Highlights from the 2008 American Heart Association Scientific Session

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The 2008 Annual Scientific Session of the American Heart Association was held in New Orleans from November 9 to 12, 2008. Many innovative clinical and scientific developments were presented and discussed at the meeting. The American Heart Association meeting is unique in that all major specialties treating cardiovascular disease are represented, including cardiac surgery, cardiology, neurology, basic science, and imaging.

This year, cardiac surgery was especially well represented. Dr Tim Gardner presented his Presidential address, Dr Philippe Menasché gave the Paul Dudley White International Lecture, and Dr Tirone David presented the William W. L. Glenn Lecture entitled ''Aortic Valve Sparing: Matching the Procedure to the Aortic Root Pathology.'' In his Presidential address, Dr Gardner challenged the audience to become citizen leaders with a ''passion for prevention'' to reduce heart disease and stroke. Worldwide heart disease mortality rates peaked approximately 30 years ago and have been declining, largely because of preventative measures. Dr Gardner noted ''Despite this progress, serious challenges remain. The major threat to continued reductions in preventable and premature deaths from cardiovascular disease and stroke is the increase in the risk factors of obesity and diabetes, untreated high blood pressure, smoking and lack of physical activity,'' especially in developing countries. Gardner called on all health care professionals to continue their work to build a healthier world by raising money to support research and providing resources to drive prevention and health promotion efforts. He concluded by promoting preventative medicine and healthy lifestyles, not only in North America and Europe but also throughout the world.

Dr Philippe Menasché gave the Paul Dudley White Lecture, entitled ''Human Cardiac Cell Therapy—Lessons Learned and Future Prospects.'' Dr Menasche reviewed studies of stem cell therapies, including intracoronary infusion of bone marrow-derived mononuclear cell and mesenchymal stem cells for the treatment of acute myocardial infarction (MI) and the delivery of embryonic stem cells for the treatment of chronic heart failure. Although Dr Menasche did outline the progress that has been made, he noted that the results to date are not what we would have hoped. With current techniques, most cells die or do not functionally engraft into the host organ. The lessons learned include the choice of cells, a better understanding of graft–host interactions, the development of methods to improve cellular survival, and the incorporation of the transplanted cells into the host so that they survive and incorporate into the host organ with real clinical improvement.

BASIC/TRANSLATIONAL RESEARCH

It was shown in a fibrillin-deficient mouse model of Marfan syndrome that pravastatin at 50 mg/kg/d attenuated aortic root dilatation and thickening of the aortic media over an observation period of 6 months.[1] Although exact mechanisms are unclear, other results obtained with this mouse model indicated that the combination of oral doxycycline and oral losartan also could prevent dilatation of the ascending aorta, with concomitant decreases in the activities of matrix metalloproteinase-2 and -9, as well as a reduction in transforming growth factor-β expression.[2] Taken together, these observations provide some hope for the possibility of future primary and secondary prevention in patents with Marfan syndrome.

In the field of cell therapy, Gorman and colleagues[3] reported that allogenic mesenchymal progenitor cells (MPCs) injected intramyocardially 1 hour after acute MI in sheep could not be found 8 weeks later. Although this has been observed by other groups, they also found that this was independent of the number of cells delivered (up to 450×10^6 cells) and that, despite the absence of cells, the functional effect on the prevention of left ventricular dilatation correlated with higher injected MPC numbers and a proportional decrease in collagen turnover.

Huang and colleagues[4] showed that the so-called immune privilege of MPCs is not sustained, and that it is lost 1 to 5 weeks post-injection, possibly coincident with myogenic differentiation of the MPCs, but without any significant impact on functional effects such as left ventricular ejection fraction.[4] Clearly, the field has much work to do to resolve such issues of ''mechanistic-functional dissociation.''

ACUTE CORONARY SYNDROME

Rosuvastatin in Patients with Elevated C-Reactive Protein

The JUPITER trial, a randomized, double-blind, placebo-controlled, multicenter trial testing whether a lipid-lowering drug reduces heart attacks in people with normal cholesterol but high levels of high-sensitivity C-reactive protein (hs-CRP), attracted much interest at the meeting. Hs-CRP is a marker of inflammation that can be associated with increased coronary disease risk. Among 17,802 patients with

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elevated hs-CRP, patients receiving 20 mg rosuvastatin had a 44% reduction in first major cardiovascular events. There was a 37% reduction in first cardiac events in the statin group who had no risk factors except elevated hs-CRP, suggesting a potential role of rosuvastatin in patients with elevated hs-CRP with normal cholesterol. This study was recently published in the *New England Journal of Medicine* in November 2008.[5]

New Anticoagulation Strategies

Anticoagulation during acute coronary syndrome introduces dilemmas to surgeons because these patients often require coronary artery bypass grafting (CABG) after cardiac catheterization. Two interesting studies on new anticoagulation strategies were presented at the late-breaking trial sessions. The first addressed the widely used clopidogrel. In 429 patients undergoing percutaneous coronary intervention (PCI) who had a low response to an initial 600 mg clopidogrel loading dose, as defined by a vasodilator-stimulated phosphoprotein (VASP) index of less than 50%, the patients were randomized to receive either the usual single 600-mg dose of clopidogrel or up to 3 additional 600-mg clopidogrel doses (up to 2400 mg) to obtain a predefined, adequate antiplatelet response (VASP index > 50%).[6] The VASP index has been shown to be a highly specific measure of a patient's antiplatelet response to clopidogrel.[7] Researchers reported that individually tailoring the loading dose of clopidogrel was associated with a significant 88% reduction in the rate of early stent thrombosis and 94% reduction in the rate of major adverse cardiovascular events compared with the standard clopidogrel dose.

In another study, 3491 patients who were already taking either aspirin alone or aspirin plus thienopyradine were randomized to also receive either placebo or rivaroxaban, a new oral, direct factor Xa inhibitor. Although there was a dose-dependent increase in mild bleeding with rivaroxaban compared with the placebo (2–4.5-fold increase with higher doses), there was also a 20% trend toward a benefit in the rate of death, MI, stroke, or need for revascularization.[8] This study thus suggests that additional benefit might be achieved in patients with acute coronary syndrome who are already receiving the usual anticoagulation regimen by the addition of rivaroxaban. On the basis of the safety and efficacy outcomes, a study of different dosing regimens of rivaroxaban is planned in a phase III trial.

Also, in a late breaking clinical trial presentation, the safety and possible benefits of rFVIIa in patients undergoing cardiac surgery were assessed. A total of 172 patients who had undergone cardiac surgery and were bleeding were randomized to receive placebo, 40 mg/kg rFVIIa, or 80 mg/kg rFVIIa. The authors reported more serious adverse events in the rFVIIa groups, but the differences did not reach statistical significance (placebo: 7%; 40 mg/kg: 14%; $P = .25$; 80 mg/kg: 12%; $P = .43$). After the trial drug administration, in comparison with the placebo, significantly fewer patients in the rFVIIa group underwent reoperation because of bleeding ($P = .03$) or required transfusions ($P = .03$). On the basis of this preliminary evidence, rFVIIa was believed to be beneficial to treat bleeding after cardiac surgery, but caution should be applied and further clinical trials are required.

INTERVENTIONAL CARDIOLOGY

Bare Metal Stent versus Drug-eluting Stent

Although drug-eluting stents (DES) have been shown to reduce the rate of repeat revascularization compared with bare metal stents (BMS), there have been recent controversies over their potential long-term safety. Several studies addressed long-term safety issues, particularly 2 abstracts by Dr Patrick Serruys' group from The Netherlands. In the first study, the 5-year clinical event rates evaluation of 958 patients treated with sirolimus-eluting stents (SES) from the RESEARCH registry (508 patients treated with SES and 450 patients treated with BMS) showed that the 5-year, all-cause mortality rates were comparable (14.0% for SES vs 13.4% for BMS, $P = .9$).[9] In the second study, the investigators compared 576 patients treated with paclitaxel-eluting stents from the T-SEARCH registry compared with 508 patients treated with SES from the RESEARCH registry.[10] The 4-year cumulative major adverse event rates were equivalent (30.5% SES vs 30.7% paclitaxel-eluting stents, $P = .9$). Further supporting this conclusion, a meta-analysis of more than 192,000 patients enrolled in 22 randomized, controlled trials and in 34 observational studies demonstrated that DES was not associated with a greater percentage of adverse safety outcomes, such as death or MI, but did achieve a significant reduction in target vessel revascularization compared with BMS.[11] Further indicating the benefit of DES compared with BMS, studies of diabetic patients from the Mass-DAC registry and patients with proximal coronary lesions from the National Heart, Lung, and Blood Institute Dynamic Registry also suggest that DES results in significant decreases in death or MI, as well as the need for repeat revascularization compared with BMS.[12,13]

Primary Percutaneous Transluminal Coronary Angioplasty versus Primary Stenting in Patients with Early Coronary Artery Bypass Grafting

Whether balloon angioplasty without stent placement (primary percutaneous transluminal coronary angioplasty [PTCA]) is adequate or stent implantation is necessary in patients presenting with ST-elevation MI for whom early CABG is planned is not known. Investigators from Duke University examined 2982 patients with ST-elevation MI treated with primary PTCA (n = 1494) or primary stenting (n = 1488) to evaluate if the strategy of primary PTCA versus primary stenting had any differences in clinical events in the first 30 days.[14] Compared with primary stenting, primary PTCA was associated with higher rates of target vessel

revascularization at 30 days, but with no increase in death or reinfarction. This study thus suggests that primary PTCA may be a reasonable option in patients who are planned for early CABG, allowing a shorter course of potent antiplatelet therapy and permitting earlier CABG compared with those patients receiving stents.

Stenting versus Coronary Artery Bypass Grafting

Malenka and colleagues,[15] for the Northern New England Cardiovascular Disease Study Group, reported on registry patients who received either PCI with DES (DES-PCI) (N = 2520) or CABG (N = 2626) for non-emergency multivessel disease. Although there was a small but statistically significant increase in 45-day mortality (0.4% for DES-PCI vs 1.8% for CABG) in favor of the DES-PCI group, these differences vanished by approximately 15 months postprocedure and actually translated into significantly higher overall mortality rate in DES-PCI (4.1%/year) compared with patients who underwent CABG (2.2%/year). Similar findings were also observed in a large single-center study from Beijing, China, where 2-year rates of target vessel revascularization (13% for DES-PCI vs 1.4% for CABG), MI rates (hazard ratio 1.6 for DES-PCI vs CABG), and total mortality (hazard ratio 1.6 for DES-PCI vs CABG) were significantly higher with DES-PCI than with CABG.[16] Furthermore, CABG was associated with significantly lower costs by 1 year post-procedure. Notably, a unique feature of these studies from New England and China is that all patients in the PCI group received DES.

McGinn and colleagues[17] presented a series of 300 consecutive patients who underwent multivessel minimally invasive CABG via a small thoracotomy, under direct vision and without the need for endoscopic or robotic assistance. The procedure was reported to be safe (0.7%), with low atrial fibrillation, stroke, and wound infection rates. It allowed for all coronary distributions to be grafted (with up to 4 grafts per patient in the series), as well as performance of total arterial grafting and hand-sewn proximal anastomoses onto the aorta, as per a standard CABG operation.

Endovascular Stent-Graft Repair of Type B Aortic Dissection

The potential effectiveness of endovascular stent-graft repair of type B aortic dissection was demonstrated by investigators from South Korea in a retrospective analysis of 73 patients who underwent stent-graft repair from 1994 to 2007.[18] The indications for case selection were progression of dissection despite adequate medical treatment, dynamic obstruction, intractable pain, aortic diameter of 6 cm or more, or continuous false lumen leakage. The analysis showed the achievement of 92% angiographic success (immediate closure of the entry site without any significant endoleak) and 73% clinical success (complete obliteration of the false lumen). The complication rate was 30% (eg, persistent endoleak, false lumen flow patency) and the mortality rate was 5.5% at 43 months follow-up. On the basis of these favorable clinical outcomes, stent-graft repair may be considered a safe and effective treatment option of type B aortic dissection, particularly in patients with a high risk for surgical morbidity or mortality.

VALVULAR DISEASE

Percutaneous Aortic Valve Replacement

Although percutaneous aortic valve replacement (PAVR) is increasingly being used to treat patients with aortic stenosis who are poor candidates for surgery, the clinical outcomes of these patients are still not fully evaluated. A study from The Netherlands followed 81 patients for 1 year who were treated between 2005 to 2008 with the CoreValve (CoreValve Inc, Irvine, Calif), a self-expanding pericardial valve system.[19] PAVR was complicated by a stroke in 4 patients (5%) and MI in 2 patients (2%). In these very high risk and mostly elderly patients, the 30-day and 1-year mortality rates were 4% and 15%, respectively, and there was no evidence of significant valvular dysfunction. Thus, these findings suggest that PAVR may be a safe and effective option for high-risk, elderly patients with severe aortic stenosis.

Aortic Valve Replacement in the Elderly

In a study from the Northern New England Cardiovascular Study Group, Likosky and coauthors[20] found in approximately 4000 patients that survivorship in very elderly patients ($\geq$85 years) after surgical AVR was 89.7% for AVR alone and 90.1% for AVR-CABG, and that in both groups the median survival was reasonable at approximately 6 years. However, it remains likely that very elderly patients who undergo surgical AVR are selected, as was reported in a smaller study indicating that 49% of patients with severe aortic stenosis (mean gradient $\geq$ 40 mm Hg) who presented to 3 tertiary centers did not undergo AVR, for a number of reasons that included age and comorbidities.[21]

ARRHYTHMIA

Ablation in Mitral Valve Surgery for Atrial Fibrillation

In the MAMA trial, 64 patients with permanent atrial fibrillation were randomly assigned to mitral valve surgery plus left and right atrial microwave ablation (31 patients) or mitral valve surgery alone (33 patients).[22] At 12 months, sinus rhythm was restored in 81% of the ablation group versus 36% of the control group. Thus, this study suggests that microwave ablation in the left and right atria in conjunction with mitral valve surgery is a safe and effective method to restore sinus rhythm in patients with long-lasting, permanent atrial fibrillation compared with mitral valve surgery alone.

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