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Clinically guided pacemaker choice and setting: pacemaker expert programming study

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Aim The aim of this multicentre, observational, transversal study was to evaluate pacemaker (PM) choice and setting in a large number of patients, in order to understand their relationship with the patients' clinical characteristics.

Methods and results The study enrolled a total of 1858 patients (71 ± 14 years, 54% male), consecutively evaluated during scheduled PM follow-up visits in 7 Italian cardiac arrhythmia centres. To evaluate the appropriateness of PM choice in relation to the patients' clinical characteristics, we analysed their rhythm disorders at the time of device implantation and the characteristics of the devices implanted. To evaluate the appropriateness of device setting, current rhythm disorders and device setting at the time of enrolment were analysed. In the overall study population, 64.3% of the patients received a PM with all of the features required for their rhythm disorder [80.8% in persistent atrioventricular (AV) block, 76.5% in atrial fibrillation needing pacing, 71.0% in sinus node disease, 58.7% in non-persistent atrioventricular block (AVB), 52.7% in neuro-mediated syncope]. The most frequent cause of inappropriate PM choice was the lack of an algorithm to promote intrinsic AV conduction in non-persistent AVB patients (38.1%). In 76.2% of the patients with an appropriate PM ($n = 1301$), the PM was optimally set for their rhythm disorder.

Conclusions In the present 'real-world' registry, a large number of patients (35.7%) did not receive an optimal PM for their rhythm disorders. Moreover, one-fourth of appropriate PMs were not programmed according to the patients' clinical characteristics.

Keywords Pacemaker • Device setting • Rhythm disorder • Bradyarrhythmias • Permanent pacing

Introduction

Pacemakers (PMs) are life-saving devices and are widely used for the treatment of bradyarrhythmias. In Italy alone, 65 554 PMs were implanted[1] in 2013 (~900 PMs/million population), a 3% increase over the 2012 figure. Moreover, this number is expected to rise as the population ages.[2] In the last 10 years, PM technology has improved, and manufacturers have developed several algorithms that have potentially useful clinical implications.

It is not currently known how technological improvements have been perceived by physicians nor whether specific disease-driven PM setting is always implemented in device programming.

The aim of this observational, multicentre study was to evaluate PM choice and programming in a large number of patients,

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What's new?

- Only 64% of patients had a pacemaker (PM) endowed with all algorithms required for their clinical condition, and 5% of PMs had none of the required algorithms.
- In only 76% of the patients who received an appropriate PM was the device setting appropriate.
- Suboptimal focus on how to choose an optimal device and how to set it once implanted could potentially reduce the expected benefit of the implant itself, increasing the risk of complications and impairing quality of life.

in order to analyse their relationship with the patients' clinical characteristics.

Methods

Pacemaker expert programming (PEP) was a multicentre, observational study on patients receiving a PM for bradyarrhythmia-related disease. The study was endorsed by the Italian Association of Arrhythmology and Cardiac Pacing (AIAC). The aim of the study was two-fold: (1) to analyse the appropriateness of PM choice according to patients' rhythm and conduction diseases on implantation and (2) to analyse the appropriateness of PM programming according to patients' rhythm and conduction defects during follow-up.

All consecutive patients who underwent routine PM follow-up examination from 1 February 2015 to 31 July 2015 at each participating study centre were evaluated. Patients aged 18 years or older in whom the PM had initially been implanted in the previous 15 years were enrolled in the study.

The study protocol was approved by each site's Medical Ethics Committee and conformed with the principles outlined in the Declaration of Helsinki. Each patient provided informed consent for data collection and analysis.

Recorded data

Patients were screened and enrolled during scheduled outpatient PM follow-up visits. Patients' characteristics at the time of PM implantation, rhythm, and conduction disturbances were recorded, as were the manufacturers, models, and embedded algorithms of all PMs. In all participating centres, the indications for PM implantation were based on ESC cardiac pacing implantation guidelines.[3] Data on the baseline characteristics of patients and PM implantation were retrospectively analysed for the purpose of this study.

During enrolment, the PM was interrogated and checked. Data on the manufacturer, model, and setting of each patient's PM were recorded. During the visit, the rhythm and conduction disturbances of each enrolled patient were reassessed and defined according to current guidelines.[3] The spontaneous rhythm was analysed by examining the intracavitary electrograms and, if needed, the 12-lead electrocardiogram. In all of the hospitals involved in the study, PM interrogation and reprogramming and reassessment of conduction disturbances were performed by electrophysiologists. In accordance with the clinical practice of all participating centres, conduction disturbances were routinely reassessed at each scheduled PM follow-up visit and were recorded in dedicated electronic medical records.

Definition of appropriate pacemaker choice and programming

In accordance with the indications reported in the literature,[4] a PM was considered appropriate if its programmable parameters promoted the most physiological cardiovascular activity, ensured patient safety, and maximized device longevity. On the basis of these criteria, appropriate device setting had to meet one or more of the following, according to the patient's rhythm: (a) preservation of atrioventricular (AV) synchrony when atrial fibrillation (AF) was not the predominant rhythm or the rhythm 'chosen' for the patient; (b) avoidance of unnecessary ventricular pacing in the absence of persistent atrioventricular block (AVB); (c) automatic management of the pacing output in the chamber presenting the primary indication for cardiac pacing;[5] (d) rate increase during exercise, with rate-responsiveness activated, when required, in the case of chronotropic incompetence (CI); and (e) prevention of syncope in the setting of neutrally mediated syndromes.

In order to identify the device characteristics and settings required, we assigned rhythm disorders needing pacing to five clinical categories: (1) sinus node disease (SND): SND, including brady-tachy form; (2) persistent AVB: persistent third- or second-degree AVB; (3) non-persistent AVB: chronic bifascicular block and/or paroxysmal third- or second-degree AVB; (4) neuro-mediated syncope (NMS): carotid sinus syncope and vasovagal syncope; and (5) AF needing pacing: AF with slow ventricular conduction and AF with intermittent/paroxysmal AVB.

The minimal appropriate device settings required according to clinical features are summarized in *Table 1*. The PM choice on implantation was deemed appropriate if the device implanted was equipped with all of the algorithms required for the specific rhythm disorder requiring permanent pacing. The PM setting on follow-up was deemed appropriate if all of the algorithms required for the patient's current rhythm disorder were activated.

In the first part of the analysis (appropriateness of PM choice on implantation), we included all patients with available detailed data on baseline rhythm disorder and on the programmable parameters of the PM which was originally implanted. Patients with more than one rhythm disorder (e.g. SND + AVB) at the time of PM implantation were excluded from this analysis. In all participating centres, the choice of device was made by the electrophysiologists involved in the implantation procedure. Devices endowed with all of the features listed in *Table 1* were available in all of the hospitals involved in the study when all PM implantations were performed.

In the second part of the analysis (appropriateness of PM setting on follow-up), we included only those patients who had received an appropriate device (according to criteria listed in *Table 1*) and in whom the rhythm disorder had subsequently been confirmed and recorded at least twice in the previous year. In this part of the analysis, we excluded patients who had developed more than one rhythm disorder (e.g. SND + AVB) and those who no longer needed pacing (i.e. SND patients who developed permanent AF without pacing indication during follow-up). Patients whose rhythm disorder had significantly evolved in comparison with their previous follow-up visit, and who therefore needed PM reprogramming (e.g. from non-persistent to persistent AVB), were also excluded.

Statistical analysis

Descriptive statistics are reported as mean ± standard deviation (SD) for normally distributed variables and were compared by means of Student's *t*-test. Continuous variables with a skewed distribution are reported as medians and 25th–75th percentiles. Categorical variables are reported as percentages and were statistically tested by means of the χ^2 and Fisher's exact tests.

Table 1 Pacemaker settings required according to clinical features

Required characteristics	SND	Persistent AVB	Non-persistent AVB	NMS	AF needing pacing
Pacing mode	DDD or AAI[a]	DDD or VDD	DDD	DDD	VVI
Rate-responsive function (yes/no)	Yes[b]	No	No	No	Yes[b]
Auto-adapted ventricular output (yes/no)	No	Yes	No	No	Yes
Algorithms to promote intrinsic AV conduction (yes/no)	Yes[c]	No	Yes	Yes	–
Specialized sensing and pacing algorithms for NMS prevention (yes/no)	No	No	No	Yes	No

AF, atrial fibrillation; AVB, atrioventricular block; NMS, neuro-mediated syncope; SND, sinus node disease.
[a]All of the patients with a single-chamber AAI PM had a SND. During the implant, an atrial pacing test was performed, and 1:1 atrioventricular conduction at 100 bpm was required for considering AAI/R PM implantation appropriates.[6]
[b]Required in the case of CI.
[c]Not available in the case of AAI PM.

Univariate Cox proportional hazards models were used to investigate the effect of variables related to patients and to enrolling hospitals on the appropriateness of PM choice at implantation, and on PM setting during follow-up. Variables that showed an effect on the appropriateness of PM choice and/or setting with a significance level of <0.2 in the univariate analysis were entered into the multivariate Cox proportional hazards models. Cox model findings are presented as hazard ratios (HRs) and 95% confidence intervals (CIs). A two-tailed *P*-value of <0.05 was considered statistically significant.

Results

Population

A total of 1858 patients were consecutively enrolled in 7 Italian arrhythmia centres during a 6-month period. Baseline characteristics of the study population and rhythm disorders at the time of PM implantation are summarized in *Table 2*. The mean age of patients was 71.3 ± 13.6 years, and 53.8% were male. The most frequent indication for PM implantation was SND (31.8%), followed by persistent third-degree AVB (20.3%), permanent AF with AVB or slow ventricular rate (11.2%), persistent second-degree AVB (11.1%), paroxysmal second- and/or third-degree AVB (7.4%), NMS (7.0%), and chronic bifascicular block (4.4%). Two or more associated rhythm disorders were recorded in 6.8% of patients. The median time from first PM implantation to enrolment was 4.5 years. Pacemakers were implanted from January 2000 to July 2015. Nearly one-fifth (19.8%) of all patients underwent one or more PM replacement.

Table 2 Characteristics of study population

Characteristics	$n = 1858$
Baseline characteristics	
Male, *n* (%)	999 (53.8)
Age on implantation, in years, mean + SD	71.3 ± 13.6
Time from implantation to enrolment, in years, median (interquartile range)	4.5 (2.3–8.3)
Patients who underwent one or more PM replacement, *n* (%)	368 (19.8)
Indication for PM implantation	
Sinus node disease, including brady-tachy form, *n* (%)	590 (31.8)
Persistent third-degree AVB, *n* (%)	378 (20.3)
Atrial fibrillation needing pacing, *n* (%)	209 (11.2)
Persistent second-degree AVB, *n* (%)	206 (11.1)
Paroxysmal second- and/or third-degree AVB, *n* (%)	137 (7.4)
Neuro-mediated syncope, *n* (%)	130 (7.0)
Two or more associated rhythm disorders, *n* (%)	126 (6.8)
Chronic bifascicular block, *n* (%)	82 (4.4)
Type of PM initially implanted	
DDD, *n* (%)	1359 (73.1)
VVI, *n* (%)	426 (22.9)
VDD, *n* (%)	68 (3.7)
AAI, *n* (%)	5 (0.3)
Manufacturers	
Medtronic, *n* (%)	675(36.3)
St Jude Medical, *n* (%)	351 (18.9)
Boston Scientific, *n* (%)	325 (17.5)
Biotronik, *n* (%)	211 (11.4)
Sorin, *n* (%)	125 (6.7)
Medico, *n* (%)	22 (1.2)
Ela, *n* (%)	21 (1.1)
Vitatron, *n* (%)	16 (0.9)
Unknown, *n* (%)	112 (6.0)

Appropriateness of pacemaker choice

Of the 1858 patients, 112 (6.0%) were excluded from this analysis because detailed data on the PMs initially implanted were not available; another 126 (6.8%) patients were excluded because they had received a PM for two or more associated rhythm disorders. The remaining 1620 patients were analysed. *Table 3* reports the rate of patients receiving a PM endowed with all of the features required for their rhythm disorder (appropriate device choice) and the rate of patients receiving a PM with none of the features required (wrong device choice). Overall, patients with NMS had the lowest probability of receiving an appropriate PM (52.7%). In this group, 7.6% of patients received a PM without any algorithms related to their rhythm disorder. The most frequent cause of inappropriate choice was the lack of dedicated algorithms for syncope prevention (absent

Table 3 Appropriateness of PM choice on implantation and of PM setting on follow-up

		SND	Persistent AVB	Non-persistent AVB	NMS	AF needing pacing	Overall population
		$n = 545$	$n = 521$	$n = 223$	$n = 131$	$n = 200$	$n = 1620$
Appropriate choice of PM on implantation	Patients receiving PM with all of the required characteristics, *n* (%)	387 (71.0)	421 (80.8)	131 (58.7)	69 (52.7)	153 (76.5)	1041 (64.3)
	Patients receiving PM with none of the required characteristics, *n* (%)	47 (8.6)	13 (2.5)	16 (7.2)	10 (7.6)	0 (0)	86 (5.3)
		$n = 369$	$n = 472$	$n = 114$	$n = 67$	$n = 279$	$n = 1301$
Appropriate PM programming on follow-up	Patients with PM programmed with all of the required settings, *n* (%)	282 (76.4)	382 (80.9)	75 (65.8)	32 (47.8)	220 (78.9)	991 (76.2)
	Patients with PM programmed with none of the required settings, *n* (%)	87 (23.6)	90 (19.1)	39 (34.2)	10 (14.9)	59 (21.1)	285 (21.9)

AF, atrial fibrillation; AVB, atrioventricular block; NMS, neuro-mediated syncope; SND, sinus node disease.

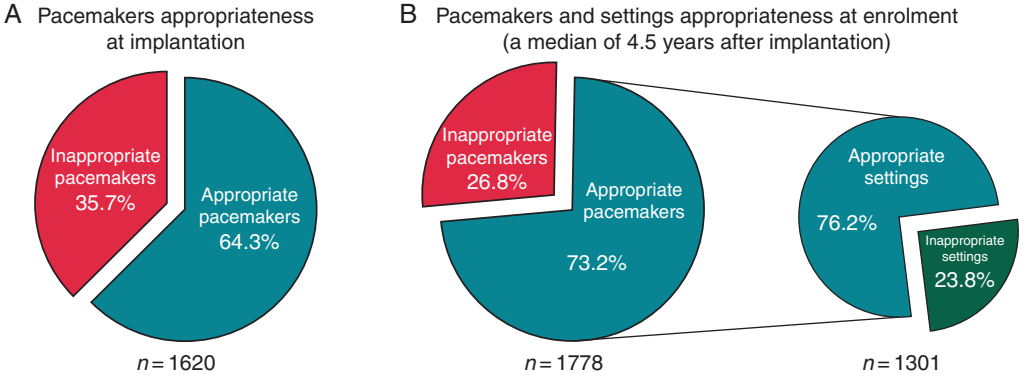

Figure 1 Rate of appropriate PMs on implantation (*A*). Rate of appropriate PMs and appropriate settings on enrolment (*B*).

in 36.8% of NMS patients). The group of patients with persistent AVB had the highest probability of receiving an appropriate PM (80.8%; $P < 0.001$ compared with NMS patients). In this group, only 2.5% of patients received a PM with none of the required features. The most frequent cause of inappropriate choice was the lack of an algorithm for automatic management of the ventricular pacing output (13.8%). Overall, the PM choice was appropriate in 64.3% of patients (*Figure 1A*). As shown in *Figure 2*, in the overall population analysed, the most frequent cause of inappropriate PM choice was the lack of an algorithm to promote intrinsic AV conduction in non-persistent AVB patients (38.1%). Multivariate analysis (*Table 4*) identified 'time from implantation to enrolment >5 years' as the only independent predictor of inappropriate PM choice (HR 3.26; $P < 0.001$). Implantation for persistent AVB and for AF needing pacing, and a high annual implantation volume (>350/year) in the enrolling hospital were independently associated with a lower probability of inappropriate PM choice (HRs 0.46, 0.59, and 0.42, respectively; all $P < 0.001$).

Appropriateness of pacemaker setting

Of the 1858 patients, 77 (4.1%) were excluded because they had two or more associated rhythm disorders; 3 (0.2%) were excluded because, during the enrolment visit, their rhythm disorder was seen to have significantly evolved in comparison with their previous indication. Of the remaining 1778 patients, 1301 (73.2%) had a PM endowed with all of the features related to their rhythm disorder and hence were included in the analysis (*Figure 1B*). *Table 3* reports the rate of patients receiving a PM with all of the algorithms required for their rhythm disorder activated, according to the criteria reported in *Table 1* (appropriate device setting), and the rate of patients with a PM with not even one of the required settings activated (wrong device setting). Overall, patients with NMS had the lowest probability of appropriate device setting (47.8%). In this group, 14.9% of patients had a PM with all of the algorithms related to their rhythm disorder inactivated (although they were all available). The most frequent cause of inappropriate setting was the failure to activate a specialized sensing and pacing algorithm for NMS prevention (not activated in 40.3% of the NMS patients, see *Figure 3*). The group of patients with persistent AVB had the highest probability of appropriate device setting (80.9%; $P < 0.001$ compared with NMS patients). In this group, 19.1% of patients had a PM with all of the algorithms related to their rhythm disorder inactivated. Overall, in 76.2% of patients, the PM setting was considered appropriate (*Figure 1B*). As shown in *Figure 3*, in the overall population, the

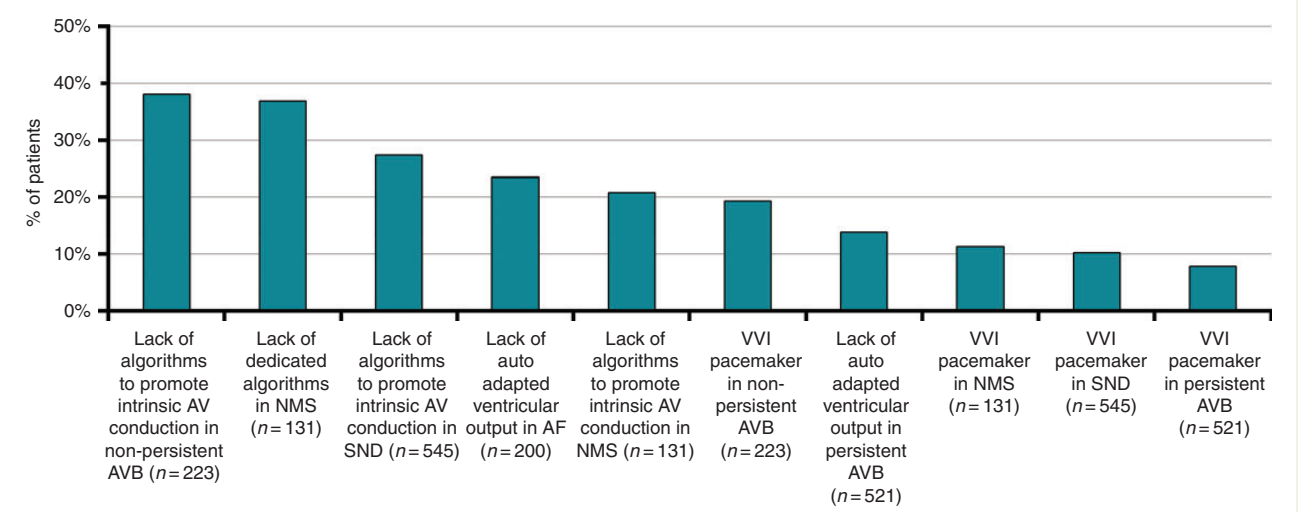

Figure 2 Causes of inappropriate PM choice. AF, atrial fibrillation; AVB, atrioventricular block; NMS, neuro-mediated syncope; SND, sinus node disease.

most frequent cause of inappropriate PM setting was the failure to activate a dedicated algorithm for syncope prevention in NMS patients (inactivated in 40.3% of patients, although this was available in all of the devices).

Multivariate analysis (*Table 4*) identified as independent predictors of inappropriate PM setting on follow-up a history of PM replacement and of PM implantation for NMS (HRs 2.42 and 3.27, respectively; both $P < 0.001$). Conversely, implantations for persistent AVB and for AF needing pacing were independently associated with a lower risk of inappropriate PM setting (HRs 0.57 and 0.57, respectively; both $P < 0.01$).

Discussion

This observational, multicentre study provides relevant data regarding the choice and the setting of devices in an unselected PM population from 'real-world' routine clinical practice. The main findings of this study were two. First, in almost one-third of cases, the devices chosen did not have all of the features recommended (or appropriate) for the patients' specific rhythm disorders.[3] This occurred despite the fact that all of the implanting physicians had access to many devices in which all of the required features were fully available. Second, during follow-up, PM programming was seen to be appropriate to the patient's clinical needs in only 76% of cases, even though the patients' rhythm disorders were periodically reassessed and recorded in all of the participating centres.

The prevalence of bradyarrhythmia requiring a PM is unknown. Pacemaker implantation has been reported to vary widely among different countries; this may reflect differences in demographics and disease prevalence. Furthermore, in addition to medical aspects, access to health resources, health policies, and economic welfare can play a role. In Italy, the PM implantation rate ranks high among western countries, being above 65 000 yearly (~900 PMs/million population).[1] What is known is that cardiac pacing prolongs survival and is a cost-effective therapy;[7] moreover, it aims to address specific clinical needs by implementing the many built-in algorithms currently available.[8–10] However, owing to the heterogeneity of the populations in published studies, the choice of the appropriate PM is seldom straightforward. Although no differences in mortality between single- and dual-chamber devices have been demonstrated, several studies have shown the benefits of atrial-tracked stimulation for the reduction of PM syndrome and crossover to dual-chamber stimulation that causes a burden of hospitalizations and upgrade-related complications.[11] Moreover, AV-synchronous stimulation significantly reduces AF development and heart failure-related hospitalizations.[12,13] Whereas ventricular stimulation is mandatory in AVB patients, it has proved detrimental in patients with preserved AV conduction; this provides the rationale behind algorithms designed to avoid unnecessary right ventricular stimulation. Our study demonstrates that, in the 'real world', only 62% of patients receive an 'appropriate' PM. Quite shockingly, single-chamber PMs were implanted in 8% of patients with a symptomatic second- or third-degree AVB; this results in the loss of atrial tracking and a non-physiologic diastolic function. In patients who have a low (<60 bpm) intrinsic rate and are nearly 100% paced, single-chamber pacing is associated with higher cardiovascular mortality and stroke rate, a risk that outweighs the functional benefit of normal ventricular filling in diastole.[6,13]

The effects of AAI or AAI-DDD pacing are more evident in SND, with or without first-degree AVB. Indeed, the DANPACE study showed that, in sick sinus syndrome, AAI/R pacing was associated with a higher incidence of paroxysmal AF than DDDR pacing, and with a two-fold increased risk of PM re-intervention, in that 0.6–1.9%/year of these patients develop AVB.[6] This evidence supports the use of dual-chamber rather than single-chamber pacing in sick sinus syndrome patients with a prolonged AV interval, which makes the strategy of avoiding right ventricular stimulation and very long AV interval (>400 ms) highly debateable.[6,10] On the basis of this evidence, more than 70% of the patients with SND in our study had a PM endowed with an algorithm that reduces unnecessary

Table 4 Predictors of inappropriate PM choice on implantation and of inappropriate PM setting on follow-up: univariate and multivariate Cox proportional hazards analysis

Predictors of inappropriate choice of PM on implantation ($n = 1620$)				
Variables	**Univariable analysis**		**Multivariable analysis**	
	Hazard ratio (95% IC)	***P***	**Hazard ratio (95% IC)**	***P***
Factors related to patients				
Age on implantation >80 years	0.965 (0.76–1.23)	0.773		
Male sex	0.963 (0.77–1.20)	0.739		
Time from implantation to enrolment >5 years	2.618 (2.07–3.31)	**<0.001**	3.258 (2.50–4.23)	**<0.001**
Indication for PM implantation				
Sinus node disease	1.050 (0.88–1.22)	0.676		
Persistent AVB	0.280 (0.21–0.37)	**<0.001**	0.457 (0.33–0.63)	**<0.001**
Non-persistent AVB	2.416 (1.67–3.49)	**<0.001**	0.871 (0.48–1.10)	0.101
Neuro-mediated syncope	1.568 (1.05–2.34)	**0.026**	1.206 (0.95–2.64)	0.461
Atrial fibrillation needing pacing	0.477 (0.33–0.70)	**<0.001**	0.589 (0.39–0.90)	**<0.001**
Factors related to enrolling centres				
University hospital	1.125 (0.88–1.44)	0.348		
No. of devices implanted >350/year	0.648 (0.50–0.84)	**<0.001**	0.422 (0.22–0.68)	**<0.001**
Predictors of inappropriate setting of PM on follow-up ($n = 1301$)				
Factors related to patients				
Age >80 years	1.012 (0.75–1.36)	0.939		
Male sex	0.992 (0.76–1.29)	0.953		
Time from implantation to enrolment >5 years	1.537 (1.18–2.00)	**0.001**	1.164 (0.81–1.67)	0.412
Pacemaker replacement	2.222 (1.67–2.96)	**<0.001**	2.419 (1.65–3.54)	**<0.001**
Conduction disturbance				
Sinus node disease	0.981 (0.79–1.22)	0.894		
Persistent AVB	0.638 (0.48–0.84)	**0.001**	0.565 (0.39–0.82)	**0.003**
Non-persistent AVB	1.563 (1.04–2.36)	**0.032**	1.297 (0.79–2.12)	0.300
Neuro-mediated syncope	3.866 (2.35–6.36)	**<0.001**	3.266 (1.85–5.76)	**<0.001**
Atrial fibrillation needing pacing	0.724 (0.52–1.00)	0.051	0.555 (0.36–0.85)	**0.007**
Factors related to enrolling centres				
University hospital	0.878 (0.67–1.15)	0.339		
No. of devices implanted >350/year	1.105 (0.83–1.47)	0.493		

Statistically significant *P*-values are in bold type.

ventricular pacing, and, when available, it was turned on in more than 80% of cases.

Auto-adaptive stimulation algorithms are the most important in ensuring patient safety and reducing replacement-related complications.[5,8] In addition to preventing loss of capture in the event of an unexpected pacing threshold increase,[5] they enable the patient's life expectancy to be matched with the service life of the PM, thereby reducing the replacement rate. For these reasons, it is recommended that algorithms for automatic management of the pacing output in the chamber representing the primary indication for cardiac pacing be activated.

There is weak evidence that a PM may be effective in reducing NMS.[14] The maintenance of AV synchrony, as opposed to simple ventricular pacing, is debateable, owing to the sporadic occurrence of symptoms and the heterogeneity of the syncope (purely cardioinhibitory vs. mixed). Small and large controlled studies have shown that dual-chamber pacing, incorporating dedicated algorithms that monitor the heart rate for faster detection of a significant rate drop and respond by pacing at a high rate, reduces syncope in patients with severe forms of NMS to a greater degree than DDD pacing.[14–17] However, our data show that PM choice is not driven by the availability of these specific algorithms when it comes to NMS patients and that these algorithms are most commonly not turned on after implantation.

In our study, more recently implanted PMs (<5 years prior to enrolment) were more likely to be appropriate for the patients' clinical characteristics. It is possible that awareness of the potential clinical benefits of technological improvements in devices has increased in recent years, which may have prompted the choice of these devices. Pacemaker implantation in a high-volume hospital was another factor significantly associated with appropriate device choice. The most likely explanation for this finding is that physicians in high-volume hospitals are more aware of the technical features of different PM models than those in less experienced centres.

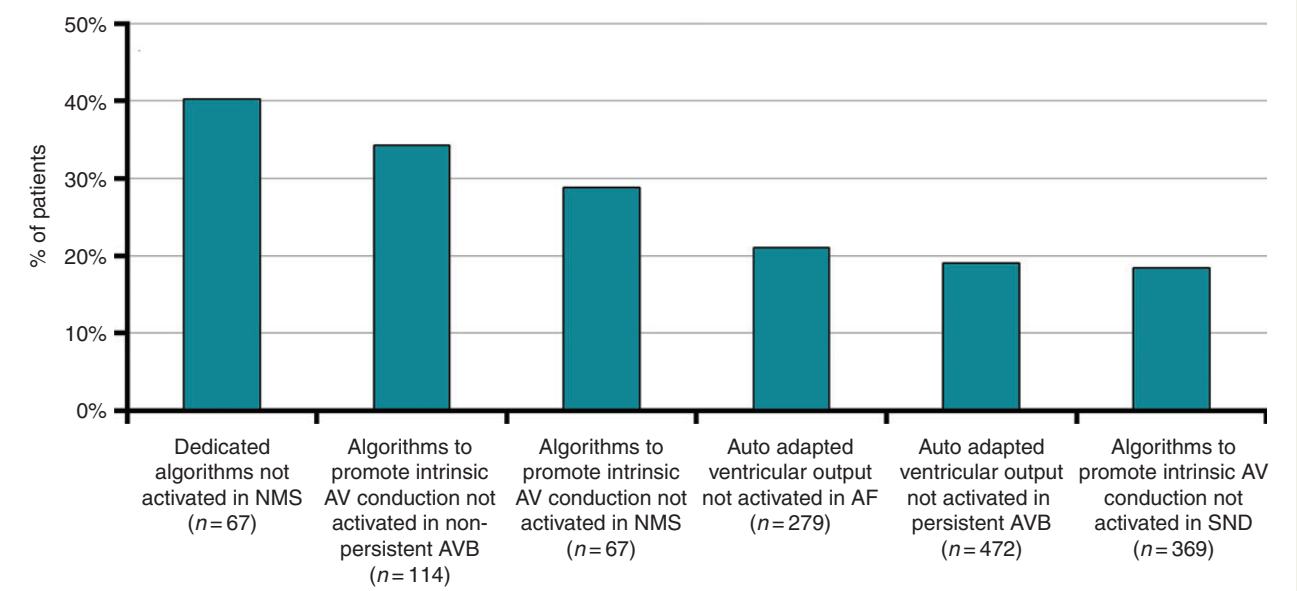

Figure 3 Causes of inappropriate PM setting. AF, atrial fibrillation; AVB, atrioventricular block; NMS, neuro-mediated syncope; SND, sinus node disease.

In patients who underwent PM replacement, the programming of the new device was less likely to be tailored to the clinical conditions of the patient. This suggests a potential lack of focus when devices are replaced in clinical practice.

Study limitations

The present study, although prospective in nature, is subject to all of the limitations of an observational study. The first limit of our study could be the definition of the 'appropriateness': in accordance with the indications reported in the literature,[4] and not only in the ESC guidelines,[3] a PM was considered appropriate if its programmable parameters promoted the most physiological cardiovascular activity, ensured patient safety, and maximized device longevity. The results of this study should therefore be interpreted with caution as confounding factors cannot be entirely excluded. Further prospective, large population analyses are needed to confirm our findings.

A rate-responsive (RR) function is useful in patients with CI.[18] A correct diagnosis of CI requires the execution of an exercise test. In this study, the incidence of CI was not evaluated, either on implantation or on enrolment. Consequently, it was not possible to evaluate activation of the RR function in patients with CI.

Conclusions

Two important results stem from this analysis: considering our definition of appropriateness, many patients still receive a PM that is inappropriate for their rhythm disorder; the pacing setting is not tailored to the clinical conditions in at least 25% of patients. Leaving aside the question of the availability of technologically advanced devices via the supply chain, the biggest challenge is to improve physicians' familiarity with PM technology. As reported in the AUTOMATICITY trial, the performances of the various algorithms are very good, and device reprogramming by physicians is rare (and often clinically unwarranted).[19] Shipment programming traditionally sticks to generic settings, which cannot be fully physiologic for all rhythm disorders. Programming should be tailored to the individual patient through the use of predefined settings that are disorder specific. In this way, the physician would only need to make individual changes (e.g. lower or upper rate, AV delay, maximum sensor rate and rate during ordinary activity), the rest being automatically managed by the pacer.

Conflicts of interest: none declared.

References

1. Proclemer A, Zecchin M, D'Onofrio A, Botto GL, Rebellato L, Ghidina M *et al.* The pacemaker and implantable cardioverter-defibrillator registry of the Italian Association Arrhythmology Cardiac Pacing and cardiac pacing—annual report 2013. *G Ital Cardiol (Rome)* 2014;**15**:638–50.
2. Loirat A, Feneon D, Behaghel A, Behar N, Le Helloco A, Mabo P *et al.* Pacemaker replacement in nonagenarians: procedural safety and long-term follow-up. *Arch Cardiovasc Dis* 2015;**108**:367–74.
3. Brignole M, Auricchio A, Baron-Esquivias G, Bordachar P, Boriani G, Breithardt OA *et al.* 2013 ESC Guidelines on cardiac pacing and cardiac resynchronization therapy. *Europace* 2013;**15**:1070–118.
4. Biffi M, Melissano D, Rossi P, Kaliska G, Havlicek A, Pelargonio G *et al.* The OPTIMIND study: a prospective, observational study of pacemaker patients according to pacing modality and primary indications. *Europace* 2014;**16**:689–97.
5. Biffi M, Bertini M, Mazzotti A, Gardini B, Mantovani V, Ziacchi M *et al.* Long-term RV threshold behavior by automated measurements: safety is the standpoint of pacemaker longevity! *Pacing Clin Electrophysiol* 2011;**34**:89–95.
6. Nielsen JC, Thomsen PE, Hojberg S, Moller M, Vesterlund T, Dalsgaard D *et al.* A comparison of single-lead atrial pacing with dual-chamber pacing in sick sinus syndrome. *Eur Heart J* 2011;**32**:686–96.
7. Boriani G, Maniadakis N, Auricchio A, Muller-Riemenschneider F, Fattore G, Leyva F *et al.* Health technology assessment in interventional electrophysiology and device therapy: a position paper of the European Heart Rhythm Association. *Eur Heart J* 2013;**34**:1869–74.

8. Biffi M, Bertini M, Saporito D, Ziacchi M, Martignani C, Diemberger I *et al.* Actual pacemaker longevity: the benefit of stimulation by automatic capture verification. *Pacing Clin Electrophysiol* 2010;**33**:873–81.
9. Capucci A, Boriani G, Specchia S, Marinelli M, Santarelli A, Magnani B. Evaluation by cardiopulmonary exercise test of DDDR versus DDD pacing. *Pacing Clin Electrophysiol* 1992;**15**:1908–13.
10. Sweeney MO, Bank AJ, Nsah E, Koullick M, Zeng QC, Hettrick D *et al.* Minimizing ventricular pacing to reduce atrial fibrillation in sinus-node disease. *N Engl J Med* 2007;**357**:1000–8.
11. Link MS, Hellkamp AS, Estes NA 3rd, Orav EJ, Ellenbogen KA, Ibrahim B *et al.* High incidence of pacemaker syndrome in patients with sinus node dysfunction treated with ventricular-based pacing in the Mode Selection Trial (MOST). *J Am Coll Cardiol* 2004;**43**:2066–71.
12. Sweeney MO, Hellkamp AS, Ellenbogen KA, Greenspon AJ, Freedman RA Lee KL *et al.* Adverse effect of ventricular pacing on heart failure and atrial fibrillation among patients with normal baseline QRS duration in a clinical trial of pacemaker therapy for sinus node dysfunction. *Circulation* 2003;**107**: 2932–7.
13. Tang AS, Roberts RS, Kerr C, Gillis AM, Green MS, Talajic M *et al.* Relationship between pacemaker dependency and the effect of pacing mode on cardiovascular outcomes. *Circulation* 2001;**103**:3081–5.
14. Brignole M, Menozzi C, Moya A, Andresen D, Blanc JJ, Krahn AD *et al.* Pacemaker therapy in patients with neurally mediated syncope and documented asystole: Third International Study on Syncope of Uncertain Etiology (ISSUE-3): a randomized trial. *Circulation* 2012;**125**:2566–71.
15. Johansen JB, Bexton RS, Simonsen EH, Markowitz T, Erickson MK. Clinical experience of a new rate drop response algorithm in the treatment of vasovagal and carotid sinus syncope. *Europace* 2000;**2**:245–50.
16. Occhetta E, Bortnik M, Audoglio R, Vassanelli C, Investigators IS. Closed loop stimulation in prevention of vasovagal syncope. Inotropy Controlled Pacing in Vasovagal Syncope (INVASY): a multicentre randomized, single blind, controlled study. *Europace* 2004;**6**:538–47.
17. Palmisano P, Zaccaria M, Luzzi G, Nacci F, Anaclerio M, Favale S. Closed-loop cardiac pacing vs. conventional dual-chamber pacing with specialized sensing and pacing algorithms for syncope prevention in patients with refractory vasovagal syncope: results of a long-term follow-up. *Europace* 2012;**14**:1038–43.
18. Sims DB, Mignatti A, Colombo PC, Uriel N, Garcia LI, Ehlert FA *et al.* Rate responsive pacing using cardiac resynchronization therapy in patients with chronotropic incompetence and chronic heart failure. *Europace* 2011;**13**:1459–63.
19. Alings M, Vireca E, Bastian D, Wardeh AJ, Nimeth C, Tukkie R *et al.* Clinical use of automatic pacemaker algorithms: results of the AUTOMATICITY registry. *Europace* 2011;**13**:976–83.

Corrigendum

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The Authors would like to apologize for errors in the in-text references to tables in this paper. These have now been corrected online and in print.