reproducible response and two had borderline responses to carotid sinus massage (2.6 s asystole and 40 mmHg fall in systolic blood pressure). Five of this group had had further unexplained falls or presyncope. Of the remaining 20 patients, only one had CSH (vasodepressor; 55 mmHg; previous borderline responses) and none had experienced falls or syncope.

The overall heart rate and systolic blood pressure responses to carotid sinus massage were the same at the follow-up study as on the inpatient study days (Figures 1 and 2). Performing carotid sinus massage during head-up tilt did not identify additional patients with CSH. Only five patients had orthostatic hypotension on any of the three study days; three of these also had CSH.

None of the patients in the study had any adverse neurological or cardiac events induced by carotid sinus massage.

Discussion

CSH is frequently overlooked as a cause of unexplained falls and syncope, particularly in elderly people. Centres which routinely perform carotid sinus massage report symptoms due to hypersensitivity in up to 45% of patients referred because of unexplained syncope or falls [13]. The carotid sinus syndrome is diagnosed when reflex hypersensitivity is documented in a patient with otherwise unexplained symptoms. Baroreflex sensitivity normally declines with advancing years, but in patients with carotid sinus syndrome the baroreflex response is exaggerated, so that a given

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Table 1. Clinical characteristics of the four patient groups

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>FNOF</th>
<th>EHS</th>
<th>Acute frail</th>
<th>Chronic frail</th>
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<tbody>
<tr>
<td>Number</td>
<td>50</td>
<td>31</td>
<td>30</td>
<td>35</td>
</tr>
<tr>
<td>Age (years)</td>
<td>81 ± 7</td>
<td>74 ± 7</td>
<td>79 ± 7</td>
<td>82 ± 8</td>
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<tr>
<td>Sex (% female)</td>
<td>78</td>
<td>58</td>
<td>70</td>
<td>66</td>
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<tr>
<td>Blessed MTS (total = 37)</td>
<td>27 ± 12</td>
<td>36 ± 1</td>
<td>52 ± 6</td>
<td>26 ± 9</td>
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<tr>
<td>Barthel ADL (total = 20)</td>
<td>18</td>
<td>19</td>
<td>18</td>
<td>16</td>
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<tr>
<td>Previous falls (%)</td>
<td>58</td>
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<td>55</td>
<td>51</td>
</tr>
<tr>
<td>Previous syncope (%)</td>
<td>6</td>
<td>3</td>
<td>0</td>
<td>8</td>
</tr>
<tr>
<td>Previous dizziness (%)</td>
<td>18</td>
<td>19</td>
<td>20</td>
<td>14</td>
</tr>
<tr>
<td>Carotid sinus hypersensitivity (%)</td>
<td>36</td>
<td>0</td>
<td>13</td>
<td>17</td>
</tr>
</tbody>
</table>

FNOF, fractured neck of femur; EHS, elective hip surgery; MTS, mental test score; ADL, activities of daily living.

*P < 0.01 compared with FNOF; †P < 0.05 compared with FNOF; ‡P = 0.08 compared with FNOF.
change in systolic blood pressure results in an excessive slowing of heart rate [14]. Patients with the syndrome may present atypically with falls and deny syncope. In one series, one-third of elderly patients had amnesia for loss of consciousness, despite witnessed syncope [15].

Carotid sinus syndrome is associated with appreciable morbidity. Approximately half of elderly patients with this diagnosis report injuries during symptomatic episodes, of which fractures (predominantly of the femoral neck) are sustained in 25% [9]. In a nursing-home population Murphy observed a threefold increase in the fracture rate associated with falls in patients who had CSH [16]. One possible explanation for the association between CSH and FNOF is that loss of consciousness occurs rapidly and patients are obtunded or unconscious as they fall, thereby preventing reflex protective hand or arm mechanisms. This fits with the published observations that FNOF is more likely if patients fail to use the protective arm reflex which would otherwise result in wrist rather than hip fractures [4].

Complications from carotid sinus massage are uncommon. A recent study of 5000 episodes of carotid sinus massage reported only a 0.2% complication rate, most of these being transient cerebral episodes [17]. In the present study no patient developed either neurological or cardiac complications. Neurovascular instability, manifesting as CSH, was present in one-third of FNOF patients and particularly in those with a previous history of unexplained falls or an unexplained

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Present</th>
<th>Absent</th>
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<tr>
<td>No. of subjects</td>
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</tr>
<tr>
<td>Mean age (years)</td>
<td>83 ± 7</td>
<td>80 ± 7</td>
</tr>
<tr>
<td>Sex (% female)</td>
<td>72</td>
<td>81</td>
</tr>
<tr>
<td>Blessed MTS (total = 37)</td>
<td>21 ± 13</td>
<td>30 ± 10^3</td>
</tr>
<tr>
<td>Barthel ADL (total = 20)</td>
<td>16</td>
<td>18</td>
</tr>
<tr>
<td>Previous falls (%)</td>
<td>78</td>
<td>47^a</td>
</tr>
<tr>
<td>Unexplained fall caused fracture (%)</td>
<td>66</td>
<td>13^a</td>
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<tr>
<td>Previous syncope (%)</td>
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<td>3</td>
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<tr>
<td>Previous dizziness (%)</td>
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<td>6</td>
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<tr>
<td>Ischaemic heart disease (%)</td>
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<td>Cerebrovascular disease (%)</td>
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<td>50</td>
<td>44</td>
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MTS, mental test score; ADL, activities of daily living.
^aP < 0.05; ^bP < 0.001.

Figure 5. Heart rate response (mean R–R interval ± SD) to carotid sinus massage at initial assessment (study 1) for patients with fractured neck of femur (FNOF), patients admitted for elective hip surgery (EHS), acutely ill elderly patients admitted to medical wards (acute frail; AF) and frail elderly outpatients (chronic frail; CF). FNOF versus EHS, P < 0.01; AF versus EHS, P < 0.01; CF versus EHS, P < 0.004.

Figure 6. Fall in systolic blood pressure (mean SBP ± SD) during carotid sinus massage at initial assessment (study 1) for patients with fractured neck of femur (FNOF), patients admitted for elective hip surgery (EHS), acutely ill elderly patients admitted to medical wards (acute frail; AF) and frail elderly outpatients (chronic frail; CF). FNOF versus EHS, P < 0.0001; AF versus EHS, P < 0.01; CF versus EHS, P < 0.001.
fall causing the index fracture. Whether these patients have had a syncopal episode and amnesia for loss of consciousness, or whether intermittent changes in heart rate and blood pressure cause gait instability and falls, is unclear.

The prevalence of reflex hypersensitivity in asymptomatic individuals is uncertain. Early investigators reported that reflex hypersensitivity could be elicited in 10% of a healthy population and that the prevalence was even higher in those with coronary artery disease or hypertension [18, 19]. Although such studies used prolonged massage and predated the standardization of diagnostic criteria for reflex hypersensitivity, they led to scepticism about the syndrome as a diagnostic entity. More recent reports cite prevalence rates of 2–5% in healthy older subjects [20, 21]. In this series, elective surgery patients had no marked cardioinhibitory or vasodepressor responses documented. There is ample evidence for a causal association between reflex hypersensitivity and spontaneously occurring bradycardic symptoms. For example, Hudson et al. [22], reported that 65% of patients attending for routine electrocardiograph who had a hypersensitive response had previously unreported syncopal and dizzy symptoms.

There were several differences between patients admitted because of fractures and those admitted for elective surgery; fracture patients were acutely ill, older and more cognitively impaired. However, age did not appear to be a responsible factor for the difference in prevalence of CSH. To determine whether these other variables were contributing to the difference, chronic and acute frail, elderly patients matched for age, sex, frailty and cognition were compared with the fracture and elective surgery patients. The prevalence of CSH was lower in both acute and chronic frail elderly subjects, indicating that the baroreflex hypersensitivity was not simply a marker for frailty or acute illness. Fracture patients with CSH had other characteristics which differed from patients with normal responses. Cognitive impairment was more marked, a previous history of recurrent unexplained falls more common and patients were less likely to recognize an accidental fall as causing the index fracture.

Our data support a causal association between CSH and falls. Most of those with a hypersensitive response had a history of unexplained falls. Fractured femur patients who had a hypersensitive response continued to have further falls during follow-up. This was not so for patients who did not have a hypersensitive response. Both the heart rate and blood pressure responses to carotid sinus massage were reproducible after discharge, indicating that hypersensitivity is not solely related to an acute event.

The most common cause of fracture is a fall, but hip fracture rates are not entirely accounted for by fall rate or altered bone mass, indicating that other factors may increase the susceptibility to hip fractures. One such factor could be haemodynamic instability manifesting as an exaggerated response to carotid sinus stimulation. The possibility that reflex hypersensitivity might be a marker for those at risk of fracture from falls could have major health care implications.

Few studies have examined the natural history of either asymptomatic subjects with CSH or patients with the syndrome. The timing of therapeutic intervention in the syndrome is controversial. Whilst most agree that treatment is necessary when a patient has had more than two syncopal episodes, there is no consensus on the management of less symptomatic individuals. In view of the high injury rate associated with symptomatic episodes, treatment should perhaps be considered even after one syncopal attack [23]. The possible role of prophylactic treatment in those with a hypersensitive response has not been addressed. Current treatment of choice for those with cardioinhibitory carotid sinus syndrome is atrioventricular sequential cardiac pacing [24]. Treatment of the vasodepressor response is less satisfactory because of our poor understanding of its pathophysiology [25]. Prospective cohort studies are required to determine whether CSH is a risk fracture for FNOF and would benefit from early pacing intervention strategies.

Key points
• Carotid sinus hypersensitivity may be a modifiable risk factor for fractured neck of femur in old people.
• Carotid sinus hypersensitivity is present in 36% of fractured neck of femur patients but absent in age-matched controls attending for elective hip surgery.
• In the majority of fractured neck of femur patients with carotid sinus hypersensitivity an unexplained fall resulted in the index fracture, and most have a history of recurrent unexplained falls.

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References
Carotid baroflex in hip fractures


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