Table 2. Event Reductions.

Center TTR Quartiles Range	D 110 mg BID vs warfarin RR (95% CI)	p value for Interaction	D 150 mg BID vs warfarin RR (95% CI)	p value for Interaction
Primary Endpoint of Stroke or Systemic Embolism				
<56.9%	1.1 (0.73, 1.6)		0.61 (0.39, 0.96)	
56.9% - 65.4%	0.74 (0.51, 1.1)		0.48 (0.32, 0.74)	
65.5% - 72.4%	1.0 (0.65, 1.5)		0.76 (0.48, 1.21)	
>72.4%	0.88 (0.57, 1.4)		0.88 (0.57, 1.37)	
		0.27		0.41
Intracranial Bleeding				
<56.9%	0.56 (0.23, 1.3)		0.62 (0.27, 1.4)	
56.9% - 65.4%	0.25 (0.12, 0.55)		0.38 (0.19, 0.74)	
65.5% - 72.4%	0.22 (0.07, 0.65)		0.44 (0.19, 1.0)	
>72.4%	0.31 (0.13, 0.73		0.30 (0.13, 0.71)	
		0.51		0.68
Major Bleeding				
<56.9%	0.66 (0.48, 0.91)		0.74 (0.54, 1.0)	
56.9% - 65.4%	0.79 (0.60, 1.0)		0.84 (0.41, 1.1)	
65.5% - 72.4%	0.90 (0.67, 1.2)		1.12 (0.85, 1.5)	
>72.4%	0.84 (0.62, 1.1)		1.08 (0.81, 1.4)	
		0.22	0.10	0.10
Total Death				
<56.9%	0.71 (0.56, 0.90)		0.68 (0.54, 0.86)	
56.9% - 65.4%	0.96 (0.75, 1.24)		0.91 (0.70, 1.2)	
65.4% - 72.4%	0.92 (0.70, 1.21)		1.0 (0.78, 1.3)	
>72.4%	1.1 (0.87, 1.5)		1.0 (0.78, 1.4)	
		0.02		0.02
All Cardiovascular Events*				
<56.9%	0.75 (0.62, 0.89)		0.69 (0.57, 0.82)	
56.9% - 65.4%	0.93 (0.78, 1.1)		0.88 (0.73, 1.1)	
65.5% - 72.4%	1.1 (0.87, 1.3)		1.1 (0.92, 1.4)	
>72.4%	1.0 (0.83, 1.2)		1.0 (0.85, 1.3)	
		0.04		0.002

* Vascular events, death, major bleeding; D = dabigatran.

Biventricular Pacing Protects Against Adverse Cardiac Remodeling Associated with Right Ventricular Pacing

Pacing both ventricles of the heart, rather than pacing the right ventricle only, prevented loss of left ventricular function among patients with sinus node dysfunction or bradycardia due to atrioventricular (AV) block, according to new findings from the Pacing to Avoid Cardiac Enlargement (PACE) trial (CUHK_CCT00037).

Right ventricular apical (RVA) pacing is associated with deleterious effects on left ventricular systolic function and adverse clinical outcomes, including progression to heart failure, in patients with standard pacing indications. By comparison, biventricular (BiV) pacing has been shown to slow or reverse progressive adverse ventricular remodeling in certain patients, such as those with heart failure. The PACE trial was designed to evaluate whether BiV pacing is superior to RVA pacing in preserving left ventricular systolic function and avoiding adverse left ventricular structural remodeling in patients with normal left ventricular ejection fraction (LVEF).

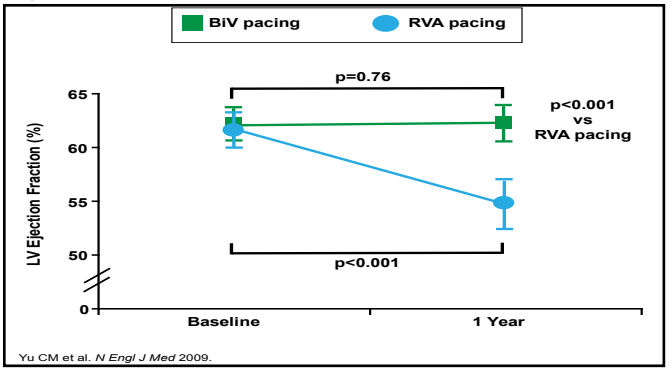
Cheuk-Man Yu, MD, Chinese University of Hong Kong, Hong Kong, China, presented results from the PACE trial, which were simultaneously published online in *The New England Journal of Medicine*.

The PACE trial included 177 patients with a normal LVEF (>45%) who had sinus node dysfunction or AV block. Patients were randomly assigned to BiV (n=89) or RVA (n=88) dual-chamber pacing. The primary endpoints were LVEF and left ventricular end-systolic volume (LVESV) at 12 months.

Baseline characteristics were similar in both treatment groups. In the BiV pacing group, the mean age was 69 years, LVEF was 61.9%, and the indication for pacing was advanced AV block in 55% of patients and sinus node dysfunction in 45% of patients.

During the first year, LVEF fell in the RVA group but remained unchanged in the BiV group, leading to an absolute difference of 7.4% between groups at 12 months (p<0.001; Figure 1). Fewer patients in the BiV group than in the RVA group experienced a decline in LVEF to <45% (1% vs 9%; p=0.02). At 12 months, LVESV was significantly lower in the BiV group than in the RVA group (27.6 ml vs 35.7 ml; p<0.001), reflecting a relative change from baseline that was 25% greater in the RVA group than in the BiV group (p<0.001).

Figure 1. LVEF at 12 Months.



Yu CM et al. *N Engl J Med* 2009.

According to a subgroup analysis, patients benefited from BiV pacing relative to RVA pacing regardless of baseline left ventricular diastolic function. Indeed, the subgroup analysis favored BiV patients in all subgroups, including those who were defined by pacing indication; age; gender; QRS duration; or comorbid hypertension, diabetes, or coronary artery disease.

No significant differences between the two groups were observed in left ventricular end-diastolic volume (p=0.25), 6-minute walk distance (p=0.81), quality of life (p=0.75), or heart failure hospitalizations (p=0.74) at 12 months.

The role of BiV pacing devices, which are more expensive and require more expertise to implant than RVA devices, remains controversial. In an editorial that accompanied the PACE trial, Bruce D. Lindsay, MD, Cleveland Clinic, Cleveland, OH, suggested that BiV pacing may not be appropriate first-line treatment for all patients with high-grade AV block. Instead, patients may be successfully managed with standard RV dual-chamber pacing, monitored with annual echocardiograms, and converted to BiV pacing only when a clinically significant change in LVEF or functional capacity occurs.

Additional reading:

Yu CM, Chan JY, Zhang Q, et al. Biventricular pacing in patients with bradycardia and normal ejection fraction. *N Engl J Med* 2009 Nov 26;361(22):2123-34.

New Findings from BARI 2D

For patients with type 2 diabetes and stable coronary artery disease (CAD), intensive medical therapy (IMT) provides similar protection against myocardial infarction (MI) and cardiac death compared with percutaneous coronary intervention (PCI) but is not as effective as coronary artery bypass grafting (CABG) among patients with more extensive CAD, according to new findings from the Bypass Angioplasty Revascularization Investigation 2 Diabetes (BARI 2D) trial (NCT00006305).

The BARI 2D trial was designed to compare treatment strategies for patients with type 2 diabetes, ischemic CAD, and no history of CABG or PCI within the last 12 months. Specifically, BARI 2D involved 2 comparisons: prompt revascularization versus IMT with delayed revascularization, if needed, and insulin sensitization (IS) or insulin provision (IP) therapy with a target HbA1c level of <7.0%.

Prior to randomization, the treating physician recommended a form of revascularization based on clinical and angiographic factors. Candidates for PCI (n=1605) were randomly assigned to treatment with PCI or IMT, and candidates for CABG (n=763) were randomly assigned to treatment with CABG or IMT. All patients underwent a second randomization to IS or IP therapy for glycemic control. Investigators stratified all endpoints by revascularization group, because it was assumed that patients who were candidates for CABG had higher baseline risk than those who were candidates for PCI.

The BARI 2D investigators previously reported no significant differences in the primary endpoint of all-cause mortality or in the principal secondary endpoint of all-cause death/MI/stroke between revascularization and IMT or between strategies of IS and IP. However, in the CABG group, early revascularization significantly reduced major cardiovascular events (22.4% vs 30.5%; p=0.02), primarily due to a reduction in MI in patients within the IS strategy (7.4% vs 14.6%) [Frye RL et al. *N Engl J Med* 2009].

Bernard R. Chaitman, MD, St. Louis University School of Medicine, St. Louis, MO, presented data on additional secondary endpoints, including MI and cardiac death. Overall, the 5-year cardiac mortality rates were similar in the revascularization and IMT groups (5.9% vs 5.7%; p=0.38) and in the IS and IP groups (5.7% vs 6.0%; p=0.76). However, important differences in secondary endpoints emerged when patients were evaluated according to revascularization strata.

Among patients who were candidates for PCI upon study enrollment, there was no difference between revascularization plus IMT and IMT alone in the risk of MI (12.3% vs 12.6%; p=0.42) or cardiac death (5.0% vs 4.2%; p=0.16). Moreover, the combined endpoint of cardiac death or MI favored treatment with IMT alone (16.0% vs 14.2%; p=0.05). In the PCI strata, there were no significant interactions between revascularization versus IMT and IP versus IS for MI, cardiac death, or the combined endpoint of cardiac death or MI.

By comparison, among patients in the CABG group, the risk of MI was significantly lower following treatment with