of any single trial did not alter the pooled effect result. Meta-regression coefficients were not significant for hypertension (p = 0.8) or aortic diameter (p = 0.8).

Most reports of post-AVR aortic dissection include a limited number of patients and do not differentiate between BAV phenotypes (1). One systematic review with 14% of BAV patients found that aortic insufficiency and fragility/thinning of the aortic wall were predictive of post-AVR dissection (4).

Study limitations include the restricted focus on BAV function only (i.e., excluding other potentially important features) and the relevant rate of missing data (i.e., regarding BAV morphotype and aortic diameters).

Our meta-analysis revealed a 10-fold higher risk of aortic dissection in patients who undergo AVR for BAV insufficiency compared with BAV stenosis. Moreover, the smaller aortic diameters in patients with BAV insufficiency indicate an increased risk of dissection at smaller diameters in this BAV cohort. In contrast, BAV stenosis-associated aortopathy seems to follow a more benign course post-AVR. Such information may be helpful when deciding on management of the aorta in BAV patients undergoing AVR surgery.

*Evaldas Girdauskas, MD, PhD  
Mina Rouman, MD  
Kushtrim Disha, MD  
Andres Espinoza, MD  
Martin Misfeld, MD, PhD  
Michael A. Borger, MD, PhD  
Thomas Kuntze, MD

*Department of Cardiac Surgery  
Central Clinic Bad Berka  
Robert-Koch-Allee 9  
99437, Bad Berka, Germany  
E-mail: egirdauskas@web.de

Please note: The authors have reported that they have no relationships relevant to the contents of this paper to disclose. These data were originally presented at the 44th Annual Meeting of the German Society for Thoracic and Cardiovascular Surgery, February 8–11, 2015, Freiburg, Germany.

REFERENCES


Protamine and Bleeding Avoidance Strategies

I read with great interest Dr. Singh’s state-of-the-art review entitled “Bleeding Avoidance Strategies During Percutaneous Coronary Interventions” (1). As he points out, the HEAT-PPCI (Unfractionated Heparin Versus Bivalirudin in Primary Percutaneous Coronary Intervention) trial (2) has renewed interest in heparin monotherapy with pre-loading of dual antiplatelet therapy during percutaneous coronary interventions (PCIs). Protamine reversal of heparin anticoagulation can also be considered as a bleeding management and/or bleeding avoidance strategy. Nonetheless, protamine may be underutilized because of concerns regarding possible heparin rebound, cardiac and peripheral thrombotic effects, and the potential for allergic or anaphylactic reactions. Protamine-related adverse events occur in ~2.6% of treated patients but may be as high as 11% with a less restrictive definition (3). Briguori et al. (4) previously concluded that patients who received protamine to reverse heparin-associated bleeding complications after coronary stent implantation did not sustain higher rates of stent thrombosis compared with similar nonprotamine-treated patients. Protamine is generally well tolerated when routinely used at the conclusion of cardiopulmonary bypass procedures in patients with cardiovascular clinical characteristics similar to patients undergoing PCI. Meta-analysis of routine utilization of protamine for the reversal of heparin anticoagulation post-PCI has shown favorable results in properly selected patients (5).

Interventionalists may consider protamine reversal of heparin anticoagulation as a reasonable strategy for the treatment of significant post-procedural bleeding events. Further clinical studies are appropriate to define the optimal role of protamine post-femoral access PCI, to reverse heparin anticoagulation, and to potentially avoid PCI-associated bleeding events in patients who have also undergone appropriate pre-loading with dual antiplatelet therapy.
RESERVE ESTIMATION NOT REQUIRING PERCUTANEOUS CORONARY INTERVENTIONS (PCI)

Heparin is used in PCI to prevent thrombosis and patency requiring anticoagulation with heparin.

There are several reasons that protamine cannot be routinely used to avoid bleeding after PCI. First, the allergic reactions to protamine are not uncommon and can lead to serious anaphylaxis. Second, even though protamine has been shown to be safe in small series, case-control, and randomized studies, its usefulness has not been proven in large contemporary randomized trials (3).

Third, its safety has been tempered with case reports of ischemic complications in patients treated with protamine. Fourth, the use of the radial artery for access has diminished the utility of protamine reversal in favor of radial artery patency requiring anticoagulation with heparin.

The role of protamine should be explored further, and larger, randomized trials need to be planned. In the meantime, patient selection for use of protamine is important. Patients with seafood allergies or previous use of protamine should not be given this drug. However, patients at very high risk of bleeding (e.g., elderly women presenting with acute coronary syndrome and who had femoral access for PCI) would be ideal candidates for protamine administration for heparin reversal, especially if there are bleeding events (i.e., hematoma, retroperitoneal bleed).

Rebound thrombogenicity and allergic reactions to protamine are valid concerns that need to be addressed. Protamine remains a useful tool in the armamentarium of interventional cardiologists, and its judicious use is recommended.

Mandeep Singh, MD, MPH
Division of Cardiovascular Diseases
Department of Internal Medicine
Mayo Clinic
Rochester, Minnesota 55902
E-mail: singh.mandeep@mayo.edu
http://dx.doi.org/10.1016/j.jacc.2015.06.1337

Please note: Dr. Singh has reported that he has no relationships relevant to the contents of this paper to disclose.

A PROPOSAL TO INCORPORATE TRIAL DATA INTO A HYBRID AMERICAN COLLEGE OF CARDIOLOGY/AMERICAN HEART ASSOCIATION ALGORITHM FOR THE ALLOCATION OF STATIN THERAPY IN PRIMARY PREVENTION

Ridker et al. (1) draw attention to the importance of statins as primary prevention agents; they endorse...