Hospitalist Medicine
NewsFlash

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Potentially practice changing articles

- Blood cultures and gram negative bacteremia
- Contrast induced AKI
- VTE and cancer
Follow up Blood Cultures in Gram Negative Bacteremia: Are They Needed?

Clinical Infectious Diseases

July 2017

Canzoneri, C, Akhavan, B, Tosur, Z, Andrade, P, and Aisenberg, G. Volume 65, Issue 11, 13 November 2017, Pages 1776-1779,
Why is this article important?

- Gram negative (GN) bacteremia
  - Accounts for 25-50% of all bacteremia
  - GN sepsis has a mortality of 12-38%
- However, gram negative bacteremia is usually transient
  - Questionable utility of follow up cultures
  - Despite this there continues to be ongoing, unrestrained use of blood cultures
- Optimal duration of treatment has not been studied in detail, so the utility of repeating blood cultures is unclear
Follow up Blood cultures (FUBC)

Blood cultures, in general, have a low yield

- True Positive 5%
- False Positive 5%
- Negative Blood cultures 90%

Risks of follow up blood cultures

- Prolonged hospital stay
- Increased healthcare costs
- Unnecessary consults
- Inappropriate use of antibiotics

Negative Blood cultures 90%
False Positive 5%
True Positive 5%
Methods

Inclusion criteria:
- Adults, admitted to tertiary care center
- Admitted with true bacteremia
- Excluded positive fungal cultures, and contaminants

Definitions:
- True bacteremia - at least 1 positive blood culture not considered a contaminant
- Contaminant - common skin organism isolated in only 1 blood culture
- Persistent bacteremia - positive culture after 24 hours
- Febrile - Temp >100.4, when at least 1 of the FUBCs were drawn
Analyzed 500 episodes of bacteremia

- Determined frequency and yield of follow up blood cultures
- Identified risk factors for persistent bacteremia
- Identified source of bacteremia
- Antibiotic status at the time of FUBC
- Mortality and ICU stay
Results

500 episodes of bacteremia

383 (77%) had at least 1 FUBC obtained

Number of FUBC obtained per organism type (% of total FUBC)

- **GPC 206 (54%)**
  - 43 (78%)
  - 21%

- **GNB 140 (37%)**
  - 8 (15%)
  - 6%

- **Polymicrobial 30 (8%)**
  - 4 (7%)
  - 10%

Positive FUBC’s (percentage of total positives)

Persistent bacteremia (+/total FUBC per organism)

55 positive FUBC’s
2.37 FUBC were obtained per patient in whole cohort
- GPC - 2.32 FUBC per patient (range 1-12)
- GNB - 2.32 FUBC per patient (range 1-6)
Mean duration of bacteremia 2.83 days (range 1-15), similar for three categories of bacteria
Average follow up 4.45 days (range 1-18 days)
Characteristics of patients who had FUBC obtained

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male sex</td>
<td>211 (55)</td>
</tr>
<tr>
<td>Age, y, mean ± standard deviation</td>
<td>53 ± 15</td>
</tr>
<tr>
<td>Known source of bacteremia</td>
<td>273 (71)</td>
</tr>
<tr>
<td>Medical (vs surgical) disease</td>
<td>314 (82)</td>
</tr>
<tr>
<td>Initial bacteremia caused by</td>
<td></td>
</tr>
<tr>
<td>Gram-positive cocci</td>
<td>206 (53.8)</td>
</tr>
<tr>
<td>Gram-negative bacilli</td>
<td>140 (37)</td>
</tr>
<tr>
<td>Polymicrobial</td>
<td>30 (8)</td>
</tr>
<tr>
<td>Gram-positive bacilli</td>
<td>6 (1.6)</td>
</tr>
<tr>
<td>Anaerobes</td>
<td>1 (0.3)</td>
</tr>
<tr>
<td>Patients on antibiotics the day of FUBC</td>
<td>347 (91)</td>
</tr>
<tr>
<td>Microorganism sensitive to those antibiotics</td>
<td>325 (86)</td>
</tr>
<tr>
<td>Fever on the day of FUBC</td>
<td>127 (33)</td>
</tr>
<tr>
<td>Presence of an IV central line</td>
<td>165 (43)</td>
</tr>
<tr>
<td>Presence of a bladder catheter or nephrostomy</td>
<td>119 (31)</td>
</tr>
<tr>
<td>Neutropenia (ANC &lt; 1000/mL)</td>
<td>36 (9)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>230 (60)</td>
</tr>
<tr>
<td>AIDS</td>
<td>28 (7)</td>
</tr>
<tr>
<td>ESRD on hemodialysis</td>
<td>92 (24)</td>
</tr>
<tr>
<td>Liver failure</td>
<td>53 (14)</td>
</tr>
<tr>
<td>Need for ICU care</td>
<td>165 (43)</td>
</tr>
<tr>
<td>In-hospital death</td>
<td>52 (14)</td>
</tr>
</tbody>
</table>

Table 4. Incidence of Bacteremia per Source (n = 273)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No.</th>
<th>Positive</th>
<th>Negative</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urinary tract infection</td>
<td>71</td>
<td>2</td>
<td>3%</td>
<td>.001</td>
</tr>
<tr>
<td>Severe skin infection</td>
<td>70</td>
<td>4</td>
<td>6%</td>
<td>.026</td>
</tr>
<tr>
<td>Intravenous catheter</td>
<td>61</td>
<td>21</td>
<td>34%</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>34</td>
<td>5</td>
<td>15%</td>
<td>.79</td>
</tr>
<tr>
<td>Intra-abdominal infection</td>
<td>21</td>
<td>2</td>
<td>10%</td>
<td>.75</td>
</tr>
<tr>
<td>Endocarditis</td>
<td>6</td>
<td>1</td>
<td>17%</td>
<td>.59</td>
</tr>
<tr>
<td>Osteomyelitis</td>
<td>5</td>
<td>0</td>
<td>0%</td>
<td>1.00</td>
</tr>
<tr>
<td>Pleural empyema</td>
<td>3</td>
<td>1</td>
<td>33%</td>
<td>.35</td>
</tr>
<tr>
<td>Septic arthritis</td>
<td>1</td>
<td>1</td>
<td>100%</td>
<td>.14</td>
</tr>
<tr>
<td>Tonsillitis</td>
<td>1</td>
<td>0</td>
<td>0%</td>
<td>1.00</td>
</tr>
</tbody>
</table>

236 negative FUBC
37 positive FUBC
## Differences Between Patients Whose FUBC Were Positive or Negative

21/24 obtained dialysis through central line

### Table 2. Differences Between Patients Whose Follow-up Blood Cultures Were Positive or Negative

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Positive (n = 55)</th>
<th>Negative (n = 328)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>On antibiotics when cultures drawn</td>
<td>54 (98%)</td>
<td>312 (95%)</td>
<td>.49</td>
</tr>
<tr>
<td>Medical disease (vs surgical)</td>
<td>49 (89%)</td>
<td>265 (81%)</td>
<td>.18</td>
</tr>
<tr>
<td>Fever when cultures drawn</td>
<td>27 (49%)</td>
<td>100 (30%)</td>
<td>.008</td>
</tr>
<tr>
<td>Presence of a urinary catheter</td>
<td>11 (20%)</td>
<td>82 (25%)</td>
<td>.50</td>
</tr>
<tr>
<td>Presence of an IV central catheter</td>
<td>34 (62%)</td>
<td>121 (37%)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Neutropenia (ANC &lt;1000/mL)</td>
<td>4 (7%)</td>
<td>29 (9%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>31 (56%)</td>
<td>121 (37%)</td>
<td>.19</td>
</tr>
<tr>
<td>HIV positive</td>
<td>3 (5%)</td>
<td>20 (6%)</td>
<td>1.00</td>
</tr>
<tr>
<td>ESRD on hemodialysis</td>
<td>24 (44%)</td>
<td>65 (20%)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Liver cirrhosis</td>
<td>5 (9%)</td>
<td>33 (10%)</td>
<td>1.00</td>
</tr>
<tr>
<td>ICU care required</td>
<td>18 (33%)</td>
<td>119 (36%)</td>
<td>.65</td>
</tr>
<tr>
<td>Death</td>
<td>3 (5%)</td>
<td>35 (11%)</td>
<td>.33</td>
</tr>
</tbody>
</table>
### Differences Between Patients Whose FUBC Were Positive or Negative

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Negative (n = 328)</th>
<th>FUBC Positive for GPC (n = 43)</th>
<th>PValue</th>
<th>FUBC Positive for GNB (n = 8)</th>
<th>PValue</th>
</tr>
</thead>
<tbody>
<tr>
<td>On antibiotics when cultures drawn</td>
<td>312 (95%)</td>
<td>42 (98%)</td>
<td>.71</td>
<td>8 (100%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Medical disease (vs surgical)</td>
<td>265 (81%)</td>
<td>39 (91%)</td>
<td>.14</td>
<td>6 (75%)</td>
<td>.65</td>
</tr>
<tr>
<td>Fever when cultures drawn</td>
<td>100 (30%)</td>
<td>21 (49%)</td>
<td>.02</td>
<td>6 (75%)</td>
<td>.01</td>
</tr>
<tr>
<td>Presence of a urinary catheter</td>
<td>82 (25%)</td>
<td>9 (21%)</td>
<td>.71</td>
<td>1 (13%)</td>
<td>.69</td>
</tr>
<tr>
<td>Presence of an IV central catheter</td>
<td>121 (37%)</td>
<td>27 (63%)</td>
<td>.002</td>
<td>5 (63%)</td>
<td>.16</td>
</tr>
<tr>
<td>Neutropenia (ANC &lt; 1000/mL)</td>
<td>29 (9%)</td>
<td>3 (7%)</td>
<td>1.00</td>
<td>1 (13%)</td>
<td>.53</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>121 (37%)</td>
<td>23 (53%)</td>
<td>.04</td>
<td>6 (75%)</td>
<td>.06</td>
</tr>
<tr>
<td>HIV positive</td>
<td>20 (6%)</td>
<td>3 (7%)</td>
<td>.74</td>
<td>0 (0%)</td>
<td>1.00</td>
</tr>
<tr>
<td>ESRD on hemodialysis</td>
<td>65 (20%)</td>
<td>20 (47%)</td>
<td>&lt;.001</td>
<td>3 (38%)</td>
<td>.21</td>
</tr>
<tr>
<td>Liver cirrhosis</td>
<td>33 (10%)</td>
<td>3 (7%)</td>
<td>&lt;.78</td>
<td>2 (25%)</td>
<td>.20</td>
</tr>
<tr>
<td>ICU care required</td>
<td>119 (36%)</td>
<td>12 (28%)</td>
<td>.31</td>
<td>4 (50%)</td>
<td>.47</td>
</tr>
<tr>
<td>Death</td>
<td>35 (11%)</td>
<td>3 (7%)</td>
<td>.60</td>
<td>0 (0%)</td>
<td>.36</td>
</tr>
</tbody>
</table>
Results

The use of antibiotics did not make a difference in the rate of positivity of FUBC.

Mortality and ICU care were not associated with positive FUBC’s.

For the cohort, the presence of fever on the day of FUBC was associated with higher rates of positive FUBC, as was ESRD on HD, and presence of an IV central catheter.

When analyzed separately:

- The presence of fever on the day of FUBC was associated with higher rates of positive FUBC for both GPC and GNB.
- In GPC bacteremia, the presence of ESRD on HD, DM, or presence of an IV central catheter was associated with higher rates of positive FUBC.
- In GNB bacteremia, only fever was associated with higher rate of positive FUBC.
- However, this is based on only a small number of positive FUBC.
Conclusions

- Authors conclude that their data supports that FUBC may have little utility in the management of GNB bacteremia.
- Currently the management of GNB bacteremia is determined by clinical judgement, no guidelines for treatment exist.
- FUBC can be cost ineffective, may lead to false positives, possibly prolonging hospital course, or leading to inappropriate antibiotic usage.
- GNB bacteremia usually resolves within a short time after initiation of appropriate antibiotics and/or source control.

Limitations:
- Small number of positive FUBC for gram negative infections
- Excluded contaminants at the beginning, possibly skewing distribution of positive cultures
- No explanation in the medical record for the 23% of patients that didn’t have FUBC (less sick?)
Take Home Points

- In GNB bacteremia 17 FUBC were drawn to yield 1 positive result.
- In the whole cohort 5 FUBCs were needed to yield 1 positive result.
- FUBC in GNB bacteremia, especially uncomplicated bacteremia, can likely be avoided.
- FUBC should still be obtained in suspected endocarditis and in other cases of endovascular infection (line infections), especially if line salvage planned.
Pole Everywhere

Which of the following patients is least likely to have a positive follow up blood culture, obtained greater than 24 hours after the initial positive culture?

A) 60 year old woman on dialysis who is admitted with sepsis and found to have MRSA bacteremia

B) 25 year old female with a port for TPN secondary to short gut syndrome presenting with sepsis and found to have Staphylococcus epidermidis bacteremia

C) 38 year old male admitted with perinephric abscess with Klebsiella bacteremia who has been persistently febrile for the last 48 hours

D) 78 year old male admitted with sepsis secondary to a UTI, found to have E. coli bacteremia, who has been afebrile since admission to the medicine floor.
you see, my friend, it’s never who you expect
folks are quick to blame seafood and ethnic foods
they’ll even avoid them for weeks
but their aversion is my diversion
w-what are you saying... that YOU did it? YOU...
give my regards to your porcelain throne.
POISONED me?!!
Other ID articles worth looking up

Treating atypical PNA (peds)\(^3\) – prospective cohort of 1400 hospitalized peds patients, with pneumonia, no difference between B-lactam monotherapy and combination therapy of B-lactam+macrolide
- 9% had an atypical bacteria detected, but no benefits of empiric macrolide therapy seen in this subgroup

Probiotics for c diff in hospitalized patients\(^4\) – Systematic review and meta-analysis showed starting probiotics early after starting antibiotics significantly decreased c diff, 50% RRR

Vanc and Zosyn and AKI\(^5\) – Retrospective review showed patients who received both vanc and zosyn had >2-fold excess risk for AKI compared with either monotherapy group, however multiple co-founding variables

Procalcitonin in respiratory tract infections\(^6\) – Meta-analysis showed procalcitonin guided treatment reduced mortality, length of antibiotic treatment, and abx related side effects
Contrast and kidneys
In patients with CKD what is the most effective way to prevent CIN?

A) Normal saline
B) IV bicarbonate
C) PO hydration
D) Oral acetylcysteine
E) None of the above
Prophylactic hydration to protect renal function from intravascular iodinated contrast material in patients at high risk of contrast-induced nephropathy (AMACING): a prospective, randomized, phase 3, controlled, open-label, non-inferiority trial.

Contrast Induced Nephropathy (CIN)

- A decline in renal function typically occurring 2-5 days after contrast
  - Has varying definitions across papers
  - Increase in creatinine of 25% or 0.5mg/dl (commonly used)
  - Usually rises within 48 hours, and peaks between 4-5 days post-contrast

More than 75 million procedures with IV contrast are done worldwide every year.

Estimated that 6-12 million patients at risk for CIN have contrasted procedures done every year.

Associated with increased morbidity and mortality.

Usually resolves and clinically relevant consequences are reported to occur in <1% of cases.

“At the current time, it is the position of ACR Committee on Drugs and Contrast Media that CIN is a real, albeit rare, entity.” Last updated 2014.
Study Design

Single hospital in the Netherlands

Elective contrast enhanced CT scans, excluded emergencies or ICU patients
- 9% were inpatients

Non-inferiority trial of guideline recommended normal saline hydration versus no treatment
- Non-inferiority was defined as absolute difference in CIN between groups of less than 2.1%
- Expected 2.4% proportion of patients to have CIN after hydration
- Average of 1.6L NS

Enrolled patients:
- GFR 45-60 at risk for CIN with:
  - Diabetes (23%) or
  - 2 of the following: >75 yo, anemia, CV disease, diuretics or NSAID use (42%)
  - OR GFR 30-45 (35% of patients)
  - OR with multiple myeloma or lymphocytoplastic lymphoma (1% each)
Results - Primary Endpoints

Mean total Cost

- Hydration patients: 1455 €
- Non-hydration patients: 792 €
- Major savings were driven by reduced hospitalization costs

Difference between groups of proportion of patients with CIN at 2-6 days

<table>
<thead>
<tr>
<th>Group size</th>
<th>Contrast-induced nephropathy incidence</th>
<th>Absolute difference</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Contrast-induced nephropathy incidence</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>H+ group</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>H- group</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>Yes</td>
<td>2/94 (2.1)</td>
<td>3/96 (3.1)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>1/202 (0.5)</td>
<td>1/211 (0.5)</td>
</tr>
<tr>
<td>eGFR&lt;45</td>
<td>Yes</td>
<td>2/204 (2.0)</td>
<td>2/204 (2.0)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>5/192 (2.6)</td>
<td>6/201 (3.0)</td>
</tr>
<tr>
<td>Contrast administration route</td>
<td>IA</td>
<td>6/144 (4.2)</td>
<td>6/145 (4.1)</td>
</tr>
<tr>
<td></td>
<td>IV</td>
<td>2/152 (2.0)</td>
<td>2/162 (2.2)</td>
</tr>
<tr>
<td>Interventional procedure</td>
<td>Yes</td>
<td>3/44 (6.8)</td>
<td>1/43 (2.3)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>2/247 (0.9)</td>
<td>7/264 (2.7)</td>
</tr>
<tr>
<td>Total population</td>
<td>603</td>
<td>8/296 (2.7)</td>
<td>8/307 (2.5)</td>
</tr>
</tbody>
</table>

Figure 2: Incidence of contrast-induced nephropathy in the total study population by patient subgroup. The dashed line indicates the non-inferiority margin of 2.1%. Error bars indicate two-sided 90% CIs. Bullets indicate the absolute difference (no hydration minus hydration) in proportion with contrast-induced nephropathy. eGFR = estimated glomerular filtration rate. IA = intra-arterial. IV = intravenous. *The no diabetes subgroup represents the guideline high-risk group with eGFR < 60 ml per min/1.73 m² and two risk factors. p values for interaction: diabetes vs non-diabetics, p = 0.5722; eGFR < 45 vs eGFR > 45, p = 0.6040; intra-arterial vs intravenous contrast administration, p = 0.9608; interventional vs diagnostic procedure, p = 0.3289.
5.5% of patients in the hydration group experienced adverse events.
**Limitations**

- Possibly underpowered study
  - smaller sample size than originally planned based on “feasibility considerations”
- Didn’t include patients with eGFR <30
- Didn’t include ICU patients or CT’s obtained secondary to an emergency
- Single center study

**Conclusions**

- No Hydration is more cost-effective than hydration
- For patients with eGFR >30, no hydration is non inferior to hydration
- Hydration can have adverse effects
Take Home Points

IV hydration prior to contrast CT scans is likely not necessary in patients with eGFR >30.

There are increased costs and potential adverse effects with IV hydration.
Is CIN even real?

**McDonald et al. (Mayo, single center)**
- 5758 patients: (1961 undergoing contrast-enhanced CT, 3797 with non-contrast enhanced)
- (1538 with stage 1-2, 2899 with stage 3, and 1321 with stage 4-5)
- Iso-osmolar contrasted CT compared to patients who received non-contrast CT
- After propensity score adjustment, rates of AKI, dialysis, and mortality were not significantly different between the two groups, for all CKD subgroups.
- However, small numbers of patients with CKD 4 and 5 (90 received contrast).

**Hinson et al. (John Hopkins Emergency room)**
- 17,934 patients (7,201 patients undergoing contrast-enhanced CT, 5,499 undergoing unenhanced CT, and 5,234 with no imaging)
- 4887 stage 1, 1878 stage 2, 1559 with stage 3, 1084 with CKD stage 4-5
- Included patients with creatinine as high as 4, however only 82 patients with CKD stage 4 or 5 had contrasted CT
- Before, and after, propensity score adjustment contrast was not associated with AKI, CKD, renal transplant, or dialysis at 6 months

**Meta-analysis Aycock et al.**
- 28 articles, all observational; 107,335 participants
- Contrast-enhanced CT compared to non-contrast CT was not significantly associated with AKI, all-cause mortality, or need for renal replacement therapy
Nephrogenic Systemic Fibrosis\textsuperscript{8} – single center, retrospective study of 3800 patients (70% on dialysis, 30% with stage 4 or 5 CKD) underwent MRI with a “group II” gadolinium contrast agent, 30% didn’t undergo dialysis afterwards, and 11% were on chronic peritoneal (not thought to clear gadolinium) and none had NSF at 6 months.

- ACR “considers the risk of NSF among patients exposed to standard or lower than standard doses of group II GBCAs (gadolinium based contrast agent) is sufficiently low or possibly nonexistent such that assessment of renal function with a questionnaire or laboratory testing is optional prior to intravenous administration\textsuperscript{2}”

Sodium bicarbonate and/or acetylcysteine to prevent CIN (PRESERVE)\textsuperscript{9} – Multicenter, double blind placebo controlled randomized trial with 5000 patients at high risk for CIN (eGFR 15-45 or 45-60 with diabetes) undergoing angiography. They received IV sodium bicarb or NS and placebo or PO acetylcysteine. No difference in death, need for dialysis, or persistent decline in kidney function (>50% decline) at 90 days, also no difference in CIN.
where ya headed, gall bladder?
I haffa get removed...

well that’s OUTRAGEOUS! WHY?!
on account of I maked all these stones...

seriously?
they’re removing you for that?

hey bladder, lookin’ good. I made these for you...

theAwkwardYeti.com
No one likes injections...

Low molecular weight heparin (LMWH) is the standard treatment for cancer-associated VTE. However, requires regular injections and can be burdensome.

- **Multicenter, prospective, randomized, open label, non-inferiority trial**
  - Hazard ratio less than 1.5 was defined as non-inferior.

- **Adult patients with active cancer** (diagnosed in previous 6 months), or cancer that had been diagnosed within the previous 2 years.

- **Had symptomatic VTE, or incidentally detected proximal DVT** or segmental or more proximal PE.

- **Exclusion criteria**: IVC filter, thrombectomy, lytics, platelets <50, CrCl<30, bleeding, uncontrolled HTN, DAPT, significant liver dysfunction.

- **Compared**:
  - Edoxaban, an oral direct Factor Xa inhibitor
  - Subcutaneous Dalteparin, a LMWH
1050 patients enrolled at 114 centers in 13 countries

1050 Patients underwent randomization

- 525 Were assigned to the edoxaban group
  - 3 Did not receive the assigned treatment
    - 522 Were included in the modified intention-to-treat and safety populations
      - 20 Had a qualifying diagnosis of venous thromboembolism that was not confirmed
      - 12 Did not receive $\geq 1$ dose of edoxaban after randomization
      - 219 Did not complete the overall trial period
        - 206 Died
        - 10 Withdrew consent
        - 3 Were lost to follow-up
    - 524 Were included in the modified intention-to-treat and safety populations
      - 16 Had a qualifying diagnosis of venous thromboembolism that was not confirmed
      - 208 Did not complete the overall trial period
        - 191 Died
        - 12 Withdrew consent
        - 5 Were lost to follow-up

- 525 Were assigned to the dalteparin group
  - 1 Did not receive the assigned treatment
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Edoxaban (N = 522)</th>
<th>Dalteparin (N = 524)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age — yr</td>
<td>64.3±11.0</td>
<td>63.7±11.7</td>
</tr>
<tr>
<td>Male sex — no. (%)</td>
<td>277 (53.1)</td>
<td>263 (50.2)</td>
</tr>
<tr>
<td>Weight</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean — kg</td>
<td>78.8±17.9</td>
<td>79.1±18.1</td>
</tr>
<tr>
<td>≤60 kg — no. (%)</td>
<td>83 (15.9)</td>
<td>78 (14.9)</td>
</tr>
<tr>
<td>Creatinine clearance of 30-50 ml/min — no. (%)</td>
<td>38 (7.3)</td>
<td>34 (6.5)</td>
</tr>
<tr>
<td>Platelet count of 50,000-100,000 per μl — no. (%)</td>
<td>32 (6.1)</td>
<td>23 (4.4)</td>
</tr>
<tr>
<td>Met criteria to receive lower dose of edoxaban — no. (%)†</td>
<td>122 (23.4)</td>
<td>117 (22.3)</td>
</tr>
<tr>
<td>Qualifying diagnosis of venous thromboembolism — no. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulmonary embolism with or without deep-vein thrombosis</td>
<td>328 (62.8)</td>
<td>329 (62.8)</td>
</tr>
<tr>
<td>Deep-vein thrombosis only</td>
<td>194 (37.2)</td>
<td>195 (37.2)</td>
</tr>
<tr>
<td>Symptomatic deep-vein thrombosis or pulmonary embolism</td>
<td>355 (68.0)</td>
<td>351 (67.0)</td>
</tr>
<tr>
<td>Incidental deep-vein thrombosis or pulmonary embolism‡</td>
<td>167 (32.0)</td>
<td>173 (33.0)</td>
</tr>
<tr>
<td>Active cancer — no. (%)</td>
<td>513 (98.3)</td>
<td>511 (97.5)</td>
</tr>
<tr>
<td>Metastatic disease — no. (%)</td>
<td>274 (52.5)</td>
<td>280 (53.4)</td>
</tr>
<tr>
<td>Recurrent cancer — no. (%)</td>
<td>163 (31.2)</td>
<td>152 (29.0)</td>
</tr>
<tr>
<td>Cancer treatment within previous 4 wk — no. (%)§</td>
<td>374 (71.6)</td>
<td>383 (73.1)</td>
</tr>
<tr>
<td>ECOG performance status — no. (%)¶</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>155 (29.7)</td>
<td>148 (28.2)</td>
</tr>
<tr>
<td>1</td>
<td>243 (46.6)</td>
<td>246 (46.9)</td>
</tr>
<tr>
<td>2</td>
<td>123 (23.6)</td>
<td>124 (23.7)</td>
</tr>
<tr>
<td>Previous venous thromboembolism — no. (%)</td>
<td>49 (9.4)</td>
<td>63 (12.0)</td>
</tr>
<tr>
<td>Risk factors for bleeding — no. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>92 (17.6)</td>
<td>92 (17.6)</td>
</tr>
<tr>
<td>1</td>
<td>148 (28.4)</td>
<td>151 (28.8)</td>
</tr>
<tr>
<td>2</td>
<td>174 (33.3)</td>
<td>159 (30.3)</td>
</tr>
<tr>
<td>≥3</td>
<td>108 (20.7)</td>
<td>122 (23.3)</td>
</tr>
</tbody>
</table>
Methods

Edoxaban was started after a 5-day course of LMWH:
- 60mg daily if normal renal function
- 30mg daily if CrCl 30-50, or weight <60kg, or if patient on potent P-glycoprotein inhibitors

Dalteparin was given subcutaneously:
- 200 IU/kg once daily for 30 days, max dose 18,000 IU.
- After 30 days decreased to 150 IU/kg daily
- Dose reduced if plt decreased to less than 100,000 during treatment

Treatment for at least 6 months, but up to 12 months, at the discretion of the treating MD.

All patients followed for 12 months or until the end of the study (minimum 9 months):
- 72 patients in edoxaban and 68 patients in dalteparin group (9-12mo)
Results

- Median duration of treatment was 211 days in edoxaban group and 184 days in dalteparin group.
- Composite outcome of recurrent VTE or major bleeding (overt bleeding associated with decrease in Hgb level of 2 or more, led to a transfusion of 2 or more units of blood, occurred in a critical site, or contributed to death).
- Reasonable adherence.

Majority of deaths related to cancer, 6 in each group from VTE or bleeding.
More Results

- Subgroup analyses – only significant subgroup analysis was the risk of bleeding in patients with GI cancer was higher in patients on edoxaban.
Conclusions

• Edoxaban is non-inferior to dalteparin in treating cancer associated VTE in regards to the composite outcome of major bleeding or recurrent VTE

• Rate of major bleeding with edoxaban was higher than with dalteparin,
  • mostly driven by upper GI bleeding, more so in GI cancers (more GI cancer in Edoxaban group)
  • Severe bleeding (3 and 4) were equal

Limitations

• Open-label

• Lower than expected number of primary outcomes

• Median duration of treatment was shorter in dalteparin
  • Primarily due to inconvenience of injections
Take Home Points

Reasonable to treat cancer associated VTE with epoxaban, patients may have better adherence with oral rather injectable medication.

May want to avoid edoxaban in GI cancers.
Other VTE articles to know about:

**YEARS** - Prospective validation of new screening tool for PE. Clinical signs of (deep vein thrombosis, hemoptysis, and whether pulmonary embolism is the most likely diagnosis), and D-dimer concentrations. PE was ruled out in patients with negative YEARS items and D-dimer less than 1000 ng/mL, or in patients with one or more YEARS items and D-dimer less than 500 ng/mL. Saw 14% decrease in CTA’s.

**DVT in calf veins** - Randomized, double blind placebo controlled, 260 patients with isolated calf DVT randomized to LMWH vs placebo, serial ultrasounds performed for 6 weeks, 4 pts in LMWH had progression or PE, versus 7 in placebo, no significant increase in progression (though underpowered to detect this), significant increase in bleeding 5 pts versus 0.

**DVT and thrombolytics** - 692 patients with proximal DVT randomized to anticoagulant therapy with or without catheter directed thrombolysis. At 2 years same rate of PTS, more severe in non-thrombolysis group, but quality of life the same. Increased risk of bleeding in thrombolysis group.

**Clinical Decision tool in Hospitalized Patients with Suspected PE** - Meta-analysis of 12 studies with 4000 inpatients with symptoms or signs suggesting acute PE. This study evaluated clinical decision tool using Modified Wells criteria (>4) plus D-dimer testing (>500), resulted in 99.7% sensitivity and 11% specificity. 8.4% of symptomatic patients will have a negative test. Imaging can be avoided in 1 in 12 symptomatic patients.
platelet party!

what's going on here?

platelet party!

why, I haven't had this much fun in years!

I think we're stuck.

no, seriously, we're stuck

platelet party.

platelet party!
References:
4) Shen NT et al. Timely use of probiotics in hospitalized adults prevents clostridium difficile infection: A systematic review with meta-regression analysis. Gastroenterology 2017 Feb 10; [e-pub].
18) Michele Sundar and Daniel Dressler. Can We Limit Imaging in Hospitalized Patients with Suspected PE? NEJM Journal watch. Jan 30 2018