Pulmonary Artery Thrombosis during Acute Chest Syndrome in Sickle Cell Disease.

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To assess for the contribution and prevalence of Pulmonary artery thrombosis (PT) in the pathophysiology of acute chest syndrome (ACS) using multidetector computed tomography (MDCT) as a tool. It was a prospective study included 18 yr or > adults with sickle cell disease and ACS were enrolled. ACS was diagnosed based on (presence of dyspnea/chest pains), abnormal lung sounds and new pulmonary infiltrates. -Total of 125 pts were screened (4 pts were excluded) and 121 underwent MDCT for a total of 140 ACS episodes (total of 19MDCT were excluded); finally 103 pts were include for a total of 121 ACS episodes. MDCT Image analysis, were done with 24hrs of ACS presentation. A positive MDCT is that which shows a thrombus up to the segmental level or multiple thrombi at the segmental level. Lower extremity ultrasound was done to assess for DVTs (using a B mode venous compression) within 48hrs of positive MDCT.

Of the 121 MDCT s studied, 101 were identified as negative, whereas 20 were positive for pulmonary artery thrombosis making the prevalence of (PT) in the study 17%. D-Dimer concentrations were similar in both groups of (PT) positive and (PT) negative pts. Pts who were PT negative had a higher level lactate dehydrogenase at time of ACS compared to pts who were PT positive. They also had a lower bilirubin levels and higher platelet counts at ACS and also had a higher peak platelet count during hospital stay.

-Pt with Pulmonary artery thrombus had less need for antibiotic use and red blood cell transfusion but had similar demand for mechanical ventilation and hospital length of stay was significantly longer in patients with PT. All pts with PT were treated with anticoagulation for at least 6months. Recurrence was seen in one pt that was not treated for up to 6 months.

TAKE HOME POINT:
- Pulmonary artery thrombosis should be evaluated in sickle cell patients presenting with ACS particularly in those with higher platelet count and lower signs of hemolysis.

-D-Dimer test is often positive in ACS and should not be used as a screening tool.

-Lower extremity Doppler are usually negative in ACS which could suggest that the formation of clots is triggered off by local (likely from hypoxia which induces adherence of sickled cells to dysfunctional endothelium of pulmonary artery and its branches causing microvascular occlusion) rather than an embolic phenomenon.

-It is suggested that
patients who have pulmonary artery thrombosis should be treated with anticoagulation to avoid recurrence.

**Warfarin Dose Assessment Every 4 Weeks Versus Every 12 Weeks in Patients With Stable International Normalized Ratios: A Randomize**

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The recent availability of dabigatran and its benefit of lack of frequent blood monitoring has led many patients to be switched to this medication for ease of management. However, given the cost of this new drug, is there a way to safely decrease the monitoring associated with coumadin use for those who may not be able to afford dabigatran? The above study addresses the question of safety of increasing the time interval between INR checks. Current ACCP recommendations call for a maximal interval of 4 weeks between PT measurements. The authors performed a non-inferiority randomized controlled trial comparing 4 week versus 12 week interval of PT monitoring over a period of 1 year. They evaluated a total of 226 patients at a single center whose coumadin dose had been stable for the past 6 months. All patients had PT measurements checked every 4 weeks, however, sham results were given to the physician managing the patient. Sham results ranged from 1.8 to 3.5 for those with goal INR between 2-3 and 2.0 to 4.0 for those with goals of 2.5 to 3.5. None of these sham results resulted in a change in coumadin dosing. A physician reviewed all of the INR results and if less than 1.5 or greater than 4.5, true results were given to the treating physician. The main endpoint was time within the therapeutic range. For those with INR checks every 4 weeks, mean time in therapeutic range was 74.1% as compared to 71.6% for those checked every 12 weeks which was within the predetermined non-inferiority margin. Secondary outcomes included, extreme INRs requiring changes in maintenance dose, major and minor bleeding events, deaths, and thromboembolic events. The number of patients with at least one change to their maintenance dosing was noted to be significantly greater in the 4 week group, otherwise, there were no significant differences in secondary outcomes. While the study appears to be good news for the veins of those patients on coumadin, it should be noted, that even the 12 week patients received follow up call every 4 weeks to provide them with their sham results and to let them know there would be no adjustment in dosage. During these calls, they were reminded about important factors for INR stability including questions regarding new medications and changes in overall health status. Also, given the small size of the study and its taking place at a single center, the results should be viewed cautiously. The study also lacked enough power to accurately comment on clinical outcomes, although no significant differences were seen. Overall, as additional studies look at increasing the interval for INR measurements in those requiring chronic anticoagulation (remember
these patients had stable coumadin dosing for AT LEAST 6 months), the use of coumadin may become more palatable to both physicians and patients.

**Screening by Chest Radiograph and Lung Cancer Mortality: The Prostate, Lung, Colorectal, and Ovarian (PLCO) Randomized Trial**


This article adds to the multiple prior studies looking to evaluate various methods for lung cancer screening. Lung cancer, as the number one cause of cancer death, is a major target for screening/early detection. Studies thus far have failed to demonstrate conclusive evidence in support of screening. This study is randomized controlled trial that is part of the larger Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial. It compared annual posteroanterior chest radiograph with usual care. The study was large, total of 154,901 participants aged between 55 and 74 that were followed for 13 years. Patients randomized to the intervention group underwent annual screening chest radiograph at baseline and annually during the subsequent 3 years. As this was a large, screening trial for multiple cancers, there was no requirement for prior or current tobacco use. So, in effect, this study is focusing on likely too broad of population, as most of us would not consider screening in our non-smoking patients. The authors realized this as well and did a sub analysis focusing on the patients with similar characteristics as patients in the National Lung Screening Trial – i.e. those with at least a 30 pack-year history of smoking who were either actively smoking or had quit within the last 15 years. The authors felt that this study could be viewed in conjunction with the NSLT study (which demonstrated a 20% reduction in lung cancer mortality with CT screening as compared to CXR alone) in that it could serve as the “control” for the NSLT since there was not a usual care arm. Not surprisingly, the results of the study demonstrated that there was no effect on lung cancer mortality with annual chest radiograph screening over a period of 4 years including the subset analysis of those with a 30+ pack-year history. However, this study taken in conjunction with the NSLT, may add further weight to the results from the NSLT, or at least provide a counter to the critics who felt the NSLT was significantly weakened from lack of a “true” control group.

“Annual CXR not a good method for lung cancer screening”

**Burnout in ICU Caregivers: A Multicenter Study of Factors Associated to Centers.**


Currently rotating on lung transplant has forced this pulmonary fellow to consider another kind of BOS – Burnout syndrome, characterized by emotional instability, feelings of futility, quitting one’s job, irritability, insomnia, and depression. It affects almost half of
all physicians and nurses working in ICUs. Merlani et al performed a prospective multicenter observational study in predominantly German-speaking Swiss hospitals to identify important risk factors for burnout in an individual. Previously, these authors and others had identified that repeated stress leads to burnout. One of the aims of the study was to identify modifiable targets. Factors associated with increased risk for high stress were university hospitals, the number of beds per unit, and a higher proportion of female physicians. The study involved questionnaires that avoided central tendency bias by forcing to choose a frequency of a symptoms (very often, often, sometimes, never). Anonymous self-administered questionnaires collected from physicians, nurses, nurse-assistants between March 2006 to April 2007 revealed that being a nurse-assistant, male, under age 40, and without children are associated with a high risk for burnout. These are not easily modifiable risk factors. The number of years of experience working in an ICU was inversely related with burnout. Exceedingly interesting was the tantalizing revelation was that a high proportion of female nurses on the ICU team actually decreased individual risk for high burnout (for both males and females)! This raises many interesting questions about how females are biologically wired and how they are socialized compared to their male counterparts. Moreover, it creates the opportunity to explore how burnout is related to the ICU caregiver’s ability to handle stress and his or her capacity for empathy. Ironically, female caregivers experienced more stress overall. Does this mean that the men did not openly respond on their questionnaires? Are there cultural differences between the Swiss/German/Italian respondents? The results should be confirmed in a larger multinational study before hospitals go on a hiring spree of female nurses.

Statins have anti-inflammatory and immunomodulatory effects and thus may be a useful additional therapy in critically ill patients. Previous studies have shown that the use of statins was associated with a decreased mortality rate and also significantly reduced risk of fatal pneumonia. These studies, however, were observational and included patients that had already been on chronic statin therapy. In the current study, the authors evaluated the effect of adding a statin at the time of admission on the frequency of ventilator-associated pneumonia. The study took place in two hospitals in Greece and included patients that were older than 18 years of age, mechanically ventilated for more than 48 hours and in the ICU for more than 48 hours. Patients were excluded if they were already on statins prior to

Effect of Pravastatin on the frequency of ventilator-associated pneumonia and on intensive care unit mortality: Open-label, randomized study.


Critical Care Medicine is reviewed by Emily Gilbert
Acute lung injury (ALI) is caused by injury to the alveolar-capillary membrane from immune cell migration. This leads to platelet activation, enhanced thromboxane A2 production and platelet aggregation. Previous studies have shown that treatment with aspirin (ASA) prior to lung injury can protect against acid-induced ALI and enhance resolution of ALI by promoting generation of anti-inflammatory lipids. A prior study performed by the authors of this paper shows that prehospitalization ASA led to a reduced rate of ALI but this was done in a single center with a homogeneous study population. Therefore, the authors looked again at prehospital use of ASA and the risk of ALI but this time, in 20 different American hospitals and 2 Turkish hospitals, making the study population much more diverse. This was a prospective cohort study in 19 of the hospitals and retrospective in 3 hospitals. Patients were included if they were admitted to the hospital, over the age of 18 and had at least one risk factor for ALI: aspiration, pneumonia, sepsis, shock, pancreatitis or high risk trauma. Surgical patients and patients who had ALI/ARDS at the time of admission were excluded. The exposure of interest was ASA therapy at the time of admission and the primary outcome was development of ALI or ARDS during hospitalization. The authors admit that observational studies risk unequal distribution of possible
confounding factors between treatment groups because random assignment is not used. Therefore, they performed a propensity score analysis to match ASA-treated and nontreated patients. They enrolled 3,855 patients (976 ASA users and 2,879 non-ASA users). Of the 3,855 patients, 240 patients developed ALI or ARDS leaving 3,615 patients without ALI/ARDS. After isolating all confounding factors and propensity score matching, they found that prehospital ASA use does NOT decrease the risk of developing ALI or ARDS (p = 0.055).

**Bottom Line:** The use of ASA prior to hospitalization does not decrease the risk for development of ALI or ARDS.

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**Beneficial effects of humidified high flow nasal oxygen in critical care patients: a prospective pilot study.**


The purpose of this study is to evaluate the efficiency, safety of high flow nasal cannula (HFNC) oxygen in ICU patients with acute respiratory failure. A total of 38 patients from a single ICU were included. All had respiratory failure requiring over 9l/min of oxygen to achieve an SpO2 over 92%, or persistent signs of distress exhibited by respiratory rate over 25 bpm, thoracoabdominal asynchrony and supraclavicular retractions. The mean age was 54.2 ± 15.4 years and the main cause of respiratory failure was pneumonia (15/38, 39%). HFNC, delivered with optiflow device, set with a mean FiO2 of 88 ± 16% with flow of 49 ± 9l/min. It was associated with a significant reduction in respiratory rate, heart rate, dyspnea score, suprclavicular retraction and thoracoabdominal asynchrony as well as improvement in pulse oximetry. ABGs drawn at 1 and 24hr after its application showed significantly improved PaO2/FiO2 ratio, and no difference in pH and PaCO2. A total of 9 patients did require secondary intubation and mechanical ventilation, done at a median of 4 hr after beginning HFNC. This subset of patients on average had a higher respiratory rate and lower SpO2 after beginning the HFNC. In conclusion, this study suggests that HFNC can give an early and sustained effect on clinical parameters and oxygenation for respiratory failure and perhaps may have helped some patients avoid mechanical ventilation. The main limitation of this study is that it is not a randomized controlled study. I would also be concerned that this approach may lead to delayed intubation in patients that need it and in effect increase their mortality. So, like with noninvasive mechanical ventilation, these patients need to be monitored very closely in the event that they may require emergent intubation. Overall it still seems like a reasonable intervention especially in our DNR patients or immunosuppressed patients where we may prefer to avoid mechanical ventilation.
Time course of organ failure in patients with septic shock treated with hydrocortisone: results of the Corticus study


The majority of studies on sepsis use 28-day mortality as the primary endpoint, including those looking at the role of corticosteroids. This study aims to evaluate morbidity and organ failure-free days in addition to the mortality data in those patients treated with hydrocortisone. This is a multicenter, randomized, double-blind, placebo-controlled study where patients over the age of 18 with infection, shock, and organ dysfunction were randomized to receive placebo or the study drug (hydrocortisone 50mg every 6 hours for 5 days then tapered). All patients also received a corticotrophin (ACTH) test and categorized as responded or non-responders (cortisol increase $<9 \text{ g/dl}$). A total of 499 patients were analyzed, with 251 in the hydrocortisone group and 248 in the placebo group. The 28-day mortality between the hydrocortisone and placebo group overall was not significantly different (34.3 vs 31.5%), nor was it different when responders and non-responders were looked at separately. The authors then investigated the rate of decrease in SOFA scores for each organ system. They found significantly faster decrease in SOFA score for the hydrocortisone group for the cardiovascular and liver components ($p<0.0001$). The patients treated with hydrocortisone had a higher mean number of vasopressor-free days ($2.5 + 2.4 \text{ vs } 1.4 + 2.4$). In regards to renal failure, at day 28 60.5% had reversal of this in hydrocortisone group compared to 44.3% in placebo group ($p=0.039$). There was no significant difference between groups for coagulation, CNS, or pulmonary components of SOFA. There was also no significant difference for ventilator-free days during first 7 days. This study like so many before it does not verify any improvement in mortality, but it may lead to faster resolution of liver dysfunction, renal failure and shock. However, previous studies have shown that the faster reversal of shock with hydrocortisone in those patients responsive to fluids and vasopressors was associated with more superinfections and recurrence of new sepsis or septic shock. Therefore, it still cannot be recommended in these patients and it is advisable to stick to the current guidelines which recommend its use for patients with refractory septic shock.

Randomized controlled trial of high concentration versus titrated oxygen therapy in severe exacerbations of asthma.

Thorax November 2011

The authors set out to demonstrate that much like in COPD, excessive Oxygen leads to an increase in CO2. They wanted to enroll a total of 150 subjects, 75 into a group that received 8l/min of O2 through a venti mask, designed to deliver an FiO2 between 0.4 and 0.78, and 75 into a group that would only receive oxygen if their saturation was less than 92% on RA. Oxygen would be titrated every 5 minutes to effect a sat between 93 and 95%. Inclusion criteria were: age 18-65, previous dx of asthma, history consistent w/ an acute exacerbation of asthma and an FEV1 <50% of predicted. Exclusion criteria: diagnosis of COPD or other disorders associated w/ hypercapnic respiratory failure, inability to speak, inability to give informed consent, or being unconscious. The primary
outcome variable was the proportion of patients with an increase in PtCO2 of ≥4mm Hg

The study was only able to enroll 53 patients in each group over 2.5 yrs which, according to the paper, provided sufficient statistical power to determine clinically relevant differences between the two treatment groups. The proportions of patients w/ an increase in PtCO2 of ≥4mm Hg at 60 min as well as an overall increase of ≥8mm Hg were statistically significantly greater in the high concentration group. 10 patients developed hypercapnia (PtCO2 > 45 mm Hg). All of them came from the high oxygen concentration group. The study indicates that much like in COPD patients who have lost their hypercapnic drive to breathe Asthmatics in the throes of an acute exacerbation are not helped by hyperoxia and in many cases can be harmed by it.

Is age-related decline in lean mass and physical accelerated by obstructive lung disease or smoking?
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A longitudinal study of 3075 well-functioning men and women between 70 and 79 was begun in 1997/8 and continued for eight years. Patients were assessed annually. The patients with Obstructive Lung Disease (OLD) were compared to smoking controls, formerly-smoking controls, and never smoking controls. Variables examined were: Lung Function checked at baseline as well as years 5 and 8, Body composition checked annually for the first six years and at year eight, Muscle Function and mobility was checked checked in years 1, 2, 4, 6, and 8.

The baseline characteristics showed that Never smokers had statistically significantly better lung function as well as lower levels of systemic inflammatory markers compared to patients w/ OLD.

The results showed that in patients with OLD and the smoking controls there were lower measures of body composition and physical functioning compared w/ never smokers. However the rate of decline in weight, lean mass, fat mass, and strength observed over the study period were comparable between the groups.

The authors felt that a common insult related to smoking must have occurred earlier in life that did not uniformly persist into old age.