Top Articles from 2017 – Part II

1. *Seymour CW, et al. Time to treatment and mortality during mandated emergency care for sepsis. N Engl J Med 2017.*
    - Study
        - Retrospective, observational, "Big DATA" study using NY DOH Sepsis database
        - 185 hospitals in the state of NY from April 2014 – June 2016
        - Comparison Groups: 49, 337 patients with severe sepsis or septic shock (Sepsis-2) who had a completed vs. did not complete the 3-hour sepsis bundle
        - 3-hour bundle included: Blood cultures before antibiotics, lactate measurement, administration of broad spectrum antibiotics
        - 6-hour bundle: 30 mL/kg fluid bolus, vasopressors for refractory hypotension, repeat lactic acid.
    - Outcomes:
        - Primary: In hospital mortality
        - Secondary: Odds ratio per hour delay of fluid, blood cultures, antibiotics
    - Results
        - Odds ratio of dying increased by 1.04 per hour of completing bundle ($p \leq 0.001$)
        - OR of dying with delayed fluid bolus p=0.21
        - OR per hour delay for blood cultures
    - **Take Home Points**
        - **Highlights that early source control is important**
        - **More rapid completion of a 3-hour bundle of sepsis care and rapid administration of antibiotics, but not rapid completion of an initial bolus of intravenous fluids, were associated with lower risk-adjusted in-hospital mortality**

2. *Andrews B, et al. Effect of an early resuscitation protocol on in-hospital mortality among adults with sepsis and hypotension: a randomized clinical trial. JAMA 2017; 318:1233-40.*
    - Background
        - Though mortality for sepsis remains unacceptably high, the use of protocols is reported to reduce mortality in developed countries
        - It is uncertain if sepsis protocols can improve mortality in resource limited settings

        - FEAST trial demonstrated increased mortality with IVF administration in a select African population
    - Objective
        - Determine if a resuscitation protocol implemented soon after ED presentation improved in-hospital mortality compared with usual care
    - Study
        - RCT in a single, university center in Zambia
        - Patients
            - Adults 18 y ears of age and older
            - Sepsis: suspected infection with 2 or more SIRS criteria
            - Hypotension (SBP <= 90 mm Hg or MAP <= 65 mm Hg)
        - Intervention
            - Initial 2 L of isotonic crystalloid within 1 hour of enrollment
            - Additional 2 L over subsequent 4 hours
            - Fluid monitored by JVP, RR, and SpO2
            - Dopamine gtt if MAP < 65 mm Hg after completion of initial 2L
            - Blood transfusion to maintain Hgb > 7 g/dL
        - Control
            - Treating clinicians determined IVF amount, vasopressors, and blood transfusions
        - Treating clinician determined antibiotic selection in all cases
        - Primary outcome: in-hospital mortality
    - Results
        - 212 patients
            - 107 in Intervention Group
            - 105 in Control Group
            - 89% of patients were HIV+
        - In-hospital mortality
            - Intervention Group: 48.1%
            - Control Group: 33%
            - NNH 7
        - Median hospital LOS lower in Intervention Group
        - Control Group
            - Received less IVFs (3.5L vs. 2.0L)
            - Only about 50% got any IVFs
            - <2% received a vasopressor
    - Limitations
        - Almost all patients HIV+ (89.5%)
        - Single center study in Zambia – limited generalizability
        - Also used convenience sampling to recruit patients
        - Dopamine used for vasopressor support
        - Patients in the Intervention Group got 2 L of IVFs in first hour

        - IVFs not titrated to hemodynamic parameters – fluids given until patient became tachypneic or hypoxemic
    - **Take Home Point**
        - **In primarily HIV+ patients a resource-limited setting, a sepsis protocol for early IVFs and vasopressors increased mortality compared with usual care.**

3. *Leisman D, et al. Delayed second dose antibiotics for patients admitted from the emergency department with sepsis: prevalence, risk factors, and outcomes. Crit Care Med. 2017.*
    - Background
        - Timely ABX administration is considered to be of particular importance
        - Current guidelines call for ABX administration within 60 minutes of "time-zero" for sepsis with organ dysfunction or septic shock
        - Timely administration of subsequent dosing has received far less attention
        - Delayed post-initial dosing could promote regrowth of resistant microbes
    - Objective
        - Quantify the frequency of delayed 2nd dose ABX administration in a sepsis and septic shock population
        - Identify risk factors for these delays in care
        - Conduct an exploratory analysis of patient outcomes - mortality, et c. associated with delays in 2nd dose administration
    - Study
        - Retrospective cohort study of patients admitted from the ED with sepsis or septic shock at a single, suburban, academic medical center in NY
        - Patients
            - Adult patients with sepsis and septic shock whose initial sepsis presentation occurred in the ED
            - Excluded
                - Less than 18 years old
                - Declined interventions
                - Advanced directives precluding bundle application
                - Directly admitted to hospice or palliative care
                - Not receiving initial ABX in the ED
                - Expiring or admitted to hospice before 2nd dose
                - Antibacterial therapy DCd after initial dose
        - Time of ABX admin
            - Determined recommended dosing intervals from Sanford's Guide to ABX therapy
            - Used recommended rather than as-ordered times for second dose
            - Stratified first to second dose time by recommended interval length; 6, 8, 12, or 24 hours

            - A priori defined major delay as greater than or equal to 25% of the recommended time interval
        - Also looked at whether the patient was admitted and boarding at the time of recommended 2nd dose
            - Care delays and poor outcomes well documented for boarding patients
        - Primary outcome: major delay;
        - Exploratory analysis: in-hospital mortality
    - Results
        - 828 patients included in study
        - 32.9% (272) had major delay in 2nd dose administration
            - Median delay was 79%
        - Boarding was an additional independent predictor of delay (OR 2.67)
        - Exploratory analysis: major delays associated with 1.6 times mortality and 2.4 times odds of mechanical ventilation
    - Limitations
        - Retrospective design
        - May preclude capture of variables that may be related to risk or outcomes from 2nd dose delay
        - Single site
        - Did not calculate illness severity scores
        - Did not record source control requirement
        - Did not record causative organisms
    - **Take Home Points**
        - **1 in 3 patients received their second dose with a delays greater than or equal to 25%**
        - **Major delays more common in those with 6-hr ABX dosing**
        - **Major delays more common in boarding patients**

4. *Fuller BM, et al. Lung-protective ventilation initiated in the emergency department (LOV_ED): A quasi-experimental, before-after trial. Ann Emerg Med 2017.*
    - Background
        - Approximately 250,000 patients receive MV in US EDs each year
        - Pulmonary complications (ARDS, VAP) develop in about 20% of ED patients receiving MV
        - Time spent in the ED is a vulnerable period
        - Recent evidence suggests that potentially injurious ventilator practices are common in the ED
        - Initial ventilator settings influence future delivery of LPV
    - Objective
        - Evaluate the effectiveness of an ED-based lung protective mechanical vent protocol on reducing the incidence of pulmonary complications
    - Study
        - Quasi-experimental, before-after study

        - Consisted of preintervention period (2009-2014), run-in period during which LPV was implemented as standard approach, and then intervention period (2014-2016
        - Single center, academic, tertiary medical center ED and ICU
        - Patients
            - Consecutively vented ED patients
            - Adults 18 years or older
            - Mechanical ventilation through an ETT
        - Interventions
            - After intubation, RT obtained accurate height with a tape measure
            - Tidal volume set to 6 ml/kg PBW (Range 6-8 ml/kg if no ARDS)
            - HOB elevation to > 30 degrees
            - Set PEEP to greater than or equal to 5 cm H2O (PEEP higher for elevated BMI)
            - Initiate FiO2 at 30-40% after intubation; titrated to maintain SpO2 90-95%; if hypoxic used PEEP table for FiO2/PEEP combination
            - Set RR to 20-30 bpm
            - Measure and limit plateau pressure < 30 cm H2O
            - All interventions performed by ED clinical staff
        - Primary Outcome
            - Composite of pulmonary complications after admission (ARDS and ventilator-associated conditions)
    - Results
        - 1705 patients
            - 1,192 in preintervention group
            - 513 in intervention group
        - Tidal volumes
            - Reduced by a median of 1.8 ml/kg PBW
            - LPV increased by 48.4% in ED
            - Also, ICU tidal volumes decreased by median of 1.1 ml/kg PBW and LPV increased by 30.7%
        - Primary outcome
            - Absolute risk reduction of 7.1% (aOR 0.47)
        - Increase in ventilator free days, ICU free days, and hospital free days
        - Absolute risk reduction for mortality of 14.5%
    - Limitations
        - Before and after study design (prone to temporal trends that may lead to independent changes in care)
        - Causation or association?
        - Single center study
        - Some imbalances between the 2 groups
    - **Take Home Point**
        - **ED ventilator setting make a difference!!**

5. *Stephens RJ, et al. Analgosedation practices and the impact of sedation depth on clinical outcomes among patients requiring mechanical ventilation in the ED: A cohort study. Chest. 2017.*
    - Background
        - Meds used to achieve analgosedation influence duration of MV and lengths of stay
        - Optimize sedation early to improve outcome
        - Little data exist regarding postinbutation analgosedation or sedation depth in MV ED patients
        - No study has examined the impact of ED-based sedation on clinically relevant outcomes
    - Objective
        - Characterize modern ED analgosedation practices
        - Assess the relationship between ED sedation depth and clinical outcomes
    - Study
        - Secondary analysis of prospective, observational cohort from single, tertiary, academic, medical center
        - Inclusion
            - Age greater than or equal to 18 years
            - Mechanical ventilation through an ETT
        - Exclusion
            - Death or DC of MV within 24 hours
            - Chronic MV
            - Presence of a trach
            - Transfer to another hospital
            - Neuro injury or sudden cardiac arrest as reason for MV
        - Measurements
            - Sedation depth - RASS
            - Defined deep sedation as RASS -3 to -5
            - In patients where no RASS was documented in the ED, used the first ICU RASS as a surrogate if measured within first 3 hours of ICU admit
        - Primary outcome: hospital mortality
        - Secondary outcomes: Ventilator, hospital, ICU free days
    - Results
        - 414 patients in final analysis
            - 317 intubated in the ED
            - Majority underwent RSI with succ or roc and etomidate or ketamine
        - Sedation practices
            - 354 received fentanyl (85.5%)
            - 254 received midazolam (61.4%)
            - 194 received propofol (46.9%)

        - 68 received ketamine (16.4%)
    - 59 patients (14.3%) received no analgesia and 63 (15.2) received no sedation while in the ED
    - Outcomes
        - Median ED RASS level was -3
        - Deep sedation observed in 64%
        - Primary outcome occurred in 60 patients (14.5%)
        - ED RASS was deeper in patients who died (-4) compared with those who survived (-3)
        - Deeper ED RASS associated with mortality (aOR 0.77; CI 0.54-0.94)
        - No difference between trauma or medical
- Limitations
    - Single center - may reflect local practices
    - Data obtained retrospectively
    - Sedation depth inconsistently recorded in the ED
- **Take Home Point**
    - **Deep sedation is common in mechanically ventilated ED patients and associated with worse outcome**