Improved Outcomes in Cardiogenic Shock

Christian Spaulding, MD, European Hospital Georges Pompidou and INSERM U 970, Paris, France, discussed the epidemiology of ST-segment elevation myocardial infarction and cardiogenic shock, and its association with the increasing use of reperfusion therapy, especially primary percutaneous coronary intervention. See page 6.

Also

New Global Agenda for CVD Prevention

Clinical Trial Highlights

Techniques to Improve Left Main Stenting
Dear Colleagues,

On behalf of the Egyptian Society of Cardiology Board and Cardiology Department of Alexandria University, I am pleased to present the official peer-reviewed highlights of Cardio Alex 2013, held in June in Alexandria, Egypt. Cardio Alex is proud to be cooperating with the Goodwin Group International LLC, publishers of *MD Conference Express* to bring practitioners this valuable resource.

Cardio Alex offers a unique opportunity for medical professionals from around the region to gather in an exciting educational environment. This special report brings the very best of Cardio Alex to your practice for the benefit of your patients. This edition covers information presented at the 2013 meeting by our own practitioners as well as our esteemed international colleagues. The topics presented in this issue include updates on the Society’s work to establish regional surgical and interventional registries, as well regional and international clinical trial updates.

The topics selected for this special edition were determined in direct consultation with the scientific leadership of Cardio Alex. All articles were written strictly from primary source data (no press releases, no third-party opinion). The faculty who presented these data live were invited to review and comment on the resulting articles. Finally, an independent board of world experts carefully peer-reviewed the content to ensure accuracy and a balanced perspective.

This is a new approach to conference highlights reports – and one which we at the Egyptian Society of Cardiology and Cardio Alex felt would be of service to our members. I hope you enjoy this special edition of *MD Conference Express* and find it to be useful to your practice.

We welcome your comments on this new initiative. Please plan to join us next year for Cardio Alex 2014. You can learn more at www.cardioalex.com.

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**Prof. Mohamed Sobhy, MD, FACC, FESC**  
*Professor of Cardiology, Faculty of Medicine, Alexandria University*  
*Chairman of International Cardiac Center (ICC)*  
*I.P. President of the Egyptian Society of Cardiology (EgSC)*  
*Governor of ACC Egypt Chapter*  
*SFIL Egypt Champion*

Cardio Alex Executive Board

**Prof. Moustafa Nawar**  
*Professor of Cardiology, Alexandria University*

**Prof. Mahmoud Hassanein**  
*Professor of Cardiology, Alexandria University*

**Prof. Tarek El Zawawy**  
*Professor of Cardiology, Alexandria University*
10-13 June 2014

The total number of delegates: 4912
Number of Junior Cardiologists: 3
Number of Chairpersons & speakers: 1148
Number of Abstracts: 427
Number of faculty guests: 94
Number of Nurses & Technicians: 41
Number of Sessions: 86
Dear Practitioner,

We are pleased to share highlights from Cardio Alex 2013 held June 11-14, 2013, in Alexandria, Egypt, with practicing clinicians. The articles selected for this issue of *MD Conference Express* represent the most newsworthy topics of relevance to a broad array of practitioners. The abstracts presented at Cardio Alex provided an exciting and innovative forum where advances in research could be translated into practical applications for the clinician.

This year’s meeting included important information from regional, clinical studies, and novel treatments. Preliminary results from an analysis of intravascular ultrasound (IVUS) data [SAUDICAT] provides a framework to better understand the characteristics of coronary atherosclerosis in a Middle Eastern population. The initial Egyptian experience with the MitraClip device shows that while there is a learning curve associated with proper device delivery, the device appears to be both safe and feasible.

Feature articles in this issue of *MD Conference Express* look at the epidemiology of ST-segment elevation myocardial infarction and cardiogenic shock, and its association with the increasing use of reperfusion therapy, especially primary percutaneous coronary intervention; the new global agenda for cardiovascular disease prevention put forth by the Noncommunicable Diseases Alliance; and an update on endovascular aortic repairs. Therapeutic update sections contain information in selected, challenging areas of cardiovascular medicine including heart failure, a new approach to treating hypercholesterolemia, techniques to improve left main stenting, renal denervation, and transcatheter aortic valve replacement. Other topics of interest include bioabsorbable stents, the updated European Society of Cardiology guidelines on valvular heart disease, and the management of STEMI in the Middle East.

We hope that you will find the articles and practical perspectives contained in the pages of this edition of *MD Conference Express* to be useful in your clinical practice. For more information about *MD Conference Express*, please visit www.mdconferencexpress.com.

Robert P. Giugliano, MD, SM  
Associate Physician, Cardiovascular Division  
Brigham & Women’s Hospital  
Associate Professor in Medicine,  
Harvard Medical School  
Boston, MA

Matthew Cavender, MD  
Cardiovascular Fellow, Cardiovascular Division  
Brigham & Women’s Hospital  
Boston, MA
Improved Outcomes in Cardiogenic Shock

Written by Nicola Parry

Christian Spaulding, MD, European Hospital Georges Pompidou and INSERM U 970, Paris, France, discussed the epidemiology of ST-segment elevation myocardial infarction (STEMI) and cardiogenic shock (CS), and its association with the increasing use of reperfusion therapy, especially primary percutaneous coronary intervention (PCI).

IMPROVED USE OF REPERFUSION THERAPY

Evaluation of French survey data showed an improved use of reperfusion therapy from 1995 to 2010, associated with an increased use of primary PCI and decreased use of thrombolysis from 2000 to 2010 (Figure 1). During the decade, the mortality rate 30 days after STEMI declined by ~9% absolute [Puymirat E et al. JAMA 2012].

Figure 1. Changes in Use of Reperfusion Therapy, PCI, and Thrombolysis Over Time

![Chart showing changes in use of reperfusion therapy, PCI, and thrombolysis over time.]

Reproduced with permission from C Spaulding, MD.

Prof. Spaulding discussed key data from three French nationwide registries [Aissaoui N et al. Eur Heart J 2012] conducted between 1995 and 2005, comparing mortality in patients with acute myocardial infarction (AMI) with versus without CS. The key findings were 1) the incidence of CS decreased over time (6.9% in 1995; 5.7% in 2005; p=0.07); 2) 30-day mortality was more than 10-fold higher in CS patients compared to those without CS (60.9% vs 5.2%); and 3) mortality decreased both among patients with CS (70% to 51%; p=0.003) and without CS (8.7% to 3.6 %; p<0.001). Correspondingly, the use of PCI increased from 20% to 50% (p<0.001), and was associated with decreased mortality (OR, 0.38; 95% CI, 0.24 to 0.58; p<0.001).

Of patients enrolled in the Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock trial (SHOCK), 302 had AMI complicated by CS. Compared with initial medical stabilization, early revascularization resulted in a 13.2% absolute and 67% relative improvement in 6-year survival, reinforcing the need to rapidly identify patients who are candidates for early revascularization [Hochman JS et al. JAMA 2006].

CARDIAC ASSIST DEVICES

Despite the lack of clear guidelines for the timing and choice of cardiac assist devices (CADs), numerous options are available:

Intraaortic Balloon Pump (IABP): Although it was considered a Class I treatment for CS complicating AMI, clinical data are lacking to confirm this. In one recent trial, intraaortic balloon counterpulsation did not significantly reduce 30-day mortality in such patients [Thiele H et al. N Engl J Med 2012] although this lack of benefit may, in part, be explained by the use of IABP in 10% of the patients in the control arm.

Extracorporeal membrane oxygenator/extracorporeal life support (ECMO/ECLS): ECLS has shown encouraging outcomes in cardiac arrest (CA), and early ECMO-assisted primary PCI improves 30-day outcomes in STEMI complicated with CS.

Between 2002 and 2009, 1650 patients with acute STEMI underwent primary PCI. Of these, 13.3% had CS and 46 patients were treated with ECMO. The outcomes of the patients treated in an era in which ECMO was available was compared with historical controls of patients who presented between 1993 and 2002 with STEMI complicated by CS who underwent primary PCI prior to the availability of ECMO. The incidence of profound shock was similar in both groups (21.7% vs 21.0%; p=0.5); however, in patients treated in the ECMO era, the mortality of patients with profound shock and total 30-day mortality were lower (all p<0.04), and hospital survival time was increased (p=0.0005) [Sheu JJ et al. Crit Care Med 2010].

ECMO for temporary circulatory support is sometimes the only option for patients with refractory CS (RCS), but is typically only available in tertiary-care centers. However, a pilot study suggested this as a feasible option even in remote hospitals. Mortality was compared between tertiary and nontertiary care centers in the greater Paris area, and results demonstrated successful transfer of 75 of 87 RCS patients to tertiary care following local ECMO support, and 32 survived to hospital discharge (overall survival rate, 36.8%; 95% CI, 27.4 to 46.2). There was no significant difference in
mortality between patients who received ECMO locally or
at a tertiary care institution (OR, 1.48; 95% CI, 0.72 to 3.00,
p=0.29) [Beutheret S et al. *Eur Heart J* 2013].

**Impella 2.5: Advantages of the Impella 2.5 system**
include the ease of percutaneous insertion, its user-
friendly console, and trends toward improved outcomes
compared with IABP-support.

The PROTECT II trial was performed in stable patients
undergoing high-risk PCI and compared the Impella
system with an IABP. The with a primary endpoint of 30-
day incidence of major adverse events (MAEs), which
were defined as all-cause death, Q-wave or non-Q-
wave MI, stroke or transient ischemic attack, any repeat
revascularization procedure (PCI or coronary artery
bypass graft), need for a cardiac or a vascular operation
(including a vascular operation for limb ischemia), acute
renal insufficiency, severe inprocedural hypotension
requiring therapy, cardiopulmonary resuscitation or
ventricular tachycardia requiring cardioversion, aortic
insufficiency and angiographic failure of PCI. MAEs at 30
days were not significantly different, but at 90-day follow-
up there was a strong trend toward reduced MAEs in the
Impella group in the intent-to-treat and per-protocol
populations (Figure 2) [O’Neill WW et al. *Circulation*
2012]. There is limited data on the use of the Impella
device in CS. Registries have shown improvement in
hemodynamic parameters.

**Figure 2. Outcomes of the PROTECT II Trial**

And due to the high potential for coronary occlusions
and difficulties in interpreting the electrocardiogram in
patients following CA, immediate angiography should be
considered when ongoing infarction is suspected.

There is also evidence that survivors of out-of-hospital
CA who are comatose have improved neurological
outcomes if cooling occurs soon after resuscitation.
These patients should considered for prompt initiation of
therapeutic hypothermia [Steg PG et al. *Eur Heart J* 2012].

**PCI IN REFRACTORY IN- OR OUT-OF-HOSPITAL CARDIAC ARREST**

Studies have shown that survival rate decreases rapidly
after 10 minutes of cardiopulmonary resuscitation (CPR),
and even more rapidly after 30 minutes.

A 3-year prospective study investigated the use of ECLS as
compared with conventional CPR for patients with
in-hospital CA of cardiac origin undergoing CPR of >10
minutes. The primary endpoint was survival to hospital
discharge. Patients randomized to extracorporeal CPR
had a higher survival rate to discharge (p<0.0001), 30-day
survival (p=0.003), and 1-year survival as compared with
the conventional CPR group (p=0.007) [Chen YS et al.
*Lancet* 2008].

**PCI IN REFRACTORY OUT-OF-HOSPITAL CARDIAC ARREST**

ECLS has recently been introduced in the treatment of
refractory CA. Time from CA to implementation of
ECLS is a major prognostic factor for survival. Data from
a pilot study has suggested that prehospital ECLS is a safe
and feasible option even if the provider is not surgeon.
Prehospital ECLS for refractory CA was implemented in
seven patients by a team of providers that did not include
surgeons. ECLS was started 22 minutes after incision
and 57 minutes after onset of advanced cardiovascular
life support. One patient survived without sequelae, and
brain death resulted in three patients [Lamhaut L et al.
*Resuscitation* 2013].

Prof. Spaulding highlighted that, although CS remains
a concern in patients with STEMI, it is rare and usually
occurs after admission. He stressed the importance of
always considering shock in the management of patients
with AMI, and noted that beyond PCI, other factors (such
as age, diabetes, past history, coronary artery bypass graft,
and AMI) also contribute to the reduced mortality of
patients with STEMI.

**SHOCK AFTER RESUSCITATED CARDIAC ARREST**

In patients with resuscitated CA in whom
electrocardiography shows ST-segment elevation, the
strategy of choice is immediate angiography with a view to
primary PCI.
New Global Agenda for CVD Prevention: 25% Reduction by Year 2025

Written by Mary Mosley

Four noncommunicable diseases (NCDs) are recognized as a global epidemic and comprise the majority of morbidity and mortality worldwide: cardiovascular disease (CVD), diabetes, cancer, and respiratory disease. Four international nongovernmental organizations (NGOs) formed the NCD Alliance (www.ncdalliance.org), which now has a network of 2000 civil society organizations in more than 170 countries. The mission of the NCD Alliance is “to combat the NCD epidemic by putting health at the center of all policies.”

The four leading NGOs of the NCD Alliance are the International Diabetes Federation, World Heart Federation, Union for International Cancer Control, and International Union Against Tuberculosis and Lung Disease.

As one step to serve this mission, the NCD Alliance campaigned for and achieved a High-Level Meeting on NCD Prevention and Control at the United Nations, held September 19 to 20, 2011, with the participation of Heads of State and Government. This is only the second health summit held in the history of the United Nations, following the one held on HIV/AIDS in 2001.

The goal of the UN High-Level Meeting was to address the growing threat of NCDs to the public health of the world. This meeting led to the development of a political strategy designed to address the global epidemic of the four main NCDs. Following this meeting, the UN General Assembly voted to adopt a resolution to begin efforts to reduce premature death from NCDs worldwide by 25% by Year 2025—the so-called “25x25” agenda. This 25x25 global agenda for the prevention of CVD was reviewed by David A. Wood, MD, MSc, Imperial College London, London, United Kingdom. The toll exacted by NCDs is illustrated in Figure 1, with some of the highest NCD death rates in low- and middle-income countries.

MEMBER STATES FORMAL MEETING

The group then worked at a formal meeting of UN Member States in November 2012 to develop a framework through which to accomplish these goals. The group established indicators of progress and nine voluntary goals to be achieved by Year 2025 (Figure 2).

The 25x25 aims to reduce utilization of tobacco by 30% in persons aged ≥15 years. The program also seeks to achieve 10% reductions in the number of people with insufficient physical activity and excess alcohol use. Given the adverse effects of salt and hypertension on CV health, the group is aiming to reduce salt intake by 30% and work towards a 25% relative reduction in the prevalence of hypertension. The framework hopes to prevent the prevalence of diabetes and obesity from increasing further.

Figure 1. Mortality From NCD in Year 2010

NCD Death Rates (per 100,000 population)

- ≤400
- 401-500
- 501-600
- 601-700
- 701-800
- >800

Data not available
Not applicable

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The group agreed on working to increase access to care by setting a target of 80% availability for affordable basic technologies. In addition, the group hopes that the use of essential medications can be increased with at least 50% of eligible people worldwide receiving drug therapy and counseling, including glycemic control, to prevent heart attacks and strokes.

**WHO NCD ACTION PLAN**

The vision of the WHO NCD Action Plan 2013 to 2020 is a world free of the avoidable burden of NCD. The group agreed on 6 objectives to help work toward achieving this goal (Table 1). Prof. Wood noted that objectives 1 to 3 are political, objective 4 is clinical, objective 5 is research, and objective 6 is an audit to evaluate progress.

**Table 1. Objectives of the WHO Noncommunicable Diseases Action Plan 2013-2020**

| Objective 1: | To strengthen international cooperation and advocacy to raise the priority accorded to prevention and control of NCDs in the development agenda and in internationally agreed development goals |
| Objective 2: | To strengthen national capacity leadership, governance, multisectional action and partnerships to accelerate country response for prevention and control of NCDs |
| Objective 3: | To reduce exposure to modifiable risk factors for NCDs through creation of health-promoting environments |
| Objective 4: | To strengthen and reorient health systems to address prevention and control of NCDs through people-centered primary health care and universal coverage |
| Objective 5: | To promote and support national capacity for high quality research and development for prevention and control of NCDs |
| Objective 6: | To monitor trends and determinants of NCDs and evaluate progress in their prevention and control |

Image: Figure 2. The Nine Voluntary Global NCD Targets for Year 2025

Reproduced with permission from DA Wood, MD.

GLOBAL ALLIANCE FOR CVD PREVENTION IN CLINICAL PRACTICE

In addition, the WHO set a goal to strengthen and reorient health systems to address prevention and control of NCD through people-centered primary health care and universal coverage. The Global Alliance for Cardiovascular Disease Prevention in Clinical Practice was created to bring together members from the European Society of Cardiology (ESC) and the European Association for Cardiovascular Disease Prevention and Rehabilitation (EACDPR) in order to work toward achieving this objective.

The Global Alliance held the CVD Prevention in Clinical Practice Global Forum in Rome in April 2013, during the EuroPrevent Congress, to determine how it will achieve 25x25. At the Global Forum, they established a target of longer and healthier lives for all patients with atherosclerotic vascular disease and asymptomatic persons at high multifactorial risk of developing CVD, including those with diabetes.

The Global Alliance also agreed that their role should include the following:

- Creation of guidelines and standards
- Provision of education and training
- Provision of health service
- Research
- Leadership

The group felt guidelines and standards for CVD prevention and rehabilitation should be tailored to appropriately meet the specific needs of each country. Also, education and training in CVD prevention and rehabilitation should be provided to physicians, nurses, and allied health professionals.

The Global Alliance agreed they should work together to strengthen health service provision for CVD prevention and rehabilitation, and to promote adequate and cost effective service delivery that is tailored to the needs of each population. Research should be conducted to understand the burden of lifestyle and related risk factors in different populations and how these change over time, and to determine the outcomes that are being achieved by patients.

Leadership in CVD prevention and rehabilitation must be built by supporting the organization of professional societies in the countries where they do not exist. Additional information about the Global Alliance for Cardiovascular Disease Prevention in Clinical Practice can be obtained at www.escardio.org/EACPR/Documents/brochure-global-forum.pdf.
Patients with a ruptured thoracic aortic aneurysm experience among the highest rates of mortality reported for any cardiovascular condition. When repair is performed before rupture, these rates can be reduced from 48% to >19% at 30 days, and from 62% to >31% through 365 days. In both situations, however, the increasing mortality after 30 days demonstrates a significant risk that extends beyond the initial perioperative period. This risk increases with age (Figure 1) [Rigberg DA et al. *J Vasc Surg* 2006].

Figure 1. Impact of Age on Mortality for Patients Undergoing TAA Repair

Approximately 30% of patients being evaluated for aortic aneurysm repair are considered at too high a risk for surgery. Endovascular aortic repair-thoracic endovascular aortic/aneurysm repair (EVAR-TEVAR) is increasingly being used in this high-risk population. Achieving procedural success depends on multiple factors but the deploying of the device so as to minimize the potential for endoleaks (leakage off blood from the graph into the aneurysm sac) is critical to achieving procedural success.

Oscar A. Mendiz, MD, Hospital Universitario, Fundación Favaloro, Buenos Aires, Argentina, discussed the techniques used to minimize the risk of endoleaks in patients being treated for aortic aneurysms with endovascular techniques. Individual variations in vascular anatomy that make EVAR-TEVAR challenging include aneurysms with a short neck (<15 mm for abdominal aneurysms, <20 mm for thoracic aneurysms), angulated aneurysm necks (>40°), mural thrombus in the neck, tapering or reverse tapering of the aneurysm sac, compromise of both iliac arteries, thoracoabdominal aneurysms, and juxtarenal aneurysms.

Despite increases in the number of endograft devices and the improved design, many patients do not meet the indications for the current Food and Drug Administration-approved devices. Although custom devices are available, these devices take considerable time to acquire. As a result, surgeons often create or modify grafts to address patients anatomical variation. Stents are deployed along with the endograft, and the resulting “chimneys” allow an adequate proximal landing zone while enabling blood flow of the branch vessels outside of the endograft. Myriad versions of the chimney technique can be employed as dictated by the anatomy; these can be a cheaper and faster solution, and seem to have acceptable outcomes.
Abdominal aortic aneurysm (AAA) often occurs in the area of the renal arteries. In the past, this has prevented the use of a stent graft since the graft itself would cover the renal arteries preventing blood flow to the kidneys. Recently, fenestrated stent grafts have been developed which have small holes in the stent graft and allow blood to flow to the important organs. Although it is a challenging procedure, successful results have been achieved using fenestrated endovascular aneurysm repair (FEVAR).

In a meta-analysis of 11 studies describing the use of FEVAR for suprarenal and juxtarenal AAAs (660 procedures), 11 deaths occurred within 30 days, yielding a 30-day proportional mortality rate of 2%. Target vessel perfusion rates ranged from 90.5% to 100% [Cross J et al. Br J Surg 2012]. Intermediate results from another study using FEVAR for juxtarenal aortic aneurysms with short proximal necks, reported no aneurysm-related deaths, ruptures, or conversions through 2 years of follow-up. No type I or II endoleaks were reported. Type II endoleaks were noted in 26.1% of patients at 12 months and 20.0% of patients at 24 months [Greenberg RK et al. J Vasc Surg 2009]. In an 8-year clinical study, cumulative visceral branch patency was 93.3±1.9% at 5 years. All visceral artery stent occlusions occurred within the first 2 postoperative years. Renal function deterioration, however, was a major concern (Figure 2) [Verhoeven EL et al. Eur J Vasc Endovasc Surg 2010].

Figure 2. Target Vessel Patency With the FEVAR Approach


About one third of patients with AAAs have anatomy that is unfavorable to the use of a stent graft [Hallet JW. Comprehensive Vascular and Endovascular Surgery. Edinburgh, Scotland; New York, NY: Mosby; 2004]. These patients can still be treated successfully with endovascular aneurysm repair [Stather PW et al. Eur J Vasc Endovasc Surg 2012] with the right selection of fenestrated endografts and proper surveillance. The design must be individualized using precise imaging of the patient’s AAA. Fenestrated endovascular repair of AAA has been proposed as an alternative to open surgery for juxtarenal and pararenal AAAs. The Global Collaborators on Advanced Stent-Graft Techniques for Aneurysm Repair [GLOBALSTAR] Registry is the largest cohort of patients with fenestrated endovascular repair of juxtarenal aortic aneurysms in the United Kingdom. Data from 318 patients were obtained from 14 centers. Primary procedural success was achieved in 99% of patients, perioperative mortality was 4.1%, and intraoperative target vessel loss was observed in 5 of 889 target vessels (0.6%). Freedom from reintervention at 1 year was 90%. After 3 years, the survival rate was 89% [British Society for Endovascular Therapy and the GLOBALSTAR Registry. Circulation 2012]. The use of fenestrated endografts for aortic aneurysm repair is safe and effective in preventing rupture in the medium term, but there is a predictable high mortality rate during follow-up in this high-risk cohort, which requires meticulous follow-up [Amiot S et al. Eur J Vasc Endovasc Surg 2010].

The chimney graft has evolved as a potential alternative to fenestrated and side-branched endografts in high-risk patients with juxtarenal, pararenal, or thoracoabdominal aneurysms. Primary technical success was achieved in all patients in one meta-analysis of 15 reports. The 30-day in-hospital mortality was 4.3%. Although this technique has achieved relatively good results, long-term endograft durability and proximal fixation remains a significant concern [Moulakakis KG et al. J Vasc Surg 2012]. The technique should be considered only in acute poor surgical risk patients, as a bailout in case of unintentional renal artery coverage, or in elective poor surgical risk cases that are not suitable for a fenestrated endograft [Karsargyris A et al. J Endovasc Ther 2013]. This approach will require further investigation before widespread adoption.

An approach using coils and external-internal iliac bypass has been used in cases of bilateral iliac aneurysms when both iliac arteries are compromised. In a long-term study of iliac aneurysm repair with an iliac-branch endograft, periprocedural technical success rate was 95% with no mortality. Estimated patency rate of internal iliac branches after 5 years was 91.4%. Freedom from any reintervention was 90% at 1 year and 81.4% at 5 years. No late ruptures occurred and there was a low risk of reintervention. This technique can be considered as a first endovascular option in patients with extensive iliac aneurysm disease and favorable anatomy [Parlani G et al. Eur J Vasc Endovasc Surg 2012]. Results comparing side-branch endograft deployment with hypogastric exclusion for endovascular treatment of iliac aneurysms showed no significant differences in the failure of hypogastric side branch deployment (2/32) compared with hypogastric coiling (3/42). Reintervention rates were also similar (5/32 vs 4/42) at 1 year. Buttock claudication or impotence was more frequent after hypogastric exclusion, however [Verzini F et al. J Vasc Surg 2009].
Preliminary Results of SAUDICAT Provides IVUS Characterization of CAD

Written by Mary Mosley

The incidence of coronary artery disease (CAD) has reached epidemic levels in Saudi Arabia [Al-Nozha MM et al. Saudi Med J 2004]. In addition, Saudi Arabia has the highest prevalence of diabetes (DM) in the Middle East [Al-Nozha MM et al. Saudi Med J 2004]. As a result, the Saudi Coronary Athero-Thrombotic disease study [SAUDICAT] sought to use intravascular ultrasound to define the spectrum of coronary atherothrombotic disease in Saudi nationals with acute coronary syndromes (ACS) [Lawand S et al. J Saudi Heart Assoc 2012]. Samih Lawand, MD, Prince Salman Heart Center, Riyadh, Saudi Arabia, presented the preliminary results of the first 59 consecutive patients enrolled in this study.

The patients were mostly men (78%), 46% currently smoked and two thirds had DM. The presenting diagnosis was ST-segment elevation myocardial infarction (STEMI) in 25% of patients, non-STEMI (NSTEMI) in 25%, and unstable angina in 32% of patients.

The rate of NSTEMI was significantly higher in the 39 patients with DM (60%) compared with those without DM (40%; p=0.009). The incidence of hypertension (75% vs 26%; p=0.053) and dyslipidemia (70% vs 30%; p=0.59) was also more prevalent in patients with NSTEMI. STEMI was more common in patients without DM.

Differences in the coronary anatomy and structure were found between patients with DM, as compared with patients without DM, including significantly smaller vessel diameters, smaller lumen diameters, smaller vessel areas, and smaller plaque areas among patients with DM (Table 1).

Table 1. IVUS Characterization of Coronary Vessels in Patients With and Without Diabetes

<table>
<thead>
<tr>
<th>Total (n=59; 435 Obs)</th>
<th>Nondiabetic (n=17; 110 Obs)</th>
<th>Diabetic (n=42; 325 Obs)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vessel area mean</td>
<td>12.8767717</td>
<td>11.3618954</td>
<td>0.0088</td>
</tr>
<tr>
<td>Average vessel diameter</td>
<td>3.988856451</td>
<td>3.74483503</td>
<td>0.0030</td>
</tr>
<tr>
<td>Plaque area mean</td>
<td>6.9733033866</td>
<td>6.09470437</td>
<td>0.0200</td>
</tr>
<tr>
<td>Lesion area mean</td>
<td>5.905379927</td>
<td>5.267276642</td>
<td>0.0632</td>
</tr>
<tr>
<td>Average percent volume obstruction</td>
<td>0.5277 (0.0787±SD)</td>
<td>0.5363 (0.0782±SD)</td>
<td>0.7795</td>
</tr>
</tbody>
</table>

Patients with DM who presented with STEMI were more likely to have significantly smaller vessel diameters, luminal diameters, and plaque areas. In contrast, patients with DM who presented with NSTEMI had significantly larger plaque areas (p=0.0003) and plaque burden (p=0.0033), and a trend for a larger remodeling index (p=0.3345) that was not significantly different compared without DM. In the setting of unstable angina, no significant differences were seen between the patients with and without DM.

Patients with diabetes presenting with STEMI or NSTEMI were more likely to have a greater plaque burden and larger plaque area, which Prof. Lawand hypothesized may be due to advanced atherosclerosis. Although patients with diabetes had smaller coronary vessels overall, he noted that the size of the plaque area and percent volume obstruction was similar to patients without diabetes.

Prof. Lawand concluded that this small, retrospective analysis of intravascular ultrasound (IVUS) data highlights the need for improvements in the use of IVUS and provides a framework to better understand the characteristics of coronary atherosclerosis in a Middle Eastern population.
MitraClip Appears Promising in First Egyptian Patients for Percutaneous Mitral Repair

Written by Mary Mosley

Surgical approaches for degenerative or functional mitral regurgitation (MR) continue to have limitations and not all patients are appropriate surgical candidates. Hazem Khamis, MD, October 6 University Hospital, Giza, Egypt, described the use of percutaneous mitral valve repair for functional MR using the MitraClip Device and the results from their initial experience in Egypt.

This percutaneous device delivers two stitches into the mitral valve leaflets that approximate the two leaflets in a manner similar to that of the surgical Alfieri technique. The MitraClip procedure requires sufficient leaflet tissue in the mitral valve for mechanical coaptation, with a flail gap <10 mm, a flail width <15 mm, and a mitral area ≥4.0 cm. To use the MitraClip, the etiology of the regurgitation cannot be due to either rheumatic fever or infective endocarditis. The MitraClip is approved in some European and Asian countries, but is available for use only within clinical trials in the United States.

In 78 high-risk surgical patients (≥12% predicted mortality) with extensive comorbidities, the MitraClip device was shown to reduce MR, improve symptoms (functional status and quality of life), and prevent ventricular reverse remodeling through 1 year, according to results from the EVEREST II High Risk Study [Whitlow PL et al. J Am Coll Cardiol 2012]. Similar clinical benefits were found in the ACCESS EU trial of functional MR in patients with extensive comorbidities [Maisano F et al. J Am Coll Cardiol 2013].

The PERMIT-CARE prospective survey in 51 symptomatic patients who were not successfully treated with cardiac resynchronization therapy (CRT) in seven European centers showed there was significant improvement in NYHA class and MR after MitraClip implantation [Auricchio A et al. J Am Coll Cardiol 2011].

Prof. Khamis stressed the importance of the multidisciplinary team for the MitraClip approach, which discusses every potential patient. The team includes the interventional cardiologist, cardiac anesthetist, echocardiogram specialists, laboratory staff, and nursing staff who were given specialized training. All patients undergo a preprocedural transthoracic echocardiogram and transesophageal echocardiogram (TEE).

At their institution, Prof. Khamis and colleagues have treated five patients, all of whom had functional MR. The baseline demographics and comorbidities of these patients are summarized in Table 1. One patient was treated with two MitraClips, and the others with a single clip. There were no procedural major adverse cardiac events. The device performance was good, without any occurrence of embolization, fracture, erosion, or migration of the percutaneous device, or single leaflet device attachment. At 1 month, all of the patients reported a marked improvement in symptoms and in exercise capacity. At 30 days, only one safety endpoint had occurred, which was a deep wound infection.

Based on the results in the first five patients treated in Egypt, as well as those who have been treated in other parts of the world, percutaneous MV repair with the MitraClip device appears both safe and feasible. However, Prof. Khamis stated there is a steep learning curve, and understanding the MV anatomy and the TEE images is essential to proper device delivery. Furthermore, he stated there is a definite need for the development of percutaneous treatment options for MR in order to treat patients who are not candidates for current surgical treatments.

Table 1. Baseline Demographics and Comorbidities

<table>
<thead>
<tr>
<th>Age</th>
<th>55±7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>4</td>
</tr>
<tr>
<td>History of heart failure</td>
<td>4</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>3</td>
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<tr>
<td>Prior myocardial infarction</td>
<td>3</td>
</tr>
<tr>
<td>Previous cardiothoracic surgery</td>
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<td>Atrial fibrillation</td>
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<tr>
<td>Chronic obstructive pulmonary disease</td>
<td>1</td>
</tr>
<tr>
<td>CRT</td>
<td>2</td>
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<tr>
<td>Diabetes mellitus</td>
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<td>Degenerative mitral regurgitation etiology</td>
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<tr>
<td>NYHA functional class III/IV</td>
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<tr>
<td>Mitral regurgitation severity 3+ to 4+</td>
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<tr>
<td>Mean ejection fraction</td>
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<tr>
<td>Mean left-ventricular end-systolic diameter</td>
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Heart Failure Update

Written by Maria Vinall

Dipti Itchhaporia, MD, Hoag Heart and Vascular Institute, Newport Beach, California, USA, reviewed data from four heart failure studies and discussed changes in the 2013 American College of Cardiology Foundation (ACCF)/American Heart Association (AHA) Heart Failure Guidelines [Yancy CW et al. J Am Coll Cardiol 2013; Circulation 2013].

The primary change is the expanded definition of heart failure (HF) to HF with reduced ejection fraction (EF ≤40%; HFrEF or systolic HF) and heart failure with preserved ejection fraction (EF ≥50%; HFrEF or diastolic HF). Two subcategories of HFrEF have also been defined: HFrEF Borderline (EF 41% to 49%) and HFrEF Improved (patients previously diagnosed with HFrEF whose EF is now >40%).

Greater emphasis has been placed on adherence to performance and quality measures, reducing readmissions, patient self-care, and team-based care. The guidelines call for a more thorough analysis of HFrEF, a continued assessment of risk factors, genetic testing, and avoidance of anticoagulation in patients with chronic reduced EF and no risk factors. For the first time, the guidelines include recommendations for optimal guideline-directed medical therapy (GDMT).

RED-HF: ADDRESSING ANEMIA

Studies have shown that anemia in HF patients is associated with worse functional capacity and poor survival. Increasing hemoglobin using an erythropoiesis-stimulating agent has been suggested to have clinical benefit. Darbepoetin alfa is a glycoprotein that stimulates erythropoietin, a hormone released from the kidney that develops red blood cells and produces hemoglobin.

The Reduction of Events With Darbepoetin Alfa in Heart Failure study [RED-HF; Swedberg K et al. N Engl J Med 2013] assessed its effects on clinical outcomes in 2778 HF patients with HFrEF and mild-to-moderate anemia. Although darbepoetin alfa significantly increased hemoglobin levels, the increase did not reduce the risk of the primary composite outcome of death or hospitalization for HF. Scores on the Kansas City Cardiomyopathy Questionnaire indicated a small, but statistically significant improvement in quality of life (QoL; p=0.005) after 6 months in patients treated with darbepoetin alfa. The risk of thromboembolic events was significantly higher in darbepoetin alfa-treated patients (13.5% vs 10% with placebo). These findings suggested that hemoglobin is simply a marker of poor prognosis in HF rather than a therapeutic target.

ASTRONAUT: TESTING ALISKIREN, A NEW DIRECT RENIN INHIBITOR

The ASTRONAUT trial [Gheorghiade M et al. JAMA 2013] was an international, randomized, controlled trial designed to evaluate the effect of inpatient initiation of the direct renin inhibitor aliskiren on postdischarge morbidity and mortality among patients with HF. The study population was comprised of patients hospitalized with HF who were hemodynamically stable with HFrEF, elevated natriuretic peptides (brain natriuretic peptide [BNP] ≥400 pg/mL or N-terminal pro-BNP [NT-proBNP] ≥1600 pg/mL), and signs and symptoms of fluid overload. Patients were recruited from 316 sites across North and South America, Europe, and Asia between May 2009 and December 2011. The follow-up period ended in July 2012. Patients were randomized to aliskiren (starting dose 150 mg, titrated to 300 mg as tolerated; n=808) or placebo (n=807), on top of standard therapy. The primary outcome of cardiovascular (CV) death or hospitalization for heart failure at 6 months occurred in 24.9% of the aliskiren group versus 26.5% of the placebo group (p=0.41).

The ASTRONAUT trial did not support routine administration of aliskiren in patients recently hospitalized for worsening chronic heart failure (Figure 1).

Data from observational studies and small trials have suggested that sildenafil, a phosphodiesterase-5 (PDE-5) inhibitor, might improve exercise capacity and clinical outcomes in HF patients compared with placebo. The Effect of Phosphodiesterase-5 Inhibition on Exercise Capacity and Clinical Status in Heart Failure With Preserved Ejection Fraction trial [RELAX; Redfield et al. JAMA 2013] showed no benefit of sildenafil in patients with HFrEF (EF >40%).
MM et al. JAMA 2013] was a randomized, controlled study that enrolled 216 patients with NYHA Class II to IV HFpEF at 26 North American centers between October 2008 through February 2012. Follow-up was through August 30, 2012. Participants were randomized to sildenafil (n=113) or placebo (n=103) administered orally at 20 mg TID for 12 weeks, followed by 60 mg TID for 12 weeks. The primary endpoint was change in peak oxygen consumption after 24 weeks of therapy. A key secondary endpoint was the composite clinical status rank score, based on time to death, time to CV or cardiorenal hospitalization, and change in QoL for participants without CV or cardiorenal hospitalization at 24 weeks.

Figure 1. CV Death or HF Rehospitalization Following Aliskiren Treatment

![Figure 1](image1.png)


At Week 24 in RELAX, the change in peak oxygen consumption was not significantly different between the two groups, and there was no significant difference in mean clinical status rank scores (Figure 2).

Figure 2. Effects of Sildenafil on Exercise Capacity and Clinical Outcome

![Figure 2](image2.png)


Even though HF remains a leading cause of hospital admission and readmission [Jencks SF et al. N Engl J Med 2009] the use of digoxin has been declining, in part due to its lack of effect on mortality and a downgrade in guideline recommendations. Older trials had shown benefit with digoxin, a drug discovered more than 2 centuries ago. The DIG trial [Digitalis Investigation Group. N Engl J Med 1997] showed that digoxin improved HF symptoms and reduced the risk of hospital admission both overall and for worsening heart failure. But, digoxin did not reduce overall mortality (Figure 4). In the RADIANCE trial [Packer M et al. N Engl J Med 1993] digoxin improved exercise tolerance and endurance, and patients switched from digoxin to placebo had lower QoL scores (p=0.04), decreased EF (p<0.001), and increases in heart rate (p=0.001) and body weight (p<0.001).

A recent post hoc analysis of the 3405 patients aged >65 years in the DIG trial showed that digoxin reduced the rate of all-cause hospital admission through 30 days (5.4% vs 8.1% with placebo) in ambulatory older patients with chronic HFpEF treated with ACE inhibitors and diuretics [Bourge RC et al. Am J Med 2013]. The absolute and relative risk for all-cause hospital admission were reduced by 2.7% and 34%, respectively, 30 days after randomization in patients randomized to digoxin. Digoxin reduced the risk of hospital admission due to CV causes by 47% (p<0.001) and worsening HF by 60% (p<0.001) during this same period.

These results are limited by their post hoc nature and other generalizability concerns. However, if they can be replicated in contemporary older HF patients discharged from the hospital after acute decompensation, digoxin may provide an inexpensive tool to reduce 30-day all-cause hospital readmission, the study authors stated.

Evidence-based, guideline-directed diagnosis, evaluation, and therapy should be the mainstay for all patients with HF, concluded Dr. Itchhaporia. Effective implementation of guideline-directed best quality care reduces mortality, improves QoL, and preserves healthcare resources. More research is needed to answer questions pertaining to prevention, nonpharmacologic therapy of HF [including dietary adjustments], treatment of HFpEF, management of hospitalized HF, effective reduction in HF readmissions, more precise use of device-based therapy, and cell-based regenerative therapy.
Monoclonal Antibody to PCSK9 Offers New Approach to Treating Hypercholesterolemia

Written by Lynne Lederman

Hypercholesterolemia, particularly an increased level of low-density lipoprotein cholesterol (LDL-C) is associated with elevated cardiovascular (CV) risk. Individuals with genetic lifelong lower levels of LDL-C are associated with a reduced risk of CV events. In addition, the reduction in coronary heart disease (CHD) risk is proportional to the decrease in LDL-C over the time period of LDL-C reduction. Statins are often used to therapeutically lower LDL-C levels, but individuals with lifelong lower LDL-C levels due to genetic variants have three times the protection from CHD as do those who begin statin therapy later in life. In a meta-analysis, the effect on reduced CHD risk was directly proportional to the decrease in LDL-C associated with each allele [Ference BA et al. J Am Coll Cardiol 2012].

Gregory S. Thomas MD, MPH, Memorial Care Heart and Vascular Institute, University of California, Irvine, Irvine, California, USA, questioned whether we should start treating patients with drugs, diet, and exercise earlier in their life span, and whether treatment decisions should be based on the 10-year or lifetime CHD risk. Dr. Thomas presented examples of individuals with heterozygous familial hyperlipidemia (HeFH), who, in contrast to those with alleles associated with lifetime lower LDL-C levels, have lifetime higher LDL-C levels. In addition to hyperlipidemia, people with HeFH experience myocardial infarctions (MI) at an early age, and may undergo repeat coronary artery bypass grafting (CABG) and stenting.

Normally, LDL receptors are expressed on the cell surface, primarily on liver cells. LDL receptors "pick up" LDL particles; via endocytosis into a clathrin-coated vesicle, the LDL is ultimately degraded in a lysosome while the LDL receptor is recycled via an endosome back to the cell surface where it can continue to regulate LDL levels. This process is regulated by the sterol regulatory element binding protein (SREBP) in the nucleus.

Proprotein convertase subtilisin/kexin type 9 (PCSK9) is an enzyme that affects the recycling of LDL receptors. Like the LDL receptor, PCSK9 is also regulated by SREBP. Circulating PCSK9 binds to the extracellular domain of the LDL receptor, followed by transport to an intracellular lysosome rather than a clathrin-coated vesicle, where the LDL receptor is degraded, rather than being recycled. Thus, increased PCSK9 activity results in fewer LDL receptors available on the cell surface to remove LDL from circulation.

Individuals with nonsense mutations in the PCSK9 gene have reduced levels of LDL-C and a significantly reduced risk of CHD [Cohen JC et al. N Engl J Med 2006]. Among 3363 black subjects, mean LDL-C was 28% lower and CHD risk was reduced by 88% in the 2.6% who had a PCSK9 nonsense mutation as compared with those subjects without the nonsense mutation (HR, 0.11; 95% CI, 0.24 to 0.97; p=0.03). Of 9524 white subjects, 3.2% had a PCSK9 sequence mutation. This mutation was associated with a 15% lower LDL-C and a 47% lower CHD event rate (adjusted HR, 0.50; 95% CI, 0.32 to 0.79; p=0.003). This observation suggested that inactivating PCSK9 in individuals with hypercholesterolemia might be a strategy to lower LDL-C levels in individuals with high LDL-C levels.

SAR236553/REGN727 (alirocumab) is a fully humanized monoclonal antibody that binds to circulating PCSK9 and prevents it from binding to the LDL receptor. Binding of SAR236553/REGN727 to PCSK9 allows normal recycling of the LDL receptor, so rather than being degraded, the LDL receptor continues to remove LDL from circulation.

Clinical trials have been conducted of SAR236553/REGN727, which is administered by subcutaneous injection. SAR236553/REGN727 lowered LDL-C in normal healthy volunteers [Stein EA et al. N Engl J Med 2012]. A dose-finding study in patients with HeFH showed SAR236553/REGN727 lowered LDL-C without adverse effects on liver function tests [Stein
EA et al. Lancet 2012. Adding SAR236553/REGN727 to atorvastatin resulted in further lowering of LDL-C levels in patients with primary hypercholesterolemia [Roth EM et al. N Engl J Med 2012]. In this study, adverse events included rash that responded to antihistamine administration, and injection-site reactions in three of the 61 patients. One patient with mild AST elevation at baseline had a further AST elevation. In another Phase 2 study, one patient experienced vasculitis that resolved with treatment [McKenney JM et al. J Am Coll Cardiol 2012]. Two weeks before and after there were no anti-SAR236553/REGN727 antibodies detectable; however, at Week 20, a follow-up assessment detected minimal (titer of 30) anti-SAR236553/REGN727 antibodies.

The Phase 3 Evaluation of Cardiovascular Outcomes After an Acute Coronary Syndrome During Treatment With Alirocumab SAR236553 [REGN727] trial [Odyssey Outcomes; NCT01663402] is testing a 150-mg dose of SAR236553/REGN727 administered subcutaneously Q2W. This randomized, double-blind, placebo-controlled, parallel-group trial will evaluate the effect of SAR236553/REGN727 compared with placebo on the occurrence of CV events. The planned enrollment is 18,000 individuals who have had an acute coronary syndrome (ACS) event 4 to 16 weeks prior to random assignment and who are being treated for dyslipidemia. The primary composite endpoint of CV events includes CHD death, nonfatal MI, fatal and nonfatal ischemic stroke, and unstable angina requiring hospitalization. The trial completion date is estimated to be 2018. Dr. Thomas suggested that the initial FDA approval for SAR236553/REGN727 may be for HeFH because statins do not achieve sufficiently low levels of LDL-C for these individuals.

The safety and efficacy of SAR236553/REGN727 continues to be evaluated in a number of clinical trials, alone and in combination with other cholesterol-lowering agents such as statins, fibrates, and cholesterol absorption inhibitors, and in patients with HeFH and those with other causes of hypercholesterolemia. It will be necessary to determine the long-term effects of administration of SAR236553/REGN727, given the reports of injection-site reactions. Patient acceptability may also be an issue, as the current administration scheme requires subcutaneous injection every 2 weeks, presumably for life. Similar Phase 2 studies have been conducted and Phase 3 trials are underway with AMG 145, a monoclonal antibody administered either every 2 or every 4 weeks.
Clopidogrel Retains Its Place in ACS Therapy

Clopidogrel appears to retain its place in the treatment of patients with acute coronary syndrome (ACS) and may have greater benefit than clopidogrel plus aspirin in patients that receive oral anticoagulant (OAC) therapy. Fausto J. Pinto, MD, PhD, Lisbon University, Lisbon, Portugal, presented clinical trial data to support what he suggests are key concepts in the treatment of ACS, with particular attention given to the role of clopidogrel.

The antithrombotic drugs that are currently available for clinical use include antiplatelet agents such as aspirin, clopidogrel, prasugrel, ticagrelor, and GPIIb/IIIa inhibitors, and anticoagulation agents such as fondaparinux, low molecular weight heparin, heparin, and bivalirudin. Prof. Pinto pointed out that physicians must always balance the axis of increased efficacy (decreased ischemic risk) without increasing the risk of bleeding (Figure 1).²

**Figure 1. Efficacy/Bleeding Risk Balance**

- Therapeutic goal: Superior outcome (decreased ischemic risk without increased bleeding)
- Reduced efficacy
- Increased bleeding
- Inferior outcome
- No increase in bleeding

In addition to clopidogrel and aspirin, two new antiplatelet agents are currently being evaluated in late-stage clinical trials. Prasugrel, like clopidogrel, is an irreversible thienopyridine prodrug with a rapid onset of action of 30 minutes (defined as 50% inhibition of platelet aggregation) that lasts for 5 to 10 days. Ticagrelor is a reversible triazolopyrimidine that does not require activation. The onset of action is 30 minutes (defined as 50% inhibition of platelet aggregation) that lasts for 5 to 10 days. Ticagrelor is a reversible triazolopyrimidine that does not require activation. The onset of action is 30 minutes (defined as 50% inhibition of platelet aggregation) that lasts for 5 to 10 days.

Prof. Pinto highlighted an early trial that showed a clear benefit for the use of antiplatelet therapy in patients with ACS. In the CURE trial, patients treated with clopidogrel demonstrated a lower cumulative hazard ratio for death from cardiovascular causes, nonfatal myocardial infarction (MI), or stroke over 12 months compared with placebo (p<0.001). Trials like the CURE study resulted in the recommendation of antithrombotic agents for first-line use in ACS by the European Society of Cardiology (ESC).

The 2012 ESC guidelines recommend aspirin plus an adenosine diphosphate-receptor blocker such as prasugrel, ticagrelor, or clopidogrel in periprocedural percutaneous coronary intervention (PCI). Clopidogrel is suggested for use when prasugrel or ticagrelor are not available or are contraindicated. The guidelines recommend the use of clopidogrel plus aspirin in fibrinolytic therapy and in patients with ST-elevation myocardial infarction (STEMI), low-dose aspirin, or prasugrel in patients intolerant to aspirin. The recommended doses of clopidogrel in primary PCI is a loading dose of 600 mg and a maintenance dose of 75 mg QD, in fibrinolytic therapy the loading dose is 300 mg and a maintenance dose of 75 mg QD, and without reperfusion therapy the dose is 75 mg QD.

Prof. Pinto presented several clinical trials on which the 2012 ESC recommendations were based. Importantly, ~40% to 60% of patients with ACS with unstable angina (UA) or non-STEMI are medically managed without revascularization, and these patients have a 2-fold greater risk of developing ischemic events. Prof. Pinto pointed out that this patient population has been traditionally underrepresented in ACS trials, but the TRILOGY ACS trial evaluated clopidogrel versus prasugrel in this ACS population.

In the TRILOGY ACS trial, 7243 medically managed UA/non-STEMI patients were randomized to receive clopidogrel 75 mg QD or prasugrel 5 or 10 mg QD for 30 months. The primary efficacy endpoint was cardiovascular death, MI, or stroke, which was similar among both treatment arms. In the clopidogrel arm, 20.3% of patients experienced the primary efficacy endpoint compared with 18.7% in the prasugrel arm, with a hazard ratio of 0.96 (95% CI, 0.86 to 1.07; p=0.45). In addition, 1.8% and 2.5% of patients who received clopidogrel or prasugrel, respectively, experienced major bleeding as identified by TIMI bleeding criteria, with a hazard ratio of 1.23 (95% CI, 0.84 to 1.81; p=0.29).

Although not performed in patients with ACS, the WOEST trial evaluated long-term OAC therapy plus aspirin 80 mg QD and clopidogrel 75 mg QD (triple therapy), or OAC plus clopidogrel 75 mg QD (dual therapy) following percutaneous coronary stenting in patients with atrial fibrillation and/or mechanical heart valves. Follow-up was for 1 year with a primary endpoint of bleeding events as determined by TIMI criteria. Secondary endpoints included the occurrence of stroke, death, MI, stent thrombosis, and target vessel revascularization (TVR).
both as a composite and individually. In the triple-therapy arm, the cumulative incidence of bleeding was 44.4% compared with 19.4% in the dual-therapy arm, with a resulting hazard ratio of 0.36 (95% CI, 0.26 to 0.50; p<0.0001; Figure 2). In the WOEST trial, the majority of the bleeding events were classified as minor (25.7% triple therapy vs 10.7% dual therapy; p<0.001), and 5.6% and 3.2% of bleeding in the triple- and dual-therapy groups, respectively, were considered to be major. Further analysis demonstrated that the worst bleeding per patient for triple therapy was located in “other” and the skin, while the worst bleeding per patient with dual therapy occurred in “other” and the access site.

Figure 2. Long-Term OAC Therapy Plus Clopidogrel Monotherapy Versus Clopidogrel and Aspirin in the WOEST Trial


The results of the secondary endpoints in the WOEST trial demonstrated that TVR trended toward occurring more frequently in the dual-therapy arm (p=0.876; Figure 3); however, death, MI, stroke, and stent thrombosis occurred more frequently in the triple-therapy arm.Overall, the all-cause mortality in the WOEST trial was greater in the triple-therapy group at 6.3% compared with 2.5% in the dual-therapy arm, with a hazard ratio of 0.39 (95% CI, 0.16 to 0.93; p=0.027). Prof. Pinto pointed out that the WOEST trial was the first randomized trial of patients receiving antiplatelet therapy with OAC and undergoing coronary stenting. Although it was expected that dual therapy would result in less bleeding than triple therapy, it was important to demonstrate this through a randomized trial. Further, Prof. Pinto pointed out that in addition to dual therapy resulting in less bleeding, dual therapy did not cause an increase in thromboembolic events or death.

Figure 3. WOEST Secondary Endpoints

Prof. Pinto concluded by stating that, in his opinion, clopidogrel is still a major tool for the treatment of patients with ACS that may or may not undergo revascularization, as well as those that may require percutaneous coronary stenting and OAC therapy. In addition, in patients that receive OAC, the use of clopidogrel only, without aspirin, provides greater benefits than clopidogrel plus aspirin.

References
Techniques to Improve Left Main Stenting

Written by Emma Hitt, PhD

Stenting of the left main coronary artery can be technically challenging due to the different diameters of the proximal and distal vessel, presence of disease in the bifurcation of the artery and limitations of the currently available stents. Bernard Chevalier, MD, Institut Cardiovasculaire Paris Sud, Massy, France, presented techniques for left main percutaneous coronary intervention (PCI). Achieving success with left main PCI is dependent on choosing proper patients, using appropriate techniques, and implanting the best type of stent for that particular patient, according to Prof. Chevalier.

There are a variety of treatment options for bifurcation lesions such as T-stenting or crush techniques which use multiple stents or provisional stenting which uses one stent to treat the main coronary artery and an additional stent in the other only if necessary. A recent analysis of the French Left Main Taxus registry of 5-year outcomes following unprotected left main stenting demonstrated a major adverse cardiac event (MACE) occurrence of 34.1% in patients with one stent compared with 17.8% in patients with two stents at 60 months (log-rank p=0.006) [Mylotte D et al. EuroIntervention 2012]. In addition, the rate of cardiac death was 18.2% in patients who received one stent and 8.5% in patients who received two stents (log-rank p=0.035). Similarly, a prospective analysis of the j-Cypher registry in Japan of 3-year outcomes following sirolimus-eluting stent (SES) implantation for unprotected left main coronary artery disease demonstrated an incidence of cardiac death of 5.5% for patients in which only the main branch was stented and 12.2% for in which the main branch and the side branch were stented at 1095 days post stent implantation (p=0.018) [Toyofuku M et al. Circulation 2009]. In the same analysis, the incidence of target lesion revascularization (TLR) was 11.1% for patients in which only the main branch was stented and 30.9% for patients in which the main branch and the side branch were stented (p<0.0001).

The impact of stenting technique—T-stenting, V-stenting, or crush stenting—was evaluated in a study of 2-year outcomes with drug-eluting stent (DES) implantation in 773 patients with unprotected left main stenosis [Palmerini T et al. Circ Cardiovasc Interv 2008]. The MACE-free survival was similar across the techniques with a MACE-free rate of 66.5% in patients who received T-stenting, 69.3% in patients who received V-stenting, and 66.9% in patients who received crush stenting. Similarly, there was no significant difference in survival, myocardial infarction (MI)-free survival, cardiac death-free survival, or TLR-free survival between the three different techniques. In addition, there appears to be no clear consensus on the use of provisional versus multiple, as studies have demonstrated favorability for both techniques for TLR and side branch restenosis. However, provisional stenting is associated with lower MI or stent thrombosis as compared with the use of two stents.

Prof. Chevalier compared the French Left Main Taxus pilot registry and the Left Main Xience [LEMAX] registry in which the same operators performed a provisional T-stenting and final kissing balloon inflation strategy for left main stenting, and the Friend registry (Table 1). In the Taxus pilot and FRIEND registries, first generation paclitaxel-eluting stents (PES) were used, whereas second generation everolimus-eluting stents (EES) were used in the LEMAX registry. In the Taxus pilot study in 2004, 78% of the 291 patients had a distal lesion and and 42% had two stents [Vaquerizo B et al. Circulation 2009]. In the FRIEND registry, 69% of the 151 patients had a distal lesion while 26% were treated with two stents [Carrié D et al. EuroIntervention 2009]. In the LEMAX registry in 2008, 81% and 19% of the 174 patients had a distal lesion and two stents, respectively [Salvatella N et al. EuroIntervention 2011].
Table 1. Comparison of Left Main Studies With Drug-Eluting Stenting

<table>
<thead>
<tr>
<th>No. of patients</th>
<th>Distal lesion (%)</th>
<th>Two stents (%)</th>
<th>Mean LM stent diameter (mm)</th>
<th>12-month TLR</th>
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</thead>
<tbody>
<tr>
<td>Pilot Taxus* 2004</td>
<td>291</td>
<td>78</td>
<td>42</td>
<td>3.44±0.39</td>
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<tr>
<td>FRIEND** 2006</td>
<td>151</td>
<td>69</td>
<td>26</td>
<td>3.59±0.49</td>
</tr>
<tr>
<td>LEMAX 2008</td>
<td>174</td>
<td>81</td>
<td>19</td>
<td>3.63±0.33</td>
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</tbody>
</table>

LM=left main; TLR=target lesion revascularization.


Prof. Chevalier stated it is important to know the maximum expansion for the DES being used to treat a coronary lesion since expansion of the stent beyond this point had not been studied. It is possible that expansion beyond recommended size could result in loss of the structural integrity of the stent, increased metal fatigue, and an increased risk of stent fracture. It is unknown whether beyond-maximal expansion can cause an increased risk of dissection or plaque prolapse. When performing left main stenting, the maximum expansion of the stent should be taken into consideration when determining which stent to use (Table 2) [Foin N et al. Int J Cardiol 2013].

Table 2. Maximum Postdilation Expansion of Drug-Eluting Stents

<table>
<thead>
<tr>
<th>Maximum Balloon Size</th>
<th>Element</th>
<th>Xience</th>
<th>Taxus</th>
<th>Integrity</th>
<th>BioMatrix</th>
<th>Cypher</th>
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<tbody>
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<td>Very small WH (2 cells); ME, 3.0 mm</td>
<td>Medium WH (6 crowns, 2 cells); ME, 4.4 mm</td>
<td>Small WH (6 crowns, 2 cells); ME, 3.4 mm</td>
<td>Small WH (7 crowns, 2 cells); ME, 4.9 mm; 1.5 cell in Resolute</td>
<td>Medium WH (6 crowns, 2 cells); ME, 4.6 mm</td>
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<td>Medium WH (10 crowns, 3 cells); ME, 5.4 mm</td>
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<td>Large WH (9 crowns, 3 cells); ME, 5.6 mm</td>
<td>Large WH (9 crowns, 3 cells); ME, 5.9 mm</td>
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<td>3.50</td>
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<td>4.00</td>
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</table>

ME=maximum exposure; WH=workhorse.

Prof. Chavalier noted that treating side branches is challenging because the diameters are frequently different from the main branch and the diameter of the branching ostia may be different from the diameter of the main branch. Prof. Chavalier recommended against using a balloon other than kissing balloon for inflation, as this technique can cause distortion of the stent [Sgueglia GA, Chevalier B. JACC Cardiovasc Interv 2012]. Instead, kissing inflation allows the use of multiple balloons of different sizes to expand the stent to the appropriate diameter. For example, before the bifurcation the main branch may have a larger diameter than after the bifurcation. In addition, different-sized balloons can expand a single stent to the correct diameter in different areas of the vessel.

In conclusion, Prof. Chevalier stated that provisional side branch stenting is a feasible and safe technique for both left main and non-left main bifurcation lesions in most patients. Using a complete simulation may be helpful in understanding the important steps of this technique, including the use of two wires, stent sizing, proximal optimization technique, and the use of kissing balloons. Prof. Chavalier pointed out that in the future, simulations may be extremely useful as a training tool, as well as a way to analyze the results of various treatments and the prediction of future events following treatment.
Renal Denervation Is Promising as a Treatment for Resistant Hypertension

Written by Emma Hitt, PhD

The sympathetic nervous system (SNS) has recently been hypothesized to play a key role in resistant hypertension. As a result, recent studies have explored renal artery denervation therapy as a potential treatment option for patients with resistant hypertension. Mohammad I. Kurdi, MBBS, Al Takhassoussi Hospital, Riyadh, Saudi Arabia, presented the current and future landscape of renal denervation therapy.

Systemic hypertension is associated with major adverse cardiac and cerebral events and pharmacologic control of hypertension has been shown to reduce cardiovascular and cerebrovascular events. However, some patients continue to have poorly controlled hypertension despite multidrug therapy or have adverse drug events or contraindications to pharmacotherapy that prevent adequate control of hypertension. Interestingly, increased sympathetic tone, in part mediated by the kidneys, has been hypothesized as a potential mechanism in the pathophysiology of hypertension. Therefore, several recent studies sought to evaluate the benefit of therapies that inhibit the effects of the kidneys on the sympathetic nervous system in patients with resistant hypertension.

Although the results of an ongoing, large randomized, controlled trial are needed to confirm the efficacy and safety of renal denervation therapy, Prof. Kurdi stated that several smaller studies have demonstrated that surgical renal sympathectomy can result in improved blood pressure control. The potential benefits of renal denervation therapy may include decreased cardiac size, improved renal function, decrease incidence of headache, decreased precordial pain, and fewer cerebrovascular events.

In the Catheter-Based Renal Sympathetic Denervation for Resistant Hypertension proof-of-principle trial [Symplicity HTN-1 Investigators; Krum H. Hypertension 2011], bilateral radiofrequency application to the renal arteries was evaluated in 45 patients with drug-resistant hypertension. Following renal artery angiography, patients received anticoagulation therapy and opioid analgesics for diffuse abdominal pain. An 8-French guide catheter was used via an 8-French femoral artery access and positioned in the renal arteries, with subsequent radiofrequency application. Patients experienced a significant decrease in systolic blood pressure of 14 mm Hg at 1 month and 27 mm Hg at 12 months. Diastolic blood pressure decreased by 10 mm Hg at 1 month and 17 mm Hg at 12 months. In addition, the antihypertensive medications were adjusted in 13 patients; 9 patients had a decrease in the number of antihypertensive medications while 4 patients had an increase. Importantly, even after adjusting for the 4 patients whose treatment was intensified, the blood pressure was significantly reduced. No response to renal denervation therapy occurred in 13% of patients.

In the Renal Sympathetic Denervation in Patients With Treatment-Resistant Hypertension trial [Symplicity HTN-2 Investigators; Esler MD et al. Circulation 2012], 106 patients with resistant hypertension were randomized to receive catheter-based renal sympathectomy plus pharmacologic treatment or pharmacologic treatment only. Patients that received catheter-based therapy experienced a significantly greater blood pressure reduction from baseline compared with pharmacologic therapy only, with a mean blood pressure decrease of 33/11 mm Hg at 6 months’ follow-up (p<0.0001; Figure 1). In addition, 84% of patients treated with renal sympathectomy experienced a blood pressure decline of at least 10 mm Hg compared with 35% of patients that received pharmacologic therapy only (p<0.001).

Prof. Kurdi explained the structure of several renal denervation systems. The Symplicity systems include the first-generation denervation system, a single-point ablation catheter that is manually rotated with 4 points of ablation, and the second generation denervation catheter with a spiral, helical-shaped wire with 4 simultaneous points of ablation. The EnligHTN System consists of a catheter with 4 electrodes placed in staggered positions in a basket configuration, each having a temperature and impedance sensor.
Emerging renal sympathectomy systems are balloon-based and include the Covidien system, which has 8 ablation sites with water irrigation and a timing of 2 minutes; the Boston Scientific Balloon with 8 ablation points and a timing of 30 seconds; and the Cordis system. Prof. Kurdi suggested that renal sympathectomy should be evaluated in the treatment of other cardiovascular diseases including, heart failure and severe hypertension with end organ damage (eg, left ventricular hypertrophy, proteinuria, or retinopathy), since reduction in blood pressure in patients with these conditions may also improve cardiovascular outcomes.

Mahmoud Hassanein, MD, Alexandria University, Alexandria, Egypt, presented potential mechanisms by which increased sympathetic activity may result in effect blood pressure. As mentioned above, recent research has implicated the SNS in the development of hypertension, as sympathetic nervous activity can initiate and sustain blood pressure elevation. Although sympathetic denervation in the thoracic, abdominal, and pelvic regions has been demonstrated to decrease blood pressure in patients with malignant hypertension, they are associated with high morbidity, such as bowel, bladder, and erectile dysfunction; severe postural hypotension, and death.

Renal denervation has emerged as a treatment of resistant hypertension due to the observation that efferent sympathetic nerves, which are located adjacent to the renal artery, are essential for systemic hypertension [DiBona GF. Curr Opin Nephrol Hypertens 2002]. An increase in renal sympathetic activity results in decreased sodium excretion, increased water retention, stimulation of the juxtaglomerular apparatus resulting in greater release of the enzyme renin, and changes to the renal blood flow. All of these characteristics contribute to both acute and long-term increases in blood pressure.

Dr. Hassanein highlighted a multicenter, proof-of-principle study, in which 45 patients with resistant hypertension with a mean of 4.7 antihypertensive medications were treated with percutaneous radiofrequency catheter-based therapy and followed for 1 year [Krum H et al. Lancet 2009]. The mean change in office blood pressure from baseline after the procedure is shown in Figure 2.

Dr. Hassanein concluded that selective renal sympathetic denervation is a promising approach for the treatment of resistant hypertension, since it interrupts renal sympathetic activity without affecting nerves in the abdominal, pelvic, or lower extremity regions of the body. Ongoing clinical outcomes trials of renal denervation will determine whether it will become a standard treatment option for patients with resistant hypertension.
Transcatheter Aortic Valve Replacement: Important Considerations

Written by Emma Hitt, PhD

Although surgical aortic valve replacement (AVR) is recommended by clinical practice guidelines in patients with severe aortic stenosis, many patients with calcific aortic stenosis are not optimal candidates for surgery due to their medical comorbidities. Transcatheter aortic valve replacement (TAVR) offers an alternative approach for this patient population that is less invasive. Martine Gilard, MD, Brest Centre Hospitalier Regional Universitaire, Brest, France, presented indications and outcomes TAVR in patients with severe aortic stenosis.

An important aspect of TAVR is appropriate patient selection. A multidisciplinary heart team is important to fully evaluate the patient, develop an individual risk profile and to determine anatomic suitability of TAVR. Prof. Gilard stated that the multidisciplinary heart team should consist of surgeons, cardiologists, anesthesiologists, imaging specialists, and other specialities, such as geriatricians [Vahanian A et al. Eur Heart J 2012].

Current indications for TAVR include severe, symptomatic aortic stenosis in patients with a life expectancy of ≥1 year who are not optimal surgical candidates. Prof. Gilard stated that comorbidities such as chronic obstructive pulmonary disease (COPD), concomitant coronary artery disease, and obesity can cause symptoms similar to those seen in severe aortic stenosis and must be ruled out prior to pursuing TAVR.

In determining feasibility of TAVR in a patient, the diameter, tortuosity, and calcifications for the transvascular approach should be evaluated via computed tomography (CT), angiography or magnetic resonance imaging (MRI). The diameter of the aortic annulus must to be determined through imaging studies and coronary angiography should be undertaken to identify potential revascularization.

Prof. Gilard highlighted that some contraindications for TAVR include absence of a heart team or cardiac surgeon, life expectancy of <1 year, unlikelihood of improvement in quality of life, and anatomical limitations such as inadequate annulus size, presence of a thrombus in the left ventricle, endocarditis, and plaques with mobile thrombi in the ascending aorta or arch [Vahanian A et al. Eur Heart J 2012]. Other comorbidities such as bicuspid or noncalcified valves, untreated coronary artery disease that requires revascularization, hemodynamic instability, and left ventricular ejection fraction of <20% are relative contraindications to TAVR. The the potential risks and benefits of TAVR in patients with these comorbidities should be assessed by the heart team.

The PARTNER A study was a noninferiority trial that evaluated TAVR and surgical AVR in high-risk surgical patients. In this trial, the mortality of patients who received TAVR was similar to patients who received surgical AVR at 12 months (HR 0.93, 95% CI, 0.71 to 1.22, p=0.62) [Smith CR et al. N Engl J Med 2010]. In the PARTNER B trial which randomized patients with severe aortic stenosis who were not candidates for surgical AVR to either medical therapy or TAVR, 1-year mortality was significantly lower in patients who underwent TAVR (67.6% vs. 43.3) [Leon MB et al. N Engl J Med 2011].

According to data from several European registries, major complications experienced by patients who underwent TAVR included major vascular complications (3.3% to 6.3%), requirement of a new pacemaker (13% to 39.3%), bleeding and tamponade (up to 17.7%), and stroke (1.2% to 5%). In the German Aortic Valve Registry (GAVR), data from 13,860 patients were analyzed and stratified by type of AVR (surgical vs transcatheter), performance of AVR plus coronary artery bypass grafting (CABG) versus AVR alone, and type of percutaneous approach to TAVR (femoral vs transapical). Cerebrovascular events occurred in 2.2% of patients who received AVR only, 3.6% of patients who received surgical AVR plus CABG, 3.7% of patients who received femoral TAVR, and 3.5% of patients who received transapical TAVR. A new pacemaker was required in 4.6% and 3.9% of...
patients who received surgical AVR only and surgical AVR plus CABG, respectively, as compared with 23.7% and 9.9% of patients who underwent femoral or transapical TAVR, respectively. In-hospital mortality was 2.1%, 4.5%, 5.1%, and 7.7% in patients who underwent surgical AVR only, surgical AVR plus CABG, femoral TAVR, and transapical TAVR, respectively.

In a follow-up study of 88 patients who had received TAVR, the cumulative survival steadily decreased over the study period of 5 years, with a 1-year survival rate of 83% and a 5-year survival rate of 35% [Toggweiler S et al. J Am Coll Cardiol 2013]. Patients with COPD and moderate or greater paravalvular regurgitation after TAVR had a lower rate of survival.

Prof. Gilard concluded that TAVR should be used as the standard of care in patients who are unable to undergo surgical AVR or in high-risk patients in whom the heart team feel TAVR would result in better outcomes than surgical AVR. Future directions include the development of a more accurate measure of risk in potential TAVR patients and methods to decrease paravalvular leaks and stroke following the TAVR.

Although TAVR appears to offer a promising alternative to surgical AVR for patients who are poor surgical candidates, Bernard Chevalier, MD, Institut Cardiovasculaire Paris Sud, Massy, France, presented strategies for appropriate patient selection for TAVR, as he pointed out that there are clearly differences in outcomes based on patient selection.

One characteristic that may be important in patient selection for TAVR is frailty. Indicators of frailty may include number and type of comorbidities, combined into a score where comorbidities such as metastatic cancer is weighted 5; congestive heart failure 2; weight loss 2; alcohol abuse 1; cardiac arrhythmias 1; and liver disease 1. Another score uses the combined score from three tests: grip strength, walking speed, and chair rise time. The Katz daily life score, which measures disability, assesses the ability of a patient to take a bath, get dressed, get washed, go from their bed to a chair, and to prepare a meal, where 0 is given for easy to do alone and 4 is given for impossible to do alone.

Prof. Chevalier suggested that another characteristic for patient selection includes analysis of the ilio-femoral vessels, which are required for vascular access during TAVR. Important features to be aware of are vessel sinuosities, angles, vessel diameter, and the presence of plaque and calcification. Location of vessel access may also be important to consider. In the PARTNER Cohort A study, mortality rates 30 days post procedure were 3.7% versus 8.2% in patients who underwent transfemoral TAVR versus surgical AVR (p=0.046), while the mortality rate in patients who received transapical arm TAVR or AVR was 8.7% and 7.6%, respectively (p=0.79) [Smith CR et al. N Engl J Med 2011]. Recent case series have described an alternative approach in which the valve is inserted via a transaortic approach. The potential advantages of a transaortic approach for TAVR include frequent use of aortic annuloplasty and ministernotomy, no left ventricular access, less chest wall complications, and the ability to convert to a full sternotomy if required. Across three studies, the observed mortality rate of TAVR via the transaortic access ranged from 6.9% to 10.9% [Hayashida K et al. Eur J Cardiothorac Surg 2013].

Valve selection is also an important feature to consider prior to TAVR. In multiple international studies, aortic regurgitation (AR) was a prominent occurrence following TAVR, ranging from 13.1% to 21% of patients. Importantly, the survival rate following TAVR decreases as AR grade worsens, regardless of ejection fraction (Figure 1). Prof. Chevalier suggested that the shape of the aortic valve annulus and its diameter may be important indicators of AR. A recent study demonstrated that CT-guided versus transesophageal echocardiography (TEE)-guided valve sizing was likely more accurate, resulting in less AR and annulus rupture [Hayashida K et al. EuroIntervention 2012].
The prevalence of ischemic heart disease is increasing among the 340 million people who live in the Arab world. Thus, a program that improves the management of ST-elevation myocardial infarction (STEMI) and access to coronary revascularization therapies is needed. Habib Gamra, MD, Fattouma Bourguiba University Hospital, Monastir, Tunisia, discussed ways to improve the management of STEMI in the Arab world.

The ACCESS Registry is a prospective, observational, multinational registry of patients from 134 sites in 19 countries in Latin America, the Middle East, and Africa who were hospitalized for an acute coronary syndrome (ACS) between January 2007 and January 2008. Of the 11,731 patients with confirmed ACS, 46% were diagnosed with STEMI and 54% with non-ST Elevation ACS (non-ST Elevation Myocardial Infarction (NSTEMI) or unstable angina). Diabetes, hypertension, abdominal obesity, and smoking were identified as significant risk factors for ACS.

While hospitalized, the majority of patients received aspirin (93%), lipid-lowering medication (94%), β-blocker (78%) and angiotensin-converting enzyme inhibitor (68%). Death at 12 months was higher in patients with STEMI (8.4%) as compared with NSTEMI (6.3%, p<0.0001). Although the use of evidence-based, pharmacologic therapies occurred in the majority of patients with ACS, the majority of patients with STEMI who were eligible for reperfusion therapy did not receive either fibrinolysis or primary percutaneous coronary intervention (PCI). These data suggests further work is necessary in order to increase access of patients in developing countries to reperfusion therapies and other therapies which reduce the risk of long-term ischemic events in patients with ACS [ACCESS Investigators. Am Heart J 2011].

While percutaneous revascularization has been shown to be preferable to thrombolysis for the management of patients with STEMI, thrombolysis is more commonly used in the Middle East. Of the 1470 patients with STEMI followed in the Monastir for Acute MI [MIRAMI] registry, 23.6% received primary angioplasty (PAMI) and 34.5% received streptokinase. Thrombolytic success (defined as chest pain relief <5 using a scale of 1 to 10 and ST-elevation resolution >50% from baseline) was achieved in 70% of the patients who received treatment within 3 hours from chest pain onset. Predictors of success were short time to treatment (<3 years), smoking, and inferior STEMI while severe heart failure was a predictor of thrombolytic failure.

The Gulf Registry of Acute Coronary Events (Gulf Race) followed 8169 consecutive patients (74% men) with ACS patients from six Middle Eastern countries. In this registry, women were more likely than men to present with unstable angina and more often had atypical presentations of STEMI. In contrast, men presented with STEMI (45%) more frequently than women (22%). Compared with men, women were significantly less likely to be treated with β-blockers and antiplatelet therapy. Among patients with STEMI eligible for reperfusion therapy, 83% received thrombolytic therapy. PCI was performed in 9% of eligible patients; another 8% were eligible but did not undergo reperfusion therapy. The percentage of patients who were eligible for reperfusion but were not treated was higher in women as compared with men (15% vs 8%; p=0.001). Women had higher in-hospital mortality and had poorer outcomes than men [El-Menyar A et al. Am J Cardiol 2009]. The finding of inadequate use of reperfusion therapy among patients with STEMI in Arab countries has also been documented in other studies [Moustaghfir A et al. Arch Cardiovasc Dis 2012]. To better achieve guideline-based treatment, the Middle East needs more catheterization laboratories with adequate geographic distribution capable.
of running a primary PCI program 24 hours a day [Knot J et al. EuroIntervention 2009]. There is also a critical need for education of the general population regarding ACS and more training for healthcare providers.

Prof. Gamra's concluded with the observation that in patients with STEMI, thrombolysis is effective if initiated soon after the onset of symptoms but primary PCI is the preferred method of revascularization.

New Thinking for the Management of Acute Interventions

Horst Sievert, MD, CardioVascular Center Frankfurt, Frankfurt, Germany, discussed new data which may change the management of patients with acute stroke. He noted that there is often a long time interval between the onset of stroke and treatment. In addition, current transfer systems for getting patients to hospital or catheterization laboratories in order to undergo treatment are poorly developed. Finally, current therapies are limited.

The amount of time in which the brain is without blood flow impacts the severity of the stroke and potential for recovery. There is often a considerable delay from the time in which patients first develop symptoms to the time in which they seek treatment. Efforts must be made to educate patients about the early signs of transient ischemic attack (TIA)/stroke and the need to quickly seek medical care when these symptoms occur. The time to treatment may also be improved by using ambulances specifically designed for transporting stroke patients. It may also be possible to reduce the amount of time needed to make the diagnosis of a stroke by utilizing mobile computed tomography (CT) scanners or bypassing the Emergency Department and taking patients directly to imaging. Providers could then take a history can be taken, perform lab tests, and ready the patient for thrombolysis while the patient is preparing to undergo imaging.

Expediting the treatment of patients with thrombolysis is important since data from a pooled analysis of early administration of recombinant tissue plasminogen activator (rTPA) after ischemic stroke showed benefit out to 4.5 hours after stroke onset. After 4.5 hours, the risk of thrombolysis may outweigh its potential benefits (Figure 1) [Lees KR et al. Lancet 2010].

Thrombolysis improves outcomes in patients with acute ischemic stroke; however, the success of thrombolysis for the recanalization of large clots is poor (~10% success) and reocclusion occurs in ~20% of patients who initially have successful reperfusion. The use of angiography allows for better localization of the occlusion and allows for direct administration of thrombolitics to thrombus. In addition, mechanical thrombectomy devices can be used to obtain immediate reperfusion.

Although thrombolysis is still the gold standard therapy for acute stroke, more centers are developing clinical pathways based on severity, duration of symptoms, and the use of catheter intervention. Data from the PROACT-II study [Furlan A et al. JAMA 1999], IMS II trial [IMS Trial Investigators. Stroke 2007], and RECANLISE registry [Sen S et al. Neurocrit Care 2009], support the use of a catheter invention approach; however, recent data show no benefit from mechanical lysis compared with IV tPA (IMS III [Broderick JP et al. N Engl J Med 2013], SYNTHESIS [Ciccone A et al. N Engl J Med 2013], and MR Rescue [Kidwell CS et al. N Engl J Med 2013]). As a result, the optimal treatment for patients with ischemic stroke remains undefined.

Prof. Sievert proposed an algorithm to guide treatment selection based on time since symptom onset (Table 1).

### Table 1. Treatment Algorithm

<table>
<thead>
<tr>
<th>Time of Symptom Onset</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;4.5 hours</td>
<td>IV tPA</td>
</tr>
<tr>
<td>NIHSS score &lt;10</td>
<td>IA lysis/mechanical</td>
</tr>
<tr>
<td>NIHSS score &gt;10</td>
<td>IA lysis/mechanical</td>
</tr>
<tr>
<td>4.5 to 6 hours</td>
<td>IA lysis/mechanical</td>
</tr>
<tr>
<td>&gt;6 hours</td>
<td>IA lysis guided by perfusion imaging</td>
</tr>
</tbody>
</table>

rTPA=recombinant tissue plasminogen activator; IA=intra-arterial; IV=intravenous; NIHSS=National Institutes of Health Stroke Scale; tPA=tissue plasminogen activator.
Under multisociety consensus quality improvement guidelines [Sacks D et al. Catheter Cardiovasc Interv 2013], patients with the following characteristic benefit the most from mechanical recanalization:

- Patients in whom IV tPA is contraindicated or in whom IV tPA has failed or is likely to fail
- Patients with large vessel occlusion
- Very symptomatic patients
- Patients with a stroke time window out to 8 hours
- Patients with a proximal artery occlusion

“There is only one effective treatment for ischemic stroke,” said Prof. Sievert, “to get the vessel open.”

**Updated Guidelines for Valvular Heart Disease**

Written by Maria Vinall

Valvular heart disease is not usually regarded as a major public health problem. However, the prevalence of both mitral and aortic valve disease is increasing and is particularly troublesome for individuals aged ≥75 years (Figure 1) [Nkomo VT et al. Lancet 2006].

Table 1. Aortic Regurgitation (Class and Level of Evidence)

<table>
<thead>
<tr>
<th>Condition</th>
<th>Class</th>
<th>Level</th>
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<tbody>
<tr>
<td>AVR</td>
<td>IIaC</td>
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</tbody>
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Table 2. Aortic Valve Replacement (Class and Level of Evidence)

<table>
<thead>
<tr>
<th>Condition</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>AVR</td>
<td>IV</td>
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European Society of Cardiology (ESC)/European Association for Cardio-Thoracic Surgery (EACTS) Guidelines on the management of valvular heart disease were updated in 2012 [Vahanian A et al. Eur Heart J 2012; Eur J Cardiothorac Surg 2012]. Fausto J. Pinto, MD, PhD, University of Lison, Lisbon, Portugal, discussed some of the major changes that resulted from new evidence regarding risk stratification, diagnostic methods, and therapeutic options.

The 2012 guidelines recommend that treatment decisions for patients with valvular heart disease be made by a “heart team” comprised of cardiologists, cardiac surgeons, imaging specialists, anesthesiologists, and others, as appropriate. The decision process should focus on disease severity, patient symptoms, the relationship of the symptoms to valvular disease, life expectancy and quality of life, whether the expected benefits of intervention outweigh the risk, the patient’s wishes, and whether local resources are optimal for the planned intervention.

All patients should receive a clinical assessment and echocardiography to confirm diagnosis and to assess severity and prognosis. Exercise testing, stress echocardiography, magnetic resonance imaging, and multislice computed tomography may provide additional useful information. Cardiac catheterization to evaluate valve function are necessary only if noninvasive findings are inconsistent with the clinical assessment.

**OTHER NEWS**

Valvular heart disease is not usually regarded as a major public health problem. However, the prevalence of both mitral and aortic valve disease is increasing and is particularly troublesome for individuals aged ≥75 years (Figure 1) [Nkomo VT et al. Lancet 2006].
Table 3. Severe Primary MR (Class and Level of Evidence)

<table>
<thead>
<tr>
<th>Symptomatic Patients</th>
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</tr>
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<tbody>
<tr>
<td>Mitril valve repair should be the preferred technique when it is expected to be durable (IC)</td>
<td></td>
</tr>
<tr>
<td>Surgery is indicated in symptomatic patients with LVEF &gt;30% and LVESD &lt;55 mm (IB)</td>
<td></td>
</tr>
<tr>
<td>Surgery should be considered in patients with severe LV dysfunction (LVEF &lt;50% and/or LVESD &gt;55 mm) refractory to medical therapy with high likelihood of durable repair and low comorbidity (IIaC)</td>
<td></td>
</tr>
<tr>
<td>Surgery may be considered in patients with severe LV dysfunction (LVEF &lt;30% and/or LVESD &gt;55 mm) refractory to medical therapy with low likelihood of durable repair and low comorbidity (IIbC)</td>
<td></td>
</tr>
<tr>
<td>Asymptomatic Patients</td>
<td></td>
</tr>
<tr>
<td>Surgery is indicated in patients with LV dysfunction (LVESD ≥45 mm and/or LVEF 60%; IC)</td>
<td></td>
</tr>
<tr>
<td>Surgery should be considered in patients with preserved LV function and new onset of atrial fibrillation or pulmonary hypertension (systolic pulmonary pressure at rest &gt;50 mm Hg; IIaC)</td>
<td></td>
</tr>
<tr>
<td>Surgery should be considered in asymptomatic patients with preserved LV function, high likelihood of durable repair, low surgical risk, flail leaflet, and LVESD ≤40 mm (IIaC)</td>
<td></td>
</tr>
<tr>
<td>Surgery may be considered in patients with preserved LV function, high likelihood of durable repair, low surgical risk, and left atrial dilatation (volume index ≥80 ml/m² BSA) and sinus rhythm, OR pulmonary hypertension on exercise (SPAP &gt;60 mm Hg at exercise; IIbC)</td>
<td></td>
</tr>
</tbody>
</table>

BSA: body surface area; LVEF: left ventricular ejection fraction; LVESD: left ventricular end systolic diameter; SPAP: systolic pulmonary artery pressure.

Table 4. PMC in Mitral Stenosis with Valve Area ≤1.5 cm² (Class and Level of Evidence)

| PMC is indicated for symptomatic patients with favorable characteristics (IB) and those with contraindications or at high risk for surgery (IC) |  |
| PMC should be considered as initial treatment for symptomatic patients with unfavorable anatomy but without unfavorable clinical characteristics (IIaC) |  |
| PMC should be considered in asymptomatic patients without unfavorable characteristics and high thromboembolic or hemodynamic decompensation risks (IIaC) |  |

PMC: percutaneous mitral commissurotomy.

Table 5. TAVI (Class and Level of Evidence)

| TAVI should only be undertaken with a multidisciplinary ‘heart team’ including cardiologists and cardiac surgeons and other specialists if necessary, and should only be performed in hospitals with cardiac surgery onsite (both IC) |  |
| TAVI is indicated in patients with severe symptomatic AS who are not suitable for AVR as assessed by a ‘heart team’ and who are likely to gain improvement in their quality of life and to have a life expectancy of more than 1 year after consideration of their comorbidities (IB) |  |
| TAVI should be considered in high-risk patients with severe symptomatic AS who may still be suitable for surgery, but in whom TAVI is favored by a ‘heart team’ based on the individual risk profile and anatomic suitability (IIaB) |  |


Stent for Life Initiative Improves Delivery of Primary PCI in Timely Manner

Written by Mary Mosley

The Stent for Life (SFL) program is a joint initiative to improve the delivery of and patient access to percutaneous coronary intervention (PCI) to reduce the morbidity and mortality of patients suffering from acute coronary syndromes (ACS). The founding partners in this program are the European Association of Percutaneous Cardiovascular Interventions (EAPCI), a registered branch of the European Society of Cardiology, and EuroPCR. Petr Kala, MD, Brno, Czech Republic, SFL Chairman, reviewed the objectives of Stent for Life and the three stages completed to date.

The objectives of Stent for Life Initiative are to define the regions and countries with an unmet medical need for optimal treatment of ACS, and to implement an action program to increase patient access to primary PCI where it is needed. In terms of patient access, the goals are to increase primary PCI to >70% among all patients with STEMI segment elevation myocardial infarction (STEMI) and to provide 24/7 service for primary PCI at all invasive facilities to meet the needs of the STEMI population.

Phase 1 of Stent for Life comprised situation mapping and data collection during 2008 and 2009 to assess the current situation in 30 countries. Along with defining the rates of primary PCI, thrombolysis, and no reperfusion for STEMI, they found that the rates of primary PCI were not correlated to gross domestic product of the country [Widimsky P et al. Eur Heart J 2010]. On average, only 51% of STEMI patients arrive to the first hospital by emergency medical services (EMS), and 46% of STEMI patients were untreated despite a nationwide “thrombolytic strategy” program.

Phase II evaluated how to improve access to primary PCI based on the experience of best practice countries. Strategies found to reduce system delays included building an effective primary PCI network, strengthening the role of EMS, and decreasing transportation time. An awareness campaign called “ACT NOW, SAVE A LIFE” was created to educate public about heart attack symptoms and the need to act and call an emergency number to reduce patient delay in seeking medical treatment [Knot J et al. EuroIntervention 2009].

The implementation of Stent for Life from 2009 to 2013 comprised Phase 3. Currently there are 17 national cardiac societies and organizations actively involved in SFL in Europe and Asia. Prof. Kala reviewed the achievements attained in Romania, which joined SFL in 2010. Five STEMI
networks with 10 hospitals with cardiac catheterization labs were identified to provide 24/7 primary PCI service under this government program.

An additional eight primary PCI centers will be opened by 2015 [Kristensen SD et al. EuroIntervention 2012]. The Romanian national program has resulted in an increase in the number of patients treated with primary PCI, decreases in the utilization of thrombolysis, and a decrease in the number of patients with STEMI who do not undergo reperfusion therapy. The number of primary PCIs performed increased from 40 per million inhabitants in 2009, to 64 in 2010, and to 210 in 2011.

The Stent for Life program identified factors that contribute to the delay in treating STEMI patients and targets for providing intervention (Figure 1). The first factor found to delay the timing of therapy was the length of time between the onset of a patient’s symptoms to the first medical contact. Public service campaigns designed to increase awareness of symptoms of myocardial infarction have been developed to reduce this potential for delay in therapy. Efforts of the Stent for Life program have focused on reducing the delays in reperfusion that can occur after patients present to the healthcare system.

Figure 1. Components That Contribute to Delayed Treatment for STEMI and Ideal Time Intervals for Intervention

Symptom onset → FMC ×10 minutes Diagnosis → Reperfusion therapy Time to reperfusion therapy → Wire passage in culprit artery if primary PCI × Bolus or infusion start if thrombolysis

FMC=first medical contact; PCI=percutaneous coronary intervention.

Addressing Tobacco Use to Reduce Cardiovascular Disease

Written by Mary Mosley

The scope of the impact of tobacco on cardiovascular disease (CVD) and its mode of action, the lack of awareness of physicians about smoking cessation tactics, and smoking cessation as a treatment for CVD were reviewed by Georges A. Saade, MD, Bellevue Medical Center, Beirut, Lebanon.

Tobacco use is a risk factor for 6 of the 8 leading causes of death worldwide and is associated with nearly 6 million deaths per year (Figure 1). The use of tobacco is associated with increased CV risk and the use of tobacco is projected to be associated with 175 million deaths worldwide by the year 2030. Given the adverse effects of tobacco utilization, at its 2012 summit on Noncommunicable Diseases, the United Nations endorsed efforts to reduce tobacco abuse in an attempt to reduce premature mortality from CVD.

Cigarette smokers die ~10 years earlier than nonsmokers and at least half of chronic smokers will die of a tobacco-related disease, according to the British Male Doctors’ Study [Doll R et al. BMJ 2004]. Smokers of waterpipes, practiced in Egypt and other countries, are also at risk for developing dependence and other adverse health-related conditions associated with smoking [Maziak W. Addict Behav 2011], contrary to popular opinion that waterpipes are safe. Newer interventions to help smokers quit offer the potential for reducing the smoking rates in the near future. An anonymous survey of 326 cardiologists in Spain revealed that 3 in 4 always ask their patients about smoking and recommend that they quit; 1 in 5 had cessation print materials in their office; and 2 in 5 checked patient progress. However, 73% were unfamiliar with cessation medications and 71% wanted to improve their tobacco treatment skills. [Dalmau R. Heart wire http://www.theheart.org/article/1531389.do].

Figure 1. Pathways Linking Tobacco and CVD

CO=carbon monoxide; CVD=cardiovascular disease; LV=left ventricular; ROS=reactive oxygen species.

IMPAKT OF SECONDHAND SMOKE

Secondhand smoke causes ~603,000 premature deaths annually, and 87% of secondhand smoking-related deaths are from ischemic heart disease [Oberg M et al. Lancet 2011]. A comprehensive literature review concluded that the CV effects of secondhand smoke are substantial and rapid, and that the effects of even brief exposure (minutes to hours) are often nearly as large (averaging 80% to 90%) as those of chronic active smoking [Barnoya J, Glantz SA. Circulation 2005]. Furthermore, they showed that long-term exposure to secondhand smoke at work or home is associated with a 30% increased risk for coronary heart disease (CHD) in adult nonsmokers.

SMOKING CESSATION AS A TREATMENT OF CVD

Smoking cessation is a powerful treatment for established CVD, reducing the risk of CV-related death by 36% and the risk of future cardiac event rates by 50%. These effects are comparable to the 15% to 35% reductions in CV-related death achieved with many widely used pharmacologic therapies (aspirin, β-blockers, ACE inhibitors, statins). Prof. Saade noted that tobacco cessation is one of the most important preventative measures available and that and no other preventive activity produces such significant results from such a small investment in time. The number needed to treat to prevent CV events or death is shown in Table 1.

Table 1. Treating Tobacco Is Effective and Efficient for Reducing Cardiovascular Events and Death

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Outcome</th>
<th>NNT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Statins</td>
<td>Prevent 1 death over 5 years</td>
<td>107</td>
</tr>
<tr>
<td>Aspirin</td>
<td>Prevent 1 MI over 5 years</td>
<td>118</td>
</tr>
<tr>
<td>Antihypertensive therapy</td>
<td>Prevent 1 stroke, MI, death over 1 year</td>
<td>700</td>
</tr>
<tr>
<td>Cervical cancer screening</td>
<td>Prevent 1 death over 10 years</td>
<td>1140</td>
</tr>
<tr>
<td>MD 5 min advice to stop smoking</td>
<td>Prevent 1 premature death</td>
<td>80</td>
</tr>
<tr>
<td>+ cessation medication</td>
<td>Prevent 1 premature death</td>
<td>38-56</td>
</tr>
<tr>
<td>+ behavioral support</td>
<td>Prevent 1 premature death</td>
<td>16-40</td>
</tr>
</tbody>
</table>

MD=doctor; MI=myocardial infarction; NNT=number needed to treat.

Tobacco treatment is also cost-effective, with cessation counseling and medications costing $2587 per life-year saved [Cromwell J et al. Health Care Financ Rev 1997]. Prof. Saade noted that the cardiology team has a professional obligation to address tobacco use and exposure, and it is an essential component of CVD treatment for all patients. Cardiologists have an important role to play, as outlined in Figure 2, in achieving the “25 by 25” CVD goals established by the World Heart Federation.

Figure 2. Role of the Cardiologist to Achieve “25 by 25” CVD Goals

Ideal Bioabsorbable Stent Scaffold Is an Achievable Dream

Written by Lynne Lederman

The development of metallic stents improved outcomes after angioplasty by reducing acute vessel occlusion. However, permanent metal-based stents have the potential for negative sequelae after several months in place that could be overcome if the stents were absorbable. Mohammad I. Kurdi, MBBS, Al Takhassoussi Hospital, Riyadh, Saudi Arabia, reviewed the advantages of having stents “disappear” and discussed progress toward development of the idea bioabsorbable stent.

Reabsorbable stents could reduce or eliminate stent-associated thrombosis, obstructions caused by stent strut side-branches, and restenosis subsequent to strut fracture. Resorption could also allow reestablishment of vascular function. After stent absorption, the stented site could more easily imaged using computed tomography or magnetic resonance and re-treated if necessary, either surgically or via percutaneous coronary intervention (PCI) procedures, although the expectation is that repeat interventions would be avoided. Furthermore, bioabsorbable stents could be used to treat pediatric patients, allowing the treated vessels to grow without requiring surgical removal of the stents.

The concept of bioabsorbable stents has been around for over 2 decades, but there are challenges to development. Ideal bioabsorbable stents must be strong enough to function for an appropriate time, have struts that are not too thick, be capable of delivering anti-proliferative drugs to control restenosis, and not cause unacceptable inflammation during breakdown. The long-term use of antiplatelet therapy that is...
required with conventional stents, which is expensive and does not eliminate all late-occurring thrombosis, could be avoided with bioabsorbable stents.

Features of five of the bioabsorbable stents in development are listed in Table 1.

### Table 1. Bioabsorbable Stents in Development

<table>
<thead>
<tr>
<th>Stent</th>
<th>Features</th>
<th>Advantages</th>
<th>Drawbacks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Igaki-Tamai bioabsorbable stent</td>
<td>PLLA zig-zag helical coil with straight bridges</td>
<td>During absorption, hydrolysis of lactic acid produces lactic acid that is metabolized to carbon dioxide and water; radiolucent with radio-opaque markers</td>
<td>Strut 170 microns, thicker than contemporary metallic stents; cumbersome to use</td>
</tr>
<tr>
<td>Bio-absorbable magnesium stent (Biobronik)</td>
<td>Laser cut from tubular magnesium WE-43, sinusoidal in-phase hoops linked by straight bridges</td>
<td>Balloon-expandable; radial strength at implantation similar to stainless steel stents; no stent thrombosis; completely absorbed</td>
<td>Strut 165 microns; radiolucent, no radio-opaque markers; placement challenging; radial support test early; no antiproliferative drug release; high rate of restenosis</td>
</tr>
<tr>
<td>Bioresorbable coronary stent (REVA Medical)</td>
<td>PLLA backbone contains and controls release of antiproliferative drug everolimus; different polymerization than Igaki-Tamai</td>
<td>Release rate of everolimus (80% by 30 days) similar to that of Xience V metallic stent and similar low internal obstruction; strut thickness and crossing profile (1.3 mm) similar to those of Cypher stent</td>
<td>Radial strength at body temperature lower than many metallic stents</td>
</tr>
<tr>
<td>Bioabsorbable Therapeutics stent</td>
<td>Repeating salicylate molecules linked by adipic acid molecules; elutes sirolimus and also releases salicylic acid</td>
<td>Modifiable absorption; balloon-expandable without distortion; iodine for radio-opacity</td>
<td>200 micron struts are thick with 1.7 mm crossing profile; side effects include O-wave myocardial infarctions, target lesion revascularization</td>
</tr>
<tr>
<td>BVS Everolimus-eluting bioabsorbable PLLA stent (Abbott Vascular)</td>
<td>PLLA backbone contains and controls release of antiproliferative drug everolimus; different polymerization than Igaki-Tamai</td>
<td>Release rate of everolimus (80% by 30 days) similar to that of Xience V metallic stent and similar low internal obstruction; strut thickness and crossing profile (1.3 mm) similar to those of Cypher stent</td>
<td>Radial strength at body temperature lower than many metallic stents</td>
</tr>
</tbody>
</table>

BVS/bioresorbable vascular scaffold; PLLA=poly-L-lactic acid.

To summarize, the ideal bioabsorbable stent should be easy to handle and implant, and be detectable by imaging to ensure accurate post-dilatation and placement of additional stents without gaps or overlaps. Having a detectable absorbable stent also means that complete resorption can be confirmed. In addition, at implantation, bioabsorbable stents should have an initial strength similar to that of conventional metal stents and be able to maintain this strength for sufficient time to help overcome the early negative remodeling forces that occur soon after PCI, this negative remodeling is the main cause of restenosis after balloon angioplasty. Stenting via PCI also causes an intimal hyperplastic or excessive healing response, hence the need for a stent that is capable of releasing antiproliferative drugs. Ideally, repair with a bioabsorbable stent would achieve and maintain vessel movement, increase blood vessel lumen size, and produce a reduction in plaque area. In addition, it would be desirable to regain appropriate physiologic responses to exercise and the ability to dilate in response to local ischemia in healed arteries.

The ideal bioabsorbable stent should also result in a healed, normally functioning vessel with no foreign body (stent) remaining, and no restenosis or late thrombosis development. Early encouraging results, particularly the results from the bioresorbable vascular scaffold everolimus-eluting bioabsorbable poly-L-lactic acid stent, although they require confirmation in larger clinical trials in patients with complex lesions, suggest the ideal bioabsorbable stent can be developed.

### Therapeutic Strategies for Hemodynamic and Circulatory Support After PCI

Written by Mary Mosely

Treatment strategies for ST-segment elevation myocardial infarction (STEMI) utilize both pharmacological therapies and devices designed to restore coronary blood flow. While these therapies are generally effective, a proportion of patients with STEMI will develop cardiogenic shock, one of the leading causes of inhospital death post MI. Despite an optimal pharmacomechanical approach, revascularization, and hemodynamic support, the mortality in patients with STEMI complicated by cardiogenic shock remains high, said Hany Eteiba, MD, University of Glasgow, Glasgow, Scotland.

Prof. Eteiba reviewed effective and active circulatory support strategies that can be used in patients with cardiogenic shock. Extracorporeal membrane oxygenation (ECMO) and left ventricular assist device (LVAD) are two of these approaches and Prof. Eteiba discussed how these devices can be utilized in clinical practice.

Hemodynamic support for patients with acute myocardial infarction complicated by shock can be provided through a variety of available devices (intraaortic balloon pump, Impella, Tandem Heart, etc) that work to increase cardiac output.

Circulatory support can also be provided by ECMO or a LVAD. ECMO is performed by obtaining venous and arterial access and does not require a sternotomy. ECMO can serve as a bridge to recovery, bridge to another...
hemodynamic support device (total artificial heart or LVAD), or transplantation. The evidence supporting the use of ECMO and the survival rates are shown in Table 1.

<table>
<thead>
<tr>
<th>Study</th>
<th>Patients</th>
<th>Survival Rate</th>
<th>Cardiogenic Shock Etiology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Golding et al. (1992)</td>
<td>91</td>
<td>25.3%</td>
<td>Post-CABG</td>
</tr>
<tr>
<td>Muehrcke et al. (1996)</td>
<td>23</td>
<td>30.4%</td>
<td>Post-CABG</td>
</tr>
<tr>
<td>Magovern et al. (1999)</td>
<td>27</td>
<td>85%</td>
<td>UA or CHF</td>
</tr>
<tr>
<td>Formica et al. (2008)</td>
<td>18</td>
<td>27.8%</td>
<td>AMI/Post-CABG</td>
</tr>
<tr>
<td>Combes et al. (2008)</td>
<td>16</td>
<td>31.3%</td>
<td>AMI</td>
</tr>
<tr>
<td>ELSO (2009)</td>
<td>153</td>
<td>22%</td>
<td>Declared by physician</td>
</tr>
</tbody>
</table>

AMI=acute myocardial infarction; CABG=coronary artery bypass graft; CHF=congestive heart failure; US=unstable angina.


The TandemHeart Pump is another circulatory support device utilized in the treatment of patients with cardiogenic shock. In two randomized, controlled trials, TandemHeart, when compared with IABP, improved some hemodynamics measurements. Treatment with TandemHeart did not reduce mortality and complications were increased.

The HeartMate II Long-Term LVAD is implanted surgically and is used as either a destination device or as a bridge to either recovery or transplantation. The HeartMate II is a rotary continuous-flow device that works in parallel with the native left ventricle. It has a percutaneous driveline, a fixed-speed operating mode, and is powered electrically. Some patients treated with a HeartMate II are able to be discharged home after implantation.

A treatment algorithm for the management of patients with cardiac failure after an MI is shown in Figure 1. Prof. Eteiba reviewed the evolution of cardiac failure in this patient population and treatment recommendations as the disease progresses (Figure 2).

Figure 1. Management of Patients With Cardiac Failure Post Myocardial Infarction

<table>
<thead>
<tr>
<th>Stage A</th>
<th>Stage B</th>
<th>Stage C</th>
<th>Stage D</th>
</tr>
</thead>
<tbody>
<tr>
<td>No symptoms</td>
<td>Heart failure, disease, no symptoms</td>
<td>Structural heart disease, previous or current symptoms</td>
<td>Refractory symptoms requiring special intervention</td>
</tr>
</tbody>
</table>

Oxygenation and Survival Rates after Cardiogenic Shock

<table>
<thead>
<tr>
<th>Study</th>
<th>Patients</th>
<th>Survival Rate</th>
<th>Shock Etiology</th>
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The incidence of cardiogenic shock for patients with STEMI continues to decrease as revascularization rates increase and medical therapy has improved. For example, the TRITON TIMI-38 study [Wiviott SD et al. Lancet 2008] compared the oral antiplatelet prasugrel with clopidogrel. The overall trial showed a reduction in cardiovascular death, MI, and stroke with prasugrel. In addition, treatment with prasugrel reduced stent thrombosis, both early (through Day 30, 0.42% of patients with prasugrel compared with 1.44% of patients with clopidogrel, 71% relative risk reduction [RRR]), and late (Day 31 to Day 450, 0.42% compared with 0.91% of patients, 54% RRR).

The incidence of cardiogenic shock is greater among patients with multivessel coronary artery disease; yet, the optimal revascularization strategy for patients with STEMI and multivessel coronary artery disease remains undefined. The 2005 Practice Guideline from the American College of Cardiology, American Heart Association, and Society for Cardiovascular Angiography and Interventions, state that PCI should not be performed in a noninfarct artery during primary PCI in patients without hemodynamic compromise. The current guidelines do note that PCI of a noninfarct-related artery could be considered for patients if the lesion “appeared to be flow limiting in patients with hemodynamic instability”. The 2012 Practice Guidelines from the European Society of Cardiology state that performing PCI in nonculprit vessels is discouraged because of a “gap of evidence.” Numerous observational studies have been published which have found differing results; however, randomized trials are required for this question to be answered in a definitive manner.
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