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Association of hypercapnia and hypercapnic acidosis on clinical outcomes in mechanically ventilated patients with cerebral injury

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Research

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Association of Hypercapnia and Hypercapnic Acidosis With Clinical Outcomes in Mechanically Ventilated Patients With Cerebral Injury

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 Editorial

Background

- Cerebral injury may be caused by traumatic brain injury, stroke, and cardiac arrest.
- Very limited research on management of hypercapnia in such patients
- The management guidelines recommend normocapnia (PCO₂ 35-45 mmHg) with no specific recommendation on pH
 - Low quality evidence

- Changes in PCO_2 are inextricably related to changes in pH
 - Acute increase in PCO_2 reduces pH
 - Chronic increase in PCO_2 leads to compensation where pH is normalised by an increase in HCO_3
- Studies so far have mainly focused on the changes in PCO_2 and pH in isolation and have not evaluated the effects of PCO_2 and pH in conjunction.

AIM

- Review the association of compensated hypercapnia and hypercapnic acidosis during the first 24 hours of intensive care unit (ICU) admission on clinical outcomes in adult mechanically ventilated patients with cerebral injury.

Methods

- Retrospective cross-sectional study using ANZICS APD over a 16 year period (Jan 2000 to Dec 2015) in 167 ICUs in ANZ.
- Adult patients with cerebral injury receiving mechanical ventilation during the first 24 hrs. of ICU admission
- Patients were classified into 3 groups
 - Normocapnia [35–45 mm Hg] and normal pH [7.35–7.45] (reference)
 - Compensated hypercapnia [normal pH with elevated carbon dioxide (45 mm Hg)]
 - Hypercapnic acidosis [$P_{CO_2} > 45$ mm Hg; pH < 7.35] during the first 24 hours of ICU stay

Outcomes

- Primary
 - Hospital mortality

- Secondary
 - Discharge destination and duration of ICU and hospital stay



Methods – Data analysis

- Assessed for normality.
- Group comparisons using χ^2 tests for categorical data
- Continuous data was analysed using analysis of variance or Kruskal-Wallis tests.

- To investigate the independent effect, hierarchical multivariable regression models were used using logistic regression for hospital death and Cox proportional hazards regression for time to death.
- Adjusted for patient severity, propensity to be hypercapnic, propensity to be hypercapnic acidotic, baseline GCS stratified into 3 groups (GCS score 3-7, 8-12, and 13-15), and year of admission.
- Additional matched sensitivity analysis was performed with patients from each of the 3 hypercapnic diagnostic categories matched for patient severity.



Results

Figure 1. Study Profile

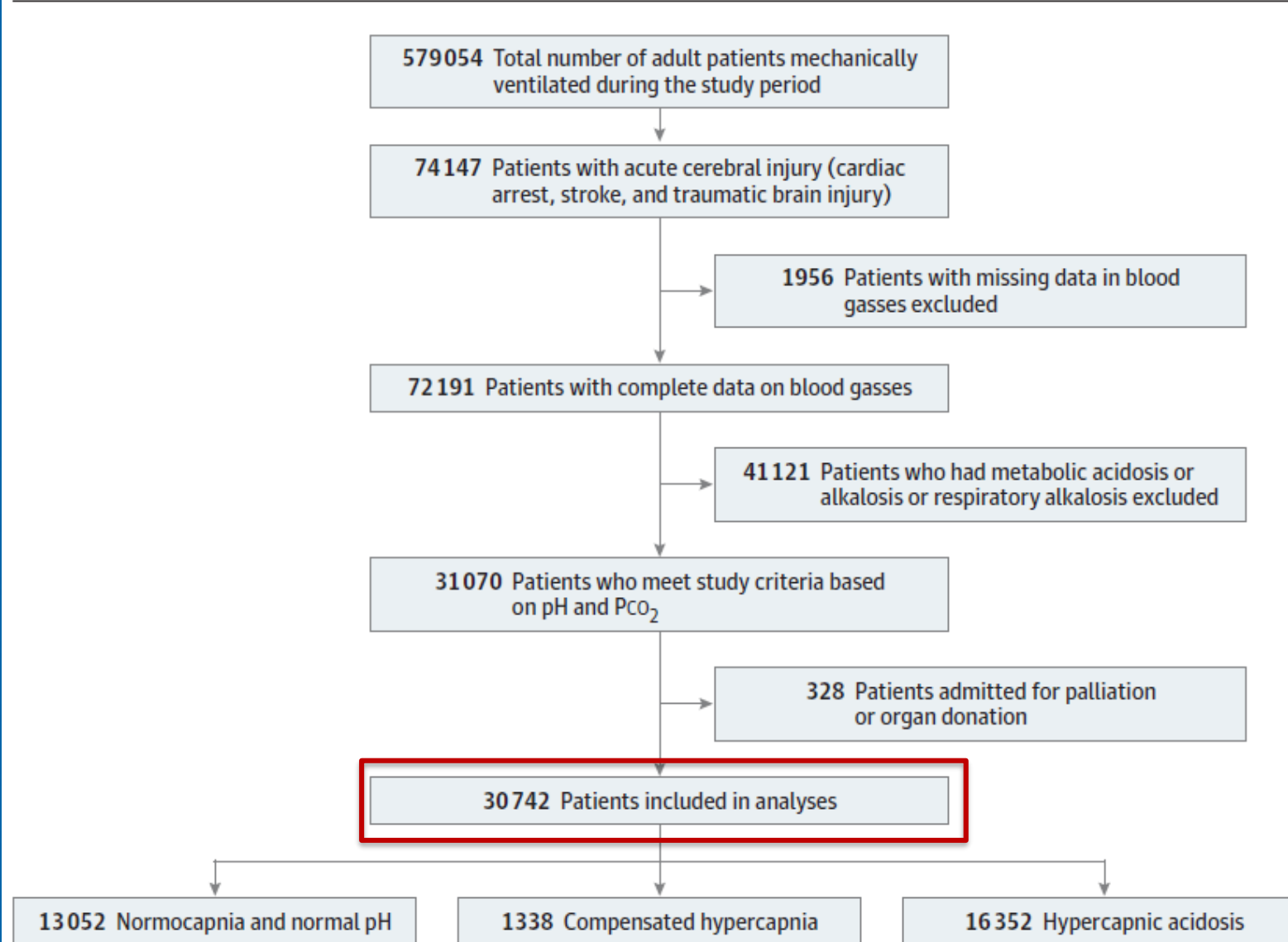




Table 1. Comparisons of Demographics, Comorbidities, and Physiological and Laboratory Data

Variable	No. (%)			P Value
	Normocapnia and Normal pH (n = 13 052)	Compensated Hypercapnia (n = 1338)	Hypercapnic Acidosis (n = 16 352)	
Age, y, mean (SD)	53.1 (20.2)	54.9 (19.9)	56.2 (18.9)	<.001
Men	8949 (68.6)	996 (74.4)	11929 (73)	<.001
Worst GCS score, mean (SD)	8.15 (4.44)	8.47 (4.66)	6.27 (4.55)	<.001
GCS score 3-7	6462 (50)	630 (47)	11125 (68)	<.001
GCS score 8-12	3237 (25)	398 (30)	2925 (18)	<.001
GCS score 13-15	3170 (24)	290 (22)	1935 (12)	<.001
Missing data on GCS score	183 (1.4)	20 (1.5)	367 (2.2)	<.001
Comorbidities				
Chronic respiratory disease	245 (1.9)	72 (5.4)	1119 (6.8)	<.001
Chronic cardiovascular disease	773 (5.9)	123 (9.2)	1620 (9.9)	<.001
Chronic liver disease	117 (0.9)	22 (1.6)	171 (1)	.03
Chronic renal failure	169 (1.3)	25 (1.9)	472 (2.9)	<.001
Immunosuppression	149 (1.1)	18 (1.3)	312 (1.9)	<.001
Physiological data				
Highest body temperature, °C	37.5 (0.9)	37.6 (0.9)	37 (1.4)	<.001
Highest heart rate, bpm	95.7 (22.8)	98.5 (23.9)	107 (25.7)	<.001
Highest respiratory rate, PM	19.1 (6.3)	20.4 (7.1)	21.4 (7.3)	<.001
Highest mean arterial pressure, mm Hg	105 (18)	106 (19)	101 (21)	<.001
Laboratory data				
Lowest sodium, mEq/L	138 (4.05)	139 (4.59)	138 (4.75)	<.001
Highest, mEq/L	4.19 (0.526)	4.23 (0.582)	4.69 (0.86)	<.001
Lowest potassium plasma, mEq/L	22.4 (2.9)	25.3 (3.9)	19.8 (4.8)	<.001
Highest creatinine, mg/dL, median (IQR)	0.85 (0.70-1.04)	0.80 (0.74-1.17)	1.18 (0.88-1.75)	<.001
Worst inspired oxygen concentration, %/100	0.53 (0.24)	0.548 (0.25)	0.729 (0.26)	<.001
Worst arterial oxygen partial pressure, mm Hg, median, (IQR)	127 (92-205)	107 (78-164)	104 (76-174)	<.001
Worst arterial CO2 partial pressure, mm Hg	39 (2.8)	52.2 (18.3)	56.7 (14.8)	<.001
Worst arterial pH	7.4 (0.03)	7.39 (0.03)	7.19 (0.13)	<.001
Highest hemoglobin, g/dL	12.5 (2.0)	12.6 (2.2)	13.1 (2.5)	<.001
Highest white blood cell count, / μ L	14 100 (7800)	13 900 (11 500)	17 800 (11 600)	<.001
Lowest platelets, $\times 10^3$ / μ L	203 (79)	201 (90)	197 (88)	<.001
Plasma albumin, mmol/L	31.3 (5.9)	30.9 (6.0)	29.8 (6.9)	<.001
Worst plasma bilirubin, mmol/L, median (IQR)	13 (9-18)	13 (9-18)	12 (8-18)	<.001
Plasma glucose, mg/dL	161.08 (63.06)	159.28 (64.86)	209.01 (106.31)	<.001
Severity of illness at ICU admission				
APACHE III Score	57.9 (28)	61.8 (30.5)	91.4 (37.3)	<.001
ANZROD, %	29.3	33.8	51.3	<.001

Table 2 - Comparison of outcomes in patients with cerebral injury based on their pH and carbon dioxide (unadjusted)

Variable	Normocapnia and normal pH (N= 13132)	Compensated Hypercapnia (N=1352)	Hypercapnic acidosis (N=16586)
Died in Hospital [n, %]	3691 (28%)	414 (31%)	8457 (51%)
Discharged Home [n, %]	4757 (36%)	505 (37%)	5064 (30%)
Discharged to Rehabilitation [n, %]	2225 (17%)	205 (15%)	1300 (8%)
Discharged to Other Hospital [n, %]	2370 (18%)	221 (16%)	1697 (10%)
ICU LOS (days) [median; IQR]	3.0 (2.9-3.2)	2.6 (2.4-2.9)	2.6 (2.5-2.7)
Hospital LOS (days) [median; IQR]	7.9 (7.3-8.6)	7.0 (6.3-7.8)	5.8 (5.4-6.3)

All comparisons were statistically significant p <0.001

Kaplan-Meier survival curves all cerebral injury patients

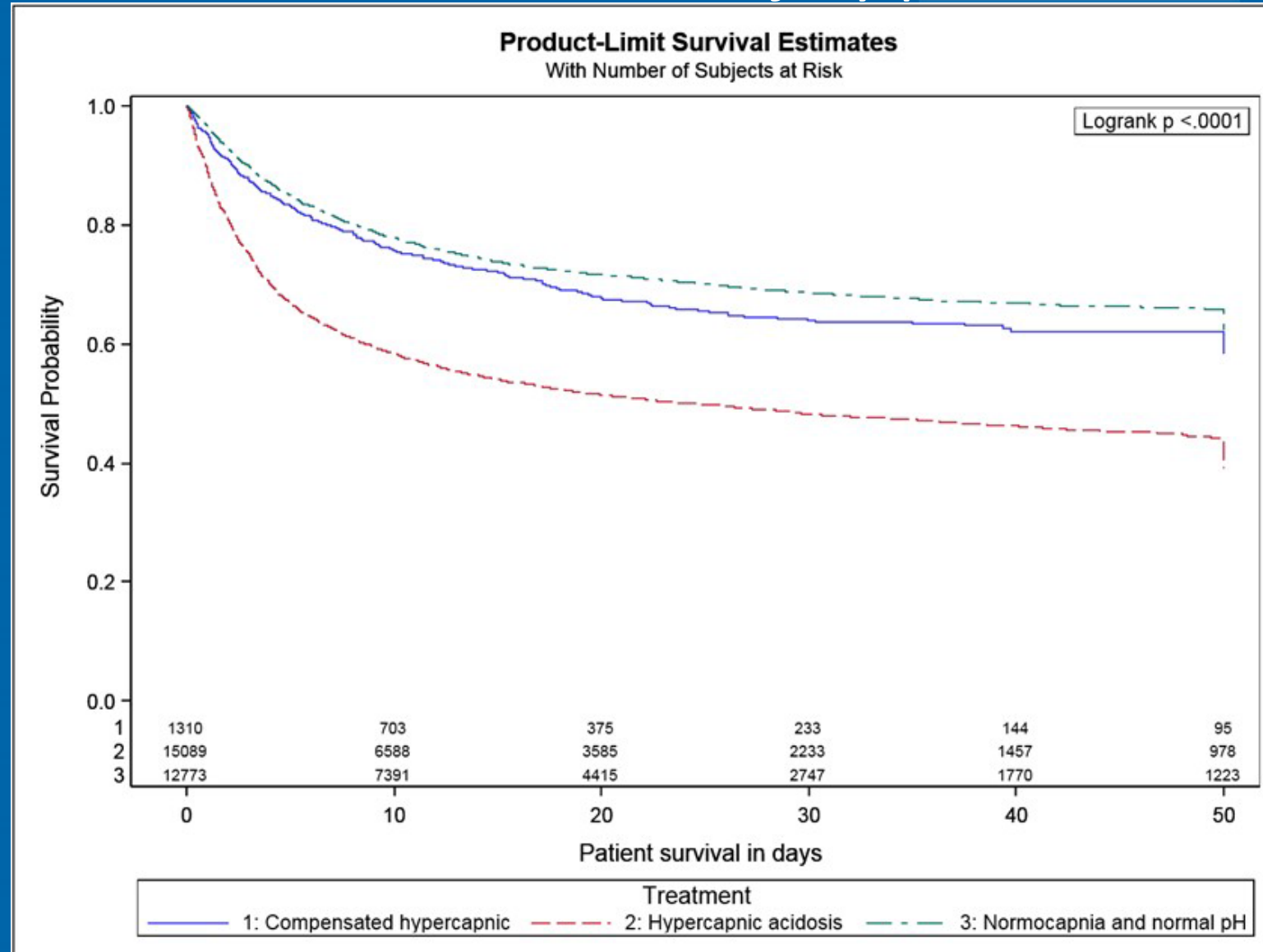




Table 3. Adjusted Hospital Mortality (Logistic Regression and Cox-Proportional Hazards) in Patients With Cerebral Injury

Diagnostic Category	Logistic Regression Analysis ^a		Cox Proportional Hazards ^b	
	OR (95% CI)	P Value	HR (95% CI)	P Value
Cardiac arrest				
Hypercapnic group				
Normocapnia and normal pH	1.00 [Reference]		1.00 [Reference]	
Compensated hypercapnia vs normocapnia and normal pH	1.04 (0.78-1.38)	<.001	0.98 (0.81-1.19)	<.001
Hypercapnic acidosis vs normocapnia and normal pH	1.51 (1.34-1.71)		1.23 (1.14-1.34)	
Stroke				
Hypercapnic group				
Normocapnia and normal pH	1.00 [Reference]		1.00 [Reference]	
Compensated hypercapnia vs normocapnia and normal pH	0.98 (0.8-1.21)	<.001	1.04 (0.9-1.2)	<.001
Hypercapnic acidosis vs normocapnia and normal pH	1.43 (1.27-1.6)		1.3 (1.21-1.4)	
Traumatic brain injury				
Hypercapnic group				
Normocapnia and normal pH	1.00 [Reference]		1.00 [Reference]	
Compensated hypercapnia vs normocapnia and normal pH	0.74 (0.5-1.11)	.004	0.85 (0.6-1.21)	.07
Hypercapnic acidosis vs normocapnia and normal pH	1.22 (1.06-1.42)		1.13 (1-1.27)	

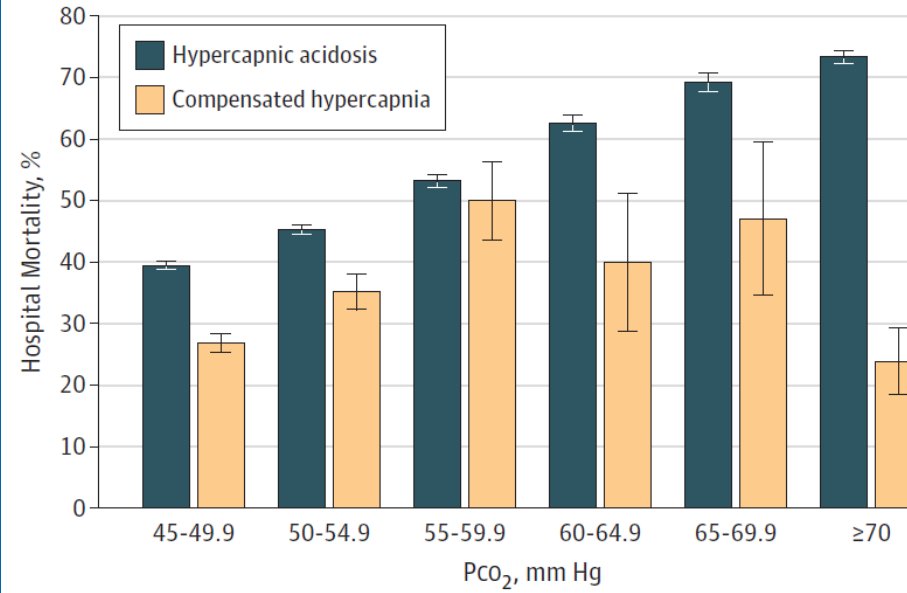


Table 4 Sensitivity analysis - Adjusted hospital mortality matched for admission severity scores

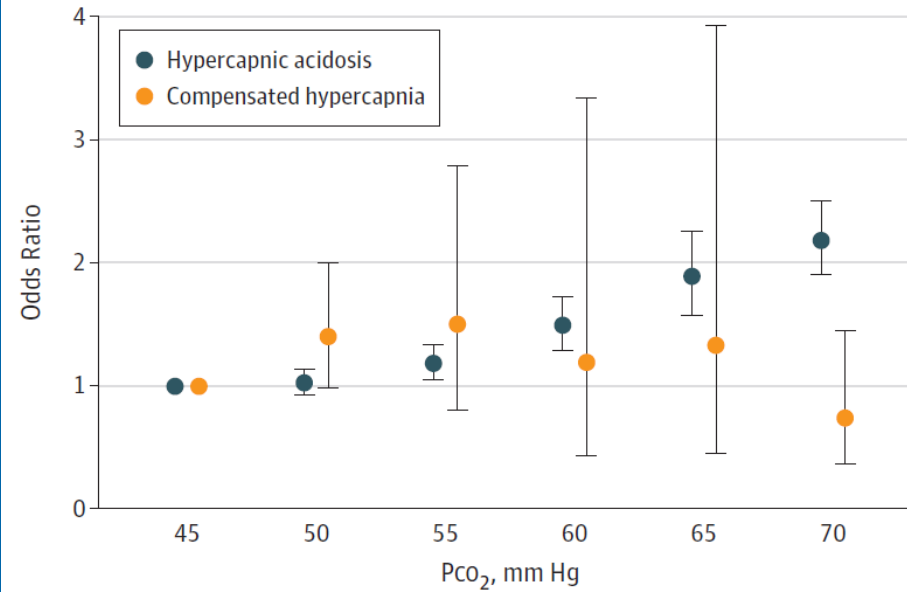
N	Diagnostic categories	Logistic regression analysis	
		OR (95% CI)	P Value
Cardiac arrest			
	Hypercapnic group		<0.0001
307	Normocapnia and normal pH	1	
307	Compensated hypercapnia vs Normocapnia and normal pH	0.97 (0.67-1.41)	
307	Hypercapnic acidosis vs Normocapnia and normal pH	2.16 (1.48-3.15)	
Stroke			
	Hypercapnic group		p=0.06
547	Normocapnia and normal pH	1	
547	Compensated hypercapnia vs Normocapnia and normal pH	1.05 (0.8-1.37)	
547	Hypercapnic acidosis vs Normocapnia and normal pH	1.34 (1.03-1.74)	
Traumatic Brain Injury			
	Hypercapnic group		p=0.13
481	Normocapnia and normal pH	1	
481	Compensated hypercapnia vs Normocapnia and normal pH	0.99 (0.6-1.64)	
481	Hypercapnic acidosis vs Normocapnia and normal pH	1.48 (0.96-2.28)	



A Unadjusted hospital mortality



B Adjusted odds ratio for hospital mortality



Conclusion

- Hypercapnic acidosis was associated with increased risk of hospital mortality in patients with cerebral injury.
- Hypercapnia, when compensated to normal pH during the first 24 hours of intensive care unit admission, may not be harmful in mechanically ventilated patients with cerebral injury.



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Questions...

