

Journal Club: Eastern Virginia Medical School

Krista Greene, MD

Date: 30 August 2010

Citation: Kilgannon JH, et al. Association between arterial hyperoxia following resuscitation from cardiac arrest and in-hospital mortality. JAMA. 2010; 303(21):2165-2171

I. WHAT IS BEING STUDIED?	To test the hypothesis that in non-traumatic post-cardiac arrest patients, exposure to hyperoxia is associated with increased mortality.
1. Study Objective: Did the review ask a clearly-focused question?	Yes. 1. Is the presence of hyperoxia commonly found in post-arrest patients? 2. Is post ROSC hyperoxia associated with lower in-hospital survival (<i>primary outcome</i>) and hospital discharge with functional independence (<i>secondary outcome</i>)
2. Study Design: Was the cohort recruited in an acceptable way?	Possibly. The cohort (critically ill post-arrest ICU patients) though there were 11/31 database hospitals that were not included. Multicenter cohort study generated from a critical care database (Project IMPACT Cerner Corporation) of intensive care units (ICUs) in 120 of 131 Project Impact US hospitals from 2001-2005. Primarily represented community hospitals (79%) settings. Subjects included 6326 adults with nontraumatic cardiopulmonary arrest who were admitted to the ICU and underwent ABG within 24 hrs of ICU admission. Groups were analyzed in three groups based upon first ABG: hypoxia (PaO ₂ <60 mm Hg), hyperoxia (PaO ₂ >300 mm Hg) normoxia: (>60 and <300mmHg)
3. Inclusion Criteria	Adult pts who sustained nontraumatic cardiac arrest and admitted to Project Impact ICU's from 2001-2005. >17yo. Nontraumatic cardiac arrest. Cardiopulmonary resuscitation within 24h prior to ICU arrival, ABG performed within 24h after ICU arrival
4. Exclusion Criteria	No ABG within the first 24h after arriving to ICU. Traumatic arrest. <17yo. Authors excluded 11/131 Project Impact hospitals without explanation.
5. Interventions Compared	Exposure to post-arrest hyperoxia (PaO ₂ > 300mmHg vs. hypoxia vs. normoxia (defined as not meeting hyperoxia or hypoxia criteria) Groups were defined a-priori to database queiry

6. Outcomes Evaluated	<ul style="list-style-type: none"> - Primary outcome: in-hospital mortality. - Secondary outcome: Survival to hospital discharge with independent functional status at discharge however authors did not describe how functional status at hospital discharge was determined. One would prefer to have a validated assessment scale (i.e. Modified Rankin-Scale)
II. Are the results of the study valid?	
1. Was the exposure accurately measured in order to minimize bias?	No. The relative time of exposure before obtaining first ABG at various levels of oxemia was not controlled for. Exposure to first ICU ABG could have ranged from 0-24 hrs and was not described.
2. Have the authors identified all important confounding factors?	The authors attempted to calculate odds ratios of independent predictors of mortality utilizing multivariable logistic regression on thirteen variables 9 of which were associated with in-hospital mortality. Important ED confounders such as post-arrest down time, CPR at scene were not controlled for.
3. Were all patients who entered the trial properly accounted for and attributed at its conclusions?	No. There were over 300 subjects lost to follow-up with over half of those disproportionately represented by the hypoxia group.
4. Was follow-up complete?	No. The authors do not explicitly state the exact term of short (in-hospital) or long-term follow up or how follow-up was performed. They did not include how subjects were assessed regarding long term functional status other than
6. Were study groups similar at the start of the trial?	Patient characteristics appeared to be similar in the respective groups except the normoxic group admitted to the ICU from the ED vs. in-patient units which was approx 15% higher and 14% lower respectively. The authors did not provide statistical significance for this difference.
7. Aside from the experimental intervention, were the groups treated equally	Unlikely- Authors did not control for interventions other than use of pressors. Authors use of pressors
III. What were the results?	
1. How large was the treatment effect? (difference between treatment and control group).	<p>3561/6326 or 56% of all subjects met primary outcome: in hospital mortality</p> <ul style="list-style-type: none"> --- 63% of hyperoxia (95% CI 60-66) --- 57% hypoxia (95% CI 43-48) --- 45% normoxia (95% CI 43-48) <p>- Proportional difference (relative risk) RR 18% in hyperoxia (95% CI 14-22%) vs.</p>

	<p>normoxia group and 6% RR (95%CI 3-9%) when compared to hypoxia group</p> <ul style="list-style-type: none"> - Hyperoxia group also demonstrated lower proportion of functionally independent pts vs. normoxia (29% vs. 38%) at time of d/c. - Using logistic regression the following RFs were associated with in hospital death: age, non-independent preadmission status, admission from ED, active chemo, CRF, hypotension on ICU arrival, tachycardia, hypoxia and... - exposure to hyperoxia significant predictor of in hospital death OR 1.8%(95% CI, 1.5-2.2) - secondary analysis with hyperoxia defined as PaO₂ > or = 400mmHg increased mortality revealed even greater mortality: 69% in hyperoxia vs. 57% in hypoxia and 50% in normoxia - Hyperoxia group had proportion difference of 19% for greater in-hospital mortality vs. normoxia and 12% vs. hypoxia
<p>2. What was the estimated treatment effect at a 95% confidence interval?</p>	<ul style="list-style-type: none"> - 63% in hospital mortality of hyperoxia group with 95% CI 60-66 - OR 1.8% (95% CI 1.5-2.2)for death of hyperoxia exposure after controlling for confounders <p>CI's 95 appear to be fairly narrow across all effects reported.</p>
<p>IV. Will the results help me in caring for my patients? (applicable?)</p>	<p>Liaison Committee on Resuscitation advocated for avoidance of hyperoxia and controlled reoxygenation strategy targeting O₂ sats 94-96%</p>
<p>1. Were all clinically important outcomes considered?</p>	<p>Yes: in-hospital mortality, functional status at discharge though authors fail to describe how this was measured.</p>
<p>2. Can the results be applied to the local population?</p>	<p>Probably. There was a proportionate representation of demographic and comorbid characteristics however a disproportionate representation of Caucasian subjects (75%)</p>
<p>3. What are the limitations?</p>	<ul style="list-style-type: none"> - Cohort study—cannot identify causality - Definition of hypoxia was only defined as P:F ratio (allowing for normoxia that requires high FiO₂) - ABG data is not time stamped precisely (some data suggests that early exposure to hyperoxia worsens ischemia-reperfusion injury whereas later hyperoxia may not)

	<ul style="list-style-type: none"> - Project IMPACT does not include data specific to arrest event, down-time etc - did not capture use of therapeutic hypothermia (6% of pts had a lowest temp < 34degC) pulmonary barotrauma is higher O2 groups not measured. - may be significant unmeasured confounders witnessed arrest, bystander CPR, transport time - exact cause of death not reported -very broad definitions of oxemia -no discussion regarding the time to correction of hyper/hypoxemia
--	---

Additional Comments: Fairly representative cohort of subjects. Large database with evidence of fairly narrow CI's. There appeared to be substantive data to identify 9 RF's for in-hospital mortality including: Age, Non-independent pre-admission functional status, ER admissions, chemotherapy(OR 2.8), CRF, hypotension on arrival to ICU (OR 2.1), tachycardia(OR 1.9) and Hyperoxia (OR 1.8) . The data is interesting and this cohort suggests an *association* between hyperoxia and mortality. That stated, there are considerable potential confounders described above. An ED study that controlled for some of these confounders (i.e. early CPR or not, level and exposure time to O2 etc.) could add substantive data to the management of the post-arrest patient.