2015 (and early 2016)
The Year in Review
No conflicts of interest

How to make this talk….
Areas Searched
- Medline
- ACP Journal Club
- Residency Journal Clubs
- Faculty Suggestion
- Practical, Applicable, Interesting
- Whatever is not being covered elsewhere….

Topics!

1- Therapeutics
   - Afib, GIB and Warfarin - dangerous brew
   - PPI's - well tolerated?
2- Screening Update
   - The dreaded AAA
3- When to refer to ortho
   3a- Meniscal tears
   3b- Knee replacements
4- Post-op analgesia

Afib, GIB and Warfarin - dangerous brew

A 75 year old woman with hypertension and diabetes arrives a week after being sent home after a three day hospitalization after having a upper GIB from a gastric ulcer. Biopsy pathology was benign and her H.Pylori testing was negative. She has longstanding atrial fibrillation and was taking warfarin which was stopped upon her admission. She feels well and wonders if she should restart her anticoagulation. You recommend which of the following:

A. Treat with clopidogrel monotherapy
B. Treat H. Pylori infection
C. **Restart warfarin for INR of 2-3**
D. Change to a novel oral anticoagulant
E. Reconsider anticoagulation a month after her bleed

2% 0% 15% 26% 57%
**Atrial Fibrillation**

<table>
<thead>
<tr>
<th>AGE</th>
<th>PREVALENCE</th>
<th>AR%</th>
<th>RR</th>
</tr>
</thead>
<tbody>
<tr>
<td>50-59 Years</td>
<td>0.5%</td>
<td>1.5%</td>
<td>4.0</td>
</tr>
<tr>
<td>60-69 Years</td>
<td>1.8%</td>
<td>2.8%</td>
<td>2.6</td>
</tr>
<tr>
<td>70-79 Years</td>
<td>4.8%</td>
<td>9.9%</td>
<td>3.3</td>
</tr>
<tr>
<td>80-89 Years</td>
<td>8.8%</td>
<td>23.5%</td>
<td>4.5</td>
</tr>
</tbody>
</table>

- Common disorder, increases with age
- AR% increases dramatically with age
  - Circulation 2010: 103:162-182
- Our patient - 75, DM, HTN
  - CHADS2 = 3
  - ~6-8%/year stroke

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**Stroke Prevention in A. Fib-Rx**

Meta-analysis Data – 9874 participants, 16 trials

1. Warfarin vs. Placebo → 62-68% RRR INR 2-3
   - Absolute risk bleeding 0.3%/year
   - Reduction of all cause mortality 26% (ARR 1.6%/Year)

2. Aspirin vs. Placebo → 21-25% RRR ANY Dose
   - Absolute risk bleeding 0.2%/Year
   - No overall reduction of mortality

WHEN/IF Restart anticoagulation?

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**Mortality after GIB with Afib + anticoagulation**

- Post-d/c cohort
- 4600 Danes, X=78yo, 45% women
- f/u started 90 days post discharge
- Two years follow-up -49% mortality
- All-cause mortality

- Staerk. BMJ 2015;351:h5876

**Outcomes:**

- Mortality RRR 61%
- Thrombosis RRR 59%

**Harms:**

- Major Bleed RRI 37%
- 2nd GIB RRI 34%

- Staerk. BMJ 2015;351:h5876
Timing of Restarting Anticoagulation

- Findings similar to Quereshi et al. AJC, Volume 113, Issue 4, 2014, 662–668

Retrospective Cohort 1329 pts
- Southeast Michigan
- 2005-2010
- X=76 years
- 45% women
- Anticoag 49% restarted
- Controlled for chads/hasbeld

33% mortality RRR

1.18 RRI recurrent GIB
P=0.47

29% thrombosis RRR

Survival analysis showing 1-year mortality stratified by duration of interruption of warfarin

- Increased GIB risk <7days
- Increased Death or Thromboembolism >30 days

Recommend 7-21 days

Anticoagulation after UGIB

- Mortality Benefit to restarting!
- 7-15 days seems to be sweet-spot
- Some increase to bleeding- carefully council and ensure INR in range

- Case resolution: 76 yo woman 10 days post-UGIB. Restart warfarin for INR=2-3 with close follow-up

Anticoagulation on Discharge

Table 3. Unadjusted and adjusted hazard ratios for continuing anticoagulation vs. cessation of anticoagulation

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Unadjusted hazard ratio (95% CI)</th>
<th>P value</th>
<th>Adjusted hazard ratio (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thromboembolism</td>
<td>0.073 (0.004–0.434)</td>
<td>0.003</td>
<td>0.121 (0.005–0.812)</td>
<td>0.03</td>
</tr>
<tr>
<td>Recurrent GIB</td>
<td>2.28 (9.29–6.83)</td>
<td>0.07</td>
<td>2.17 (0.961–6.67)</td>
<td>0.10</td>
</tr>
<tr>
<td>Death</td>
<td>0.471 (0.172–1.28)</td>
<td>0.138</td>
<td>0.632 (0.216–1.89)</td>
<td>0.40</td>
</tr>
</tbody>
</table>

CI, confidence interval; GIB, gastrointestinal bleeding

Sengupta, Am J Gastroenterol 2015; 110:328–335

Prospective Cohort restarted on anticoagulation on discharge
- 90 day outcomes, 197 patients
Case #2

60 year old woman is concerned about her medications. She has heard that her chronic omeprazole that she has taken for several years for her heartburn can cause other medical problems. You say she is right and tell her PPIs are associated with the following complications except:

A. Increased risk for C. Dificle infection
B. Renal insufficiency
C. Drug interaction leading to Clopidogrel failure
D. Dementia
E. All of the above
F. A and C only

Also CAP, B12 deficiency, fracture risk

Risk of C. Dif with PPI Use
- OR = 1.74 increase in CID with PPI
- Heterogeneity
- Consistency across studies


PPI and Renal Damage?

- Chronic kidney disease (CKD) affects approximately 13.6% of adults in United States
- Increased risk of death and cardiovascular events
- PPIs amongst most commonly used drugs worldwide
  - 40% to 60% no appropriate indication

- Large database study examines relationship
  - Atherosclerosis Risk in Communities (ARIC) prospective cohort study 10,482 participants, 63.0 yo, 56% women
  - Replication Cohort 248,751 patients with an outpatient eGFR of at least 60
    - Lazarus et al. JAMA Intern Med. 2016;176(2)
Prevalence of Proton Pump Inhibitor (PPI) Ever Use
Over Time in the Atherosclerosis Risk in Communities Study


Proton Pump Inhibitor Use and the Risk of Chronic Kidney Disease

Table 2. Proton Pump Inhibitor Use and the Risk of Incident Chronic Kidney Disease

<table>
<thead>
<tr>
<th>Variable</th>
<th>Atherosclerosis Risk in Communities Study</th>
<th>Simon Heart Health System Replication Cohort</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of Events</td>
<td>No. of Participants</td>
</tr>
<tr>
<td>PPI users</td>
<td>36</td>
<td>1924</td>
</tr>
<tr>
<td>PPI non-users</td>
<td>906</td>
<td>2904</td>
</tr>
<tr>
<td>PPI non-users and Incident CKD</td>
<td>1.40 (1.13-1.73)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Baseline PPI use vs no PPI use</td>
<td>1.50 (1.46-2.96)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Baseline PPI use vs no PPI use</td>
<td>1.39 (1.15-2.35)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Baseline PPI use vs no PPI use</td>
<td>1.39 (1.15-2.35)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Baseline PPI use vs no PPI use</td>
<td>1.76 (1.53-2.04)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Baseline PPI use vs no PPI use</td>
<td>1.24 (0.86-1.79)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>


Proton Pump Inhibitor Use and the Risk of Chronic Kidney Disease

Table 3. Proton Pump Inhibitor use and the Risk of Incident Acute Kidney Injury

<table>
<thead>
<tr>
<th>Variable</th>
<th>Atherosclerosis Risk in Communities Study</th>
<th>Simon Heart Health System Replication Cohort</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of Events</td>
<td>No. of Participants</td>
</tr>
<tr>
<td>PPI users</td>
<td>67</td>
<td>1034</td>
</tr>
<tr>
<td>PPI non-users</td>
<td>953</td>
<td>2121</td>
</tr>
<tr>
<td>PPI non-users and Incident CKD</td>
<td>1.26 (1.12-1.42)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Baseline PPI use vs no PPI use</td>
<td>1.49 (1.26-2.77)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Baseline PPI use vs no PPI use</td>
<td>1.50 (1.15-2.80)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Baseline PPI use vs no PPI use</td>
<td>2.06 (1.84-2.32)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

Lazarus et al. JAMA Intern Med. 2016;176(2)

PPI and Dementia

- German Study on Aging, Cognition and Dementia in Primary Care Patients
- 73K participants free of dementia
- X=83 yo, 74% women
- Community dwelling at enrollment
- q18 month follow up
- Memory testing
**Figure Legend:**

hazard ratio 1.44

44% increase risk of dementia with PPI use over 6 years


**Table 3. Data on Risk of Incident Dementia by PPI Use, Age-Group Analysis**

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>75-79 y</th>
<th>80-84 y</th>
<th>85+ y</th>
</tr>
</thead>
<tbody>
<tr>
<td>No PPI use</td>
<td>1.00 (1.00-1.00)</td>
<td>1.00 (1.00-1.00)</td>
<td>1.00 (1.00-1.00)</td>
</tr>
<tr>
<td>PPI use</td>
<td>1.09 (1.00-1.20)</td>
<td>1.09 (1.00-1.20)</td>
<td>1.09 (1.00-1.20)</td>
</tr>
</tbody>
</table>

**Bottom Line:**

- **Long Term PPI Indications:**
  - Barrett’s or Erosive esophagitis, Hypergastrinemic states, Long term NSAIDS in high risk patients, DAPT
  - AGA recommends lowest shortest exposure possible

- **Re-evaluate:**
  - Needs assessment for PPI - frequently
  - Try protocol


Anderson and Kotwani - reproduced with permission
Case #3-
When talking about Abdominal Aortic Aneurysms which of the following statements is true?

A. Risk of rupture increases exponentially when AAA measures >4.5cm
B. Smoking is the biggest risk factor for AAA
C. Family history of AAA is not a risk factor
D. Screening for AAA has no impact on disease specific mortality
E. All of the above are false

Abdominal Aortic Aneurysm

- AAA >2.9 cm 6% at 65yo
  - Increases 6%/decade
  - 90% smokers
  - Ehlers Danlos, Marfans
  - Familial (30%, 6%)
- Obvious risk=rupture
  - 90% mortality!
  - 9K deaths
  - 2-6% operative mortality
  - 1400-2800 deaths

Who to screen for AAA?

- Poking a skunk...
- Ultrasound Sn=95%, Sp=99%
  - CT- similar test characteristics, more dye
- USPSTF
  - Male smoker 65-75 years- Grade B (fair data)
    - Family Hx, Erhlers Danlos, Marfans
    - AAA mortality screened- OR = 0.57
  - Non-smoking Males- Grade C- no rec.
  - Females 65-75 years- Grade D
    - OR = 0.98 mortality. Only one trial
**MASS Trial** (multicenter aneurysm screening study)

- 68K men in UK 65-75yrs, 10 yrs of follow-up
- HR=0.52 (intention to screen)
- HR=0.40 (actually screened)
- NNS= 243
- $11,400 per QALY

![Graph showing MASS Trial results](image)

- Thompson et al. BMJ 2009;338:b2307

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**How to repair a AAA?**

**DREAM Trial- >5 cms**

- (Dutch Randomized EVR Aneurysm Trial)
- 345 patients
  - Open-174, EVR-171
  - 4.6% (8) 1.2% (2)
  - Mortality
    - 9.8% (17) 4.7% (8)
  - Mortality or severe complications @30 days

![Graph showing DREAM Trial results](image)

- www.marketwire.com/mw/release_html_b17release...

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**Not so Sweet DREAM- 2 year outcomes**

- Large retrospective Medicare database evaluation
- **40K matched pairs** of patients who had undergone either open repair or endovascular repair.
- **Perioperative mortality** 1.6%-EVR vs. 5.2% with open repair (P<0.001)
- From 2001 through 2008, perioperative mortality decreased 1% both
- **8 years** of follow-up

![Graph showing DREAM 2-year outcomes](image)

**3 Possible Explanations**

1- Chance driving outcomes since small study
2- Frail patients survived EVR but later died
3- Long term EV repair inferior to open?

- NEJM 352:23 June 9 2005

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**Long-Term Outcomes of Abdominal Aortic Aneurysm in the Medicare Population**

- NEJM 351;16, Oct 14, 2004

- NEJM 352:23 June 9 2005

Freedom from Rupture, Aneurysm, or Reintervention for Complications Related to Laparotomy.

8 year outcomes
Aneurysm rupture:
5.4% EVR
1.4% open repair (P<0.001)

Bottom Line- AAA

- **Screen** smoking men 65-75, +FH, Marfans
  - Non-smokers, women??
- **>5.4 cm refer for repair**
  - (or for >1 cm expansion/yr)
  - Short term survival benefit for EVR
  - Endovascular repair high risk patients

  - Mortality risk crosses between 2-3 years
  - Annual U/S post procedure

Case 5

60 yo woman arrives in your office complaining of right knee pain that began while playing golf where she twisted after hitting the ball. The pain has persisted despite 2 weeks of APAP. She endorses her knee catches with walking and occasionally feels like it could collapse. Xrays show no fractures or significant DJD. You advise.

A. Vitamin D 800iu daily
B. Physical therapy
C. Arthroscopic partial meniscectomy
D. Glucosamine sulfate orally

Fidelity Study- what is known

**RCT- sham-controlled meniscectomy.**

- **146 patients** 35-65 yo
- Degenerative medial meniscus tear
- Arthroscopic partial meniscectomy vs. sham arthroscopy
- Pain scores 12 mos.
- **NO DIFFERENCE**

Meniscectomy for Tears

- 700,000 annually
- Previous research no difference from PT and fewer complications
- NOT examined for mechanical symptoms manifest by: locking, popping or collapse
  – May represent larger tears

Fidelity Subgroup- Mechanical s/s

| Table 2. Course of Mechanical Symptoms After APM or Sham Surgery (n = 144)* |
|---------------------------------|------------------|------------------|------------------|
| Mechanical Symptoms             | Before Surgery   | After Surgery    | After Surgery    |
| -                               | APM              | Sham             | APM              |
| -                               | Sham             | APM              | Sham             |
| -                               | APM              | Sham             | APM              |
| -                               | Sham             | APM              | Sham             |
| Present, n                      | 32               | 37               | 17              |
| Absent, n                       | 38               | 39               | 53              |
| Relative risk (95% CI)          | 0.24             | 0.32             | 0.21            |
| Absolute risk                   | -                | -                | 0.04            |
| Risk difference (95% CI)        | -0.01 (-0.22 to 0.007) | 0.04 (-0.01 to 0.18) | 0.07 (-0.16 to 0.21) |
| Relative risk (95% CI)          | 0.77 (0.62 to 1.24) | 1.24 (0.68 to 2.30) | 1.38 (0.73 to 2.60) |

*Results are expressed as the number of patients with a degenerative meniscal tear who still have mechanical symptoms at 2, 6, and 12 mo after APM (n = 70) or sham surgery procedure (diagnostic arthroscopy followed by simulated APM (n = 74).

Mechanical symptoms:
- 32 patients (46%) in the APM vs. 37 (49%) sham
  - No Difference post procedure…

CAUTION in using surgery for reported mechanical s/s…

Case 5

80 yo woman arrives in your office complaining of right knee pain that is ongoing. You recently diagnosed her with severe DJD for which she has had only transient relief from APAP. You advise.

A. Vitamin D 800iu daily (neg RCT**)
B. Physical therapy, nutrition
C. Total knee replacement
D. Foot insoles
E. B and D


Total Knee Replacement

- Effective for severe knee DJD
  – 670K TKA’s in 2012, 900+K in 2015
  – Aggregate charges $36 billion
- Multi-specialty care also effective
  – Exercise, diet, insoles, pain relief
  – AGS step care approach endorsed
- Comparison study needed
RCT Total Knee Replacement

100 Patients mod-to-severe knee osteoarthritis

TKA + 12 weeks non-surgical Rx (PT, nutrition, exercise, education, insoles, pain rx) Vs. 12 weeks non-surgical Rx

Outcome: 4 Knee Injury and Osteoarthritis Outcome Score subscales, covering pain, symptoms, activities of daily living, and QOL (KOOS4)

KOOS improvement:
- Both groups improved
- 32.5 surgery
- 16 non-surgical
- Only 26% crossed over to surgery


NNT 5.7 for 15% improvement

More side effects in surgical group

DVT, deep infection, femur fx, mobilization procedure

Bottom Line: Better outcomes with surgery BUT 70% avoided surgery with intense non-surgical intervention- trial everyone first!

Pre-op pain advice for TKA

Your 80 yo woman decides to go for TKA after only mild relief from intensive non-surgical intervention. She wants to minimize pain medications. What do you advise?

A. Avoid narcotics to prevent addiction
B. General rather than regional anesthesia
C. Go to low volume center to ensure more personalized care
D. Listen to music post-operatively
Last case: Post-op pain relief

- **Meta-analysis of 73 RCTs**
- **Music type, timing, duration variable**
- **Reduced pain, anxiety, analgesic use**
- **Improved patient satisfaction**


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**Final Review**

- **Therapeutics**
  - Restart anticoagulation 7-14 days post UGIB in afib
  - Review needs for PPI frequently and minimize use

- **Imaging**
  - Ultrasound imaging AAA in smokers
  - Endovascular repair outcomes cross over after 3 years

- **Surgery for Knees**
  - No meniscectomy for most mechanical symptoms
  - TKA only after intensive non-surgical intervention
  - Music for post-op pain is good!

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Thanks for your attention!!
**CHADS\textsubscript{2} Prediction Rule**

**AFI, SPAF - 2 large prediction rule trials**
- don’t always agree
- **Framingham** hard to use

C – CHF in last 100 days
H – Hypertension
A – Age >75 Years
D – Diabetes
S\textsubscript{2} – x2 previous Stroke or TIA

<table>
<thead>
<tr>
<th>Score</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1%</td>
</tr>
<tr>
<td>1</td>
<td>2.5%/year (4=8%)</td>
</tr>
<tr>
<td>2</td>
<td>4%</td>
</tr>
<tr>
<td>3</td>
<td>6%</td>
</tr>
<tr>
<td>4</td>
<td>8%</td>
</tr>
<tr>
<td>5</td>
<td>12%</td>
</tr>
<tr>
<td>6</td>
<td>18%</td>
</tr>
</tbody>
</table>

Gage et al. JAMA June 13, 2001

**Match Trial**

**Secondary Prevention: Plavix + Aspirin or Plavix + Placebo**

- **N=7599 followed for 18 months**

- Outcomes: CVA, MI, hospitalization or death
  - Dual Rx. 596/3793 (15.7%)
  - Clopidogrel 636/3802 (16.7%) - no asa alone arm….
  - RRR 6.4% (-4.6-16.3)
  - Significant increase in bleeding on dual therapy

- **Conclusions: Dual Rx no better than clopidogrel alone**
  - VA Neuro- change antiplatelet agent
  - Lancet Vol. 364 July, 2004

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**How to follow a AAA..**

- **Society of Vascular Surgery**
  - U/S annually 3-4cm
  - U/S q6 mos. 4-4.5cm
  - U/S q6 mos. and vascular referral for >4.5 cm

**Patient- 5.8cm AAA on U/S**

Aorta
Rupture

Ann Intern Med. 2005 Feb 1;142(3):203-11