Result of the Pacing to Avoid Cardiac Enlargement (PACE) Trial

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Presenter Disclosure Information

- *< Cheuk-Man, YU >*
- *<Result of the Pacing to Avoid Cardiac Enlargement (PACE) Trial >*

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PACE study

Steering Committee:

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Background

Right ventricular apical (RVA) pacing

- Deleterious effect on LV systolic function has long been recognized
- Unexpected increased rates of death and heart failure admissions (DAVID trial)
- Adverse clinical outcomes in patients with standard pacing indications
- Easy accessibility, relative stability, though the optimal mode and site of pacing?

Biventricular (BiV) pacing vs. RVA pacing

- Preclinical data: BiV > RVA to preserve myocardial performance *(normal EF)*
- Acute hemodynamic study: BiV > RVA to preserve LV systolic function *(normal EF)*
- Clinical study: BiV > RVA to improve exercise capacity & quality of life *(LV dysfunction)*

Hypothesis & Study Design

A prospective, multicenter, double-blinded, randomized study to examine if atrial-synchronized BiV pacing is superior to RVA pacing in preserving LV systolic function & avoiding adverse LV structural remodeling in patients with standard pacing indication and normal LV ejection fraction

Patients

Inclusion criteria

- Patients with normal LV ejection fraction (≥45%) who had standard pacing indications

Exclusion criteria

- Persistent atrial fibrillation
- Acute coronary syndrome
- Percutaneous coronary intervention or CABG <3months
- Life expectancy of <6 months
- Heart transplant recipients
- Pregnant women

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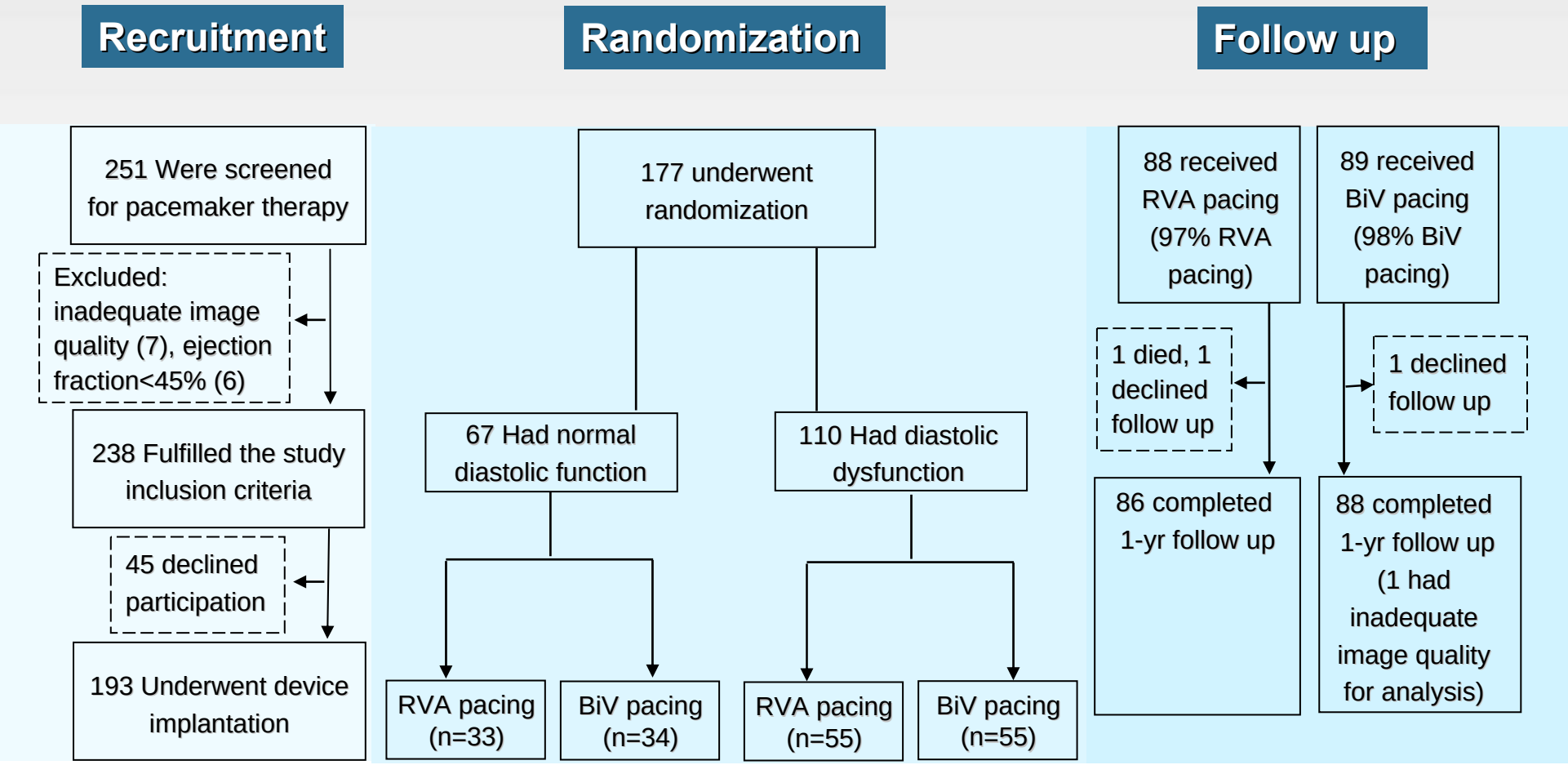
Study flowchart



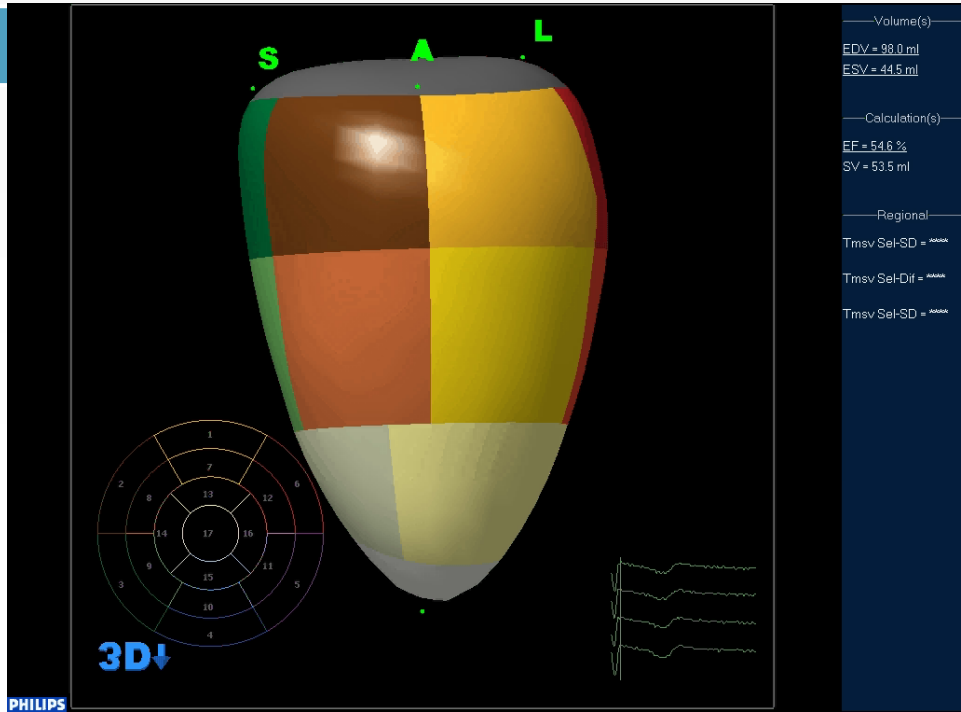
Study End-points

Primary End-points

- LV ejection fraction at 12 months
- LV end-systolic volume at 12 months

Secondary End-points

- LV end-diastolic volume
- 6-min hall walk distance
- Quality of life scores (SF-36)



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Assessment

Time points: baseline, 1 month, 3, 6, 9, 12 months.

Echocardiography

- Real-time 3-dimensional echocardiography (iE33 & Q-Lab 7.0, Phillips, Andover, MA)
- LV volumes and ejection fraction, dyssynchrony index
- Off-line analysis blinded to treatment and clinical data
- Inter-/intra-observer variability: 3.9 & 4.2% (ejection fraction), 6.7 & 6.5% (LV volume)

Clinical status

- Blinded to treatment and echocardiographic data
- 6-min hall walk distance
- Quality of life scores (SF-36 health survey questionnaire)

Statistical Analysis

Sample size calculation

- To detect difference in LV ejection fraction of 5% and LV end-systolic volume of 5ml between the 2 groups at 12 months
- N = 85 in each group: at least 90% power with a 2-sided 5% Type 1 error

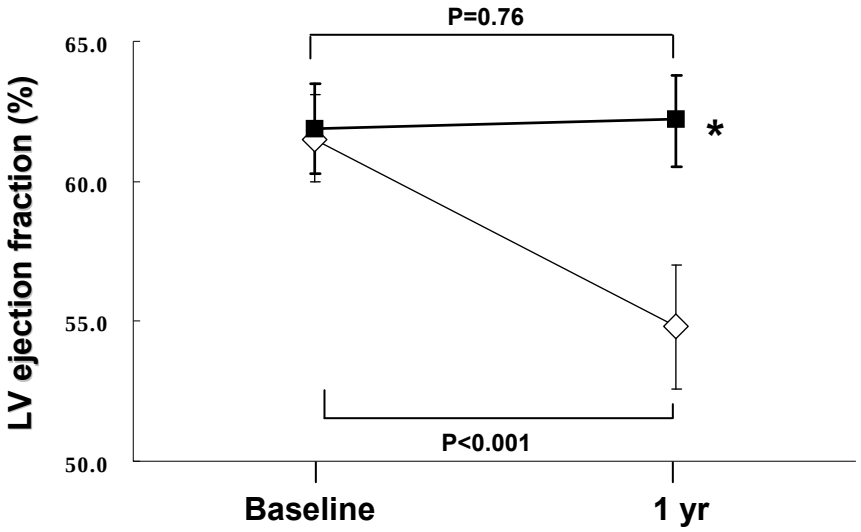
Statistical analysis on end-points

- Intention-to-treat: patients with ≥3 months follow up were included
- Analysis was also performed based on final pacing sites
- Two-sided t-test or non-parametric test: for differences in end-points
- General Liner Model: potential interaction of clinical factors on primary end-points

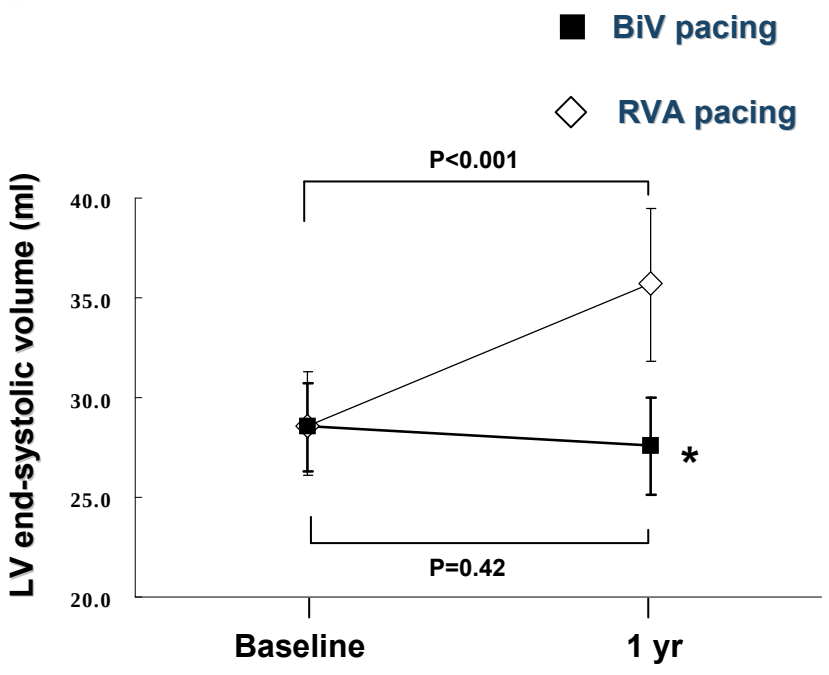
Baseline Characteristics

Parameters	RVA pacing (n=88)	BiV pacing (n=89)	P value
Age – years	68±11	69±11	0.76
Male sex – no. (%)	49 (56)	47 (53)	0.70
Systolic blood pressure – mmHg	143±22	148±24	0.14
Diastolic blood pressure – mmHg	69±12	73±12	0.01
Heart rate – bpm	59±18	59±17	0.98
QRS duration – ms	107±30	107±27	0.98
Left ventricular ejection fraction – %	61.5±6.6	61.9±6.7	0.86
Dyssynchrony Index – ms	12.4±8.1	14.0±10.6	0.43
Indication for pacing – no. (%)			0.24
Advanced atrioventricular block	55 (63)	49 (55)	
Sinus node dysfunction	33 (37)	40 (45)	
Medical history – no. (%)			
Hypertension	55 (62)	62 (70)	0.24
Diabetes mellitus	26 (29)	23 (26)	0.70
Coronary heart disease	20 (23)	19 (21)	0.71
Heart failure	12 (14)	10 (11)	0.63
Chronic renal failure	4 (5)	2 (2)	0.44

Comparison of Primary End-points



*P<0.001 vs RVA pacing



*P<0.001 vs RVA pacing

Absolute difference of EF by 7%

Absolute difference of LVESV by 8.1ml

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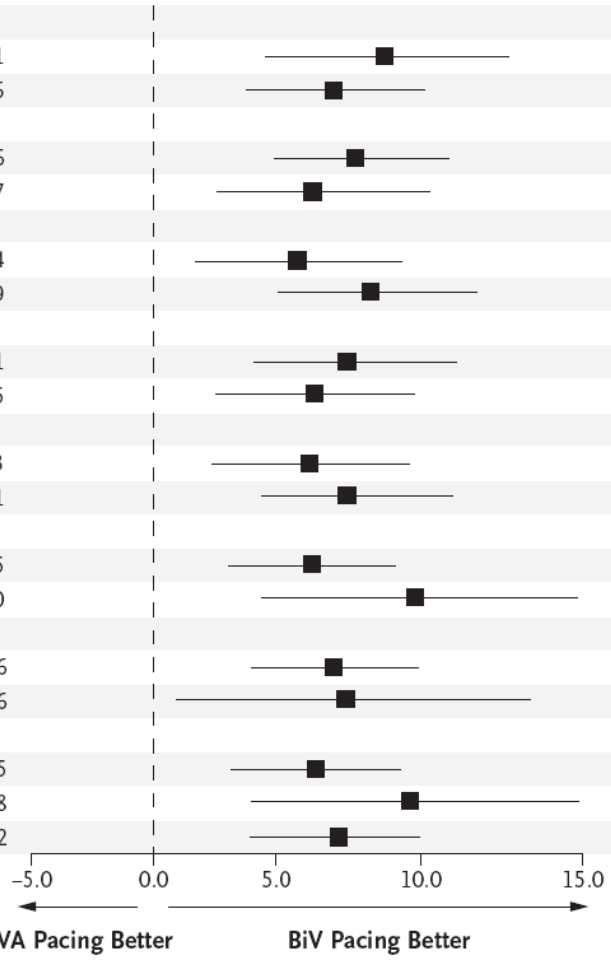
Subgroup Analysis – LV Ejection Fraction

Subgroup	No. of Patients	LV Ejection Fraction (%) RVA	BiV	P Value for Interaction
Diastolic dysfunction				0.46
No	66	54.4	63.1	
Yes	107	55.0	61.6	
Pacing indication				0.53
Heart block	102	54.5	62.6	
Sinus-node dysfunction	71	55.3	61.7	
Age				0.20
<70 yr	86	54.8	60.4	
≥70 yr	87	54.8	63.9	
Sex				0.62
Male	95	53.2	61.1	
Female	78	57.0	63.5	
Hypertension				0.53
No	60	56.1	62.3	
Yes	113	54.0	62.1	
Diabetes				0.67
No	125	56.3	62.5	
Yes	48	51.2	61.0	
Coronary heart disease				0.93
No	135	55.4	62.6	
Yes	38	53.1	60.6	
QRS duration				0.24
<110 msec	113	56.2	62.5	
≥110 msec	60	52.2	61.8	
All patients	173	54.8	62.2	



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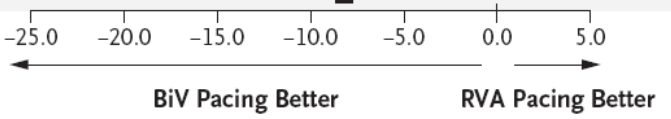
Subgroup Analysis – LV End-Systolic Volume

Subgroup	No. of Patients	LV End-Systolic Volume (ml) RVA	BiV	Difference (ml)	P Value for Interaction
Diastolic dysfunction					0.39
No	66	36.9	26.4		
Yes	107	34.9	28.4		
Pacing indication					0.16
Heart block	102	38.6	28.0		
Sinus-node dysfunction	71	31.2	27.1		
Age					0.17
<70 yr	86	37.4	31.8		
≥70 yr	87	33.8	23.4		
Sex					0.83
Male	95	39.4	31.1		
Female	78	30.6	23.3		
Hypertension					0.10
No	60	32.2	29.4		
Yes	113	37.7	26.8		
Diabetes					0.53
No	125	33.5	26.6		
Yes	48	40.8	30.6		
Coronary heart disease					0.52
No	135	34.0	27.0		
Yes	38	40.1	29.6		
QRS duration					0.94
<110 msec	113	34.3	25.9		
≥110 msec	60	38.1	29.2		
All patients	173	35.7	27.6		



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Comparison of Secondary End-points

Parameters		RVA pacing (n=86)	BiV pacing (n=87)	P value
6-min hall walk – meter	Baseline	335±98	345±105	0.88
	12-month	374±112	380±110	0.81
LV end-diastolic volume – ml	Baseline	73.3±19.8	74.3±17.5	0.61
	12-month	76.7±22.5	71.5±17.8	0.25
SF-36 score				
Physical function	Baseline	65±30	68±25	0.63
	12-month	71±23	70±28	0.75
Role physical	Baseline	38±45	42±45	0.74
	12-month	61±43	72±40	0.14
Bodily pain	Baseline	68±30	78±28	0.04
	12-month	72±26	77±26	0.21
General health	Baseline	42±23	50±24	0.05
	12-month	45±28	53±24	0.05
Mental health	Baseline	72±22	77±20	0.13
	12-month	77±18	78±20	0.31
Role emotional	Baseline	62±42	69±42	0.22
	12-month	67±42	73±38	0.39
Social function	Baseline	49±17	49±13	0.88
	12-month	49±6	50±9	0.27
Vitality	Baseline	56±25	64±23	0.06
	12-month	66±21	64±24	0.67

Discussion

Major findings in the study

- LV ejection fraction reduced by 7% in the first year in RVA pacing
- 9 patients had ejection fraction <45% at 12 months, 8 (89%) in RVA pacing
- Both patients with normal and abnormal baseline LV diastolic function benefited from BiV pacing
- No difference in 6-min walk or quality of life between RVA and BiV pacing

Study limitations

- Small sample size, not powered at any difference in clinical events
- Lower success rate for BiV pacing (92%) than conventional dual chamber pacing

Conclusion

The PACE study

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ORIGINAL ARTICLE

Biventricular Pacing in Patients with Bradycardia and Normal Ejection Fraction

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