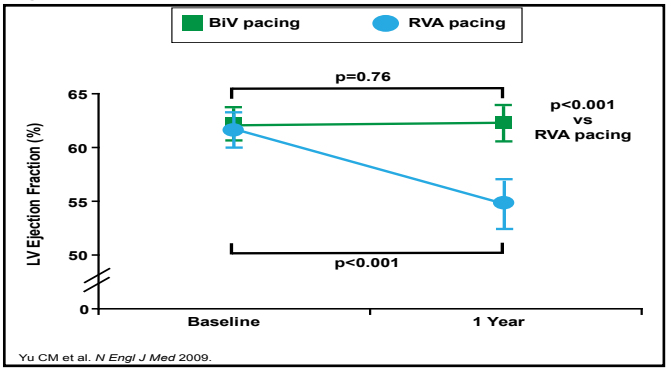
Figure 1. LVEF at 12 Months.



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

revascularization plus IMT compared with IMT alone (10.0% vs 17.6%; p=0.003). Revascularization plus IMT also reduced the risk of the composite endpoints of all-cause death or MI (21.1% vs 29.2%; p=0.01) and cardiac death or MI (15.8% vs 21.9%; p=0.03) relative to IMT alone.

Whereas CABG reduced the risk of MI relative to IMT by 68% among patients who were treated with IS (HR, 0.32; p=0.001), early CABG did not protect against MI in patients who were treated with IP (HR, 0.79; p=0.40). Similarly, CABG reduced the combined endpoint of cardiac death or MI relative to IMT only in the IS group (HR, 0.41; p=0.0002), not in the IP group (HR, 1.03; p=0.91).

Findings from BARI 2D suggest that the optimal treatment strategy may depend on the extent and severity of CAD. "In many patients with type 2 diabetes and stable ischemic CAD, an initial strategy of IMT should be considered and does not require immediate PCI to prevent cardiac death or MI when angina symptoms are controlled," Dr. Chaitman said. "In patients with more extensive coronary disease, a strategy of prompt CABG, intensive medical therapy, and insulin sensitization therapy should be considered the preferred strategy to reduce the incidence of spontaneous MI," he concluded.

Platelet Reactivity Tests Predict Thrombotic Events After PCI

Three tests of platelet reactivity were able to predict one-year risk of thrombotic events in patients who were undergoing elective percutaneous coronary intervention (PCI), according to new findings from the POPular study.

Dual antiplatelet therapy with aspirin and clopidogrel is the standard of care for patients who are undergoing PCI with stent implantation; yet, up to 36% of patients show decreased responsiveness to clopidogrel. These patients exhibit high on-treatment platelet reactivity, which is associated with an increased risk of thromboischemic events. Today, Nicoline J. Breet, MD, St. Antonius Hospital, Nieuwegein, the Netherlands (lead investigator JM ten Berg, MD, PhD), presented results from the POPular study, which was designed to identify which platelet function tests predict thrombotic risk in patients who receive antiplatelet therapy following PCI.

The POPular trial included 1069 consecutive patients who were treated with aspirin and clopidogrel after undergoing elective PCI with stent implantation. In a head-to-head comparison, investigators evaluated seven platelet reactivity tests in parallel:

- Light transmittance aggregometry (LTA) 5 µmol/L adenosine diphosphate (ADP) and 20 µmol/L ADP
- VerifyNow® P2Y12
- Plateletworks®
- Impact-R
- Impact-R ADP
- PFA-100 COL/ADP
- INNOVANCE® PFA P2Y®

The primary endpoint was a composite of death, myocardial infarction, stent thrombosis, and stroke at 1 year. Primary safety endpoints included TIMI major and minor bleeding at 1 year.

Three platelet function tests were able to correlate high platelet reactivity with an increased risk of thrombotic complications at 1 year, including both versions of the LTA test, the VerifyNow® P2Y12 assay, and the Plateletworks® assay.

When the LTA test was used with 5 µmol/L ADP, 6% of patients with normal reactivity and 11.7% of patients with high reactivity reached the primary endpoint (p<0.0001). When used with 20 µmol/L ADP, the risk of complications was 6.2% in the normal reactivity group and 12% in the high reactivity group (p<0.0001). The LTA test is the most labor-intensive and time-consuming of the platelet reactivity tests and can not be performed at the patient's bedside, Dr. Breet said.

Patients with normal and high platelet reactivity according to the VerifyNow® P2Y12 assay had a 5.7% and 13.3% risk of reaching the primary endpoint, respectively (p<0.0001). The VerifyNow® test is fully automated and can be performed at the bedside in the cardiac catheterization laboratory.

Using the Plateletworks® assay, normal and high platelet reactivity corresponded with a 1-year risk of thrombotic events of 6.7% and 12.6%, respectively (p=0.002). The Plateletworks® assay is a semiautomated test that can be performed at the bedside, but it is limited by the requirement that it must be performed within 10 minutes of drawing blood.

The four remaining tests – Impact-R, Impact-R ADP, PFA-100 COL/ADP, and INNOVANCE® PFA P2Y® – were not able to identify an association between high platelet reactivity and thrombotic complications at 1 year. None of the tests that were included in the analysis was able to identify patients with an increased risk of TIMI major or minor bleeding.

Currently, platelet reactivity tests are used primarily in research rather than in the clinical setting. However, large randomized trials are currently underway to evaluate whether these tests can guide clinical decision-making for patients who receive antiplatelet therapy following PCI, Dr. Breet said.