HYPER OXYGÉNATION VERSUS NORMO OXYGÉNATION EN REANIMATION

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16 Novembre 2018, Congrès National de l'Association Tunisienne de Réanimation

OXYGÈNE:

- Découvert par **Scheele** en 1772
- « redécouvert » par **Priestley** quelques années plus tard
- **Lavoisier**: identification de l'oxygène dans l'air et de son rôle capital dans la combustion.

- Oxygène: élément familier indispensable aux organismes aérobies (métabolisme aérobie)
- Intérêt clinique très tôt: premières utilisations pour l'assistance respiratoire dans la pneumonie datant du début du 20ème siècle

Statut de médicament en France en 1998
(décret 98-79 du 11 février 1998)

- Toxicité soulevée par une première étude animale de **Lavoisier** sur des porcs, en 1783.

- Toxicité « réapparue » dans les années 1950, à la suite d'une épidémie de fibroplasie rétrolentale chez les nouveaux-nés traités par des pressions partielles élevées en oxygène

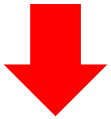
Priestley: « Oxygen might not be so proper for us in the usual healthy state of the body »

MÉCANISMES DE TOXICITÉ DE L'O2

Étudiés sur cellules épithéliales alvéolaires et endothéliales en culture soumises à des concentrations en O2 comprises entre 80 et 100 % pour des durées allant de 30 min à 48 h.

Augmentation de la PaO2 et de la concentration tissulaire en oxygène

Augmentation de la production d'espèces radicalaires dans les mitochondries, les microsomes et les fractions nucléaires



Mort cellulaire par apoptose ou nécrose

- **Effets biochimiques de l'hyperoxie:**
  - altérations mitochondriales,
  - chute du glucose et de l'ATP,
  - altérations de l'ADN,
  - peroxydation lipidique,
  - oxydation des protéines
  - activation de la NO-synthétase inductible.

  - Réponse inflammatoire dans les tissus pulmonaires, avec production accrue des cytokines (TNFα, IL-1, IL-6 et IL-8) et activation des PNN grands producteurs de ROS (reactive oxygen species)

TOXICITÉ DE L'OXYGÈNE CHEZ L'HOMME SAIN

- Résultats chez l'animal et rares observations en clinique humaine: seuil de FiO2 induisant une toxicité estimé à 85 %.

- Toxicité pulmonaire déjà pour des expositions prolongées aux FiO2 > 50%

- Syndrome de souffrance par hyperoxie: en trois phases :
  - trachéo-bronchite,
  - SDRA
  - fibrose interstitielle pulmonaire avec dégâts alvéolaires étendus

Vilar RE. Biochem J 1997;324:473-9

- Premiers signes de toxicité:
  - irritation trachéo-bronchique,
  - contraction thoracique et toux après une exposition d'environ 10 h à 100 % d'O2 à pression atmosphérique : rapidement réversible
  - SDRA à H24

- H24 à H48:
  - augmentation de la concentration en albumine dans les liquides de lavage broncho-alvéolaire
  - altération de la barrière alvéolo-capillaire
  - confirmation d'une atteinte précoce de l'endothélium des capillaires pulmonaires

- Pour les expositions de longue durée aux FiO2 supérieures à 85%: chute progressive de la tension artérielle en O2 et augmentation du shunt.
- A 50% d'O2 administré pour des périodes prolongées: altérations pulmonaires démontrées par l'analyse des liquides de lavage broncho-alvéolaire.
- FiO2 inférieures à 50% en période prolongée et en normobare: aucune altération observable chez l'homme sain.
- A faible pression: pas d'effets nocifs des concentrations élevées en O2.
- Lors des vols spatiaux: pas d'altération pulmonaire décrite chez les astronautes soumis à 100 % d'O2 à 250 mmHg durant des périodes prolongées.

N Engl J Med 1980;303:76-86

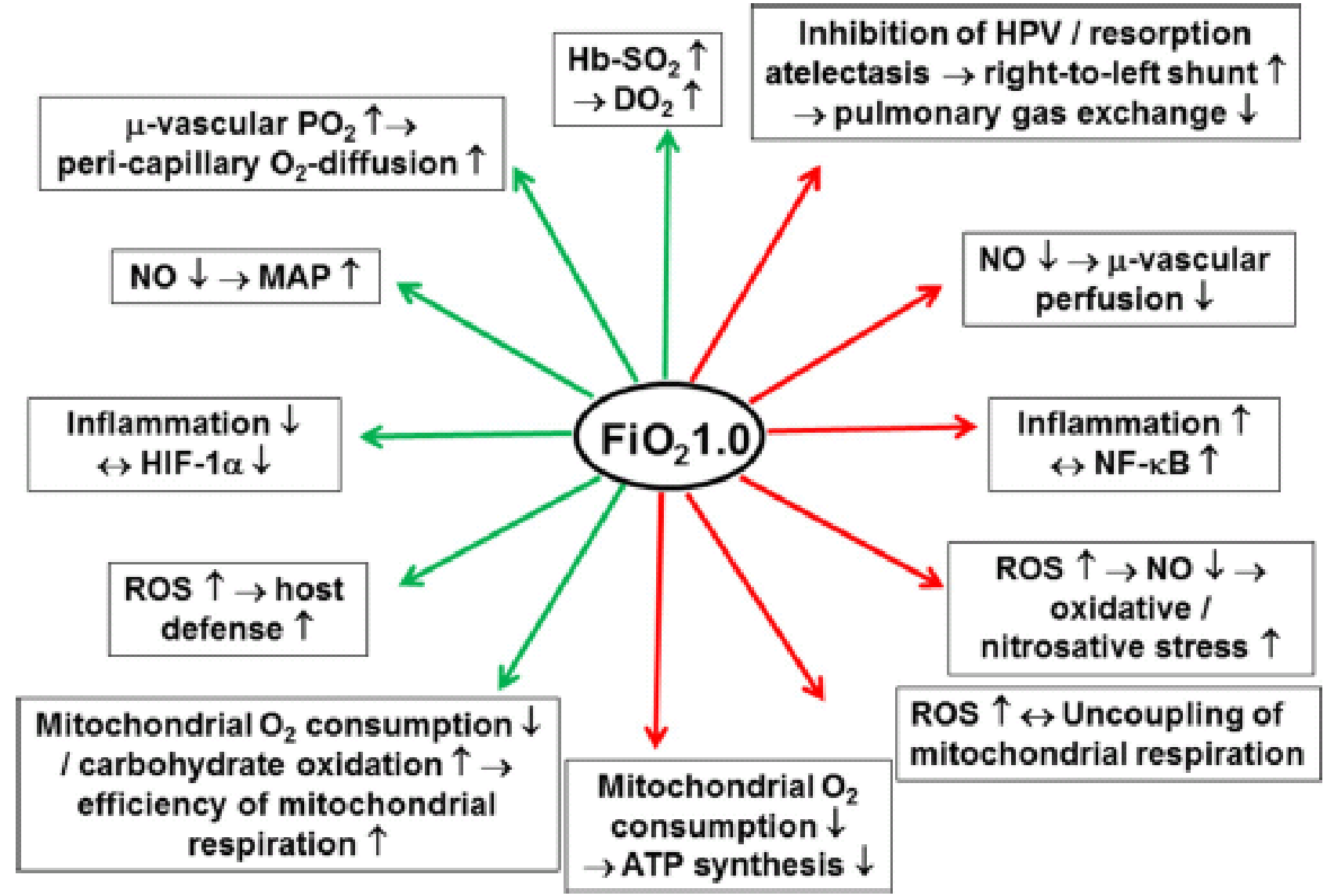


Fig. 1 Beneficial (*green arrows*) and deleterious (*red arrows*) effects of hyperoxia, i.e., breathing pure oxygen, during circulatory shock and/or in medical emergencies. FIO_2 fraction of inspired oxygen, PO_2 oxygen partial pressure, *µ* micro, *Hb* haemoglobin, SO_2 oxygen saturation, DO_2 systemic oxygen transport, *HPV* hypoxic pulmonary vasoconstriction, *MAP* mean arterial pressure, *SVR* systemic vascular resistance, *NO*: nitric oxide, *HIF-1α*: hypoxia-inducible factor 1 alpha, *NF-κB* nuclear transcription factor kappaB, *ROS* reactive oxygen species, *ATP* adenosine triphosphate; adapted from Asfar et al. [16] with kind permission from Springer Science and Business Media

OXYGÉNOTHÉRAPIE EN RÉANIMATION

- **Recommandations d'Experts de la Société de Réanimation de Langue Française**

J.C. Richard, Ch. Girault, S. Leteurtre et le groupe d'Experts de la SRLF

Janvier 2006

Toxicité de l'oxygène:

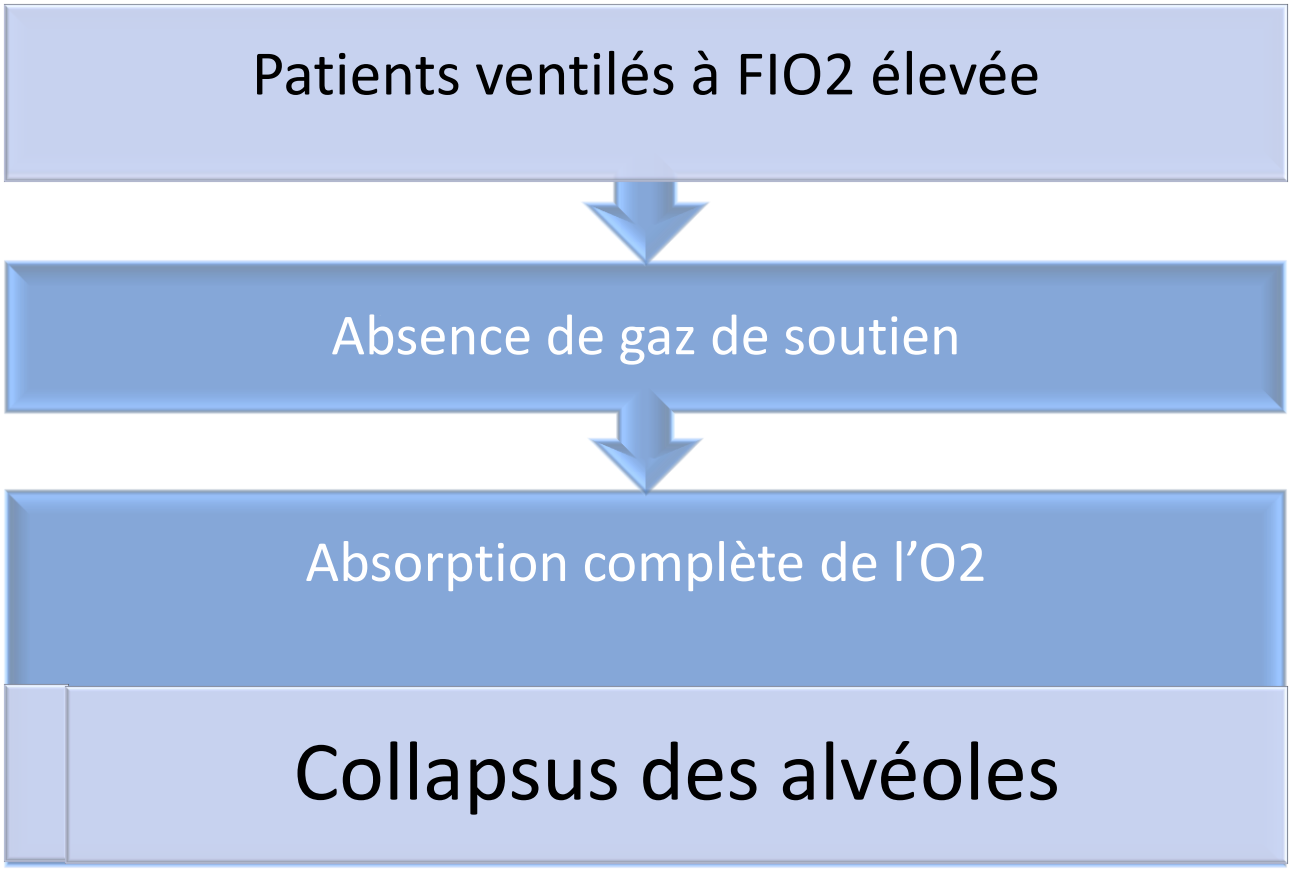
Sur ce sujet extrêmement important pour la pratique, les experts s'accordent pour dire que :

- Il n'y a pas à ce jour de démonstration de la toxicité de l'oxygène administré à forte concentration chez l'homme ***(accord fort).***

Néanmoins, tous ne sont pas d'accords sur les points suivants :

- L'innocuité pulmonaire de l'O2 pur au cours du SDRA n'est pas prouvée ***(accord faible).***
- L'utilisation de FiO2 élevées (> 80%) peut favoriser la survenue d'atélectasies dites de dénitrogénation, en particulier quand elle est associée à des niveaux de PEP faibles ***(accord faible).***

L'atélectasie d'absorption/dénitrogénation



Atelectasis and mechanical ventilation mode during conservative oxygen therapy: A before-and-after study

Satoshi Suzuki, MD, PhD [a], Glenn M. Eastwood, PhD [a], Mark D. Goodwin, MD, FRANZCR [b], Geertje D. Noë, MD, FRANZCR [b], Paul E. Smith, MD, FRANZCR [b], Neil Glassford, MD [a], Antoine G. Schneider, MD [a], Rinaldo Bellomo, MD, FCICM [a,c,*]

Phase I: oxygénothérapie conventionnelle

Phase II: oxygénothérapie pour objectif de SaO2= 90% à 92%

Table 2A

Comparisons of atelectasis scoring according to oxygen therapy–chest radiography–based analysis

Variable	Total	Conventional	Conservative	*P*
No. of CXRs	555	270	285	
Interobserver agreement of atelectasis scoring				.13
Minimal discrepancy	538 (97%)	264 (98%)	274 (96%)	
All 3 agreed	231 (42%)	123 (46%)	108 (38%)	
2 of 3 agreed	307 (55%)	141 (52%)	166 (58%)	
Discrepancy (all 3 disagreed)	17 (3%)	6 (2%)	11 (4%)	
Atelectasis score				.005
0	97 (17%)	35 (13%)	62 (22%)	
1	98 (18%)	43 (16%)	55 (19%)	
2	286 (52%)	146 (54%)	140 (49%)	
3	73 (13%)	45 (17%)	28 (10%)	
4	1 (0.2%)	1 (0.4%)	0 (0%)	

Journal of Critical Care 30 (2015) 1232–1237

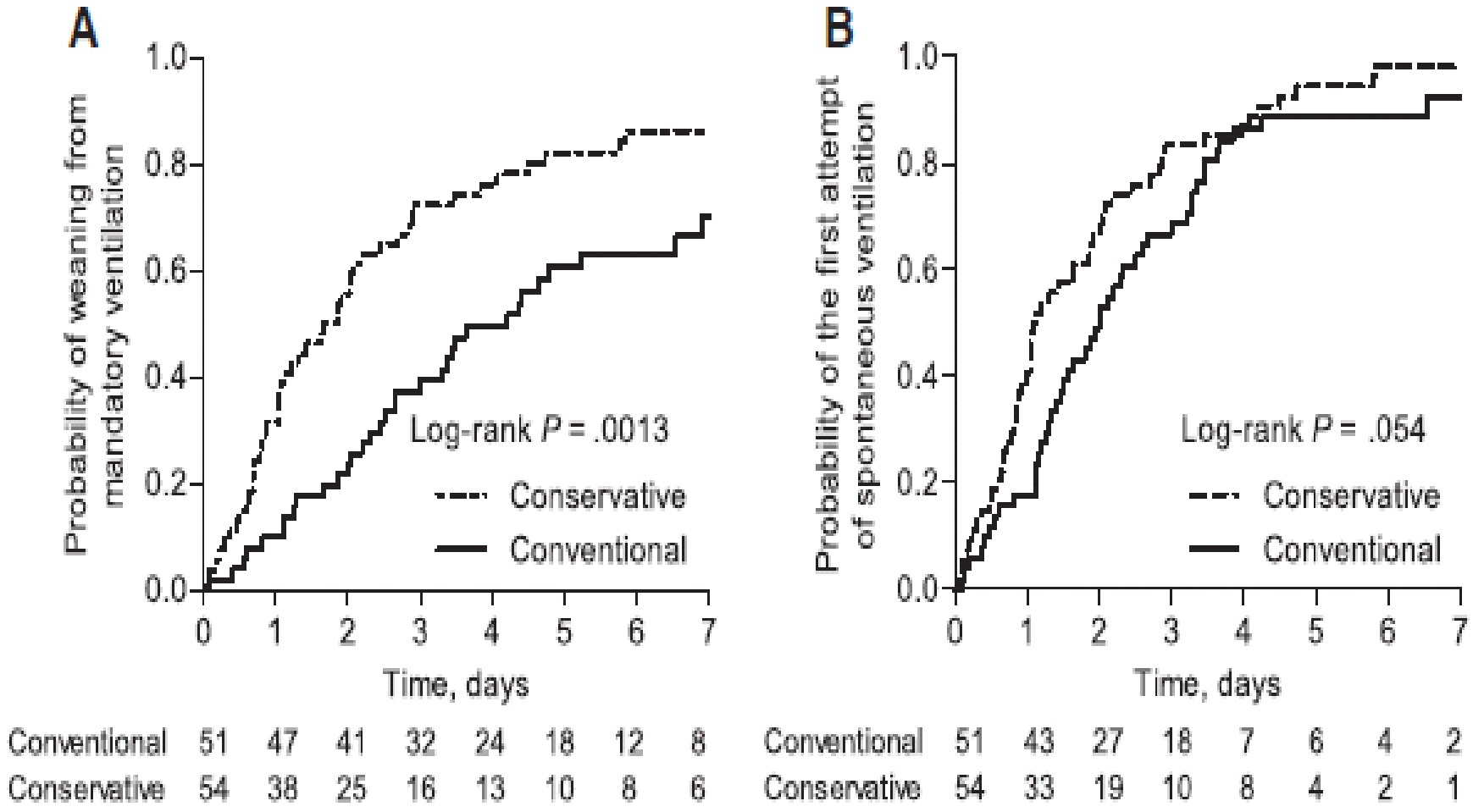


Fig. 2. Kaplan-Meier analysis of time to weaning from mandatory ventilation mode (A) and first SVT (B) in the first 7 days.

ORIGINAL ARTICLE

Conservative versus Liberal Oxygenation Targets for Mechanically Ventilated Patients

A Pilot Multicenter Randomized Controlled Trial

Critères d'inclusion:

•Age>18 ans

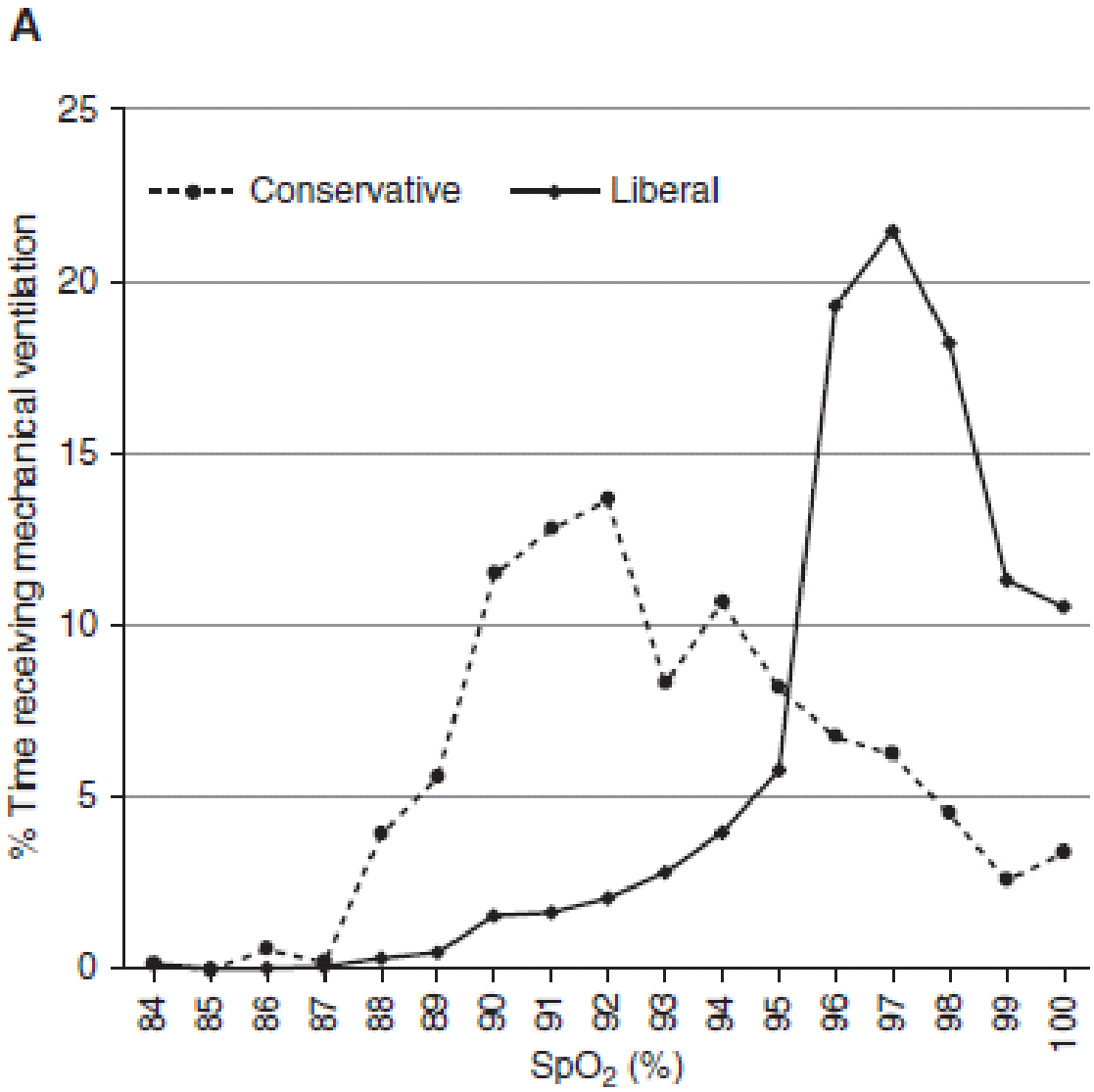
•VM< 24H

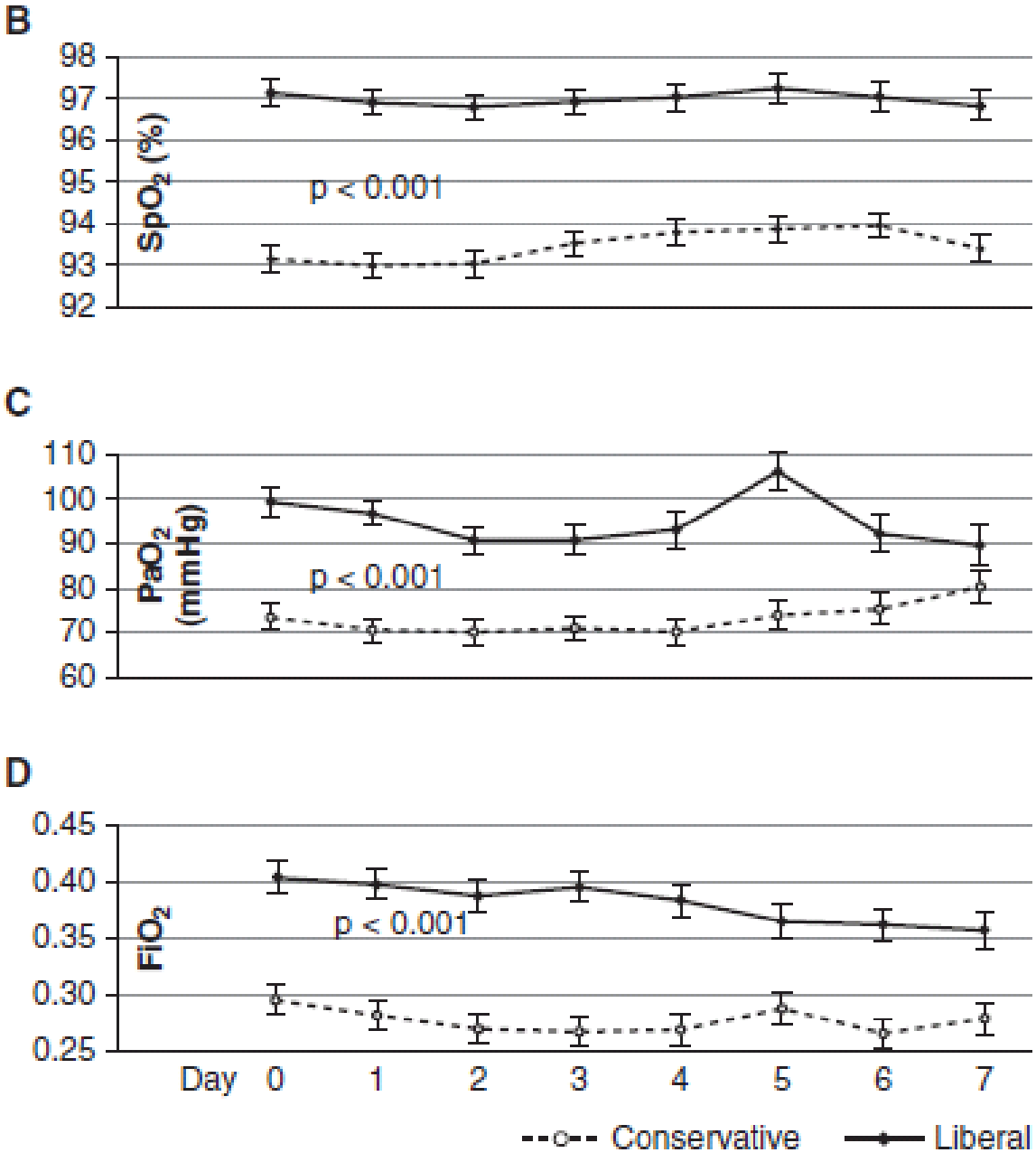
2 bras:

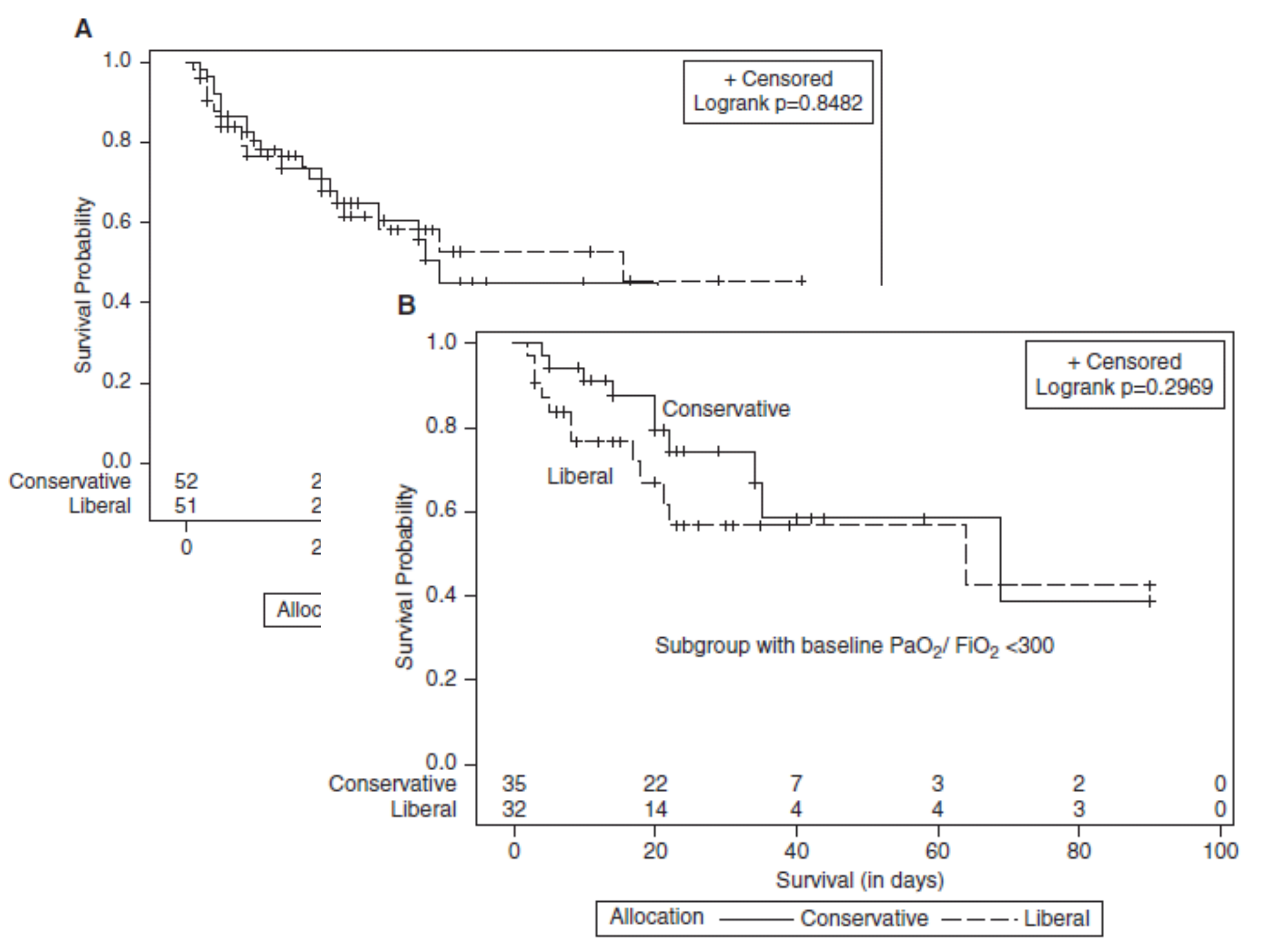
• Oxygénothérapie conservatrice: SpO2 à 88-92% (n=52)

• Oxygénothérapie libérale: SpO2 > 96% (n=51)

Am J Respir Crit Care Med 2016; 193 (1): 43–51


A
25
20
15
10
5
0
Conservative
Liberal
% Time receiving mechanical ventilation
84
85
86
87
88
89
90
91
92
93
94
95
96
97
98
99
100
SpO2 (%)


B
98
97
96
95
94
93
92
SpO2 (%)
p < 0.001
C
110
100
90
80
70
60
PaO2 (mmHg)
p < 0.001
D
0.45
0.40
0.35
0.30
0.25
FiO2
p < 0.001
Day 0 1 2 3 4 5 6 7
Conservative
Liberal


A
1.0
0.8
0.6
0.4
0.2
0.0
Survival Probability
+ Censored
Logrank p=0.8482
Conservative 52
Liberal 51
0
Alloc
B
1.0
0.8
0.6
0.4
0.2
0.0
Survival Probability
+ Censored
Logrank p=0.2969
Conservative
Liberal
Subgroup with baseline PaO2/ FiO2 <300
Conservative 35 22 7 3 2 0
Liberal 32 14 4 4 3 0
0 20 40 60 80 100
Survival (in days)
Allocation Conservative Liberal

Raj et al. Critical Care 2013, 17:R177
http://ccforum.com/content/17/4/R177

CRITICAL CARE

RESEARCH Open Access

Hyperoxemia and long-term outcome after traumatic brain injury

Hyperoxémie: PaO2 < 10 Kpa
Normoxémie: PaO2 = 10-13,3 KPa
Hyperoxémie: PaO2 > 13,3 KPa

Table 2 Unadjusted outcomes

	All patients (n = 1116)	Hypoxemia (n = 174)	Normoxemia (n = 375)	Hyperoxemia (n = 567)	*P*-value
Mortality, number of patients (%)					
In-ICU	201 (18)	42 (24)	61 (16)	98 (17)	0.067
In-hospital	313 (28)	64 (37)	105 (28)	144 (25)	0.014
6-month	435 (39)	83 (48)	151 (40)	201 (35)	0.012

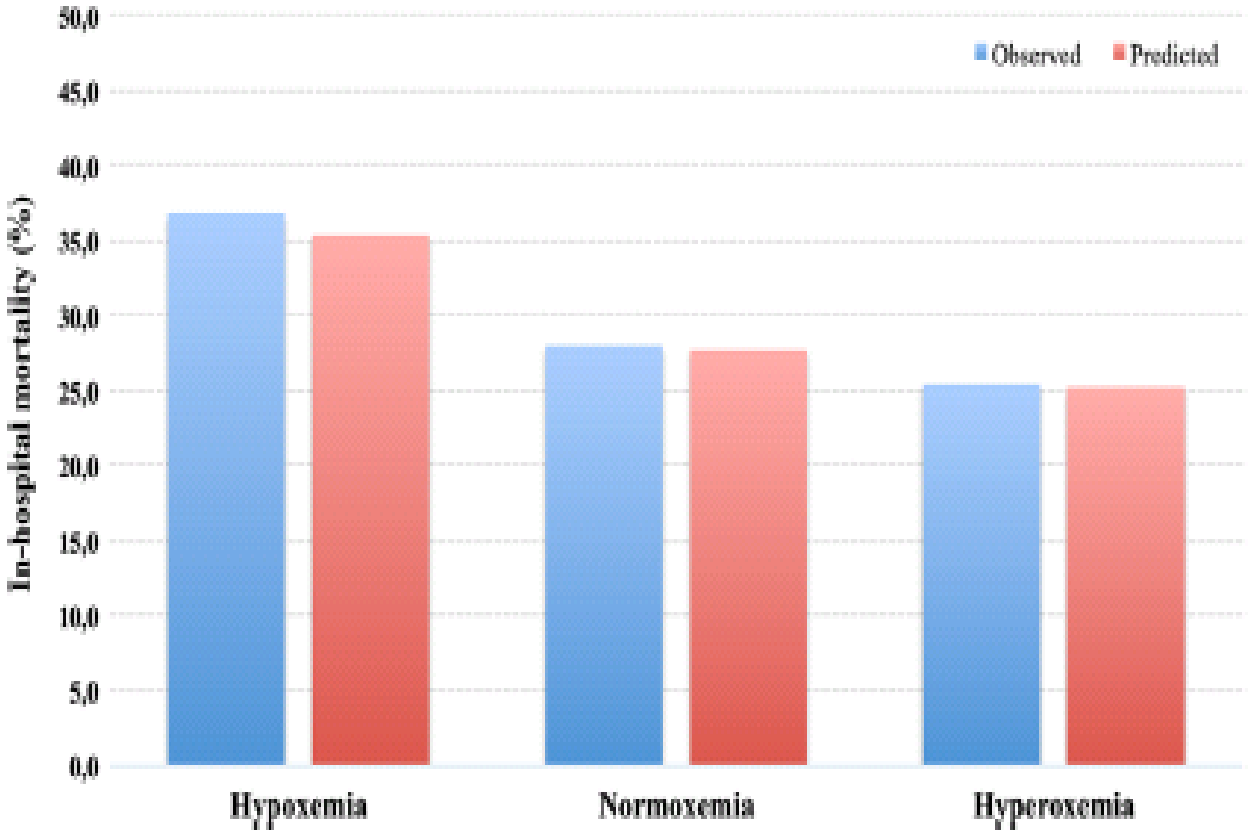


Figure 3 Observed and mean predicted in-hospital mortality differences between arterial oxygen tension (PaO_2) groups.

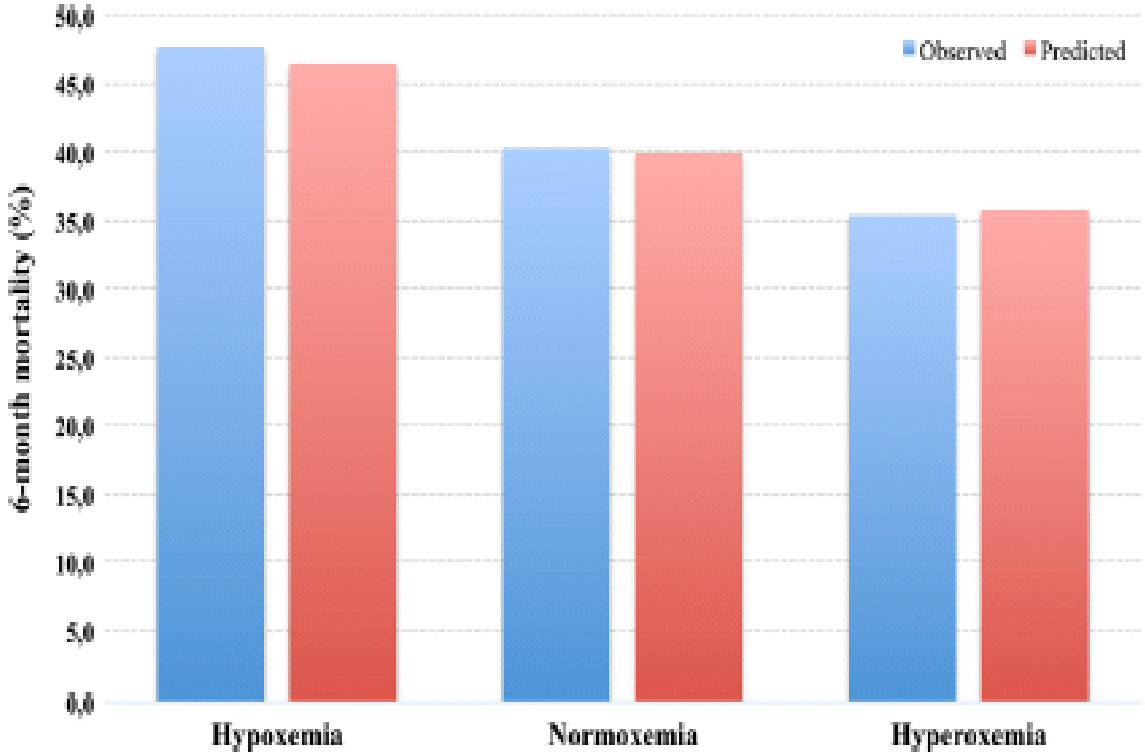


Figure 4 Observed and mean predicted 6-month mortality differences between PaO_2 groups. The difference in mean predicted risk of death is significantly different among the groups ($p < 0.001$), being highest in the hypoxemia group and lowest in the hyperoxemia group. Predicted risk of death matched observed mortality very well within the quartiles with R_L^2 values between 0.519 and 0.603.

Table 3 Adjusted outcomes by multivariable logistic regression model showing relationship between PaO_2 groups and outcome

Variable	Odds ratio (95% CI)	*P*-value
	6-month mortality	
Hypoxemia versus normoxemia	0.90 (0.57, 1.41)	0.648
Hyperoxemia versus normoxemia	0.88 (0.63, 1.22)	0.429
Hyperoxemia versus hypoxemia	0.97 (0.63, 1.50)	0.898
	In-hospital mortality	
Hypoxemia versus normoxemia	1.01 (0.63, 1.62)	0.967
Hyperoxemia versus normoxemia	0.94 (0.65, 1.36)	0.753
Hyperoxemia versus hypoxemia	0.93 (0.59, 1.47)	0.766

Air Versus Oxygen in ST-Segment–Elevation Myocardial Infarction

Groupe 1: oxygène à 8L/min
Groupe 2: pas d'oxygène

Table 4. Adverse Clinical End Points at Hospital Discharge and the 6-Month Follow-Up in Patients With Confirmed STEMI

Clinical End Point	Oxygen Arm (n=218)	No Oxygen Arm (n=223)	*P* Value
At hospital discharge, n (%)			
Mortality, any cause	4 (1.8)	10 (4.5)	0.11
Cardiac cause	4 (1.8)	7 (3.1)	…
Massive hemorrhage	0	2 (0.8)	…
Sepsis	0	1 (0.4)	…
Recurrent myocardial infarction	12 (5.5)	2 (0.9)	0.006
Stroke or transient ischemic attack	3 (1.4)	1 (0.4)	0.30
Cardiogenic shock	20 (9.2)	20 (9.0)	0.94
Coronary artery bypass grafting	5 (2.3)	9 (4.0)	0.30
Major bleeding	9 (4.1)	6 (2.7)	0.41
Arrhythmia	88 (40.4)	70 (31.4)	0.05

Circulation. 2015;131:2143-2150

At the 6-mo follow-up, n (%)*			
Mortality, any cause	8 (3.8)	13 (5.9)	0.32
Cardiac cause	6 (2.9)	9 (4.1)	…
Massive hemorrhage	0	2 (0.9)	…
Sepsis	0	1 (0.5)	…
Renal failure	1 (0.5)	0	…
Cancer	0	1 (0.5)	…
Recurrent myocardial infarction	16 (7.6)	8 (3.6)	0.07
Stroke or transient ischemic attack	5 (2.4)	3 (1.4)	0.43
Repeat revascularization	23 (11.0)	16 (7.2)	0.17
MACEs	46 (21.9)	34 (15.4)	0.08

MACE indicates major adverse cardiac events (all-cause mortality, recurrent myocardial infarction, repeat revascularization, stroke); and STEMI, ST-segment–elevation myocardial infarction.

Six et al. Critical Care (2016) 20:195
DOI 10.1186/s13054-016-1368-4

Critical Care

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Hyperoxemia as a risk factor for ventilator-associated pneumonia

	VAP		P
	Yes	No	
	n = 141	n = 362	
Stress ulcer prophylaxis			0.002
Proton-pump inhibitor	122 (86)	279 (77)	
Sucralfate	9 (6)	46 (13)	
No	10 (7)	40 (11)	
Tracheostomy	24 (17)	47 (13)	0.243
Red blood cell transfusion	86 (61)	139 (38)	<0.001[a]
Sedation	122 (86)	284 (78)	0.039[b]
Neuromuscular-blocking agent use	10 (7)	20 (6)	0.505
Mean number of ABG per day	3 (1–6)	2 (1–5)	0.261
Number of days with PaO_2 > 120 mmHg	5 (2–7)	3 (1–5)	<0.001
Percentage of days with PaO_2 > 120 mmHg	0.33 (0.19–0.58)	0.33 (0.14–0.50)	0.282
Duration of MV prior to VAP, days	14 (8–23)	9 (5–17)	<0.001
Total duration of MV, days	30 (17–43)	9 (5–17)	<0.001
Length of ICU stay, days	34 (19–45.5)	12 (7–21)	<0.001
ICU mortality	73 (52)	130 (35)	0.001[c]

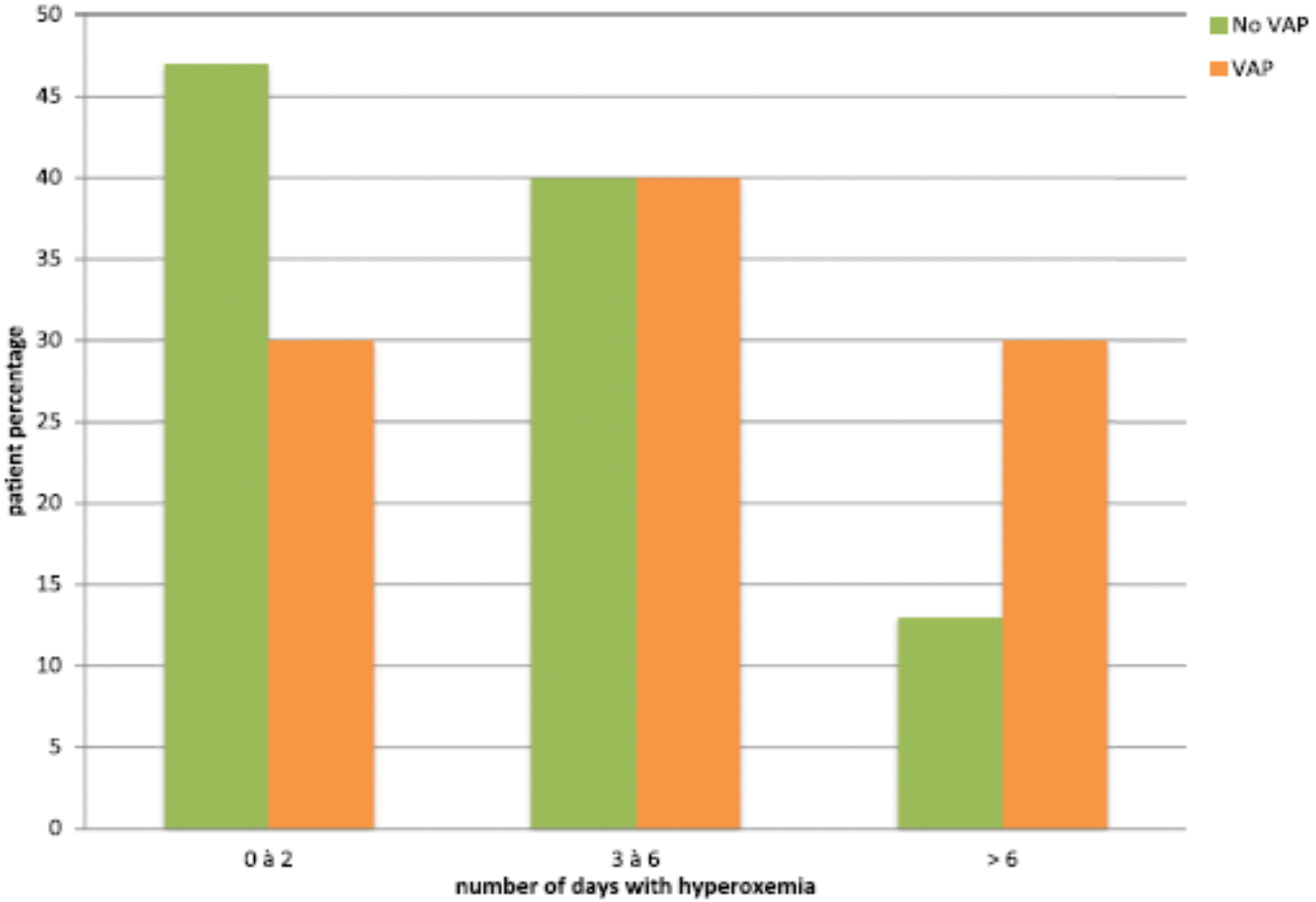

50
45
40
35
30
25
20
15
10
5
0
patient percentage
No VAP
VAP
0 à 2
3 à 6
> 6
number of days with hyperoxemia

Table 5 Risk factors for ventilator-associated pneumonia by Cox proportional hazards model

Variable	Univariate analysis		Multivariate analysis (model 1)		Multivariate analysis (model 2)	
	HR (95 % CI)	*P*	HR (95 % CI)	*P*	HR (95 % CI)	*P*
At ICU admission						
LOD score	1.04 (1.01, 1.09)	0.044	-	0.922	-	0.138
Transfer from other wards	0.65 (0.45, 0.93)	0.018	-	0.356	-	0.952
Prior antibiotic treatment	0.67 (0.48, 0.94)	0.021	-	0.483	-	0.184
Neurologic failure	1.82 (1.07, 3.09)	0.027	-	0.111	-	0.197
Poisoning	3.24 (1.9, 5.51)	<0.001	2.49 (1.31, 4.72)	0.005	2.16 (1.14, 4.09)	0.018
COPD	0.55 (0.37, 0.89)	0.003	-	0.063	-	0.065
McCabe score >2	0.76 (0.59, 0.99)	0.042	-	0.169		0.726
PaO2 > 120 mmHg	1.58 (1.11, 2.25)	0.011	NA	NA	1.68 (1.16, 2.42)	0.006
During ICU stay						
Percentage of days with PaO2 > 120 mmHg	5.67 (3.15, 10.20)	<0.001	6.23 (3.26, 11.9)	<0.001	NA	NA

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Effect of High-Flow Nasal Oxygen vs Standard Oxygen on 28-Day Mortality in Immunocompromised Patients With Acute Respiratory Failure

The HIGH Randomized Clinical Trial

JAMA. doi:10.1001/jama.2018.14282

Figure 1. Flow of Patients Through the HIGH Trial

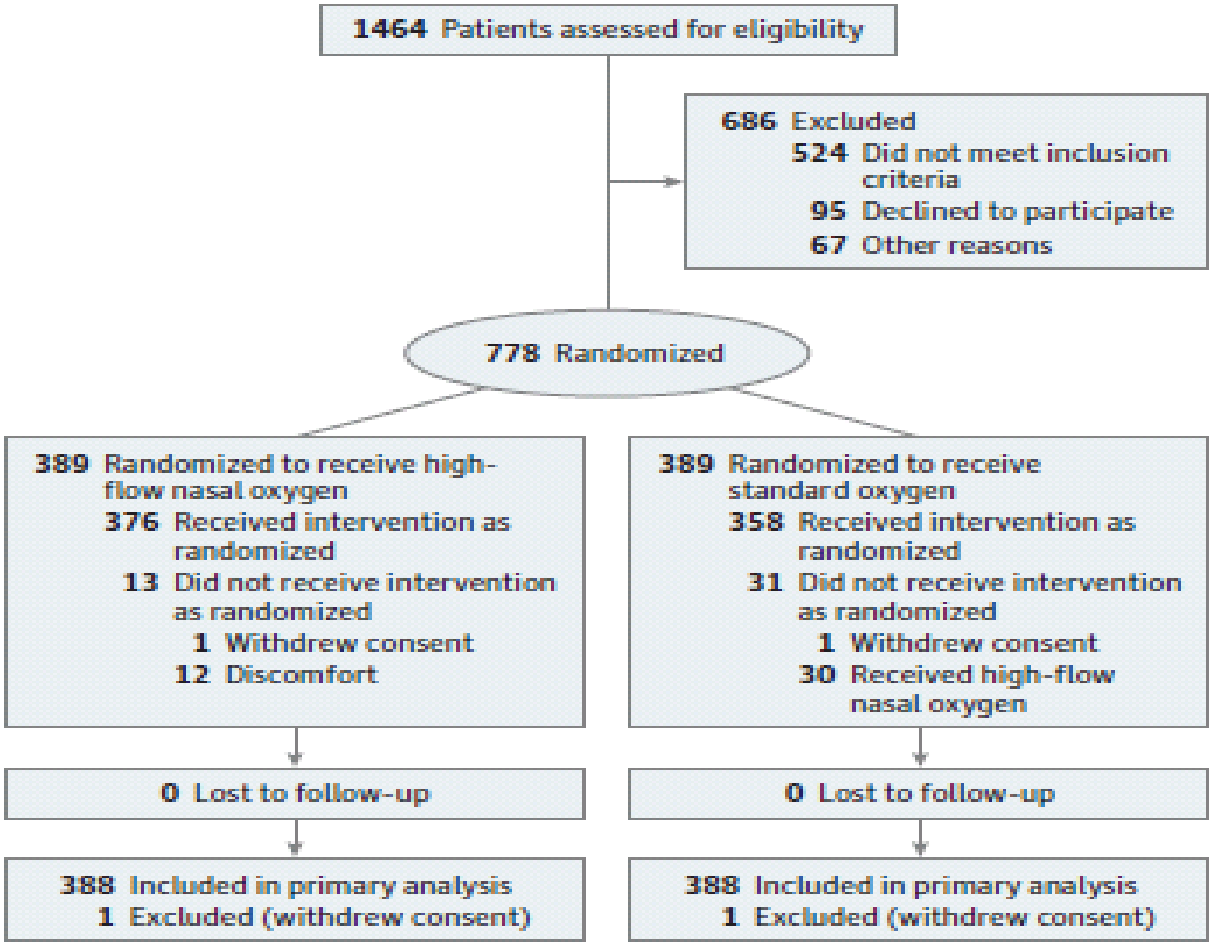
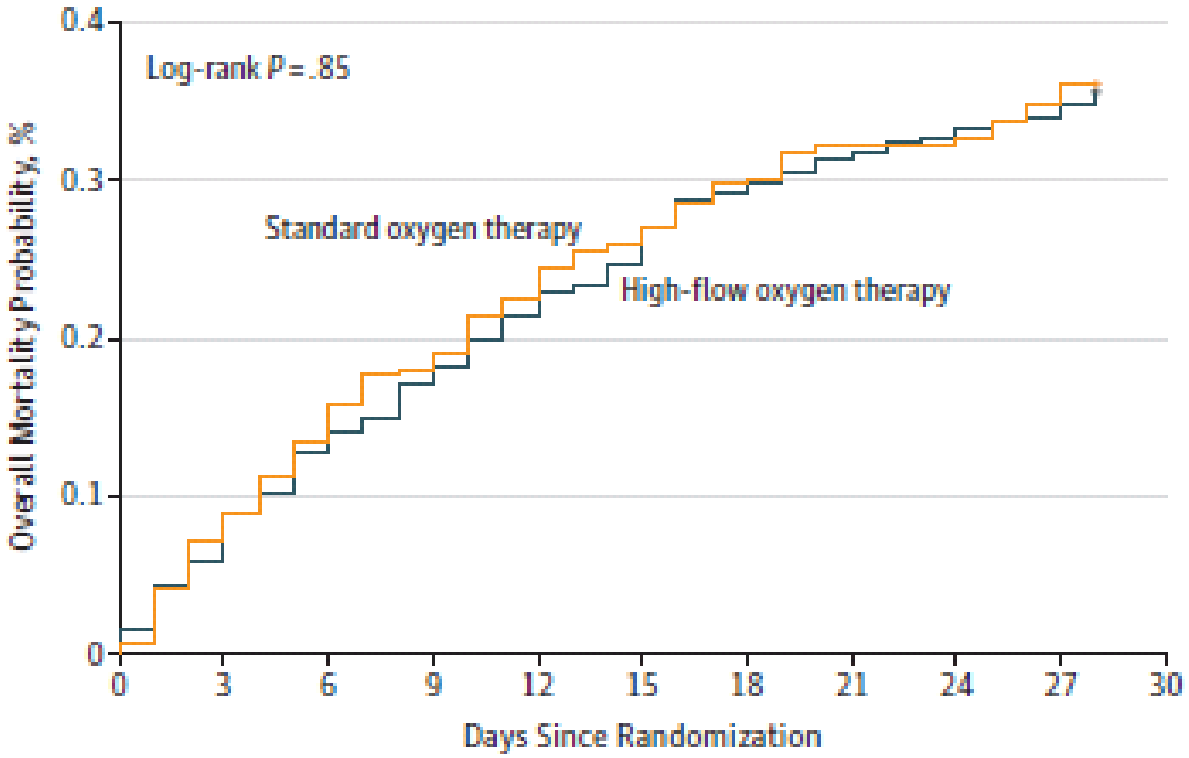


Table 2. Primary and Secondary End Points[a]

End Points	No. (%)		Mean Difference, % (95% CI)[b]	Relative Difference (95% CI)	*P* Value
	High-Flow Oxygen Therapy (n = 388)	Standard Oxygen Therapy (n = 388)			
Primary					
All-cause day-28 mortality	138 (35.6)	140 (36.1)	−0.5 (−7.3 to 6.3)	HR, 0.98 (0.77 to 1.24)	.94
Secondary					
Invasive mechanical ventilation[c]	150 (38.7)	170 (43.8)	−5.1 (−12.3 to 2.0)	HR, 0.85 (0.68 to 1.06)[d]	.17
ICU-acquired infection	39 (10.0)	41 (10.6)	−0.6 (−4.6 to 4.1)	HR, 1.01 (0.96 to 1.06)[d]	.91
ICU mortality	123 (31.7)	122 (31.4)	0.3 (−6.3 to 6.8)	RR, 1.01 (0.82 to 1.24)	.64
Hospital mortality	160 (41.2)	162 (41.7)	−0.5 (−7.5 to 6.4)	RR, 0.99 (0.84 to 1.17)	.77
Length of stay, median (IQR), d					
ICU	8 (4-14)	6 (4-13)	0.6 (−1.0 to 2.2)	NA[e]	.07
Hospital	24 (14-40)	27 (15-42)	−2 (−7.3 to 3.3)	NA[e]	.60

Figure 2. Probability of Day-28 Mortality in Immunocompromised Patients With Acute Respiratory Failure Receiving High-Flow Oxygen Therapy or Standard Oxygen Therapy



No. at risk

High-flow oxygen therapy	388	365	338	322	305	292	275	266	261	256	0
Standard oxygen therapy	388	360	336	318	301	287	272	263	263	253	0

Association Between Arterial Hyperoxia and Outcome in Subsets of Critical Illness: A Systematic Review, Meta-Analysis, and Meta-Regression of Cohort Studies*

Hendrik J. F. Helmerhorst, MD[1,2]; Marie-José Roos-Blom, MSc[3]; David J. van Westerloo, MD, PhD[1]; Evert de Jonge, MD, PhD[1]

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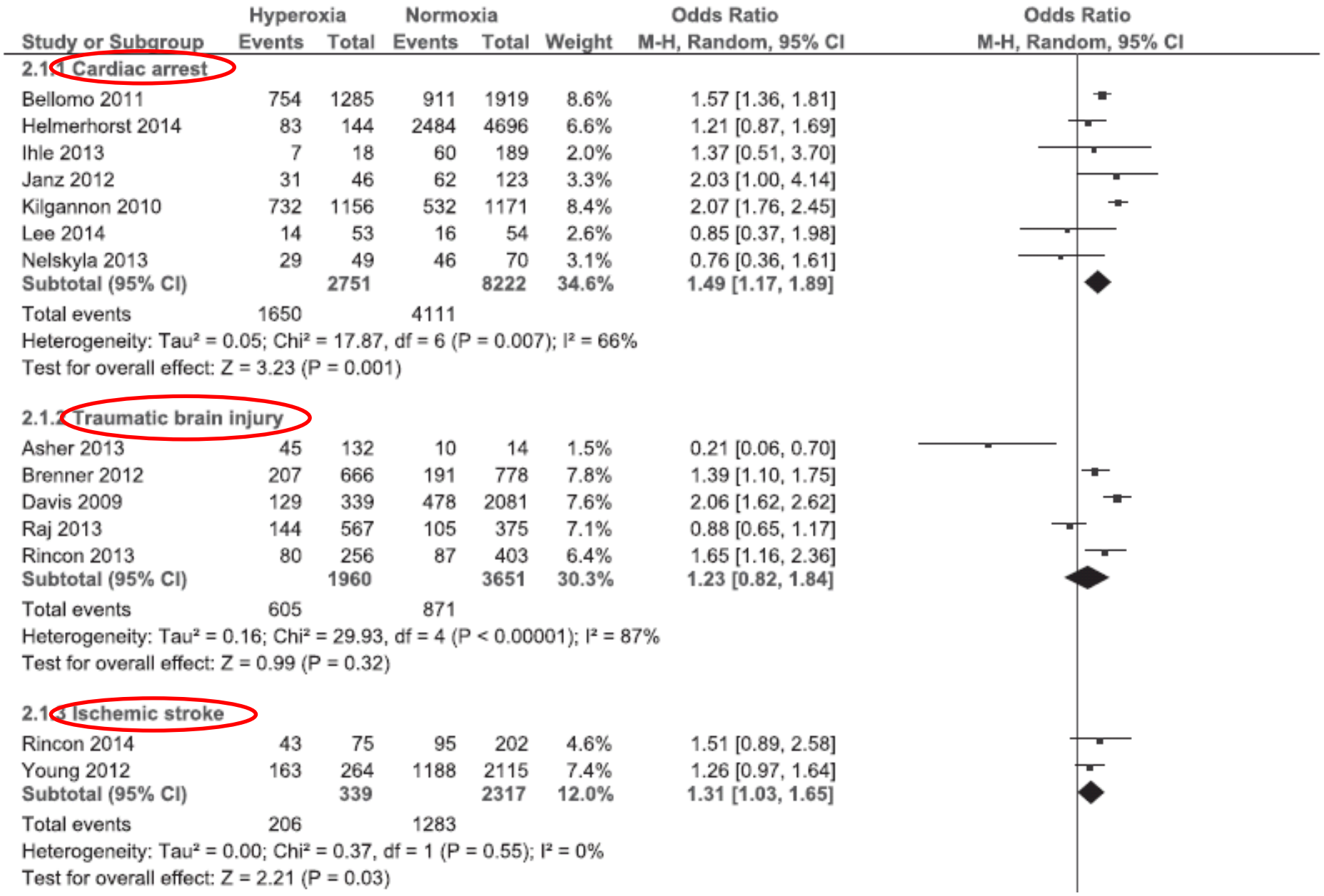
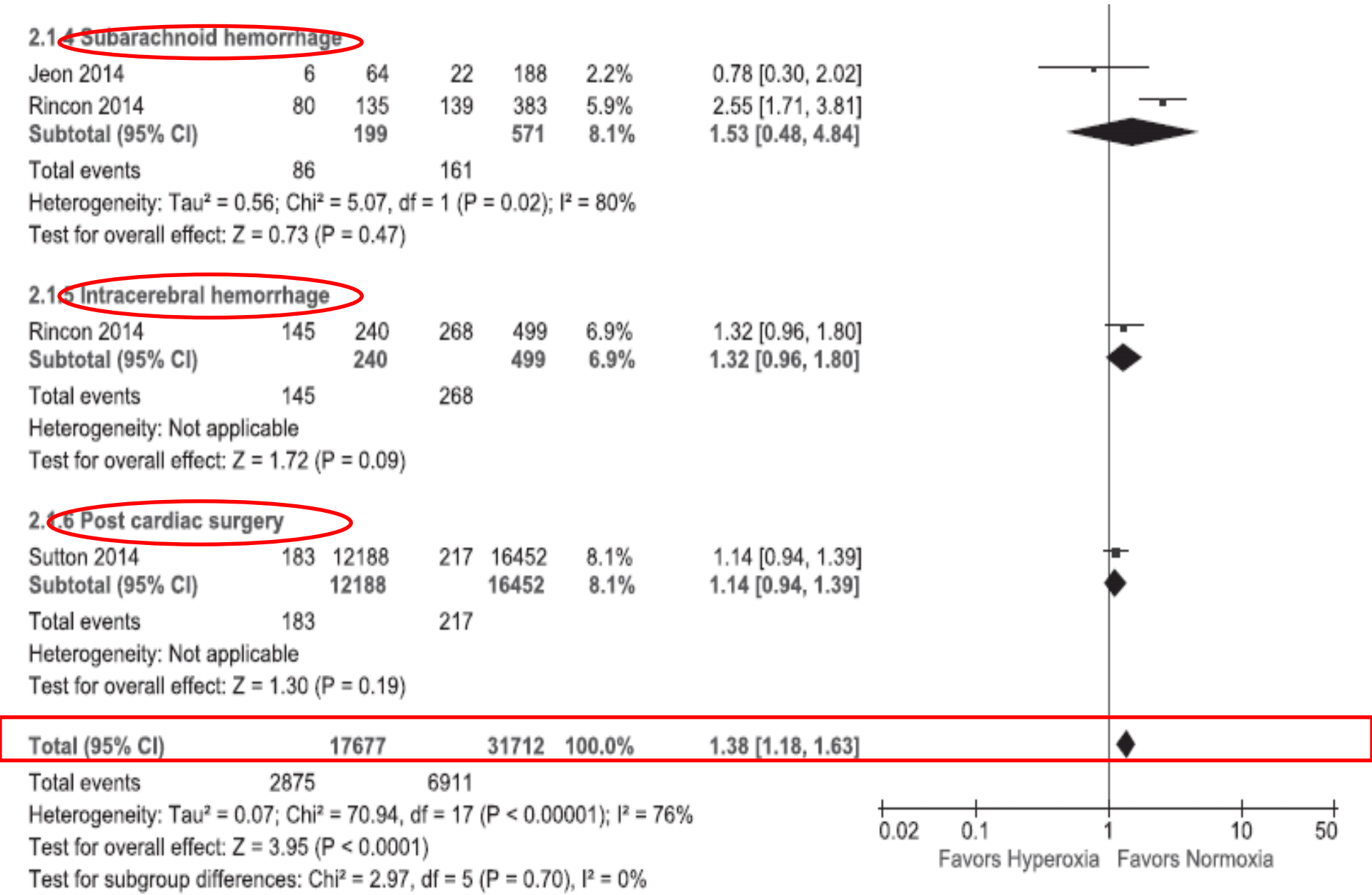

Hyperoxia
Normoxia
Odds Ratio
Odds Ratio
Study or Subgroup
Events
Total
Events
Total
Weight
M-H, Random, 95% CI
M-H, Random, 95% CI
2.1.1 Cardiac arrest
Bellomo 2011 754 1285 911 1919 8.6% 1.57 [1.36, 1.81]
Helmerhorst 2014 83 144 2484 4696 6.6% 1.21 [0.87, 1.69]
Ihle 2013 7 18 60 189 2.0% 1.37 [0.51, 3.70]
Janz 2012 31 46 62 123 3.3% 2.03 [1.00, 4.14]
Kilgannon 2010 732 1156 532 1171 8.4% 2.07 [1.76, 2.45]
Lee 2014 14 53 16 54 2.6% 0.85 [0.37, 1.98]
Nelskyla 2013 29 49 46 70 3.1% 0.76 [0.36, 1.61]
Subtotal (95% CI) 2751 8222 34.6% 1.49 [1.17, 1.89]
Total events 1650 4111
Heterogeneity: Tau² = 0.05; Chi² = 17.87, df = 6 (P = 0.007); I² = 66%
Test for overall effect: Z = 3.23 (P = 0.001)
2.1.2 Traumatic brain injury
Asher 2013 45 132 10 14 1.5% 0.21 [0.06, 0.70]
Brenner 2012 207 666 191 778 7.8% 1.39 [1.10, 1.75]
Davis 2009 129 339 478 2081 7.6% 2.06 [1.62, 2.62]
Raj 2013 144 567 105 375 7.1% 0.88 [0.65, 1.17]
Rincon 2013 80 256 87 403 6.4% 1.65 [1.16, 2.36]
Subtotal (95% CI) 1960 3651 30.3% 1.23 [0.82, 1.84]
Total events 605 871
Heterogeneity: Tau² = 0.16; Chi² = 29.93, df = 4 (P < 0.00001); I² = 87%
Test for overall effect: Z = 0.99 (P = 0.32)
2.1.3 Ischemic stroke
Rincon 2014 43 75 95 202 4.6% 1.51 [0.89, 2.58]
Young 2012 163 264 1188 2115 7.4% 1.26 [0.97, 1.64]
Subtotal (95% CI) 339 2317 12.0% 1.31 [1.03, 1.65]
Total events 206 1283
Heterogeneity: Tau² = 0.00; Chi² = 0.37, df = 1 (P = 0.55); I² = 0%
Test for overall effect: Z = 2.21 (P = 0.03)


2.14 Subarachnoid hemorrhage
Jeon 2014 6 64 22 188 2.2% 0.78 [0.30, 2.02]
Rincon 2014 80 135 139 383 5.9% 2.55 [1.71, 3.81]
Subtotal (95% CI) 199 571 8.1% 1.53 [0.48, 4.84]
Total events 86 161
Heterogeneity: Tau² = 0.56; Chi² = 5.07, df = 1 (P = 0.02); I² = 80%
Test for overall effect: Z = 0.73 (P = 0.47)
2.15 Intracerebral hemorrhage
Rincon 2014 145 240 268 499 6.9% 1.32 [0.96, 1.80]
Subtotal (95% CI) 240 499 6.9% 1.32 [0.96, 1.80]
Total events 145 268
Heterogeneity: Not applicable
Test for overall effect: Z = 1.72 (P = 0.09)
2.16 Post cardiac surgery
Sutton 2014 183 12188 217 16452 8.1% 1.14 [0.94, 1.39]
Subtotal (95% CI) 12188 16452 8.1% 1.14 [0.94, 1.39]
Total events 183 217
Heterogeneity: Not applicable
Test for overall effect: Z = 1.30 (P = 0.19)
Total (95% CI) 17677 31712 100.0% 1.38 [1.18, 1.63]
Total events 2875 6911
Heterogeneity: Tau² = 0.07; Chi² = 70.94, df = 17 (P < 0.00001); I² = 76%
Test for overall effect: Z = 3.95 (P < 0.0001)
Test for subgroup differences: Chi² = 2.97, df = 5 (P = 0.70), I² = 0%
0.02
0.1
1
10
50
Favors Hyperoxia
Favors Normoxia

Mortality and morbidity in acutely ill adults treated with liberal versus conservative oxygen therapy (IOTA): a systematic review and meta-analysis

Lancet 2018; 391: 1693–705

Derek K Chu*†, Lisa H-Y Kim*†, Paul J Young, Nima Zamiri, Saleh A Almenawer, Roman Jaeschke, Wojciech Szczeklik, Holger J Schünemann, John D Neary, Waleed Alhazzani

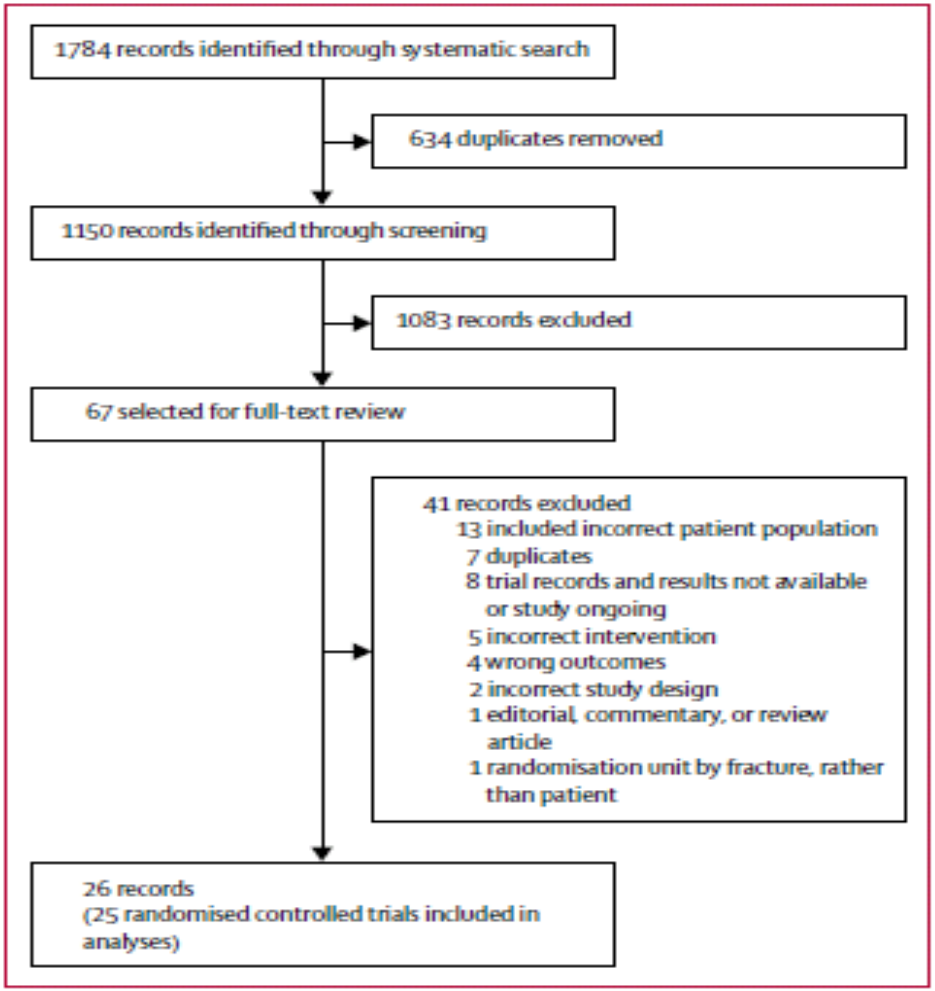
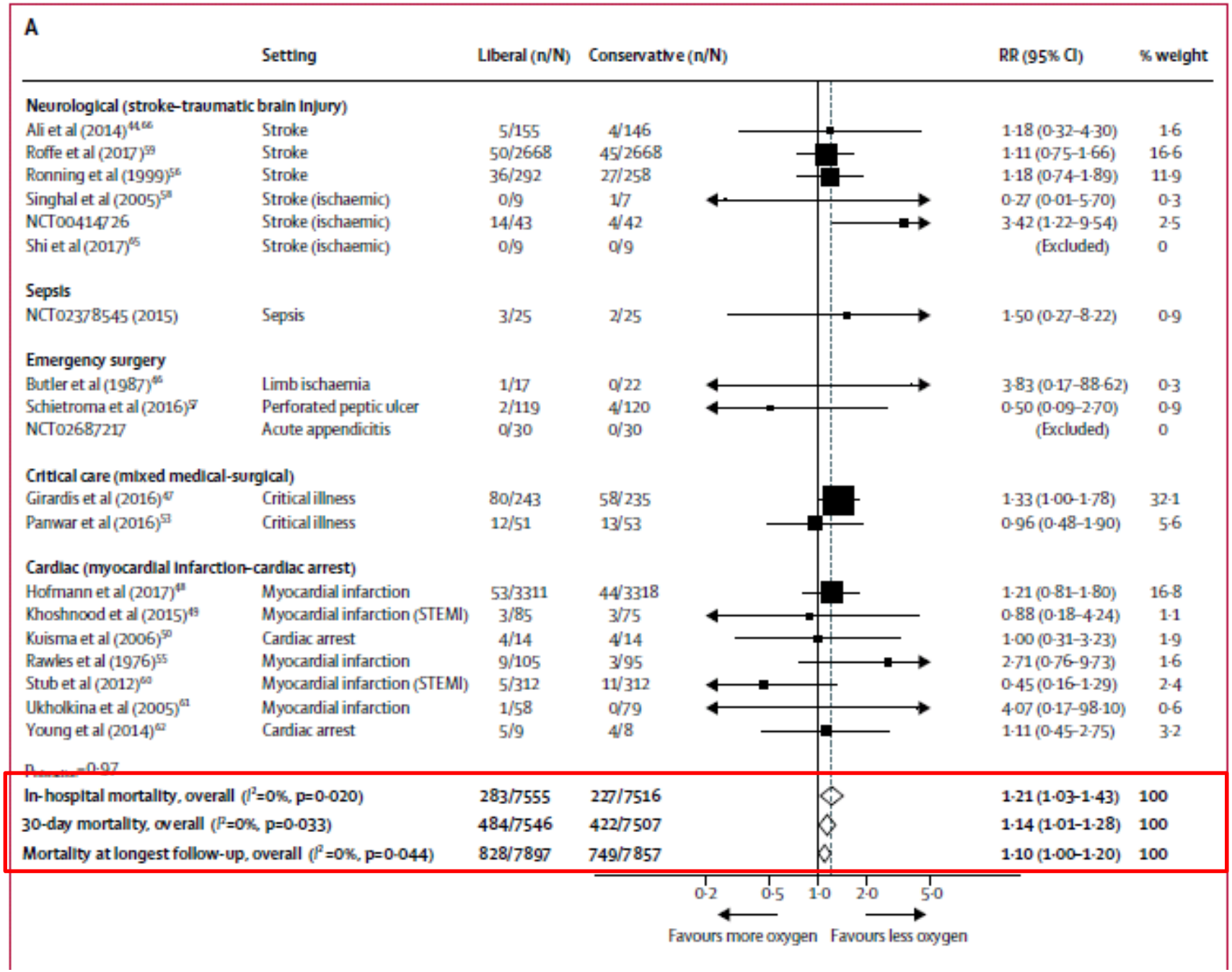


Figure 1: Study selection


A
Setting
Liberal (n/N)
Conservative (n/N)
RR (95% CI)
% weight
Neurological (stroke–traumatic brain injury)
Ali et al (2014)[44,66] Stroke 5/155 4/146 1·18 (0·32–4·30) 1·6
Roffe et al (2017)[59] Stroke 50/2668 45/2668 1·11 (0·75–1·66) 16·6
Ronning et al (1999)[56] Stroke 36/292 27/258 1·18 (0·74–1·89) 11·9
Singhal et al (2005)[58] Stroke (ischaemic) 0/9 1/7 0·27 (0·01–5·70) 0·3
NCT00414726 Stroke (ischaemic) 14/43 4/42 3·42 (1·22–9·54) 2·5
Shi et al (2017)[65] Stroke (ischaemic) 0/9 0/9 (Excluded) 0
Sepsis
NCT02378545 (2015) Sepsis 3/25 2/25 1·50 (0·27–8·22) 0·9
Emergency surgery
Butler et al (1987)[46] Limb ischaemia 1/17 0/22 3·83 (0·17–88·62) 0·3
Schietroma et al (2016)[57] Perforated peptic ulcer 2/119 4/120 0·50 (0·09–2·70) 0·9
NCT02687217 Acute appendicitis 0/30 0/30 (Excluded) 0
Critical care (mixed medical-surgical)
Girardis et al (2016)[47] Critical illness 80/243 58/235 1·33 (1·00–1·78) 32·1
Panwar et al (2016)[53] Critical illness 12/51 13/53 0·96 (0·48–1·90) 5·6
Cardiac (myocardial infarction–cardiac arrest)
Hofmann et al (2017)[48] Myocardial infarction 53/3311 44/3318 1·21 (0·81–1·80) 16·8
Khoshnood et al (2015)[49] Myocardial infarction (STEMI) 3/85 3/75 0·88 (0·18–4·24) 1·1
Kuisma et al (2006)[50] Cardiac arrest 4/14 4/14 1·00 (0·31–3·23) 1·9
Rawles et al (1976)[55] Myocardial infarction 9/105 3/95 2·71 (0·76–9·73) 1·6
Stub et al (2012)[60] Myocardial infarction (STEMI) 5/312 11/312 0·45 (0·16–1·29) 2·4
Ukholkina et al (2005)[61] Myocardial infarction 1/58 0/79 4·07 (0·17–98·10) 0·6
Young et al (2014)[62] Cardiac arrest 5/9 4/8 1·11 (0·45–2·75) 3·2
p=0·97
In-hospital mortality, overall (I²=0%, p=0·020) 283/7555 227/7516 1·21 (1·03–1·43) 100
30-day mortality, overall (I²=0%, p=0·033) 484/7546 422/7507 1·14 (1·01–1·28) 100
Mortality at longest follow-up, overall (I²=0%, p=0·044) 828/7897 749/7857 1·10 (1·00–1·20) 100
0·2
0·5
1·0
2·0
5·0
Favours more oxygen
Favours less oxygen

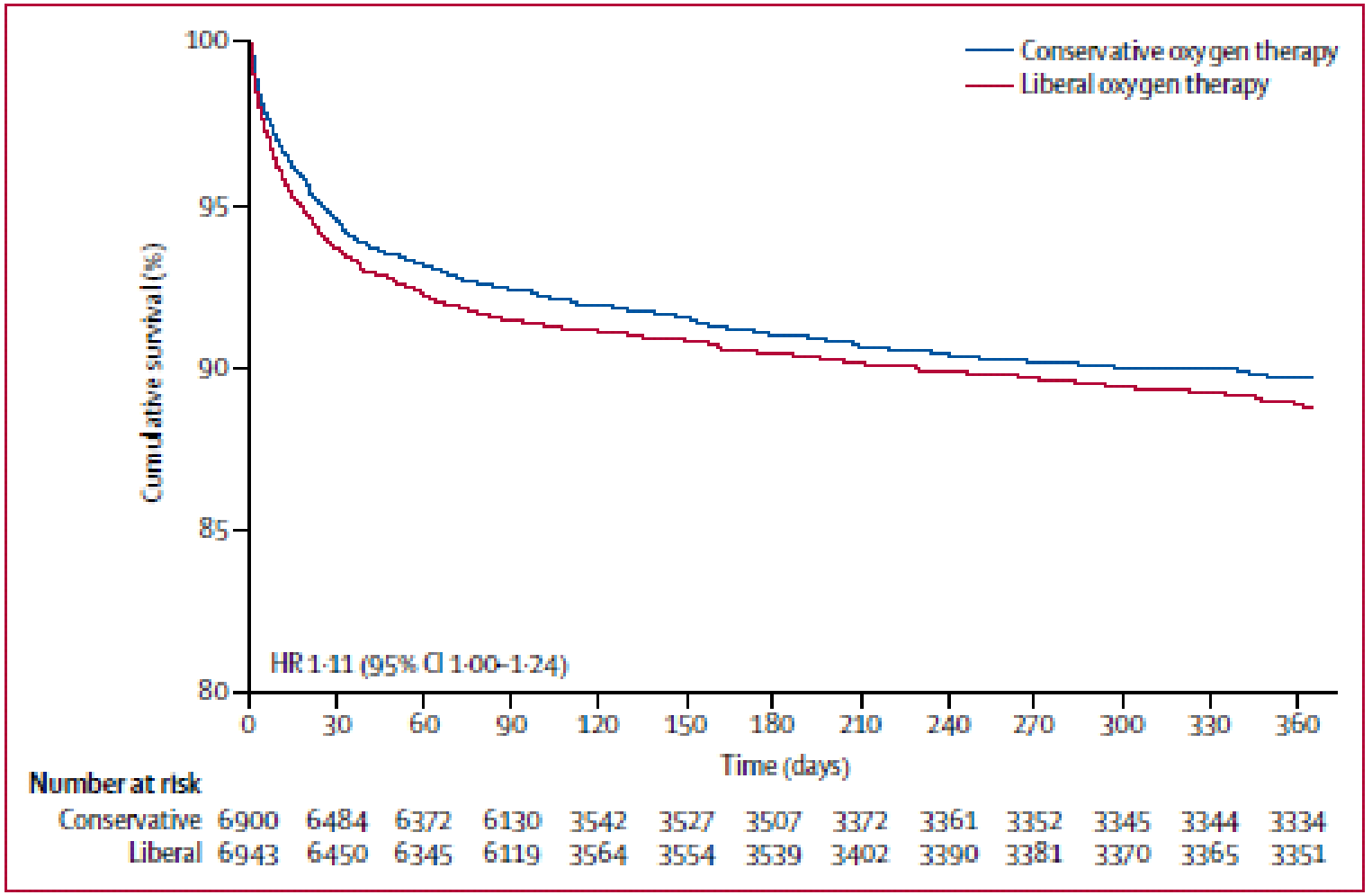


Figure 5: **Kaplan-Meier analysis of cumulative survival for liberal versus conservative oxygen therapy**
We extracted patient-level data from eight randomised controlled trials with various follow-up durations for this analysis: in the study by Panwar and colleagues[53] patient follow-up was 60 days, in the study by Ali and coworkers[44] patients were followed up for 6 months, and in the studies by Hofmann and colleagues[48] and Rønning and coworkers[52] patients were followed up for 1 year. In all other studies, patient follow-up was 90 days. HR=hazard ratio.

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Review Article

A Systematic Review of the Effects of Hyperoxia in Acutely Ill Patients: Should We Aim for Less?

Table 1: Association between hyperoxemia and clinically relevant outcomes after myocardial infarction and cardiac arrest.

Reference	Study design	Sample size	Hyperoxemia definition	Condition	Location	Conclusion
[20], Ranchordet al.	RCT	136	6 L O_2/min	STEMI	-	High-O_2 therapy had no effect on mortality or infarct size
[21], Spindelboeck et al.	Retrospective cohort	1015	PaO_2 > 40.0 kPa	Cardiac arrest	Pre-hospital	Higher hospital admission rates when during CPR
[22], Vaahersalo et al.	Prospective cohort	409	PaO_2 > 40.0 kPa	Cardiac arrest	ICU	No association with different 12 month outcome
[23], Ihle et al.	Retrospective cohort	584	PaO_2 > 40.0 kPa	Cardiac arrest	ICU	No association with in-hospital mortality
[24], Helmerhorst et al.	Retrospective cohort	5258	PaO_2 > 39.9 kPa	Cardiac arrest	ICU	Hyperoxia not associated with higher mortality rates
[25], Bellomo et al.	Retrospective cohort	12,108	PaO_2 > 40.0 kPa	Cardiac arrest	ICU	No association with mortality
[26], Chirst et al.	Retrospective cohort	134	-	Cardiac arrest	-	Hyperoxia in the first 60 minutes after return of circulation is associated with better survival rates
[27], Lee et al.	Retrospective cohort	213	-	Cardiac arrest	-	Hypocarbia associated with in-hospital mortality. Hypoxemia and hyperoxemia associated with poor neurological outcome.
[28], Kilgannon et al.	Retrospective cohort	6,326	PaO_2 > 40.0 kPa	Cardiac arrest	ICU	Higher mortality rates, even when compared to hypoxemia
[29], Elmer et al.	Retrospective analysis of prospective registry	184	Severe: PaO_2 > 40.0 kPa Moderate/ probable: PaO_2 13.5–39.9 kPa	Cardiac arrest	ICU	Severe associated with higher in-hospital mortality. Moderate/probable was not but was associated with improved organ function after 24 hours.
[30], Kilgannon et al.	Retrospective cohort	4,459	-	Cardiac arrest	ICU	Dose-dependent association with in-hospital mortality

Table 2: Association between hyperoxemia and clinically relevant outcomes after stroke and traumatic brain injury.

Reference	Study design	Sample size	Hyperoxemia definition	Condition	Location	Conclusion
[33], Young et al.	Retrospective cohort	2,643	-	Ischaemic stroke	ICU	No association with mortality.
[34], Rincon et al.	Retrospective cohort	2,894	PaO_2 > 40.0 kPa	Ischaemic stroke, subarachnoid or intracerebral hemorrhage	ICU	Associated with higher in-hospital mortality, also when compared to hypoxemia.
[35], Lång et al.	Retrospective cohort	432	-	Subarachnoidal hemorrhage	ICU	Unfavorable outcome associated with higher PaO_2, but higher PaO_2 levels after multivariate analysis not associated with unfavorable outcome or mortality
[36], Singhal et al.	Randomized pilot study, partially blinded	16	O_2 45 L/min, 8 hours	Ischaemic stroke	-	Transient improvement of clinical deficits and MRI abnormalities after 24 hours
[37], Padma et al.	Randomized pilot study, partially blinded	40	O_2 10 L/min, 12 hours	Ischaemic stroke	-	No improvement in functional or neurological outcome after 3 months
[43], Davis et al.	Retrospective cohort	3,420	PaO_2 > 64.9 kPa	TBI	-	Independently associated with increased mortality and decrease in good outcomes.
[44], Rincon et al.	Retrospective cohort	1,212	PaO_2 > 40.0 kPa	TBI	ICU	Independently associated with higher in-hospital mortality.
[45], Asher et al.	Retrospective cohort	193	PaO_2 > 64.8 kPa	TBI	-	Decrease in survival
[46], Raj et al.	Retrospective cohort	1,116	PaO_2 > 13.3 kPa	TBI	ICU	No effect on 6 month mortality

Table 3: Association between hyperoxemia and clinically relevant outcomes in sepsis.

Reference	Study design	Sample size	Hyperoxemia definition	Condition	Location	Conclusion
[19], Stolmeijer et al.	Prospective cohort	83	PaO_2 > 13.5 kPa	Sepsis	ED	More than 64% of patients were hyperoxemic with 10 L O_2/min. No association with mortality.
[47], Rossi et al.	Prospective cohort	14	FiO_2 100%	Sepsis	ICU	Decreases oxygen delivery in upper limbs.
[48], Pope et al.	Retrospective cohort	619	Central venous saturation ($ScvO_2$) 90–100%	Sepsis	ED	Associated with increased mortality.
[49], Dahl et al.	Retrospective cohort	1,770	PaO_2 > 16.0 kPa	Sepsis	ICU	No effect on mortality, but hypoxemia and FiO_2 > 60% increased mortality.

CONCLUSION

- Peu d'études prospectives randomisées étudiant l'impact de l'hyperoxygénation en réanimation notamment dans le cadre du sepsis.

- Pas d'impact évident de l'hyperoxémie sur la morbi-mortalité .

- Viser une normoxémie semble judicieux.

- Étude randomisée contrôlée en réanimation avec:
  - Définitions bien établies des niveaux d'hyperoxémie et de normoxémie
  - 800 patients à inclure (400 dans chaque bras) pour une puissance statistique significative

A BONS ENTENDEURS