



Update in Hospital Medicine

January 24, 2014

Amy (Rybak) O'Linn DO, FHM, FACP

Staff, Cleveland Clinic

Dept. of Hospital Medicine

olinna2@ccf.org



Fairview Hospital

517 beds



Fairview Hospitalist Team



Not pictured: Brent Burkey MD, Khaldoon Shaheen MD and our cadre of night docs.

Disclosures

- None

Methods

- Reviewed literature (primary studies and guidelines) relevant to hospital medicine over the past 15 months.
- Summarized most relevant studies

Talk Outline

- **New Anticoagulants Update- Apixaban, nOAC GIB risk**
- **Stroke prevention**
- **Meds: Zolpidem (Ambien)**
- **Perioperative Troponin**
- **IVCF**
- **New Infections, Choosing Wisely**
- **Current Trends: OUTs and INs**

Case Presentation

- **ED calls: 41 year old man with acute shortness of breath, CT PE protocol diagnoses a right sided pulmonary embolus.**

Which treatment would you order?

- A.** LMWH SQ and VKA (warfarin) PO
- B.** Long-term LMWH (enoxaparin)
- C.** Dabigatran (Pradaxa) PO alone
- D.** Rivaroxaban (Xarelto) PO alone
- E.** Apixaban (Eliquis) PO alone
- F.** Fondaparinux (Arixtra) SQ daily
- G.** IVC Filter and an anticoagulant

Apixaban alone to treat Acute VTE

Question: Is Apixaban alone noninferior to standard therapy (LMWH to warfarin)?

Design: Randomized, double-blind, noninferiority trial. AMPLIFY trial

N=5395 patients w/ acute symptomatic VTE

Intervention: Apixaban (10 mg BID x 7d, then 5mg po BID x 6 mos) v. standard therapy with enoxaparin and coumadin

Agnelli G. et al, NEJM, 2013, July 1.

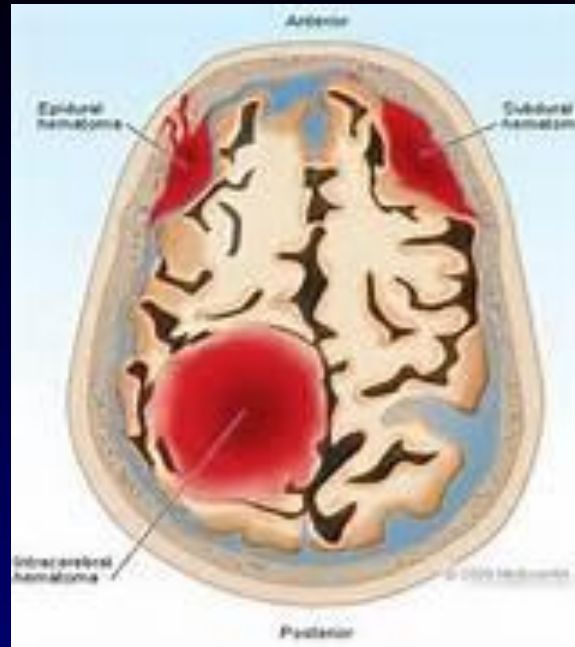
Apixaban to treat acute VTE outcomes

| | Apixaban, n=2609 | Standard, n=2635 |
|--|----------------------------|----------------------------|
| Recurrent VTE or VTE related death no. (%) | 59 (2.3%)* ^{***} | 71 (2.7%)* ^{***} |
| Major Bleeding- no. (%) | 15 (0.6%)* ^{***} | 49 (1.8%)* ^{***} |
| Major bleeding or clinically relevant nonmajor bleeding- no. (%) | 115 (4.3%)* ^{***} | 261 (9.7%)* ^{***} |

*^{***} p<0.001

Agnelli, G., et al. NEJM, 2013, July 1.

**What will
you tell him
about the
Bleeding
Risk?**



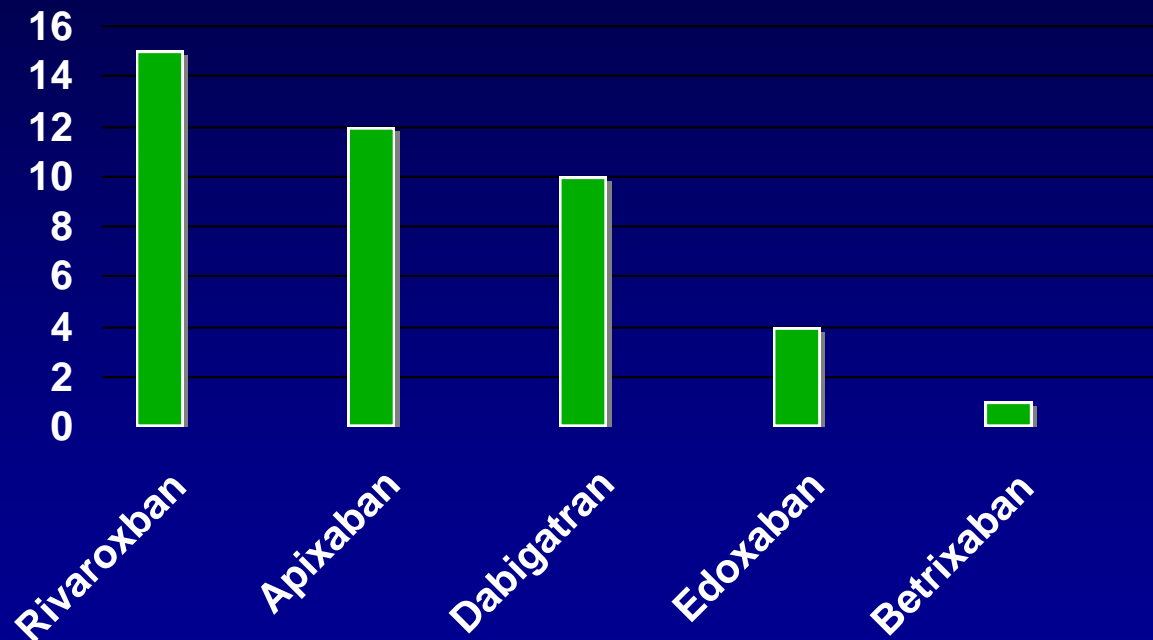
New Oral Anticoagulants Increased Risk of GIB

- **Systematic review and meta-analysis**
- **43 RCT (151,578 patients) that compared nOAC with standard of care.**
- **Primary outcome: risk of GIB**
- **Comprehensive lit review: Medline, EMbase, Cochrane Central Register of Controlled Trials.**

New Oral Anticoagulants and Increased risk of GIB

- **Odds ratio and associated 95% CI were calculated for each RCT.**
- **Prespecified subgroup analysis according to type of nOAC + indication.**

New Oral Anticoagulants Increased Risk of GIB



NUMBER OF STUDIES

Odds Ratio dependent on Indication

- Overall Odds Ratio for GIB in patients taking nOAC was 1.45 (95% CI 1.07-1.97), ($I^2 = 61\%$)
- Subgroup analysis
 - Thromboprophylaxis after orthopedic surgery
 - Atrial fib
 - Treatment of Acute DVT/PE
 - Acute Coronary Syndrome

Odds Ratio dependent on Indication

- Subgroup analysis
 - 0.78 for Thromboprophylaxis after orthopedic surgery (95% CI, 0.31-1.96)
 - 1.21 for Atrial fib (95% CI, 0.96-1.61)
 - 1.59 for Tx of DVT/PE (95% CI, 1.03-2.44)
 - 5.21 for ACS (95% CI, 2.58-10.53)

Odds Ratio for GIB dependent on Drug

- 0.31 for edoxaban (95% CI, 0.01-7.69)
- 1.23 for apixaban (95% CI, 0.56-2.31)
- 1.48 for rivaroxaban (95% CI, 1.21-1.82)
- 1.58 for dabigatran (95% CI, 1.29-1.93)

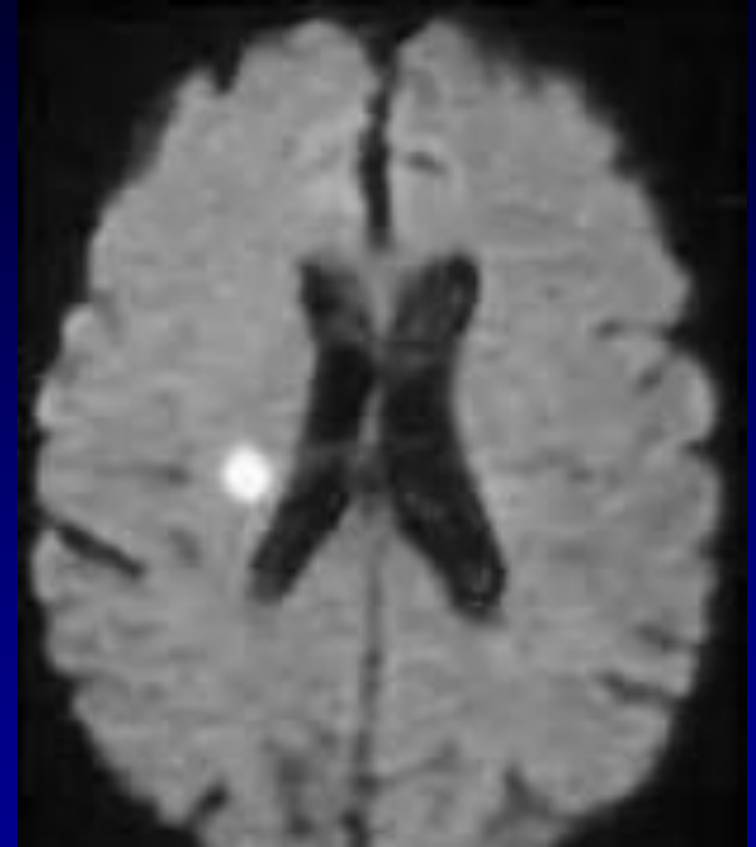
Odds Ratio for Clinically Relevant Bleeding

- Overall risk of clinically relevant bleeding was significantly higher with the use of nOAC compared with standard care (OR 1.16; 95% 1.00-1.34).
- Considerable overall heterogeneity was observed ($I^2=83\%$)



Case Presentation

75 year old Caucasian female with history of HTN, HPL on daily Aspirin 325mg presents with paresthesia right leg. MRI showing acute lacunar thalamic CVA. Should you double-up on the antiplatelets to prevent future stroke, ie. add Clopidogrel?



A. Yes

B. No

Antithrombotics in Stroke: SPS3 Trial

- **Question: Does adding clopidogrel (75mg) to aspirin (325mg) reduce CVA recurrence in patients with recent lacunar stroke?**
- **Design: double blind, randomized, placebo-controlled, multicenter trial [Secondary Prevention of Small Subcortical Strokes (SPS3) trial]**
- **Intervention: ASA 325 + Clopidogrel; or ASA + placebo**
- **N=3020 patients**
- **Mean follow-up period: 3.4 yr**

ASA + Clopidogrel more harm than benefit

| Outcomes | ASA + Clopidogrel n=1517 | ASA + Placebo n=1503 |
|-------------------------------|-----------------------------|-------------------------|
| Recurrent CVA | 125 (2.5%/year) | 138 (2.7%/year) |
| Major Extracranial hemorrhage | 105 (2.1%/year)*** | 56 (1.1%/year)*** |
| All-cause mortality | 113 (7.4%) | 77 (5.1%) |

***p<0.001

Benavente OR, Hart RG, et al. N Engl J Med. 2012; 367:817-25 (August 2012).

Antithrombotics in Stroke

Summary: Usefulness of clopidogrel for the treatment of acute ischemic CVA is not well established.

American Heart Association/American Stroke Association Guidelines for the Early Management of Patients With Acute Ischemic Stroke, January 2013.



Antiplatelets in Stroke

- **Q: Does loading-dose (300mg) then maintenance (75mg) clopidogrel in addition to ASA (75mg) reduce recurrent stroke? (CHANCE trial)**
- **Design: randomized, double blind, placebo-controlled, multicenter trial**
- **Intervention: Clopidogrel 300mg followed by 75mg daily x 90 days + ASA 75mg x 21 days; or ASA 75mg + Placebo daily x 90 days.**
- **N=5170**
- **90 day follow up**

**TIA with
moderate-to-
high risk of
stroke
recurrence
(ABCD² ≥ 4)**

| Risk Factor | Points | S |
|--|--------|--------------------------|
| Age | | |
| ≥ 60 years | 1 | <input type="checkbox"/> |
| Blood Pressure (at initial acute evaluation) | | |
| Systolic BP ≥ 140 mm Hg OR Diastolic BP ≥ 90 mm Hg | 1 | <input type="checkbox"/> |
| Clinical Features of TIA | | |
| Unilateral weakness | 2 | <input type="checkbox"/> |
| Speech impairment without weakness | 1 | <input type="checkbox"/> |
| Duration | | |
| TIA duration ≥ 60 minutes | 2 | <input type="checkbox"/> |
| TIA duration 10-59 minutes | 1 | <input type="checkbox"/> |
| Diabetes | 1 | <input type="checkbox"/> |
| Total ABCD ² score | 0-7 | <input type="checkbox"/> |

Acute minor stroke, defined as NIHSS ≤ 3

| Medscape® www.medscape.com | | |
|--|---|---------|
| Category | Results | Scoring |
| 1a. Level of consciousness (LOC; patients who score 2 or 3 on this item should be assessed using the Glasgow Coma Scale) | Alert, keenly responsive | 0 |
| | Not alert (arousable—minor stimulation) | 1 |
| | Not alert (arousable—painful stimulation) | 2 |
| | Unresponsive | 3 |
| 1b. LOC questions (month, age) | Answers both correctly | 0 |
| | Answers one correctly | 1 |
| | Answers neither correctly | 2 |
| 1c. LOC commands (open and close eyes, make fist, release fist) | Performs both tasks correctly | 0 |
| | Performs one correctly | 1 |
| | Performs neither correctly | 2 |
| 2. Best gaze | Normal | 0 |
| | Partial gaze palsy | 1 |
| | Forced deviation | 2 |
| 3. Visual | No visual loss | 0 |
| | Partial hemianopia | 1 |
| | Complete hemianopia | 2 |
| | Bilateral hemianopia | 3 |
| 4. Facial palsy | Normal | 0 |
| | Minor paralysis | 1 |
| | Partial paralysis | 2 |
| | Complete | 3 |
| 5. Motor function (arm) | No drift | 0 |
| | Drift before 5 seconds | 1 |
| | Drift before 10 seconds | 2 |
| | No effort against gravity | 3 |
| | No movement | 4 |
| 6. Motor function (leg) | No drift | 0 |
| | Drift before 5 seconds | 1 |
| | Drift before 10 seconds | 2 |
| | No effort against gravity | 3 |
| | No movement | 4 |
| 7. Limb ataxia | No ataxia | 0 |
| | Ataxia—one limb | 1 |
| | Ataxia—two limbs | 2 |
| 8. Sensory | No sensory loss | 0 |
| | Mild sensory loss | 1 |
| | Severe sensory loss | 2 |
| 9. Language | Normal | 0 |
| | Mild aphasia | 1 |
| | Severe aphasia | 2 |
| | Mute or global aphasia | 3 |
| 10. Articulation | Normal | 0 |
| | Mild to moderate dysarthria | 1 |
| | Severe dysarthria | 2 |
| 11. Extinction and inattention | Absent | 0 |
| | Mild (1 sensory modality) | 1 |
| | Severe (2 modalities) | 2 |

Note. The full NIH Stroke Scale is available at www.ninds.nih.gov/doctors/NIH_Stroke_Scale.pdf.

Source: J Neurosci Nurs © 2007 American Association of Neuroscience Nurses

ASA + Clopidogrel more benefit than harm?

| Outcomes | ASA + Clopidogrel n=2584 | ASA + Placebo N= 2586 |
|-------------------------------|-----------------------------|--------------------------|
| Recurrent CVA | 212 (8.2%)*** | 303 (11.7%)*** |
| Moderate/severe hemorrhage | 7 (0.3%) | 8 (0.3%) |

***p<0.001

Wang NEJM July 2013.

Commentary on Stroke Trials

- Timing was different (semi-acute v. acute)
- CHANCE trial: 12% of patients screened were eligible. Generalizable?
- Secondary Prevention differs in China.
- Distribution of stroke subtypes differs in China.

Case Presentation (cont'd)

The first night in the hospital, patient needs a sleeping aide. The house officer prescribes Ambien 10mg PO x1.

At 3am, patient arises without notifying the nurse and she slips and breaks her hip.



Inpatient Zolpidem Use

Question: Does Zolpidem increase risk of inpatient falls?

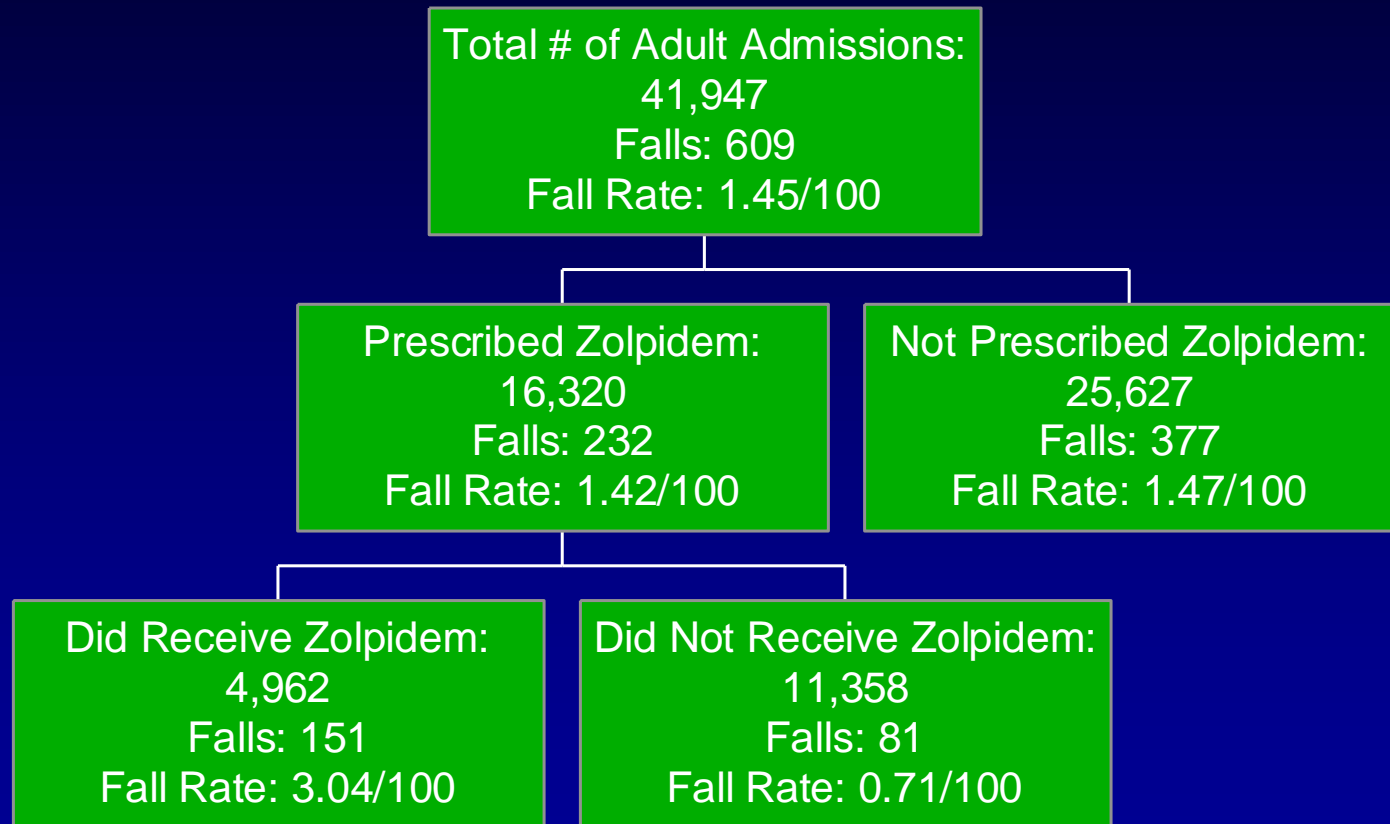
Design: Retrospective cohort study

N= 41,947 inpatients

Methods: Review of electronic medical records to determine demographics, other risk factors for falls, and prescription and administration of zolpidem.

Multivariate analysis to determine whether zolpidem was independently associated with falls.

Zolpidem and Inpatient Falls



Inpatient Zolpidem Use

Question: Does Zolpidem increase risk of inpatient falls?

Design: Retrospective cohort study

N= 41,947 inpatients

Methods: EMR Review and multivariate analysis.

Results: Zolpidem is an independent risk factor for inpatient falls. This is after accounting for age, gender, insomnia, delirium status, zolpidem dose, Charlson comorbidity index, Hendrich's fall risk score, length of hospital stay, presence of visual impairment, gait abnormalities, and dementia/cognitive impairment. NNH = 55 patients

Comment on Sleep

- **Hard to interpret studies on sleeping aides and falls.**
- **Insomnia itself is a risk factor for falls.**



Zolpidem = Danger for Inpatients



Zolpidem = Danger for Inpatients

FDA Recommends to reduce the dose in WOMEN.

- **5mg for immediate-release**
- **6.25mg for extended release**

**Patient is now status-post ORIF right hip.
On the evening of POD #0, pt complains
of indigestion. The nurse suggests
TUMS.**

**But you remember a recent article about
perioperative troponins...**

Vascular Events In Noncardiac Surgery Patients Cohort Evaluation (VISION)

Question: Does peak 4th generation troponin measurement in the first 3 days after noncardiac surgery predict 30-day mortality?

**Design: Prospective, international cohort study
N= 15,133 pts.**

Method: Measured TnT levels at 6-12 hours after surgery, then Day 1, 2 and 3.

Devereaux PJ, JAMA, 2012; 307 (21): 2295-2304.



Peak Troponin-Mortality

| Peak TnT Level | </0.01ng/mL N=13,376 | 0.02ng/mL N= 494 | 0.03-0.29ng/mL N= 1121 | >/0.30 ng/mL N=142 |
|--------------------------------------|-------------------------|---------------------|---------------------------|-----------------------|
| No. of Deaths within 30 days post-op | 134 (1%) | 20 (4%) | 104 (9.3%) | 24 (16.9%) |

Devereaux PJ, et al. JAMA; 2012;307(21):2295-2304.

Vascular Events In Noncardiac Surgery Patients Cohort Evaluation (VISION)

Question: Does peak 4th generation troponin measurement in the first 3 days after noncardiac surgery predict 30-day mortality?

Design: Prospective, international cohort study
N= 15,133 pts.

Result: Multivariable analysis showed that peak TnT values of at least 0.02ng/mL, occurring in 11.6% of patients, were associated with higher 30-day mortality compared to the reference group.

Perioperative MI

- **Question: How does perioperative MI present in the elderly with hip fracture and what are the outcomes?**
- **Design: population-based retrospective, case control study.**
- **N= 1212 hip fracture surgeries.**
- **Mean age: 85 years old.**

Perioperative MI

- Question: How does perioperative MI present in the elderly with hip fracture and what are the outcomes?
- Design: population-based retrospective, case control study.
- N= 1212 hip fracture surgeries.
- 167 (13.8%) cases of perioperative MI within first 7 days.
- 92% within the first 48 hours

Of the patients with perioperative MI...

Of the patients with perioperative MI...
25.2% experienced symptoms of ischemia
7% reported chest pain
12% dyspnea

**Only 22.8% had EKG changes consistent
with ischemia**

What else?

| | Perioperative MI N= 167 | No Perioperative MI N= 334 |
|---------------------------|----------------------------|-------------------------------|
| Median Length of Stay | 11.6 days** | 7.4 days** |
| No. of In-hospital Deaths | 24 (14.4%)*** | 4 (1.2%)*** |
| No. of Deaths at 30 days | 29 (17.4%)*** | 14 (4.2%)*** |
| No. of Deaths at 1-year | 66 (39.5%)*** | 77 (23%)*** |

** p +/- 0.001, ***p <0.001

Gupta BP, et al. J of Hospital Med. 2012;7:713-6.

**Doctor Beware:
Perioperative ischemic
symptoms are masked by
analgesia, sedation, and
transient/subtle EKG
changes.**





Third Universal Definition of MI

European Society of Cardiology

American College of Cardiology Foundation

American Heart Association

World Health Federation

“Routine monitoring of cardiac biomarkers in high-risk patients, both prior to and 48–72 h after major surgery, is therefore recommended.”

Circulation 2012; 126: 2020-2035

Patient declines the IPC, and develops red, swollen painful leg with duplex ultrasound revealing proximal DVT.

Patient receives rivaroxaban, develops BRBPR and hemoglobin drops 2 grams.

Do you consult vascular surgery for an IVCF?

a. Yes

b. No

Inferior Vena Cava Filters

Question: What information on complications, follow-up data, concomitant anticoagulation medication use, and rate of retrieval can be collected from patients with retrievable IVCF?

Design: Retrospective review of IVCF from 2003-2011. N= 978 patients.

Intervention: placement of an IVC filter.



IVCF (cont'd)

Of 679 retrievable IVC filters placed, attempts were made to retrieve only 71 filters.

- 58 (8.5%) successful.**
- 13 (18.3% of attempts) unsuccessful.**

7.8% (74 patients) of patients in this study (total n=952) acquired VTE

- Including 25 PE (with Filter in place)**
- 48% of the new VTE were in patients without VTE at time of filter placement.**
- Nearly 25% were discharged on a regimen of anticoagulant therapy**

Summary IVCF

- **Ticking Time Bomb?**



Case Presentation (cont'd)

Finally, patient is discharged to a Skilled Nursing Facility.

14 days later, you are back on service, and the ED calls: UTI. Culture from SNF is growing a difficult to treat organism, but the ED health care provider cannot remember the name of the bug. You check the cultures. It's...

Carbapenem Resistant Enterobacteriaceae (CRE)

- 1) You've never heard of this before-- is it like MRSA?**
- 2) You shudder. No antibiotics to treat it-- maybe polymixin. This is a chance for you to respect the bug and prevent further transmission.**
- 3) A nurse mentions contact precautions, but you think, "Nah. I'm going in. I've got 10 more patients to see. Where's the contact precautions cart anyway?"**

Carbapenem Resistant Enterobacteriaceae (CRE)

A Family of Bacteria

Klebsiella

E. Coli

Citrobacter

Enterobacter

Spread their genetic tricks (via plasmid) to each other. Very Dangerous and difficult if not impossible to treat.

Carbapenem Resistant Enterobacteriaceae (CRE)

What to do when you see it:

- **Stop transmission.**
 - **Contact Precautions**
 - **Dedicated Equipment**
 - **Dedicated Staff.**
 - **Hand hygiene.**
- **Inform facilities when transferring patients (and ask about it in incoming patients)**
- **Remove catheters and other devices ASAP.**
- **Continue Antibiotic stewardship.**

ABIM Choosing Wisely Campaign

Choosing Wisely Campaign Society of Hospital Medicine (SHM) Adult Contribution

- 1) Don't place, or leave in place, urinary catheters for incontinence or convenience or monitoring of output for non-critically ill patients (acceptable indications: critical illness, obstruction, hospice, perioperatively <2 days for urologic procedures; use weights instead to monitor diuresis).**

Choosing Wisely Campaign SHM Adult Contribution

2) Don't prescribe medications for stress ulcer prophylaxis to medical inpatients unless at high risk for GI complications.



- **3) Avoid transfusions of RBC for arbitrary hemoglobin or hematocrit thresholds and in the absence of symptoms of active coronary artery disease, heart failure or stroke.**



Choosing Wisely Campaign SHM Adult Contribution

- 4) Don't order continuous telemetry monitoring outside of the ICU without a protocol that governs continuation.



- **5) Don't perform repetitive CBC and chemistry testing in the face of clinical and lab stability.**

The OUTs and INs

OUT

- Opioid Rx (Recent MMWR)
- Clarithromycin/Erithromycin + Statin

IN

- I COUGH (Incentive spirometry, Coughing/deep breathing, Oral care, Understanding, Getting out of bed, HOB elevation)
- Financial Awareness
- Duration COPD (5 days prednisone)
- Nonpharmacological Sleep Assistance

The OUTs and INs

OUT

- **Probiotics to Prevent CDiff**
 - **PLACIDE Trial**
 - **Randomized, double-blind, placebo-controlled, multicenter trial.**
 - **Lactobacilli + Bifidobacteria daily x 21 days v. placebo**
 - **No significant reduction CDAD**

IN

- **Probiotics to Prevent CDiff**
 - **2 MetaAnalyses**
 - **20 Trials**
 - **3818 Participants**
 - **Probiotics reduced CDAD incidence by 66%**

The OUTs and INs

OUT

- **Liberal blood transfusions** (Carson JL, et al. Red Blood Cell Transfusion Guideliness from AABB, Ann Intern Med 26 March 2012.)
- **Confusing ways to write sodium bicarb** (Klima T, et al. Sodium chloride vs. sodium bicarbonate for the prevention of contrast medium-induced nephropathy: a RCT. Europ Heart J (2012); 33, 2071.)

IN

- **Fecal Microbiota Transplant**
- **Better Transitions**
- **Post-Hospital Syndrome (NEJM Jan 10)**

Post-Hospital Syndrome

Teach Me Back

Thank you for your attention.



Every life deserves world class care.