Obesity Is a Determinant of Asthma Control Independent of Inflammation and Lung Mechanics

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Previous studies have shown that obese persons have an increased prevalence of asthma. In addition, obese asthmatics have been shown to have worse asthma control as evaluated by the Asthma Control Questionnaire. The cause of this worse control has yet to be fully elucidated. Studies have looked at airway obstruction, airway hyperresponsiveness, and eosinophilic airway inflammation, but have not been able to demonstrate any significant differences in these areas between obese and non-obese asthmatics.

It is known that obesity decreases functional residual capacity which can decrease airway caliber and increase airway resistance. Whether or not the altered lung mechanics in obesity could be the culprit in worse asthma control, rather than obesity leading to changes in asthma pathophysiology, has yet to be fully teased out.

The authors hypothesize that obesity’s effect on asthma control is independent of spirometry, airway inflammation, and airway hyperresponsiveness, and as such, is not modifiable by high dose inhaled corticosteroid treatment. The further hypothesize that any residual symptoms present are due to altered lung mechanics.

Subjects were tested on two occasions: at baseline and following 12 weeks of treatment with ICS +/- LABA. At each of the two visits, subjects did the following:

- Asthma control questionnaire
- Exhaled nitric oxide – served as a marker of inflammation
- Forced oscillation technique - to measure respiratory system
- Spirometry and plethysmography
- Methacholine bronchial provocation test – to determine airway hyperresponsiveness-defined by methacholine causing a 20% fall in FEV1 (range of dose of methacholine from 0.05 to 6.1)

The authors feel that they were able to successfully isolate the effects of obesity on asthma control by targeting airway inflammation with high dose inhaled corticosteroids for a period of three months. The fact that airway hyperresponsiveness, spirometry, and inflammatory markers all improved with treatment across all subgroups, and were no longer independent predictors of ACQ-5 support this. After treatment, the multivariate analysis demonstrated only BMI and resistance as independent predictors. Because resistance was a separate variable, the authors feel that the effect of obesity was not related to reduced airway caliber. The exact cause of obesity's
Obesity perse, may be a determinant for asthma control independent of its effect on lung mechanics.

Effect was not determined. However, as mentioned, the effect of obesity was independent of airway resistance. They also felt that because reactance at the frequency tested is a reflection of compliance and were not deemed to be an independent predictor of asthma control, that the effect of obesity was not related to lung mechanics.

This study has many weaknesses, but does address most of the common measures of airway hyperresponsiveness, airway inflammation, and airflow in its evaluation. Their data does support the idea of obesity as an independent risk factor of asthma control, but does not shed any light as to possible mechanisms. They suggest that clinicians take into account obesity – related factors when dealing with patients who are not fully responding to ICS, but do not really suggest treatment modalities other than weight loss. Further prospective studies addressing possible confounding factors such as undiagnosed sleep apnea and deconditioning should be addressed.

Grading the Severity of Obstruction in Mixed Obstructive-Restrictive Lung Disease

Current ATS/ERS guidelines recommend the use of FEV1% predicted to determine the grading of severity of obstruction during the evaluation of pulmonary function tests. In straightforward obstructive disease, this works well and provides an accurate assessment of the degree of obstruction. However, if a patient has concomitant restrictive disease, thus causing an additional decrease in their FEV1% predicted, will this significantly overestimate their degree of obstruction?

Gardner et al decided to further investigate. They reviewed a large PFT database and identified patients who met criteria for both restrictive lung disease (TLC <80% predicted) as well as and FEV1/FVC less than the lower limit of normal – a total of 199 patients over a ~ 6 year period. They initially graded the degree of obstruction using current ATS/ERS guidelines i.e. based solely on FEV1% predicted. They subsequently adjusted the FEV1% predicted by dividing it by the TLC % predicted. After the adjustment, they re-graded the degree of obstruction. To assess if the adjusted FEV1 was a more accurate reflection of the degree of obstruction, the adjusted and unadjusted values were correlated with the degree of air trapping (RV/TLC).

Their results were notable for several points. First of all, the grading using the two different FEV1 values was significantly different. The unadjusted FEV1% predicted resulted in 76% of patients classified as having severe or very severe obstructive disease, whereas with the adjusted values only 33% of patients were characterized as such. Also, correlation between FEV1 and RV/TLC was significantly greater when the adjusted value was used suggesting that the adjusted value is a better reflection of true obstructive physiology.
This study highlights an interesting problem that is seen not uncommonly in our patients. I think that their proposed correction factor is a simple and quick method to better estimate the functional obstruction of patients with combination lung disorders. However, I disagree that it will significantly change their management. Most of us recognize when our patient has both restrictive and obstructive disease and thus take the FEV1% predicted value with a “grain of salt”. Given that, we do not necessarily “over treat” that number as the authors suggest. Rather, I think we use the FEV1% predicted as one part in the larger picture of our patients' management and place as much, if not more, weight on the functionality and clinical status of our patients. Thus, this article would not likely significantly change my practice, but may more accurately allow me to assess how much of my patients symptoms may be due to obstruction versus restrictive disease.

Randomized, Placebo-controlled Clinical Trial of an Aerosolized β2-Agonist for Treatment of Acute Lung Injury

NHLBI network

The authors discuss that resolution of pulmonary edema is essential to recovery from ALI. They mention that in ex vivo lungs the rate of alveolar fluid clearance has been doubled by treatment with cyclic AMP Beta-2 Agonist Receptor. This was their basis for initiating the trial. They screened 2688 and enrolled 282 into two groups: albuterol and saline. The albuterol dose was 5mg administered every 4 hrs for 10 days. If the pt had persistent tachycardia related to the albuterol the dose could be halved. The primary end point was the number of ventilator free days up to day 28. They were not able to measure albuterol levels in the distal airspaces. Instead they checked plasma levels 15 minutes after administration. The study was stopped secondary to futility as the difference in number of ventilator free days in the albuterol group was -2.2, lower than the futility boundary of -0.4. The authors explanations for why the study was negative include: inadequate delivery of the albuterol to the alveoli; inability of the injured epithelium to respond to the albuterol; the Beta-2 receptors may have been down-regulated.

Noninvasive Ventilation and Weaning in Patients with Chronic Hypercapnic Respiratory failure


Noninvasive ventilation (NIV) has the advantage of avoiding mechanical ventilation and its associated complications in select patients, particularly those with hypercapnic respiratory failure. The authors of this study sought to determine whether or not NIV
could be used to facilitate early extubation in patients with chronic respiratory failure. The study was performed in 13 ICUs in France and Tunisia in centers experienced with NIV, and in 208 patients with COPD (70%), asthma, obesity-hypoventilation syndrome, or other restrictive processes. Patients were included in the study if they tolerated a T-piece trial for anywhere between 5 min and two hours. Patients were subsequently extubated and placed into one of 3 groups – conventional invasive weaning – pressure support weans/t-piece trials until the patient was deemed ready for extubation by traditional criteria, - oxygen therapy – extubation (even if tolerated SBT for only 5 minutes) followed by supplemental oxygen therapy, or – NIV – applied for 6 hours and then intermittently as tolerated. All patients were subsequently eligible for NIV or reintubation as deemed necessary for 'rescue', clinically. The authors report that while there was no overall difference between the groups in terms of probability of reintubation, the NIV group was significantly less susceptible to post extubation acute respiratory failure, reintubation, or death.

There were numerous problems with this study, which should not change our practice. In particular, patients were extubated after failing a spontaneous breathing trial. One arm of these patients was provided only supplemental oxygen. Understandably, the purpose of this study was to examine the effects of NIV on early extubation, but it seems that patients extubated prematurely and receiving oxygen therapy only, were put at unnecessary risk. Furthermore, the reported rate of reintubation in the traditionally weaned group was 30% - above normal expected rates. Thus, any subsequent comparisons between the 3 arms must be interpreted with caution. It is difficult to draw a firm conclusion from this study, except that its findings are consistent with previous studies demonstrating some benefit to NIV in patients with hypercapnic respiratory failure.

Detection of Pulmonary Emboli with 99mTc-Labeled Anti-D-dimer (DI80B3) Fab' Fragments (Thromboview).


CT scan and V/Q scan are the current mainstays for detection of pulmonary embolism (PE). Both scans rely on absence of perfusion to make a diagnosis. The authors describe a new technique involving single photon emission computerized tomography (SPECT) to detect a positive PE signal. The test is a radionuclide test, performed by injecting one dose of radiolabeled antibody fragments into the subject, followed by a baseline SPECT scan, and a repeat SPECT scan 2.5 hours later. During the interval, the radiolabeled antibodies bind to d-dimer regions of fibrin in a clot. These antibodies subsequently 'light up'
on a SPECT scan. The authors performed a prospective trial in order to determine the sensitivity and specificity of this novel test (compared to CT scan).

Patients enrolled in the study had either a positive d-dimer test, or moderate to high clinical probability of PE. They underwent both a CT PE protocol, as well as radiolabeled SPECT scan. All SPECT images were interpreted by three nuclear medicine specialists at different centers. The physicians were blinded to CT results as well as patient clinical information. Of note, the kappa for agreement in interpretation between the 3 reviewers was a modest 0.4–0.6. 5 of the 52 SPECTs performed were ‘un evaluable’. The sensitivity of the SPECT scan was 76.2%, with a PPV of 88.9%. Specificity was 90.5% with a NPV of 79.2%. Likelihood ration of a positive scan was 8.02, and likelihood ratio of a negative scan was 0.26. In terms of safety, the authors attributed a transient elevation in hepatic enzymes to 5 of the 52 subjects. Subjects were asymptomatic, and lab values returned to baseline at 30 day follow-up.

Radiolabeled SPECT is a novel method for PE detection, which demonstrates promise and warrants continued study. It appears safe, and it has the potential for a place beyond that of V/Q scans, and possibly alongside CT scans as a reliable diagnostic modality for PEs. Although, it does not carry the radiation or contrast burden of CT scans, further study is required in those with renal failure (the radionuclide is partially excreted through the kidneys). In addition, the test itself takes 20 minutes to perform, and the time delay required for binding and interpretation may be an issue in certain clinical scenarios. Finally, the relatively moderate agreement between the 3 trained interpreters reading a limited number of studies suggests that the above noted statistics may change significantly - for better or worse in larger trials. Widespread use and implementation are still several years away, and will require significant experience and training.

This study investigates BIBF 1120, a tyrosine kinase inhibitor, as a potential treatment option for Idiopathic Pulmonary Fibrosis. Targets of this drug include platelet-derived growth factor receptors, vascular endothelial growth factor receptors, and fibroblast growth factor receptors; these have all been shown to be involved in the development of pulmonary fibrosis. This was a Phase 2 trial investigating BIBF 1120. Patients 40 years or older with IPF consistent with ATS/ERS criteria were eligible; they also had to have a FVC 50% or more of predicted, a DLCO that was 30-79% predicted, and a PO2 of 55mmHg or greater (50mgHg if they lived at altitude of > 1500 meters). Concomitant use of up to 15mg of prednisone was allowed as long as the dose was stable. Patients were assigned randomly to either placebo, or increasing doses of BIBF 1120: 50mg daily, 50mg bid, 100mg bid, or 150mg bid. Medication was administered for 52 weeks. A total of 428 patients were enrolled with 85-86 patients in each arm (1 placebo arm and 4 treatment arms). The primary endpoint, annual rate of decline in FVC, trended towards an improvement in the 150mg bid group when compared to placebo (0.06L vs 0.19L, p=0.06). Several
secondary end points did demonstrate statistically significant improvements in the 150mg bid treatment arm when compared to placebo; these included number of patients with a 10% or 200ml decrease in FVC (20 patients in the 150mg bid treatment arm (23.8%) vs 37 patients in placebo arm(44%), p=0.04); proportion of patients with more than a 4% decrease in resting SpO2 (3.6% vs 11.0%, p=0.03); as well as incidence of acute exacerbations (2.4 vs 15.7 per 100 patient-years, p=0.02).

Overall adverse events were similar in both groups. There were no significant differences in DLCO or 6 minute walk amongst groups. Overall the data appears promising for BIBF 1120, as it appears that this medication may be successful in slowing the rate of progression of IPF. At the very least this warrants further studies.

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**Placebo-Controlled Trial of Cytisine for Smoking Cessation.**


Of the world’s 1 billion smokers, over 2/3 live in countries with an average household income of less than $200. Most forms of smoking cessation is not economically feasible in this situation. Cytisine (a partial agonist of the α4β2 subtype of the nicotinic acetylcholine receptor) has been used for many years in countries such as Poland for smoking cessation due to its favorable pricing point, but there has never been an RCT evaluating efficacy. This study was conducted at a smoking cessation clinic in Warsaw, Poland. Eligible patients were adults who smoked 10 or more cigarettes per day and were willing to quit. Patients with current psychiatric disorders, arterial hypertension, or advanced atherosclerosis were excluded. 740 patients were randomized either to placebo or the treatment regimen (1.5mg tablets; 6 tablets the first 3 days, 5 tablets for 9 days, 4 tablets for four days, and 2 tablets for 5 days. The target quit date was day 5. There were clinic visits at initial enrollment, 4 weeks after the quit date, and 6 and 12 months after the quit date. Abstinence was characterized by an exhaled carbon monoxide concentration of less than 10ppm. If patients were lost to followup, it was assumed that they had resumed smoking. For the primary outcome, abstinence at 12 months, there was significantly greater success in the treatment group vs the placebo group (8.4% vs 2.4%, p<0.001). The rate of drug discontinuation was similar, though there was a higher rate of all GI adverse events in the cytosine group. There was no difference in the rate of serious adverse events. This study does demonstrate that cytisine may be effective for smoking cessation. The low overall rate of abstinence likely is related to the lack of other forms of support such as counseling or behavioral modification. This may not be as applicable here in the US, but should be considered as a low cost alternative for smoking cessation where available.
Biochemical markers of cardiac dysfunction predict mortality in acute exacerbations of COPD

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Cardiovascular disease is often associated with a poorer prognosis in COPD exacerbations. This prospective study looked at the association between NT-BNP and troponin T levels and mortality in consecutive patients admitted to a New Zealand hospital with COPD exacerbations. Patients were excluded if they had another respiratory illness such as asthma or pneumonia or if they were diagnosed with coronary ischemia. NT-BNP and troponin T were measured within 24 hours of admission. Primary and secondary end points were 30-day mortality and 30-day to 1-year mortality respectively. The study included 250 patients with COPD exacerbation admitted to the hospital over a 1-year period. The 30-day and 1-year mortality was 8.5% and 18.5% respectively. The study found that elevated NT-proBNP levels >220pmol/L predicted 30-day mortality from a COPD exacerbation with an odds ratio of 9.0 but did not predict 1-year mortality. Troponin T levels >0.03ug/L predicted 30-day mortality with an odds ratio of 6.3 but again, did not predict 1-year mortality. The Kaplan-Meier survival curve stratified according to cardiac biomarker status showed the patients with both NT-proBNP and troponin T elevation had the highest risk of 30-day mortality (15-fold higher mortality than those with normal values for both markers). One notable weakness of the study was that clinicians were not blinded to the results of the biomarkers and thus, treatment is likely to have been affected by these results. Cardiac failure was found to be the leading cause of death in a recent autopsy series of consecutive patients who died of acute COPD exacerbation. Therefore, patients admitted to the hospital with COPD exacerbation and found to have elevated cardiac biomarkers but no clinical evidence of acute cardiac dysfunction should likely be treated differently than those with negative cardiac markers. Future research is needed on this subject.

Bottom line: Elevated troponin T and NT-proBNP levels strongly predict 30-day mortality in patients with acute exacerbations of COPD.

The impact of traffic air pollution on bronchiolitis obliterans syndrome and mortality after lung transplantation

Tim S Nawrot et al.

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Bronchiolitis obliterans syndrome (BOS) is the most important cause of late mortality after lung transplantation (25-35%). It is known to be triggered by HLA mismatch, acute rejection, age, CMV status, colonization by Pseudomonas and GERD. These factors induce airway inflammation via the innate immune
system which is also activated by air pollution. The authors questioned whether air pollution could be another risk factor for BOS and therefore looked at the association between proximity of the patients’ homes to major roads and the risk of BOS and death. The study included 281 patients who had a lung transplant between 1997 and 2008 in Belgium. Patients were excluded if they lived outside of Belgium, if BOS could not be diagnosed or if they were part of a study where azithromycin was started 1 month after lung transplantation. BOS and death were the main outcomes. Distances between homes and major roads (either a highway or major local road) was calculated and used a cut-off point of <171 meters (or 1/10 mile) based on the lowest tertile of distances between home and nearest major road. To assess background air pollution, they calculated daily mean values for particulate matter with diameter <10um (PM$_{10}$) and NO2 at each patient’s home for the year 2002. Median follow-up for the 281 patients was 2.7 years; 41% of the patients developed BOS and 21% died. Of the patients living <171 meters from a major road, 51% developed BOS verses 35% who lived >171 meters from a major road (p=0.01). Mortality was also higher in those living <171 meters from a major road (28% vs. 18%, p=0.04). The risk of dying after lung transplantation decreased by 31% for each 10-fold increase in distance between home and a major road. Hazard ratios increased after adjustment for age, gender, acute rejection rate, CMV infections and the average background level of PM$_{10}$. BAL neutrophils, BAL IL-16 and plasma CRP were inversely associated with the distance of the home to the nearest major road. Weaknesses of this study included the inability to truly measure the exposure variable (air pollution). Also, they admit that Belgium is a small country with a high population density and thus has only a few areas of low pollution. But they did see a decline in inflammatory markers, rates of BOS and death as the distance between the home and a major road increased and they did adjust for potential confounders.

**Bottom Line:** Exposure to traffic-related air pollution is a risk factor for the development of BOS and death following lung transplantation.

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**Short-term effects of combining upright and prone position in patients with ARDS: a prospective randomized study**

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Improved oxygenation in ARDS patients placed in the prone position has been demonstrated previously by aerating the atelectatic areas and avoiding over-ventilation/barotraumas of the non-dependent parts, although the mechanisms are neither quite that clear nor simple. There are hypothesized improvements in V/Q mismatch, possibly compliance, and decreasing PaCO2 that in turn improve oxygenation. In this prospective randomized cross-over study in an Austrian hospital, 20 patients were randomized into two matched groups. Exclusions were mostly hemodynamically unstable patients (including PaO2/FiO2 < 60 among other variables). There were
more females and the median age 67, PaO2/FiO2 138, PEEP 12, days in the ICU, days of mechanical ventilation, and days of ARDS were all 2, FiO2 70%, SAPS II scores 57. The patients were all in pressure-control mode, the median PIP was 30 (minimum pressure to achieve 6cc/kg IBW). One patient had extrapulmonary ARDS (vasculitis) and the majority had pneumonias as the major diagnoses. If patients were deemed candidates for prone positioning, they were included. Adding the upright position was easy to achieve. To exclude the possibility that any improvement is time-dependent, the sequence of positioning was randomized; moreover, one group had worsening of oxygenation almost immediately after reversing the upright position seemingly indicating time-independence. Baseline measurements were obtained, then Group A was proned for 2 hours, then proned and uprighted for 2 hours (Group B was the opposite) followed by either prone alone for 4 hours in Group A or prone+upright for 4 hours in Group B. PaO2/FiO2 was measured every hour, as that was the primary endpoint. There were 14 responders with PaO2/FiO2 improving most in the combined prone+upright position (going up from 135 supine at baseline up to 191 with p<0.05). Significant differences in PaCO2 or lung compliance were not detected during the brief observation period of this study. The upright prone position described is 20-30 degrees (in reverse Trendelenberg). The other two major studies showing improved oxygenation in ALI or ARDS patients had patients closer to 45 degrees of head elevation. It should be noted that even in this seemingly small number of patients, individual responses varied greatly, so strict observation is mandatory. The authors conclude that combining upright with the prone position can improve oxygenation. What they only very briefly mention, however, is that improved oxygenation has not been shown to improve outcome (but a decrease in PaCO2 in prone position has been associated with higher survival rates).

Red blood cell transfusion and outcomes in patients with acute lung injury, sepsis and shock

Elizabeth C Parsons et al. NLBI ARDS Network

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Blood transfusions are quite common in the ICU. Does it improve outcomes beyond the first 6 hours as previously shown? Prior studies suggest more harm than benefit, often leading to infections, ALI, and death. Many physicians do not follow the Surviving Sepsis Campaign from 2004 within the first 6 hours of admission to the ICU. Patients are
often transfused in the name of better O2 delivery. The authors of this article performed secondary analysis in 85 patients from the prior ARDSNet Fluid and Catheter Treatment Trial (FACTT from 2000-2005) who had diagnosed shock and sepsis/ALI risk factor within 24 hrs of admit to look at RBC transfusion’s association with adjusted 28-day mortality (and secondary endpoints of 90-day mortality, ventilator free days). The authors also tried to see if certain physiologic criteria would help identify patients who are most likely to benefit from transfusion. The patients had Hgb< 10.2 g/dL; MVO2 < 70%, CVP > 8, MAP < 65 and on pressors. As in any large long study, there was much missing data that was filled in. Multivariate regression was used to assess for any independent association between RBC transfusion and 28-day mortality. The study failed to show benefit or harm in transfusing patients with ALI and severe sepsis: there was no difference in the odds ratio for death or statistically significant difference in ventilator free days. Besides incomplete data, the study was limited by not knowing which indications clinicians were using to transfuse or how fresh the transfused blood was, in addition to the authors’ conclusions that larger cohorts and accounting for other modifiers would be important in future studies.

CPAP for acute cardiogenic pulmonary edema from out-of-hospital to cardiac intensive care unit: a randomised multicentre study.


**Rationale:** To demonstrate the effectiveness of CPAP in the management of cardiogenic pulmonary edema leading to prevention of intubation and decrease in symptoms.

This was a multi-center, prospective randomised, open and intention to treat clinical trial performed in 10 hospital centers with cardiac ICUs as well as mobile emergency medical service. The primary end point which was assessed within 48 hrs was death, necessity of intubation and presence of inclusion criteria. Secondary endpoints included: - Composite primary endpoint without intubation criteria (mortality during hospitalization; length of stay in the cardiac ICU, BNP levels from inclusion to 24 hrs, progression of physiological parameters, peak troponin levels.

The usefulness of CPAP in decreasing both right and left ventricular preload and left ventricular afterload. It is also known to decrease work of breathing as well as pulmonary shunt. Only one single centered prospective randomized study has demonstrated the benefit of early initiation of CPAP in patients with cardiogenic pulmonary edema.

Patients were included in the study if they met the following criteria:

- Orthopnea, diffuse crackles, respiratory rate > 25 breaths/min and a pulse oximetry > 90% on
room air

Exclusion criteria: History of COPD, asthma, severe stenotic valvular disease, immediate need for intubation(loss of consciousness, bradypnoea) cardiovascular collapse or suspicion of ST elevation MI

*CPAP was generated by use of a venture device which delivers a high gas flow with adjustable Fio2(ranging from 30% -60%). The high flow device was connected to a face mask. The generated positive pressure range from 5cmH20 to 10cmH20. ABGs were sampled and venous blood was collected for BNPs at the beginning prior to randomization(at the out of hospital location). Patients were randomized to either receive (oxygen @15l/min: control grp.) or CPAP(using a pressure of 7.5cmH20 initially and could increase to 10cmH20). *

Pharmacological therapy was given to the patients in each grp: Lasix 40mg up to 120mg or bumetanide 1mg up to 3mg. Patients could also receive high-dose nitrites either as repeated boluses(1m per 3mins) or continuous infusion. Dobutamine could be added ONLY if the was cardiogenic shock(SBP <90mmgh) with presence of peripheral hypoperfusion. Intubation was decided if patients had refractory hypoxemia (Sao2 <85%) after 30mins of continuous o2 with 15l/min or with CPAP at 60% Fio2 or if there was respiratory arrest, loss of consciousness, psychomotor agitation with increased dyspnea or hemodynamic instability w2ith SBP<80mmgh).

**In-hospital setting:** ABGs were analysed on admission. BNP was measured @ 6hrs and 24hrs after inclusion. Echocardiogram was done at 24hrs and 72hrs. Diagnosis of cardiopulmonary edema was confirmed by a cardiologist. Parameters including respiratory rate, Killip score(to assess for diffuse crackles) Sao2, intubation criteria HR, systolic mean and diastolic pressures were collected as data at time of inclusion. Circulatory failure was assessed by presence of at least 2 of the following: SBP<90mmgh, need for vasopressor, urine output <0.5ml/kg/h, encephalopathy(altered mental status) or signs of peripheral hypoperfusion.

**RESULTS:** Total of 207 Patients were enrolled for the study. 100 patients were assigned to the control and 107 to the CPAP grp. Both grps. were matched for demographics. The time between out of hospital inclusion and hospital admission was similar in both groups. At 48hrs the success rate was higher in the CPAP grp compare d to the control group especially for persistence of inclusion criteria) even after adjusting for baseline Left ventricular ejection fraction. When intubation criteria was excluded from the primary composite endpoint the number of successful endpoint was still higher in the CPAP group. Changes in BNP were similar in both groups. Death @ 7 days was less in the CPAP group, in hospital mortality was less in the CPAP group. Other measures which include: The HR, Respiratory rate, pH, Paco2 were significantly better in the CPAP group. * There was cross over from the control group to the CPAP group in patients who met intubation criteria and their outcome was good.

**SUMMARY:** This is one study that has re demonstrated the effectiveness of CPAP use for effective management of cardiogenic pulmonary edema. The study goes on to demonstrate that positive pressure ventilation by way of CPAP if started early could prevent...
intubation in patients with CPE.

**DOWN SIDE OF THE STUDY:**

- Open, non-blinded study (cannot completely remove bias from investigators).
- The study was terminated early as it could not include patients consecutively so makes it difficult to generalize.
- There was crossover from the control to the treatment arm of the study which could have skewed the results towards to treatment group.

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Lung ultrasound in critically ill patients: comparison with bedside chest radiography

Nektaria Xirouchaki et al.

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The aim of the study was to compare the diagnostic performance of lung ultrasound and bedside chest (CXR) for the detection of various pathologic abnormalities. This was a single center prospective blinded study in a med-surgical ICU. 42 patients who were mechanically ventilated were recruited for the study. There was no inclusion criteria other than patients were enrolled in the study when a thoracic CT scan (iodine contrast) was ordered by the primary physician (who was not involved in the study). Prior to CT scans the bedside chest x-ray was performed and a lung ultrasound was done. Four pathological entities were being assessed:

1) Consolidation
2) Interstitial syndrome
3) Pneumothorax
4) Pleural effusion

Anterior chest x-rays were performed by an expert radiologist; consolidation, interstitial syndrome, PTX and pleural effusion were identified. Anatomical landmarks were used: Lung apex, mid-axillary line, hilar line and external limit of the rib cage, mediastinal border and diaphragm. High resolution CT scans were performed and spiral CT scans were done (as the standard procedure to identify ground glass opacities, septal or no septal lines and fibrotic changes (architectural distortion).

*Interstitial syndrome was defined as presence of ground glass, septal or non septal lines or fibrotic changes*

*Consolidation was defined as presence of atelectasis, alveolar consolidation or parenchymal bands.*

*Lung regions were same at that of the CXRs.*

Ultrasound was done using a micro-convex 5-9MHZ transducer appropriate for transthoracic exam. It was done by a single person (who was unaware of the CT scan and CXR findings). Lung regions were divided...
into 12. Anterior surface: area defined by the clavicle, parasternal, anterior axillary line and diaphragm which was further divided to upper and lower. Posterior surface: defined as posterior axillary and the paravertebral lines (divided into upper and lower zones).

DATA ANALYSIS: Each lung region was evaluated and characterized as positive or negative for each abnormality. A hemi thorax was characterized as positive for an abnormality if it presented at least one positive region, negative if all regions were negative.

RESULTS: Interstitial syndrome: Lung ultrasound: 94% sensitive and diagnostic accuracy. Lung ultrasound was more sensitive and specific than bedside chest x-ray for identifying interstitial syndrome. Consolidation: Lung ultrasound had a sensitivity 100% and diagnostic accuracy of 95%. While CXR had a sensitivity of 38% and diagnostic accuracy of 49%. Lung ultrasound had 4 false positive cases with specificity of 78%. (*reason might have been the time interval of performing the lung ultrasound relative to when the CT scan was done which might have accounted for changes). Pleural Effusion: Lung ultrasound had a sensitivity and specificity of 100% while the bedside chest x-ray had a sensitivity of 65% and diagnostic accuracy of 69%). Pneumothorax: Lung ultrasound identified 6 out of the 8 PTXs. While a chest x-ray did not (**the patients were in SUPINE POSITION)

SUMMARY: CXR has long been the fast and easiest means of making bedside diagnosis in the ICU that have to do with lung pathologies. This study however brings to the table the importance and reliability of using other means of diagnosis that could potentially improve diagnostic capabilities.

DOWN SIDE OF THE STUDY:

a) Small group
b) There was no control with regards to timing of doing the CT scan of the lungs and either lung ultrasound and CXR
c) There were technical difficulties in performing the Lung ultrasound in certain patients
d) Only selection criteria used to enroll the patient was decision of the primary physician to perform thoracic CT scan; thus the pop patients used might have been pre-selected.