Trial Commentary: Effect of Clopidogrel and Aspirin vs. Aspirin Alone on Migraine Headaches After Transcatheter Atrial Septal Closure: The CANOA Randomized Trial

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Research Question

To evaluate the incidence and severity of new-onset migraine headache episodes following transcatheter ASD closure in patients treated with aspirin alone compared to those on aspirin + clopidogrel therapy as antithrombotic treatment after the procedure.
Importance

• Atrial septal defects are a common adult congenital heart defect that can lead to heart failure and pulmonary HTN

• The majority of secundum ASDs are percutaneously closed
  – Lower complication rate than surgical closure

• Migraine headache (MHA) is not considered a complication of ASD closure in device trials but has implications for patient QOL
Potential Mechanisms of MHA with ASD Closure

• Liberation of vasoactive substances with atrial stretch
  – Plasma calcitonin gene-related peptide (CGRP)
• Microthrombi formation on left atrial surface*
  – Microemboli from thrombus
  – Platelet release of serotonin
• Nickel release from device
• Change in cardiac output and stroke volume influencing ocular hemodynamics

Study Design

• Multicenter, prospective, double blind randomized trial
• Randomization prior to successful ASD closure
  – 22% patients in each group excluded for no ASD closure or dropped out
• Primary endpoint
  – Mean number of monthly migraine days per patient
    • Evaluation by 2 neurologists blinded to group assignment
    • Validated and HA measures (MIDAS) and diary
    • Universal definition HA (IHS criteria)
Results

• Baseline characteristics well balanced
  – ASD and device size, residual shunt

• Endpoints of MHA reduction with DAPT met
  – Migraine days per month low
    • 1.4 (4.1) ASA vs. 0.4 (1.4) DAPT (IRR 0.61 (0.41-0.91))
  – New onset migraines higher than expected
    • 21.8% ASA vs. 9.5% DAPT (OR 0.38 (0.15-.089))
  – Results consistent ITT and as treated analysis
    • 91% received assigned treatment
Unanswered Questions and Future Considerations

• Confirm mechanism of benefit and nonresponse
• Not generalizable to other devices
  – Cardioseal higher thrombus
• Optimal duration DAPT
  – Device endothelialization
• Does DAPT reduce other potential device complications?
  – TIA, study not powered (1 vs 0)
• Pediatric patients

Astroulakis Z Heart 2008;94:580; Anzai H AJC 2004, 93(4):426-31
Impact on clinical practice

• Most centers currently using DAPT 3-6 months post ASD/FPO closure
  – Practice empirically started
  – Regimen used in many RCTs (MIST)
  – Registries of serial imaging of devices report high use of DAPT

• Study provides rationale for DAPT use and will increase adoption

• For patients at high risk for bleeding risks and benefits of DAPT should be considered