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Prehospital Supplemental Oxygen for Acute Stroke – a Retrospective Analysis

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Abstract

Objective: Brief early administration of supplemental oxygen (sO₂) to create hyperoxia may increase oxygenation to penumbral tissue and improve stroke outcomes. Hyperoxia may also result in respiratory compromise and vasoconstriction leading to worse outcomes. This study examines the effects of prehospital sO₂ in stroke.

Methods: This is a retrospective analysis of adult acute stroke patients (aged ≥18 years) presenting via EMS to an academic Comprehensive Stroke Center between January 1, 2013 and December 31, 2017. Demographic and clinical characteristics obtained from Get with the Guidelines-Stroke registry and subjects' medical records were compared across three groups based on prehospital oxygen saturation and sO₂ administration. Chi-square, ANOVA, and multivariate logistic regression were used to determine if sO₂ status was associated with neurological outcomes or respiratory complications.

Results: 1,352 eligible patients were identified. 62.7% (n=848) did not receive sO₂ ("controls"), 10.7% (n=144) received sO₂ due to hypoxia ("hypoxia"), and 26.6% (n=360) received sO₂ despite normoxia ("hyperoxia"). The groups represented a continuum from more severe deficits (hypoxia) to less severe deficits (controls): mean prehospital GCS (hypoxia -12, hyperoxia -2, controls -14 p<0.001), mean initial NIHSS (hypoxia -15, hyperoxia -13, controls -8 p<0.001). After

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controlling for potential confounders, all groups had similar rates of respiratory complications and favorable neurological outcomes.

Conclusions: Hyperoxic subjects had no significant increase in respiratory complications, nor did they differ in neurologic outcomes at discharge when controlling for confounders. While limited by the retrospective nature, this suggests brief, early sO₂ for stroke may be safe to evaluate prospectively.

Keywords

Acute Ischemic Stroke; Prehospital; Hyperoxia

1. Introduction:

Every year in the United States alone, nearly 800,000 people will experience a new or recurrent stroke, with the vast majority of these being an Acute Ischemic Stroke (AIS).[1] The time to reperfusion and penumbral salvage are key determinants of stroke outcomes and while the time window for systemic thrombolysis and endovascular treatments continues to expand, many AIS victims may be ineligible for either option.[1] With approximately 50% of patients experiencing a stroke entering the healthcare system via Emergency Medical Services (EMS),[2] evaluating potential interventions in the prehospital and Emergency Department (ED) phases of care are key, but understudied, components of stroke treatment.

Administration of oxygen is a low cost, potentially beneficial component of stroke care that can be implemented in the prehospital and ED phases of care. However, there is little conclusive evidence that directly addresses the putative benefits and potential harms of hyperoxia (i.e. administration of high levels of supplemental oxygen (sO₂) to patients who are not hypoxic), in the early stages of AIS. Most preclinical data suggest beneficial effects during this specific therapeutic window, but the clinical data remain more controversial.[3-9]

Rodent stroke models have demonstrated a multitude of potential benefits of hyperoxia: return of penumbral brain tissue oxygenation levels to near pre-ischemic levels; increased cerebral blood flow to ischemic tissues; no increase in the production of markers of oxidative stress and reactive nitrogen species; and maintenance of the blood-brain barrier after an AIS.[4-7, 9, 10] These models of large vessel occlusion (LVO) also suggest that the window in which hyperoxia is provided is a key determinant of the potential therapeutic benefit, with the benefits being lost when hyperoxia was applied during reperfusion.[11, 12] A pilot study of hyperoxia by delivery of 45 liters (L)/min humidified oxygen via facemask in AIS demonstrated reduced markers of anaerobic metabolism and increased markers of neuronal integrity and mitochondrial function, and improved neurological function, but without a significant change in infarct volumes in the hyperoxia treated groups.[8],[13] However, providing 45 liters (L)/min humidified oxygen via facemask in the prehospital setting is not feasible in most systems.

Despite these potentially promising studies, others have failed to demonstrate a benefit and some have even demonstrated potential harm. In patients treated with hyperoxia in the form of 3L nasal cannula for the first 24 hours after admission, there was no difference in

neurological outcomes.[14] Additionally, analysis of mechanically ventilated stroke patients in the intensive care unit (ICU) found that those who were hyperoxic (Partial pressure of arterial oxygen (PaO₂) > 300mmHg) had a 20% higher in-hospital mortality compared to normoxia or hypoxia.[3] These data underscore the preclinical data suggesting that the timing and duration of sO₂ administration are key factors. This study examines the effects of delivery of prehospital sO₂ to normoxic patients to create potential hyperoxia compared to those who received sO₂ due to hypoxia and controls who did not receive sO₂.

2. Methods:

2.1 Study Population and Data abstraction:

This study is a retrospective analysis of discharge diagnosed adult acute stroke patients (aged ≥ 18years) presenting via EMS to a single academic Comprehensive Stroke Center between January 1, 2013 and December 31, 2017. Demographic and key clinical characteristics were obtained from Get with the Guidelines-Stroke (GWTG-S) registry and extracted from subjects' medical records. Variables extracted from GWTG-S registry included: basic demographics (age, gender, race, ethnicity), baseline comorbidities (history of prior transient ischemic attack or cerebrovascular accident, dyslipidemia, hypertension, diabetes mellitus, atrial fibrillation, and/or smoking), initial National Institutes of Health Stroke Scale (NIHSS) score, ambulatory status prior to admission and at discharge, time from last known well, discharge modified Rankin Score (mRS), treatment for hospital acquired pneumonia, acute stroke treatments (ie systemic thrombolysis (tissue Plasminogen Activator (tPA)), intraarterial tPA (IAtPA), or endovascular thrombectomy (EVT)). Prehospital records were reviewed for: first documented vitals, lowest documented pulse oximetry, the time of initiation of supplemental oxygen and the initial amount and type provided, Glasgow Coma Scale (GCS), initial respiratory exam findings (clear lungs versus the presence of wheezing, coarse breath sounds, rales/rhonchi, tachypnea, labored breathing, or "respiratory distress"). Subjects' ED charts were reviewed for: timing of sO₂ removal if documented while in the ED or if it was continued upon admission, ED vital signs (measured within 30minutes of arrival, 1hour of arrival, and 2 hours of arrival). Discharge summaries were reviewed for the development of respiratory complications for any reason (i.e. intubation and mechanical ventilation (MV), non-invasive positive pressure ventilation (NIPPV), respiratory failure, acute respiratory distress syndrome (ARDS), pulmonary edema, pneumonia). Data were entered into a REDCap Database (Vanderbilt University) for subsequent data analysis. This study was approved by the Research Subjects Review Board.

2.2 Data Analysis:

Variables were compared across the three groups using SAS 9.4 software (SAS Institute, Cary, NC) based on prehospital oxygen level with normoxia defined as an initial EMS room air pulse oximetry >94% before sO₂ administration: those who received sO₂ despite normoxia ("hyperoxia"), those who received sO₂ for hypoxia ("hypoxia") and those who did not receive sO₂ ("controls") using chi-square tests for independence and ANOVA. Tukey post-hoc analysis was performed for intergroup significance when the ANOVA was significant. Multivariate logistic regression was used to compare rates of in-hospital respiratory complications and rates of favorable discharge mRS (defined as mRS of 0-2)

while controlling for baseline confounders (i.e. age, initial GCS, initial NIHSS, prior ambulatory status, smoking history, past medical history of respiratory comorbidities and prior stroke).

3. Results:

A total of 1,352 patients were identified from GWTG-S records that also had complete prehospital records. 62.7% (n=848) did not receive sO₂ ("controls"), 10.7% (n=144) received sO₂ due to hypoxia ("hypoxia"), and 26.6% (n=360) received sO₂ despite normoxia ("hyperoxia"). Basic demographic and baseline comorbidities are shown in Table 1. With exception of age, hypoxia and hyperoxia subjects had a similar demographic composition. Hyperoxia subjects were significantly more likely to have atrial fibrillation and/or Chronic Obstructive Pulmonary Disorder (COPD) compared to controls.

In terms of clinical presentation (Table 2) and patient outcomes (Table 3), the three groups represented a continuum of disease from more severe deficits/higher complication rates (hypoxia group) to less severe deficits/lower complication rates (control group), including: documented normal respiratory exam (lack of apparent respiratory distress and/or labored tachypneic breathing, presence of clear breath sounds) (hypoxia-79.2%, hyperoxia-92.5%, controls-97.4%, $p<0.001$), mean prehospital GCS (14, 14, 15, $p<0.001$), and mean initial NIHSS (15, 13, 8, $p<0.001$). Initial vital signs by EMS were similar among the three groups with exception of the lowest EMS pulse oximetry which ranged from 95.8% in the hyperoxia group to 94.7% in the control group and 89.9% in the hypoxia group ($p<0.001$).

There were significantly more respiratory complications among those receiving sO₂ compared to controls, including rates of intubation (Table 3). However, there was no difference in the rates of respiratory complications between hyperoxia and hypoxia subjects. However, the mean discharge mRS (3 in all groups, $p=0.953$) and their ambulatory status upon discharge was similar among all three groups.

A series of multivariate logistic regression analyses were performed controlling for age, initial EMS GCS, initial NIHSS, baseline history of any respiratory comorbidity or smoking, and a history of prior transient ischemic attack (TIA) or cerebrovascular accident (CVA) to determine the effects of sO₂ on respiratory complications. Additional multivariate logistic regressions analyses controlling for baseline ambulatory status and time to last known well were performed to assess the effect on having a favorable discharge mRS. Results indicated that those in the hyperoxia group had similar rates of any respiratory complication compared to controls (OR -1.377; 95% CI 0.966-1.963) and the hypoxia group (OR -0.656; 95% CI 0.399-1.078). Those in the hypoxia group had 2.101 times the odds of any having any respiratory complication compared to controls (95% CI 1.314-3.358). There was no significant difference in favorable discharge mRS between the hyperoxia group and either the control group (OR- 0.926, 95% CI 0.658-1.303) or the hypoxia group (OR - 1.105; 95% CI 0.644-1.895).

4. Discussion:

This report is the first observational study to examine the effects of unindicated sO₂ administered in the prehospital and ED settings for acute stroke. Despite the general trend among ED and prehospital providers to not give sO₂ unless indicated (pulse oximetry <94% according to AHA guidelines[15]), this study identifies a high proportion of patients (over 25%) receiving sO₂, with over 70% of patients receiving sO₂ without evidence of hypoxia. Several factors may have contributed to these patients receiving sO₂ despite normoxia. Compared to controls, those in the hyperoxia group had higher rates of atrial fibrillation, lower initial EMS GCS, more severe stroke symptoms, and were less likely to have a documented normal respiratory exam. Although the decision by prehospital providers to administer sO₂ in these cases may be based on the perception that these patients appeared to be “sicker” patients, the exact rationale is unknown and requires further evaluation.

While an initial EMS room air pulse oximetry of >94% was used to determine whether oxygen was indicated or not, findings in this study reflect the frequency of stroke encounters in other studies that result in a patient receiving supplemental oxygen. In unpublished data from the 2014 Greater Cincinnati Northern Kentucky Stroke Study, there were also high rates of sO₂ use for any reason in the prehospital setting (over 2/3 of the entire population) with those receiving sO₂ having lower EMS GCS and higher admission NIHSS scores.[16] Using multivariable logistic regression of the 2014 data to control for stroke severity (initial EMS GCS and admission NIHSS), former smoker status remained significantly associated with sO₂ use. Together, these data illustrate a high rate of sO₂ use across geographic regions and the complexity of clinical care with regards to sO₂ use, the effects of which need to be fully evaluated.

Despite the high rates of sO₂ in this setting, multivariate analysis in this study failed to show hyperoxia resulted in an increase in either respiratory complications or poorer neurologic outcomes. A previous study reported higher 28-day mortality associated with hyperoxia in mechanically ventilated ICU stroke patients who were found to have a PaO₂ >300mmHg.[3] However, upon subgroup analysis of AIS patients, there was no difference in mortality between those found to be hyperoxic compared to controls. A second study of AIS ICU patients also failed to demonstrate a correlation between PaO₂ and mortality.[17] These data suggest that the response to hyperoxia is different in the ischemic and hemorrhagic stroke populations. However, in the prehospital setting it is difficult to distinguish these two populations, limiting the ability to prospectively evaluate prehospital sO₂ use in only AIS patients.

Reported concerns related to oxygen toxicity include increased free radical damage, impaired immune responses, and potential for hyperoxic lung injury. A previous study of severe stroke patients who received sO₂ via a 40% Venturi mask compared to nasal canula also showed a non-significant trend toward lower rates of in-hospital mortality and co-morbidities such as fever, pneumonia and respiratory failure.[18] Similarly, the retrospective data presented here were limited to the analysis of in-hospital respiratory complications and neurological outcomes due to incomplete data with regards to hemorrhagic conversion and other systemic bleeding complications (over 75% with missing data). Additionally, a 90-day

mRS was not included in this dataset and thereby neurological outcome was limited to only the discharge mRS. However, when analyzing only respiratory complications for which the data was complete and controlling for likely confounders (i.e. stroke severity, age, prior stroke, baseline respiratory comorbidities), acute stroke patients who received sO₂ despite normoxia had no significant difference in the odds of developing any respiratory complication compared to either controls or those receiving sO₂ for hypoxia. It is unclear, given the retrospective nature, if this lack of complications was related to the level of sO₂ received as hyperoxia subjects similar oxygen flow rates and only differed from hypoxia subjects in their initial room air pulse oximetry. Future studies that prospectively collect arterial blood gas data to confirm hyperoxia are needed to fully understand the potential consequences of such an intervention in stroke.

Hyperoxia for AIS may have numerous benefits including the potential to increase cerebral blood flow to penumbral tissue, decrease free radical production leading to reperfusion injury, maintain the blood-brain barrier, decrease the final infarct volume, and improve neurological function. A small pilot study of hyperoxia for eight hours demonstrated a significant improvement in 24-hour NIHSS and a significant reduction in infarct volume at 4hours, but no difference in later neurological outcomes.[4, 5, 7-10, 13, 19, 20] The data presented here used multivariate logistic regression to control for potential confounders (stroke severity, baseline ambulatory status, prior stroke or transient ischemic attack, time to last known well, age, respiratory comorbidities) to determine the effect of hyperoxia on the odds of having a favorable mRS (0-2) at discharge. Unfortunately, there was no statistical difference in outcome among the hyperoxia group compared to the control group or hypoxia groups. Given that 60% of the hyperoxia group had oxygen continued upon admission, this finding may underscore the importance of the time of potential hyperoxia and reflect the similar trend seen in previous pilot studies, where there may be an initial improvement, followed by loss of that difference with time.[13] In rodent models, the timing of hyperoxia administration is a key factor in the potential effects, with hyperoxia prior to reperfusion being beneficial and these effects being attenuated and even reversed when continued into reperfusion.[21]

This study had several important limitations given the retrospective nature from a single large academic center. Given the retrospective nature and lack of the ability to randomize subjects, indication bias as to who received supplemental may account for some of the lack of differences in outcomes. This is evident by the fact that those who received supplemental oxygen for any reason were overall sicker with lower GCS scores, higher NIHSS scores and increased likelihood of an abnormal respiratory exam by EMS. After multivariate analysis that controlled for these confounders, there was no difference in respiratory complications or neurological outcomes between the hyperoxia and hypoxia groups. Even after adjustment for these factors, hyperoxia was associated with increased respiratory complications compared to controls. It is possible that there are other unknown or unmeasured confounders that could contribute to this difference.

This study was also limited by an inability to correlate unindicated supplemental oxygen use with the development of hyperoxia as defined in preclinical models by a PaO₂ >200mmHg. Additionally, given the changing data collection forms for the GWTG-S registry during the

study period, many early subjects lacked data on bleeding complications making analysis of the effects of sO₂ on non-respiratory complications impossible. However, if hyperoxia was to increase hemorrhagic conversion rates, free radical production and/or cerebral edema, this might be reflected by a change in neurological function at discharge.

5. Conclusions:

In summary, this study identifies a high rate of prehospital sO₂ use despite normoxia that may lead to potential hyperoxia. While, hyperoxia subjects did not differ in their neurologic outcomes compared to hypoxia or control subjects, this study also did not find a significant difference in rates of respiratory complications after controlling for potential confounders. The lack of significant development of respiratory complications and the relatively high rates of ongoing sO₂ use in the prehospital setting, suggests that brief, early hyperoxia may be safe for further investigation through larger, well-designed clinical trials to explore its potential therapeutic role in treatment for patients with acute ischemic stroke.

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Abbreviations:

AIS	acute ischemic stroke
EVT	endovascular therapy
GCS	Glasgow coma scale
GWTG-S	Get with the Guidelines Stroke
ICU	intensive care unit
IAtPA	intraarterial tissue plasminogen activator
LVO	large vessel occlusion
mRS	modified Rankin Scale
MV	mechanical ventilation
NIHSS	National Institutes of Health Stroke Scale
NIPPV	non-invasive positive pressure ventilation
sO₂	supplemental oxygen
tPA	tissue plasminogen activator

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Table 1:

Baseline Demographic and Comorbidities:

Characteristic		Hyperoxia (n=360)	Hypoxia (n=144)	Controls (n=848)
Age (Mean, SD) ^a		70 (15) [#]	76 (14) ⁺	69 (16)
Gender (n, %)	Female ^a	188 (53%)	74 (54%)	374 (45%)
Stroke Type (n, %)	Ischemic ^a	262 (74%)	100 (73%)	673 (82%)
	Hemorrhagic ^a	94 (26%)	38 (27%)	152 (18%)
Ethnicity (n, %)	Hispanic	4 (1%)	3 (2%)	17 (2%)
Race (n, %)	White ^a	311 (86%)	119 (83%)	673 (80%)
	African American	34 (9%)	17 (12%)	120 (14%)
	Other	6 (2%)	1 (1%)	26 (3%)
	Not documented	9 (3%)	7 (5%)	29 (3%)
Past Medical History (n, %)	Prior TIA and/or CVA	90 (25%)	48 (35%)	217 (26%)
	Dyslipidemia	181 (50%)	73 (53%)	436 (53%)
	Hypertension	271 (76%)	115 (83%)	619 (75%)
	Atrial Fibrillation ^a	108 (30%)	43 (31%)	183 (22%)
	Diabetes Mellitus	90 (25%)	41 (30%)	214 (26%)
Respiratory Comorbidities (n, %)	Smoking ^a	62 (17%)	12 (9%)	142 (17%)
	COPD ^a	38 (11%)	18 (13%)	56 (7%)
	Asthma	18 (5%)	8 (6%)	39 (5%)
	Sleep Apnea ^a	17 (5%)	11 (8%)	27 (3%)

^aChi-squared p<0.05^bANOVA p<0.05Tukey analysis p<0.05 compared to control (⁺), to hypoxia ([#]).

Table 2:

EMS and ED Presentation and Clinical Course

Characteristic		Hyperoxia (n=360)	Hypoxia (n=144)	Controls (n=848)
Highest Level of EMS Provider (n, %)	BLS	0 (0%)	1 (0%)	39 (4%)
	ALS ^a	359 (100%)	142 (100%)	805 (95%)
	Not documented	1 (0%)	1 (0%)	4 (1%)
Symptom Onset while in: (n, %)	Healthcare Setting ^a	32 (9)	25 (18%)	55 (7%)
	Non-healthcare Setting	324 (91%)	112 (81%)	769 (93%)
Patient Transferred from: (n, %)	Home or scene ^a	170 (48%)	109 (79%)	658 (80%)
	Another Hospital	185 (52%)	29 (21%)	166 (20%)
Cincinnati Prehospital Stroke Score (CPSS) Completed (n, %)		140 (40%)	65 (46%)	377 (45%)
CPSS positive (n, %) ^a		113 (81%)	57 (88%)	124 (25%)
Initial GCS (mean, SD) ^b		12 (4) ⁺	12 (4) ⁺	14 (2)
EMS Initial Vital Signs (mean, SD)	Heart Rate (bpm)	79.6 (19.5)	82.2 (20.1)	82.0 (18.3)
	Systolic Blood Pressure	153.5 (32.7)	155.8 (37.3)	160.5 (70.6)
	Diastolic Blood Pressure	87.1 (19.5)	89.7 (23.1)	89.2 (21.6)
	Respiratory Rate	17.8 (3.7)	18.2 (4.6)	17.6 (3.1)
	Lowest Pulse Oximetry (mean, SD) ^b	95.8 (6.0) ^{+, #}	89.9 (4.6) ⁺	94.7 (6.6)
Type of Oxygen Provided by EMS(n, %)	Nasal Canula	275 (76.8%)	108 (75.5%)	n/a
	NRBM	46 (12.9%)	23 (16.1%)	n/a
	NIPPV	5 (1.4%)	5 (3.5%)	n/a
	MV	32 (8.9%)	7 (4.9%)	n/a
Amount sO ₂ in LPM excluding intubated patients by EMS (mean, SD) ^c		4.5 (4.2)	5.4 (4.7)	n/a
Amount sO ₂ in LPM excluding intubated patients by ED (mean, SD)		3.9 (3.7)	4.3 (4.5)	n/a
Initial Respiratory Exam (n, %)	Lungs Clear Bilaterally ^a	333 (93%)	114 (79%)	826 (97%)
	Adventitious Breath Sounds (wheeze, rales, rhonchi, coarse) ^a	13 (4%)	17 (12%)	15 (2%)
	Diminished Breath Sounds ^a	7 (2%)	8 (6%)	6 (1%)
	Apparent Respiratory Distress (includes tachypnea and labored) ^a	19 (5%)	15 (10%)	14 (12%)
Initial NIHSS (mean, SD) ^b		13 (9) ^{+, #}	15 (10) ⁺	8 (8)
Ambulatory Status prior to Admission (n, %)	Able to Ambulate without personal assistance ^a	293 (94%)	109 (92%)	732 (96%)
	Ambulates with personal assistance	6 (2%)	5 (4%)	11 (1%)
	Unable to ambulate	12 (4%)	4 (3%)	19 (3%)
ED Vital Signs in first 3 hours (mean, SD)	Heart Rate (bpm)	78.8 (15.7)	80.3 (17.8)	79.1 (15.7)
	Systolic Blood Pressure (mmHg)	158.2 (22.3)	146 (24.0)	148.9 (23.0)

Characteristic		Hyperoxia (n=360)	Hypoxia (n=144)	Controls (n=848)
	Diastolic Blood Pressure (mmHg) ^b	78.9 (17.2) ⁺	82.2 (18.9)	85.2 (15.0)
	Respiratory Rate (bpm)	18.5 (3.4) ⁺	19.1 (3.7) ⁺	18.0 (3.0)
	Pulse Oximetry (%) ^b	97.9 (3.5) [#]	96.8 (2.9) ⁺	97.7 (3.8)
	Lowest Pulse Oximetry (%) ^b	96.9 (6.0) [#]	95.7 (3.5) ⁺	96.8 (2.5)
Supplemental Oxygen continued in the ED or upon admission (n, %) ^a		218 (60.6%)	106 (73.6%)	124 (14.6%)
Time to LKW in hours (mean, SD) ^b		4.3 (3.0) ⁺	3.7 (3.1) ⁺	3.8 (3.2)

^aChi-squared p<0.05

^bANOVA p<0.05

Tukey analysis p<0.05 compared to control (⁺), to hypoxia ([#]).

^cStudent's t-test p<0.05

Abbreviations: BLS (basic life support), ALS (Advanced Life Support), SD (standard deviation), bpm (beats per minute), NRBM (non-rebreather mask), NIPPV (non-invasive positive pressure ventilation), MV (mechanical ventilation), SEM (standard error of the mean)

Table 3:**Patient Outcomes**

Outcome		Hyperoxia (n=360)	Hypoxia (n=144)	Control (n=848)
Ambulatory Status at Discharge (n, %)	Able to Ambulate without personal assistance	152 (49%)	59 (49%)	372 (53%)
	Ambulates with personal assistance	93 (30%)	34 (28%)	197 (28%)
	Unable to ambulate	66 (21%)	27 (23%)	138 (20%)
Stroke Interventions (n, %)	tPA	51 (17%)	23 (20%)	136 (20%)
	EVT	6 (2%)	3 (2%)	25 (3%)
	IAtPA	7 (2%)	3 (3%)	30 (4%)
Total LOS in days (mean, SD)		9.6 (13.0)	7.8 (9.0)	8.6 (32.6)
In-hospital Respiratory Complications (n, %)	Requiring NIPPV	6 (2%)	5 (4%)	9 (1%)
	Requiring MV ^a	89 (25%)	39 (27%)	75 (9%)
	Pulmonary Edema	6 (2%)	3 (2%)	10 (1%)
	Treatment for Hospital Acquired Pneumonia	10 (5%)	8 (10%)	47 (9%)
	Any documentation of pneumonia in discharge summary ^a	18 (5%)	17 (12%)	24 (3%)
	Any Respiratory Complication ^a	111 (31%)	56 (39%)	136 (16%)
Favorable discharge mRS (mRS 0-2) (n,%)		85 (34%)	31 (33%)	189 (34%)

^aChi-squared p<0.05^bANOVA p<0.05

Tukey analysis p<0.05 compared to control (+), to hypoxia (#)