BARI 2D: Up-Front CABG Shows Advantages

BY BRUCE JANCIN

ORLANDO — Type 2 diabetes patients with stable but severe and extensive coronary disease are best served by a management strategy of prompt coronary artery bypass graft surgery with intensive medical and insulin-sensitization therapy, according to a new secondary analysis from the BARI 2D trial.

This approach provides significantly greater clinical and quality of life benefits and is more cost-effective than is trying medical management first and holding CABG in reserve for the suboptimal responders, investigators from BARI 2D (the Bypass Angioplasty Revascularization Investigation 2 Diabetes study) reported at the annual scientific sessions of the American Heart Association.

BARI 2D showed that an up-front revascularization strategy was advantageous only in the sorts of diabetes patients whose ischemic heart disease was better suited for CABG than for percutaneous coronary intervention: generally, those with three-vessel disease, more total occlusions, and/or significant proximal left anterior descending lesions.

In contrast, a wait-and-see approach to revascularization is preferable in type 2 diabetes patients with less extensive coronary disease that is suitable for PCI. In such patients— the majority of type 2 diabetics with ischemic heart disease—intensive medical treatment alone should be the first-line therapy. BARI 2D showed that it is significantly less costly and no less effective than up-front PCI in terms of hard cardiac end points at 5 years of follow-up, said Dr. Bernard R. Chaitman, professor of medicine and director of cardiovascular research at St. Louis University.

"If angina symptoms are controlled and the patient is satisfied with [his or her] quality of life, a strategy of watchful waiting is more appropriate," he added.

BARI 2D involved 2,368 type 2 diabetes patients with stable coronary disease. On the basis of their angiographic findings, their treating physicians assigned 1,605 of them to the PCI stratum and 763 to the CABG stratum. Within each stratum, participants were randomized to prompt revascularization plus intensive medical management or to intensive medical management alone, with delayed revascularization as clinically indicated. Patients were further randomized to insulin provision or insulin sensitization therapy for their diabetes management.

In the patients with more severe coronary disease deemed most suitable for CABG, prompt revascularization was associated with significantly lower 5-year rates of MI, the composite end point of all-cause mortality or MI, and the composite of cardiac death or MI (see box). These benefits were significant only in the subgroup on insulin sensitization therapy, which is why up-front CABG combined with intensive medical management and insulin sensitization is the preferred strategy, Dr. Chaitman said.

BARI 2D: Key 5-Year Outcomes by Early Revascularization Strategy

	PCI stratum (1,605)		CABG stratum (763)	
	Intensive medical therapy	*PCI*	*Intensive medical therapy*	*CABG*
MI	12.6%	12.3%	6.0%	4.3%*
All-cause mortality or MI	19.6%	21.1%	29.2%	21.1%*
Cardiac death or MI	14.2%	16.0%	21.9%	15.8%*

*Significantly different from intensive medical therapy group.
Source: Dr. Chaitman

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Dr. Mark A. Hlatky presented a cost-benefit analysis of BARI 2D based on 4 years of economic data. Lifetime projections suggested that prompt CABG in patients with more severe coronary disease may be cost-effective, with a cost of $47,000 per life-year added, just under the benchmark of $50,000 per life-year added. Initial medical therapy is the more cost-effective strategy in patients similar to those in the PCI stratum, with a cost of only $600 per life-year added.

Cumulative 4-year total costs in the PCI stratum averaged $67,800 per patient assigned to initial medical management compared with $73,400 with up-front PCI. In the CABG stratum, the figures were $60,600 with initial medical management, compared with $80,900 with early revascularization, according to Dr. Hlatky, professor of health research and policy and professor of medicine at Stanford (Calif.) University.

Noting that only 43% of deaths at 5 years in BARI 2D were attributable to cardiac causes, compared with an anticipated 60%-75% based on earlier studies, Dr. Hlatky said this is striking evidence of the effectiveness of modern medical management using statins, beta-blockers, ACE inhibitors, and aspirin. Medical therapy is "a lot better than it used to be. I think that's one of the main messages of the trial," he said.

Insulin sensitization therapy cost an average of $1,100 more than did insulin therapy over 4 years. From a cost-effectiveness standpoint, the two diabetes management strategies were "essentially a toss-up," he noted.

A quality of life analysis by Maria M. Brooks, Ph.D., of the University of Pittsburgh, concluded that 1 year into BARI 2D, all participants reported significant improvements over baseline. The gains were greater in patients randomized to early revascularization, whether by CABG or PCI.

Discussant Lars Ryden took issue with Dr. Chaitman's conclusions about PCI's role in patients with type 2 diabetes. Dr. Ryden, professor emeritus of cardiology at the Karolinska Institute, Stockholm, argued in favor of an even stronger endorsement of intensive medical management as the front-line therapy.

"When we're dealing with patients we have to give them all the information we have," Dr. Chaitman replied. "If patients are really not satisfied with their quality of life and they're willing to accept the slight risks of a periprocedural event, then I think that's reasonable."

BARI 2D was funded by the National Heart, Lung, and Blood Institute and the National Institute of Diabetes and Digestive and Kidney Diseases. Dr. Chaitman has been a consultant to Eli Lilly & Co. Dr. Hlatky and Dr. Brooks reported no financial conflicts. ■

Best Shunt for Norwood Operation Remains Unresolved

VITALS

Major Findings: At 1 year, infants who received the RVPAS had a significant absolute reduction in death or need for transplant vs. those who received the MBTS; after 1 year that rate was higher in the RVPAS patients.

Source of Data: The Single Ventricle Reconstruction Trial, involving 555 infants.

Disclosures: The National Heart, Lung, and Blood Institute sponsored the trial. Dr. Ohye had no conflicts.

BY MITCHEL L. ZOLER

ORLANDO — The best shunt to use in the Norwood operation, during the first stage of repairing hypoplastic left heart syndrome, remains a toss-up despite completion of a yearlong randomized trial with more than 500 infants.

"What we see at 12 months is a survival advantage" for a right ventricle-to-pulmonary artery shunt (RVPAS) compared with the alternative, modified Blalock Taussig shunt (MBTS), Dr. Richard G. Ohye said at the annual scientific sessions of the American Heart Association.

"The concern is that the [survival] curves begin to converge, and in the future will they remain parallel or cross?" As a result of this uncertainty about long-term survival, "concrete recommendation will have to wait for further follow-up," said Dr. Ohye, director of pediatric cardiac surgery at the University of Michigan, Ann Arbor.

The MBTS has been the traditional option during the Norwood operation, but concerns about its safety focused on the retrograde coronary flow it allows that could potentially interfere with coronary perfusion and lead to ischemia and possibly death. The other option, the RVPAS, requires a ventriculotomy, which could compromise right ventricular function and might also trigger arrhythmias.

Uncertainty over which shunt produced the best outcomes led to the Single Ventricle Reconstruction Trial, done through the Pediatric Heart Network at 15 U.S. sites. It randomized 555 infants scheduled for the Norwood operation to either of the two shunt strategies.

One year after randomization, the incidence of death or need for heart transplant was 26% in patients getting the RVPAS and 36% in those getting the MBTS, a statistically significant 10% absolute difference in the primary end point in favor of the RVPAS. Although this was the primary end point, it did not tell the entire story.

Follow-up continued and after an average of 32 months, 16 additional deaths or heart transplants occurred in the RVPAS group compared with 7 of these events in the MBTS infants, a trend that led to the observation that the event curves may be converging over time.

Another worrisome finding was that unintended cardiac procedures such as balloon dilatations of the shunt or neoaorta, shunt revisions, or unplanned pulmonary artery reconstructions, were significantly more common in the RVPAS infants, 54%, compared with those who received MBTS, 44%. The RVPAS also produced smaller pulmonary arteries by the Nakata index.

By most other criteria, the two procedures produced similar outcomes. Time to extubation during surgery, duration of ventilation, and total days spent in the ICU and in the hospital were identical, as was the percentage of infants who required an open sternum or extracorporeal membrane oxygenation. The incidence of nonfatal serious adverse events was similar in the two arms, as was long-term right ventricular function. Infants treated with a RVPAS had the advantage of a significantly reduced need for cardiopulmonary resuscitation, 13%, compared with 20% in the MBTS infants.

"Although 12-month, transplant-free survival is higher with RVPAS, the emergence of later mortality with RVPAS is of concern. Continued follow-up of the cohort will be important to determine intermediate and long-term outcomes," Dr. Ohye said. ■