Heart and Vascular Update

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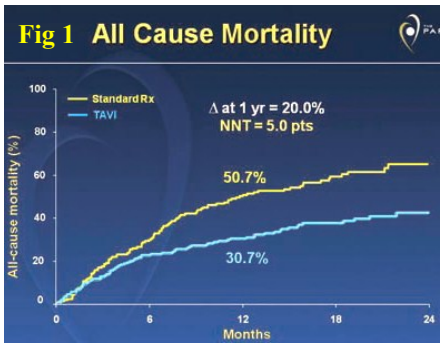
Transcatheter Aortic Valve Replacement

A randomized trial (PARTNERS) reported in Sep. 2010 demonstrated significant reductions in all-cause mortality with transcatheter aortic valve implantation (TAVI) compared with standard therapy in patients who are not candidates for surgery (Fig 1).

The PARTNER investigators randomized 358 patients with severe symptomatic aortic stenosis who were unable to undergo surgery. They then assessed the safety and effectiveness of TAVI (n=179) vs. standard medical therapy which also included balloon valvuloplasty (n=179). At one year there was a 20% absolute reduction in mortality in TAVI patients. The number needed to treat to prevent one death is 5.5 patients. The patients had a better functional status and less likelihood of repeat hospitalizations.

From this data and other registries we can conclude today that **TAVI should be the new standard of care for patients with severe aortic stenosis who are not suitable candidates for surgery** (On-line NEJM Sep 2010).

This balloon-expandable valve and the *Medtronic self-expanding GoreValve* are not approved in the U.S., however they are approved in Europe since 2007 and more than 15,000 implants have already been performed worldwide. The second cohort of PARTNERS has randomized 700 patients to either standard AVR or TAVI, results are still pending.



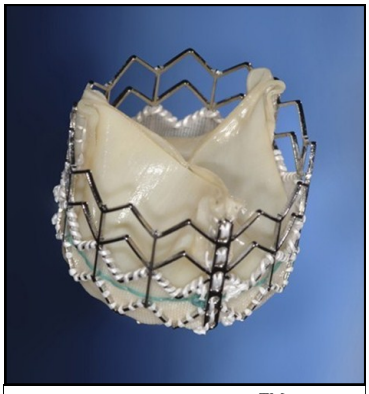


Fig 2. ***Edwards Sapien***™ ***Valve*** is made from bovine pericardium and attached to a balloon-expandable stainless steel stent.

We must emphasize that operator experience and newer generations of the valve will reduce procedural complications. In March of this year the *Sapien XT,* an 18F device (as compared with the 22-24F device used in PARTNERS) with a Cobalt Chromium stent was approved in Europe.

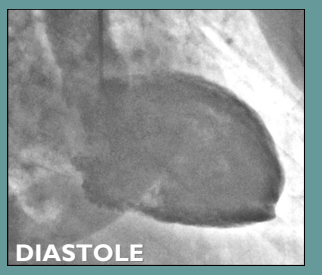
We expect and hope to have this technology commercially available in the U.S. at the end of 2011.

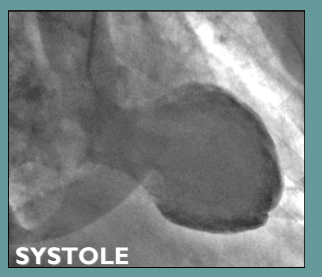
Is Platelet Reactivity Testing Necessary in PCI?

The short answer is yes. In essence "one size does not fit all". The frequency of poor responders to Plavix -and less to aspirin – has been shown in many studies. The relation of poor response with subsequent adverse outcomes and stent thrombosis is strong.

A bedside point-of-care test, VerifyNow™ by Accumetrics is available at MRH. We tested 100 consecutive patients on Plavix who were undergoing procedures in our Cath Lab in 2009. Only 43% of them had a good platelet inhibition (<240 PRU).

The options for poor responders? Increasing loading dose of Plavix, addition of cilostazol (Pletal) - which potentiates the effect of Plavix- or using Prasugrel. The latter has been shown to have a faster, more consistent and more powerful antiplatelet effect than Plavix. Prasugrel (Effient™) is now our preferred drug in ACS patients especially in those with diabetes. Only contraindications are active bleeding or any h/o TIA or stroke. Caution is advised in patients older than 75 and less than 60 kg in whom a lower dose (5 mg instead of 10) may be enough. Another drug, Ticagrelor may be available soon.





Takotsubo Cardiomyopathy: Apical and mid-ventricular akinesis. Only the basal LV remained with good contractility.

About the so-called "Broken Heart Syndrome"

Stress-Induced Myocardial Stunning: How Frequent is it?

I always remember the 69 yr. old woman who was told over the telephone that her daughter had died. She described an "immediate heavy pressure in the chest and felt like dying". After EMS arrived, a 12-lead revealed anterior ST elevation and rushed her to MRH for emergency catheterization. She was intubated and sedated. Her coronaries were normal and her LV is shown (see Figure). She was extubated within 24 hrs and finally went home in 5 days. Her LVF normalized on a follow up echo 2 weeks later.

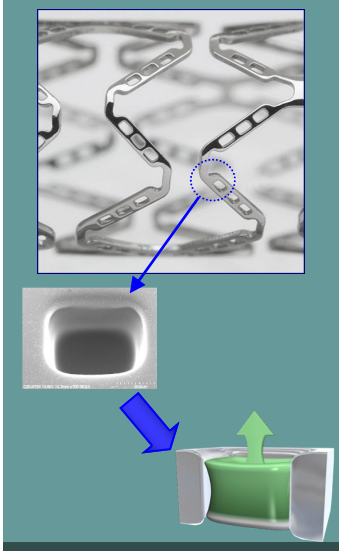
*T*akotsubo cardiomyopathy was described in Japan in 1991. Since then it has been increasingly reported in Western countries. At MRH we have seen close to 100 cases in the last several years. All but 2 were women. The youngest was 38 yrs. (1 year after her premature menopause) and the oldest was 92 yrs. old. Stressors included emotional events or physical stress such as an operation, infection or intracranial bleeding. Occasionally stressors were not found. Patients typically presented as a NSTEMI or STEMI with minimally elevated cardiac enzymes and total CKs usually less than 200. Cardiac catheterization is critical to confirm the absence of obstructive CAD. The characteristic appearance of the LV is the hallmark for the diagnosis of this condition. Either hypokinesis or akinesis of the apex (typical variety or Takotsubo) and/or the midventricle. Localized forms have also been described and a diffuse form is likely.

*T*he prognosis after the acute phase is excellent with full recovery of the LV. The pathogenesis involves cathecolamine-induced acute cardiotoxicity. The exact mechanism remains unknown. The distribution/ sensitivity of cathecolamine receptors and the distribution of adrenergic fibers in the myocardium may explain the characteristic LV appearance.

*E*xperimental models of stress induced cardiomyopathy in ovariectomized rats demonstrated the protective role of estrogens. Therefore it is provocative to postulate a pathogenic role of the lack of estrogen seen in postmenopausal women. Although physicians recognize this syndrome better, we believe that its incidence has increased over the last 6-7 yrs. We now see 2-4 cases every month. It might be that the marked reduction of Premarin prescriptions in this country play a role.

*T*reatment is conservative. Correct diagnosis is important to reassure patients of an excellent prognosis. Confirmation of the diagnosis requires recovery of the LVF. The spectrum of manifestations extends from minimal symptoms and positive cardiac enzymes to cardiogenic shock and death. Lack of recognition led to inappropriate ICD implantation in 2 patients!

Are All Drug Eluting Stents (DES) the Same?



The upcoming NEVO stent is designed specifically as DES. It has reservoirs for the drug-polymer combination. Both will elute completely by 3 months leaving behind only the metallic stent.

*T*he current DES available in the US are:

1. **Cypher stent** (Cordis Corp.) the first DES available, - since April 2003.
2. **Taxus stent** (Boston Scientific), approved a year later.
3. **Endeavor stent** (Medtronic) approved in Feb 2008.
4. **Xience stent** (Abbott) also marketed as **Promus stent** (Boston Scientific), approved in July 2008. Current leaders in the U.S. Market.

*A*ll four DES are made of a previously designed metallic stent platform which is coated with an antiproliferative drug contained in a durable, non-absorbable polymer. The drug released is a "Limus" drug in 3 of them: Sirolimus in Cypher, Zotarolimus in Endeavor Everolimus in Xience/Promus. Paclitaxel is the drug in Taxus stents (which is incompletely released from the stent). The drug and the polymer influence the efficacy and safety of these devices.

*M*ultiple studies indicate that very late stent thrombosis (beyond one year) is a risk of all DES. This risk is lower in the two newer stents probably because of a more biologically compatible polymer. This is especially true for Endeavor which may be seen as the safest in term of late and very late stent thrombosis- at the expense of an increase in restenosis. Additionally, recent large studies demonstrated that Taxus stents are inferior DES when compared to Cypher and Xience/Promus.

What is coming next?

*N*ewly designed DES will be available in the US soon: The ***Nevo stent*** by Cordis have reservoirs (see Figure) for the drug and polymer (and BOTH will be eluted completely in about 3 months, leaving behind only the bare metal stent). This will probably reduce the risk of late stent thrombosis. Medtronic will introduce the ***Resolute stent*** with slower drug release than that of Endeavor, a change that have more antirestenotic potency. The latter stent is already available in Europe.

The future trend is clear: absorbable polymers or no polymers at all. It may be that even a "temporary" (fully absorbable) stent is enough. The additional benefit of safer and still effective DES is to shorten the need for dual antiplatelet therapy without risk of late stent thrombosis.

Carotid Stenting (CAS): Is It Ready for Prime Time?

Without question CAS has been the most scrutinized vascular procedure. CAS was approved by the FDA in 2004 as an alternative for Carotid Endarterectomy (CAE) in high-surgical risk patients. Currently, it is reimbursed by CMS only for **symptomatic patients with greater than 70% stenosis** (unless patient is enrolled in a clinical trial). At MRH, we have participated of the CHOICE (Abbott) and SAPPHIRE WW (Cordis Corp.) trials for several years now.

After long 10 years, the Carotid Revascularization Vs Stenting Trial (**CREST**) was completed and published (NEJM 363:11-23, 2010). This was a NIH-sponsored randomized study involving nearly 220 centers and 224 interventionalists. It is the largest trial comparing CAS Vs CAE (2,502 patients randomized). The primary endpoint was any stroke, myocardial infarction or death at 30 days. The results were: 7.2% and 6.8% for stenting and surgery respectively (p=NS). There was slight higher rate of minor strokes with stenting. However, more myocardial infarctions and cranial nerve palsies with surgery. Interestingly younger patients (less than 70) did better with stenting rather than surgery. Conversely, the older patients did better with surgery, especially if symptomatic.

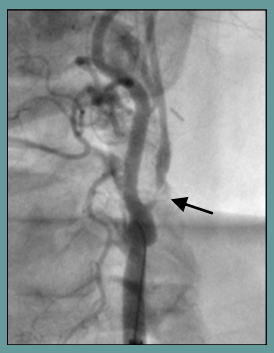
Overall these results were remarkable and reassuring since earlier smaller studies in Europe favored surgery. The lack of operator experience and lack of uniform cerebral protection probably affected their results.

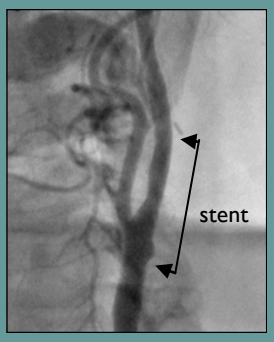
Over the past 10 years however, there has been significant improvements in technology and current studies using newer cerebral protection devices showed better results with 30-day all-stroke/MI/death of 2.3% (ARMOUR trial) and 3.7% (EMPIRE trial).

If CMS will change the reimbursement policies remains to be seen.

High surgical risk factors include serious comorbidities such as severe heart disease: unstable coronary syndromes, valvular heart disease, or any situation that requires heart surgery within the next 6 weeks, severe COPD, etc. Local anatomic factors are a short neck, high or low lesions in the neck, restenosis after CAE, contralateral occlusion, history of prior surgical neck dissection or radiation for cancer among others.

The role in CAS today will depend on further analysis of the recently presented CREST, center experience/outcomes and CMS reimbursement.





63 yr. old diabetic presented with a TIA 1 year after left CAE. Angiography revealed 99% restenosis (arrow). Successful stenting performed without complications.

PAD: Opportunity to Reduce Symptom and Prevent CV Death!

For many years we have known that the diagnosis of Peripheral Arterial Disease (PAD) carries a poor prognosis with high 5-year mortality rates - comparable to some types of cancer!. The reason is that essentially all 11 patients with PAD have concomitant Coronary Artery Disease (CAD). Although the higher the severity of PAD the higher the CV mortality, even asymptomatic patients face a significant risk. The presence of additional diabetes confers a particularly poor prognosis.

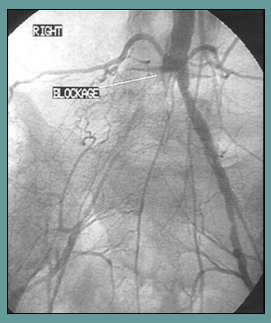
Examination should include measurement of the pressure at the ankle level and calculation of the Ankle-Brachial Index (ABI). The best correlate of the symptomatic status is the ABI immediately after walking ("post-exercise ABI"). This is especially helpful in patients with leg pain of mixed etiologies i.e. arthritis, spinal stenosis and peripheral neuropathy, or patients requiring intervention. Once the diagnosis is made we should consider in ***every*** patient:

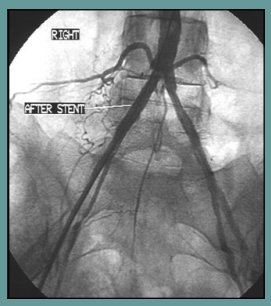
1. **Antiplatelet therapy: Plavix or ASA** (or both if a recent coronary event or any vascular intervention done). Plavix better than ASA in CAPRIE.
2. **Lipid lowering agents: Statins** with a goal of less than 70 mg/dL (or 100 mg/dL by Guidelines)
3. **ACE inhibitors** especially in diabetics or hypertensive patients. The HOPE trial showed benefit even in normotensive patients.

Symptomatic patients should be evaluated functionally (post-exercise ABIs) and anatomically (Duplex US, MRA or CTA).

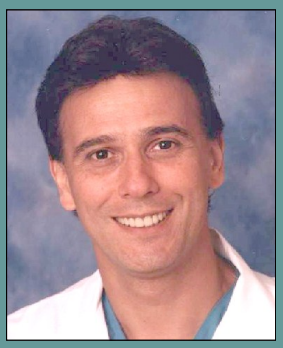
Advances in the non-surgical treatment of PAD have created the opportunity for less invasive treatment for the vast majority of patients. New technology and the improved health of older Americans are changing the previous "indifferent" approach for a new, more active and aggressive attitude that emphasizes early diagnosis and the use of less invasive treatment modalities.

Additionally, clinical evaluation (and when indicated appropriate non-invasive testing) for aneurysms, carotid disease (bruits), CAD (angina/SOB), renal artery stenosis (resistant HTN) and subclavian artery stenosis (arm BP difference) is recommended for *ALL* patients.



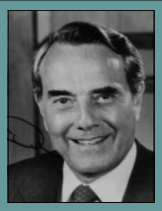


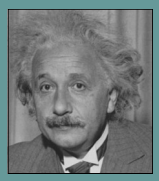
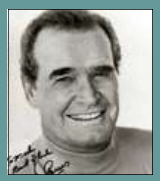
69 yr. old woman refused surgery and came for percutaneous revascularization. Two iliac stents placed and discharged the next morning.

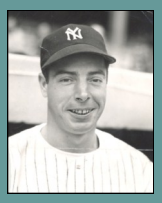


Luis F. Tami, MD

Among people affected by AAA…..



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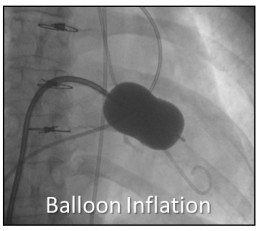
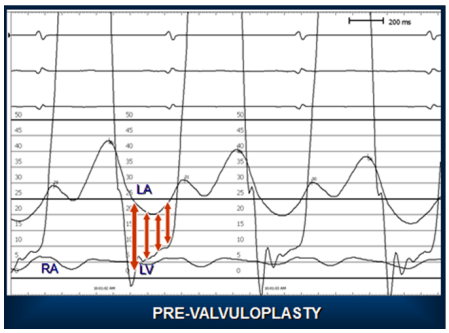
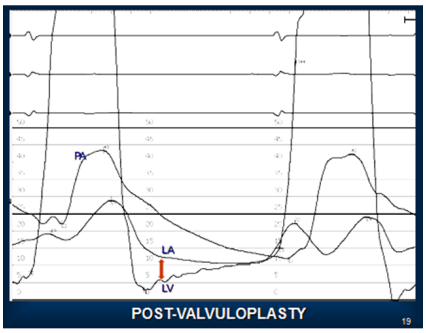
CASE
Mitral Valvuloplasty

A 48-year-old female with history of rheumatic fever and an open mitral commissurotomy 14 years ago was seen in our clinic for mitral valve re-stenosis presenting with shortness of breath on minimal exertion. She had a MVA of 1.0 cm^2 with a mean gradient of 12 mmHg at rest and an echo score of 8.







Abdominal Aortic Aneurysm Stent Graft Repair

Aortic aneurysms occurs most commonly in the abdominal aorta (AAA). This condition remains extensively underdiagnosed. However, its detection is quite simple: **Duplex US**.

It is important to screen male patients after age 65 with h/o ever smoking (Fig 1) or FHx of AAA.

Initial detection and periodic surveillance are done by Duplex US. When the aneurysm size is 5 - 5.5 cm, an Abdominal CTA will assess the precise size, anatomy and feasibility of stent-graft repair (see Fig 2).

Open AAA repair was developed in the 1960s with mortality 2-5% and significant 30-40% postoperative morbidity, especially in elderly individuals. Patients are discharged typically after 7-10 days. Durability of the open repair is excellent.

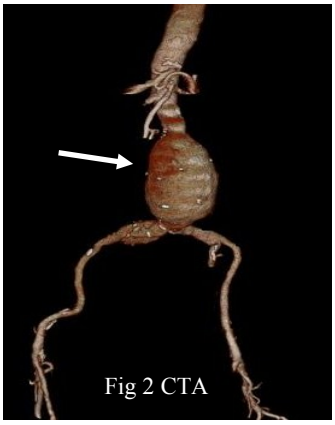
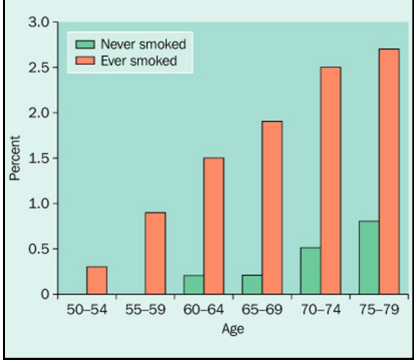


Fig 2 CTA

pair has 1-2% perioperative mortality and 5-10% morbidity (mostly related to femoral access). Usually there is no need for ICU and hospital stay is 1-2 days.

Long term outcome studies have demonstrated good durability, although there is a need for periodic follow up to detect endoleaks and graft migration. Not infrequently secondary procedures are required.

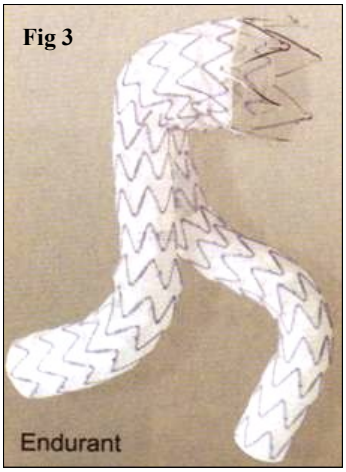
Prevalence of AAA ≥ 4 cm in Men



Parodi performed the first stent graft case in humans on Sep 7, 1990. Nine years later the first devices (Ancure, Guidant and AneuRx, Medtronic) were approved in the U.S. Subsequently the Gore Excluder, Cook Zenith, Medtronic Talent and Endologix Powerlink were added to the list. Newer devices are in the pipeline waiting for approval in the U.S. (Fig 3)

The typical stent graft re-

Fig 3



Medtronic Endurant™ graft is the most used device in Europe. Approved on Dec 21st, 2010 in the U.S.