

We are IntechOpen, the world's leading publisher of Open Access books Built by scientists, for scientists

4,800

Open access books available

122,000

International authors and editors

135M

Downloads

Our authors are among the

154

Countries delivered to

TOP 1%

most cited scientists

12.2%

Contributors from top 500 universities



WEB OF SCIENCE™

Selection of our books indexed in the Book Citation Index
in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?
Contact book.department@intechopen.com

Numbers displayed above are based on latest data collected.

For more information visit www.intechopen.com



Role of Pacing in Neurally Mediated Syncope

Vikas Kuriachan and Robert Sheldon

Libin Cardiovascular Institute of Alberta, University of Calgary, Calgary, Alberta, Canada

1. Introduction

Neurally mediated syncope syndromes involve autonomic reflexes causing bradycardia and/or hypotension resulting in a transient loss of consciousness (Brignole et al., 2004). These episodes can result in injuries and emotional stress. Recurrent vasovagal syncope can have a significant detrimental effect on the quality of life comparable to chronic disease patients with chronic back pain or rheumatoid arthritis (Linzer et al., 1991; Rose, Koshman, Spreng, & Sheldon, 2000). Hence management strategies have targeted vasodepression and bradycardia. Pacing has been a tempting solution that treats the cardioinhibitory response.

2. Vasovagal syncope

Vasovagal syncope is one of the common causes of syncope and a common reason for emergency room encounters (Savage, Corwin, McGee, Kannel, & Wolf, 1985). Vasovagal syncope is seen in younger patients and the reflex may have triggers such as sight of blood, venipuncture, or prolonged standing (Brignole et al., 2004). Some patients may have a prodrome of nausea and diaphoresis prior to loss of consciousness due to hypotension and/or bradycardia. Usually the syncopal episode lasts less than a minute but accompanying nausea, diaphoresis, and pallor can last longer. Many patients do not have a prodrome sufficiently long upon which to act, and therefore are unable to use preventive techniques such as counterpressure maneuvers or sitting/lying down to avoid or minimize a full episode. Unlike patients with cardiac or neurologic cause for syncope, patients with vasovagal syncope have no increased risk of cardiovascular morbidity or mortality (Soteriades et al., 2002). Hence in patients with vasovagal syncope preventing injury and maintaining a good quality of life are the primary goals for management (Kuriachan & Sheldon, 2008).

3. Initial pacing studies for vasovagal syncope

Bradycardia has long been recognized as a component of vasovagal syncope (Sharpey-Schafer, 1956). In recent years, bradycardia was seen during tilt table test studies in patients with vasovagal syncope during the induced episodes (Mosqueda-Garcia et al., 1997). Bradycardic problems have also been detected by pacemaker and implantable loop recorders during clinic episodes of vasovagal syncope (Krahn, Klein, & Yee, 1997). This suggested that pacing could prevent vasovagal syncope by treating the bradycardia component. This was initially looked at in patients with tilt table induced syncope associated with bradycardia (Fitzpatrick, Theodorakis, Ahmed, Williams, & Sutton, 1991). These patients underwent repeat tilt table test

with temporary pacing. This prevented syncope in over half the patients although they still experienced vasovagal symptoms and presyncope. The results of this study should also be interpreted with caution since repeated tilt table testing can have a training effect and may reduce syncopal episodes (Reybrouck, Heidbuchel, Van De Werf, & Ector, 2002). Also the hemodynamic changes seen on tilt table induced syncopal episodes may not correlate with clinical episodes (Menozzi et al., 1993).

Initial observational studies seemed to show benefit with pacing as a treatment for vasovagal syncope (Sheldon, Koshman, Wilson, Kieser, & Rose, 1998; Petersen et al., 1994; Benditt et al., 1997). These initial studies were mainly a sequential design, with no placebo group, and included highly symptomatic patients, who received a pacemaker. Open label studies then followed which also showed impressive results with pacing. The North American Vasovagal Pacemaker Study (VPS) randomized 54 vasovagal syncope patients to a pacemaker or optimal medical treatment (Connolly, Sheldon, Roberts, & Gent, 1999a). Impressive results, as shown in Figure 1, were seen with 19/27 in the medical treatment group and only 6/27 in the pacemaker arm having one or more recurrences of syncope. The Vasovagal Syncope International Study (VASIS) randomized 42 syncope patients with cardioinhibitory responses on tilt table testing to pacemaker or medical therapy (Sutton et al., 2000). Again, an impressive reduction in syncope was seen, with only 5% in the pacemaker group and 61% in the medical therapy having syncope recurrence. Another open label study, Syncope Diagnosis and Treatment Study (SYDAT), randomized 93 syncope patients to a pacemaker or atenolol (Ammirati, Colivicchi, & Santini, 2001). This also showed a significant reduction in syncope with pacing (4.3%) versus atenolol (26%). Hence initial observational and open-label studies suggest a significant reduction in syncope recurrence with pacing with up to 87% relative risk reduction (Sud et al., 2007a; Connolly, Sheldon, Roberts, & Gent, 1999b). Summaries of the observational and randomized open-label pacing studies in vasovagal syncope are shown in Table 1.

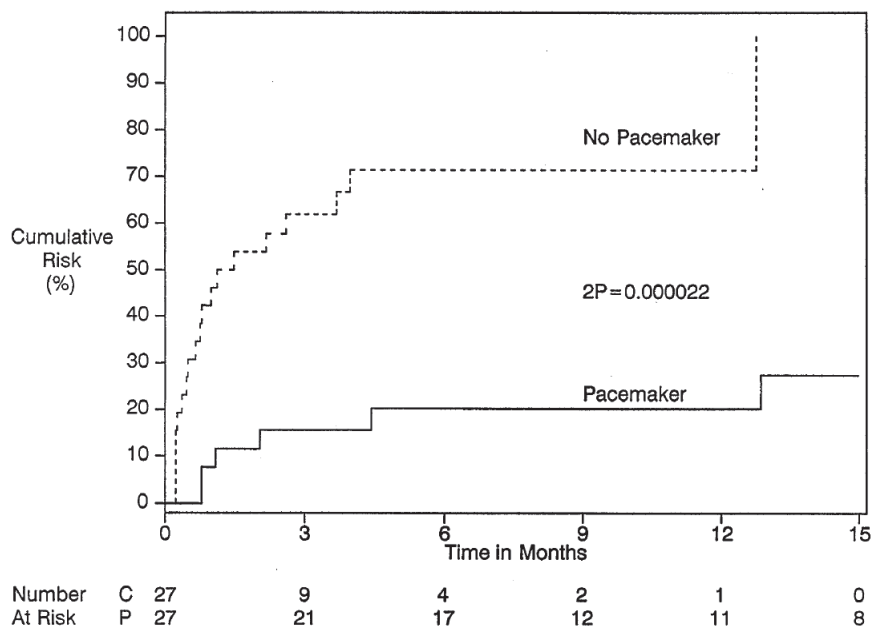


Fig. 1. Kaplan-Meier plot of time to first recurrence in VPS I of the 27 patients with pacemaker and the 27 patients without a pacemaker by intention-to-treat analysis. Figure from (Connolly et al., 1999a)

Study (year)	Type of Study	Tilt Testing part of inclusion	Study Arms	Results
Sheldon et al. (1998)	Observational	Yes	12 patients with VVS. Rate drop pacing in all patients	No syncope in 50%
Peterson et al. (1994)	Observational	Yes	37 patients with VVS. 35 had DDD and 2 had VVI	No syncope in 62%
Benditt et al (1997)	Observational	No	31 patients with VVS or CSS. Rate drop pacing in all patients	No syncope in 80%
VPS I (1999)	Open-label randomized	Yes	54 patients with VVS randomized to rate drop pacing or no implant	85% relative risk reduction
SYDAT (2001)	Open-label randomized	Yes	93 patients with VVS randomized to ppm with rate drop response or to atenolol	83 % reduction of syncope with pacing
VASIS (2000)	Open-label randomized	Yes	42 patients with VVS randomized to ppm with hysteresis and 23 with no implant	90% reduction of syncope with pacing

VVS = vasovagal syncope, CSS = carotid sinus syncope, ppm = pacemaker

Table 1. Summary of major open-label and observational studies for pacing in vasovagal syncope

4. Pacemaker programming

Various pacemaker settings have been tried in patients with vasovagal syncope. In general dual chamber (AV sequential) pacing is preferred, since both sinus and atrioventricular nodal function can be affected during a vasovagal episode. DDD pacing was compared to VVI and to sensing only (ODO) in 12 children with vasovagal syncope and found both modes of pacing to prevent syncope (McLeod, Wilson, Hewitt, Norrie, & Stephenson, 1999). All 12 were implanted with dual chamber pacemakers. Then programmed to ODO, VVI, and DDD with rate drop response for four month periods. Parents and patients were blinded to the pacemaker mode. Physician analyzing the results were blinded to patient and pacemaker mode. Even though both pacing modes prevented syncope, DDD was better than VVI for reducing presyncopal events.

Rate-changing programming has also been examined including rate hysteresis, rate smoothing, and rate drop response. The goals of these programming strategies are to treat the bradycardia and also to compensate for the hypotensive/vasodepressive response. Rate hysteresis triggers pacing at a higher rate when the intrinsic heart rate falls below a preset rate. Rate smoothing prevents sudden changes in heart rate by pacing when there is an abrupt drop in intrinsic heart rate even in just 1-2 beats. (This is also used in patients with atrial fibrillation.) Rate drop response, the most sophisticated of the three, results in high rate pacing for a few minutes when a drop in native heart rate is detected. This hopes to achieve pacing support that can overcome bradycardia and hypotension. Rate response programming has been used in many syncope studies including VPS and VPS II. One study compared DDD with rate drop response to DDI with rate hysteresis in vasovagal syncope (Ammirati et al., 1998). This study randomized 20 vasovagal syncope patients with cardioinhibitory response during tilt testing to rate drop response or rate hysteresis. During the 17 month follow up, no patients with rate drop response had syncope but 3 of 8 in the rate hysteresis group had recurrence of syncope.

Hence rate drop response was found to be more effective. Recent studies have also looked at closed loop stimulation (CLS). In closed loop stimulation variation of intracardiac impedance is tracked every beat, so that contractility changes can be detected in the early phase (prior to changes in heart rate) of a vasovagal episode and dual chamber pacing is activated (Occhetta, Bortnik, Audoglio, & Vassanelli, 2004a), as shown in Figure 2. This early initiation of pacing is believed to not only treat the bradycardic response that may follow but also overcome the transient hypotension. The INVASY trial randomized 55 patients with vasovagal syncope and positive tilt test to a CLS pacemaker or DDI and found CLS to be effective in preventing syncope over two-year follow-up period (Occhetta et al., 2004a). None of the patients had recurrences of syncope while in a CLS mode. However both groups had a reduction in syncope, likely due to a placebo effect. The recently completed, but not published, SCANSYNC study also used CLS pacing, described below. A preceding single blind cross-over study of 23 patients used a microaccelerator-equipped ventricular pace/sense leads (Sorin Biomedica, Saluggia, Italy) with a sensor at the tip that measures peak endocardial acceleration that correlates with measurements of left ventricular contractility (Deharo et al., 2003). This study compared standard DDI pacing to a rate adaptive (DDDR) specialized pacing system with a microaccelerometer in the right ventricular lead to detect myocardial contractivity. Both modalities were found to decrease syncopal episodes; in addition, the contractility-driven DDDR might have an additive benefit to conventional DDI pacing (Deharo et al., 2003).

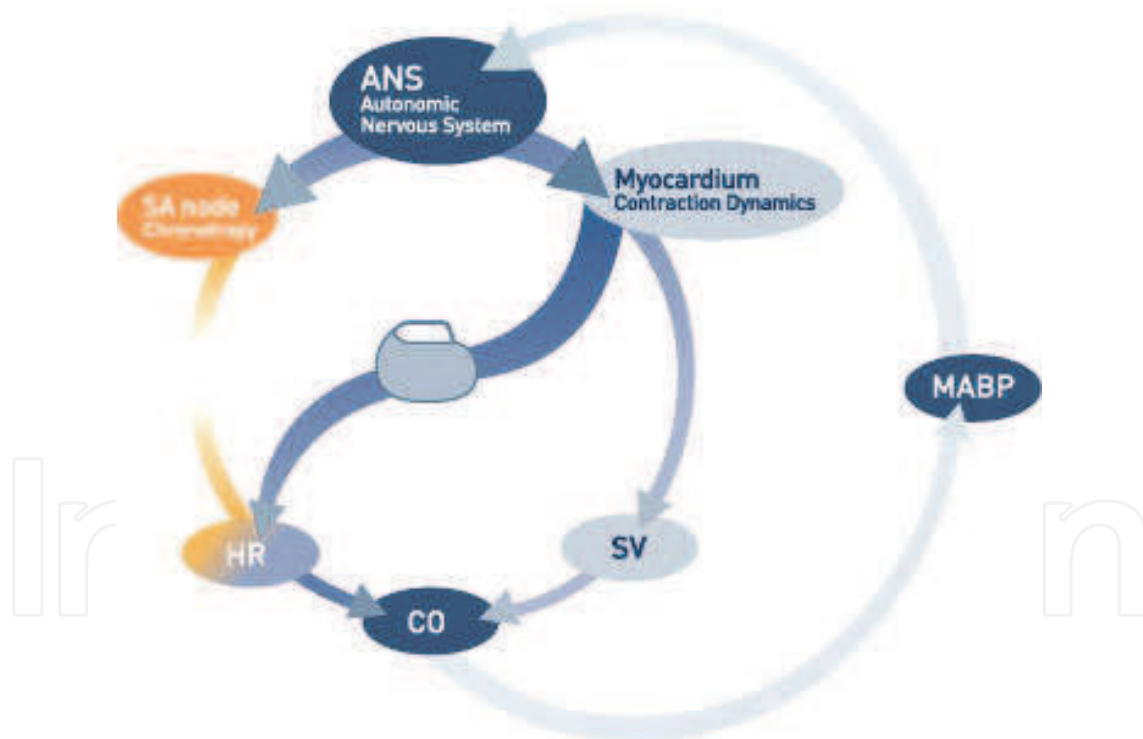


Fig. 2. Autonomic nervous system (ANS) monitors cardiac output (CO) via the mean arterial blood pressure (MABP). Cardiac output is a product of heart rate (HR) and stroke volume (SV). Myocardial contraction dynamics are monitored and changes detected early on by the closed loop stimulation pacemaker. Which enables the CLS pacemaker to provide heart rate changes help improve cardiac output. Figure taken from <http://www.biotronik.com/en/in/1088> (c) Biotronik. Reproduced with permission from BIOTRONIK

5. Randomized, double blind studies comparing active pacing to sensing only

The great success of the initial studies raised the possibility a placebo effect with implant of a pacemaker for treatment of vasovagal syncope. Hence the first randomized, multicenter, double blinded study was designed and completed. VPS II, in which all 100 patients received pacemakers but were randomized to dual chamber pacing with rate drop sensing or sensing only (Connolly et al., 2003). After six months of follow up, there was no significant benefit with pacing and showed a 40% cumulative risk of syncope in the sensing group and 31% in the pacing group. This was also confirmed in a smaller study that included 29 patients with recurrent tilt-induced vasovagal syncope and one relapse after tilt testing (SYNPACE) (Raviele et al., 2004). In this study, patients all received a pacemaker and then were randomized to pacing or no pacing. Results of the first interim analysis and VPS II stopped this trial prematurely. They were unable to show a benefit with active pacing in preventing syncope.

A recent meta-analysis examined the role of pacing in vasovagal syncope (Sud et al., 2007b). Nine randomized trials were looked at in the meta-analysis, which included open label, single blind, and double blind trials. Interestingly, in contrast to open label trials, blinded trials for pacing in vasovagal syncope do not show a benefit, even in patients with marked cardioinhibitory response on tilt table testing (Sud et al., 2007a). Therefore, a cardioinhibitory response on tilt table testing probably is neither an appropriate surrogate marker for pacing studies, nor can it be used to predict patients who might respond to pacing. The authors of the meta-analysis described that the benefits seen in open label, unblinded trials as being due to an expectation effect, by both patients and physicians. The authors of this meta-analysis synthesized a unique comparison between "inactive" pacing and no treatment and found that the expectation response alone reduces the odds of syncope by 84% (Figure 3).

Study (year)	Number of Patients	Type	Tilt Testing part of inclusion	Study Arms	Results
VPS II (2003)	100	Double blind randomized	No	Rate drop pacing vs ODO	Pacing did not reduce risk of syncope
SYNPACE (2004)	29	Double blind randomized	Yes	DDD rate drop vs ODO	Pacing did not reduce risk of syncope
Deharo et al. (2003)	23	Single blind randomized crossover	No	Contractility driven DDDR vs DDI	Both reduced syncope. Contractility driven may be better than DDI
INVASY (2004)	50	Single blind randomized crossover	Yes	DDD-CLS compared to DDI	Both reduced syncope. CLS pacing seems to be better than DDI.
Mcleod et al. (1999)	12	Double blind randomized	No	DDD vs VVI vs ODO	Pacing prevented syncope. DDD further reduced presyncope.

Table 2. Randomized blinded studies in pacing for Vasovagal Syncope

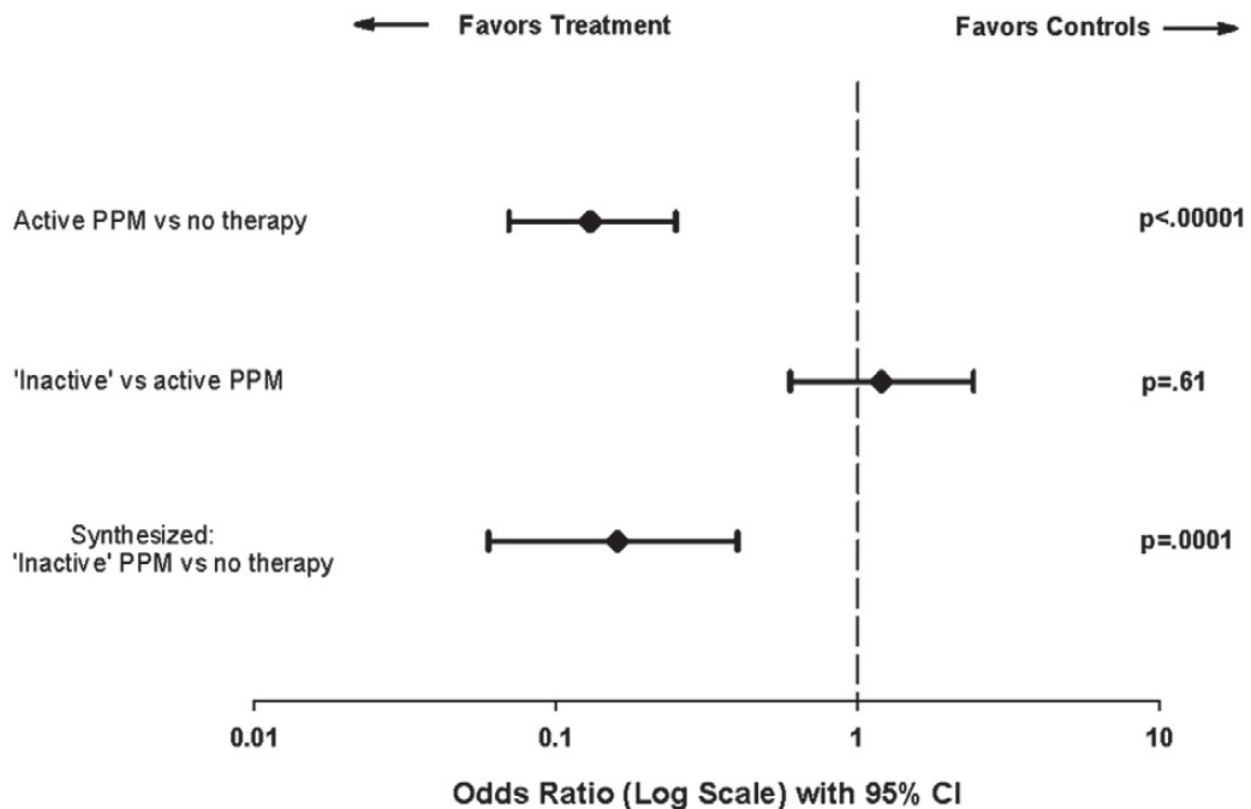


Fig. 3. Odds ratios comparing active cardiac pacing versus no therapy, “inactive” pacing versus active pacing, and a synthesized “inactive” versus no therapy. Line at OR 1.0 indicates no difference between the two groups. Estimates to the left of 1 represent treatment is better and estimates to the right represent control is better. Hence the bottom comparison represents the “expectation” effect. Figure from Sud et al 2007.

6. Placebo effect in pacing for vasovagal syncope

The placebo effect can be powerful and may be due to expectation effects of patients and health care providers, conditioning effects in patients, along with biases in patient assessment and reporting (Olshansky, 2007). Patients who receive pacemakers, due to the expense and invasive nature of the treatment, may be more willing to consider it as being a beneficial treatment for their problems. Healthcare workers who are involved in the care of these patients may not be conscious of biases they are exhibiting in assessment and reporting, and may also apparently observe a benefit from an ineffective intervention. Conversely those patients who did not receive pacemakers in studies may be disappointed and more inclined to report symptoms. Similar situations have also been encountered in the past with hypertrophic cardiomyopathy, where pacing was initially thought to improve functional status in open label studies (Nishimura et al., 1997). Similarly, atrial pacing was first reported to reduce atrial fibrillation, stroke, and death in patients with pacemakers (Gillis et al., 1999; Connolly et al., 2000). However, randomized, controlled studies did not show the benefits that were seen in the open label studies in any of these situations (Gillis et al., 1999; Connolly et al., 2000; Nishimura et al., 1997). Hence interpretation of studies in pacing that are not randomized, double blind, placebo-controlled should be done with caution since there may be important placebo effects. The vasodepressor and cardioinhibitory components may vary in each patient

with different episodes and 50% to 83% of syncopal episodes may not have a cardioinhibitory component (Sheldon & Connolly, 2003). This may also explain why pacing does not seem to be of benefit in vasovagal syncope. Pacing alone may not be enough to overcome vasodepression.

7. Ongoing studies

Although the two blinded randomized trials are small (VPS II and SYNPACE), it seems pacing may not benefit most patients with vasovagal syncope. The ISSUE 2 study reported 392 patients with recurrent syncope and an implantable loop recorder (ILR) (Brignole et al., 2006). Specific treatment was then given to 53 patients based on the monitoring findings, of whom 47 received a pacemaker for asystole and 6 received anti-tachycardia treatments. A marked decrease in syncopal episodes was noted in the group that received specific treatment. In the 53 patients receiving specific treatment, the 1-year syncope recurrence rate was 10% compared to 41% in the patients without specific treatment. However the study is limited by lack of blinding and having only a minority of patients receiving specific treatment. To overcome the limitation of ISSUE 2, the ISSUE 3 study was designed (Brignole, 2007). Patients found to have asystolic pauses associated with syncope on ILR monitoring were randomized to pacemaker On or Off. This is a multicenter, randomized, placebo-controlled, prospective study of patients with a documented pause during syncope on an implantable loop recorder and then randomized to a pacemaker with pacing or only sensing. ISSUE 3 has finished recruitment and is now in the follow-up phase. The results of this study will help to clarify whether pacing may be of benefit in vasovagal syncope patients with prolonged asystolic pauses. As mentioned previously, initial studies also suggest that using a closed loop pacing (CLS) that detects contractility may be able to detect a neurocardiogenic episode early and provide pacing support better than a rate drop system (Kanjwal, Karabin, Kanjwal, & Grubb, 2010; Occhetta, Bortnik, & Vassanelli, 2003; Occhetta, Bortnik, Audoglio, & Vassanelli, 2004b). A randomized, prospective, double blind, cross over study (SCANSYNC) compared active (CLS pacing) to passive (VVI 30) pacing in patients with recurrent vasovagal syncope has been completed and is awaiting publication.

8. Other treatment options in vasovagal syncope

Other treatments for vasovagal syncope have also had similar findings with open label and observational studies showing benefit but double blind, randomized studies showing minimal benefit or no difference from placebo (Kuriachan, Sheldon, & Platonov, 2008). In patients with an identifiable prodrome there may be some benefit to using physical counterpressure maneuvers (PCM) which are safe and cost free (van et al., 2006). The maneuvers used are usually leg crossing with tensing of abdominal, buttock, and lower extremity muscles and/or gripping hands while abducting both arms. These maneuvers should be tried as first line treatments in patients with vasovagal syncope and an identifiable prodrome. Ensuring adequate volume repletion is important with salt and fluid intake. Various medications have also been studied, including beta-blockers, selective serotonin re-uptake inhibitors (SSRI), Fludrocortisone, and Midodrine. In general, no clear benefit has thus far been seen from studies with beta-blockers, SSRIs, and fludrocortisone (Kuriachan & Sheldon, 2008). The POST II study is comparing fludrocortisone to placebo in a randomized, double blind fashion and is in the follow-up phase (Raj, Rose, Ritchie, & Sheldon, 2006). Midodrine, a peripherally acting alpha-agonist, does seem to have some benefit in adults and children. Frequent dosing and

some side effects, such as supine hypertension, may limit its use (Kuriachan et al., 2008). POST IV will be a double blind, randomized, placebo controlled study comparing midodrine to placebo in patients with vasovagal syncope.

The initial management approach to a patient with vasovagal syncope should include education about the condition, reassurance, and dietary intake (particularly salt and fluid). PCM should be taught to patients with a prodrome. If they still have frequent recurrent symptoms then medication attempts should be made. Pacing should be reserved as a last resort and ideally in patients documented with asystole during their syncopal episodes. A frank and open discussion should be held with the patient about the limited benefit that has been seen in studies for medications and pacing. Refer to Figure 4 for management approach for vasovagal syncope.

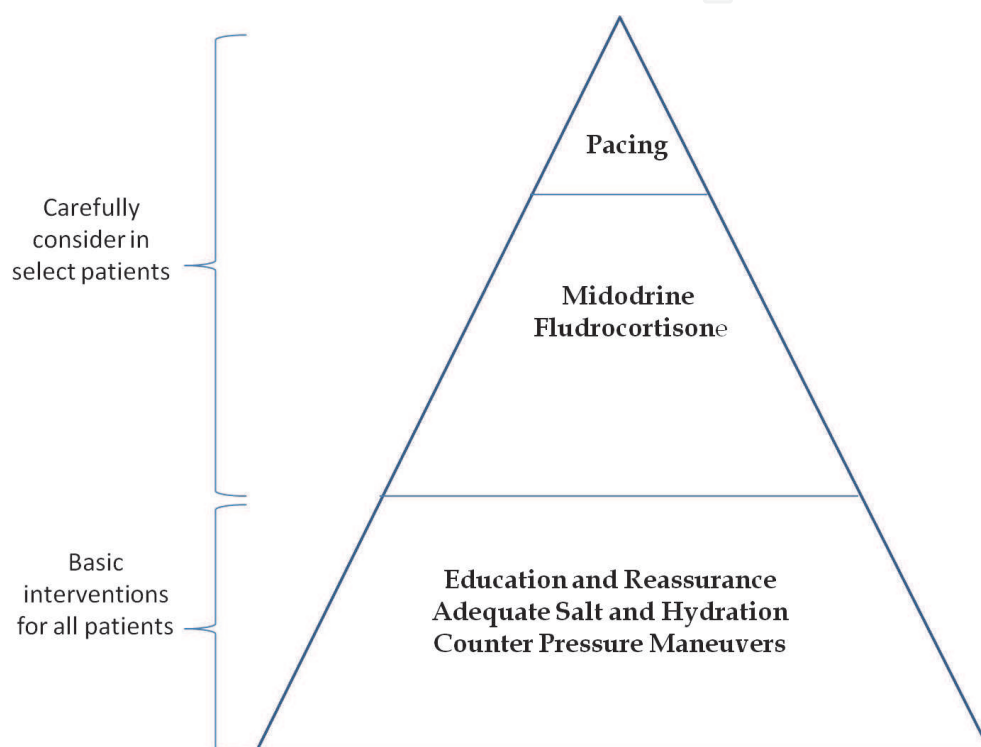


Fig. 4. Pyramid scheme of treatment for vasovagal syncope. All patients should receive the basic interventions as appropriate. Currently limited evidence for medications and pacing, hence use should be limited in very select patients who have significant, recurrent episodes after the basic interventions.

9. Carotid sinus hypersensitivity

Carotid sinus hypersensitivity and association with syncope have been known for many years. Carotid sinus hypersensitivity (CSH) is defined as a fall in systolic BP > 50 mmHg and/or asystolic pause > 3 seconds with carotid sinus massage. Carotid sinus syndrome is when CSH is associated with spontaneous syncope that can be reproduced with carotid sinus massage (CSM). Carotid sinus syncope tends to happen in elderly men and the prevalence increases with cardiovascular, cerebrovascular, and neurodegenerative disease (Claesson, Kristensson, Edvardsson, & Wahrborg, 2007). A fall from syncope can result in significant injuries given the older age of this patient population. Although there is

limited evidence, carotid sinus syncope has been believed to occur in the context head turning movements that may cause pressure on the carotid, such as shoulder checking in a car with shoulder seat belt putting pressure or wearing a tight collar.

It is important to differentiate carotid sinus hypersensitivity from carotid sinus syndrome. A positive carotid sinus massage was noted in 32% of patients having an angiogram who had no history of carotid sinus syncope (Brown, Maloney, Smith, Haritzler, & Ilstrup, 1980). Asymptomatic carotid sinus hypersensitivity may be common in the elderly. Carotid sinus reflex helps with hemodynamic regulation. The vagal efferent signals increases cardiac vagal input resulting in lowering heart rate and peripheral vasodilation lowering blood pressure (LOWN & LEVINE, 1961). Hence an abnormal reflex can cause significant changes in blood pressure and heart rate which decreases brain perfusion and results in syncope.

10. Carotid sinus massage

Various protocols have been used for carotid sinus massage (Brignole et al., 2001). In one method, the carotid artery is firmly massaged at the anterior margin of the sternocleidomastoid at the cricoid cartilage level for up to 5 seconds, while the patient is in a supine position. If the first side does not yield a positive result then CSM is performed on the other side. Asystolic pause > 3 seconds (sinus pause or at times due to AV block), fall in BP > 50mmHg, and development of symptoms are necessary for a truly positive test. Abnormal responses can also be seen in patients with a history of spontaneous syncope. Some protocols use longer duration of massage to reproduce spontaneous symptoms, as well as both supine and upright positions (ensure patient safety in upright position). Heart rate changes can be readily seen on cardiac monitoring but a blood pressure drop is difficult to document without invasive monitoring (not usually practical) or noninvasive continuous digital plethysmography. CSM is contraindicated in patients with carotid bruits or history of prior stroke/TIA, due to concerns that the CSM may result in carotid plaque disruption and embolization resulting in a cerebrovascular event. Studies have looked at the safety of CSM, totaling over 5000 patients and found complication rates in the 0.1 - 0.2% range, of which most were transient neurological symptoms and full recovery was made except in two patients (Munro et al., 1994; Davies & Kenny, 1998).

11. Pacing studies in carotid sinus syncope

One of the first studies in carotid sinus syncope reported 70 patients with CSH and syncope, and found pacing to be very effective (Morley et al., 1982a). Subsequently a second study assessed 56 consecutive patients with CSH and syncope who had received no treatment (13 patients), anticholinergic medications (20), and pacemaker implant (23). In this study, pacing was effective in preventing syncope but a high rate of spontaneous remission was also observed (Sugrue et al., 1986). Another study with 21 patients, in which 13 received pacemakers, found only minimal benefit with pacing (Huang, Ezri, Hauser, & Denes, 1988). However, none of the patients with pacemakers had recurrences of syncope and only one patient had recurrence in the no pacemaker group of eight patients, demonstrating a very low recurrence rate even without receiving treatment. Other observational studies also found benefits from pacing and are listed in Table 3 (Brignole et al., 1991; Brignole, Menozzi, Lolli, Sartore, & Barra, 1988). Hence some benefit was observed with pacing in CSH and syncope in the initial studies, but there were high rates of spontaneous remission.

Since many elderly patients who have syncope may not remember the details of the event and prodrome, they may present with a non-accidental fall. Hence it was thought that in many elderly patients, carotid sinus syncope might be responsible for non-accidental falls. This was first examined in the SAFE-PACE trial (Kenny et al., 2001). This open-label study included 175 consecutive patients over the age of 50 with non-accidental falls attending an accident and emergency facility. Those with carotid sinus hypersensitivity were randomized to rate drop dual chamber pacemaker or standard treatment. Paced patients were significantly less likely to fall (odds ratio 0.42) and reduced injurious event by 70%. SAFE-PACE 2 was a double blind, randomized study done to assess this (Daniel, Steen, Seifer, & Kenny, 2010). 141 patients with unexplained falls and cardioinhibitory carotid sinus hypersensitivity were randomized to a rate responsive pacemaker or implantable loop recorder. No significant reduction was seen in the pacemaker group, but this small sample size led to an underpowered study. Again, due to concerns of the open-label nature of the initial SAFE-PACE, a randomized study was conducted in which 25 patients received pacemakers but was randomized to pacemaker On (DDD) or Off (ODO) (Parry, Steen, Bexton, Tynan, & Kenny, 2009). This was a double blind study with a cross over design. There was a mean of 3.48 falls in the ODO mode and 4.04 in the DDD mode. Survival analysis showed no significant differences in time to first fall between the two groups (Figure 5). Hence no benefit was seen with pacing in this group for fall reduction. Further supporting the placebo effect in this study was the fall reduction that was seen in both groups, pacemaker On or Off, in the first six months after implant. However, this study was underpowered and should be interpreted with caution. Hence the initial impressive benefits seen in SAFE-PACE may be due to a placebo effect similar to the open-label vasovagal pacing studies.

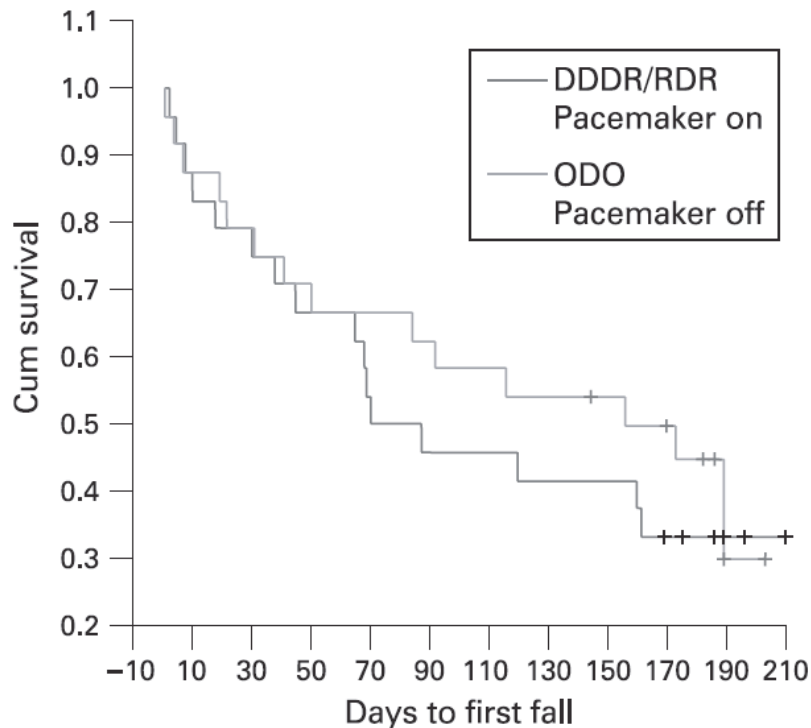


Fig. 5. Survival analysis (treating each group as independent samples) showed no significant differences in time to first fall between DDD and ODO modes. $P=0.57$. Figure from Parry et al. 2009.

Study (year)	Number of Patients	Methodology	Study Arms	Results
Sugrue et al. (1986)	56	Observational	13 no treatment 23 pacemaker 20 anticholinergics	Pacing was effective but high rate of spontaneous remission
Morley et al. (1982)	70	Observational	54 patients VVI 13 patients DVI 18 patients DDD	89% asymptomatic with pacing
Huang et al. (1988)	21	Observational	13 with pacemaker 8 with no implant	Pacing found to be beneficial. However only one patient had recurrence (in no pacer group)
Brignole et al. (1991)	60	Observational Crossover	26 with DDD 34 with VVI	DDD found to have less symptoms overall
Brignole et al.(1988)	35	Observational	19 no implant 11 with VVI 5 with DDD	Pacing prevented syncope recurrence
SAFEPACE 1 (2001)	175	Open label	87 with pacemaker 88 no implant	Pacing reduced falls and minimal reduction of syncope
SAFEPACE 2 (2010)	141	Double blind	71 with pacemaker 70 with loop recorder	No significant reduction in falls seen
Parry et al. (2009)	25	Double blind Crossover	25 DDD and crossover to ODO	Pacing had no effect of falls

Table 3. Pacing studies in context of Carotid Sinus Hypersensitivity, Syncope, and Falls.

Although only a few small studies have shown benefit, pacing has generally been felt to be beneficial in this condition, especially in elderly patients with a predominantly cardioinhibitory response to CSM and present with symptoms suggestive of carotid sinus syncope (Brignole, Menozzi, Lolli, Bottoni, & Gaggioli, 1992; Morley et al., 1982b; Claesson et al., 2007; Moya et al., 2009). Management should also include volume repletion and recommendations on avoiding situations that may cause syncope, such as tight collars and ties. Volume expanders and vasopressors may also be helpful but usually are limited due to problems with heart failure and hypertension that is common in the elderly population.

12. Conclusion

Initial steps in the management of vasovagal syncope should include education about the diagnosis and reassurance. Patients should be instructed on liberal intake of salt and fluid. Counterpressure maneuvers should be taught to patients with a prodrome. If they still have frequent recurrent symptoms, then medications attempts should be made. Pacing should be reserved as a last resort and ideally in patients documented with asystole during their syncopal episodes. For patients with carotid sinus syncope, pacing should be considered. Additional management should also include volume repletion and recommendations on avoiding situations that may cause syncope.

13. References

- Ammirati, F., Colivicchi, F., & Santini, M. (2001). Permanent cardiac pacing versus medical treatment for the prevention of recurrent vasovagal syncope: a multicenter, randomized, controlled trial. *Circulation*, *104*, 52-57.
- Ammirati, F., Colivicchi, F., Toscano, S., Pandozi, C., Laudadio, M. T., De, S. F. et al. (1998). DDD pacing with rate drop response function versus DDI with rate hysteresis pacing for cardioinhibitory vasovagal syncope. *Pacing Clin.Electrophysiol.*, *21*, 2178-2181.
- Benditt, D. G., Sutton, R., Gammage, M. D., Markowitz, T., Gorski, J., Nygaard, G. A. et al. (1997). Clinical experience with Thera DR rate-drop response pacing algorithm in carotid sinus syndrome and vasovagal syncope. The International Rate-Drop Investigators Group. *Pacing Clin.Electrophysiol.*, *20*, 832-839.
- Brignole, M. (2007). International study on syncope of uncertain aetiology 3 (ISSUE 3): pacemaker therapy for patients with asystolic neurally-mediated syncope: rationale and study design. *Europace.*, *9*, 25-30.
- Brignole, M., Alboni, P., Benditt, D., Bergfeldt, L., Blanc, J. J., Bloch Thomsen, P. E. et al. (2001). Guidelines on management (diagnosis and treatment) of syncope. *Eur.Heart J.*, *22*, 1256-1306.
- Brignole, M., Alboni, P., Benditt, D. G., Bergfeldt, L., Blanc, J. J., Thomsen, P. E. et al. (2004). Guidelines on management (diagnosis and treatment) of syncope-update 2004. Executive Summary. *Eur.Heart J.*, *25*, 2054-2072.
- Brignole, M., Menozzi, C., Lolli, G., Bottoni, N., & Gaggioli, G. (1992). Long-term outcome of paced and nonpaced patients with severe carotid sinus syndrome. *Am.J.Cardiol.*, *69*, 1039-1043.
- Brignole, M., Menozzi, C., Lolli, G., Oddone, D., Gianfranchi, L., & Bertulla, A. (1991). Validation of a method for choice of pacing mode in carotid sinus syndrome with or without sinus bradycardia. *Pacing Clin.Electrophysiol.*, *14*, 196-203.
- Brignole, M., Menozzi, C., Lolli, G., Sartore, B., & Barra, M. (1988). Natural and unnatural history of patients with severe carotid sinus hypersensitivity: a preliminary study. *Pacing Clin.Electrophysiol.*, *11*, 1628-1635.
- Brignole, M., Sutton, R., Menozzi, C., Garcia-Civera, R., Moya, A., Wieling, W. et al. (2006). Early application of an implantable loop recorder allows effective specific therapy in patients with recurrent suspected neurally mediated syncope. *Eur.Heart J.*, *27*, 1085-1092.
- Brown, K. A., Maloney, J. D., Smith, C. H., Haritzler, G. O., & Ilstrup, D. M. (1980). Carotid sinus reflex in patients undergoing coronary angiography: relationship of degree and location of coronary artery disease to response to carotid sinus massage. *Circulation*, *62*, 697-703.
- Claesson, J. E., Kristensson, B. E., Edvardsson, N., & Wahrborg, P. (2007). Less syncope and milder symptoms in patients treated with pacing for induced cardioinhibitory carotid sinus syndrome: a randomized study. *Europace.*, *9*, 932-936.
- Connolly, S. J., Kerr, C. R., Gent, M., Roberts, R. S., Yusuf, S., Gillis, A. M. et al. (2000). Effects of physiologic pacing versus ventricular pacing on the risk of stroke and

- death due to cardiovascular causes. Canadian Trial of Physiologic Pacing Investigators. *N.Engl.J.Med.*, 342, 1385-1391.
- Connolly, S. J., Sheldon, R., Roberts, R. S., & Gent, M. (1999a). The North American Vasovagal Pacemaker Study (VPS). A randomized trial of permanent cardiac pacing for the prevention of vasovagal syncope. *J.Am.Coll.Cardiol.*, 33, 16-20.
- Connolly, S. J., Sheldon, R., Roberts, R. S., & Gent, M. (1999b). The North American Vasovagal Pacemaker Study (VPS). A randomized trial of permanent cardiac pacing for the prevention of vasovagal syncope. *J.Am.Coll.Cardiol.*, 33, 16-20.
- Connolly, S. J., Sheldon, R., Thorpe, K. E., Roberts, R. S., Ellenbogen, K. A., Wilkoff, B. L. et al. (2003). Pacemaker therapy for prevention of syncope in patients with recurrent severe vasovagal syncope: Second Vasovagal Pacemaker Study (VPS II): a randomized trial. *JAMA*, 289, 2224-2229.
- Daniel, J. R., Steen, N., Seifer, M. C., & Kenny, R. (2010). Carotid sinus syndrome, should we pace? A multicentre, randomised control trial (Safespace 2). *Heart*, 96, 347-351.
- Davies, A. J. & Kenny, R. A. (1998). Frequency of neurologic complications following carotid sinus massage. *Am.J.Cardiol.*, 81, 1256-1257.
- Deharo, J. C., Brunetto, A. B., Bellocchi, F., Barbonaglia, L., Occhetta, E., Fasciolo, L. et al. (2003). DDDR pacing driven by contractility versus DDI pacing in vasovagal syncope: a multicenter, randomized study. *Pacing Clin.Electrophysiol.*, 26, 447-450.
- Fitzpatrick, A., Theodorakis, G., Ahmed, R., Williams, T., & Sutton, R. (1991). Dual chamber pacing aborts vasovagal syncope induced by head-up 60 degrees tilt. *Pacing Clin.Electrophysiol.*, 14, 13-19.
- Gillis, A. M., Wyse, D. G., Connolly, S. J., Dubuc, M., Philippon, F., Yee, R. et al. (1999). Atrial pacing periablation for prevention of paroxysmal atrial fibrillation. *Circulation*, 99, 2553-2558.
- Huang, S. K., Ezri, M. D., Hauser, R. G., & Denes, P. (1988). Carotid sinus hypersensitivity in patients with unexplained syncope: clinical, electrophysiologic, and long-term follow-up observations. *Am.Heart J.*, 116, 989-996.
- Kanjwal, K., Karabin, B., Kanjwal, Y., & Grubb, B. P. (2010). Preliminary observations on the use of closed-loop cardiac pacing in patients with refractory neurocardiogenic syncope. *J.Interv.Card Electrophysiol.*, 27, 69-73.
- Kenny, R. A., Richardson, D. A., Steen, N., Bexton, R. S., Shaw, F. E., & Bond, J. (2001). Carotid sinus syndrome: a modifiable risk factor for nonaccidental falls in older adults (SAFE PACE). *J.Am.Coll.Cardiol.*, 38, 1491-1496.
- Krahn, A. D., Klein, G. J., & Yee, R. (1997). Recurrent syncope. Experience with an implantable loop recorder. *Cardiol.Clin.*, 15, 313-326.
- Kuriachan, V. & Sheldon, R. S. (2008). Current concepts in the evaluation and management of syncope. *Curr.Cardiol.Rep.*, 10, 384-390.
- Kuriachan, V., Sheldon, R. S., & Platonov, M. (2008). Evidence-based treatment for vasovagal syncope. *Heart Rhythm.*, 5, 1609-1614.
- Linzer, M., Pontinen, M., Gold, D. T., Divine, G. W., Felder, A., & Brooks, W. B. (1991). Impairment of physical and psychosocial function in recurrent syncope. *J.Clin.Epidemiol.*, 44, 1037-1043.

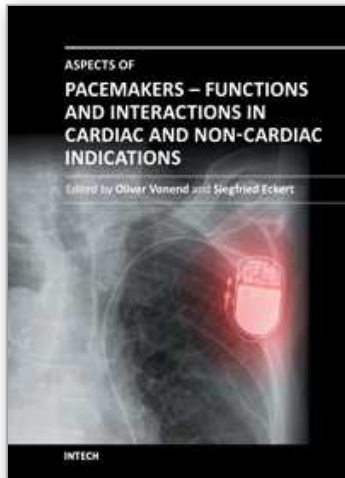
- LOWN, B. & LEVINE, S. A. (1961). The carotid sinus. Clinical value of its stimulation. *Circulation*, 23, 766-789.
- McLeod, K. A., Wilson, N., Hewitt, J., Norrie, J., & Stephenson, J. B. (1999). Cardiac pacing for severe childhood neurally mediated syncope with reflex anoxic seizures. *Heart*, 82, 721-725.
- Menozzi, C., Brignole, M., Lolli, G., Bottoni, N., Oddone, D., Gianfranchi, L. et al. (1993). Follow-up of asystolic episodes in patients with cardioinhibitory, neurally mediated syncope and VVI pacemaker. *Am.J.Cardiol.*, 72, 1152-1155.
- Morley, C. A., Perrins, E. J., Grant, P., Chan, S. L., McBrien, D. J., & Sutton, R. (1982a). Carotid sinus syncope treated by pacing. Analysis of persistent symptoms and role of atrioventricular sequential pacing. *Br.Heart J.*, 47, 411-418.
- Morley, C. A., Perrins, E. J., Grant, P., Chan, S. L., McBrien, D. J., & Sutton, R. (1982b). Carotid sinus syncope treated by pacing. Analysis of persistent symptoms and role of atrioventricular sequential pacing. *Br.Heart J.*, 47, 411-418.
- Mosqueda-Garcia, R., Furlan, R., Fernandez-Violante, R., Desai, T., Snell, M., Jarai, Z. et al. (1997). Sympathetic and baroreceptor reflex function in neurally mediated syncope evoked by tilt. *J.Clin.Invest*, 99, 2736-2744.
- Moya, A., Sutton, R., Ammirati, F., Blanc, J. J., Brignole, M., Dahm, J. B. et al. (2009). 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.*, 30, 2631-2671.
- Munro, N. C., McIntosh, S., Lawson, J., Morley, C. A., Sutton, R., & Kenny, R. A. (1994). Incidence of complications after carotid sinus massage in older patients with syncope. *J.Am.Geriatr.Soc.*, 42, 1248-1251.
- Nishimura, R. A., Trusty, J. M., Hayes, D. L., Ilstrup, D. M., Larson, D. R., Hayes, S. N. et al. (1997). Dual-chamber pacing for hypertrophic cardiomyopathy: a randomized, double-blind, crossover trial. *J.Am.Coll.Cardiol.*, 29, 435-441.
- Occhetta, E., Bortnik, M., Audoglio, R., & Vassanelli, C. (2004a). Closed loop stimulation in prevention of vasovagal syncope. Inotropy Controlled Pacing in Vasovagal Syncope (INVASY): a multicentre randomized, single blind, controlled study. *Europace.*, 6, 538-547.
- Occhetta, E., Bortnik, M., Audoglio, R., & Vassanelli, C. (2004b). Closed loop stimulation in prevention of vasovagal syncope. Inotropy Controlled Pacing in Vasovagal Syncope (INVASY): a multicentre randomized, single blind, controlled study. *Europace.*, 6, 538-547.
- Occhetta, E., Bortnik, M., & Vassanelli, C. (2003). The DDDR closed loop stimulation for the prevention of vasovagal syncope: results from the INVASY prospective feasibility registry. *Europace.*, 5, 153-162.
- Olshansky, B. (2007). Placebo and nocebo in cardiovascular health: implications for healthcare, research, and the doctor-patient relationship. *J.Am.Coll.Cardiol.*, 49, 415-421.
- Parry, S. W., Steen, N., Bexton, R. S., Tynan, M., & Kenny, R. A. (2009). Pacing in elderly recurrent fallers with carotid sinus hypersensitivity: a randomised, double-blind, placebo controlled crossover trial. *Heart*, 95, 405-409.

- Petersen, M. E., Chamberlain-Webber, R., Fitzpatrick, A. P., Ingram, A., Williams, T., & Sutton, R. (1994). Permanent pacing for cardioinhibitory malignant vasovagal syndrome. *Br.Heart J.*, *71*, 274-281.
- Raj, S. R., Rose, S., Ritchie, D., & Sheldon, R. S. (2006). The Second Prevention of Syncope Trial (POST II)--a randomized clinical trial of fludrocortisone for the prevention of neurally mediated syncope: rationale and study design. *Am.Heart J.*, *151*, 1186-1187.
- Raviele, A., Giada, F., Menozzi, C., Speca, G., Orazi, S., Gasparini, G. et al. (2004). A randomized, double-blind, placebo-controlled study of permanent cardiac pacing for the treatment of recurrent tilt-induced vasovagal syncope. The vasovagal syncope and pacing trial (SYNPACE). *Eur.Heart J.*, *25*, 1741-1748.
- Reybrouck, T., Heidbuchel, H., Van De Werf, F., & Ector, H. (2002). Long-term follow-up results of tilt training therapy in patients with recurrent neurocardiogenic syncope. *Pacing Clin.Electrophysiol.*, *25*, 1441-1446.
- Rose, M. S., Koshman, M. L., Spreng, S., & Sheldon, R. (2000). The relationship between health-related quality of life and frequency of spells in patients with syncope. *J.Clin.Epidemiol.*, *53*, 1209-1216.
- Savage, D. D., Corwin, L., McGee, D. L., Kannel, W. B., & Wolf, P. A. (1985). Epidemiologic features of isolated syncope: the Framingham Study. *Stroke*, *16*, 626-629.
- Sharpey-Schafer, E. P. (1956). *British Medical Journal*, *1*, 506-509.
- Sheldon, R. & Connolly, S. (2003). Second Vasovagal Pacemaker Study (VPS II): rationale, design, results, and implications for practice and future clinical trials. *Card Electrophysiol.Rev.*, *7*, 411-415.
- Sheldon, R., Koshman, M. L., Wilson, W., Kieser, T., & Rose, S. (1998). Effect of dual-chamber pacing with automatic rate-drop sensing on recurrent neurally mediated syncope. *Am.J.Cardiol.*, *81*, 158-162.
- Soteriades, E. S., Evans, J. C., Larson, M. G., Chen, M. H., Chen, L., Benjamin, E. J. et al. (2002). Incidence and prognosis of syncope. *N.Engl.J.Med.*, *347*, 878-885.
- Sud, S., Massel, D., Klein, G. J., Leong-Sit, P., Yee, R., Skanes, A. C. et al. (2007a). The expectation effect and cardiac pacing for refractory vasovagal syncope. *Am.J.Med.*, *120*, 54-62.
- Sud, S., Massel, D., Klein, G. J., Leong-Sit, P., Yee, R., Skanes, A. C. et al. (2007b). The expectation effect and cardiac pacing for refractory vasovagal syncope. *Am.J.Med.*, *120*, 54-62.
- Sugrue, D. D., Gersh, B. J., Holmes, D. R., Jr., Wood, D. L., Osborn, M. J., & Hammill, S. C. (1986). Symptomatic "isolated" carotid sinus hypersensitivity: natural history and results of treatment with anticholinergic drugs or pacemaker. *J.Am.Coll.Cardiol.*, *7*, 158-162.
- Sutton, R., Brignole, M., Menozzi, C., Raviele, A., Alboni, P., Giani, P. et al. (2000). Dual-chamber pacing in the treatment of neurally mediated tilt-positive cardioinhibitory syncope : pacemaker versus no therapy: a multicenter randomized study. The Vasovagal Syncope International Study (VASIS) Investigators. *Circulation*, *102*, 294-299.

van, D. N., Quartieri, F., Blanc, J. J., Garcia-Civera, R., Brignole, M., Moya, A. et al. (2006). Effectiveness of physical counterpressure maneuvers in preventing vasovagal syncope: the Physical Counterpressure Manoeuvres Trial (PC-Trial). *J.Am.Coll.Cardiol.*, 48, 1652-1657.

IntechOpen

IntechOpen



Aspects of Pacemakers - Functions and Interactions in Cardiac and Non-Cardiac Indications

Edited by Dr. Oliver Vonend

ISBN 978-953-307-616-4

Hard cover, 194 pages

Publisher InTech

Published online 15, September, 2011

Published in print edition September, 2011

Outstanding steps forward were made in the last decades in terms of identification of endogenous pacemakers and the exploration of their controllability. New “artificial” devices were developed and are now able to do much more than solely pacemaking of the heart. In this book different aspects of pacemaker “functions and interactions, in various organ systems were examined. In addition, various areas of application and the potential side effects and complications of the devices were discussed.

How to reference

In order to correctly reference this scholarly work, feel free to copy and paste the following:

Vikas Kuriachan and Robert Sheldon (2011). Role of Pacing in Neurally Mediated Syncope, Aspects of Pacemakers - Functions and Interactions in Cardiac and Non-Cardiac Indications, Dr. Oliver Vonend (Ed.), ISBN: 978-953-307-616-4, InTech, Available from: <http://www.intechopen.com/books/aspects-of-pacemakers-functions-and-interactions-in-cardiac-and-non-cardiac-indications/role-of-pacing-in-neurally-mediated-syncope>

INTECH
open science | open minds

InTech Europe

University Campus STeP Ri
Slavka Krautzeka 83/A
51000 Rijeka, Croatia
Phone: +385 (51) 770 447
Fax: +385 (51) 686 166
www.intechopen.com

InTech China

Unit 405, Office Block, Hotel Equatorial Shanghai
No.65, Yan An Road (West), Shanghai, 200040, China
中国上海市延安西路65号上海国际贵都大饭店办公楼405单元
Phone: +86-21-62489820
Fax: +86-21-62489821

© 2011 The Author(s). Licensee IntechOpen. This chapter is distributed under the terms of the [Creative Commons Attribution-NonCommercial-ShareAlike-3.0 License](https://creativecommons.org/licenses/by-nc-sa/3.0/), which permits use, distribution and reproduction for non-commercial purposes, provided the original is properly cited and derivative works building on this content are distributed under the same license.

IntechOpen

IntechOpen