The Year in Interventional Cardiology

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We are delighted to provide readers of the Journal with this review of major scientific work published in the field of interventional cardiology in 2010. In addition, we have included late-breaking trials presented at the American College of Cardiology, Transcatheter Cardiovascular Therapeutics, European Society of Cardiology, and American Heart Association conferences. We hope that the paper 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.

Structural Heart Disease

Aortic valve replacement. Perhaps the most important and exciting report from 2010 was publication of the first randomized trial of transcatheter aortic valve implantation (TAVI) for aortic stenosis (AS). The PARTNER (Placement of Aortic Transcatheter Valves) trial randomly assigned 358 high-risk patients with severe AS who were not suitable candidates for surgery to standard therapy (including balloon aortic valvuloplasty) or TAVI with the Edwards SAPIEN balloon-expandable bovine pericardial valve (Edwards Lifesciences, Irvine, California) (1). The mean STS (Society of Thoracic Surgeons) score was 11.6 ± 6.0%. The TAVI arm had a dramatically lower rate of death at 1 year compared with the standard therapy arm (30.7% vs. 50.7%, p < 0.001) (Fig. 1). The TAVI patients were less likely to have class III or IV heart failure (25.2% vs. 58%, p < 0.001). A higher incidence of stroke and major vascular complications was observed in the TAVI arm. There was no echocardiographic evidence of valve dysfunction at 1 year. Results of this landmark trial will revolutionize the care of inoperable AS patients.

The year also saw many other scientific reports regarding TAVI. Gurvitch et al. (2) reported durability of the Edwards valve in patients beyond 3 years in a large patient cohort. Several institutional registries reported excellent clinical outcomes in high-risk patients (3–5). In a large European registry of 1,038 patients using the Edwards valve (both transfemoral and transapical) procedural success was observed in 93.8% (6). Stroke occurred in 2.5%. Thirty-day mortality was 6.3% in transfemoral patients and 10.3% in transapical patients. Clavel et al. (7) compared the effects of TAVI and surgical aortic valve implantation on left ventricular (LV) function in patients with reduced baseline ejection fraction. At 1 year, TAVI was associated with significantly greater recovery of LV function compared with surgery (change in LV ejection fraction 14 ± 15% vs. 7 ± 11%, p = 0.005). In another report, Messika-Zeitoun et al. (8) demonstrated significant differences in measurement of the aortic annulus diameter using echocardiography and multislice computed tomography, which has important potential implications for valve sizing.

Finally, 2 studies addressed stroke after TAVI (10,11). With diffusion-weighted magnetic resonance imaging, evidence of cerebral embolization was observed in 72% to 84% of patients, but in almost all cases, this was clinically silent. The presence of new cerebral lesions did not appear to impact neurocognitive function at 3-month follow-up.

Mitral valve repair. Another major development this year was presentation of data from the first randomized trial of percutaneous versus surgical mitral valve repair, EVEREST II (Endovascular Edge-to-Edge Repair Study) (12). A total of 279 patients with significant (3 to 4+) mitral regurgitation was randomly allocated on a 2:1 basis to catheter-based repair with the MitraClip (Evalve, Inc., Menlo Park, California) versus surgery (repair or replacement). At 30 days, the primary safety endpoint, a composite of major adverse events, was markedly lower in the MitraClip arm (9.6% vs. 57%, p < 0.0001). Clinical success at 12 months (the primary effectiveness endpoint) defined as freedom from death, mitral valve surgery, or mitral regurgitation ≥2+, was 72.4% in the device arm and 87.8% in the surgical arm (p = 0.0012 for noninferiority). Improvements in LV function, functional class, and quality of life were
verified the long-term safety and efficacy of unprotected left main coronary artery (LMCA) stenting compared with coronary artery bypass graft surgery (CABG). Park et al. (16) evaluated 2,204 LMCA disease patients who were treated with either percutaneous coronary intervention (PCI), bare-metal stent (BMS), or drug-eluting stent (DES), or CABG in a nonrandomized fashion. At a median of 5.2 years of follow-up, death, myocardial infarction (MI), or stroke was similar, but target vessel revascularization (TVR) was higher in the PCI group. In a smaller cohort with 10-year follow-up, mortality, MI, and stroke rates remained equivalent (17). Chieffo et al. (18) reported 5-year outcomes in 249 unprotected LMCA disease patients treated with either DES or CABG (nonrandomized), and found a significant reduction in composite death, MI, or stroke in the DES group, but a higher rate of TVR (18).

The SYNTAX (Synergy Between PCI With TAXUS and Cardiac Surgery) Investigators published 1-year outcomes in the 705 patients with unprotected LMCA disease randomly assigned to TAXUS stenting versus CABG (19). Major adverse cardiovascular events (MACE) were similar between the 2 groups; however, stroke was significantly higher in the CABG cohort (2.7% vs. 0.3%, p = 0.004). Revascularization was higher in the PCI arm (11.8% vs. 6.5%, p = 0.02). Low or intermediate SYNTAX scores (<33) predicted good outcomes with PCI for unprotected LMCA (Fig. 2). At the Transcatheter Cardiovascular Therapeutics meeting, Serruys (20) confirmed these results were maintained at 3-year follow-up. Similarly, among 452 diabetic patients with LMCA or 3-vessel disease in the SYNTAX trial (21), TVR was higher after TAXUS compared with CABG, but death, stroke, and MI rates were equivalent.

**Multivessel disease.** The MASS-II (Medicine, Angioplasty or Surgery Study) reported 10-year outcomes among 611 randomized patients with stable angina and multivessel disease (22). Medical therapy was an inferior strategy compared with CABG and PCI, respectively, with lower survival (69% vs. 74.9% and 75.1%, p = 0.089) and higher infarction (20.7% vs. 10.3% and 13.3%, p < 0.01). Both medical therapy and PCI had higher rates of revascularization than CABG. The CARDia (Coronary Artery Revascularization in Diabetes) trial randomized 510 diabetic patients with multivessel disease to PCI (BMS or sirolimus-eluting stent [SES]) or CABG (23). One-year mortality was identical (3.2% vs. 3.2%), and combined death, MI, and stroke were similar (10.5% vs. 13.0%, p = 0.39) between CABG and PCI arms. Similarly, the ARTS-II (Arterial Revascularization Therapies Study II) found similar freedom from death, MI, or stroke in the patients with multivessel disease treated with SES compared with CABG, but superior to the BMS cohort from ARTS-I (24). Interestingly, in this era of short (3-month) duration dual antiplatelet therapy (DAPT), 32% of the MACE events were attributed to stent thrombosis. In the SYNTAX multivessel cohort, stent thrombosis occurred in 4.1% of
TAXUS-treated patients, and by 3 years, a significant increase in MI (7.1% vs. 3.3%, \( p < 0.005 \)) and increased mortality (9.5% vs. 5.7%, \( p = 0.02 \)) was observed compared with CABG (25). In our opinion, these findings speak for longer duration DAPT or for avoiding devices such as paclitaxel-eluting stents (PES) thought to have higher stent thrombosis rates compared with other DES.

**Fractional flow reserve guidance.** Fractional flow reserve measurement is useful to reduce adverse events in multivessel disease patients undergoing PCI. The FAME (FFR Versus Angiography for Multivessel Evaluation) trial randomized 1,005 patients with multivessel disease. Among lesions with 50% to 70% stenosis, 35% were functionally significant; lesions with 71% to 90% stenosis, 80% were functionally significant; and lesions >90%, 96% were functionally significant (26). The group randomly assigned to fractional flow reserve had lower utilization of stents (1.9 vs. 2.7, \( p < 0.001 \)) and reduced death or MI at 2 years (8.4% vs. 12.9%, \( p = 0.02 \)) (27).

**Bifurcation.** Although a single stent strategy for bifurcation lesions appears to be preferred when using BMS, limited data exist regarding DES. The British Bifurcation Group randomly assigned 500 patients with bifurcation lesions to simple versus 2-stent technique using DES (28). As expected, the 2-stent technique was longer in duration and required more radiation, and also increased the risk of peri-procedural MI. A Korean registry found lower rates of revascularization when bifurcation lesions were treated with SES rather than PES (29).

**Coronary total occlusion.** A meta-analysis of 14 publications comparing DES with BMS among 4,394 patients with coronary total occlusion found that DES significantly reduced restenosis and reocclusion, with similar rates of death or MI compared with BMS (30).

**High-risk PCI.** The BCIS (Balloon Pump Assisted Coronary Intervention Study) randomized 301 patients with extensive multivessel disease and ejection fraction ≤30% to intra-aortic balloon pump versus none before PCI (31). Although fewer procedural complications occurred in the intra-aortic balloon pump group (1.3% vs. 10.7%, \( p < 0.001 \)), access site complications were increased (3.3% vs. 0%, \( p = 0.06 \)) and MACE rates were similar. The authors concluded that the results did not support routine intra-aortic balloon pump for high-risk coronary intervention.

**Vascular access and closure.** Methods to reduce vascular access complications have included use of radial access, smaller sheaths, modifying antithrombotics, and vascular closure devices. The American Heart Association released a scientific statement on arteriotomy closure devices concluding that, although arteriotomy closure devices (ACDs) improve patient comfort and shorten the time to ambulation, they have not been shown to reduce vascular complications (32). We believe that this may be due, in part, to higher complication rates of some devices (VASOSeal, PLC Medical Systems Inc., Franklin, Massachusetts) and lack of studies enrolling highest risk patients. Interestingly, a trial randomizing 1,004 patients undergoing femoral access to ultrasound versus fluoroscopic guidance (33) found that ultrasound was faster, and reduced the number of attempts, risk of venipuncture, and vascular complications (1.4% vs. 3.4%, \( p = 0.04 \)).

**Contrast nephropathy.** Prevention of contrast-induced nephropathy remains a problem. In a Korean study of 382 diabetic patients, the use of sodium bicarbonate (1 h before, 6 h after) was not superior to saline hydration for 24 h (34). In this study, the amount of contrast used and lower ejection fraction were predictors of contrast-induced nephropathy. Bartorelli (35) reported a trial utilizing saline hydration with forced diuresis with nurse monitoring compared with the RenalGuard device (PLC Medical Systems Inc.), which automatically gives intravenous hydration based on urine output. In this study, after 30 min of hydration, furosemide was given (0.5 mg/kg, and 20% of patients received addi-
tional doses) resulting in urine output of 826 ± 342 ml/h. Accordingly, the RenalGuard device hydrated the patient at a rate of 1 l/h and rates of contrast-induced nephropathy and MACE were reduced. We do not know whether these results were due to the adverse effects of furosemide in a control group that was not adequately hydrated.

Unfortunately, 2010 was a bad year for N-acetylcysteine. Two trials utilizing high doses (1,200 mg twice a day for 48 h) found no advantage over saline hydration alone in a randomized trial of 250 STEMI patients (36) or in a randomized trial of 2,308 high-risk patients (37). In summary, these data suggest that N-acetylcysteine is not beneficial, and hydration with sodium bicarbonate is more convenient but not superior to prolonged hydration with normal saline.

Intravascular ultrasonography. One method to potentially improve outcomes after DES is to perform intravascular ultrasonography (IVUS) to optimize stent deployment. However, Colombo (38) reported a trial randomizing 284 patients with complex lesions to the IVUS versus angiography-guided stent deployment. Although IVUS resulted in larger lumen measurements, there was no difference in MACE, target lesion revascularization (TLR) (7.0% vs. 5.0%), or stent thrombosis (0.7% vs. 0.0%) compared with angiography-guided implantation.

Drug-Eluting Stents

DES versus BMS. It has been suggested that large vessels treated with a DES may have higher adverse events compared with BMS. Kaiser et al. (39) randomly assigned 2,314 patients with large coronaries (≥3.0 mm) to DES (SES or everolimus-eluting stent [EES]) versus BMS. The DES was superior at reducing TVR, while rates of death and MI were similar. The benefit of DES in a saphenous vein graft disease is also controversial. Lateib et al. (40) performed a retrospective review of 127 patients receiving DES in a saphenous vein graft compared with 131 patients receiving BMS. Although the DES group was far more complex, clinical outcomes were similar, and a propensity analysis suggested reduction in TVR (hazard ratio: 0.31, 95% confidence interval: 0.14 to 0.66; p = 0.002).

DES thrombosis. Stent thrombosis (ST) continues to be a topic of interest, and was reviewed in a JACC White Paper by Holmes et al. (41). The RESTART (Registry of Stent Thrombosis for Review and Reevaluation) reported 611 patients with definite ST of a SES (322 early, 105 late, and 184 very late, >1 year) (42). Mortality 1 year after ST varied depending on the timing of ST: 22.4% for early, 23.5% for late, and 10.5% for very late. Predictors of late and very late ST included chronic kidney disease, prior PCI, PCI of total occlusion, and age <65 years. When implanting multiple DES within the same vessel, it may be better to avoid overlap. In 1 study, overlapping DES was associated with more late loss, TLR, death or MI compared with multiple non-overlapped DES or single DES (43).

Second-generation DES. Second-generation DES (zotarolimus-eluting stent [ZES] and EES) were developed to reduce restenosis, but also be more deliverable and reduce ST compared with first-generation DES. Several studies were presented regarding ZES. Leon et al. (44,45) reported a trial of 1,548 patients randomly allocated to a ZES or PES. The PES was associated with higher rates of periprocedural MI and very late stent thrombosis, but similar definite/probable ST and TLR at 3-year follow-up (44,45). Park et al. (46) randomly assigned 2,645 patients to ZES, PES, or SES and found the SES superior to both ZES and PES at reducing TVR and ST. Similarly, a European trial of 2,332 patients found the ZES inferior to SES with regard to MACE (10% vs. 5%, p < 0.0001) at 18 months (47).

Numerous trials evaluating EES were published or presented in 2010. Stone et al. (48) randomized 3,687 patients to EES or PES and found EES resulted in a significantly lower rate of target lesion failure at 1 year (4.2% vs. 6.8%, p = 0.001). Similarly, the COMPARE trial (n = 1,800) found significant reductions in TVR, MI, and ST with Xience compared with the Taxus Liberté PES (49). The benefit of EES was even greater at 2 years, with an absolute difference of 4.7% in the rate of the combined endpoint of death, nonfatal MI, and TVR (50). In another trial, Ribichini (51) found a significantly lower rate of late loss at 9 months with EES compared with PES (0.08 mm vs. 0.22 mm, p = 0.018).

The first randomized comparisons of EES and SES were also reported in 2010 (Table 1). Kim (52) found a lower incidence of angiographic late loss with EES. Two randomized trials demonstrated similar clinical outcomes with EES (53,54), while a propensity-matched study found a lower rate of ST with EES (55).

Serruys et al. (56) compared 2,292 patients who were randomly assigned to EES or ZES, and found target lesion failure at 1 year was similar between both second-generation stents.

To summarize, these data suggest that PES is inferior in many respects, and unlike early reports, the ZES does not appear to reduce the risk of ST compared with SES or EES. Clinical and angiographic results seem to be best in SES- or EES-treated groups.

DES restenosis. The optimal treatment strategy for treatment of DES restenosis has not been well established. The j-Cypher registry reported 1,094 restenotic lesions after SES that were treated with additional SES (n = 537) or percutaneous transluminal coronary angioplasty (n = 557) (57). Recurrent TLR occurred less frequently in the repeat SES group (23.8% vs. 37.7%, p < 0.0001) at 2-year follow-up. Some have suggested that a different drug should be utilized after restenosis of DES. Mehilli et al. (58) randomly assigned 450 patients with SES restenosis to PCI with repeat SES or switching to PES. Either strategy was associated with comparable safety and efficacy (binary restenosis at 6 to 8 months: SES 19.6% vs. PES 20.6%, p = 0.69). The CRISTAL trial randomly allocated 281 patients.
with DES restenosis (SES or PES) to SES versus percutaneous transluminal coronary angiography (59). Angiographic outcomes at 9 to 12 months favored SES implantation compared with percutaneous transluminal coronary angiography (minimal lumen diameter 2.14 ± 0.62 vs. 1.71 ± 0.55, p < 0.0001), with a trend toward reduced TVR.

**Nonpolymer DES.** Because polymer residue has been implicated as a potential etiologic factor for late adverse events after DES implantation, several groups have investigated polymer-free stent platforms. Byrne et al. (60) found excellent angiographic and clinical outcomes at 2 years with a polymer-free rapamycin and probucol-eluting stent compared with either a ZES (Endeavor, Medtronic, Santa Rosa, California) or permanent-polymer SES. In a larger 3,002-patient randomized trial, the polymer-free rapamycin and probucol-eluting stent was noninferior to a ZES (Endeavor Resolute) with comparable angiographic and clinical endpoints at 12 months (61). Grube (62) reported excellent 12-month angiographic outcomes with a novel polymer-free biolimus A9-eluting stent (BioFreedom, Biosensors International, Morges, Switzerland) compared with a PES (TAXUS Liberté [late loss 0.19 mm]) with a 2% decrease in scaffold area, with late loss 0.19 mm, p = 0.001 for noninferiority).

**New DES.** Kereiakes et al. (63) reported a randomized study comparing a novel thin-strut (81 μm) platinum chromium alloy SES (Taxus Element, Boston Scientific, Natick, Massachusetts) to the Taxus Express SES in 1,262 patients. Clinical and angiographic endpoints at 12 months were similar between the 2 groups. A small randomized trial demonstrated improved angiographic and clinical outcomes with a combined paclitaxel-eluting balloon plus endothelial progenitor cell-capturing stent compared with endothelial progenitor cell-capturing stent alone (64). In another trial, Beijj et al. (65) found a higher rate of 1-year target vessel failure (TVF) with an EPC stent compared with a PES (17.3% vs. 10.6%).

Serruys et al. (66) reported results with a second-generation bioresorbable EES. At 6 months, there was only a 2% decrease in scaffold area, with late loss 0.19 ± 0.18 mm, and 96.8% strut coverage by optical coherence tomography. These findings represent an exciting step forward in the bioresorbable vascular scaffold field.

**Acute MI**

**Time to treatment.** Several studies investigated the impact of time to reperfusion on clinical outcomes. Brodie et al. (67) evaluated the impact of door-to-balloon time on mortality depending on clinical risk and time to presentation in 4,548 nonshock acute MI patients. Short door-to-balloon times (≤90 min) had greatest impact in patients presenting early (≤90 min), especially in high-risk patients (TIMI [Thrombolysis In Myocardial Infarction] risk score ≥2) (67). A short door-to-balloon time had less impact on mortality in patients presenting after 90 min. Lambert et al. (68) studied outcomes in a large registry of ST-segment elevation myocardial infarction (STEMI) patients in Quebec (n = 2,356) (68). Patients who received reperfusion therapy outside of guideline recommended maximum delay (30 min for fibrinolysis; 90 min for PCI) had significantly higher 30-day mortality (6.6% vs. 3.3%). In another analysis, Terkelsen et al. (69) focused on system delay (time from first contact with health care system) to reperfusion. System

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### Table 1  
**Studies of Everolimus-Eluting Stents Published or Reported in 2010**

<table>
<thead>
<tr>
<th>First Author (Ref. #)</th>
<th>Acronym</th>
<th>n</th>
<th>Stents</th>
<th>Primary Endpoint</th>
<th>Main Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stone et al. (48)</td>
<td>SPIRIT IV</td>
<td>3,687</td>
<td>XIENCE vs. TAXUS Express</td>
<td>Target lesion failure (death, MI, ischemia-driven TLR) at 1 yr</td>
<td>Rate of target-lesion failure at 1 yr with EES (4.2% vs. 6.8%, p = 0.001); ST with EES (0.17% vs. 0.85%, p = 0.004)</td>
</tr>
<tr>
<td>Kedhi et al. (49)</td>
<td>COMPARE</td>
<td>1,800</td>
<td>XIENCE vs. TAXUS Liberté</td>
<td>Composite death, MI, TVR within 12 months</td>
<td>Endpoint with EES (6% vs. 9%, p = 0.02)</td>
</tr>
<tr>
<td>Ribichini et al. (51)</td>
<td>EXECUTIVE</td>
<td>200</td>
<td>XIENCE vs. TAXUS Liberté</td>
<td>In-stent late loss at 9 months</td>
<td>Late loss with EES (0.08 mm vs. 0.22 mm)</td>
</tr>
<tr>
<td>Byrne (53)</td>
<td>ISAR-TEST 4</td>
<td>1,304</td>
<td>XIENCE vs. Cypher</td>
<td>Death, MI, TLR at 2 years</td>
<td>No difference in clinical outcomes at 2 yrs</td>
</tr>
<tr>
<td>Jensen (54)</td>
<td>SORT OUT IV</td>
<td>2,774</td>
<td>XIENCE V vs. Cypher Select</td>
<td>MACE at 9 months (death, MI, definite ST, clinically driven TVR)</td>
<td>EES noninferior to SES; Rate ST with EES</td>
</tr>
<tr>
<td>Kim (52)</td>
<td>EXCELLENT</td>
<td>1,372</td>
<td>XIENCE V vs. Cypher Select</td>
<td>In-segment late loss at 9 months</td>
<td>Similar rate of LL (EES 0.10 mm vs. SES 0.05 mm, p = 0.023 for noninferiority)</td>
</tr>
<tr>
<td>Raber (55)</td>
<td>LESSON-I</td>
<td>2,684</td>
<td>XIENCE V vs. Cypher</td>
<td>Propensity-matched comparison death/MI/TVR at 3 yrs</td>
<td>Rate of events at 3 yrs with EES (14.9% vs. 18.0%, p = 0.056); Rate of ST with EES (0.5% vs. 1.6%, p = 0.02)</td>
</tr>
<tr>
<td>Serruys et al. (56)</td>
<td>RESOLUTE All Comers</td>
<td>2,292</td>
<td>Resolute ZES vs. XIENCE V</td>
<td>Target lesion failure (death, MI, clinically indicated TLR) within 1 yr</td>
<td>Similar rate of primary endpoint (ZES 8.2% vs. EES 8.3%) and other outcomes; ST 2.3% with ZES, 1.5% with EES</td>
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</tbody>
</table>

**Legend:** EES = everolimus-eluting stent(s); LL = late loss; MACE = major adverse cardiovascular events; MI = myocardial infarction; SES = sirolimus-eluting stent(s); ST = stent thrombosis; TLR = target lesion revascularization; TVR = target vessel revascularization; ZES = zotarolimus-eluting stent(s).
delay was associated with worse survival in patients treated with PCI (69).

**Drug-eluting stents.** Although DES improve short-term outcomes in STEMI patients, it has been unclear whether these benefits are sustained at late follow-up. Stone (70) presented 3-year results of the HORIZONS-AMI (Harmonizing Outcomes With Revascularization and Stents in AMI) trial (70). Implantation of the Taxus PES resulted in a 40% reduction in ischemic TLR at 3 years, without any increased risk of stent thrombosis, reinfarction, or all-cause mortality. Two other trials reported similar findings at 3 years with a significant reduction in MACE, driven primarily by the lower rate of TLR with DES (mostly in the first year) (71,72). One study provided 5-year follow-up data (73), and reported no difference in MACE but a small increased risk of very late stent thrombosis with a PES. An increased risk of stent thrombosis was also observed in another trial (74) when routine filter-based distal protection was used during primary PCI. One potential factor that might lead to late ST is stent malapposition. Guo et al. (75) performed a detailed IVUS analysis of 241 patients with baseline and 13-month imaging in the HORIZONS-AMI trial (75). Acute stent malapposition was common in both BMS and DES lesions (~35% to 40%), with similar rates of resolution in each group at follow-up. Conversely, late acquired malapposition was more common in PES-treated lesions compared with BMS-treated lesions (30.8% vs. 8.1%, p = 0.023), due to positive remodeling and resolution of thrombus/plaque. However, the clinical impact of late acquired malapposition remains uncertain at this time. Another trial reported that patients treated with a PES had a significant reduction in late loss at 12 months compared with a BMS, but there was no difference in binary restenosis (76).

Stone et al. (77) also provided a clinically useful analysis from the HORIZONS trial to assist with stent selection in AMI patients. Patients with 2 or 3 well-known risk factors for restenosis (insulin-treated diabetes mellitus, reference vessel diameter ≤3 mm, and lesion length ≥30 mm) had the greatest benefit with a DES compared with BMS (12-month TLR 19.8% vs. 8.1%, p = 0.003). Patients with 1 risk factor had a modest benefit (7.3% vs. 4.3%, p = 0.02), whereas patients with no risk factors had similar outcomes to those with BMS.

**Thrombectomy.** Use of rheolytic thrombectomy before direct stenting was studied in a 501-patient multicenter randomized trial (78). In contrast to prior studies, all patients had angiographic evidence of thrombus (thrombus grades 3 to 5). Early ST-segment resolution was more frequent in the rheolytic thrombectomy arm; however there was no difference in final infarct size at 1 month. Event-free survival was higher in the rheolytic thrombectomy arm. In another report, Mongeon et al. (79) performed a Bayesian meta-analysis of 21 trials of adjunctive thrombectomy and found that thrombectomy improved early markers of reperfusion, but had no impact on 30-day mortality or clinical outcomes.

**Adjunctive agents.** Several studies in 2010 evaluated novel approaches to enhance myocardial salvage. Three trials investigated use of erythropoietin in patients with STEMI (2 studies used single-dose erythropoietin after reperfusion (80,81); 1 study used 3 doses after PCI (82)). Overall, these studies demonstrated no benefit of erythropoietin on infarct size, ejection fraction, or LV remodeling. In 2 studies, a higher incidence of adverse effects was observed in patients treated with erythropoietin (80,82). In another report, Newton et al. (83) presented results of a cardiac MRI substudy (n = 28) of a trial using cyclosporine before reperfusion. At 6 months, the cyclosporine group had a significant reduction in infarct size and LV end-systolic volume compared with the control group. Two studies evaluated the cardioprotective effects of ischemic conditioning (84,85). In 1 trial, remote ischemic conditioning was performed en route to hospital using 4 cycles of 5-min blood pressure cuff inflation-deflation (84). A higher rate of myocardial salvage was observed in the ischemic conditioning arm. In the other trial, ischemic post-conditioning performed immediately after reperfusion (using 4 balloon occlusions, each lasting 30 s), resulted in a 19% relative reduction in infarct size (85).

**PCI after thrombolysis.** A Norwegian trial evaluated the safety and efficacy of immediate angioplasty versus ischemia-guided therapy after thrombolysis in 266 AMI patients presenting to remote non-PCI hospitals (86). The group randomly assigned to immediate transfer for PCI had reduced ischemia at 30 days and improved composite endpoint of death, reinfarction, or stroke at 12 months. Borgia et al. (87) performed a meta-analysis of 7 trials of routine PCI versus standard care after fibrinolysis. The early routine invasive strategy was associated with significant reductions in reinfarction and recurrent ischemia compared with standard therapy, both at 30 days and at 6 to 12 months of follow-up.

Nielsen et al. (88) reported late follow-up (median 7.8 years) of the DANAMI-2 (Danish Acute Myocardial Infarction-2) trial in which 1,572 STEMI patients were randomly allocated to PCI or fibrinolysis. The short-term benefit of PCI over fibrinolysis was maintained at long-term follow-up with a reduced the risk of reinfarction and (11.7% vs. 18.5%) and death/reinfarction (34.8% vs. 41.3%).

**Cardiogenic shock.** The optimal timing for intra-aortic balloon pump support in patients with cardiogenic shock is unclear. Findings of a retrospective study suggest that intra-aortic balloon pump insertion before PCI is associated with better outcomes compared with intra-aortic balloon pump placement after PCI (89).

**Acute Coronary Syndromes**

An early invasive strategy is currently recommended in patients with non–ST-segment elevation acute coronary
syndrome (ACS) and high-risk features. In 2010, Fox et al. (90) performed a meta-analysis of 3 randomized trials (n = 5,467) comparing a routine early invasive versus selective invasive strategy. Over 5 years, a routine early invasive strategy was associated with a significant reduction in death or myocardial infarction (14.7% vs. 17.9%, p = 0.002) compared with the selective approach (greatest benefit was observed in the highest-risk patients). In contrast, Damman et al. (91) provided 5-year follow-up of the ICTUS (Invasive Versus Conservative Treatment in Unstable coronary Syndromes) trial, which randomized 1,200 troponin positive ACS patients to an early (24 to 48 h) invasive or selective invasive strategy and found no difference in the incidence of death or MI (91).

In contrast to STEMI, the impact of time-to-PCI has not been well studied in ACS. Sorajja et al. (92) studied outcomes in 7,749 patients in the ACUITY (Acute Catheterization and Urgent Intervention Triage Strategy) trial according to timing of PCI. Delay to PCI >24 h was an independent predictor of 30-day and 1-year mortality, especially in patients with high-risk features. These data suggest that urgent angiography and triage to revascularization is important in ACS patients.

Pharmacotherapy

**Clopidogrel.** Dual Antiplatelet Therapy. The optimal duration of DAPT after DES implantation has not been established. Park et al. (93) randomly assigned 2,701 patients who received a DES to continue DAPT or aspirin alone after 12 months. At median follow-up of 19.2 months, there was no significant difference in event rates including death, MI, stroke, or ST. A series of larger DAPT trials are ongoing and will provide the basis for clinical recommendations regarding duration of DAPT.

LOADING DOSE. Clopidogrel pre-treatment has been shown to improve clinical outcomes after PCI; however, these studies did not evaluate a high-dose in laboratory strategy. Di Sciascio et al. (94) randomly allocated 409 patients to clopidogrel pre-treatment (600 mg 4 to 8 h before PCI) or to a clopidogrel 600 mg loading dose given in the catheterization laboratory after angiography. At 30 days, there was no difference in clinical events, thus suggesting the in-lab strategy is a reasonable alternative when patients cannot be pre-treated. In another study, the same investigators demonstrated that there is no benefit from reloading patients who are on chronic clopidogrel therapy (95).

MAINTENANCE DOSE. The CURRENT OASIS-7 (Clopidogrel and Aspirin Optimal Dose Usage to Reduce Recurrent Events–Seventh Organization to Assess Strategies in Ischemic Symptoms) trial randomly allocated 17,000 ACS patients undergoing PCI to double-dose clopidogrel (600 mg load and 150 mg/day × 7 days followed by 75 mg/day) versus conventional dosing (96). The double-dose group had significant reductions in death, MI, and stroke, and a 42% decrease in ST, leading to rapid adoption of this approach in many centers. Whether a higher dosing strategy is also beneficial in patients with suboptimal platelet inhibition has been in question. Price et al. (97) randomly assigned 2,214 patients with high residual platelet reactivity (platelet reactivity units ≥230) to high-dose (150 mg daily) versus standard-dose clopidogrel for 6 months. High-dose clopidogrel caused a modest improvement in platelet inhibition; however, there was no difference in clinical events. In another study, Sibbing et al. (98) found no benefit of tapering clopidogrel or evidence of a rebound phenomenon after discontinuing therapy.

**PLATELET FUNCTION TESTING.** Breet et al. (99) evaluated the value of on-treatment platelet reactivity to predict clinical outcomes measured using several different platelet function assays. Interestingly, only 3 of 6 assays studied provided prognostic information, and the predictive accuracy of these 3 tests was quite modest (area under the curve between 0.61 and 0.63). These data suggest that routine platelet function testing is not helpful in elective PCI.

**GENOTYPING.** Several studies evaluated CYP2C19 polymorphisms and the antiplatelet effect of clopidogrel. In a meta-analysis of 9,685 PCI patients, carriage of even 1 loss-of-function CYP2C19 allele was significantly associated with adverse events including ST (100); however, a smaller study (n = 760) suggested that genotyping may not be helpful (101). Bonello et al. (102) demonstrated that tailored clopidogrel dosing can be used to achieve adequate platelet inhibition in patients carrying the CYP2C19*2 loss-of-function polymorphism. In contrast, the CYP2C19*17 allelic variant appears to result in enhanced response to clopidogrel and an increased risk of bleeding (103). In another study, polymorphisms of ABCB1 also were found to be associated with reduced platelet inhibition and increased risk of ischemic events during clopidogrel therapy (104).

**DRUG INTERACTIONS.** Recently, there has been controversy about use of proton pump inhibitors (PPI) in patients requiring clopidogrel. An expert consensus document on this topic was published in 2010 (105). In brief, routine PPI are recommended in patients with prior gastrointestinal bleeding, and multiple risk factors for gastrointestinal bleeding, but not patients at low risk for gastrointestinal bleeding. Concomitant use of PPI (especially omeprazole) does appear to reduce the antiplatelet effect of clopidogrel, irrespective of when the PPI is given (106), but recent studies suggest that this drug interaction does not significantly impact clinical outcomes (107). In other studies, the addition of omega-3 ethyl esters or clofazimide to aspirin and clopidogrel were shown to potentiate the effect of standard DAPT (108,109).

**P2Y12 inhibitors.** Mahoney et al. (110) performed a cost analysis of the TRITON–TIMI 38 (Trial to Assess Improvement in Therapeutic Outcomes by Optimizing Plate-
let Inhibition With Prasugrel–Thrombolysis In Myocardial Infarction 38). At a median follow-up of 14.7 months, average total costs were $221 lower with prasugrel compared with clopidogrel, largely due to a lower rate of rehospitalization with prasugrel.

Ticagrelor is an oral reversible adenosine diphosphate inhibitor with more rapid and consistent platelet inhibition than clopidogrel. Results of 2 planned substudies of the PLATO (Platelet Inhibition and Patient Outcomes) trial were published in 2010. In patients with STEMI (n = 8,430) and ACS patients with a planned invasive strategy (n = 13,408), ticagrelor was associated with significant reductions in death, MI, and ST without an increased risk of major bleeding (111, 112). Similar benefits were observed in a subgroup with chronic kidney disease (creatinine clearance <60 ml/min) (113). In other substudies, ticagrelor was shown to achieve greater platelet inhibition than clopidogrel, both after a loading dose and during maintenance therapy (114). Ticagrelor was also shown to be beneficial in patients with clopidogrel nonresponsiveness (115). In a genetic substudy, Wallentin et al. (116) reported that CYP2C19 and ABCB1 polymorphisms did not influence that efficacy of ticagrelor. Finally, Bellemain-Appaix et al. (117) performed a meta-analysis of 8 randomized trials that compared new P2Y12 inhibitors with clopidogrel. All-cause mortality was significantly decreased for PCI patients, especially among those with STEMI (odds ratio: 0.78, 95% confidence interval: 0.66 to 0.92, p = 0.003). Stent thrombosis was also significantly lower in PCI patients (decreased 40%). These agents, therefore, represent an important step forward in antiplatelet therapy for PCI patients.

Elinogrel, a reversible, competitive P2Y12 inhibitor that can be administered both orally and intravenously (half-life 12 h), also appeared promising in a phase II clinical trial (118).

**Glycoprotein IIb/IIIa inhibitors.** Several trials in 2010 expanded the evidence base regarding the benefits of glycoprotein IIb/IIIa inhibitors in primary PCI, and in particular, the role of small molecule agents. In a 427-patient randomized trial, eptifibatide was found to result in similar rates of complete ST-segment resolution after PCI compared with abciximab (119). In a large Swedish registry of 11,479 STEMI patients, similar rates of death/myocardial infarction at 1 year were observed in patients receiving either abciximab or eptifibatide (15.7% vs. 15.0%), suggesting the small molecule agent is noninferior to abciximab (120).

Early, pre-hospital administration of tirofiban in STEMI also appears to be beneficial, with improved 30-day and 1-year clinical outcomes (121). A meta-analysis of randomized trials with tirofiban in ACS and PCI suggested tirofiban reduces mortality, but an early ischemic hazard was observed with tirofiban when compared with abciximab in studies with the lower 10 μg/kg dose (but not 25 μg/kg dose) (122).

Two studies evaluated intracoronary versus intravenous (IV) administration of glycoprotein IIb/IIIa agents. Deibele et al. (123) randomly assigned ACS patients to intracoronary or IV eptifibatide. Intracoronary eptifibatide resulted in higher local platelet IIb/IIIa receptor occupancy and improved microvascular perfusion as measured by the corrected TIMI frame count. In another trial, Gu et al. (124) compared intracoronary versus IV abciximab in STEMI patients, and found no difference in the incidence of complete ST-segment resolution, but higher rate of myocardial blush grade 2/3 and lower enzymatic infarct size in the intracoronary group.

**Low-molecular-weight heparin.** Montalescot et al. (125) presented results of a randomized trial of IV enoxaparin (0.5 mg/kg with or without glycoprotein IIb/IIIa inhibitor) versus unfractionated heparin (UFH) in primary PCI. At 30 days, the primary endpoint (death, complications of MI, procedural failure, and non-CABG major bleeding) was lower in the enoxaparin arm (28.0% vs. 33.7%, p = 0.07). A lower incidence of ischemic endpoints was also observed with enoxaparin. Rao et al. (126) reported results of a safety and feasibility trial of a novel low-molecular weight heparin (M118) in elective PCI (126). Advantages of this new agent include potent activity against factor Xa and IIa, monitoring by use of point-of-care assays, and reversibility with protamine.

The optimal UFH dosing regimen was studied in 2,026 high-risk non-STEMI patients initially treated with fondaparinux and referred for early coronary angiography (127). Patients were randomly assigned to receive either low-dose UFH (50 U/kg) or standard-dose UFH (85 U/kg) adjusted by blinded activated clotting time. The primary outcome, a composite of major bleeding, minor bleeding, or major vascular access-site complications up to 48 h, occurred in 4.7% in the low-dose group and 5.8% in the standard-dose group (p = 0.27). At this time, therefore, ACS patients who are initially treated with fondaparinux should continue to receive activated clotting time-guided standard-dose UFH during PCI.

**Statins.** Statin pre-treatment has been shown to reduce periprocedural myocardial injury during elective PCI. In a Korean study, 171 STEMI patients were randomly assigned to high-dose atorvastatin (80 mg) or atorvastatin 10 mg before primary PCI (128). At 30 days, the incidence of MACE was similar between groups; however, myocardial perfusion was improved in the high-dose arm (assessed by ST-segment resolution, myocardial blush grade, and corrected TIMI frame count). Winchester et al. (129) provided a meta-analysis of 21 trials of pre-procedure statin therapy, and demonstrated a reduction in MI in both PCI and noncardiac surgical procedures, but not CABG.

**Peripheral Vascular Disease**

**Renal denervation.** In one of the most exciting developments of the year, results of a 106-patient randomized trial of catheter-based renal sympathetic denervation for treatment of resistant hypertension (systolic blood pressure...
≥160 mm Hg despite taking 3 or more antihypertensive medications) were published (130). At 6 months, the office-based blood pressure was substantially lower in patients treated with renal denervation (decrease 32/12 mm Hg vs. no difference in the control group) (Fig. 3). Eighty-four percent of renal denervation patients had a reduction in systolic blood pressure 10 mm Hg versus 35% of controls (p ≤ 0.0001). There were no device-related complications. Future studies will evaluate the effectiveness of this innovative technique in treating patients with mild hypertension, congestive heart failure, and other disease states.

**Carotid disease.** The optimal revascularization strategy for carotid artery disease remains controversial, but several studies in 2010 provided important additional data. In the CREST (Carotid Revascularization Endarterectomy vs. Stenting Trial), 2,502 symptomatic or asymptomatic patients were randomly assigned to either carotid artery stenting (CAS [embolic protection used in 96.1%]) or carotid artery endarterectomy (CEA) (131). During the periprocedural period, there was a higher risk of stroke with stenting (4.1% vs. 2.3%, p = 0.01) but lower risk of MI (1.1% vs. 2.3%, p = 0.03). At a median follow-up of 2.5 years, however, there was no difference in the primary endpoint of stroke, MI, or death between the treatment groups. In another randomized trial, ICSS (International Carotid Stenting Study), which studied 1,713 symptomatic patients, results of an interim safety analysis were published (132). At 120 days, the incidence of disabling stroke or death was 4.0% with stenting versus 3.2% with CEA. The rate of cranial nerve palsy was substantially lower with CAS (1 event vs. 43 events). Results of the primary endpoint of the trial (the 3-year rate of fatal or disabling stroke) are awaited. The same investigators also performed a meta-analysis of short-term outcomes (120 days) in 3 randomized trials of symptomatic patients (n = 3,433), and reported a higher risk of death or stroke with CAS versus CEA in patients ages 70 years or older (12.0% vs. 5.9%), but similar outcomes in younger patients (133). In another report, Bangalore et al. (134) performed a propensity-matched analysis of 3,412 patients in a large registry and observed similar late outcomes (2 years) between CAS and CEA.

Proximal embolic protection appears to be an alternative protection strategy among patients undergoing CAS. In a registry of 1,300 patients, Stabile et al. (135) reported a high procedural success with the technique and overall 30-day risk of death or stroke of 1.38%.

The impact of training for CAS was evaluated in the CASES-PMS (Carotid Artery Stenting With Embolic Protection Surveillance–Post-Marketing Study). Schreiber et al. (136) reported that physicians with varied experience can achieve short- and long-term results similar to those seen in randomized trials with a formal training program.

**Aortic aneurysm.** Long-term outcomes from 2 randomized trials evaluating endovascular repair of abdominal aortic aneurysm were published by the EVAR (Endovascular Aneurysm Repair) study investigators in 2010 (137,138). In the EVAR-1 trial, 1,252 patients with aortic aneurysm (≥5.5 cm diameter) were randomly allocated to endovascular...
lar versus open repair. At a median follow-up of 6 years, there was no difference in all-cause mortality between treatment arms. The previously reported early survival advantage of endovascular repair was lost by 4 years, due to an increase in aneurysm-related mortality. Additionally, endovascular repair was associated with higher rates of graft-related complications and reintervention. In the EVAR-2 trial, 404 patients deemed physically ineligible for open repair were randomly allocated to endovascular repair or no repair (median follow-up was 3.1 years). Endovascular repair was associated with a lower rate of aneurysm-related mortality than no repair; however, there was no difference in overall all-cause mortality, with very few patients surviving after 8 years.

**Peripheral vascular disease.** Several studies in 2010 evaluated strategies to improve the results of endovascular intervention in lower extremity arterial disease. In 206 patients with symptomatic superficial femoral artery disease, implantation of a self-expanding nitinol stent was shown to improve acute and long-term outcomes compared with balloon angioplasty with provisional stent implantation (139). At 12 months, there was a significantly lower rate of revascularization and higher patency rate (by Duplex ultrasonography) in the stent group. In a small randomized trial, use of a paclitaxel-coated balloon was found to significantly reduce angiographic late loss compared with balloon angioplasty alone (140). In another report, implantation of a PES was associated with higher 12-month patency than either angioplasty alone or provisional BMS (141).

DES also appear to be beneficial in patients with infrapopliteal disease (142). In a 106-patient randomized trial, implantation of a SES was shown to result in significantly higher patency rates at 1 year compared with BMS (143).

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