YEAR IN CARDIOLOGY SERIES

The Year in Interventional Cardiology

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We are honored to provide readers of the Journal with this review of major scientific work published in the field of interventional cardiology in 2008. In addition, we have included late-breaking trials presented at the American College of Cardiology (ACC), Transcatheter Cardiovascular Therapeutics, and American Heart Association (AHA) conferences. We hope that this report will provide a broad overview of the field for general cardiologists, as well as a framework for more detailed study for those with a specific interest in interventional cardiology.

Percutaneous Coronary Intervention (PCI) Guideline Update

An update of the ACC/AHA/Society for Cardiac Angiography and Interventions 2005 Guideline Update for PCI was published early in 2008 (1). This focused update provides revisions to existing guideline recommendations based on new clinical trial data and opinion in this rapidly evolving field. The document highlights certain key areas, including unstable angina/non–ST-segment elevation myocardial infarction (NSTEMI), facilitated PCI, rescue PCI, PCI after fibrinolysis, ancillary therapy for ST-segment elevation myocardial infarction (STEMI), antiplatelet therapy, bare-metal stents (BMS) and drug-eluting stents (DES), and finally, secondary prevention. Full review of the updated guideline recommendations is beyond the scope of this article. Careful reading of this document is essential for all those involved in the practice of interventional cardiology.

Acute Myocardial Infarction (AMI)

STEMI update. The ACC/AHA STEMI guidelines were revised and published as a focused update in 2008 (2). Essential changes in the guidelines include: 1) emphasis on pre-hospital electrocardiography and transport of STEMI patients directly to a PCI facility (bypassing hospitals that are not PCI capable); 2) facilitated PCI with full-dose thrombolytic agents may be harmful (Class IIIb); 3) clopidogrel should be added to aspirin in STEMI patients regardless of reperfusion status (Class Ia) and long-term

maintenance (e.g., 1 year) is reasonable (Class IIa, Level of Evidence: C); 4) intravenous beta-blockers should not be given to STEMI patients with signs of congestive heart failure (CHF) or low cardiac output (Class IIIa); 5) non-steroidal anti-inflammatory drugs (except for aspirin) should not be given (Class IIIc); and 6) routine coronary angiography may be considered after thrombolytic therapy in patients not receiving reperfusion therapy (Class IIb) with PCI of a hemodynamically significant stenosis in a patent vessel (Class IIb). However, late PCI of a totally occluded infarct artery is not recommended in asymptomatic patients who are hemodynamically and electrically stable and do not have ischemia. Stone (3,4) provided an excellent 2-part review article on primary angioplasty.

Regional care systems. Several groups reported findings after development of regional systems for STEMI care. Le May et al. (5) reported that acceptable door-to-balloon times are more often achieved when paramedics triage and transport STEMI patients directly to a PCI center compared with patient referral from the emergency department. Aguirre et al. (6), Flesch et al. (7), and Holmes et al. (8) showed that timely mechanical reperfusion can be achieved for patients initially presenting to a non-PCI center, with well-organized transfer protocols and coordinated systems of care.

Time to treatment. Excessive delay to primary PCI continues to be an issue, especially when the patient presents to a non-PCI facility. The National Cardiovascular Data Registry (NCDR) (9) reported that 15,049 patients at 491 hospitals underwent primary PCI after being transferred from a non-PCI facility between 2005 and 2006 (the median door-to-balloon time was 152 min (door-to-door: 109 min and PCI hospital door-to-balloon: 38 min). Although the delay was shortened compared with earlier years (180 min), there remains room for improvement. The Get With the Guidelines database (10) reported 62,814 AMI patients, of whom 5,649 arrived during off hours (nights, weekends, and holidays). Although off-hour patients had longer door-to-balloon times (110 min vs. 85 min, p < 0.001), no measurable differences were found in mortality.

Quality of care. Two important ACC/AHA reports on performance measures for patients with STEMI and NSTEMI were published in 2008 (11,12). These documents are an update of the ACC/AHA report on performance measures in 2006. Key changes include: deletion of

beta-blocker on arrival, revision of 9 measures, and addition of 4 new measures, including evaluation of left ventricular (LV) systolic function, time to transfer and time to PCI for STEMI patients presenting initially to a facility without PCI, and inpatient referral for cardiac rehabilitation. The second article focuses on measurement of time to reperfusion, and provides clarification on specific inclusions and exclusions for this measure, as well as the time point when reperfusion is achieved. Readers are encouraged to examine these documents for more detail.

In other articles, Glaser et al. (13) examined factors contributing to the worse prognosis of STEMI patients presenting during off hours, and found that this seemed to be related to both diurnal differences in patient and lesion characteristics (e.g., more shock and multivessel disease), as well as increased risk of procedural complications (13). Lev et al. (14) compared the predictive value of 4 different risk scores and found that the CADILLAC (Controlled Abciximab and Device Investigation to Lower Late Angioplasty Complications), Thrombolysis In Myocardial Infarction, and PAMI (Primary Angioplasty in Myocardial Infarction) risk scores all had a high predictive accuracy for 30-day and 1-year mortality; however, the Global Registry of Acute Coronary Events risk score had a low predictive value for outcomes.

PCI after thrombolysis. The CARESS in AMI (Combined Abciximab Retaplase Stent Study in Acute Myocardial Infarction) trial (7) treated 600 STEMI patients <75 years of age with half-dose retaplase, abciximab, aspirin, and heparin, then randomized to immediate transfer for PCI versus transfer only for rescue PCI (persistent ST-segment elevation) (15). The combined end point of death, myocardial infarction (MI), or refractory ischemia was improved in the immediate PCI group (4.4% vs. 10.7%, p = 0.004); however, bleeding was increased. In a large French registry, early PCI after full-dose thrombolysis was associated with similar 1-year survival to primary PCI alone (16).

Facilitated PCI. Although facilitated PCI with full-dose thrombolytic agents was found to be harmful, Denktas et al. (17) found that facilitation with reduced-dose thrombolytic agents was safe and effective in a nonrandomized observational experience. A large randomized trial comparing half-dose retaplase plus abciximab had improved ST-segment resolution but no improvement in clinical outcomes to primary PCI (18). Several randomized trials investigated the use of glycoprotein (GP) IIb/IIIa agents for facilitated PCI. Consistently, there was no improvement over primary PCI in randomized comparisons with pre-hospital eptifibatide (19), tirofiban (20), or abciximab (18). These data confirm previous reports that primary PCI without facilitation is the strategy of choice.

GP IIb/IIIa inhibitors. A previous meta-analysis suggested improved mortality using abciximab during primary PCI. The FATA (Facilitated Angioplasty with Tirofiban or Abciximab) trial randomized 738 patients to abciximab versus tirofiban and found better ST-segment resolution in the abciximab group (21). Although abciximab has been shown to reduce stent thrombosis and acute ischemia, a randomized trial of 800 primary PCI patients found no improvement in infarct size with abciximab compared with placebo (22). In another randomized trial, intracoronary abciximab bolus (followed by 12-h intravenous infusion) was superior to intravenous bolus and infusion at improving perfusion and reducing infarct size after primary PCI (23).

Although STEMI studies showing the benefits of GP IIb/IIIa agents have used abciximab, eptifibatide is used more frequently because of cost concerns. In a retrospective analysis of 3,541 STEMI patients undergoing primary PCI use of eptifibatide (n = 2,812) compared with abciximab (n = 729) resulted in similar rates of in-hospital death, MI, or stroke (24). In a retrospective analysis of patients receiving bolus only (n = 1,565) compared with bolus plus infusion (n = 1,064) of GP IIb/IIIa showed similar ischemic outcomes, but reduced bleeding and cost compared with the bolus-only strategy (25).

Bivalirudin. Bivalirudin was found to be superior to heparin (either enoxaparin or unfractionated heparin [UFH]) plus GP IIb/IIIa agents in the HORIZONS AMI (Harmonizing Outcomes with Revascularization and Stents in Acute Myocardial Infarction) trial. Despite an increased risk of acute stent thrombosis with bivalirudin, bleeding and clinical outcomes were improved at 1 month (26) and remained significant at 1 year.

DES. Several registries of DES for AMI found clinical event rates that were similar to (27) or superior to those for BMS (28–31). An editorial suggested a need for better large randomized trials and longer follow-up to address late stent thrombosis and poor patient compliance with medication (32).

Kelbæk et al. (33) randomized 625 STEMI patients to DES versus BMS. At 8 months, angiographic restenosis and target lesion revascularization (TLR) were improved with DES; however, there was a trend for higher mortality. Van der Hoeven et al. (34) found that sirolimus-eluting stents (SES) reduced angiographic restenosis and TLR but were associated with a higher incidence of late stent malapposition. Valgimigli et al. (35) randomized 745 STEMI patients to SES versus BMS and found reduced major adverse cardiac events (MACE) at 8 months. The HORIZONS AMI trial randomized 3,006 patients to paclitaxel-eluting stents (PES) versus BMS; PES was superior at reduction in angiographic restenosis and TLR at 1 year (4.5% vs. 7.5%, p = 0.002) with similar rates of stent thrombosis, MI, and death (36). Lee (37) randomized 328 STEMI patients to zotarolimus-eluting stent (ZES), SES, or PES. Angiographic restenosis was significantly lower with SES compared with other DES; however, clinical outcomes were similar. These data add to the evidence that DES reduce target vessel revascularization (TVR) after primary PCI, and in the short term, seem to be safe.

Late reperfusion. There is still controversy about the role of PCI in patients presenting late after the onset of AMI (>12 h). Abbate et al. (38) performed a meta-analysis of 3,560 patients undergoing PCI versus medical therapy

alone. Late PCI (median 12 days) was associated with a significant improvement in survival (mortality 6.3% vs. 8.4%, odds ratio [OR]: 0.49, p = 0.03) and favorable effect on ventricular function and remodeling. In contrast, the OAT (Occluded Artery Trial) investigators (39) found no benefit of late reperfusion for persistent infarct artery occlusion in stable patients 3 to 28 days after MI.

Distal embolization. Distal embolization is common during infarct angioplasty. Using a Doppler guidewire, Okamura et al. (40) showed that embolization occurs most frequently after stenting, followed by first balloon inflation. Until now, however, most studies have shown little or no benefit of routine thrombectomy in AMI. In the largest trial to date, Svilaas et al. (41) randomized 1,071 AMI patients to adjunctive thrombus aspiration with the 6-F Export catheter (Medtronic, Minneapolis, Minnesota) versus conventional PCI. Thrombus aspiration was associated with a significant improvement in myocardial blush and ST-segment resolution. At 1 year, the thrombus-aspiration group also had a lower incidence of death or re-infarction (42). In another smaller randomized trial, VAMPIRE (VAcuuM asPIration thrombus REmoval), thrombus aspiration was also associated with an improved rate of myocardial blush grade 3, and lower MACE rate at 8 months (43). Vlaar et al. (44) also compared the effectiveness of 2 aspiration catheters (Diver [Invatec, Roncadelle, Italy] versus Export [Medtronic]) and found no difference in size distribution of retrieved thrombotic particles with either device.

A small randomized trial evaluating use of embolic protection showed improved ST-segment resolution in patients treated with a proximal occlusion device (45). In contrast, Kelbæk et al. (46). found no benefit of distal embolic protection with the FilterWire device (Boston Scientific, Santa Clara, California). Dangas et al. (47) also reported that distal protection does not seem to be beneficial in rescue PCI. Finally, Kramer et al. (48) performed histological analysis of aspirated material in 1,315 AMI patients, and found that older thrombus (>1 day) was an independent predictor of long-term mortality.

Adjunctive therapies. Several studies in 2008 investigated novel pharmacologic or mechanical adjuncts to limit myocardial injury in AMI. In a small pilot trial, 58 patients were randomized to receive intravenous cyclosporine or saline immediately before PCI. Infarct size, measured by release of creatine kinase, troponin I, and magnetic resonance imaging in a subgroup, was significantly smaller in patients who received cyclosporine (49). In another trial, intracoronary KAI-9803 in anterior MI patients with total occlusion of the left anterior descending artery (LAD) led to favorable improvements in ST-segment resolution, creatine kinase release kinetics, myocardial perfusion grade, and infarct size (50). Ishii et al. (51) provided a review article summarizing the role of various other pharmacologic adjuncts to reperfusion therapy, including adenosine, atrial natriuretic peptide, nicorandil, and statins. Left ventricular unloading seems to be another promising strategy for reducing infarct size. Sjauw et al. (52) studied the effect of unloading with the Impella 2.5 (Abiomed, Danvers, Massachusetts) percutaneous LV assist device in nonshock anterior AMI. Patients treated with the Impella 2.5 device had a greater improvement in LV ejection fraction at 4 months compared with a control group.

Cardiogenic shock. Seyfarth et al. (53) reported results of a small randomized trial evaluating the Impella 2.5 device in cardiogenic shock. Compared with intra-aortic balloon pump, patients treated with the Impella 2.5 device had a higher cardiac index and less lactic acidosis. An interesting report from Apolito et al. (54) suggests that public reporting of outcome data may deter physicians from providing revascularization to shock patients. In this analysis, New York patients were less likely to receive angiography or PCI, and also waited significantly longer to receive a coronary artery bypass graft (CABG) than non–New York patients with shock. Reynolds et al. (55) provided a comprehensive review article of etiology, pathophysiology, and contemporary treatment of cardiogenic shock complicating AMI.

Cell therapy. Two meta-analyses examined the concept of stem cell therapy after AMI. Zohlnhöfer et al. (56) reported 10 trials that randomized 445 patients to control versus granulocyte colony stimulating factor to augment the number of circulating stem cells after AMI. There was no significant difference in infarct size and ejection fraction between the treatment groups. Conversely, selective infusion of stem cells into the infarct artery resulted in improved ejection fraction and reduced infarct size in a meta-analysis of 13 trials and 811 patients (57).

Acute Coronary Syndromes (ACS)

Steg et al. (58) studied outcomes in patients with NSTEMI and CHF in the Global Registry of Acute Coronary Events. Patients with CHF were less likely to undergo revascularization than those without CHF. After adjustment for differences in baseline risk, revascularized patients had lower 6-month mortality, suggesting that broader use of PCI in these high-risk patients may be beneficial. Ndrepepa et al. (59) reported 1-year outcomes of the ISAR-REACT 2 (Intracoronary Stenting and Antithrombotic Regimen–Rapid Early Action for Coronary Treatment 2) randomized trial. In high-risk patients with NSTEMI undergoing PCI after pre-treatment with 600 mg clopidogrel, adverse events occurred less frequently with abciximab. Mehta (60) presented results of a randomized trial of an early (within 24 h of symptom onset) versus delayed (>36 h) invasive strategy in high-risk ACS patients. The early strategy did not reduce the incidence of the composite end point of death, MI, or stroke at 6 months; however, there was a reduction in the incidence of refractory ischemia in the early invasive arm.

Elective PCI

Left main disease. Current American and European guidelines recommend CABG for unprotected left main (ULM) disease, with PCI reserved only for patients who are high risk, inoperable, or refuse surgery. Taggart et al. (61) summarized the surgical consensus, namely that CABG is proven therapy, and that PCI has limited value and may even be inferior to medical therapy for patients not suitable for surgery. Teirstein (62) provided a more balanced overview, and pointed out that numerous unanswered questions remain before routine PCI of ULM disease can be recommended.

In 2008, a number of registries and randomized trials began to provide clarity on the role of ULM PCI. Biondi-Zoccai et al. (63) performed a meta-analysis of 16 studies of DES implantation for ULM disease. Among 1,278 patients treated with a DES, in-hospital and 6-month mortality were 2.3% and 5.5%, respectively. The MACE and TVR rates were significantly lower in ostial and shaft lesions versus distal bifurcation disease. The rate of MACE was lower for DES compared with BMS, driven mainly by a lower rate of restenosis and TVR. The DELFT (Drug Eluting stent for LeFT main) registry (64) reported outcomes for 358 consecutive patients with ULM disease. Procedural success was 89.6%, and in-hospital mortality was 3%. Overall 3-year mortality was 9.2%.

The optimal technical approach to distal left main stenting is unclear. Palmerini et al. (65) provided data from a large, multicenter Italian registry in which 773 patients underwent PCI for distal left main disease (1 stent in 456 patients, 2 stents in 317). The adjusted 2-year survival was significantly better for the single- versus 2-stent strategy. When 2 stents were used, there was no difference between crush versus T-stent versus culotte techniques. Thus, like other bifurcation disease, distal left main disease should be treated with single stent implantation if technically possible.

Mehilli (66) presented results of a randomized trial of SES versus PES in 607 low-risk patients with ULM disease (ISAR-LEFT MAIN [Intracoronary Stenting and Angiograpic Results: Drug Eluting Stents for Unprotected Coronary Left Main Lesions]). The primary end point, 1-year MACE, was similar between SES- and PES-treated patients (15.8% vs. 13.6%). Angiographic restenosis was also similar (19.4% vs. 16.0%).

Several nonrandomized comparisons of PCI versus CABG for ULM disease were published in 2008. Seung et al. (67) reported outcomes in 2,240 patients treated with PCI or CABG from January 2000 to June 2006. In this matched comparison, there was no difference in long-term mortality or the composite of death, MI, or stroke, but a higher rate of TVR was observed in patients treated with PCI. Other studies also reported similar survival between PCI- and CABG-treated patients (68–70). White et al. (71) provided further insight by stratifying outcomes according to baseline risk. Survival was similar for low-risk

patients. However, survival was lower among high-risk patients treated with PCI. In aggregate these registries suggest equipoise for low-risk patients with ULM disease and provide an excellent foundation for several recently completed randomized trials.

The first of these randomized trials is the Polish LE MANS (Study of Unprotected Left Main Stenting Versus Bypass Surgery) trial (72). Buszman et al. (72) randomized 105 low-risk patients (age 60 years, LV ejection fraction 53%) and found greater improvement in late LV ejection fraction (3.3 ± 6.7% vs. 0.5 ± 0.8%, p = 0.047) for PCI-treated patients compared with CABG.

Serruys (73) presented results of the left main subset of the SYNTAX (Synergy between Percutaneous Coronary Intervention with Taxus and cardiac surgery) study (348 patients randomized to CABG, 357 randomized to Taxus stent implantation [Boston Scientific, Minneapolis, Minnesota]). Patients were low risk (Euroscore 3.9, age 65 years, 75% male). At 1 year, mortality was similar in both arms (4.4% CABG vs. 4.2% PCI, p = NS), but there was a higher incidence of stroke in the CABG group (2.7% vs. 0.3%, p = 0.009). Repeat revascularization at 1 year was higher in the PCI arm (12.0% vs. 6.7%, p = 0.02). The combination of these registries and the SYNTAX trial now allow clinicians to make more scientific decisions about revascularization for ULM disease. The higher the patient risk, the more likely that CABG improves survival. Conversely, low-risk patients, especially those without bifurcation disease, seem to be well suited for PCI with DES implantation.

Multivessel disease. The year 2008 started with an anti-PCI groundswell. The New York State database was analyzed by Hannan et al. (74). This large, prominently publicized article reported on all New York State patients with multivessel disease who had PCI or CABG from January 2003 to December 2004 and were followed up until December 2005. A total of 9,965 patients underwent PCI, and 7,437 patients underwent surgery. Patients with ULM and AMI were excluded. Unadjusted survival was similar. After adjustment for differences in baseline variables, CABG treated patients with 3- and 2-vessel disease with proximal LAD involvement had lower mortality. Park et al. (75) studied 3,042 patients with multivessel disease treated from January 2003 to December 2004. Unadjusted 3-year mortality was higher for CABG (7.0% vs. 4.4%, p = 0.01). Adjusted mortality was similar. These 2 large registries show that such large differences are present in baseline severity of illness and surgical and PCI outcomes that fundamental scientific differences cannot be found without properly sized randomized trials.

Two moderate-sized randomized trials presented midterm follow-up. Booth et al. (76) followed up 988 patients for 6 years who were treated with PCI (n = 488) or CABG (n = 500). Mortality was greater for PCI patients at 2 years, and this persisted at 6-year follow-up (10.9% vs. 6.8%, p = 0.02). The ARTS (Arterial Revascularization Therapies

Study) investigators (77) followed up 607 multivessel DES-treated patients for 3 years. Outcomes were compared with surgical patients and non-DES stent patients in the ARTS I study. In addition, outcomes for the 159 diabetic patients in ARTS II were compared with the ARTS I cohort. These data show that for ARTS-eligible patients, overall 3-year survival and 3-year risk of stroke is similar for DES, non-DES, and CABG therapy. Differences in outcomes were greater in the diabetic subgroups. There was a trend toward lower mortality for CABG and DES compared with non-DES therapy. In addition, risk of cerebrovascular accident diverges for the 3 treatments. Daemen et al. (78) provide a meta-analysis of the ARTS I, ERACI II (Argentine Randomized Trial of Coronary Angioplasty with Stenting Versus Coronary Bypass Surgery in Patients with Multiple Vessel Disease), MASS II (Medicine, Angioplasty, or Surgery Study II), and SOS (Stenting Of Saphenous vein grafts) trials. Five-year follow-up in the 3,051 patients randomized to stent or surgery therapy are presented. Risk of death, stroke, and MI was 16.7% vs. 16.9% (p = NS). Risk for TVR was higher for the stent therapy (29% vs. 7.9%, p = 0.001). For diabetic patients, mortality trended higher in the PCI group (12.4% vs. 7.9%, p = 0.09).

Results of the 3-vessel disease subset of the SYNTAX (Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery) study were also presented; 1,095 patients were randomized to CABG (n = 549) or multivessel PCI with the Taxus DES (n = 546) (79). At 1 year there was no difference in the incidence of death, MI, or stroke; however, the rate of revascularization was significantly higher in the PCI group (14.7% vs. 5.4%, p < 0.001). The difference in MACE was greatest in patients with high baseline risk (SYNTAX score ≥33).

Finally, Pijls (80) presented results of the FAME (Fractional Flow Reserve versus Angiography for Multivessel Evaluation) trial, which randomized 1,005 patients with stenoses ≥50% to angiography-guided PCI or fractional flow reserve (FFR)-guided PCI. Patients in the FFR-guided group were less likely to receive a stent (1.9 ± 1.3 vs. 2.7 ± 1.2 stents/patient). At 1 year, patients in both groups had similar angina relief; however, the composite end point of death, MI, or TVR was significantly lower in the FFR group (13.2% vs. 18.4%, p = 0.02).

Isolated proximal LAD disease. Goy et al. (81) presented 10-year follow-up of 123 patients treated with PCI (n = 52) or CABG (n = 59). MI-free survival was excellent at 90% for both groups. PCI patients had a 26% rate of TVR, whereas no CABG-related patients required TVR at 10-year follow-up. Kapoor et al. (82) performed a meta-analysis of 9 randomized trials of PCI or CABG for proximal LAD disease (633 PCI-treated patients, 577 CABG-treated patients). The 5-year survival was similar (92.8% vs. 90.6%); TVR was higher for PCI (33% vs. 7.3%). Angina relief was greater with CABG.

PCI versus medical therapy. Holmes (83) provided an excellent review of the subject and concluded that PCI provides superior angina relief versus medical therapy, but does not prevent MI or death. Weintraub et al. (84) confirmed these findings in a quality-of-life analysis from the COURAGE (Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation) trial. Angina relief and quality of life was better initially for PCI therapy, but this benefit disappeared at 3 years. Both authors conclude that for patients with stable coronary artery disease and mild or no symptoms, initial medical therapy is an acceptable alternative to initial PCI therapy. Schomig et al. (85) performed a meta-analysis of 17 randomized trials comparing PCI and medical therapy. Unlike the COURAGE trial, Schomig included stable post-MI patients. In this analysis, mortality was lower for PCI therapy, especially in patients with recent MI who had angina or exercise-induced ischemia.

No surgery on site. There has been debate about the safety and results of PCI at facilities without on-site cardiac surgery. In one of the largest series to date, Frutkin et al. (86) reported outcomes of 1,090 elective PCIs performed at a hospital without cardiac surgery. A low incidence of complications was observed, and only 2 patients required transfer for emergency CABG. It is important to note that this center has highly experienced interventionalists and well-defined protocols for transfer.

Outcomes research. In 2008, there were many reports addressing clinical outcomes after PCI. Singh et al. (87) studied sex differences in mortality after PCI among 18,885 patients treated at the Mayo Clinic. A significant improvement in survival was seen for both men and women over the past 25 years. After adjustment for baseline risk, no difference in short- or long-term mortality was observed between men and women. In another report, Singh et al. (88) provided validation for the new Mayo Clinic Risk Score model in a large patient cohort from the NCDR. This risk score, which uses 7 simple clinical and noninvasive variables, provides clinicians an excellent tool for risk assessment and decision making before diagnostic angiography.

Rao et al. (89) studied trends in use of the radial approach for PCI. Among 593,094 patients, radial PCI was performed in only 1.32% of total procedures, although an increase was observed in 2007. Lower rates of bleeding and vascular complications were seen with the radial approach.

Applegate et al. (90) examined trends in vascular complications after diagnostic catheterization and PCI in 35,016 procedures from 1998 to 2007. A significantly lower incidence of vascular complications was observed during this time, which the investigators attributed to improvements in procedural factors such as use of fluoroscopy-guided femoral access and smaller sheath sizes. Similarly, Doyle et al. (91) reported a marked decline in the incidence of major femoral bleeding after PCI over the past decade. The relationship between peri-procedural bleeding and 1-year outcome was emphasized in a report from Ndrepepa et al. (92). Bleeding within 30 days independently predicted 1-year mortality (hazard ratio: 2.96, p < 0.001).

Two studies evaluated the impact of pre-procedural cardiac troponin levels on outcome after PCI (93,94). Both studies showed that baseline elevation of the cardiac troponin level is an important predictor of ischemic complications and prognosis. In another report, Wang et al. (95) found that the majority of hospitals in the U.S. do not systematically assess cardiac markers after elective PCI. As expected, hospitals that routinely performed biomarker testing had higher rates of periprocedural MI; however, these hospitals had a trend toward lower mortality and greater adherence to recommended medications.

From et al. (96) examined outcomes in 138 nonagenarians undergoing PCI and observed high technical success and good clinical outcomes in carefully selected patients. In other reports, Mercado (97) found that urinary dipstick proteinuria was independently associated with mortality in patients undergoing PCI. Kip et al. (98) highlighted the wide heterogeneity in definition of the term MACE, and recommend that investigators design separate composite end points for evaluation of safety and effectiveness outcomes.

Bifurcation disease. Percutaneous treatment of bifurcation disease remains challenging. Ormiston et al. (99). provided insight into crush bifurcation stenting and post-dilation strategies using microcomputed tomography in bench deployments. Importantly, less side-branch ostial stenosis was observed with 2-step kissing post-dilation, the minicrush technique compared with conventional crush, and use of stents with larger cell size (>3.5 mm).

Three clinical trials evaluating treatment of bifurcation lesions were presented at the Transcatheter Cardiovascular Therapeutics conference. The BBC-ONE (British Bifurcation Coronary study: Old, New and Evolving strategies) study (100) randomized 500 patients with bifurcation lesions to complex stenting (crush or culotte) or simple stenting (main vessel with provisional T-stent) using the Taxus stent. At 9 months, the primary end point, a composite of death, MI, and target vessel failure, was significantly lower in the simple stent arm (8.0% vs. 15.2%, p = 0.009). Stent thrombosis was higher with complex stenting (2.0% vs. 0.4%). In another study, Routledge et al. (101) also showed excellent clinical outcomes associated with a simple stent strategy. Among 424 consecutive patients, the provisional side-branch stent strategy was used in 92% of patients with a high initial success rate, and a low rate of MACE at 2 years (13.6%). This important shift in thinking to use a 1-stent technique as the default for most patients was further emphasized in a review by Latib and Colombo (102).

The Nordic Bifurcation Stent Technique study (103) compared outcomes with the crush and culotte stent strategies in 424 patients using the Cypher (Cordis Corp., Miami, Florida) SES. There was no difference in clinical outcomes at 6 months. Angiographic follow-up at 8 months showed a very low rate of restenosis in the main vessel with either stent technique, but a higher restenosis rate in the side branch with the crush technique (9.8% vs. 3.8%).

The DIVERGE (Drug-Eluting Stent Intervention for Treating Side Branches Effectively) trial (104) evaluated the Axxess biolimus A9-eluting stent in 302 patients. At 9 months there was a low rate of MACE (7.7%) and ischemic TLR (4.3%) with this novel self-expanding stent.

Vein graft disease. The AMEthyst (Assessment of the Medtronic AVE Interceptor Saphenous Vein Graft Filter System) trial (105) compared use of the Interceptor PLUS Coronary Filter System (Medtronic Vascular, Santa Rosa, California) with approved devices during vein graft intervention. At 30 days the primary end point MACE occurred in 8% of Interceptor and 7.3% of control patients, thus showing noninferiority of this novel embolic protection device.

Two studies evaluated determinants of adverse outcome after vein graft PCI. In a pooled analysis of 3,958 patients, Coolong et al. (106) identified angiographic variables, including saphenous vein graft (SVG) degeneration and estimated plaque volume, as the strongest predictors of 30-day MACE. Similarly, Kirtane et al. (107) found that lesion length was the strongest correlate of outcome in a substudy of the PRIDE (PRotection during saphenous vein graft Intervention to prevent Distal Embolization) trial. Additionally, both analyses confirmed a clear benefit of embolic protection across a range of angiographic risk, including patients with relatively short lesions.

Chronic occlusion. Safley et al. (108) studied long-term survival in 2,608 patients undergoing PCI for chronic total occlusion (CTO). Notably, successful PCI for CTO of the LAD was associated with an improved 5-year survival; however, there was no difference in outcome for successful recanalization of the circumflex or right coronary arteries. To evaluate the physiologic effect of CTO revascularization, Cheng et al. (109) performed serial cardiac MRI in 17 patients undergoing CTO PCI. Successful PCI resulted in a significant increase in myocardial blood flow and contractility at 24 h that persisted at 6 months. Courtney et al. (110) published an excellent review article describing the role of cardiac imaging techniques in assisting with patient selection for PCI, as well as innovative technologies that may enhance procedural success.

Direct stenting. Two studies published in 2008 showed a benefit of direct stenting compared with stenting after pre-dilation. Ormiston et al. (111) found that direct stenting with the Taxus Liberté PES in carefully selected lesions was associated with significantly reduced procedural time, procedural complications, and possibly restenosis. In a small randomized trial, Cuisset et al. (112) measured microcirculatory resistance with an intracoronary pressure/temperature sensor-tipped guidewire and found less microcirculatory dysfunction in patients with stable angina treated with direct stenting compared with conventional stenting.

Radiation safety. There has been increasing awareness about radiation exposure to the interventionalist. Brasselet et al. (113) compared radiation dosage to the operator between femoral and radial coronary procedures. Radiation

exposure to operators was significantly higher using the radial approach compared with the femoral approach despite optimizing radiation protection. This study clearly highlights the need for novel radiation protection systems to reduce operator risk.

DES

Stent thrombosis. In a registry of 8,146 patients treated with DES, stent thrombosis was observed in 3.3% at 4 years (114). Diabetes was predictive of early stent thrombosis, whereas ACS, younger age, and use of PES were associated with late stent thrombosis. In a Spanish registry of 23,500 patients treated with DES, stent thrombosis was observed in 2% at 3 years (115). Predictors of early stent thrombosis included diabetes and renal failure; both early and late stent thrombosis was increased in patients with ACS, LAD stenting, and longer stent length.

Based on predictors of stent thrombosis, Baran et al. (116) developed a risk score (discontinuation of thienopyridine <6 months, diabetes mellitus, lesion length >28 mm, multiple stents, vessel <3 mm diameter, calcification, or left main stent). Stent thrombosis occurred in 0.8% of low-risk patients, 3.6% of medium-risk patients, and 12.6% of high-risk patients.

Although the Endeavor (Medtronic, Santa Rosa, California) DES was thought to have low rates of stent thrombosis, a registry of 3,680 patients treated with second-generation DES (117) found no difference in stent thrombosis rates between Xience (Abbott Vascular, Santa Clara, California) and Endeavor DES. Of concern, Maeng (118) reported 6,122 patients treated with Endeavor or SES in the Western Denmark Heart Registry and found that adjusted rates of death, TVR, and stent thrombosis were higher with Endeavor.

SORT OUT III (The Danish Organization on Randomized Trials with Clinical Outcome), a randomized trial of 2,333 patients, found higher rates of stent thrombosis, MI, and TVR with Endeavor compared with SES (119). Reassuringly, the SORT OUT II trial found no differences in MACE among 2,098 patients randomized to SES versus PES (120).

Mechanisms of DES thrombosis. Numerous articles were published in 2008 attempting to elucidate mechanisms of stent thrombosis. In a porcine model, overlapping PES resulted in marked intramural thrombi and impaired vasoreactivity (121). An intravascular ultrasound substudy of the Taxus trials found that PES was associated with reduced intimal hyperplasia but expansive remodeling at 9 months (122), possibly contributing to late malapposition.

Acute stent malapposition was observed in 35% of STEMI patients undergoing DES or BMS, and late stent malapposition was observed in DES patients because of positive remodeling (123). An autopsy study (124) suggested that delayed healing and stent thrombosis occurred more frequently when DES was placed in unstable compared with stable plaques. An optical coherence tomography study (125) found that neointimal coverage improved between 3 and 24 months, but the majority of DES still had some uncovered struts. A rabbit study (126) suggested that delayed healing was caused by the polymer (not the drug) on the DES. Another rabbit study (127) found that everolimus-eluting stent had superior endothelialization compared with SES, PES, or ZES. Finally, first-generation DES have been associated with endothelial dysfunction distal to the stent (128–130), and this may be improved with second-generation DES (131). These data suggest that newer-generation stents may improve endothelialization and vasomotor dysfunction.

Late outcome of DES versus BMS. The New York State Registry (132) compared 11,436 patients treated with BMS (before the release of DES) and 12,526 patients treated with DES. The risk-adjusted 2-year outcomes were favorable in the DES group, including improved nonfatal MI and TVR; mortality rates were similar. Likewise, the Medicare database (133) found reduced rates of repeat PCI, CABG, and STEMI after stenting in the DES era (61.5% received DES, 38.5% BMS) compared with the BMS era. Another Medicare analysis of 76,525 patients who received DES (134) was compared with 2 matched cohort control groups. The DES patients were found to have improved survival as well as reduced TVR and MI compared with both BMS cohorts. The Massachusetts registry (135) compared 11,556 DES patients and 6,237 BMS patients. Two-year risk-adjusted outcomes were superior in the DES group, including mortality (9.8% vs. 12.0%, p = 0.0002), MI (8.3% vs. 10.3%, p = 0.0005), and TVR (11.0% vs. 16.8%, p < 0.0001). The Cleveland Clinic group (136) examined 832 patients who died over a 4.5-year follow-up after stenting. They reported that DES-treated patients had lower all-cause mortality in unadjusted and adjusted Cox proportional models and propensity-matched groups.

Off-label use of DES. Several groups reported comparisons of DES versus BMS in off-label applications (137–142). In general, off-label use of both DES and BMS are associated with higher event rates compared with on-label use (consistent with higher-risk clinical and lesion characteristics). However, DES seemed to have similar or improved rates of death or MI compared with BMS, and consistently reduced need for TVR. Overall, these data support the use of DES for off-label indications.

DES in diabetic patients. Diabetes is a powerful predictor of adverse clinical and angiographic events after PCI. Three separate registries compared DES with BMS in diabetic patients and found reduced TVR with similar or improved rates of MI or death (143–145). Subgroup analysis from randomized trials of DES versus BMS found markedly lower rates of TVR, with similar rates of death, MI, and stent thrombosis at 4 years (146). A meta-analysis of registries and randomized trials including more than 11,000 diabetic patients reported revascularization rates of <10% with similar outcomes comparing PES and SES (147). Conversely, a

subgroup analysis of the SIRTAX (Sirolimus-Eluting versus Paclitaxel-Eluting Stents for Coronary Revascularization) trial (148) showed reduced TVR with SES compared with PES, and a prospective trial randomizing 400 diabetic patients to SES versus PES (149) found reduced angiographic restenosis at 6 months (3.4% vs. 18.2%, p < 0.001) and TVR at 9 months (2.0% vs. 7.5%, p = 0.017) after SES.

DES in vein grafts. Saphenous vein graft interventions remain a higher-risk subgroup for PCI. Pucelikova et al. (150) reported 110 patients undergoing SVG stenting (DES in 91%). At 1 year, death occurred in 7.4%, TVR in 19.0%, and MACE in 30.5%. Predictors of MACE included thrombus and length of stented segment. Okabe et al. (151) reported a retrospective series of 138 patients treated with DES in SVG compared with 344 patients treated with BMS to SVG. At 1 year, there was no advantage to DES with regard to death, MI, or TVR. The SOS study (152) randomized 80 patients to undergo stenting of SVG with PES versus BMS. The lesions were relatively focal with mean stent length 16 ± 6 mm. At 12-month angiography, late loss and restenosis (9% vs. 51%, p < 0.0001) favored PES, and at 1.5-year follow up, TLR was reduced (5% vs. 28%, p = 0.003).

DES for in-stent restenosis. Long-term (>3 years) follow-up of a trial that randomized 150 patients with in-stent restenosis to SES versus percutaneous transluminal coronary angioplasty (153) reported that stent thrombosis was similar in the 2 groups but event-free survival was superior with SES (76% vs. 65%, p = 0.019). The 24-month follow-up of the Taxus V in-stent restenosis trial (154) found reduced TLR with PES compared with brachytherapy (18.1% vs. 27.5%, p = 0.03) with similar rates of death, MI, and stent thrombosis. In another trial, Holmes (155) also found improved outcomes with SES versus brachytherapy at 3-year follow-up.

New Stent Technologies

New DES and polymers. In 2008, there were several publications of new DES technologies. In the SPIRIT III trial, 1,002 patients were randomly assigned to receive either an everolimus-eluting stent or a PES (156). The primary end point, angiographic in-segment late loss at 8 months, was significantly less in the everolimus stent group (0.14 mm vs. 0.28 mm, p ≤ 0.004). The rate of MACE at 9 and 12 months was lower in the everolimus group. In a small randomized trial, a novel ZES (ZoMaxx, Abbott Laboratories, Abbott Park, Illinois) resulted in significantly greater late lumen loss compared with a PES (157).

Turco et al. (158) studied outcomes with the thinner-strut Taxus Liberté stent compared with the Taxus Express stent. In small vessels and long lesions, lower rates of restenosis were observed with the Liberté DES.

Several trials evaluated new DES technologies with biodegradable polymers or polymer-free stents. These new-generation stents were designed to improve the safety profile of first-generation DES. Windecker et al. (159) randomized 1,707 patients to a novel biolimus-eluting stent with a biodegradable polymer or SES (with durable polymer). At 9 months, the biolimus-eluting stent was noninferior to the SES for the composite clinical end point. Byrne (160) studied a novel polymer-free dual probucol and rapamycin–eluting stent. Angiographic restenosis and late loss were similar to a permanent polymer SES, but superior to a ZES. In the ISAR-TEST 3 (Intracoronary Stenting and Angiographic Restenosis–Test Efficacy of Rapamycin-eluting Stents with Different Polymer Coating Strategies) trial, Mehilli et al. (161) compared 3 rapamycin-eluting stents (biodegradable polymer vs. permanent polymer vs. polymer-free). The biodegradable SES had a similar rate of angiographic late loss to the permanent polymer stent; however, the polymer-free stent had a significantly higher late loss (0.17 mm vs. 0.23 mm vs. 0.47 mm, respectively). Jabara et al. (162) showed improved vascular healing in an animal model using a new DES with a slow-release biodegradable polylactide polymer and low-dose paclitaxel. In a first-in-man study, Costa et al. (163) evaluated a novel stainless-steel platform with a nanothin-microporous hydroxyapatite surface coating impregnated with a polymer-free sirolimus formulation (Vestasync-eluting stent, MIV Therapeutics, Inc., Atlanta, Georgia). At 4 months, in-stent late loss was 0.30 ± 0.25 mm). No adverse events were observed at 6 months.

In contrast to these promising results, a randomized trial evaluating the CoStar DES (Conor MedSystems, Menlo Park, California) (164) found that this novel platform was not noninferior to a Taxus DES. At 8 months, the incidence of MACE (11.0% vs. 6.9%, p < 0.005) and late loss (0.49 mm vs. 0.18 mm, p < 0.0001) were significantly higher with the CoStar stent.

Bioabsorbable stents. There has been tremendous interest in fully biodegradable coronary DES. Ormiston et al. (165) reported findings from a 30-patient study using a bioabsorbable everolimus-eluting stent that has a backbone of poly-L-lactic acid. At 6 months, angiographic late loss was 0.44 mm, mainly because of a mild reduction of the stent area, with minimal neointimal hyperplasia. Device success was 94%. This study represents a major step forward in clinical investigation of bioabsorbable stent technologies.

Pharmacotherapy

Clopidogrel. Given the short door-to-balloon times, some have questioned the benefit of pre-treatment with clopidogrel before primary PCI. Vlaar et al. (166) performed a meta-analysis of all primary PCI trials with core laboratory angiographic reviews in which pre-treatment status with clopidogrel was known (n = 8,429). In multivariate analysis, pre-treatment with clopidogrel was an independent predictor of early reperfusion (OR: 1.51, 95% confidence interval: 1.31 to 1.74, p < 0.0001) and improved clinical outcome. Conversely, the PRAGUE-8 trial (167) randomized 1,028

patients with stable angina to pre-treatment with 600 mg clopidogrel >6 h before catheterization versus selective administration after initial angiography showed the need for PCI. Pre-treatment with a high loading dose was associated with increased bleeding risk, but no difference in ischemic end points. However, this study was underpowered given the low event rate (0.8%).

Other studies have shown that 600-mg loading doses of clopidogrel achieve stronger platelet inhibition compared with conventional regimens (168). Even patients on chronic clopidogrel therapy have improved platelet inhibition if reloaded with clopidogrel (169). Moreover, the ARMYDA (Antiplatelet therapy for Reduction of MYocardial Damage during Angioplasty) Reload trial (170) showed that ACS patients on chronic clopidogrel therapy benefited from 600-mg reload. The primary end point of 30-day death, MI, or TVR was significantly reduced in the reload group (7% vs. 18%, p = 0.035).

Clopidogrel hyporesponsiveness continued to be an important topic in 2008. Gori et al. (171) showed that dual nonresponsiveness to both aspirin and clopidogrel was infrequent (6%) but identified patients at high risk of DES thrombosis or death. Studies utilizing the Accumetrics (San Diego, California) device (a more rapid and specific measure of P2Y12 responsiveness) found that pre-PCI (172) and post-PCI (173) platelet reactivity was associated with MACE. Increasing the clopidogrel dose in patients who were resistant to the first 600-mg load (vasodilator-stimulated phosphoprotein index >50%) was found to be safe and improved clinical outcomes (174).

Although a number of factors may influence clopidogrel hyporesponsiveness, Trenk et al. (175) found a genetic pre-disposition that influenced the cytochrome P450–dependent conversion of clopidogrel to its active metabolite. External influences may include smoking, which increases active metabolites (176), or medications, such as the proton pump inhibitor omeprazole, which decreased the antiplatelet effect of clopidogrel (177).

Prasugrel. More potent or more-rapid-acting oral antiplatelet regimens seem to be superior to conventional dual antiplatelet therapy with clopidogrel and aspirin. In the TRITON–TIMI (TRial to Assess Improvement in Therapeutic Outcomes by Optimizing Platelet InhibitioN with Prasugrel–Thrombolysis In Myocardial Infarction) 38 trial (178), prasugrel plus aspirin was superior to clopidogrel plus aspirin with regard to stent thrombosis (1.13% vs. 2.35%, p < 0.0001) and the primary end point of cardiovascular death, MI, or stroke (9.7% vs. 11.9%, p = 0.0001). Significant advantages of prasugrel were observed regardless of whether patients received DES (n = 5,743) or BMS (n = 6,461). Because prasugrel was associated with more bleeding than clopidogrel, a landmark analysis (179) found that net clinical benefit favored prasugrel both early (day 0 to 3) and later (day 3 to end of trial).

Cilostazol. Triple antiplatelet therapy (adding cilostazol to clopidogrel + aspirin) has previously been shown to reduce platelet aggregation and restenosis. Park (180) reported a registry of 3,099 patients undergoing successful DES placement who were treated with triple (n = 1,443) or dual (n = 1,656) antiplatelet therapy. After adjustment for selection bias (multiple high-risk features were more common in the cilostazol group), triple antiplatelet therapy was associated with reduced stent thrombosis and MI. Lee et al. (181) randomized 400 diabetic patients treated with DES to receive triple (with cilostazol) versus dual antiplatelet therapy. Triple antiplatelet therapy significantly reduced angiographic restenosis at 6 months (8.0% vs. 15.6%, p = 0.03), 9-month TLR (2.5% vs. 7.0%, p = 0.03), and MACE (3.0% vs. 7.0%, p = 0.066).

Bivalirudin. Several studies examined the use of bivalirudin during PCI. Bivalirudin was found to be cost effective compared with UFH and GP IIb/IIIa (182). One-year follow-up of the ACUITY (Acute Catheterization and Urgent Intervention Triage Strategy) trial found similar rates of ischemia and mortality but a trend for higher rates of MI in the bivalirudin arm (9.3% vs. 7.8%, p = 0.06) compared with UFH and GP IIb/IIIa (183,184).

The ARNO (Antithrombotic Regimens aNd Outcome) trial (185) randomized 900 patients undergoing PCI to bivalirudin versus UFH 100 μ/kg; both groups were pre-treated with clopidogrel and had immediate sheath removal and closure devices. Bivalirudin was associated with a reduction in major bleeding and improved net clinical benefit. The NAPLES (Novel Approaches for Preventing or Limiting Event Study) trial (186) randomized 335 diabetic patients pre-treated with clopidogrel to bivalirudin versus UFH with tirofiban. At 30 days, ischemic events were similar and bleeding was reduced in the bivalirudin arm. Feit et al. (187) reported similar results from subgroup analysis of diabetic patients from the ACUITY trial.

The ISAR-REACT 3 trial (188) randomized 4,570 patients pre-treated with 600 mg clopidogrel to UFH versus bivalirudin. Net clinical benefit was not different between the 2 groups, but bleeding was lower with bivalirudin (3.1% vs. 4.6%, p = 0.008).

Finally, given concerns about the early increase in ischemic events observed in bivalirudin patients not adequately pre-treated with clopidogrel, Cortese (189) reported a study of 178 patients requiring complex PCI who were randomized to conventional versus prolonged (4 h post-PCI) infusion of bivalirudin. Bleeding rates were similar (87% radial access), but reduced post-PCI MI was observed with the prolonged infusion.

Fondaparinux. Mehta et al. (190) pooled the OASIS (Organization to Assess Strategies in Ischemic Syndromes) 5 and 6 trials comparing fondaparinux with heparin (or enoxaparin) and reported a beneficial effect in patients treated with an invasive (cardiac catheterization) strategy. However, among patients undergoing PCI, there was a significant increased risk of catheter thrombosis with fondaparinux compared with enoxaparin (OR: 3.98, 95%

confidence interval: 1.74 to 9.09) and compared with UFH (OR: 8.98, 95% confidence interval: 1.14 to 71.43).

No antithrombin therapy. The CIAO (Coronary Interventional Antiplatelet-based Only) study (191) randomized 700 stable angina patients with uncomplicated lesions who were pre-treated with aspirin and clopidogrel to heparin versus placebo. Catheters were flushed with heparinized saline (up to 100 times per procedure) and procedure times were short (mean 11 min). Bleeding and clinical events were reduced in the no heparin arm, suggesting that antithrombins may be unnecessary in highly selective, simple elective PCI cases.

Patients on warfarin. There are few data regarding management of PCI patients requiring long-term anticoagulation with warfarin. Karjalainen et al. (192) reviewed outcomes in 241 PCI patients (80% femoral approach). Mean international normalized ratio at PCI was 2.2 ± 0.5. Access site complications and major bleeding occurred in 5.0% and 1.2% of patients, respectively. These data suggest that uninterrupted anticoagulation is a reasonably safe approach in carefully selected patients. Rossini et al. (193) studied outcomes in patients requiring triple therapy compared with dual antiplatelet therapy alone. As expected, bleeding was more frequent in patients with triple therapy; however, this excess risk was seen mostly in patients with an international normalized ratio >2.6.

Contrast Nephropathy

Results of 2 randomized trials evaluating the effect of sodium bicarbonate infusion for prevention of contrast-induced nephropathy (CIN) were published in 2008 (194,195). Both trials enrolled patients with stable renal dysfunction (creatinine clearance <60 ml/min) undergoing coronary angiography or PCI. Compared with saline infusion alone, there was no difference in the incidence of CIN with bicarbonate in either trial. A 1,307-patient meta-analysis by Hogan et al. (196) suggested a possible benefit of bicarbonate; however, this study was limited by marked heterogeneity and probable publication bias, and did not include data from the largest randomized trial by Maioli et al. (195). Kane et al. (197) provided a report emphasizing the importance of minimizing contrast dose in patients with renal dysfunction, and showed a very low rate of CIN in those who receive ultra-low-dose contrast. Harjai et al. (198) compared the value of 4 different definitions for CIN commonly used in studies and found that only 2 (serum creatinine >25% and serum creatinine >0.5 mg/dl) were consistently predictive of clinical outcomes. Based on these data, a novel nephropathy grading system was developed to predict 6-month events. Stone (199) reported findings from of a trial evaluating systemic cooling to prevent CIN. Unfortunately, only 136 of the planned 400 patients were enrolled because the study sponsor became insolvent. Cooling was safe and well tolerated, but no benefit of hypothermia was observed. Finally, McCullough (200) provided an excellent review article on contrast-induced acute kidney injury, covering pathogenesis, risk assessment, prevention, and management of CIN.

Peripheral Vascular Disease

AHA Conference on Atherosclerotic Vascular Disease. Proceedings of the second AHA Conference on Atherosclerotic Vascular Disease were published in 2008 (201–209). The report includes 8 excellent summaries of areas that were addressed at the symposium, including nomenclature for atherosclerotic vascular disease, screening, magnetic resonance and computed tomographic imaging, stroke intervention, carotid artery revascularization, abdominal aortic aneurysm repair, lower-extremity revascularization, and renal artery disease. Readers are referred to the proceedings for detailed information on these subjects.

Carotid disease. There has been controversy about the safety of carotid stenting. Gurm et al. (210) performed a meta-analysis of 5 trials with 2,122 patients undergoing stenting or endarterectomy for symptomatic carotid disease. There was no difference in the risk of 30-day mortality, stroke, or disabling stroke among patients randomized to either strategy. In another report, Iyer (211) presented 1-year outcomes of the BEACH (Boston Scientific EPI: A Carotid Stenting Trial for High-Risk Surgical Patients) trial, which evaluated high-surgical-risk patients undergoing stenting with the Wallstent plus FilterWire embolic protection device (Boston Scientific, Minneapolis, Minnesota). At 1 year, the primary composite end point occurred in 8.9% of patients; this rate was noninferior to outcomes in similar patients after surgical endarterectomy.

Two trials investigating new embolic protection devices for carotid artery stenting were presented at the Transcatheter Cardiovascular Therapeutics conference (212,213). The EPIC (Evaluating the Use of the FiberNet Embolic Protection System in Carotid Artery Stenting) trial evaluated the FiberNet (Lumen Biomedical, Plymouth, Minnesota) Embolic Protection System (212), whereas the EMPIRE (A Multicenter Registry Evaluating Neuroprotection During Carotid Stenting with a Novel Flow Reversal System) trial evaluated the GORE (WL Gore and Associates) Flow Reversal System (213). Both studies showed a high procedural success and low rate of stroke and major adverse events at 30 days.

Schofer et al. (214) assessed the timing of embolic events after carotid stenting with serial magnetic resonance imaging; 20% of patients had ipsilateral injury at 3.5 h. Of note, 17% of patients had further evidence of emboli occurring between 3.5 and 18 h after embolic-protected stenting, involving both hemispheres. Causes of late embolization remain unclear but may be related to manipulation of catheters in the aortic arch.

Lin et al. (215) provided a report on feasibility and outcomes after endovascular recanalization for chronic cer-

vical internal carotid artery occlusion. Successful recanalization was achieved in 35 of 54 patients (65%). Two patients had a stroke (4%), and vascular complications occurred in 3 patients, including 1 late pseudoaneurysm, 1 carotid-cavernous fistula, and 1 extravasation. Finally, Levy et al. (216) published a comprehensive review on the treatment of carotid artery disease.

Renal stenting. Cooper et al. (217) investigated whether adjunctive use of an embolic protection device (Angio-Guard, Cordis, Miami, Florida) or GP IIb/IIIa receptor inhibitor (abciximab) during renal artery stenting would improve renal function. At 1 month, a decline in renal function was observed with stenting alone, stenting with embolic protection, and stenting with abciximab alone. However, with combination therapy no change in renal function was noted.

Mahmud et al. (218) reported a novel angiographic method for assessing renal microvascular perfusion—the renal frame count and renal blush grade. Both parameters were impaired in hypertensive patients with unilateral renal artery stenosis, and improved after stenting. Reduction in renal frame count was associated with a blood pressure reduction.

Superficial femoral artery disease. Two studies published in 2008 investigated use of paclitaxel-coated angioplasty balloons to limit restenosis during endovascular treatment of femoropopliteal disease. Tepe et al. (219) randomized 154 patients to a paclitaxel-coated balloon, uncoated balloon with paclitaxel dissolved in the contrast medium, or uncoated balloon alone. At 6 months, late lumen loss (the primary end point) and the rate of revascularization was significantly lower in the group treated with the paclitaxel-coated balloon. No benefit was seen with paclitaxel in the contrast medium. In another smaller randomized trial, similar benefits were also observed with a paclitaxel-coated balloon (220).

Structural Heart Disease

Percutaneous aortic valve replacement. Percutaneous aortic valve replacement has emerged as a promising new treatment option for aortic stenosis. Grube et al. (221) reported outcomes in 136 patients treated with the CoreValve (Core-Valve Inc., Irvine, California) prosthesis. Procedural success with the third-generation valve was 91.2%, and there was a low rate of death, stroke, or MI at 30 days (14.7%). A marked improvement in functional status was observed. A case report (222) of a patient who died 425 days after implant of a CoreValve showed ingrowth of tissue covering the lower part of the valve situated in the LV outflow tract. Schofer et al. (223) published results of a first-in-man study with the novel repositionable prosthesis in high-surgical-risk patients with severe aortic stenosis (Direct Flow Medical, Santa Rosa, California). Valve implantation was achieved in 12 of 15 patients and was associated with a reasonable safety profile. Two reports described new left

bundle branch block and atrioventricular block after percutaneous valve implantation (224,225). In the series by Webb (225), 7 of 123 (5.7%) patients required a permanent pacemaker. In another report, Babaliaros et al. (226) reported the use of balloon aortic valvuloplasty to help size the annulus before valve implantation. Zegdi et al. (227) provided important observations regarding post-deployment characteristics of a self-expanding valve stent in 35 patients undergoing surgical valve replacement. In bicuspid valves, the stent was often distorted and underdeployed, which may influence valve results and durability. Chiam et al. (228) and Webb (229) provided nice review articles on transcatheter aortic valve implantation. Finally, Vahanaian et al. (230) published a position statement on transcatheter aortic valve implantation from the European Association of Cardio-Thoracic Surgery and European Society of Cardiology. The document summarizes current techniques and results, as well as recommendations for patient selection, performance of valve implantation, and evaluation of procedural results.

Mitral valve repair. Sorajja et al. (231) reported a novel method of percutaneous mitral valve repair in which an annulus reduction device is implanted into the myocardium at the posteromedial mitral annulus via the coronary sinus. A significant reduction in mitral annular area was observed, which persisted at 3 months. Compared with other coronary sinus technologies, this technique may be advantageous when the coronary sinus lies superior to the mitral annulus, and also may lessen risk of injury to the circumflex artery.

Pulmonary valve replacement. Lurz et al. (232) published results with a percutaneous pulmonary valve in 155 patients with pulmonary conduit stenosis or regurgitation. Most patients had tetralogy of Fallot. Valve implantation was achieved with a very high success rate, and freedom from reoperation was 70% at 70 months.

Patent foramen ovale (PFO). A randomized trial of PFO closure in 432 patients with migraine (STARflex device, NMT Medical Inc., Boston, Massachusetts) (233) found no difference in cessation of migraine headache, and patients in the implantation arm had more serious adverse effects. Taafe et al. (234) performed a randomized trial in 660 patients comparing 3 PFO closure devices. Excellent outcomes were achieved with all devices; however, patients treated with the Helex (WL Gore and Associates, Flagstaff, Arizona) devices were more likely to have a residual shunt at 30 days compared with the other devices. In another study, Hildick-Smith et al. (235) reported that many PFO closure procedures can be performed safely with fluoroscopy alone.

Alcohol septal ablation (ASA). Three articles in 2008 addressed outcomes after ASA for hypertrophic cardiomyopathy (236–238). All studies showed a reduction in LV outflow tract gradient with ASA and improvement in functional class. Death occurred in 1% to 1.4%, and pacemaker implantation was required in 8.2% to 26%. In the Mayo series, the procedural complication rate was higher than that in matched controls who underwent surgical

myomectomy; however, 4-year survival was similar between both groups.

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