Carotid Sinus Syndrome: A Modifiable Risk Factor for Nonaccidental Falls in Older Adults (SAFE PACE)

Rose Anne M. Kenny, MD, FRCP,* David A. Richardson, MRCP,* Nick Steen, PhD;† Rodney S. Bexton, DM, FRCP;‡ Fiona E. Shaw, MRCP,* John Bond, BA†

Newcastle Upon Tyne, United Kingdom

OBJECTIVES The aim of the study was to determine whether cardiac pacing reduces falls in older adults with cardioinhibitory carotid sinus hypersensitivity (CSH).

BACKGROUND Cardioinhibitory carotid sinus syndrome causes syncope, and symptoms respond to cardiac pacing. There is circumstantial evidence for an association between falls and the syndrome.

METHODS A randomized controlled trial was done of consecutive older patients (>50 years) attending an accident and emergency facility because of a non-accidental fall. Patients were randomized to dual-chamber pacemaker implant (paced patients) or standard treatment (controls). The primary outcome was the number of falls during one year of follow-up.

RESULTS One hundred seventy-five eligible patients (mean age 73 ± 10 years; 60% women) were randomized to the trial: pacemaker 87; controls 88. Falls (without loss of consciousness) were reduced by two-thirds: controls reported 669 falls (mean 9.3; range 0 to 89), and paced patients 216 falls (mean 4.1; range 0 to 29). Thus, paced patients were significantly less likely to fall (odds ratio 0.42; 95% confidence interval: 0.23, 0.75) than were controls. Syncopal events were also reduced during the follow-up period, but there were much fewer syncopal events than falls—28 episodes in paced patients and 47 in controls. Injurious events were reduced by 70% (202 in controls compared to 61 in paced patients).

CONCLUSIONS There is a strong association between non-accidental falls and cardioinhibitory CSH. These patients would not usually be referred for cardiovascular assessment. Carotid sinus hypersensitivity should be considered in all older adults who have non-accidental falls.

(From the *Cardiovascular Investigation Unit, Royal Victoria Infirmary/MRC Development Centre for Clinical Brain Ageing, Newcastle General Hospital, Newcastle Upon Tyne; †Centre for Health Services Research, University of Newcastle Upon Tyne; ‡Regional Cardiothoracic Unit, Freeman Hospital, Newcastle Upon Tyne, United Kingdom. This work was supported by a grant from the National Health Service Cardiovascular Research and Development Programme, by Research Into Ageing and by an education grant from Medtronic, Minneapolis, Minnesota. Manuscript received March 30, 2001; revised manuscript received June 20, 2001, accepted August 1, 2001.)

See page 1497

Carotid sinus syndrome is characterized by exaggerated bradycardia and hypotension in response to carotid sinus stimulation. The clinical manifestation of the syndrome is typically of recurrent syncope, and the syndrome is predominantly either “cardioinhibitory” or “vasodepressor.” The “cardioinhibitory” type is characterized by asystole during carotid sinus massage (CSM), the vasodepressor type by hypotension during CSM (1). Patients with recurrent syncope who have the cardioinhibitory type benefit from dual-chamber cardiac pacing—80% to 90% of syncopal episodes are abolished (2–4). The present American College of Cardiology/American Heart Association pacing guidelines recommend dual-chamber cardiac pacing for repeated syncope in patients in whom the cardioinhibitory response is considered to be the attributable cause of symptoms (2). There are no recommendations for pacing in patients with falls who have a cardioinhibitory response, yet preliminary data suggest an association between falls and carotid sinus hypersensitivity (CSH) (5–8).

Falls are a major health care and cost priority (9). Each year approximately 30% of people over 65 years, living at home, will fall (10,11). This figure rises to 60% in long-term care populations (12). Approximately 10% to 20% of falls result in injury and 2% to 6% in fractures (11). Falls are the sixth leading cause of death in older adults (13). There is a critical need for new strategies to prevent falls in older people, yet few single interventions are of proven benefit (14).

Recent series have reported some overlap between symptoms of falls and syncope (5,11). One explanation for this is amnesia for loss of consciousness (6). Another is that older patients who have gait and/or balance problems may experience balance instability and consequently fall during an episode of bradycardia-induced hypotension. Syncopal episodes or falls are unwitnessed in 40% to 60% of older people over 65, thus rendering a diagnosis of syncope in the absence of an accurate history and witness account more difficult (15).

We hypothesize that there is a causal association between falls and CSH. Individuals who fall may not meet the current criteria for pacing in the absence of a clear history of recurrent syncope, but these patients may be missing out on effective treatment because of this. Our question was...
whether cardiac pacing would reduce subsequent falls in older patients who presented with non-accidental falls and who had a cardioinhibitory response to carotid sinus stimulation.

METHODS

This was a randomized controlled trial of cardiac pacing in a consecutive series of cognitively normal (mini-mental state examination [MMSE] in excess of 23 out of a total of 30 points) (16) adults (age 50 years or over) attending the accident and emergency department because of a non-accidental fall. This was defined as coming to rest on the ground or another lower level, and which was unexplained and not due to an accidental event such as a slip or trip, or not attributable to a medical cause such as epilepsy, stroke, alcohol excess, orthostatic hypotension, other bradyarrhythmias or tachyarrhythmias, and so forth.

Identification of participants. Consecutive adult attendees, 50 years or over, were screened for 29 months by dedicated research staff in the accident and emergency department. Initial screening included age and the reason for attendance. This was followed by a more detailed screening of people who had fallen, including the type of fall, the explanation for the fall and cognitive status (MMSE). A fall was defined as an event whereby an individual came to rest on the ground or another lower level.

Participants were excluded from further study if they had: 1) cognitive impairment (MMSE <24)—because the details of the event would possibly be unreliable; 2) a medical explanation for the event within 10 days of presentation; 3) an accidental fall; 4) were blind; 5) lived outside of the 15-mile radius of the accident and emergency department; 6) had a contraindication to CSM (17,18); or 7) were receiving medications known to cause a hypersensitive response to CSM (16).

Clinical assessment. Eligible participants were invited to attend the Cardiovascular Investigation Unit for a more detailed history and assessment including frequency of injuries, medications (in particular those known to be risk factors for falls [2,11]), and full physical examination including neurological, cardiovascular and gait and balance assessment (11).

Carotid sinus massage was carried out during continuous, noninvasive blood pressure (digital photoplethysmography; Finapres; Ohmeda) and heart rate (surface electrocardiogram) monitoring using standard methods for CSM (19). Patients rested supine for 5 min and firm massage was then applied over the carotid sinus on the right side and then left side, for 5 s each with a 1-min interval between sides. The sinus is located at the point of maximum impulse of the carotid artery, level with the cricoid cartilage and two finger breadths below the angle of the jaw. If no abnormal response was elicited supine, patients were tilted head-up to 70° and the procedure was repeated (20). A significant cardioinhibitory response was defined as 3 s or more asystole, a significant vasodepressor response as 50 mm Hg or more drop in systolic blood pressure (when asystole was <3 s), and a “mixed” response was combined cardioinhibitory and vasodepressor responses.

Assessment of outcome. The primary outcome was the number of falls during the year after randomization. Secondary outcomes were the number of syncopal episodes and the number of injurious events. Symptom recurrence (falls, syncope) was recorded daily on self-completion diary cards, which were returned at the end of each week for one year.

Trial participants. Participants who had cardioinhibitory CSH were randomized to receive a pacemaker or no-pacing intervention (by block randomization; in blocks of eight). All paced patients received a rate drop response physiologic dual-chamber pacemaker (Thera RDR, Medtronic, Minneapolis, Minnesota). This is a physiologic dual-chamber pacemaker that paces if the patient’s heart rate falls below a predetermined rate (50 beats/min) and paces at a predetermined higher rate (100 beats/min) for a fixed time period, gradually decreasing the pacing rate by 5 beats/min at 1-min intervals to a programmed lower rate or until the patient’s own rate intervenes if this is higher than the programmed lower rate.

Sample size. The sample size was based on detecting a 40% difference in the number of falls (from 10 falls per year to 6 falls per year), assuming a standard deviation (SD) of 8 falls per year (21). Using standard methods for a continuous variable, it was determined that 85 subjects in each group would give us 90% power to detect this difference assuming a type 1 error rate of 5% (5).

Methods of analysis. The primary hypothesis was that pacing would reduce the number of falls in patients who had a pacemaker implanted. Two outcome measures were considered: 1) falls with no reported loss of consciousness—whether accidental or non-accidental; and 2) episodes of syncope. Whether or not a participant fell in a particular week was analyzed using multilevel modeling with occasions nested within participants (22).

All study participants gave informed written consent. The study was approved by the Newcastle and North Tyneside Ethics Committee.

RESULTS

An audit trail of participants throughout the study is shown in Figure 1. Of 71,299 attendees over 50 years of age, 24,251 presented because of a fall or syncopal event (34%).

Thirty-nine percent (n = 9,397) had an accidental fall,
26% (n = 6,217) a medical explanation for the fall, 16% (n = 3,937) had cognitive impairment, and falls were non-accidental in the remainder (n = 3,384; 14%). Six percent (199) of these had predetermined contraindications to CSM, carotid stenosis >70% (n = 34; 17%), recent stroke or transient ischemic attack (n = 104; 52%), severe aortic stenosis (n = 2; 1%), myocardial infarction (n = 47; 24%), ventricular fibrillation or tachycardia (n = 9; 5%), and gross obesity (n = 3; 2%). A further 38% (n = 1,270) declined CSM. Of 1,624 patients who were suitable for and agreed to CSM, 34% had CSH—cardioinhibitory or “mixed” in 16% (n = 257), and vasodepressor in 17% (n = 283). Of those with a cardioinhibitory response, 43 declined entry into the randomization phase of the study and a further 39 were on cardiovascular medications, which could not be discontinued and which may have contributed to the abnormal heart rate responses to CSM (Fig. 1).

One hundred seventy-five trial participants were randomized: 87 paced patients and 88 controls (mean age 73 ± 10 years; 60% were women). One hundred fifty-nine partici-
pants completed the study (83 paced patients; 76 controls). Reasons for failure to complete were death (8 patients) and withdrawal from study (8 patients). Reasons for withdrawal were inability to continue in study—changed domicile, intercurrent illness, disinterest. None of the control subjects who withdrew received pacemakers during the follow-up period. Participants who withdrew or died had slightly more falls in the year preceding the study (median 3 patients) compared with those who completed the study (median 2 patients); this difference was not significant.

One hundred fifty-nine patients who completed one year of follow-up returned 7,311 diaries—a completion rate of 88% (paced patients 85%; controls 92%).

Clinical investigations. Trial participants had a median of two falls (mean 9.3; range 0 to >100) before the index presentation (range 0 to 16). Seventy percent (122 patients) had previously sustained at least one serious injury and 30% (52 patients) a previous fracture. The baseline clinical characteristics of paced patients and controls did not differ significantly. Gait was abnormal in 45% overall, and balance was abnormal in 79% of all patients. Medication use was similar in both groups (Table 1). Seventy-five percent of paced patients and 72% controls had a positive response to CSM when supine, and 24% of paced patients and 28% controls had a positive response only when upright. The duration of the cardioinhibitory response was 4,367 ± 1,073 s. Fifty-two patients (30%) had witnessed loss of consciousness during CSM; 41 (80%) had amnesia for this. No patients had persistent neurological symptoms in response to CSM, but 8 (0.8%) had transient neurological symptoms, which data has been recently reported (20).

Falls with no reported loss of consciousness. The number of falls was reduced by 70%; 699 in controls and 216 in paced patients. The mean number of falls was considerably smaller for paced patients than for controls (4.1; range 0 to 29 vs. 9.3; range 0 to 89). The spread of observations was also smaller (the SD of the number of falls was 8.3 for paced patients and 18.1 for controls). Fitting a multilevel logistic model (weeks nested within participants) indicated that paced patients were less likely to fall than were controls (OR [odds ratio] 0.42; 95% CI [confidence interval] 0.23, 0.75). The benefit of pacing was similar for paced patients with a single fall and paced patients with recurrent falls (OR 1.26; 95% CI: 0.38, 4.14) (Table 2).

Diaries completed by paced patients after they were paced were compared with those they completed while waiting for pacing (mean 7, range 1 to 30 weeks). Eighty-two paced patients completed 659 diaries before pacing. During this period 35 (43%) paced patients fell: a total of 92 falls. Adjusting for the number of diaries returned, the mean number of falls before pacing was 8.2 compared with 4.1 falls per year after pacing. Fitting a multilevel logistic model indicates that paced patients are less likely to fall after pacing than before (OR 0.42; 95% CI: 0.38, 0.47).

Episodes of syncope. Only 28 (16%) participants reported syncope: total of 60 episodes; 22 syncopal events were reported by paced patients and 47 by controls (Table 2). There was no significant difference overall between the proportion of paced patients who reported syncope (11%) and the proportion of controls (22%; the Fisher exact test p = 0.063). When participants with a history of recurrent falling (two or more falls in previous year) were considered separately, more controls (29%) reported syncope than did paced patients (8%; the Fisher exact test p = 0.04).

Fitting a multilevel logistic model (weeks nested within participants) indicated that paced patients were less likely to report an episode of syncope than were controls. This was not significant (OR 0.53; 95% CI: 0.23, 1.20). However, paced patients with a previous history of recurrent falls were less likely to experience syncope than controls who had previous history of recurrent falls (OR 0.38; 95% CI: 0.14, 0.97).

While waiting for a pacemaker, 9 of 82 paced patients recorded a total of 23 episodes of syncope. Adjusting for the number of diaries returned, the mean number of episodes before pacing was 1.9 compared with 0.2 episodes per year.
reported after pacing: paced patients are less likely to experience syncope after pacing than before (OR 0.24; 95% CI: 0.12, 0.48).

Impact of falls. Fifty-two controls experienced 716 events (combined falls and syncope), 4 suffered a fracture, and 32 had a total of 198 soft tissue injuries. Forty-nine paced patients experienced 238 events, 3 suffered a fracture and 26 experienced 58 soft tissue injuries. The presence of hypertension, stroke, diabetes, ischemic heart disease, cardiovascular drugs, resting heart rate, the duration of the cardioinhibitory pause or patient’s age did not correlate with event rates during follow-up.

DISCUSSION

Falls were the commonest single reason for older adults to attend the accident and emergency department. Over one-third of adults over 50 years attended because of a “fall.” Of those, 14% attended because of nonaccidental falls, and one in three of these had vasodepressor carotid sinus hypersensitivity or cardioinhibitory CSH. Although all adults over 50 years were screened, the mean age of eligible subjects was 74. We have previously reported that the prevalence of a hypersensitive response increases with advancing age (23).

In routine practice, most of these patients never receive further cardiovascular assessment. Yet this study clearly shows that for patients with non-accidental falls and the cardioinhibitory component, cardiac pacing significantly reduces subsequent falls. The total number of falls was reduced by over two-thirds in patients who received cardiac pacemakers. The benefits of pacing were similar for paced patients who either had recurrent falls or a single fall at presentation. Evidence that pacing reduces the probability of falling is provided by two sources. First, paced patients were less likely to fall in the weeks after they were implanted than in the weeks before. Second, paced patients were less likely to fall after they had been implanted than controls were throughout the study. The magnitude of both of these effects was identical (OR 0.42 in both cases).

No other single intervention for falls has demonstrated this magnitude of benefit, albeit in a select series of individuals who experienced nonaccidental falls. Future guidelines for use in the accident and emergency department should ensure that the characteristics of such individuals are determined and that such guidelines recommend cardiovascular assessment of older adults with non-accidental falls.

The main effect of the study was to reduce the number of falls. It is well documented that fall-related morbidity and mortality increase significantly with the number of fall events (13,24). Although there was no difference in the fracture rates—the number in each group was small—three and four, respectively, in pacemaker patients and controls, the number of other injuries was reduced. It is noteworthy that a high proportion of these patients—over 30%—had sustained a fracture prior to recruitment, and over 70% had soft tissue injuries during events before recruitment. A much larger sample size would be required to determine whether pacing reduces fracture rates, hospitalizations and mortality in older adults with CSH and nonaccidental falls.

It is now timely to explore the cost benefits of pacing patients with non-accidental falls who had a cardioinhibitory response.

Consistent evidence showed that cardiac pacing also significantly reduced episodes of syncope in those participants with a history of recurrent falling (47 syncope events during one-year follow-up in controls vs. 22 in paced patients). Previous studies have shown a benefit for syncope with pacing but not in patients who have falls (3,4,25). Participants who had just a single fall reported very few subsequent episodes of syncope during follow-up, and there was no evidence that cardiac pacing had any significant effect on reported syncope for this group, although subsequent falls were significantly reduced.
We have previously published data supporting amnesia for witnessed loss of consciousness during asystole induced by upright CSM as one explanation for the overlap of index symptoms of falls and syncope (6,26). The present data support this hypothesis. It is also possible that moderate hypotensive changes, insufficient to cause loss of consciousness, cause balance instability and falls in older patients. In this series, half of the participants had abnormal gait and two-thirds had abnormal balance. It is well reported that balance and gait stability and righting reflexes decline considerably with advancing years (11,27). Pacing may have prevented subsequent falls by modifying bradycardia-induced hypotension, insufficient to cause loss of consciousness, which would otherwise have resulted in gait and balance instability.

This study has important service implications for referral pathways of older patients who fall. Staff who assess older patients with non-accidental falls in the accident and emergency department should be aware that these patients require further cardiovascular evaluation.

Reprint requests and correspondence: Professor Rose Anne Kenny, Cardiovascular Investigation Unit and Institute for the Health of the Elderly, Victoria Wing, Royal Victoria Infirmary, Queen Victoria Road, Newcastle Upon Tyne NE1 4LP, UK. E-mail: r.a.kenny@ncl.ac.uk.

REFERENCES