Within patient comparison of His-bundle pacing, right ventricular pacing and right ventricular pacing avoidance algorithms in patients with PR prolongation: Acute haemodynamic study

Daniel Keene [1,2], Matthew J Shun-Shin[1], Ahran D Arnold[1], Katherine March[1], Norman Qureshi[2], Fu S Ng[1], Mark Tanner[2], Nick Linton[2], Phang Boon Lim[2], David Lefroy[2], Prapa Kanagaratnam[2], Nicholas S Peters[1], Darrel P Francis[2] and Zachary I Whinnett[1,2]

Corresponding Author: Dr Daniel Keene, National Heart and Lung Institute, Imperial College London. Hammersmith Hospital, London, UK, W12 0HS. d.keene@imperial.ac.uk

Institutional Affiliations:

1 National Heart and Lung Institute, Imperial College London, Hammersmith Hospital, London, UK, W12 0HS

2 Imperial College Healthcare NHS Trust, Hammersmith Hospital, London, UK W12 0HS

Abstract (250 words)

Aims:

A prolonged PR interval may adversely affect ventricular filling and therefore cardiac function. AV delay can be corrected using right-ventricular-pacing (RVP) but this induces ventricular dyssynchrony, itself harmful. Therefore, in intermittent heart-block, pacing-avoidance algorithms are often implemented. We tested His-bundle pacing (HBP) as an alternative.

Methods:

Out-patients with a long PR interval(>200ms) and intermittent need for ventricular pacing were recruited. We measured within patient differences in high-precision haemodynamics between AV-optimized RVP, and HBP, as well as a pacing-avoidance algorithm [Managed Ventricular Pacing (MVP)].

Results

We recruited 18 patients. Mean left ventricular ejection fraction was 44.3±9%. Mean intrinsic PR interval was 266±42ms and QRS duration was 123±29ms. RVP lengthened QRS duration(+54 ms, 95%CI 42 to 67ms, $p<0.0001$) whilst HBP delivered a shorter QRS duration than RVP(-56 ms, 95%CI -67 to -46ms, $p<0.0001$). HBP did not increase QRS duration(-2ms 95%CI -8 to 13ms, $p=0.6$).

HBP improved acute systolic blood pressure by mean of 5.0 mmHg(95%CI 2.8 to 7.1mmHg, $p<0.0001$) compared to RVP and by 3.5 mmHg(95%CI 1.9 to 5.0mmHg, $p=0.0002$) compared to the pacing avoidance algorithm. There was no significant difference in haemodynamics between RVP and ventricular pacing avoidance ($p=0.055$).

Conclusions

HBP provides better acute cardiac function than pacing avoidance algorithms and RVP, in patients with prolonged PR intervals. HBP allows normalisation of prolonged AV delays (unlike pacing avoidance) and does not cause ventricular dyssynchrony (unlike RVP). Clinical trials may be justified to assess whether these acute improvements translate into longer term clinical benefits in patients with bradycardia indications for pacing.

Key Words: His-bundle pacing, Pacing Avoidance Algorithms, Prolonged PR interval, AV Optimisation

Introduction

In patients who have intermittent higher degree conduction block and a long PR interval there are two major considerations when selecting a pacing strategy. A prolonged PR interval adversely effects ventricular filling and therefore may compromise cardiac function[1]. Therefore, shortening a pathologically prolonged PR intervals has the potential to improve cardiac function. However utilising right ventricular pacing to shorten prolonged PR intervals can bring its own problems, namely ventricular dyssynchrony which itself compromises cardiac function, increases the risk of developing AF[2] and increases mortality[3]. Therefore, in patients with only intermittent bradycardia it is currently common practice to use ventricular pacing avoidance algorithms in order to minimise ventricular pacing and therefore preserve physiological ventricular activation wherever possible.

In people with preserved ventricular function, current strategies to minimise ventricular pacing include programming long AV delays, setting AV hysteresis or applying dedicated ventricular-pacing avoidance algorithms. However, if AV delay is long, this itself interferes with cardiac function in several ways. First, the energy expended on the atrial kick is wasted, because it occurs too early, either before the E wave (passive ventricular filling) has finished or even during the preceding systole. Second, after the atrial kick, there is a pathologically long delay before systole. This allows blood that had been pumped from the atrium to ventricles to drift back into the atrium since the papillary muscles which tense to seal the mitral valve have not yet been activated by systole. These mechanisms combine to impair ventricular filling and reduce stroke volume[1,4].

In many patients with a long PR interval and an intermittent ventricular pacing requirement due to higher degree conduction block we are therefore faced with the choice of continuous right-ventricular pacing (which causes undesirable ventricular dyssynchrony) or taking steps to minimise ventricular pacing (which leaves the patient with undesirable AV dyssynchrony). Results of trials comparing these strategies suggest that the two undesirable desynchronies are of approximately equal size so that outcomes are the same with both options[5,6]. Biventricular pacing is an alternative option, but is a more complex procedure, which utilises more expensive technology.

His-bundle pacing allows correction of AV dyssynchrony without inducing ventricular dyssynchrony

His-bundle pacing provides a potential alternative to the two established pacing strategies. By directly stimulating the His-bundle normal physiological ventricular activation via the conduction system can be

maintained in patients with intrinsic narrow QRS. His-bundle pacing may even improve ventricular activation time and pattern in people who have bundle branch block and an indication for pacing.

Therefore, His-bundle pacing allows AV delay to be shortened without causing ventricular dyssynchrony. We have previously observed acute haemodynamic improvements in patients with a long PR interval and severely impaired left ventricular function (ejection fraction below 35%)[7]. What is not known is whether acute haemodynamic improvements occur when patients are selected on the basis of a bradycardia indication for pacing, rather than wholly for resynchronisation in those with heart failure.

His-bundle pacing has the potential to have an increased energy utilisation cost compared to the other pacing strategies. Compared to pacing-avoidance algorithms AV optimised His-bundle pacing will lead to a higher proportion of ventricular pacing. Compared to right-ventricular pacing, His-bundle pacing capture thresholds may be higher, which may also lead to increased energy utilisation.

We studied a group of patients with long PR intervals, who had a bradycardia indication for pacing in whom both a His lead and RV lead were implanted. In this study we performed an acute within patient comparison between AV optimised; His-bundle pacing, right-ventricular pacing and ventricular pacing-avoidance algorithms, using high precision acute haemodynamic measurements. We also compare the device energy utilisation and effect on predicted battery longevity between the different pacing strategies.

Methods

We recruited 18 patients with sinus rhythm and an intrinsic PR interval >200ms who had devices with pacing leads in the right atrium, His-bundle and right ventricle (RV leads were sited either for pacing back-up or defibrillator capability). All recruits were ambulatory outpatients who presented for a device check at least 3 months after their device implant and had evidence of at least 5% ventricular pacing despite the prior programming of pacing-avoidance algorithms.

All patients gave written informed consent for the study which was approved by the local research ethics committee.

His-bundle pacing

His-bundle pacing was delivered using a Medtronic SelectSecure 3830 lead (Medtronic, MN, USA). His-bundle capture was confirmed using established criteria[8] before enrolment. Both selective and non-selective capture were acceptable for enrolment. We did not recruit patients with typical LBBB and QRS duration above 140ms. If the intrinsic QRS demonstrated either right bundle branch block (RBBB) or non-specific inter-ventricular conduction delay (IVCD) this was noted and any effect of shortening QRS duration by His-bundle pacing recorded.

AV delay optimisation and haemodynamic assessment

AV delay optimisation was performed using a validated, high precision, non-invasive haemodynamic method which has been previously described[9]. In brief, this uses continuous non-invasive beat-by-beat blood pressure from the Finapres Nova device (Finapres Medical Systems, The Netherlands). The method is designed to minimise the effect of noise on calculation of the optimal AV delay, through repeated alternations between test settings (the available programmable AV delays) and a reference setting, all conducted at a constant atrially paced based rate, in this case 80bpm. We tested AV delays of 40ms, 80ms, 120ms, 160ms, 200ms, 240ms, 280ms and 320ms etc or until fusion occurred. The reference setting was the pacing avoidance algorithm with the same programmed heart rate.

The relative change in mean systolic blood pressure between the reference setting (8 beats of the reference setting immediately before transitioning to a test setting) and the tested setting (8 beats immediately after the transition to the tested AV delay) was calculated. A minimum of six such transitions were performed between the reference setting and the atrial synchronous dual chamber pacing mode at each AV delay. The mean of all of

these alternations was used to calculate the relative change for that particular programmed AV delay compared with the reference setting. The blood pressure changes for all tested AV delays were plotted on a parabola and the optimal AV delay derived, defined as the one that gave the greatest increment in cardiac function relative to the pacing avoidance algorithm.

Thus, the mean change in systolic blood pressure from the reference state to each dual-chamber pacing mode at the optimal AV delay was calculated. This permitted the haemodynamics of the three pacing modes (His dual-chamber pacing, RV dual-chamber pacing and the pacing-avoidance algorithms) to be compared *within each patient.*

Pacing Avoidance Algorithm

The pacing avoidance algorithm utilised in this study was the Managed Ventricular Pacing (MVP) algorithm (Medtronic MN, USA). In brief this algorithm operates in an AAI/(R) mode whilst monitoring for the presence of AV conduction. Should a persistent loss of AV conduction be detected the device then switches to a dual-chamber pacing mode until consistent AV conduction returns.

Should AV conduction be transiently lost, the algorithm allows the device to initially remain in an AAI/(R) mode but provides a backup ventricular paced beat after one missed ventricular sensed event has been detected. Should two out of four A-A intervals not have a sensed ventricular event between them the algorithm initiates a switch in pacing mode to a dual-chamber pacing mode. The algorithm then performs periodic checks for resolution of intrinsic AV conduction, and if detected will return to the AAI/(R) mode.

Battery Longevity Assessment

Lead impedance, pacing thresholds and programmed lead output with suitable safety margins were known. For each patient the projected device longevity in each of the three modes was calculated. The calculation was based on a Medtronic Azure XT device (Medtronic MN, USA) with a programmed rate of 60bpm. The states compared were: (1) Pacing-Avoidance Algorithm with 50% atrial pacing and 5% RV pacing, (2) Dual-chamber His pacing with 25% atrial pacing and 100% His pacing and (3) Dual-chamber RV pacing with 25% atrial pacing and 100% RV pacing.

Data acquisition and statistical analysis

Haemodynamic and electrocardiographic data were acquired by using an analogue-to-digital card (National Instruments, Texas) and Labview (National instruments, Texas). The data were then processed with custom software written in Python. Statistical analyses were performed in R version 3.0.2 (R Project, Austria). Baseline characteristics were summarised as means and standard deviations. Paired and unpaired t-tests were used as appropriate.

Results

Patients

The 18 patients had a mean left ventricular ejection fraction 44.3 (SD±9)%, of whom 8 had a CRT-defibrillator implanted and the others a 3-chamber pacemaker **(Table 1)**. All patients were implanted with a His lead due to evidence of intermittent AV block and a degree of LV dysfunction and all patients had received at least 5% ventricular pacing despite the programming of pacing avoidance algorithms. During intrinsic conduction, 2 patients had right bundle branch block and 2 patients had non-specific interventricular conduction delay.

Electrocardiogram Assessment

Both of the dual-chamber modes resolved the PR prolongation. Dual-chamber RV pacing however increased QRS duration from 123±29 to 177±17ms (+54 ms, 95% CI 42 to 67ms, p<0.0001) whilst dual-chamber His-bundle pacing had no significant effect on QRS duration compared to intrinsic conduction (123±29 vs 121±17 ms, -2.6 ms, 95% CI -8 to 13ms, p=0.6). As compared to RV pacing, His pacing delivered a significantly shorter QRS duration (-56 ms, 95% CI -67 to -46 ms, p < 0.0001). **Figure 1** shows a single patient ECG example of the three pacing modes.

The effect of His-bundle pacing on QRS duration depended on two factors. First, the pacing response achieved, this could be either selective or non-selective capture. 9 patients with His-bundle pacing had evidence of non-selective capture and the presence of a pseudo-delta wave which resulted in prolongation of the measured QRS. Or, secondly whether bundle branch block was present at baseline. In the two patients with RBBB, QRS duration shortened from 188 to 133ms (-55 ms, 95% CI -93 to 17ms, p=0.035). In those without bundle branch block, QRS duration overall was only minimally increased from 115 to 119ms (4 ms, 0.3 to 8.3ms, p=0.07) reflecting non-selective capture and the addition of a slurred upstroke between pacing stimulus and onset of QRS.

Haemodynamic Assessment

His-bundle pacing produced significantly higher acute systolic blood pressure compared with right-ventricular pacing by 5.0mmHg (95% CI 2.8 to 7.1mmHg, p<0.0001). There was no significant difference in acute systolic blood pressure when dual-chamber right-ventricular pacing was used to shorten AV delay compared with the pacing avoidance algorithm [-1.5mmHg (95% CI -3.1 to 0.0mmHg, p=0.055)]. Dual-chamber His-bundle

pacing produced a significant increase in systolic blood pressure 3.5mmHg (95% CI 1.9 to 5.0mmHg, p=0.0002) compared with the pacing avoidance algorithm. **Figure 2** shows a summary of the acute haemodynamic change at the optimal AV delay for all patients and **Figure 3** shows the individual patient data. In 16/18 (89%) patients, His-bundle pacing performed best out of the three pacing modes. In the remaining 2 patients, it was pacing avoidance that performed best. RV pacing did not deliver the best haemodynamic response in any of the patients.

In six patients AV delay shortening with dual chamber right-ventricular pacing as compared to pacing avoidance algorithm resulted in an improvement in acute haemodynamics. No significant differences in ECG parameters were found between these two small groups (Table 2). Furthermore, across the whole cohort, there was no significant association between the haemodynamic benefit of RV pacing and either longer intrinsic PR interval or broader QRS (p=0.4 and p=0.2 respectively).

Device longevity assessment

Mean lead impedances, thresholds and programmed outputs for the right atrial, right ventricular and His leads are shown in **Table 1**. Duration of pacing stimulus was 0.4ms for right-ventricular and right-atrial leads but typically 1.0 ms for His leads. Right-atrial and right-ventricular lead outputs were set using the device's auto adjustment process, with the proviso of being at least twice the threshold and a minimum output of 2 Volts. For the His lead, each patient had a fixed output programmed based on similar principles.

With dual-chamber His-bundle pacing, calculated battery longevity was 3.5 years shorter (9.3 ± 2.3years) than with pacing-avoidance (12.9 ± 0.7years, p<0.0001) and 2.6 years shorter than with dual chamber RV pacing (12.0 ±1.0 years, p=0.003).

Discussion

This is the first within patient comparison of AV optimised right ventricular pacing, a ventricular pacing avoidance algorithm and AV optimised His bundle pacing, using high precision haemodynamic measurements in patients with conduction system disease and a bradycardia indication for pacing. We found that His-bundle pacing delivers a significantly shorter QRS duration compared with RV pacing and that this more rapid ventricular activation translates into significant improvements in acute haemodynamic function.

Shortening AV delay using His bundle pacing also produced a significant improvement in acute haemodynamic function compared with a pacing-avoidance algorithm. Whereas using RV pacing to shorten AV delay did not improve acute cardiac function.

His bundle pacing compared with right-ventricular pacing

We found that His bundle pacing produced a significantly shorter QRS duration compared with right-ventricular pacing and resulted in significant improvements in acute systolic blood-pressure.

Right-ventricular pacing is a very reliable method for preventing bradycardia in people with higher degree conduction block. However, right-ventricular pacing is known to be harmful when delivered to patients with left-ventricular impairment. In the DAVID trial RV pacing resulted in a ~50% increase in mortality. Chronic right-ventricular pacing can also lead to left-ventricular impairment in patients with previously normal ventricular function[10].

The mechanism of harm for right-ventricular pacing is believed to occur as a result of dyssynchronous non-physiological ventricular activation. This occurs because with direct stimulation of right-ventricular myocardial cells the activation wavefront spreads slowly via cell-cell conduction.

His bundle pacing has been proposed as an alternative pacing strategy, which aims to produce physiological ventricular activation by utilising the hearts natural conduction system which produces rapid and synchronous ventricular activation.

There is a growing body of evidence from observational studies that His bundle pacing is technically feasible, associated with a narrow QRS duration and associated with encouraging outcomes including heart failure hospitilisations and death when compared to alternate pacing modes in clinically similar patients[10].

Our study is the first to perform a within patient comparison of His-bundle pacing with RV pacing using high precision haemodynamic measurements. Our finding that His-bundle pacing results in significantly improved acute haemodynamic function, suggests that the observed beneficial effect of His-bundle pacing are delivered through improvements in cardiac function. These improvements in cardiac function are most likely to be delivered as a result of more efficient ventricular activation, this is supported by our finding that His-bundle pacing produced a significantly shorter QRS duration compared to RV pacing. We recently found that when His pacing is used for ventricular resynchronisation therapy in patients with LBBB and left ventricular impairment, that this produces a greater acute haemodynamic response compared to biventricular pacing. We demonstrated an incremental response between reduction in ventricular activation time and acute haemodynamic response.[11]

Padeletti et al unexpectedly did not find a beneficial haemodynamic difference with His pacing compared to RV pacing[12]. It may be that this apparent difference can be explained by differences in methodology. In the previous study haemodynamic measurements were acquired from only a single alternation from AAI pacing to the tested pacing mode rather than calculating the mean from multiple alternations as was the case in our study. It is known that when acute haemodynamic measurements are used to assess the effect of pacing interventions that if multiple repeated measurements are not made this can result in wide error bars and a less reliable assessment of acute response.[13]

Our acute haemodynamic study supports the concept that delivering more physiological ventricular activation using His-bundle pacing avoids the negative effects that right-ventricular pacing has on cardiac function. This supports the need for randomised-control-trials to prospectively assess this treatment approach on hard clinical endpoints.

Pacing options in patients with PR interval prolongation and a bradycardia indication for pacing

When dual-chamber pacing with a right-ventricular lead is used to treat patients who have a long PR interval and intermittent conduction block, there are two competing physiological considerations. On the one hand while it is very effective in normalising PR interval, chronic right-ventricular pacing is known to be potentially harmful. RV pacing increases hospitilisations (e.g. HR 1.37, P=0.02, in MOST trial)[14] and increases the risk of death and heart-failure (HR 1.61, P<0.03 in DAVID trial)[3]. Therefore, ventricular pacing-avoidance algorithms have been developed and utilised to mitigate this problem. However, pacing-avoidance algorithms permit the existence of very long PR intervals which can be detrimental to cardiac function since long PR interval impairs ventricular filling, because it disrupts efficient diastole.

In this study we investigated the within patient effect of AV delay optimisation using RV pacing and His bundle pacing. AV optimisation delivered using right-ventricular pacing did not significantly change acute haemodynamic function, indeed there was a non-significant trend for a decrease in acute cardiac function. This suggests that the benefits of AV optimisation were outweighed by the detrimental effects of right-ventricular pacing. A randomised cross-over study assessing quality of life, LV function and exercise capacity measured by cardio-pulmonary exercise testing in 14 patients previously showed approximate equivalence between pacing-avoidance algorithms and dual-chamber RV pacing, which is consistent with our findings [5].

AV optimised His-bundle pacing resulted in a significant improvement in acute systolic blood pressure. This suggests that if physiological ventricular activation can be maintained then there is the opportunity to improve cardiac function in this group of patients, which has the potential to lead to an improvement in symptoms.
We previously found a haemodynamic improvement with AV optimised His bundle pacing in patients with severe left ventricular dysfunction and no bradycardia pacing indication. His optimised pacing in this group of patients is currently being evaluated in the HOPE-HF trial[9]. In the current study we investigated patients who had a bradycardia indication for pacing, LV function was not an entry criterion for the study and therefore we included a spectrum of different LV function. Our findings that shortening a pathologically long AV delay in this group of patients improves acute cardiac function supports further investigation of the role of AV optimised His bundle pacing in patients with a long PR interval regardless of underlying LV function.
Long PR interval can be detrimental to cardiac function since it impairs ventricular filling by disrupting efficient diastole. The effects on ventricular filling and subsequent reductions in stroke volume and cardiac output seemingly though can be offset by shortening the PR delay with pacing that allows physiological ventricular activation. This is illustrated in **figure 4**.

Patients with long PR interval have been seen in population studies to have an association with increased (1) mortality, (2) atrial fibrillation, (3) heart-failure, (4) coronary artery disease and (5) progression of conduction disease.[15,16] Similar findings have also been reported in subgroup analyses of randomised controlled trials.[17]

Biventricular pacing (although not tested in this study) is an alternative method of resolving AV dyssynchrony while producing less ventricular dyssynchrony than RV pacing. Results with biventricular pacing studies of patients with bradycardia have been mixed, with improved clinical outcomes in the BLOCK HF trial of patients with impaired LV function[18] and neutral results in the BIOPACE trial in patients with relatively normal LV function[19]. Caution should be exercised when postulating potential benefit of biventricular pacing in patients other than in those with broad QRS and LV impairment due to the increased mortality seen in the ECHO CRT trial which looked at patients with heart failure, objective mechanical dyssynchrony and narrow QRS[20].

Need for a trial

In patients with long PR, His bundle pacing results in distinctly better haemodynamics in almost all cases but involves continuous ventricular pacing, thereby consuming more energy than the pacing-avoidance algorithms. His pacing thresholds also tend to be higher than RV pacing thresholds. Both of these factors mean that chronic AV optimised His pacing would lead to greater battery usage, which would mean more frequent generator changes. A trial is needed to determine whether the improved haemodynamics seen translate into better patient outcomes despite higher energy requirements.

Future developments could improve the energy demands of His-bundle pacing. For example, the Medtronic SelectSecure 3830 is the most commonly used lead to pace the His-bundle has a lower impedance than general purpose pacing leads, which means more energy is wasted. As another example, there are no reliable automatic capture management algorithms for dynamically determining the pacing output threshold to safely permit minimisation of energy utilisation on His leads, this could also be a major step forward in reducing energy wastage in the future, as currently fixed outputs with adequate safety margins are mandated.

Study limitations

This is a short-term n-of-1 study focusing on cardiac function, rather than a long-term endpoint trial. Whether the energy price of His bundle pacing is worth paying depends on whether the haemodynamic benefits translate into clinical benefits. Determining the latter requires a suitably sized randomised-controlled-trial. Our study was conducted in an outpatient environment in patients who already had a His pacing device. It therefore could only compare modes achievable by that implanted system which did not include biventricular pacing. Therefore, this trial and any other in an outpatient setting cannot compare within patient differences of His-bundle to traditional biventricular pacing. However, separately, we have carried out an invasive, implant-time haemodynamic comparison of His pacing versus biventricular pacing in a cohort with heart failure and LBBB[11] In this study, both His pacing and biventricular pacing improved haemodynamics but His pacing achieved significantly better haemodynamics than biventricular pacing (4.6mmHG to 12.4mmHG, p=0.04). The patients recruited into this study had a range of LV function, ranging from normal to severely impaired. It was however, encouraging that acute haemodynamic improvements were observed in patients with normal ventricular function as well as those with impaired cardiac function.

Conclusions

This mechanistic study using high precision haemodynamic measurements and within patient comparison found that His-bundle pacing leads to improved acute haemodynamics compared with right-ventricular pacing in patients with a bradycardia indication for pacing. Interestingly, our findings also suggest that in patients with a long PR interval that AV optimised His-bundle pacing is advantageous compared with a ventricular pacing avoidance algorithm. The His pacing strategy does however come at the cost of greater device energy requirements compared with the other two strategies. The study supports the need for randomised trials to assess whether the beneficial effects on cardiac function outweigh the risks associated with the requirement for more frequent pacing generator changes.

Table 1

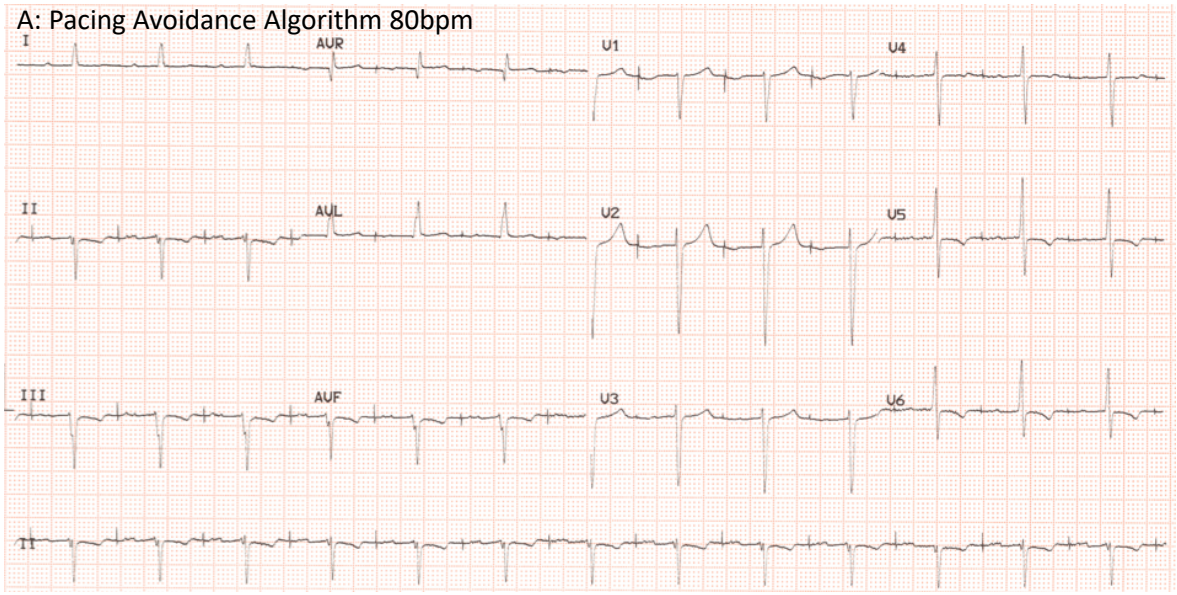
Table 1 Patient and Pacing Characteristics of the 18 patients	
Male n (%)	15 (83%)
Age years	65.5 ± 8.6
Left Ventricular Ejection Fraction (%)	44.3 ± 8.8
Intrinsic PR interval (ms)	266 ± 42
Intrinsic QRS (ms)	123 ± 29
IVCD (n) % mean QRS (ms)	2 (11%) 140 ± 2.8
RBBB (n) % mean QRS (ms)	2 (11%) 188 ± 8.5
CRT-D implanted	8 (44%)
CRT-P implanted	10 (56%)
His pacing characteristics	
Selective capture	9 (50%)
Non-selective capture	9 (50%)
Paced QRS duration (ms)	121 ± 17
Lead impedance (ohms)	315 ± 54
Threshold (V) at (ms)	0.75 ± 0.5 at 0.83 ± 0.3
Output (V) at (ms)	2.27 ± 0.5 at 0.87 ±0.3
RV pacing characteristics	
Paced QRS duration (ms)	178 ± 17
Lead impedance (ohms)	459 ±85.6
Threshold (V) at 0.4ms	0.72 ± 0.32
Output (V) at 0.4ms	2.17 ± 0.30
RA pacing characteristics	
Lead impedance (ohms)	476 ± 65.0
Threshold (V) at 0.4ms	0.70 ± 0.39
Output (V) at 0.4ms	2.10 ± 0.57
IVCD – Interventricular conduction delay RBBB – right bundle branch block	

Table 2

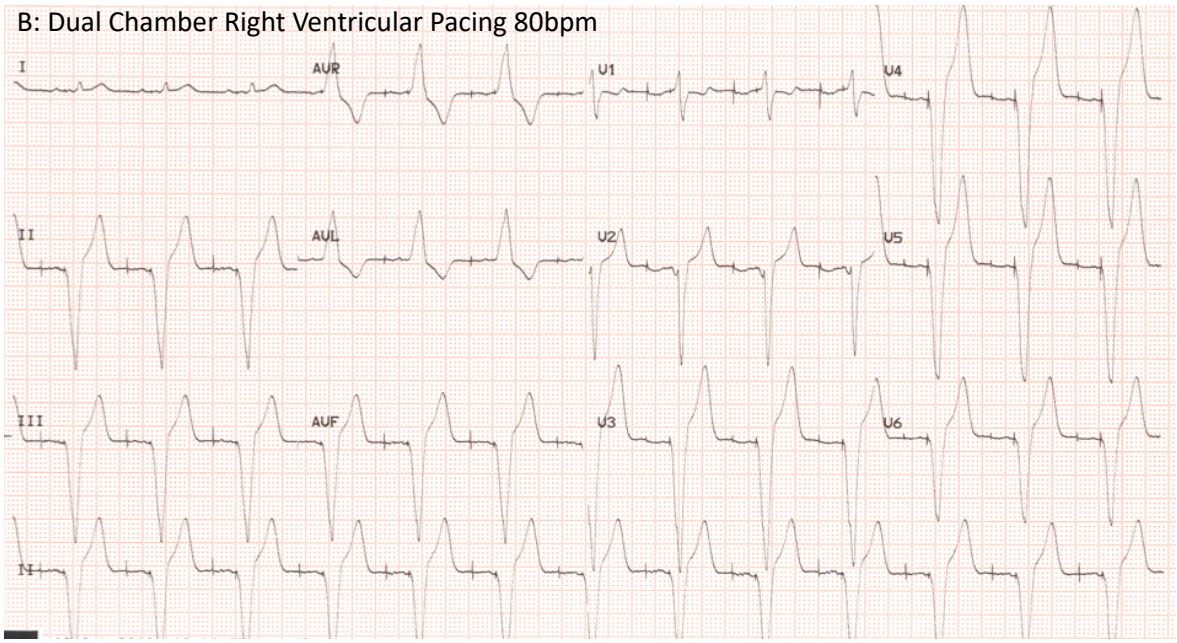
	Pacing avoidance superior to dual chamber RV Pacing	**Dual Chamber RV pacing superior to pacing avoidance**	**p**
N (%)	12 (67%)	6 (33%)	
Acute haemodynamic effect of dual chamber RV pacing compared to Pacing Avoidance (mmHg)	- 3.4 ± 1.3	+ 2.0 ± 2.2	NA
Intrinsic PR (ms)	256 ± 41	284 ± 40	0.2
Intrinsic QRS (ms)	116 ± 17	138 ± 42	0.3
Baseline left ventricular ejection fraction % (SD)	42.3 ± 10.0	39.2 ± 6.1	0.42
Reduction in surface PR interval to the optimal AV delay with dual chamber RV pacing (ms)	61 ± 31	78 ± 56	0.51
Prolongation in surface QRS duration with dual chamber RV pacing (ms)	62 ± 19	39 ± 31	0.14

Figure 1

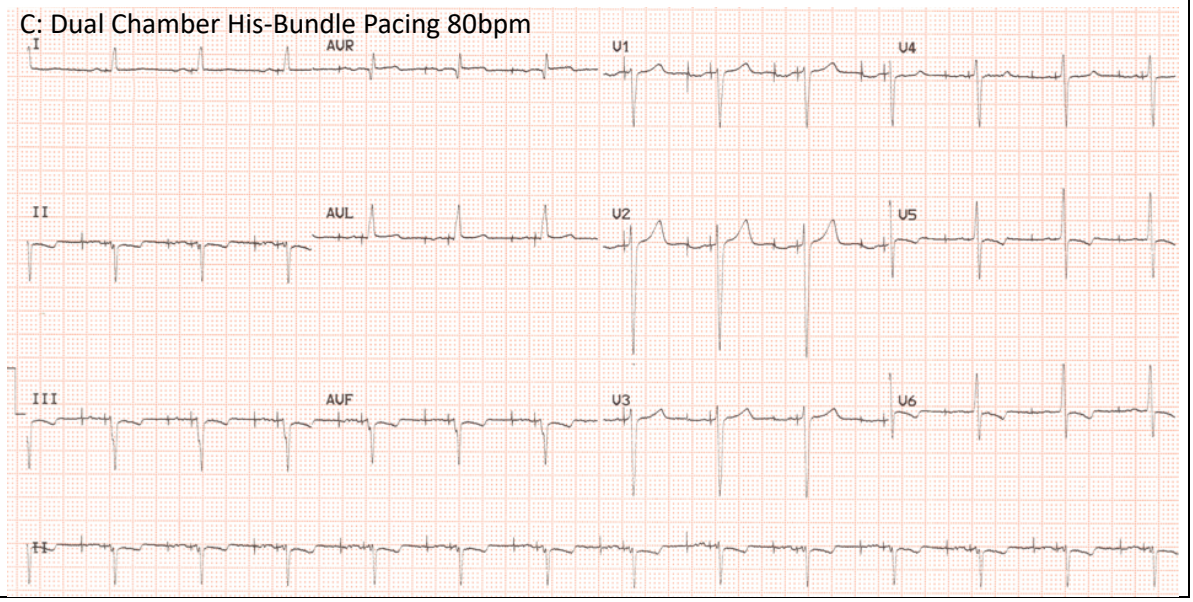
A: Pacing Avoidance Algorithm 80bpm



B: Dual Chamber Right Ventricular Pacing 80bpm

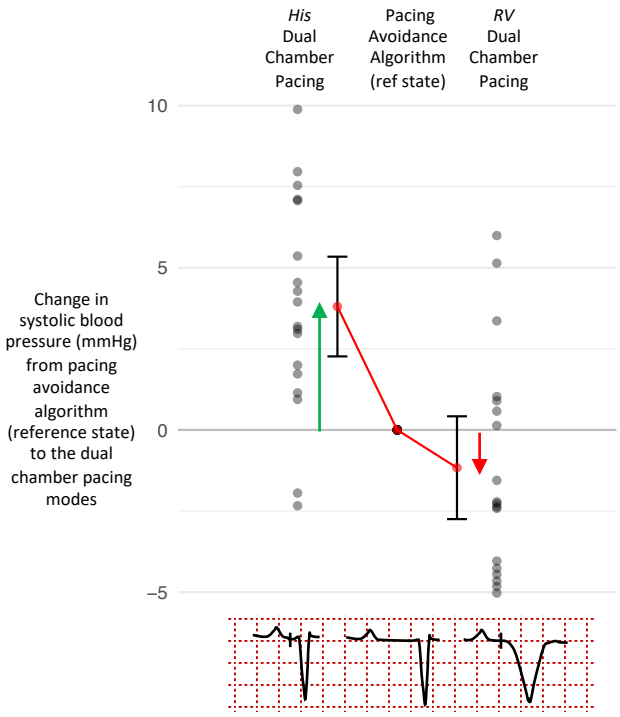


C: Dual Chamber His-Bundle Pacing 80bpm



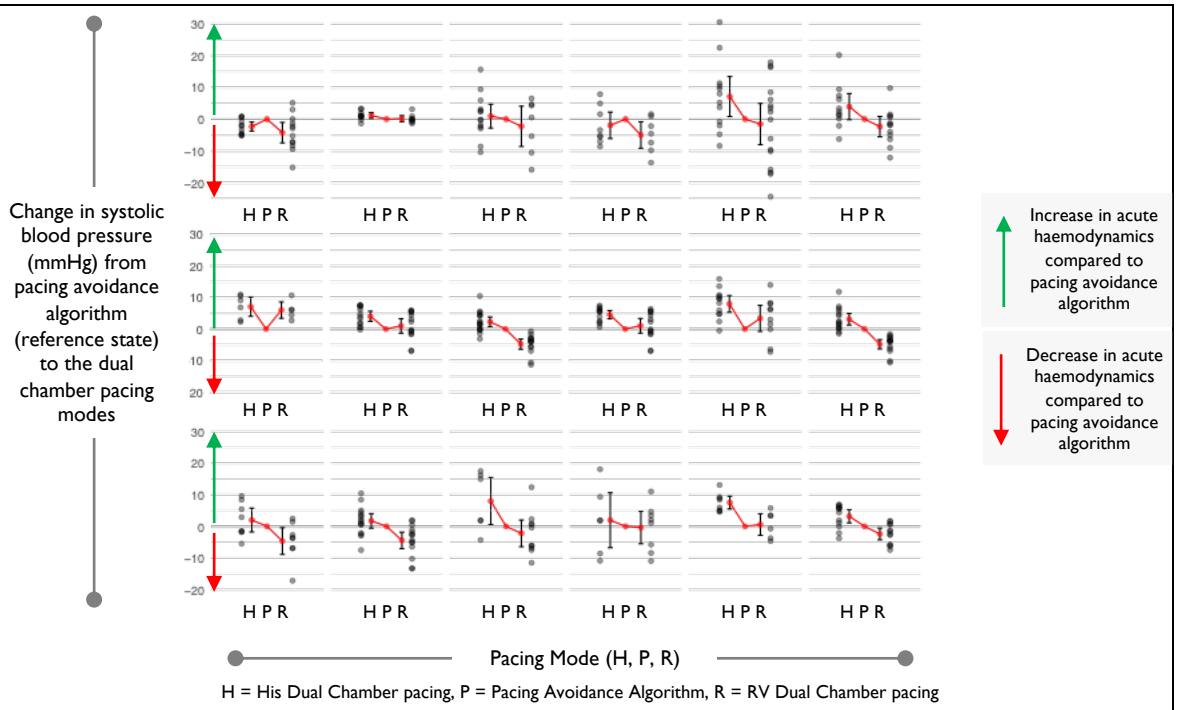
This figure shows 12 lead ECGs for the three pacing modes for an individual patient.
A, shows the ECG during pacing avoidance algorithm. This in shows an atrially paced rhythm at 80bpm with intrinsically activated QRS but with a prolonged PR interval.
B, shows the ECG during dual chamber RV pacing at 80bpm. This shows correction of the prolonged PR interval but the presence of ventricular dyssynchrony induced by right ventricular apical pacing.
C, shows the ECG during dual chamber His-bundle pacing at 80bpm. This shows correction of the prolonged PR interval and the presence of physiologically activated synchronous QRS complexes

Figure 2



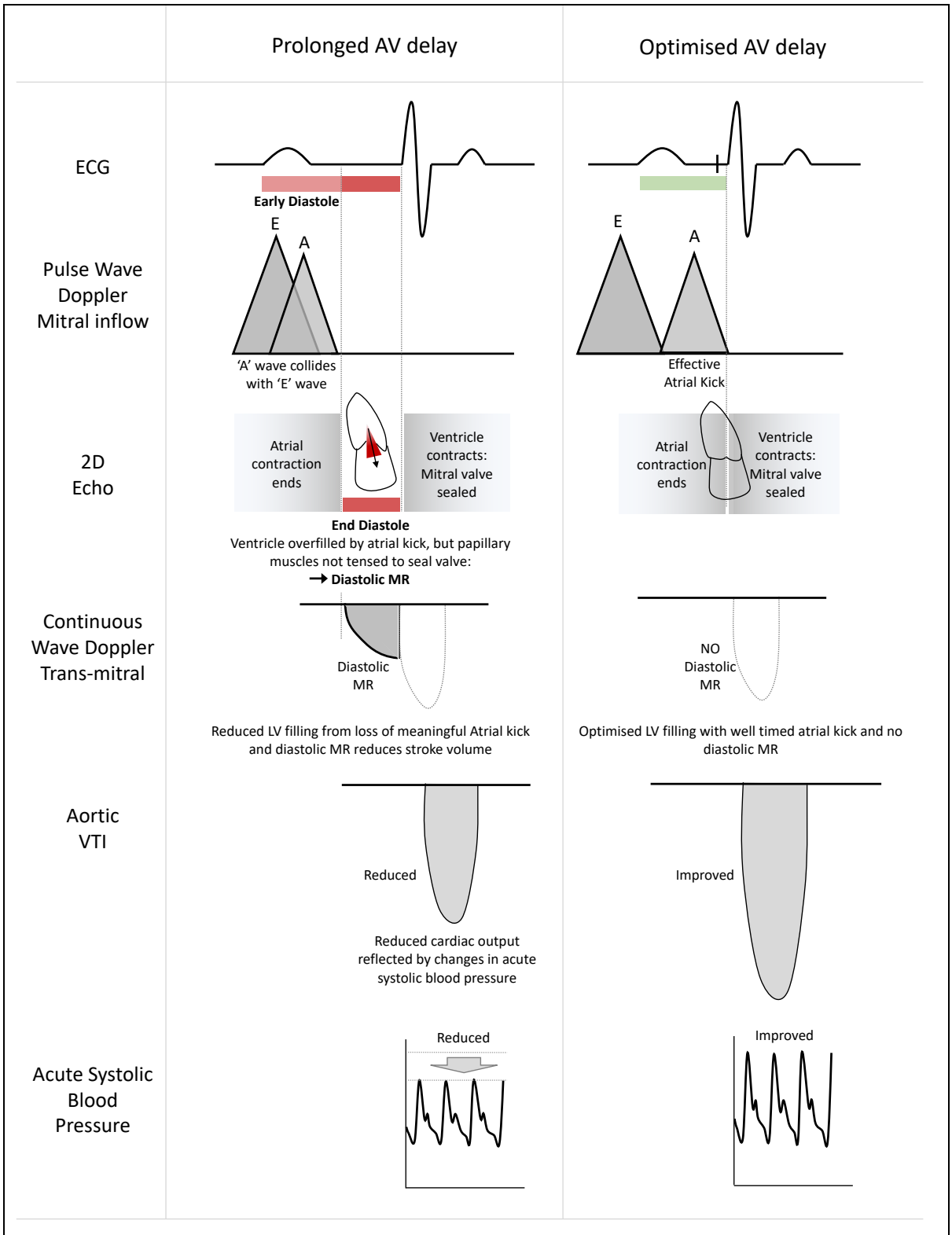
Summary data for all 18 patients is displayed here. The mean change in systolic blood pressure at the optimal AV delay during both dual chamber His and RV pacing is plotted for each patient relative to the haemodynamic response during the pacing avoidance algorithm mode. Overall dual chamber His pacing improved acute haemodynamic response and RV pacing reduced it.

Figure 3



Individual patient data for each of the 18 patients is shown here comparing the changes in acute systolic blood pressure for each patient between AV optimised dual chamber His pacing and RV pacing relative to the pacing avoidance algorithms.

Figure 4



The left side of the figure demonstrates the physiological effects of prolonged AV delay and the right side of the figure the positive haemodynamic effects of correcting this. Ideally there is a passive early diastolic phase of ventricular filling followed by an atrial kick and then immediately ventricular contraction (without leaving

any time for the blood pushed into the ventricle by the atrial kick to passively drain back into the atrium). When the PR interval is abnormally long, the atrial kick occurs earlier (with respect to the preceding ventricular relaxation and the succeeding ventricular contraction). This has dual disadvantage. First, the atrial kick occurs during the E wave, wasting the opportunity for maximum spontaneous filling at no energy cost, or even earlier, during late ventricular systole which is even more wasteful. Second, after the atrium has forced blood into the ventricles there is a pathological pause before the ventricles and papillary muscles contract sealing the mitral valve. This pathological pause permits blood to drain backward from ventricle to atrium (diastolic mitral regurgitation). Both mechanisms reduce ventricular filling and thereby reduce stroke volume and cardiac output, and both waste energy. These detrimental effects are corrected by dual chamber pacing at an optimal AV delay if the pacing mode does not induce its own dyssynchrony.

References

1. Nishimura RA, Hayes DL, Holmes DR, Tajik AJ. Mechanism of hemodynamic improvement by dual-chamber pacing for severe left ventricular dysfunction: an acute Doppler and catheterization hemodynamic study. J Am Coll Cardiol 1995;25(2):281–8.
2. Sweeney MO, Bank AJ, Nsah E, et al. Minimizing ventricular pacing to reduce atrial fibrillation in sinus-node disease. N Engl J Med 2007;357(10):1000–8.
3. Wilkoff BL, Cook JR, Epstein AE, et al. Dual-chamber pacing or ventricular backup pacing in patients with an implantable defibrillator: the Dual Chamber and VVI Implantable Defibrillator (DAVID) Trial. JAMA 2002;288(24):3115–23.
4. Hu Y, Gurev V, Constantino J, Trayanova N. Efficient preloading of the ventricles by a properly timed atrial contraction underlies stroke work improvement in the acute response to cardiac resynchronization therapy. Heart Rhythm 2013;10(12):1800–6.
5. Maurer D. Quality of life and exercise capacity in patients with prolonged PQ interval and dual chamber pacemakers: a randomized comparison of permanent ventricular stimulation vs intrinsic AV conduction. Europace 2003;5(4):411–7.
6. Shurrab M, Healey JS, Haj-Yahia S, et al. Reduction in unnecessary ventricular pacing fails to affect hard clinical outcomes in patients with preserved left ventricular function: a meta-analysis. Europace 2017;19(2):282–8.
7. Sohaib SMA, Wright I, Lim E, et al. Atrioventricular optimized direct his bundle pacing improves acute hemodynamic function in patients with heart failure and PR interval prolongation without left bundle branch block. JACC: Clinical Electrophysiology 2015;1(6):582–91.
8. Vijayaraman P, Dandamudi G, Zanon F, et al. Permanent His bundle pacing: Recommendations from a Multicenter His Bundle Pacing Collaborative Working Group for standardization of definitions, implant measurements, and follow-up. Heart Rhythm 2017;
9. Keene D, Arnold A, Shun-Shin MJ, et al. Rationale and design of the randomized multicentre His Optimized Pacing Evaluated for Heart Failure (HOPE-HF) trial. ESC Heart Fail 2018;5(5):965–76.
10. Abdelrahman M, Subzposh FA, Beer D, et al. Clinical outcomes of his bundle pacing compared to right ventricular pacing. J Am Coll Cardiol 2018;71(20):2319–30.
11. Arnold AD, Shun-Shin MJ, Keene D, et al. His resynchronization versus biventricular pacing in patients with heart failure and left bundle branch block. J Am Coll Cardiol 2018;72(24):3112–22.
12. Padeletti L, Lieberman R, Schreuder J, et al. Acute effects of His bundle pacing versus left ventricular and right ventricular pacing on left ventricular function. Am J Cardiol 2007;100(10):1556–60.
13. Francis DP. How to reliably deliver narrow individual-patient error bars for optimization of pacemaker AV or VV delay using a “pick-the-highest” strategy with haemodynamic measurements. Int J Cardiol 2013;163(3):221–5.
14. Lamas GA, Lee KL, Sweeney MO, et al. Ventricular pacing or dual-chamber pacing for sinus-node dysfunction. N Engl J Med 2002;346(24):1854–62.
15. Cheng S, Keyes MJ, Larson MG, et al. Long-term outcomes in individuals with prolonged PR interval or first-degree atrioventricular block. JAMA 2009;301(24):2571–7.
16. Magnani JW, Wang N, Nelson KP, et al. Electrocardiographic PR interval and adverse outcomes in older adults: the Health, Aging, and Body Composition study. Circ Arrhythm Electrophysiol 2013;6(1):84–90.
17. Holmqvist F, Hellkamp AS, Lee KL, Lamas GA, Daubert JP, MOST investigators. Adverse effects of first-degree AV-block in patients with sinus node dysfunction: data from the mode selection trial. Pacing Clin Electrophysiol 2014;37(9):1111–9.
18. Curtis AB, Worley SJ, Adamson PB, et al. Biventricular pacing for atrioventricular block and systolic dysfunction. N Engl J Med 2013;368(17):1585–93.
19. Beck H, Curtis AB. Right ventricular versus biventricular pacing for heart failure and atrioventricular block. Curr Heart Fail Rep 2016;13(5):230–6.
20. Ruschitzka F, Abraham WT, Singh JP, et al. Cardiac-resynchronization therapy in heart failure with a narrow QRS complex. N Engl J Med 2013;369(15):1395–405.