DDW 2016: Controversies in GIB

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Hot Topics

- Acute Management Strategies
  - Hemospray
  - Early vs. Late resumption of ASA
  - Platelet transfusion
- DOACs
  - Head to head risk study
  - Idarucizumab interim analysis
  - GPA and edoxaban bleeding rates
- LVADs
  - Target INR post bleed

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Hemospray vs. Combined Conventional Technique for Bleeding PUD (Kwok et al)

- Adsorbs water and clotting factors to create a mechanical tamponnade
- Randomized, parallel group trial of N=20 (Forrest 1A, 1B, 2A and 2B)
  - Injection + heater probe vs. hemospray
  - Second-look EGD to assess re-bleed
- Outcomes
  - Immediate hemostasis 19/20
  - Re-bleed (2^{nd} look EGD) 33% hemospray vs. 10% conventional
- Take-Home Message
  - Not ready for prime time
  - Washes off in 12 hours
  - Use as an adjunct only or temporizing measure until definitive therapy occurs (within 12 hours)
  - Bad choice for patient with a high risk stigmata (1A and 1B lesions)

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Early and Late Resumption of ASA after endoscopic therapy for bleeding peptic ulcers (Lin et al)

- Hong Kong group: RCT post ulcer bleed ASA vs. place– NNH 13 for mortality
- Cohort study to assess risk associated with early (w/in 7 day) vs. late (>7 days) resumption of ASA following bleeding peptic ulcer treatment
- Outcomes: re-bleeding, CV events, 30 day mortality
- Results: n=327 patients (105 early; 156 late)
  - No difference in re-bleed rate
  - Higher risk of CVA in late group (4.5% vs. 1.9%)
  - 65 patients no resumption of ASA- higher mortality (26% vs. 4%)

MUST resume ASA within 7 days of endoscopy!

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Platelet transfusion for acute GIB in patients taking antiplatelet agent: is there benefit or harm? (Zakko et al).

- GIB patients on clopidogrel, aspirin at Yale (2009-2014)
- Case-control study; 1:1 matching (age,sex, GIB location)
- Outcomes: recurrent GIB, major adverse CV events, mortality, RBC transfusion and LOS
- Results: 204 cases/204 controls
  - Cases had more severe GIB (hemodynamics) and more DAPT use (30% vs. 24%)
  - Controls – higher pre-GIB PPI use (30% vs. 21%)
  - Platelet transfusion without thrombocytopenia did NOT reduce rebleeding or need for RBC transfusion
  - Platelet transfusion associated with increased mortality (OR 5.57; 1.52-27.1) after adjustment for stents, hemodynamics initial Hg <7 mg/dL, initial ICU admission status
- Take-Home Message: No role unless thrombocytopenia (<50,000)
- CardioGI Pearl: only with prasugrel and ticagrelor
  - reversible P2Y12 agent ticagrelor and PAR-1 inhibitor vorapaxar will re-distribute on transfused platelets, so not helpful.

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Gastrointestinal Safety of Direct Oral Anticoagulants: A Head-to-Head Study (Abraham)

- No prior head-to-head DOAC safety trials. Indirect comparisons are of limited clinical utility for risk-prediction. Ascertain which DOAC has the most favorable GI safety profile.
- Methods:
  - Propensity-matched cohort study
  - New users of DOACs
  - Atrial fibrillation patients
  - Optum Labs Data Warehouse: large administrative data source which includes >120 million geographically diverse, non-elderly and elderly individuals, privately insured or enrolled in Medicare Advantage.
  - Cox proportional Hazards Models, incidence rates, absolute risk reduction and age-stratified analysis
- Outcomes of interest:
  - Stroke/SE, major bleeding, GIB

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- N= 43,303
  - Apixaban 6,576
  - Dabigatran 17,426
  - Rivaroxaban 19,301

- 1:1 Propensity Matched* Sub-cohorts
  - API vs. DABI (N=13,084)
  - API vs. RIVA (N= 13,130)
  - RIVA vs. DABI (N=31,574)

**PS Model: baseline characteristics, prior warfarin use, socio-demographic factors*

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Results: Comparative Risks

	RIVA vs. DABI		ARR	API vs. DABI		ARR	API vs. RIVA		ARR
Stroke or Emboli	1.4	1.4	0.02 (0.21, 0.25)	1.4	1.5	-0.13 (0.57, 0.30)	1.4	1.3	0.10 (0.37, 0.57)
Major Bleeding	3.8	2.6	1.20 (0.67, 1.72)	2.1	3.3	-1.20** (-1.99, -0.41)	2.0	4.6	-2.54*** (-3.47, -1.61)
GIB	2.7	2.0	0.72 (0.27, 1.17)	1.4	2.7	-1.35*** (-2.03,-0.67)	1.3	3.5	-2.20*** (-3.00, -1.40)

*p<0.05, **p<0.01, ***p<0.001

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Conclusions

- DOACs similar with regard to cardiac benefit
- Apixaban has most favorable bleeding profile
  - 35% safer than DABI
  - 2.2 X safer than RIVA
- DABI was 28% safer (GIB) and 20% safer (major bleed) than RIVA
- All DOACs: GIB risk highest in patients ≥ 75 yrs
  - >2X higher risk with each comparison
  - API appears safer in the very elderly

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Idarucizumab for Emergent Reversal of Dabigatran Anticoagulation during Gastrointestinal Hemorrhage: Interim Results of the Reverse-AD study (Aisenberg)

- Ongoing Reverse-AD Study enrollees presenting with severe GIB
- Interim analysis cohort (n=123)
- Results:
  - 66 patients had severe bleeding; 27 GIB
  - Mean age GIB 77.5 yrs (60-93); 56% male; renal impairment in 22/23 of those with CrCl measured
  - Afib indication for use in 93%; 74% took last dose <24 hours prior to presentation
  - 10/27 had UGIB (37%); 8/27 (30%) LGIB
    - 24/27 received >1 unit PRBC (mean 4.5 units); 9 received FFP and platelets transfused in 1 patient
  - Time to cessation of GIB after IDA use was 4.5 hours (0-645 hours)
    - Serum assays to confirm above-therapy levels not shown
  - 20/27 patients had resumption of antithrombotic post bleed (74%)

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Concurrent GPA and Edoxaban-GIB Rates: Engage-AF TIMI 48 trial (Aisenberg)

- Engage-AF TIMI 48 trial: high vs. low dose EDX (60 mg vs. 30 mg/day) vs. warfarin for stroke prevention n=21,105)
  - Major GIB (MGIB) captured as a safety outcome
- Post-Hoc analysis of patients with MGIB
  - 579 patients with MGIB (2.75%)
  - 1,691 patients (8%) daily PPI; 91/579 had MGIB (15.7% of GIB)
  - High-EDX > warfarin > low-EDX (Dose dependent MGIB)
  - PPI use increased MGIB bleed rates in all arms
    - LGIB increased in all arms
    - UGIB increased in high and low dose EDX
  - Take-home message: Confounding by indication

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The Role of Goal INR and Re-Bleeding for the LVAD patient (Storm)

- Retrospective review of LVAD bleeding experience 2012-2014 (Brigham and Women's)
- Aim to identify a threshold INR level which increased GIB re-bleed risk
- 24 patients with LVADs had GIB
  - 64 admissions (2.7 times/patient)
  - 77 GI procedures ; source found in 25%; AVM most common
  - INR >2.5 had earlier re-bleed (p=0.03); HR 2.03 (1.04, 4.14)
  - Concomitant ASA and AP increased re-bleed risk (p=0.09); NS on MVA
  - Endoscopic therapy did not reduce re-bleed; low risk of finding a bleeding lesion
- Take Home Message: Goal INR should be 2.5 or less to decrease re-bleed
  - My approach:
    - 1st decrease ASA to 81 mg or, no AP if possible
    - 2nd decrease INR to 2.0-2.5

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Take Home Messages from DDW 16 Abstracts

- Hemospray should not be your “go-to method”
  - High-risk of rebleed when compared to conventional therapy
- Must resume cardiac ASA within 7 days following urgent GIB management
  - Increased death without it! No increased re-bleed
  - Higher CVA risk with delay
- Platelet transfusion increases mortality unless patient is thrombocytopenic
- Time to cessation of GIB after IDA use was 4.5 hours
  - Assays to confirm above-therapy levels not shown; ?C/E
- ALL DOACs increase risk of GIB in patients ≥ 75 yr
  - Apixaban has the safest GIB profile
- LVAD re-bleed prevention– lower goal INR to 2.5

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