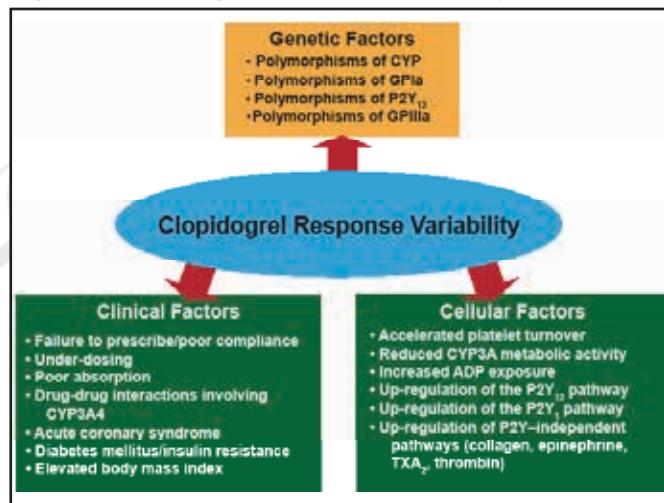


In the last 2 decades, dual antiplatelet therapy with clopidogrel and acetylsalicylic acid has become the standard of care for patients with ACS.

However, clopidogrel has drawbacks that include delayed therapeutic effect, significant interindividual variability of platelet aggregation inhibition or reduced action on thrombocytes due to interaction with other drugs or genetic polymorphisms. Although aspirin enhances the effects of clopidogrel, numerous *in vitro* studies have still verified that individual responsiveness to clopidogrel is not uniform in all patients and varies in response to genetic, clinical, and cellular factors (Figure 1) [Angiolillo DJ et al. *J Am Coll Cardiol* 2007].

Figure 1. Clopidogrel Response Variability.



ADP=adenosine diphosphate; CYP=cytochrome P450; GP=glycoprotein.

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Prasugrel, which represents the third generation of thienopyridines, inhibits platelet aggregation by irreversibly blocking the adenosine diphosphate P2Y12 receptor. In a randomized trial that compared prasugrel and clopidogrel loading doses (LDs) on rate of onset, magnitude, and consistency of platelet inhibition, Brandt et al. [*Am Heart J* 2007] found that a 60-mg LD of prasugrel resulted in more rapid ($p<0.001$), potent ($p<0.001$), and consistent ($p<0.01$) inhibition of platelet function than a 300-mg LD of clopidogrel. In the Trial to Assess Improvement in Therapeutic Outcomes by Optimizing Platelet Inhibition with Prasugrel-Thrombolysis in Myocardial Infarction [TRITON-TIMI] 38, treatment with prasugrel compared with clopidogrel resulted in a significantly lower rate of ischemic events (HR, 0.81; 95% CI, 0.73 to 0.90; $p<0.001$) [Wiviott S et al. *N Engl J Med* 2007].

Ticagrelor is an oral, reversible, direct-acting inhibitor of the adenosine diphosphate receptor P2Y12 that has a more rapid onset and more pronounced platelet inhibition

than clopidogrel [Wallentin L et al. *N Engl J Med* 2009]. The Platelet Inhibition and Patient Outcomes [PLATO] trial demonstrated that treatment with ticagrelor versus clopidogrel in a broad population of patients with ACS substantially reduced the primary composite endpoint of death, myocardial infarction, or stroke by 16% (95% CI, 8 to 21), as well as the rates of all-cause death and death from vascular causes [Wallentin L et al. *N Engl J Med* 2009].

According to Prof. Al-Mousa, 1000 ACS patients using ticagrelor versus clopidogrel for 12 months resulted in 14 fewer deaths, 11 fewer myocardial infarctions, and 7 fewer cases with stent thrombosis, with no increase in bleedings requiring transfusion. "Platelets are the principal effectors of hemostasis and key mediators in the pathogenesis of thrombosis. With clopidogrel, a wide response variability may exist and a substantial percentage of patients can exhibit nonresponsiveness," he explained.

GSA Holds Promise for Treatment of Hypertrophic Obstructive Cardiomyopathy

Written by Rita Buckley

Cyanoacrylates are the main liquid adhesives used in the vascular system and have an important role in managing vascular abnormalities, especially arteriovenous malformations [Pollack JS, White RI, Jr. *J Vasc Interv Radiol* 2001]. Ali Oto, MD, Hacettepe University, Ankara, Turkey, discussed the use of glue septal ablation (GSA) treatment for hypertrophic obstructive cardiomyopathy (HOCM).

HOCM is characterized by asymmetric myocardial hypertrophy that is most pronounced in the interventricular septum and is responsible for the dynamic obstruction of the left ventricular outflow tract (LVOT) [Fifer MA et al. *Circulation* 2008]. Prof. Oto explained that LVOT obstruction is due to the hypertrophied septum and mitral regurgitation.

Alcohol septal ablation (ASA) for HOCM is a less invasive alternative to surgical myectomy to reduce the LVOT gradient in patients resistant to drug therapy [Alam M et al. *Eur Heart J* 2009]. A recent assessment of the technique found that a significant decrease in mean peak gradient ($p<0.0001$) in the LVOT was associated with a decrease in LV mass ($p=0.0006$) and with regression of LV hypertrophy outside the scar after ASA [Timmer SA et al. *Am J Physiol* 2011].

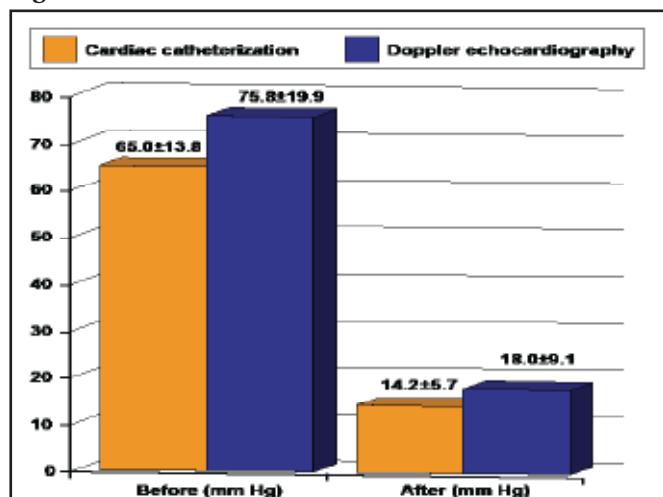
According to Prof. Oto, limitations of the ASA led him and his colleagues to publish their first-in-man GSA case in an HOCM patient with extensive collaterals to the posterior

descending coronary artery that precluded alcohol ablation [Oto A et al. *Catheter Cardiovasc Interv* 2007].

Last year, Prof. Oto and colleagues described an approach for septal ablation with glue in HOCM patients with collateral formation to the right coronary artery in whom ASA was contraindicated [Oto A et al. *J Interv Cardiol* 2011]. GSA was performed in 18 patients, 6 of whom had collateral branches to the RCA. The left coronary ostium was cannulated with 6F to 8F guiding catheter. The septal branch was cannulated with a 4F catheter and microcatheter, and then cyanoacrylate mixture was instilled into the septal artery. Immediate polymerization prevented leakage into the left anterior descending (LAD) coronary artery, and also into the RCA via septal collaterals.

Immediately after the procedure, peak LVOT gradient reduced significantly in both cardiac catheterization (65.0 ± 13.8 vs 14.2 ± 5.7 mm Hg; $p < 0.001$) and Doppler echocardiographic measurements (75.8 ± 19.9 vs 18.0 ± 9.1 mm Hg; $p < 0.001$; Figure 1). Reduction in LVOT gradient persisted after 6 months of follow-up. Furthermore, septal wall thickness (20.2 ± 3.7 vs 16.5 ± 3.2 mm; $p = 0.003$) significantly decreased while NYHA functional class improved (3.1 ± 0.4 vs 2.2 ± 0.3 ; $p < 0.001$). No significant complications occurred during the procedure or within 6 months of follow-up [Oto A et al. *J Interv Cardiol* 2011].

Figure 1. Left Ventricular Outflow Tract Gradient.



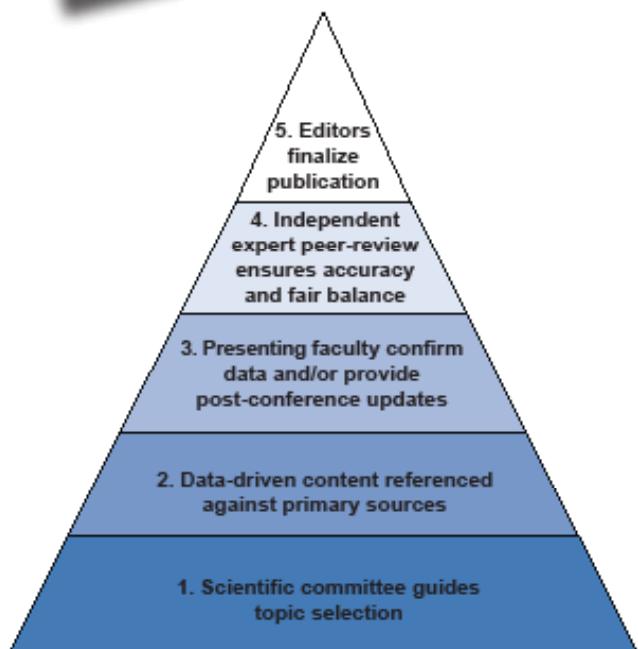
Prof. Oto and colleagues concluded that GSA is a promising alternative for treating patients with HOCM. Their experience suggests that GSA is safe, effective, and can be performed without serious complications.

Glue seems to be superior to alcohol; immediate freezing prevents leakage to the LAD coronary artery and is thought to be particularly useful in the presence of collaterals. Further experience is needed to assess the long-term efficacy and safety of the technique.

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