Papers That Changed My Practice: 2014 Edition

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Objectives

• Analyze recent studies regarding rational treatment strategies in patients with gastrointestinal bleeding
• Appraise the recent literature regarding common conditions in both outpatient and inpatient venues (e.g., β blockers in cirrhosis, gallbladder disease)
• Apply recent evidence to the care of patients with abnormal thyroid or ovarian imaging
Disclosures

• None

Disclaimers

• “Nothing I say is always true. There is usually some truth in it.”
  ▪ Mark Reid, MD @medicalaxioms

• "We got the dietary guidelines wrong. They've been wrong for decades."
  ▪ Steve Nissen, MD, 2/11/15
Case 1

• 67 yo man admitted with suspected UGIB
• **PMH**: Afib, stable CAD s/p remote NSTEMI and BMS 2005, HTN.
• **Meds**: warfarin, aspirin 81 mg, metoprolol, amlodipine
• ~6 beers weekly, remote tobacco use, 1-2 BC Powders weekly for headache or back pain
• BP 110/84, HR 98, RR 16, afebrile
• PPI infusion is started (80 mg bolus, then 8 mg/h). Warfarin and aspirin are not continued
• **EGD**: 2 small gastric ulcers, 1 with nonbleeding visible vessel & 1 with adherent clot. Hemostasis achieved with epinephrine injections and endoclips
• What is the next best step?
What is the next best step?

A. Add sucralfate
B. Add octreotide
C. Administer prothrombin complex concentrate
D. Switch to oral PPI BID and discharge patient
E. Switch to IV PPI twice daily
**Background**

- **High-dose IV PPI** (80 mg bolus, then 8 mg/h x 72) is more effective than **placebo** is decreasing rebleeding, surgery and mortality in high-risk PUD after endoscopic therapy
  – Recommended by guidelines
- **Intermittent PPI** is also better than **placebo** in decreasing rebleeding
- PPIs, whether given continuously or intermittently, IV or Oral have **comparable pharmacodynamics** (Freston JW, 2004) and effects on gastric pH
- Previous trials not adequately powered to assess noninferiority of intermittent PPI v continuous
13 RCTs of patients with UBIG due to gastric or duodenal ulcers with high-risk features successfully treated endoscopically and randomized to Continuous versus Intermittent PPI (IV or PO)
- Active bleeding
- Nonbleeding visible vessel
- Adherent clot

1° outcome: rebleeding within 7 days
2° outcomes: rebleeding between days 3-30, need for urgent intervention, mortality, transfusion, and LOS

Noninferiority margin predefined as an absolute risk difference of 3%
In all 1° and 2° outcomes, Intermittent PPIs were non-inferior to Continuous-Infusion PPIs

(In 4/13 trials the intermittent PPI was PO)
Effects of Intravenous and Oral Esomeprazole in the Prevention of Recurrent Bleeding from Peptic Ulcers after Endoscopic Therapy

Joseph J.Y. Sung, MD, PhD; Bing-Yee Suen, RN; Justin C.Y. Wu, MD; James Y.W. Lau, MD; Jessica Y.L. Ching, MPH; Vivian W.Y. Lee, PharmD; Philip W.Y. Chiu, MD; Kelvin K.F. Tsoi, PhD and Francis K.L. Chan, MD

- Single-center RDBPCT comparing standard continuous-infusion PPI to esomeprazole 40 mg PO every 12 h
- High-risk PUD patients (Forrest IA, IB, IIA, IIB)
- 1° outcome: rebleeding within 30 days
  - No difference: 7.7% (IV group) v 6.4% (PO group) (95% CI: −7.7% to 5.1%)
  - No difference in transfusion, repeat EGD, LOS
- But trial underpowered to prove noninferiority (N= 244, needed 406)
Pearl #1

• For patients with endoscopic control of high-risk UGIB, intermittent PPI twice daily is non-inferior to continuous-infusion PPI
Back to our case…

• Patient is anxious about his stroke risk while being off warfarin
  • Should anticoagulation be restarted?
  • If so, when?
  • How about the aspirin?
You Recommend:

A. Resume warfarin after 1 week
B. Resume warfarin and aspirin after 1 week
C. Resume warfarin in 4 weeks
D. Resume warfarin and aspirin in 4 weeks
E. Start dabigatran in 2 weeks
• Retrospective cohort study (Henry Ford)
• 1329 patients with GIB (upper and/or lower) on warfarin for nonvalvular AF between 2005-2010
  – Mean age 76, women 45%
  – Median CHADS2 and HAS-BLED scores = 3
• **GIB**: 2 gm drop in Hgb (or transfused 2 U), visible bleeding (clinically or endoscopically)
• **Outcomes**: recurrent GIB, thromboembolism (VTE, arterial, stroke/TIA), mortality

Am J Cardiol 2014;113:662–668
Main Results

- Warfarin restarted in 49% (different start times)
  - No increase in recurrent GIB, **unless restarted before day 7**
  - No difference in CHADS2 and HAS-BLED scores between groups
  - For those who restarted warfarin:

<table>
<thead>
<tr>
<th>Outcome</th>
<th>HR</th>
<th>95% CI</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thromboembolism</td>
<td>0.71</td>
<td>0.54-0.93</td>
<td>0.01</td>
</tr>
<tr>
<td>Mortality</td>
<td>0.67</td>
<td>0.56-0.81</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Recurrent GIB</td>
<td>1.18</td>
<td>0.94-1.10</td>
<td>0.47</td>
</tr>
</tbody>
</table>
Freedom from Recurrent Gastrointestinal Bleeding

- <7 days
- 7 - 15 days
- 16 - 21 days
- 22 - 30 days
- >30 days
- Not restarted

Time (days)
Another Pearl

• For patients who experience UGIB while anticoagulated, anticoagulation should generally be resumed within 1 week.
Case 2

• 71 yo white male with systolic HF (EF 30%) and severe COPD (FEV1 40%) presents for follow-up. Three hospitalizations for HF in past 18 months; none for COPD. Doing reasonably well, although daily activities are limited by breathlessness. Denies lightheadedness

• **Meds**: lisinopril 20 mg, carvedilol 12.5 mg BID, spironolactone 25 mg, digoxin 250 mcg, bumetanide 1 mg, tiotropium daily, fluticasone 250/salmeterol 50 BID, albuterol PRN

• BP 110/74, HR 70, RR 20

• No JVD or S3. Biventricular-ICD site looks good. Trace edema. Poor air entry with mild scattered wheezes (unchanged).

• What is the next best step?
What is the best next step?

A. Check BNP
B. Repeat PFTs
C. Increase lisinopril to 30 mg
D. Add hydralazine and isosorbide dinitrate TID
E. Continue present management
Effect of B-type natriuretic peptide-guided treatment of chronic heart failure on total mortality and hospitalization: an individual patient meta-analysis

Richard W. Troughton¹*, Christopher M. Frampton¹, Hans-Peter Brunner-La Rocca⁴, Matthias Pfisterer³, Luc W.M. Eurlings⁴, Hans Erntell⁵, Hans Persson⁵, Christopher M. O’Connor⁶, Deddo Moertl⁸, Patric Karlström⁹, Ulf Dahlström¹⁰, Hanna K. Gaggin¹¹, James L. Januzzi¹¹, Rudolf Berger⁷, A. Mark Richards¹,², Yigal M. Pinto¹², and M. Gary Nicholls¹

- B-type natriuretic peptides provide an objective index of circulatory status
- Evidence-based target doses of proven medications are often not achieved
- Previous BNP-guided trials small and not powered to assess all-cause mortality
- ACC/AHA, ESC and NICE currently state that evidence is insufficient to support routine BNP-guided care over conventional care
BNP-guided HF Treatment

- Meta-analysis of 9 trials with individual patient data
  - N=2000 (1006 BNP-guided, 994 clinically-guided)
  - BNP or NT-proBNP ("BNP")
  - Different BNP targets
- 1° outcome: all-cause mortality
- 2° outcomes: HF hospitalizations, cardiovascular hospitalizations, all-cause hospitalizations
- Average age 72, two-thirds men, 90% had EF <45
BNP-guided HF Treatment

- ACEI/ARB, BB, MRA, loop doses similar at baseline
- At end, ACEI dose increased 8.4% in BNP-guided patients v. decreased 1.2% in clinically-guided patients (P=0.007)
- BB increased in both groups (12.6% and 13.4%, P=NS)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>BNP-guided (%)</th>
<th>Clinically-guided (%)</th>
<th>HR</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All-cause mortality</td>
<td>17.1</td>
<td>20.8</td>
<td>0.62 (CI0.45-0.86)</td>
<td>0.004</td>
</tr>
<tr>
<td>HF hospitalization</td>
<td>24.6</td>
<td>29.5</td>
<td>0.80 (0.67-0.94)</td>
<td>0.009</td>
</tr>
<tr>
<td>CV hospitalization</td>
<td>42.7</td>
<td>44.6</td>
<td>0.82 (0.67--.99)</td>
<td>0.048</td>
</tr>
</tbody>
</table>
Pearl #2

- For systolic HF patients aged <75 years, BNP-guided treatment reduces all-cause mortality compared with clinically guided therapy. This strategy also reduces hospitalizations for heart failure and cardiovascular disorders, irrespective of age.
Case 3

- 69 yo woman with severe COPD (FEV1 32% in 2010) is hospitalized with COPD exacerbation. Rapid influenza is negative. She requires NIPPV and in admitted to the ICU.
- **PMH**: osteoporosis, remote fungal infection (RUL)
- **Meds**: tiotropium, fluticasone 220 mcg INH BID, cetirizine, alendronate, vitamin D3
- **BP** 164/82, **HR** 130 (sinus), **RR** 36, **T** 99.1°
- Marked bilateral wheezes with poor air entry and markedly prolonged expiratory phase
- **WBC** 6700/µL
- **CXR**: no new infiltrate, old RUL scarring
In addition to ceftriaxone, azithromycin and bronchodilators, you should order

A. Methylprednisolone 40 mg every 12 h
B. Methylprednisolone 60 mg every 6 h
C. Methylprednisolone 125 mg every 6 h
D. Hydrocortisone 50 mg every 6 h
Lower doses and shorter courses (e.g. prednisone 40 mg x 5 d) of steroids improve outcomes and decrease adverse effects in non-ICU AECOPD patients. There is a paucity of data to guide treatment in AECOPD patients in the ICU, though many use very high doses. This strategy might expose patients to greater risks of adverse effects without additional clinical benefit.
Lower-dose steroids for AECOPD in the ICU

- Observational pharmacoepidemiologic cohort study
  - 32% NIPPV, 15% invasive ventilation day 1 or 2
  - 77% >age 60, 46% male, 31% active smokers
- Attending physician
  - IM/Hospitalist (56%)
  - Family medicine (19%)
  - Pulmonary medicine (16%)
- High dose (>240 mg methylprednisolone): 64%
Steroid Conversions

http://www.globalrph.com/corticocalc.htm

• **Average lower-dose/day** (day 1-2)
  – Methylprednisolone 96 mg
  – Equiv to prednisone 120

• **Average high-dose/day** (day 1-2)
  – Methylprednisolone 312
  – Equiv to prednisone 390

• Methylprednisolone 500 = hydrocortisone 2500
# Lower-Dose Steroids for AECOPD in the ICU

## Inclusion Criteria
- Principal dx AECOPD
- >40 years old
- Steroids given
- No admission in previous 30 days
- Admitted to ICU on day 1 or 2

## Exclusion Criteria
- Pulmonary embolism
- Pneumothorax
- Pneumonia
- Solid organ transplant
- Vasopressors day 1 or 2
Main Results

After propensity score matching and adjustment for unbalanced covariates, lower-dose steroid group associated with trend toward ↓ mortality (OR 0.85 [0.71-1.01]; P=0.06)

<table>
<thead>
<tr>
<th>Outcomes in the LOWER-DOSE group</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>↓ Hospital LOS</td>
<td>-0.44 d (-0.67 to -0.21)</td>
</tr>
<tr>
<td>↓ ICU LOS</td>
<td>-0.31 d (-0.46 to -0.16)</td>
</tr>
<tr>
<td>↓ Hospital cost</td>
<td>-$2,559 (-$4,508 to -$609)</td>
</tr>
<tr>
<td>↓ Length of invasive ventilation</td>
<td>-0.29 (-0.52 to -0.06)</td>
</tr>
<tr>
<td>↓ Need for insulin</td>
<td>22.7% v. 25.1%</td>
</tr>
<tr>
<td>↓ Fungal infections</td>
<td>3.3% v. 4.4%</td>
</tr>
</tbody>
</table>
Do steroids help AECOPD (as opposed to asthma)?

- **RCT, N=271, 25 VAMC**
  - 80 – steroids x 8 weeks
  - 80 – steroids x 2 weeks
  - 111 – placebo

- Steroid dose: *methylprednisolone* 125 mg Q 6° x 72 hr, then taper
Niewoehner, et al

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Steroids (both)</th>
<th>Placebo</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment failure at 30 d</td>
<td>23%</td>
<td>33%</td>
<td>0.04</td>
</tr>
<tr>
<td>Treatment failure at 90 d</td>
<td>37%</td>
<td>48%</td>
<td>0.04</td>
</tr>
<tr>
<td>LOS</td>
<td>8.5 d</td>
<td>9.7d</td>
<td>0.03</td>
</tr>
<tr>
<td>Hyperglycemia requiring Rx</td>
<td>15%</td>
<td>4%</td>
<td>0.002</td>
</tr>
</tbody>
</table>

- No difference between the 2 steroid groups at any time
Pearl #3

• Treating patients admitted to the ICU with AECOPD with lower doses of steroids (e.g., <100 mg methylprednisolone) is associated with improved clinical outcomes, decreased steroid-related side effects, and a trend toward a reduction in mortality.
• The optimal dose, route, or duration steroids is not known.
Case 4

- 57 yo woman presents with the onset of 8/10 central and RUQ abdominal pain. No similar symptoms in past. No NSAIDS. Rare alcohol.

- BP 146/80, HR 94, RR 18, T 101.0. Predominantly RUQ pain. Murphy sign present without mass. No jaundice.

- WBC 14,000, AST 160, ALT 150, bilirubin 1.6, lipase 74

- Ultrasound confirms gallstones, gallbladder wall thickening (7 mm), and perivesicular fluid. CBD 7 mm – no stone seen
In addition to bowel rest, IVF, analgesia and ceftriaxone, you recommend

A. Consult gastroenterology for endoscopic ultrasound (EUS) assessment of the CBD
B. Consult gastroenterology for ERCP to assess and clear the CBD
C. Order MRCP to assess the CBD
D. Consult general surgery to proceed directly to OR
CBD stones often pass, but present in
- 5-10% of patients with symptomatic cholelithiasis
- 18-33% of patients with clinical biliary pancreatitis

What is the best strategy for patients at intermediate risk of a retained stone?
Choledocholithiasis

- **LFTs**
  - If normal, NPV for CBD stones is 97%
  - Any abnormality, PPV 15%
  - Bili >1.6 (specificity 60%)
  - Bili >4 (specificity 75%)

<table>
<thead>
<tr>
<th>Image</th>
<th>Sensitivity for CBD stones (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdo US</td>
<td>22 – 55 (sensitivity for CBD dilation 77 – 87)</td>
</tr>
<tr>
<td>CT (helical)</td>
<td>65 – 88</td>
</tr>
<tr>
<td>MRCP</td>
<td>85 – 92 (33 – 71 for small stones &lt;6 mm)</td>
</tr>
<tr>
<td>Endoscopic US (EUS)</td>
<td>90 – 95 (including small stones)</td>
</tr>
<tr>
<td>ERCP</td>
<td>90 – 93 (more adverse events)</td>
</tr>
<tr>
<td>IOC</td>
<td>59 – 100 (~15 minutes)</td>
</tr>
</tbody>
</table>
Risk of Choledocholithiasis

**Low (<10%)**
- No jaundice
- Normal CBD on US

**Intermediate (10%-50%)**
- Elevated LFTs other than Bilirubin
- Age >55
- Clinical biliary pancreatitis

**High (>50%)**
- Visualized CBD stone
- Cholangitis
- Bilirubin >4
- Bili >1.7 + CBD >6 mm

Lap Chole (± IOC) → ??? → ERCP

Iranmanesh, et al

- N=100, single institution in Switzerland
  - 50 – lap chole + IOC $\rightarrow$ ERCP if needed
  - 50 – preop EUS $\pm$ ERCP $\rightarrow$ lap chole
  - Women 2:1, Age $\sim$47, $\sim$45% had acute cholecystitis, AST & ALT $\sim$150 U/L

- **1° outcome**: LOS
- **2° outcomes**
  - # of CBD studies (EUS, ERCP, MRCP)
  - QOL at 1 and 6 months
Methods

Inclusion Criteria

• Age ≥16 years
• Presentation through the ED
• Clinical suspicion of choledocholithiasis
  – Sudden RUQ pain, epigastric pain or both
  – **AST or ALT >2 X ULN**
  – Presence of a gallstone on an ultrasound (performed by Radiology)
• **With or without associated acute cholecystitis**
  – Fever
  – Murphy sign
  – GBWT >4 mm, striated gallbladder wall, perivesicular fluid

Exclusion Criteria

• Severe sepsis and septic shock
• Radiologically proven CBD stone
• Bilirubin >4 mg/dL
• Alternative diagnosis (e.g., acute hepatitis)
• Medical conditions precluding surgery or MRCP (e.g., pacemaker), previous cholecystectomy, etc.
• **Pancreatitis (although this usually makes one intermediate risk)**
Main Results

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Lap chole + IOC</th>
<th>Preop Assessment</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LOS</td>
<td>5 d</td>
<td>8 d</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CBD studies</td>
<td>25</td>
<td>71</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Confirmed CBD stone</td>
<td>22%</td>
<td>20%</td>
<td>0.81</td>
</tr>
</tbody>
</table>

- No differences in morbidity, mortality or QOL
- In lap chole group, 60% did not need any additional studies
Pearl #4

- Among patients at intermediate risk of choledocholithiasis, initial laparoscopic cholecystectomy with IOC, compared with preoperative CBD assessment and subsequent surgery, results in a shorter length of stay and fewer CBD studies.
Back to our patient…

- BP 146/80, HR 94, RR 18, **T 101.0**. Predominantly RUQ pain. **Murphy sign** present. No jaundice.
- **WBC 14,000**, AST 160, ALT 150, bilirubin 1.6, lipase 54
- **Ultrasound confirms gallstones, gallbladder wall thickening** (6 mm), and **perivesicular** fluid. A common duct stone or dilatation is not seen
- She did well with laparoscopic cholecystectomy. The IOC was negative for CBD stones. She has had return of bowel function and is tolerating PO. She desires discharge to home as soon as feasible
You recommend:

A. Continue ceftriaxone for 72 hours post-op, then discharge
B. Discharge on amoxicillin-clavulanate for 5 days
C. Discharge without additional antibiotics
Cholecystitis: Background

• 150,000 cholecystectomies each year (U.S) for calculous cholecystitis
  – 90% are mild-moderate
  – Bile culture are positive in 40% - 60%
• Postop antibiotics are very often given (~85%) to reduce subsequent infections despite a dearth of evidence for this practice
• Avoiding unnecessary antibiotics is desirable
Very little data

**Grade I:** stop within 24 hours of surgery

**Grade II-III:** generally continue for 4-7 days after surgery

*Enterococcal* coverage **not** required for community-acquired infections and *anaerobic* coverage **not** recommend unless biliary-enteric anastamosis present
Regimbeau, et al.

• N=414, 17 centers (2010-2012)
• Open-label, randomized, noninferiority trial of mild-moderate cholecystitis
• Amoxicillin-clavulanate (IV or PO) before and during surgery
  – Group 1: Stop antibiotics post-op
  – Group 2: Continue amox-clav TID x 5 days post-op
• 1° outcome: surgical site and other infections within 4 weeks
• Average age 55, 49% men
• Laparoscopic 85%, conversion rate <10%
Methods

Inclusion Criteria
• ≥18 yo
• **Acute calculous chole**
  – Murphy sign or RUQ pain
  – T >38°C, CRP >5 mg/L or WBC >10,000
  – Typical US findings
• **Mild-moderate**
  – Tokyo Guidelines

Exclusion Criteria
• Acalculous
• **Severe** (grade III)
• **Duration** >5 days
• Cholangitis
• Biliary peritonitis
• Acute pancreatitis
• CBD stones discovered at surgery
• Cirrhosis
• Biliary cancer
• Pregnant, breast-feeding
TG13 diagnostic criteria and severity grading of acute cholecystitis (with videos)

**Moderate (Grade II) [any one]**
- WBC >18,000
- Palpable tender RUQ mass
- Duration of complaints >72 h
- **Marked** local inflammation
  - Gangrenous
  - Emphysematous
  - Pericholecystic abscess
  - Hepatic abscess
  - Biliary peritonitis

**Severe (Grade III) [any one]**
- CV: hypotension requiring pressors
- **Neuro**: ↓ LOC
- **Resp**: PaO2/FiO2 <300
- **Renal**: Cr >2.0 or oliguria
- **Hepatic**: INR >1.5
- **Heme**: Plt <100,000

**Mild (Grade I)**
- No organ dysfunction
- **Mild** inflammatory GB changes
Main Results

Infections by Week 4

<table>
<thead>
<tr>
<th></th>
<th>No ABX (%)</th>
<th>ABX (%)</th>
<th>Absolute difference (%)</th>
<th>95% CI</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ITT</td>
<td>17</td>
<td>15</td>
<td>1.93</td>
<td>-9.0 to 5.1</td>
<td>0.007</td>
</tr>
<tr>
<td>Per Protocol</td>
<td>13</td>
<td>13</td>
<td>0.3</td>
<td>-5.0 to 6.3</td>
<td>0.001</td>
</tr>
<tr>
<td>ITT (Grade I)</td>
<td>15</td>
<td>13</td>
<td>1.16</td>
<td>-8.5 to 10.8</td>
<td>0.03</td>
</tr>
<tr>
<td>PP (Grade I)</td>
<td>12</td>
<td>11</td>
<td>1.36</td>
<td>-7.6 to 10.3</td>
<td>0.02</td>
</tr>
<tr>
<td>ITT (Grade II)</td>
<td>19</td>
<td>16</td>
<td>2.78</td>
<td>-7.4 to 13.1</td>
<td>0.04</td>
</tr>
<tr>
<td>PP (Grade II)</td>
<td>17</td>
<td>16</td>
<td>1.24</td>
<td>-8.8 to 11.2</td>
<td>0.03</td>
</tr>
</tbody>
</table>

- No difference in infections (above), LOS or readmissions
- 61% of bile culture were sterile (c/w earlier studies)
Another Pearl

• Among patients with mild or moderate calculous cholecystitis who receive preoperative and intraoperative antibiotics, postoperative antibiotics do not appear to be helpful.
Case 5

- 52 yo man with hx of cirrhosis due to alcoholism and HCV presents with increasing encephalopathy and ascites
- **PMH**: varices without hemorrhage
- **Meds**: furosemide 80 mg, spironolactone 200 mg and propranolol 80 mg daily
- **BP** 102/66 (MAP 78), **HR** 66, **T** 99.5°F
- Confused, stigmata of chronic liver disease, asterixis present, mild diffuse abdo pain with obvious ascites
- **Creatinine** 1.5 mg/dL (baseline 0.6), **ammonia** 102, ascites WBC 752 (68% PMN) [**ANC 435**]
Which of the following is the least appropriate

A. Continue propranolol
B. Start ceftriaxone 2 gm daily
C. Administer albumin 1.5 g/kg
D. Start lactulose and rifaximin
E. Hold furosemide and spironolactone
Background

- Non-specific β blockers (NSBB) are well-established for the 1° and 2° prevention of variceal hemorrhage
- But, NSBB are ineffective in EARLY cirrhosis
  - Increase adverse events
  - Do not prevent the development of varices
  - No effect on survival,
- And recent studies demonstrate ↓ survival in patients with ADVANCED cirrhosis with refractory ascites (RA) treated with NSBB
- Original NSBB studies (Lebrec 1981) specifically excluded patients with ascites
- Effect of NSBB in patients w/ ascites only recently studies (Serste 2010)
Nonselective β Blockers Increase Risk for Hepatorenal Syndrome and Death in Patients With Cirrhosis and Spontaneous Bacterial Peritonitis

Mattias Mandorfer,1,2 Simona Bota,1,2 Philipp Schwabl,1,2 Theresa Bucsics,1,2 Nikolaus Pfisterer,1,2 Matthias Kruzik,1,2 Michael Hagmann,3 Alexander Blacky,4 Arnulf Ferlitsch,1,2 Wolfgang Sieghart,1,2 Michael Trauner,1,2 Markus Peck-Radosavljevic,1,2 and Thomas Reiberger1,2

Gastroenterology 2014;146:1680–1690

• Retrospective cohort study of 607 patients with cirrhosis
  – 182 developed SBP
• Statistical models adjusted for Child–Pugh stage and presence of varices
Main Results

- NSBB associated with ↑ transplant-free survival ↓ hospitalization in patients WITHOUT SBP

- However, with the first diagnosis of SBP, NSBB were associated with
  - Reduced transplant-free survival
  - Increased hospitalizations
  - Increased HRS and AKI
Figure 3. Influence of NSBB treatment on transplant-free survival after the first SBP diagnosis.
Figure 4. Influence of NSBB treatment on HRS and grade C AKI development within 90 days after the first SBP diagnosis.
## MAP is Critical in Cirrhosis

<table>
<thead>
<tr>
<th>Survival</th>
<th>MAP $\leq 82$ mm Hg</th>
<th>MAP $&gt;82$ mm Hg</th>
</tr>
</thead>
<tbody>
<tr>
<td>24 months</td>
<td>20%</td>
<td>70%</td>
</tr>
<tr>
<td>48 months</td>
<td>0</td>
<td>50%</td>
</tr>
</tbody>
</table>

Early cirrhosis

- Beta-blockers are not indicated in early cirrhosis, may increase adverse events
- Beta-blockers may be indicated for cardiovascular indications

Window opens

- Beta-blockers are indicated for primary prophylaxis of variceal bleeding
- Beta-blockers are indicated for secondary prophylaxis of variceal bleeding

Window closes

- Beta-blockers are contraindicated under the following situations:
  - Refractory ascites
  - Systolic blood pressure < 100mm Hg
  - Mean arterial pressure < 82mm Hg
  - Acute kidney injury
  - Hepatorenal syndrome
  - Spontaneous bacterial peritonitis
  - Sepsis
  - Poor medical follow-up
  - Patient noncompliance

Window does not re-open

Ge PS and Runyon BA. *Gastroenterology* 2014;146(7);1597-9
Pearl #5

- NSBB appear to have a detrimental effect after the development of SBP.
- SBP is likely a critical clinical event that “closes the therapeutic window” for NSBB treatment.
Summary: The Best of 2014

- Intermittent PPI are effective for high-risk UGIB
- Restart warfarin within 7 days after UGIB
- Metoclopramide works well for migraines
- Adding niacin-ER to a statin increases adverse effects without clinical benefits
- US follow-up of nondiagnostic thyroid FNA and small adnexal masses is rational
- BNPs can optimize management of chronic HF
- Avoid high-dose steroids for AECOPD in the ICU
- Patients at moderate risk for CBD stones can go straight to the OR
- Stop β-blockers in cirrhotics with h/o SBP, refractory ascites, MAP <82