Original Article

Assessment of Adaptive Rate Response Provided by Accelerometer, Minute Ventilation and Dual Sensor Compared with Normal Sinus Rhythm During Exercise: A Self-controlled Study in Chronotropically Competent Subjects

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Abstract

Background: Dual sensor (DS) for rate adaption was supposed to be more physiological. To evaluate its superiority, the DS (accelerometer [ACC] and minute ventilation [MV]) and normal sinus rate response were compared in a self-controlled way during exercise treadmill testing.

Methods: This self-controlled study was performed in atrioventricular block patients with normal sinus function who met the indications of pacemaker implant. Twenty-one patients came to the 1-month follow-up visit. Patients performed a treadmill test 1-month post implant while programmed in DDDR and sensor passive mode. For these patients, sensor response factors were left at default settings (ACC = 8, MV = 3) and sensor indicated rates (SIRs) for DS, ACC and MV sensor were retrieved from the pacemaker memories, along with measured sinus node (SN) rates from the beginning to 1-minute after the end of the treadmill test, and compared among study groups. Repeated measures analysis of variance and profile analysis, as well as variance analysis of randomized block designs, were used for statistical analysis.

Results: Fifteen patients (15/21) were determined to be chronotropically competent. The mean differences between DS SIRs and intrinsic sinus rates during treadmill testing were smaller than those for ACC and MV sensor (mean difference between SIR and SN rate: ACC vs. SN, MV vs. SN, DS vs. SN, respectively, 34.84, 17.60, 16.15 beats/min), though no sensors could mimic sinus rates under the default settings for sensor response factor (ACC vs. SN *P*-adjusted < 0.001; MV vs. SN *P*-adjusted = 0.002; DS vs. SN *P*-adjusted = 0.005). However, both in the range of 1st minute and first 3 minutes of exercise, only the DS SIR profile did not differ from sinus rates (*P*-adjusted = 0.09, 0.90, respectively).

Conclusions: The DS under default settings provides more physiological rate response during physical activity than the corresponding single sensors (ACC or MV sensor). Further study is needed to determine if individual optimization would further improve adaptive performance of the DS.

Key words: Accelerometer; Adaptive Rate Pacing; Dual Sensor; Minute Ventilation

Introduction

Modern rate-adaptive pacemakers are designed to simulate the chronotropic response of a normal sinus node (SN), incrementally increasing the heart rate (and cardiac output) of patients with chronotropic incompetence in proportion to metabolic demands, emotional needs and stress.[1,2] Activity-based rate-adaptive sensors (i.e. vibration sensor) have been widely used since 1983. However, these sensors have drawbacks[3,4] because a physiologic heart rate is modulated by complicated reflexes and neurohormonal factors acting on the SN. Therefore, the idea of combining a fast reacting, but low specificity activity-based sensor with a high specificity, but slower responding physiologic sensor was explored to better simulate normal sinus rhythm.[4] Dual sensor (DS) devices, combining an accelerometer (ACC) based activity sensor and a minute ventilation (MV) based physiologic sensor, have shown promise in preserving physiological rate response and have been commercially available over the last two decades. Bonnet *et al.*[5] carried out a self-controlled study and reported that the DS (MV + ACC) response rates were perfectly correlated to normal sinus rhythm and there was a linear relation between heart reserve

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and metabolic reserve. Page *et al*.[6] confirmed that a DS based pacemaker properly adapted to metabolic demand in patients with chronotropic incompetence when compared to a healthy control group. Rate responsiveness during intense exercise was attributed to the MV sensor, while a faster response at the onset and end of exercise was attributed to the ACC sensor. However, the study was not designed to assess whether the DS could reproduce a normal sinus rhythm. The LIFE study,[7] a multicenter trial, reported that DS (MV + ACC) was superior to the single ACC sensor in restoration of the chronotropic response in chronotropically incompetent patients, but still differed from the normal SN. None of the studies provided a detailed comparison of rate adaption associated with single ACC sensor based devices, the DS devices and a normally functioning SN. As there was not a consistent methodology to select chronotropically incompetent patients in these studies,[7] our study focuses on evaluating sensor indicated rates (SIRs) in chronotropically competent pacemaker patients with normal sinus function in a self-controlled way in order to eliminate the bias of patient selection. Herein, we directly compare SIRs for ACC, MV, and DS device configurations with actual sinus response rates measured during exercise. Moreover, we report peak rate, average rate, peak time and the average rate of change in different stages of exercise to assess how well the DS simulates normal sinus rhythm.

Methods

Study design and patient population

This study was a self-controlled single-center clinical trial that included 21 patients hospitalized in the Department of Cardiology, Zhongshan Hospital Affiliated to Fudan University between August 2012 and May 2013. Patients were eligible for the study if they were at least 18 years old and had high degree atrioventricular block (AVB) or intermittent or persistent third-degree AVB which met Class 1 or 2A indication[8] for an initial pacemaker implantation. Enrolled patients should have normal sinus function. Our study defined normal sinus function as that the heart rate during the treadmill testing should exceed 85% maximum predicted heart rate (85% × [220 − age]). Exclusion criteria before pacemaker implantation included sick SN syndrome, atrial tachycardia, atrial flutter, atrial fibrillation, symptomatic heart failure (NYHA Class II or higher), coronary arterial disease (CCS Class II or higher), uncontrolled hypertension, impaired mobility caused by neuromuscular, orthopedic, or vascular disability such as arthritis, intermittent claudication, serious pulmonary disease, e.g. chronic obstructive pulmonary disease, uncontrolled asthma, requirement of drug therapy that affects sinus function.

Eligible patients were implanted with a Boston Scientific ALTRUA S404 Pacemaker (Boston Scientific Corporation, St. Paul, MN, USA) after signing a written informed consent. At the time of implant, all patients were programmed to DDD mode. At the 1-month follow-up visit, all implanted patients performed a treadmill exercise test to determine their normal sinus function while programmed in DDDR mode and sensor passive mode. Patients with abnormal sinus function or complicated with other arrhythmias that had not been diagnosed previously were excluded. Patients were told not to speak during the treadmill testing as well as 3 minutes before and after it unless they felt uncomfortable or physically tired. Blood pressure, heart rate and rhythm were monitored during the whole process of exercise. Exercise endpoint was when patients felt uncomfortable or ran out of strength or when the exercise sinus rate exceeded 85% maximum predicted heart rate. SIRs for ACC, MV, and DS sensing modes, as well as actual heart rates representative of sinus response rates, were retrieved from the pacemaker memories. We evaluated DS SIRs compared with ACC and MV single sensor for superiority in physiologic pacing. The study complies with the Declaration of Helsinki, and the research protocol is approved by the locally appointed ethics committee.

Pacemaker and parameter programming

The ALTRUA S404 pacemaker has both MV and ACC rate-adaptive sensors. The two kinds of sensors can be used alone or combined as a DS via different sensor configurations. Due to the availability of a sensor passive mode, the pacemaker can record true sinus rate, as well as SIRs of ACC, MV and DS simultaneously and continuously during exercise. Data can be retrieved from the pacemaker after exercise. Sinus rates are the actual heart rates tracking from the atria under sensor passive mode in which rate-adaptive pacing is inactivated.

Uniform program settings were performed to assure the consistency of pacemaker function. Pacemakers of all the eligible patients were programmed to have: (1) A lower rate limit of 60 beats/min; (2) a maximum sensor rate equal to the maximum predicted heart rate (220−age); and (3) DDDR therapy mode; (4) dynamic atrioventricular delay mode was programmed ON, providing a shorter atrioventricular delay at faster heart rate; (5) recording method was programmed to high resolution at which setting the ventricular rate was averaged and recorded every 16 s and the ACC and MV raw sensor data were collected; (6) the sensor response factors were programmed passive during the treadmill testing and converted to the default settings of ACC = 8, MV = 3 when analyzing the SIR data; (7) the baseline sensor rate was set accordingly with the sinus rate at rest.

Exercise testing

The instrument of treadmill we used was 3017 Full Vision Drive (Newton, Kansas, USA), and the electrocardiography acquisition and analysis system was Mortara Instrument X-Scribe (Milwaukee, Wisconsin, USA). The treadmill testing had three stages, the first stage: Speed 1.7 mile/h, slope 0% grade, for 1 minute; the second stage: Speed 1.7 mile/h, slope 7% grade, for 5 minutes; the third stage: Speed 2.0 mile/h, slope 10% grade, for 10 minutes.

Statistical analysis

Statistical analysis were performed using Statistical Package for the Social Sciences Version 16.0 (SAS Inc., USA) and

Stata 10.0 (StataCorp., College Station, Texas, USA) and all P values were deemed significant at a level of 0.05 or below. Normal distribution data were presented as mean and standard deviation. Categorical variables were expressed as frequencies and percentages. Paired t-tests were used for comparisons between sinus rates of patients and their own target rates. Repeated measures analysis of variance and Profile analysis were used to compare curves of ACC, MV and DS SIRs, and measured sinus rate. Variance analysis of randomized block designs was used for parametric data and Friedman test for nonparametric data. P values were corrected by Bonferroni method when compared in pairs.

Results

Patients

Twenty-one patients participated in the exercise treadmill testing, and six of them were excluded because they couldn't reach the target rate which was equal to 85% maximum predicted heart rate during the treadmill testing. The remaining fifteen patients met the criteria and were considered to have normal sinus function. Table 1 shows the baseline characteristics of these patients, along with their target heart rates and actual maximum sinus rates during exercise. All patients had AVB: Persistent III degree AVB in 13% (2 of 15), intermittent III degree AVB in 60% (9 of 15) and advanced II degree AVB in 27% (4 of 15). The average maximum sinus rate was (152 ± 13) beats/min, significantly higher than the average mean target rate of (139 ± 10) beats/min ($P < 0.001$).

Profiles of accelerometer, minute ventilation and dual sensor indicated rates and sinus rate variations

Figure 1 shows profiles of ACC, MV and DS SIRs and the corresponding intrinsic sinus rates during the treadmill testing, averaged across the patient pool at seven fixed time points as follows: At onset of the treadmill testing, then 1, 2, and 3 minutes after onset, the time of peak sinus rate, the end of the treadmill testing, and 1 minute after the test. None of the three SIR profiles was statistically similar to intrinsic rate profile (ACC vs. SN P-adjusted < 0.001; MV vs. SN P-adjusted = 0.002; DS vs. SN P-adjusted = 0.005; Table 2), but the mean difference between the DS and sinus rate profiles was smaller (mean difference between SIR and SN rate: ACC vs. SN, MV vs. SN, DS vs. SN, respectively, 34.84, 17.60, 16.15 beats/min; Table 2). SIR profiles for ACC and DS were significantly different while SIR profiles for MV and DS were similar (ACC vs. DS P-adjusted = 0.001, MV vs. DS P-adjusted > 0.99; Table 2). In the first 3 min of the test, there were no significant differences between

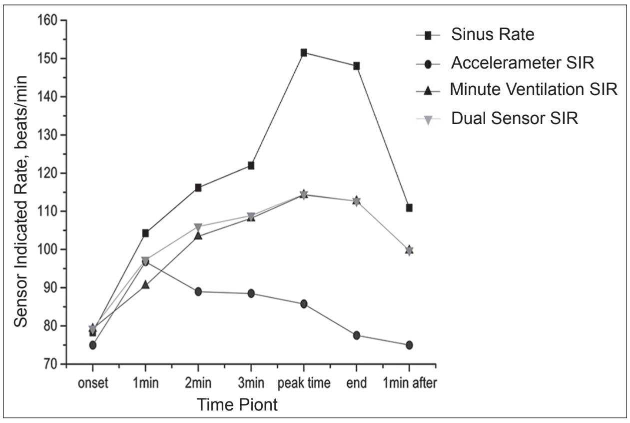

Figure 1: Profile analysis of the heart rate variations of accelerometer, minute ventilation and dual sensor sensor indicated rate, and intrinsic sinus rates measured at discrete time points during treadmill test: Onset, the onset of treadmill test; 1 min, 1 minute after test began; 2 min, 2 minutes after test began; 3 min, 3 minutes after test began; peak time, the time point to peak sinus rate; end, the end of the treadmill test; 1 minute after, 1 min after the end of test.

Table 1: Baseline characteristics of chronotropically competent patients, their target maximum heart rates and actual maximum sinus rates during exercise treadmill testing

Number	Gender	Age (years)	Diseases	Target rate* (beats/min)	Maximum sinus rate† (beats/min)
1	Female	56	Intermittent III degree AVB	139	170
2	Male	39	Persistent III degree AVB	154	170
3	Male	45	Advanced II degree AVB	149	150
4	Female	57	Intermittent III degree AVB	139	156
5	Male	43	Intermittent III degree AVB	150	152
6	Male	68	Intermittent III degree AVB	129	134
7	Female	59	Persistent III degree AVB	137	156
8	Male	63	Advanced II degree AVB	133	135
9	Male	70	Intermittent III degree AVB	128	144
10	Male	61	Advanced II degree AVB	135	156
11	Male	43	Intermittent III degree AVB	150	156
12	Male	40	Advanced II degree AVB	153	156
13	Male	57	Intermittent III degree AVB	139	158
14	Male	77	Intermittent III degree AVB	122	124
15	Female	61	Intermittent III degree AVB	135	156
Sum	4 female/11 male	56±12	–	139±10‡	152±13‡

Target rate means 85% maximum predicted heart rate equal to 85% (220-age), †Maximum sinus rate (beats/min) means the actual maximum sinus rate during the treadmill testing for every patient, ‡Maximum sinus rates were significantly higher than the target rates ($P < 0.001$). AVB: Atrioventricular block.

SIRs for DS and MV vs. intrinsic sinus rates (DS vs. SN, P-adjusted = 0.90; MV vs. SN, P-adjusted = 0.33; Table 3). On the contrary, significant differences were observed between ACC SIRs and intrinsic sinus rates (ACC vs. SN, P-adjusted = 0.005; Table 3).

Time averaged rates

The average time of the whole treadmill exercise from the onset to 1 min after the end was (10 ± 2) minutes. The time averaged SIRs for ACC, MV and DS were significantly lower than the time averaged intrinsic sinus rates (all P-adjusted < 0.001). Significant differences were also observed between the time average SIRs for ACC versus MV and DS (all P-adjusted < 0.001), but not for MV versus DS (P-adjusted > 0.99; Tables 4 and 5).

Peak sensor indicated rates and sinus node rates

All the three peak SIRs were significantly lower than the sinus rate (SN = 152 ± 13; ACC = 116 ± 25; MV = 120 ± 11; DS = 122 ± 9 beats/min; all P-adjusted < 0.001). However, no significant differences were measured among the peak SIRs for ACC, MV and DS (all P-adjusted > 0.99; Tables 4 and 5).

Peak time

The time to peak SIR was termed as peak time. The peak times of DS and ACC response rates were significantly shorter than that of SN ([5 ± 3] and [3 ± 2] minutes respectively vs. [7 ± 2] minutes; P-adjusted = 0.016; <0.001) while no significant differences were found between MV and SN ([6 ± 3] minutes vs. [7 ± 2] minutes; P-adjusted > 0.99). The peak times of DS were significantly longer than that of ACC, but similar to MV (DS vs. ACC P-adjusted = 0.039, DS vs. MV P-adjusted = 0.306). The peak times of ACC were significantly shorter than MV (P-adjusted < 0.001; Tables 4 and 5).

Average rate of change in different stages of exercise

Average rates of change of ACC, MV, DS SIRs and the intrinsic sinus rate in the 1st, 2nd, and 3rd minute of the treadmill testing, between the 3rd minute and the time of peak sinus rate, and in the 1st minute after the test were calculated and shown in Tables 4, 5 and Figure 2. Sinus rates, in the 1st minute of the exercise, increased rapidly with an average increment of (26 ± 10) beats/min. The subsequent average increments became smaller and smaller, (12 ± 12) beats/min in the 2nd min, (6 ± 4) beats/min in the 3rd min. Sinus rates were still increasing after the 3rd min and before the peak time with an average change of (9 ± 5) beats/min. In the 1st minute after the end of exercise, the sinus rates decreased with an average value of (37 ± 7) beats/min. In the 1st minute of the exercise, the ACC SIRs increased to a similar extent as the sinus rates ([21 ± 18] vs. [26 ± 10] beats/min; P-adjusted = 0.474). After that, the rates of change of ACC sensor and SN diverged. MV SIRs increased to a similar extent as sinus rates during the 2nd and 3rd minute of the exercise (both P-adjusted > 0.99) but exhibited a significantly less pronounced increase than sinus rates in the 1st minute (P-adjusted = 0.002). No significant differences of rate increase in the first 3 minute of exercise were observed between DS and SN (P-adjusted one by one in the 1st, 2nd, 3rd minute: 0.09, >0.99, >0.99). The average rates of change of MV and DS SIRs after the 3rd minute were significant different from sinus rates, including the 1st minute after the end of the test (all P-adjusted < 0.001).

Table 2: Mean differences and adjusted *P* values of profiles of heart rate variations of ACC, MV and DS SIRs, and sinus rates measured at discrete time intervals during treadmill testing compared with each other in the whole process

Group 1	Group 2	Mean difference	SE	Adjusted-*P**	95% *CI*	
SN	ACC	34.8	4.6	<0.001	22.3	47.4
SN	MV	17.6	4.6	0.002	5.0	30.2
SN	DS	16.2	4.6	0.005	3.6	28.7
DS	ACC	18.7	4.6	0.001	6.1	31.3
DS	MV	1.5	4.6	>0.99	−11.1	14.0
MV	ACC	17.2	4.6	0.003	4.7	29.8

*The mean difference is significant at the 0.05 level. *P* value was adjusted by Bonferroni method. SN: Sinus node; ACC: Accelerometer; MV: Minute ventilation; DS: Dual sensor; CI: Confidence interval; SE: Standard error.

Table 3: Mean differences and adjusted *P* values of profiles of heart rate variations of ACC, MV and DS SIRs, and sinus rates measured at discrete time intervals for the treadmill testing compared with each other in the first 3 minutes

Group 1	Group 2	Mean difference	SE	Adjusted-*P**	95% *CI*	
SN	ACC	17.9	5.0	0.005	4.1	31.7
SN	MV	9.8	5.0	0.33	−3.9	23.6
SN	DS	7.4	5.0	0.90	−6.4	21.1
DS	ACC	10.6	5.0	0.24	−3.2	24.3
DS	MV	2.5	5.0	>0.99	−11.3	16.3
MV	ACC	8.1	5.0	0.69	−5.7	21.8

*The mean difference is significant at the. 05 level. *P* value was adjusted by Bonferroni method. SN: Sinus node; ACC: Accelerometer; MV: Minute ventilation; DS: Dual sensor; CI: Confidence interval; SE: Standard error.

Table 4: Peak rate, average rate, peak time of ACC, MV, and DS SIRs and SN rate and average rate of change in different stages of exercise

Items	SN	ACC	MV	DS
Average rate (beats/min)	124 ± 13	87 ± 15	106 ± 10	107 ± 10
Peak rate (beats/min)	152 ± 13	116 ± 25	120 ± 11	122 ± 9
Peak time (minutes)	7 ± 2	3 ± 2	6 ± 3	5 ± 3
Average rate of change				
In the 1st minute	26 ± 10	21 ± 18	11 ± 7	18 ± 7
In the 2nd minute	12 ± 12	−8 ± 20	13 ± 7	9 ± 10
In the 3rd minute	6 ± 4	0 ± 12	5 ± 7	3 ± 7
Between the 3rd minute and the time of peak sinus rate	9 ± 5	−2 ± 6	1 ± 4	1 ± 4
In the 1st minute after test	−37 ± 7	−3 ± 6	−13 ± 15	−13 ± 15

SIR: Sensor indicated rate; SN: Sinus node; ACC: Accelerometer; MV: Minute ventilation; DS: Dual sensor.

Table 5: Adjusted P values for the intergroup comparison of ACC, MV, and DS SIRs and SN rates

Items	P (SN vs. ACC)	P (SN vs. MV)	P (SN vs. DS)	P (DS vs. ACC)	P (DS vs. MV)	P (MV vs. ACC)
Average rate	<0.001	<0.001	<0.001	<0.001	>0.99	<0.001
Peak rate	<0.001	<0.001	<0.001	>0.99	>0.99	>0.99
Peak time	<0.001	>0.99	0.016	0.039	0.306	<0.001
Average rate of change						
In the 1st minute	0.474	0.002	0.09	>0.99	>0.99	0.282
In the 2nd minute	<0.001	>0.99	>0.99	0.002	>0.99	<0.001
In the 3rd minute	0.356*	>0.99	>0.99	>0.99	>0.99	>0.99
Between the 3rd minute and the time of peak sinus rate	<0.001	<0.001	<0.001	0.031	>0.99	0.008
In the 1st min after test	<0.001	<0.001	<0.001	0.124	>0.99	0.124

*The average rate of change of ACC and SN in the 3rd min was clinically different while no statistical difference was found. SIR: Sensor indicated rate, SN: Sinus node, ACC: Accelerometer, MV: Minute ventilation, DS: Dual sensor.

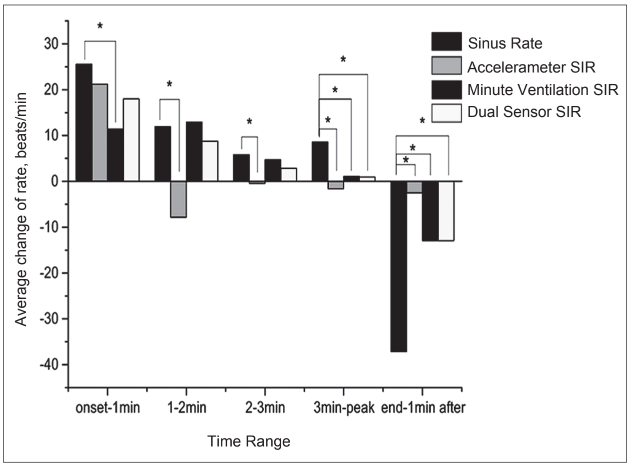

Figure 2: Average rates of change of accelerometer, minute ventilation and dual sensor sensor indicated rate, and intrinsic sinus rates in different stages of exercise: Onset - 1 min, in 1st minute after the onset of treadmill test; 1–2 min, in 2nd minute after onset of test; 2–3 min, in 3rd minute after the onset of treadmill test; 3 min-peak, the time ranging from the 3rd minute to the time of peak sinus rate; end - 1 min after, in 1st minute after the end of test (*P < 0.05).

Discussion

Restoration of the chronotropic competence of sinus rhythm is the primary goal of the application of rate adaptive pacing. The DS responded to the treadmill exercise test more favorably than the single ACC sensor on the whole in our study though both the DS and single sensor response rates differed from the SN significantly. The differences were minimum between DS and SN and maximum between ACC and SN. The superiority of DS in the adaptive response was attributed to the blending of minute sensor and ACC sensor response profiles, leveraging their advantages and minimizing their drawbacks.[9]

The single ACC sensor provided inappropriate rates at most stages of the treadmill exercise test except during the 1st min, after which the adaption was almost totally opposite to the SN and body metabolic demands. This result reflects the major disadvantage of activity-based sensor systems which are nonphysiologic[9] and hardly distinguish between mild and vigorous physical activities, and are unable to provide a sustained rate increase in response to an oxygen debt after long exercise. Matula *et al*.[10] held the opinion that ACC-controlled pacemakers showed a physiological rate behavior for everyday activities at normal walking speed. The conclusion may be one-sided because they only compared the daily average rate of ACC sensor to the SN irrespective of the differences of the peak rate, peak time, the course of the heart rates and activity level. Although the obvious differences between the ACC SIRs and sinus rates existed, we still observed that in the 1st minute of exercise the ACC sensor could mimic the SN as a result of the fast reaction of the ACC to exercise induced vibration.

Minute ventilation sensors are supposed to be promising for rate adaption. These systems are based on the measurement of transthoracic impedance that correlates with respiration and oxygen consumption and is proportional to metabolic demand.[10] As a single sensor, the MV sensor responds more proportionally to metabolic demand, but rather slowly to exercise. Therefore, the blending of MV with ACC sensor is a sensible strategy. In our study, DS (and ACC sensor) did respond rapidly in the 1st minutes of the exercise, while MV alone did not. The leading cause was the fast response of the ACC sensor. In the first 3 minutes, the absolute change of rate of DS was similar to that of the intrinsic SN, whereas both the single ACC and MV SIRs were not. Thus, blending of the ACC and MV in a DS produced a SIR that substantially reproduced behavior of the chronotropically competent SN in the first 3 minutes of exercise. In the middle and later stages of the exercise test, the profile of response rate variations of DS overlapped that of MV. This result follows from the design of the blending algorithm, which specifies that the DS response be 100% MV-based whenever the ACC response rate is less than the MV response rate. Therefore, the MV sensor was the primary contributor to the rate response of DS in our study. The importance of the ACC sensor might be underestimated in our study design partly because the treadmill exercise test was less laborious due to the slower speeds and more flat slopes when compared to the Bruce protocol. Even so, the independent application of single ACC sensors in the future may be limited because of the apparent deviation from the SN. Viewed from the whole process of the treadmill testing, DS at the default settings did not faithfully reproduce chronotropically competent SN function during prolonged exercise (beyond 3 minutes). Specifically, DS did not reach a peak rate as high as the normal SN at an appropriate timing, and did not simulate the SN physiologically when the intrinsic heart rate decelerated at rest, although these situations were significantly improved compared to ACC sensor. To some extent, the default setting of the MV response factor is conservative.[11,12] In this regard, patient specific optimization of sensor parameters is considered an important factor, not addressed in this study.

Chronotropic incompetence is associated with increased major adverse cardiovascular events and mortality in asymptomatic[13] and selected clinical populations, including those with coronary artery disease or heart failure,[14-16] and contributes to exercise intolerance which leads to impaired quality of life.[17] However, rate adaptive pacing, the main therapy for chronotropic incompetence,[18] wasn't proved to be clinically beneficial in improving the functional status or quality of life of patients with a bradycardia indication for dual-chamber pacing in large trials,[19,20] though some small-sample studies reported positive results.[21,22] Dual-chamber pacing leads to atrioventricular synchrony improving the cardiac output and quality of life.[23] While the potential benefits of rate adaptive pacing do not prove significant in the general pacemaker population, superiority is observed in a selected patient population, especially for the DS-driven pacemakers.[21,24] Our study participants were younger than those reported in the studies mentioned above, and their average and peak sinus rates reflected a need for higher heart rate support. Therefore, it is unknown whether DS devices might stand out for the relative young and physically active patient population with marked chronotropic incompetence. The proper application of rate adaptive pacemakers and sensors may need further study.

A major limitation in this study is a small sample that may have undesirable influence on the results. This is partly caused by the fact that this is a single center study and it is not easy to find AVB patients with normal sinus function and indication for pacemaker implant and also willing to participate in the study. Additionally, the amount of exercise in our study is relatively small, and supposed to be easy to the relatively young and physically active patients so that we may lose the potential eligible patients regarded as chronotropic incompetence because they cannot reach their target heart rates in the effortless treadmill test. Moreover, exercise treadmill testing is an artificial physical stress that may not accurately reproduce the physical stress of normal activity. DS may not be superior to ACC or MV sensor alone if assessed during other types of real world activity. Another limitation is that response factors were not individually optimized. By giving every patient, the same default setting would not necessarily lead to best performances of the single sensors or the DS pacemakers. If the settings were adjusted, DS, ACC, and MV sensor could have performed better compared to the measured sinus rate. There is even a chance with a given setting that ACC and MV may be found to be superior to DS. Additionally, when applying the results to the real cochlear implant patients, we should take subjective feelings into consideration.

Neither the ACC, MV sensor, or the DS configuration provided rate adaptive pacing in an absolute physiological way when programmed to their default settings of response factor and compared with intrinsic SN rates achieved in chronotropically competent patients during heavy exertion (>85% of maximum heart rate). However, the DS configuration seemed to be superior to the single sensors in rate adaptive pacing especially in the first 3 minutes of the treadmill testing.

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