Top 10 Articles of 2015
Turning Evidence into Practice

Mel L. Anderson, MD, FACP
Associate Professor of Medicine
University of Colorado School of Medicine

Chief, Hospital Medicine Section
Denver VA Medical Center
Disclosures

- None relevant
Learning Objectives

1. *Describe* the primary conclusions
2. *Identify* changes to your practice
3. *Implement* these practice changes
Roadmap

- Case based interactive format
- Multiple articles per case
- Quick hitters and Short takes
- Summary of suggested practice changes
Journals Reviewed...

Jan 2015 – Dec 2015

- N Engl J Med
- JAMA; JAMA Intern Med
- J Gen Intern Med
- J Hospit Med, PLoS Medicine
- Lancet; Stroke; Ann Emerg Med
- Am J Med; Am Heart J; Am J Cardiol
- Ann Intern Med + ACP J Club
- Crit Care Med; Am J Respir Crit Care Med
- Circulation, J Am Coll Cardiol
- ACP Plus, BMJ Online update, J Watch
Acknowledgements

- Jeffrey J. Glasheen, MD
  University of Colorado School of Medicine
- Joseph Li, MD
  Harvard Medical School
- Anneliese Schleyer, MD
  University of Washington
- Brad Sharpe, MD
  UCSF School of Medicine
2015 Notables

Recommendation on the Nomenclature for Oral Anticoagulants: communication from the SSC of the ISTH

“NOAC” →
“TSOAC” →
“DOAC”

2015 Notables

Cardiovascular and Cerebrovascular Effects in Response to Red Bull Consumption Combined With Mental Stress

Erik Konrad Grasser, PhD, MD, BSEE*, Abdul G. Dulloo, PhD, and Jean-Pierre Montani, MD

2015 Notables

Cardiovascular and Cerebrovascular Effects in Response to Red Bull Consumption Combined With Mental Stress

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2015 Notables

Special Communication | LESS IS MORE
Update on Medical Practices That Should Be Questioned in 2015

Daniel J. Morgan, MD, MS; Sanket S. Dhruva, MD; Scott M. Wright, MD; Deborah Korenstein, MD

Inadequacies of Physical Examination as a Cause of Medical Errors and Adverse Events: A Collection of Vignettes

Abraham Verghese, MD, Blake Charlton, MD, Jerome P. Kassirer, MD, Meghan Ramsey, MD, John P.A. Ioannidis, MD, DSc

CLINICAL SIGNIFICANCE
- Most errors in the physical examination that lead to consequences are related to not performing an examination.
- Failure to undress the patient and examine the skin is a frequent cause of error.
- In a patient with abdominal pain, failure to examine the groin, rectal area, and hernia orifices can have dire consequences.

Case 1

A 67 y/o man presents 3 hours after the sudden onset of R arm and leg weakness and difficulty speaking.

BP 160/95, alert/oriented w/ expressive aphasia and 3/5 R sided strength, NIHSS score of 12

STAT CT scan of the brain is normal. The ER prepares to begin IV rt-PA...
Acute Ischemic Stroke

1. Ensure aspirin is also administered asap
2. Perform transcranial ultrasound
3. Order stat CT angiography
4. Curse the cruel fates in iambic pentameter…
A Randomized Trial of Intraarterial Treatment for Acute Ischemic Stroke


MR CLEAN

Question: Effect of intra-arterial treatment on functional outcomes with acute stroke?

Design: Single blind RCT

Patients: 500 patients, anterior stroke, < 6 hours

1° Outcome: Modified Rankin score < 2 at 90 days, i.e. functionally independent

## MR CLEAN: Results

<table>
<thead>
<tr>
<th></th>
<th>UC</th>
<th>Interv.</th>
<th>OR (95% CI)</th>
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<tbody>
<tr>
<td>Primary Endpoint</td>
<td></td>
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<td>Death/bleeding</td>
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*No difference*

Question: Effect of intra-arterial treatment on functional outcomes with acute stroke?

Design: Single blind RCT

Patients: 500 patients, anterior stroke, < 6 hours

1° Outcome: Modified Rankin score < 2 at 90 days, i.e. functionally independent

Conclusion: Intra-arterial treatment, when added to thrombolytic, is safe and effective for acute anterior stroke

Endovascular Therapy for Ischemic Stroke with Perfusion-Imaging Selection


3/12/2015

Randomized Assessment of Rapid Endovascular Treatment of Ischemic Stroke


3/12/2015

The NEW ENGLAND JOURNAL of MEDICINE

Stent-Retriever Thrombectomy after Intravenous t-PA vs. t-PA Alone in Stroke


6/11/2015

Thrombectomy within 8 Hours after Symptom Onset in Ischemic Stroke


6/11/2015

## Stroke Trials Summary

<table>
<thead>
<tr>
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Meta Analyses x 3

Original Investigation
Endovascular Thrombectomy for Acute Ischemic Stroke
A Meta-analysis

*JAMA* 2015;314:1832-1843.

Original Investigation
Mechanical Thrombectomy for Acute Ischemic Stroke
A Meta-Analysis of Randomized Trials

Meta Analyses x 3

Endovascular Thrombectomy for Anterior Circulation Stroke
Systematic Review and Meta-Analysis

Chester K. Yarbrough, MD, MPH*; Charlene J. Ong, MD*; Alexander B. Beyer, MD, MPH*
Kim Lipsey, MLS; Colin P. Derdeyn, MD

Endovascular Therapy for Stroke — It’s about Time

Anthony J. Furlan, M.D.

Now, even skeptics of endovascular therapy will be convinced. The real winners are our patients with devastating strokes. Endovascular equipoise no longer exists. It’s about time.

6/11/2015

Acute Ischemic Stroke

A. Ensure aspirin is also administered asap
B. Perform transcranial ultrasound
C. Order stat CT angiography
D. Curse the cruel fates in iambic pentameter!
Between 4 and 14 days was the optimal time to start anticoagulation in acute cardio-embolic stroke. *Stroke* 2015;46:2175-2182.

Bloodcurdling movies and measures of coagulation: Fear Factor crossover trial

Banne Nemeth medical doctor, Luuk J J Scheres medical doctor, Willem M Lijfering postdoctoral researcher, Frits R Rosendaal professor of clinical epidemiology

BMJ 2015;351:h6367.
63 y/o woman presents for well pt appt. HTN, tobacco/COPD, HLP, stable claudication. Meds: thiazide, inhalers BP 136/92, HR 78, PVD findings. Creat 1.3 mg/dL With respect to her blood pressure…
Do you...

1. Add an alpha blocker 25%
2. Keep regimen unchanged: at goal 25%
3. Add an ACEI 25%
4. Wonder why you didn’t sleep at the Holiday Inn Express 25%

0 / 0 30 Cross-tab label
A Randomized Trial of Intensive versus Standard Blood-Pressure Control

The SPRINT Research Group*
SPRINT

Question: What is the benefit of SBP target < 120 mm Hg vs. < 140 mm Hg

Design: Multicenter RCT, open label

Patients: 9361 patients. Age 50+, no DM or stroke
Other CV dz; CKD; Framingham 15%; 75 y/o

1° Outcome: Composite of MI/ACS, stroke, heart failure, or death from CV causes

<table>
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<tr>
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<td>2.8</td>
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<tr>
<td>1° Endpoint</td>
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<tr>
<td>1° Endpoint</td>
<td>6.8%</td>
<td>5.2%</td>
<td>61</td>
<td>&lt;0.001</td>
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<tr>
<td>Death</td>
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SPRINT @ 3.26 years

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<tr>
<td>Death</td>
<td>4.5%</td>
<td>3.3%</td>
<td>90</td>
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## SPRINT Adverse Events

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<td>0.25</td>
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<tr>
<td><strong>Sx ortho hypo</strong></td>
<td>1.5%</td>
<td>1.3%</td>
<td>--</td>
<td>0.35</td>
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SPRINT

Question: What is the benefit of SBP target < 120 mm Hg vs. < 140 mm Hg

Design: Multicenter RCT, open label

Patients: 9361 patients. Age 50+, no DM or stroke
Other CV dz; CKD; Framingham 15%; 75 y/o

1° Outcome: Composite of MI/ACS, stroke, heart failure, or death from CV causes

Conclusion: Targeting SBP < 120 mm Hg lowers major CV events and death from all causes, but with increased adverse events

Do you...

A. Add an alpha blocker
B. Keep regimen unchanged: at goal
C. Add an ACEI
D. Wonder why you didn’t sleep at a Holiday Inn Express

VA Diabetes Trial at 10 years: intensive control associated with reduced macrovascular events (8.6 major events per 1000 person-years) N Engl J Med 2015;372:2197-206.
Search for humorous and extravagant acronyms and thoroughly inappropriate names for important clinical trials (SCIENTIFIC): qualitative and quantitative systematic study

Positive criteria

BEAUTY—Boosting Elegant Acronyms Using a Tally Yardstick

Negative criteria

CHEATING—obSCure and awkHward use of lettArs Trying to spell somethING
Case 3 Curbside

67 y/o woman with DVT and PE diagnosed 3 months ago following hip surgery, now needs lap chole for worsening biliary colic

Admission is planned for next week on Thursday

Anticoagulation clinic on vacation…
What do you recommend?

A. Continue warfarin without cessation
B. Stop warfarin and bridge with LMWH
C. Stop warfarin and bridge with IVUFH
D. Stop warfarin and don’t bridge
E. Facebook stalk pharmacist
What do you recommend?

1. Continue warfarin without cessation 20%
2. Stop warfarin and bridge with LMWH 20%
3. Stop warfarin and bridge with IVUFH 20%
4. Stop warfarin and don’t bridge 20%
5. Facebook stalk pharmacist 20%

0 / 0
Perioperative Bridging Anticoagulation in Patients with Atrial Fibrillation


Question: Is heparin bridging needed?

Design: Double blind placebo-controlled non-inferiority RCT of LMWH 3 days prior and 5-10 days after procedure. Warfarin held 5 d prior, started within 24 hours post-op

Patients: 1884 patients, CHADS$_2$ $\geq$ 1, avg. 2.3; nearly 40% were 3 or higher

1° Outcome: Thromboembolism and major bleeding

<table>
<thead>
<tr>
<th>Condition</th>
<th>Plac.</th>
<th>LMWH</th>
<th>NNH</th>
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<tr>
<td>Arterial emb.</td>
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<td></td>
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</tr>
<tr>
<td>Major bleed</td>
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</tr>
<tr>
<td>Arterial emb.</td>
<td>0.4%</td>
<td>0.3%</td>
<td>n/a</td>
<td>0.01*</td>
</tr>
<tr>
<td>Major bleed</td>
<td></td>
<td></td>
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* P value for non-inferiority
# BRIDGE Results

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<td>Arterial emb.</td>
<td>0.4%</td>
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<td>n/a</td>
<td>0.01*</td>
</tr>
<tr>
<td>Major bleed</td>
<td>1.3%</td>
<td>3.2%</td>
<td>52</td>
<td>0.005**</td>
</tr>
<tr>
<td>Minor bleed</td>
<td></td>
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* P value for non-inferiority, ** P value for superiority
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<td>0.005**</td>
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<td>Minor bleed</td>
<td>12.0%</td>
<td>20.9%</td>
<td>11</td>
<td>&lt;0.001**</td>
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* P value for non-inferiority, ** P value for superiority
Question: Is heparin bridging needed?

Design: Double blind placebo-controlled non-inferiority RCT of LMWH 3 days prior and 5-10 days after procedure. Warfarin held 5 d prior, started within 24 hours post-op

Patients: 1884 patients, CHADS$_2$ $\geq$ 1, avg. 2.3; nearly 40% were 3 or higher

1° Outcome: Thromboembolism and major bleeding

Conclusion: Forgoing bridging anticoagulation was non-inferior to bridging and decreased bleeding

Retrospective cohort 1178 patients
20% were intermediate / high risk: VTE in last year, multiple prior VTE, genetic abnl, APL, active cancer
## Kaiser Bridging Results

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<td><strong>VTE</strong></td>
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<td>0.0%</td>
<td>n/a</td>
<td>NS</td>
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<tr>
<td><strong>Clinical bleed</strong></td>
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<tr>
<td><strong>30 d M</strong></td>
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Registry of AF patients having procedures, n=7372
25% were bridged, CHA$_2$DS$_2$-VASc not different
MI / major bleed / stroke / death higher, 13% versus 6.3%, $p=0.0001$

_Circulation_ 2015;131:488-494.
What do you recommend?

A. Continue warfarin without cessation
B. Stop warfarin and bridge with LMWH
C. Stop warfarin and bridge with IVUFH
D. Stop warfarin and don’t bridge
E. Facebook stalk pharmacist
VTE Short Takes

Reversing VKA anticoagulation with 4F-PCC is more effective than FFP. *Lancet* 2015;385:2077-87.


PREPIC2: RCT of IVC filter for 3 months in 400 acute PE patients, all anticoagulated. 6/6 fatal PE in filter group, 2/3 fatal PE in no filter. *N Engl J Med* 2015;372:825-34.
Wells score for DVT performs only slightly better than chance in the inpatient setting – be not reassured. *JAMA Intern Med* 2015;175:1112-1117.

Misc. Quick Hitter:

2 x 2 RCT of ETOH Hepatitis in 1103 patients.
Pentoxifylline of no benefit
Prednisolone lowered 28d M but p=0.06

RCT of 413 patients with SVT, standard vs. modified Valsalva: 40 mm Hg 15s strain, then supine w/ passive leg raise (both semi-recumbent to start) NSR increased from 17% to 43%
PCV 13 (Prevnar) was effective in preventing vaccine type CAP (whether invasive or not), but not all cause CAP. *N Engl J Med* 2015;372:1114-25.

In 2011 there were half a million *C difficile* infections in the U.S., and 29,000 deaths. *N Engl J Med* 2015;372:825-34.

**DELIRIA-J:** Ramelteon (melatonin) reduced the risk of delirium in hospitalized elders. *JAMA Psychiatry* 2015;71:397-403.

Practice Summary

Things to Do:

1. Check out Verghese article on inadequacies of physical exam.
2. Obtain CT and CTA in acute stroke and refer for neuro-interventional care.
3. Wait about a week (4-14 days) to anticoagulate after cardio-embolic stroke.
4. Target SBP < 120 mm Hg in SPRINT patients
Practice Summary

Things to Do:

5. Remember spironolactone in resistant HTN
6. Use 4F-PCC over FFP to reverse VKA associated bleeding if time is of the essence.
7. Modified Valsalva manoeuvre for SVT.
8. Give PCV-13 (Prevnar) to eligible patients.
Practice Summary

Things to Consider:

1. Stopping statins in Palliative Care patients.
2. Ramelteon (melatonin) in hospitalized elders as part of delirium prevention package.
Things Not To Do:

1. Bridging anticoagulation except in very high risk patients...
2. Wells score in inpatients to guide decision-making.
3. CT scan for occult ca in idiopathic VTE.
4. Pentoxifylline for ETOH hepatitis.
5. TMP/SMX + spironolactone prescription.
Thank you!

Colorado Chapter
Scientific Meeting
2016

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