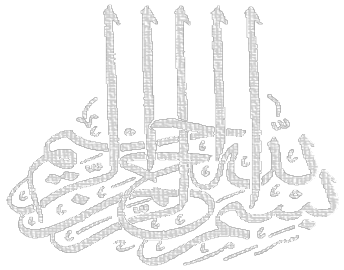

Respiratory Management

in the Potential Brain-Dead Organ Donor

Objectives

- Assess the appropriate lung donor
- Use recruitment maneuvers after apnea test
- Apply protective lung strategy for all brain death donors
- Describe the management of neurogenic pulmonary edema

Acute and Critical Care

Acute and Critical Care 2019 February 34(1):14-29
https://doi.org/10.4266/acc.2019.00430

| pISSN 2586-6052 | eISSN 2586-6060

Medical Management of Brain-Dead Organ Donors

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REVIEW

Management of the brain-dead donor in the ICU: general and specific therapy to improve transplantable organ quality

Geert Meyfroidt[1*], Jan Gunst[1], Ignacio Martin-Loeches[2], Martin Smith[3], Chiara Robba[4], Fabio Silvio Taccone[5] and Giuseppe Citerio[6,7]

Intensive Care Medicine · February 2019

Management of the neurologically deceased organ donor: A Canadian clinical practice guideline

Ian M. Ball MD MSc, Laura Hornby MSc, Bram Rochwerg MD MSc, Matthew J. Weiss MD, Clay Gillrie RN MSN, Michaël Chassé MD PhD, Frederick D'Aragon MD MSc, Maureen O. Meade MD MSc, Karim Soliman MD, Aadil Ali BSc, Samantha Arora MD, John Basmaji MD, J. Gordon Boyd MD PhD, Bernard Cantin MD PhD, Prosanto Chaudhury MD MSc, Marcelo Cypel MD MSc, Darren Freed MD, Anne Julie Frenette PharmD PhD, Pam Hruska RN MSc, Constantine J. Karvellas MD SM, Sean Keenan MD, Andreas Kramer MD, Demetrios James Kutsogiannis MD, Dale Lien MD, Patrick Luke MD, Meagan Mahoney MD, Jeffrey M. Singh MD, Lindsay C. Wilson MHA, Alissa Wright MD MSc, Jeffrey Zaltzman MD MSc, Sam D. Shemie MD

■ Cite as: *CMAJ* 2020 April 6;192:E361-9. doi: 10.1503/cmaj.190631

RESEARCH Open Access

Brazilian guidelines for the management of brain-dead potential organ donors. The task force of the AMIB, ABTO, BRICNet, and the General Coordination of the National Transplant System

Glauco Adrieno Westphal[1,2,3*], Caroline Cabral Robinson[1], Alexandre Biasi Cavalcanti[4], Anderson Ricardo Roman Gonçalves[5,6], Cátia Moreira Guterres[1], Cassiano Teixeira[7,8], Cinara Stein[1], Cristiano Augusto Franke[7,9], Daiana Barbosa da Silva[1], Daniela Ferreira Salomão Pontes[10], Diego Silva Leite Nunes[10], Edson Abdala[11], Felipe Dal-Pizzol[12,13], Fernando Augusto Bozza[14,15], Flávia Ribeiro Machado[16], Joel de Andrade[17], Luciane Nascimento Cruz[1], Luciano Cesar Pontes de Azevedo[18], Miriam Cristine Vahl Machado[3], Regis Goulart Rosa[1], Roberto Ceratti Manfro[7,19], Rosana Reis Nothen[19], Suzana Margareth Lobo[20], Tatiana Helena Rech[7], Thiago Lisboa[7], Verônica Colpani[1] and Maicon Falavigna[1,21,22]

Westphal *et al. Ann. Intensive Care (2020) 10:169*

Intensivists need to play a vital role in the management of potential organ donors through identification of potential donors, declaration of brain death, and proper medical care, all of which can improve the rates of graft survival

Table 1. Frequency of pathophysiological changes in irreversible loss of brain function

Variable	Cause	Frequency (%)
Hypothermia	Hypothalamic dysfunction, vasoplegia	100
Hypotension	Vasoplegia, hypovolemia, myocardial dysfunction	80–97
Diabetes insipidus	Hypothalamic/pituitary dysfunction	65–90
Arrhythmias	Catecholamine release, myocardial injury	25–32
Pulmonary edema	Injury to vascular endothelium	15–20
Cardiac arrest	Prolonged hypotension, arrhythmia	5–10

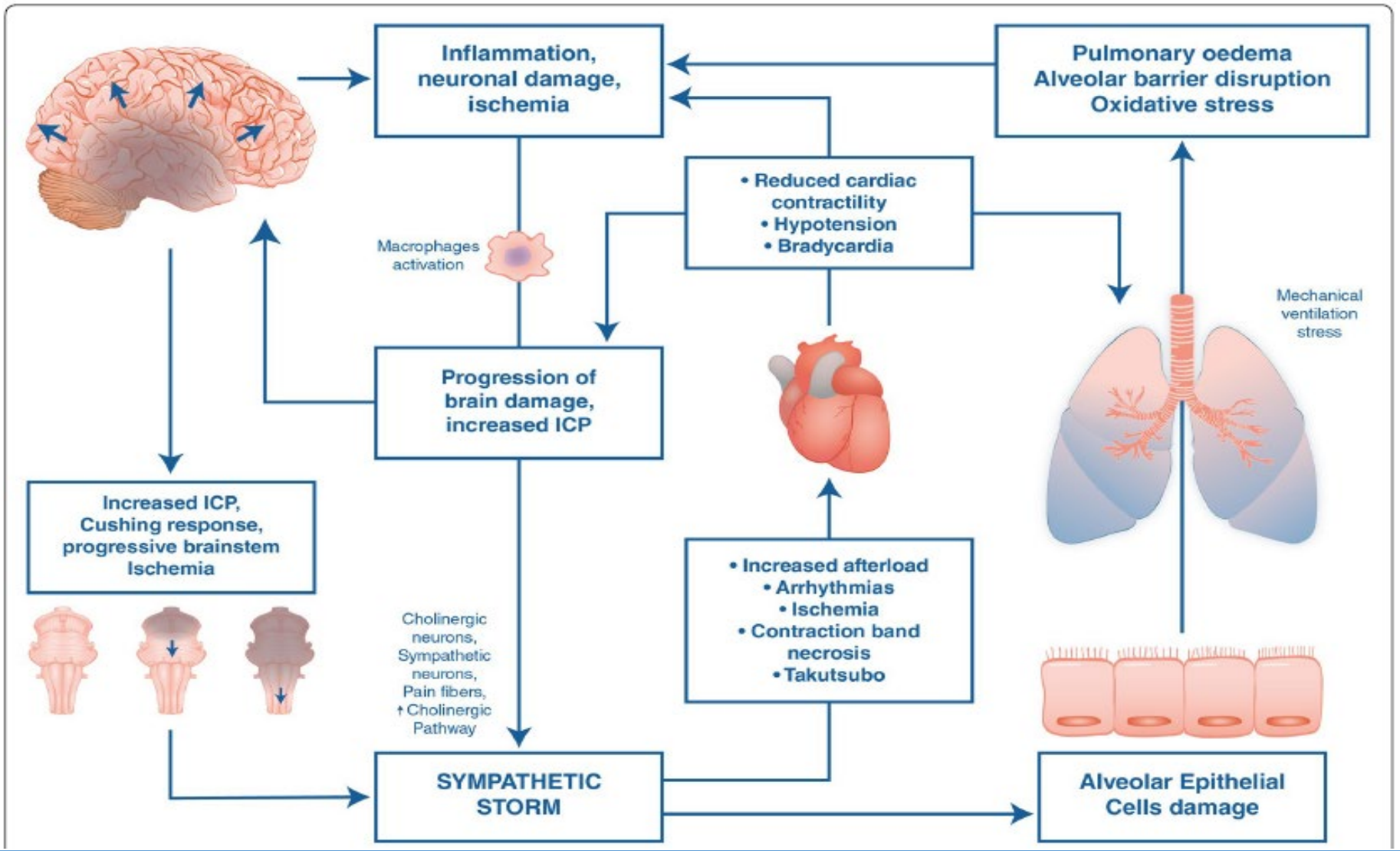
Adapted from Hahnenkamp et al. Dtsch Arztebl Int 2016;113:552-8 [13].

The lungs are the organs most often assumed to be medically unsuitable for transplants, with only 10%–20% of lungs eligible for transplantation

Acute and Critical Care 2019 February 34(1):14-29

An observational survey conducted in 13 Italian centers revealed that nearly half of potential lung donors had a PaO2/FiO2 ratio of < 300, making them ineligible for lung donation.

Mascia L, Bosma K, Pasero D et al (2006) Ventilatory and hemodynamic management of potential organ donors: an observational survey*. CritCare Med 34(2):321–327


Inflammation, neuronal damage, ischemia
Pulmonary oedema
Alveolar barrier disruption
Oxidative stress
• Reduced cardiac contractility
• Hypotension
• Bradycardia
Macrophages activation
Mechanical ventilation stress
Progression of brain damage, increased ICP
Increased ICP, Cushing response, progressive brainstem Ischemia
• Increased afterload
• Arrhythmias
• Ischemia
• Contraction band necrosis
• Takutsubo
Cholinergic neurons, Sympathetic neurons, Pain fibers, ↑ Cholinergic Pathway
SYMPATHETIC STORM
Alveolar Epithelial Cells damage

STANDARD (“IDEAL”) LUNG DONOR CRITERIA

- Age < 55 year
- Clear serial chest X-ray
- Normal gas exchange (PaO2 > 300 mm Hg on FIO2 = 1.0, PEEP 5 cm H2O)
- Absence of chest trauma
- No evidence of aspiration or sepsis
- Absence of purulent secretions at bronchoscopy
- Absence of organisms on sputum gram stain
- No history of primary pulmonary disease or active pulmonary infection
- Tobacco history < 20 pack-years
- ABO compatibility
- No prior cardiopulmonary surgery
- Appropriate size match with prospective recipient

Lung harvest rates of only 15% to 25%

Assessment of Appropriate Lung Donor

- Normal chest X-ray
- PaO_2 was > 400 mm Hg with an FIO2 of 100%
- PaO_2/FiO_2 ratio of greater than 300mm Hg
- Normal bronchoscopy:
  - Abnormal findings were found in 38% of donors with normal CXR and PaO_2 was > 400 mm Hg
- Measurement of pulmonary shunt

B Riou, R Guesde, Y Jacquens, R Duranteau, and P Viars "Fiberoptic bronchoscopy in brain-dead organ donors." American Journal of Respiratory and Critical Care Medicine, Vol. 150, No. 2(1994), pp. 558-60.

Chest X-Ray

- 37% of donors have infiltrates on the initial film, of which 51% resolved completely after proper donor management (McCowin)
- Donors with strong unilateral abnormalities on chest X-ray should not be excluded for donation of the contralateral lung
- Lungs should not be used if heavy, pneumonic infiltrates are confirmed during organ retrieval

McCowin MJ, Hall TS, Babcock WD, Solinger LL, Hall KW, Jablons DM. Changes in radiographic abnormalities in organ donors: associations with lung transplantation. J Heart Lung Transplant 2005;24: 323–330

Does every donor need a bronch?

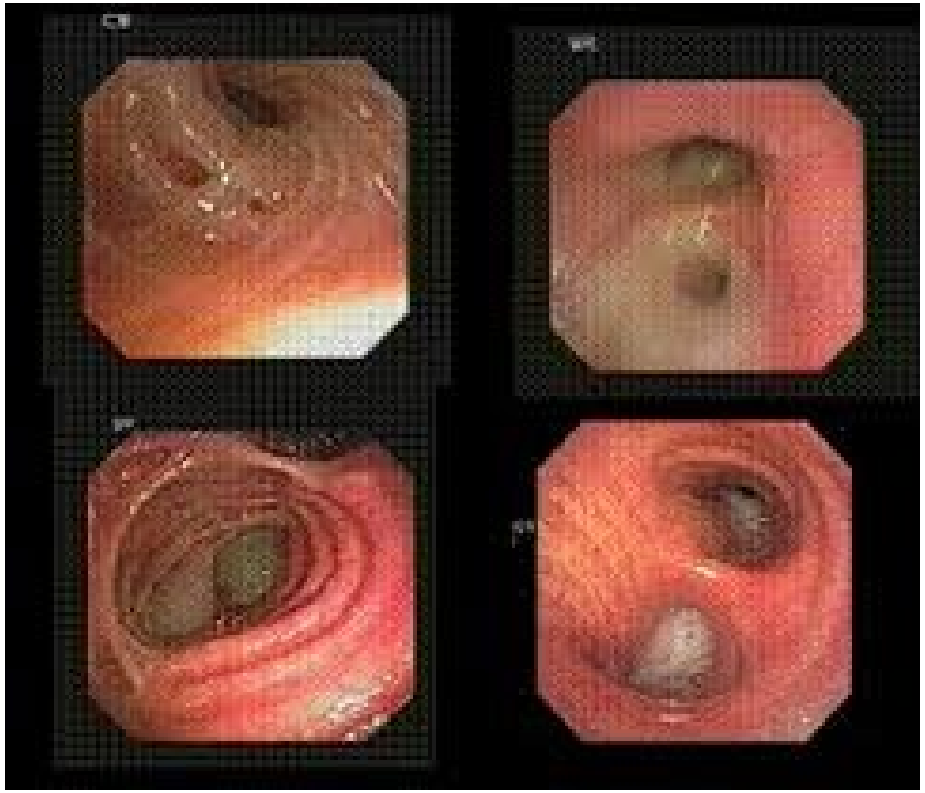
- Yes
  - One study found that bronchoscopy was abnormal in 10 of 26 potential organ donors (38%) with normal radiographs and Pao2 more than 400 mm Hg.

- Advantages:
  - Remove aspirated material, blood and purulent secretions and mucus plugs
  - Inspect airways for abnormalities (occult cancer)
  - Best bronchs for training purposes ☺

Riou B, Guesde R, Jacquens Y, et al: Fiberoptic bronchoscopy in brain-dead organ donors. Am J Respir Crit Care Med 1994; 150:558–560

Bronchoscopy

- Total of 72 organ donors
- Normal CXR in 51%
- PaO_2 was > 400 mm Hg with an FIO2 of 100% in 47%
- Normal bronchoscopy in 33% only (24 donors)
- In the 26 donors with normal chest X-ray and PaO2 > 400 mm Hg with FIO2 of 100%, bronchoscopy was abnormal in 10 donors (38%)
- Abnormal findings included:
  - Inhalation of gastric contents (n = 26)
  - Blood (n = 17)
  - Pulmonary contusion (n = 5)
  - Purulent bronchial secretions (n = 4



B Riou, R Guesde, Y Jacquens, R Duranteau, and P Viars "Fiberoptic bronchoscopy in brain-dead organ donors." American Journal of Respiratory and Critical Care Medicine, Vol. 150, No. 2(1994), pp. 558-60.

Paries *et al. Critical Care* 2012, **16**:R116
http://ccforum.com/content/16/4/R116

CRITICAL CARE

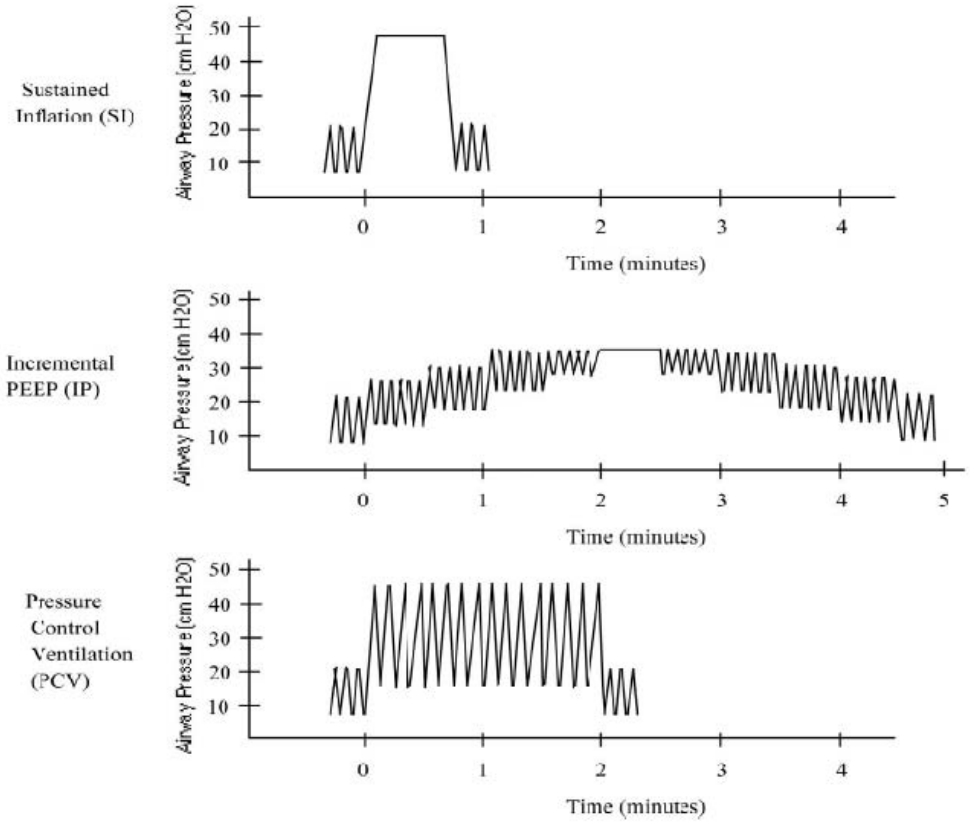
RESEARCH Open Access

Benefit of a single recruitment maneuver after an apnea test for the diagnosis of brain death

Marie Paries[1], Nicolas Boccheciampe[1], Mathieu Raux[1,2], Bruno Riou[3,4], Olivier Langeron[1,4] and Armelle Nicolas-Robin[1,4*]

Single Recruitment Maneuver After an Apnea Test For The Diagnosis Of Brain Death

- The apnea test was associated with a marked decrease in PaO_2/FiO_2 ratio
- Potential loss of potential lung donors
- Ratio could be restored by an RM performed immediately after the reconnection to the ventilator



Paries et al. Critical Care 2012, 16 :R116

Single Recruitment Maneuver After An Apnea Test For The Diagnosis Of Brain Death

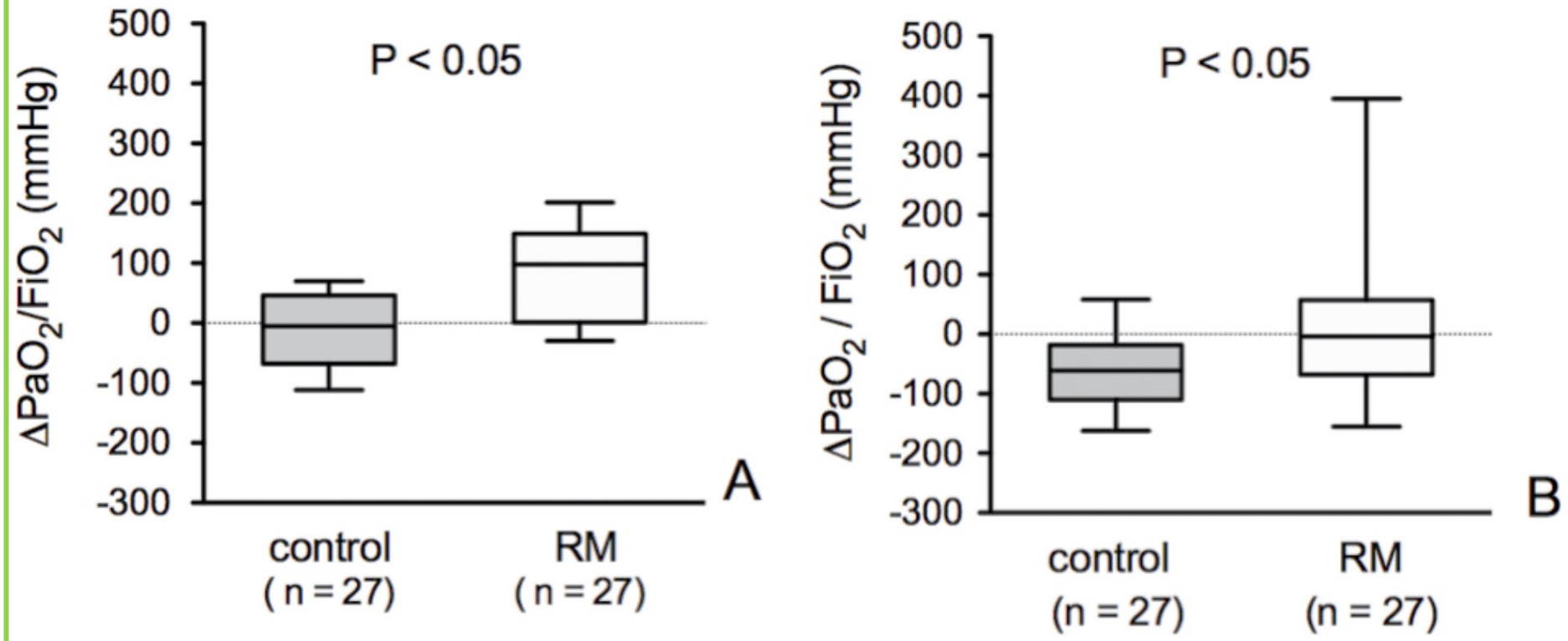


Figure 2 Variation of arterial oxygen tension/fractional inspired oxygen (PaO_2/FiO_2) ratio. **(a)** From the end of the apnea test before reconnection (T2) to 2 hours after reconnection (T3). **(b)** From before the apnea test (T1) to 2 hours after reconnection (T3). Values are medians with 25th and 75th percentiles (boxes) and 95th and 5th percentiles (whiskers). RM, recruitment maneuver.

Single Recruitment Maneuver After An Apnea Test For The Diagnosis Of Brain Death

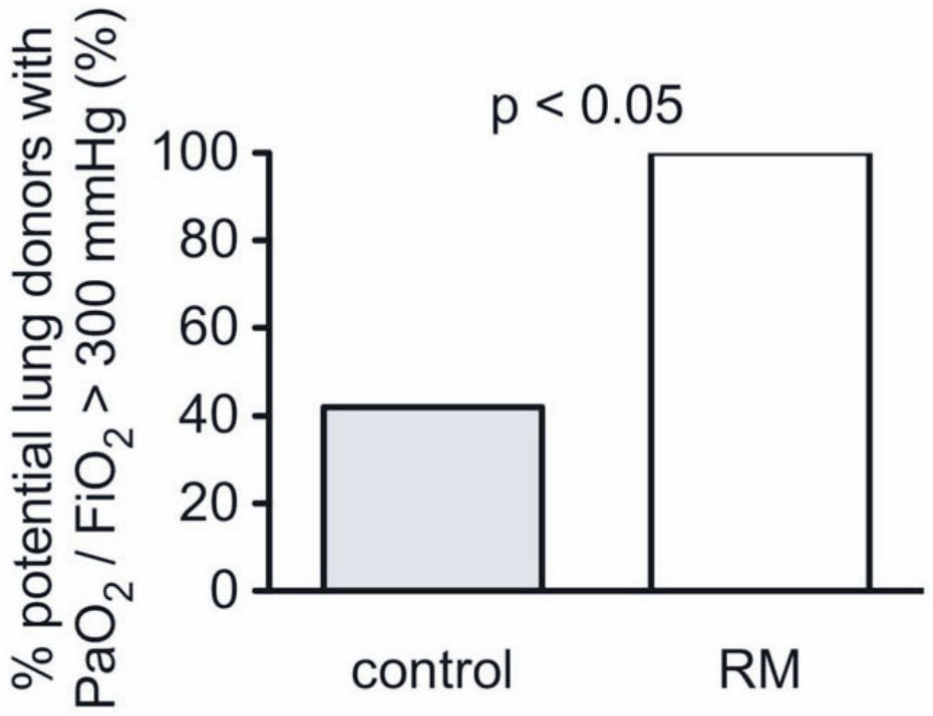
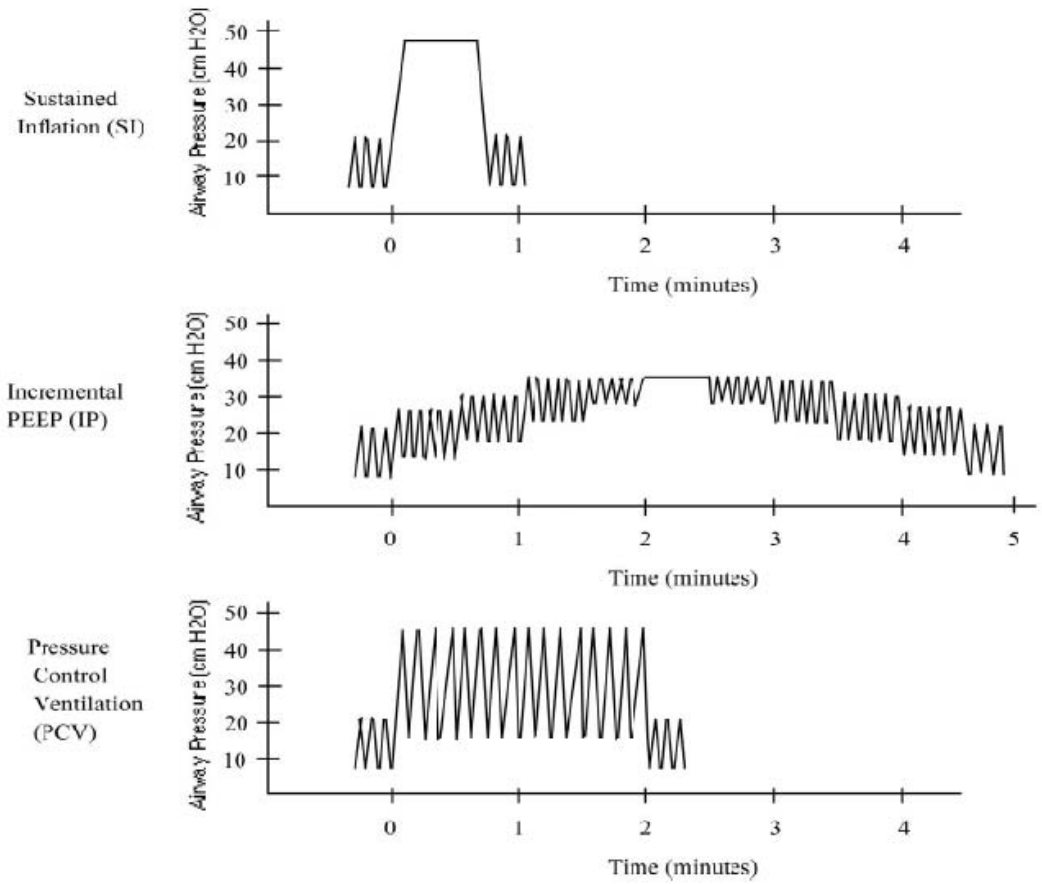


Figure 3 Variation of percentage of potential lung donors according to PaO_2/FiO_2 criterion (between T1 and T3 from 100% at T1. PaO_2/FiO_2, arterial oxygen tension/fractional inspired oxygen. RM, recruitment maneuver.

Paries et al. Critical Care 2012, 16 :R116

Recruitment Maneuvers



Ventilatory and hemodynamic management of potential organ donors: An observational survey*

Luciana Mascia, MD, PhD; Karen Bosma, MD, FRCPC; Daniela Pasero, MD; Tamara Galli, MD; Gerardo Cortese, MD; Pierpaolo Donadio, MD; Riccardo Bosco, MD

LEARNING OBJECTIVES
On completion of this article, the reader should be able to:
1. Explain the issues related to harvesting lungs for transplantation.
2. Describe the management of potential lung donors.
3. Use this information in a clinical setting.
All of the authors have disclosed that they have no financial relationships with or interests in any commercial companies pertaining to this educational activity.
Wolters Kluwer Health has identified and resolved all faculty conflicts of interest regarding this educational activity.
Visit the *Critical Care Medicine* Web site (www.ccmjournal.org) for information on obtaining continuing medical education credit.

Objective: **To determine the current standard ventilatory and cardiovascular management in potential organ donors.**

Design: **Prospective, multiple-center, observational survey.**

Setting: **A total of 15 intensive care units in 13 hospitals in Piedmont, Italy.**

Patients: **A total of 34 brain-dead patients enrolled in 6 months.**

Measurements and Main Results: **Demographics and reasons for lung transplant exclusion were recorded. Ventilatory and hemodynamic variables were compared before and after confirmation of brain death. A total of 23 potential donors were ineligible for lung donation based on pulmonary status and age. Of the 11 eligible lung donors, only two donated the lungs because five had Pao_2/Fio_2 ratios of <300 and four were ineligible for logistic problems. Tidal volume was 10 ± 2 mL/kg, positive end-expiratory pressure was 3.3 ± 2.7 cm H_2O, Fio_2 was 50% ± 18% before brain death diagnosis, and no changes were made after brain death confirmation. In potential lung donors, apnea tests were performed with apneic oxygenation after disconnection from the ventilator in all cases; tracheal suction was performed with an open circuit in eight cases, and no recruitment maneuvers were performed. Crystalloid infusion was increased after diagnosis of brain death from 187 ± 151 to 275 ± 158 mL/hr ($p < .05$), and central venous pressure increased from 6 ± 3 to 7 ± 3 mm Hg ($p < .05$). Inotropic support was used in 24 donors (70%).**

Conclusions: **Five of 11 potential lung donors (45%) had a Pao_2/Fio_2 ratio of <300, making them ineligible for lung donation. After the diagnosis of brain death, ventilatory management remained the same, no maneuvers for prevention of derecruitment of the lung were performed, and cardiovascular management was modified to optimize peripheral organ perfusion. These data represent the current standard of care for ventilatory management of potential organ donors and may be suboptimal in preserving lung function. (Crit Care Med 2006; 34:321–327)**

Key Words: lung protective strategy; organ donors; brain death

Ventilatory Settings and Pulmonary Status in 34 Potential Organ Donors

		Ventilatory Settings				Respiratory Status	
	n	VT/kg IBW, ml/kg	RR, beats/min	PEEP, cm H_2O	FiO2, %	PaO_2/FiO_2	Abnormal CXR, No. of Patients
Chest trauma with ALI/ARDS	5	10 ± 3	12 ± 2	3 ± 3	60 ± 30	159 ± 30	5
Pulmonary infection or aspiration	12	9 ± 1	13 ± 2	4 ± 3	45 ± 20	279 ± 101	10
Potential organ donors (age of >65 yrs)	6	9 ± 1	11 ± 1	2 ± 3	45 ± 10	369 ± 137	0
Potential organ donors (age of <65 yrs)	11	10 ± 2	12 ± 2	3 ± 2	55 ± 20	292 ± 135	0

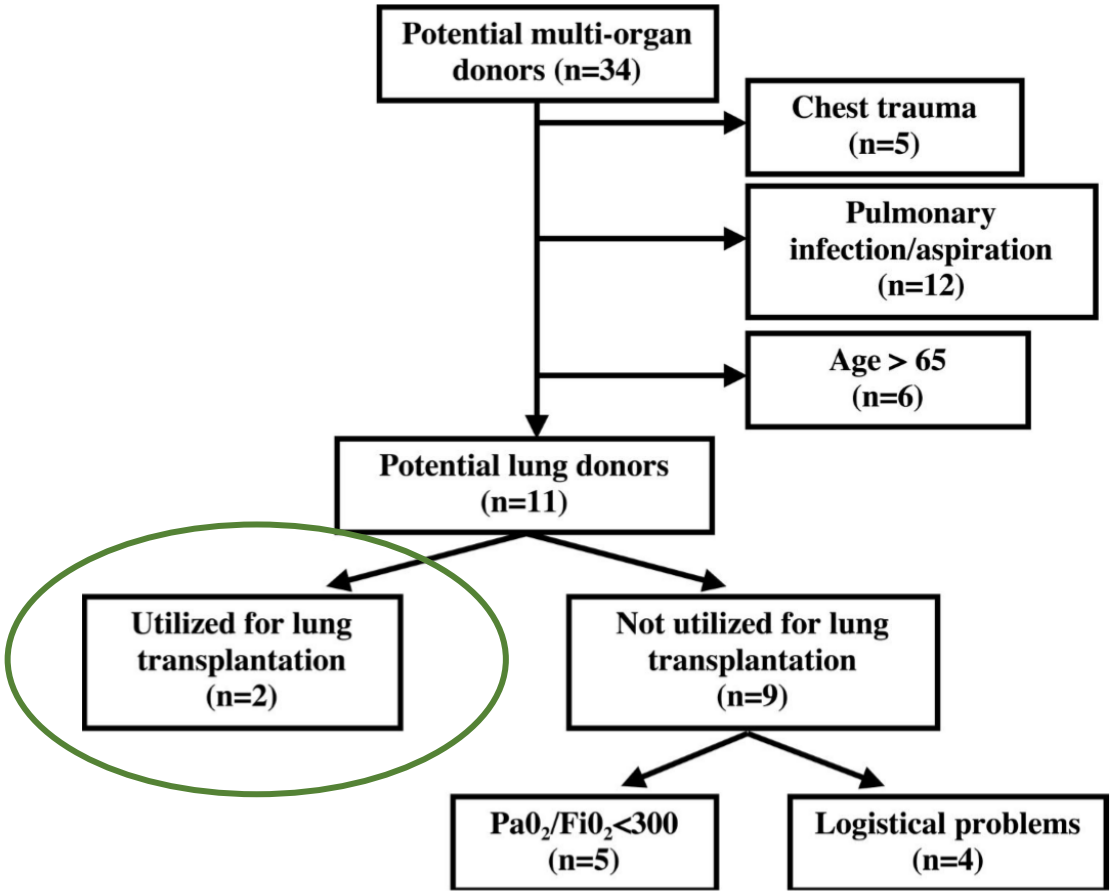
Crit Care Med. 2006 Feb;34(2):321-7

Ventilatory and Hemodynamic Parameters Before and after the Diagnosis of Brain Death In 34 Potential Donor

Parameters	Before Brain Death	After Brain Death	P value
VT/IBW, mL/kg	9.7 ± 1.6	9.7 ± 1.6	N/A
RR, breaths/min	12 ± 2	12 ± 2	N/A
PEEP, cm H_2O	3.3 ± 2.7	3.3 ± 2.7	N/A
F_IO_2, %	50 ± 18	49 ± 16	NS
Crystalloids, mL/hr	187 ± 151	275 ± 158	<0.05
Colloids, mL/hr	67 ± 40	101 ± 71	N/A
Urine output, mL/hr	191 ± 114	246 ± 131	0.07
CVP, mm Hg	6 ± 3	7 ± 3	<0.05
MAP, mm Hg	90 ± 19	83 ± 16	NS
Dopamine, µg/g/min	7.5 ± 3.5	8 ± 4	NS
Noradrenaline, µg/g/min	0.5 ± 0.5	0.3 ± 0.1	NS

Crit Care Med. 2006 Feb;34(2):321-7

Flow Chart Showing Exclusion Criteria For Lung Procurement in The Total Population Of 34 Potential Multiple-organ Donors Included in The Study.



Can we improve the P/F ratio?

- If initial PaO2/FiO2 <100 or CXR c/w pulm edema / atelectectasis
  - Recruitment maneuver, PCV PIP 35 cm H2O / PEEP 15 cm H2O for 2 h

Impact of a Lung Transplantation Donor–Management Protocol on Lung Donation and Recipient Outcomes

Luis F. Angel, Deborah J. Levine, Marcos I. Restrepo, Scott Johnson, Edward Sako, Andrea Carpenter, John Calhoon, John E. Cornell, Sandra G. Adams, Gary B. Chisholm, Joe Nespral, Ann Roberson, and Stephanie M. Levine

Division of Pulmonary and Critical Care Medicine, Division of Cardiothoracic Surgery, and Center for Epidemiology and Biostatistics, University of Texas Health Science Center at San Antonio; Veterans Evidence-based Research, Dissemination, and Implementation Center (VERDICT) Center of Excellence, Audie L. Murphy VA Hospital; and the Texas Organ Sharing Alliance, San Antonio, Texas

Am J Respir Crit Care Med 2006;174:710–71

Results

	Pre-Protocol phase 4 years	Protocol phase 4 years	p-value	RR
Mean rate of lung procurement	11.5%	25.5%	0.0001	2.2
Number of transplants	53	121	0.0001	

- Of the 98 actual lung donors during the protocol period, 53 (54%) had initially been considered poor donors; these donors provided 64 (53%) of the 121 lung transplants.

How should we ventilate lung donors?

PRELIMINARY COMMUNICATION

Effect of a Lung Protective Strategy for Organ Donors on Eligibility and Availability of Lungs for Transplantation

A Randomized Controlled Trial

Luciana Mascia, MD, PhD
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M. Jose Arguis, MD
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Salvatore Grasso, MD
Marina Munari, MD
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Francesco Della Corte, MD
Nicoletta Vivaldi, MD
Paolo Malacarne, MD
Paolo Del Gaudio, MD
Sergio Livigni, MD
Elisabeth Zavala, MD

Context Many potential donor lungs deteriorate between the time of brain death and evaluation for transplantation suitability, possibly because of the ventilatory strategy used after brain death.

Objective To test whether a lung protective strategy increases the number of lungs available for transplantation.

Design, Setting, and Patients Multicenter randomized controlled trial of patients with beating hearts who were potential organ donors conducted at 12 European intensive care units from September 2004 to May 2009 in the Protective Ventilatory Strategy in Potential Lung Donors Study.

Interventions Potential donors were randomized to the conventional ventilatory strategy (with tidal volumes of 10-12 mL/kg of predicted body weight, positive end-expiratory pressure [PEEP] of 3-5 cm H_2O, apnea tests performed by disconnecting the ventilator, and open circuit for airway suction) or the protective ventilatory strategy (with tidal volumes of 6-8 mL/kg of predicted body weight, PEEP of 8-10 cm H_2O, apnea tests performed by using continuous positive airway pressure, and closed circuit for airway suction).

Main Outcome Measures The number of organ donors meeting eligibility criteria for harvesting, number of lungs harvested, and 6-month survival of lung transplant recipients.

JAMA. 2010;304(23):2620-2627

How should we ventilate lung donors?

- Multicenter RCT (2004-2009)
- Conventional arm (n=59):
  - Vt of 10-12 mL/kg IBW, PEEP of 3-5 cm H2O, open circuits for suctioning, apnea tests performed by disconnecting the ventilator
- Protective ventilation arm (n=59):
  - Vt of 6-8 mL/kg IBW, PEEP of 6-8 cm H2O, apnea tests done on CPAP and closed circuit for suctioning

Mascia L., et al. JAMA. 2010 Dec 15;304(23):2620-7

Effect of a Lung Protective Strategy For Organ Donors On Eligibility and Availability of Lungs For Transplantation: A Randomized Controlled Trial.

Multicenter Randomized Controlled Trial

12 European Intensive Care Units September 2004 to May 2009		
	Conventional Ventilatory Strategy	**Protective Ventilatory Strategy**
VT	10-12 mL/kg	6-8 mL/kg
PEEP	3-5 cm H_2O	8-10 cm H_2O
Apnea Test	Disconnect from the ventilator	Continuous positive airway pressure
Suctioning	Open circuit	Closed circuit

Mascia L., et al. JAMA. 2010 Dec 15;304(23):2620-7

Effect of a Lung Protective Strategy For Organ Donors On Eligibility and Availability of Lungs For Transplantation: A Randomized Controlled Trial.

Multicenter Randomized Controlled Trial

12 European Intensive Care Units September 2004 to May 2009			
	Conventional Ventilatory Strategy	**Protective Ventilatory Strategy**	**P value**
n	59	59	
Met lung donor eligibility criteria	32 (54%)	56 (95%)	P <.001
Harvested lung	16 (27%)	32 (54%)	P = .004
Survival of lung transplant receovers	11/16 [69%]	24/32 [75%],	

Mascia L., et al. JAMA. 2010 Dec 15;304(23):2620-7

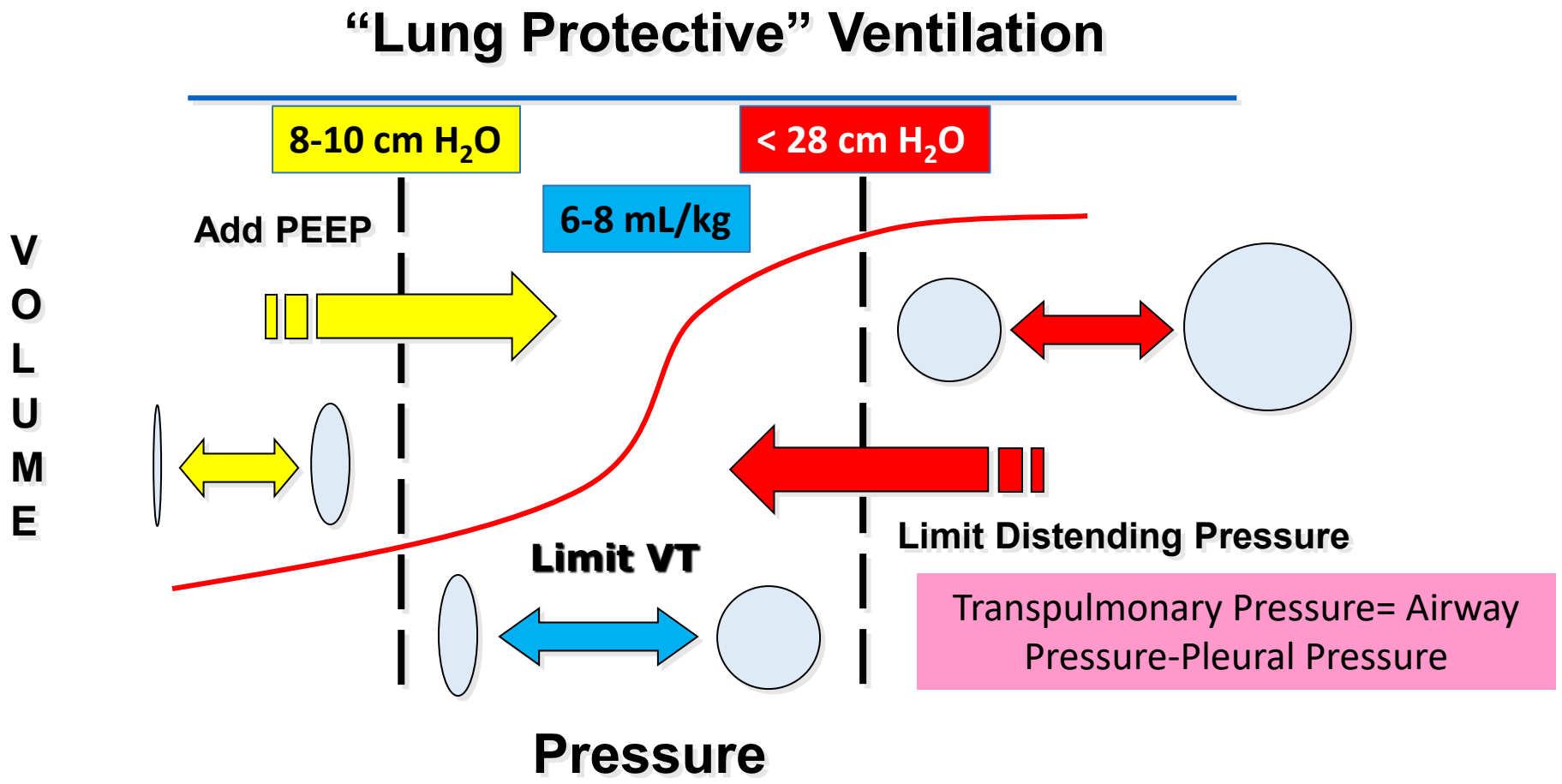
Effect of a Lung Protective Strategy For Organ Donors On Eligibility and Availability of Lungs For Transplantation: A Randomized Controlled Trial.

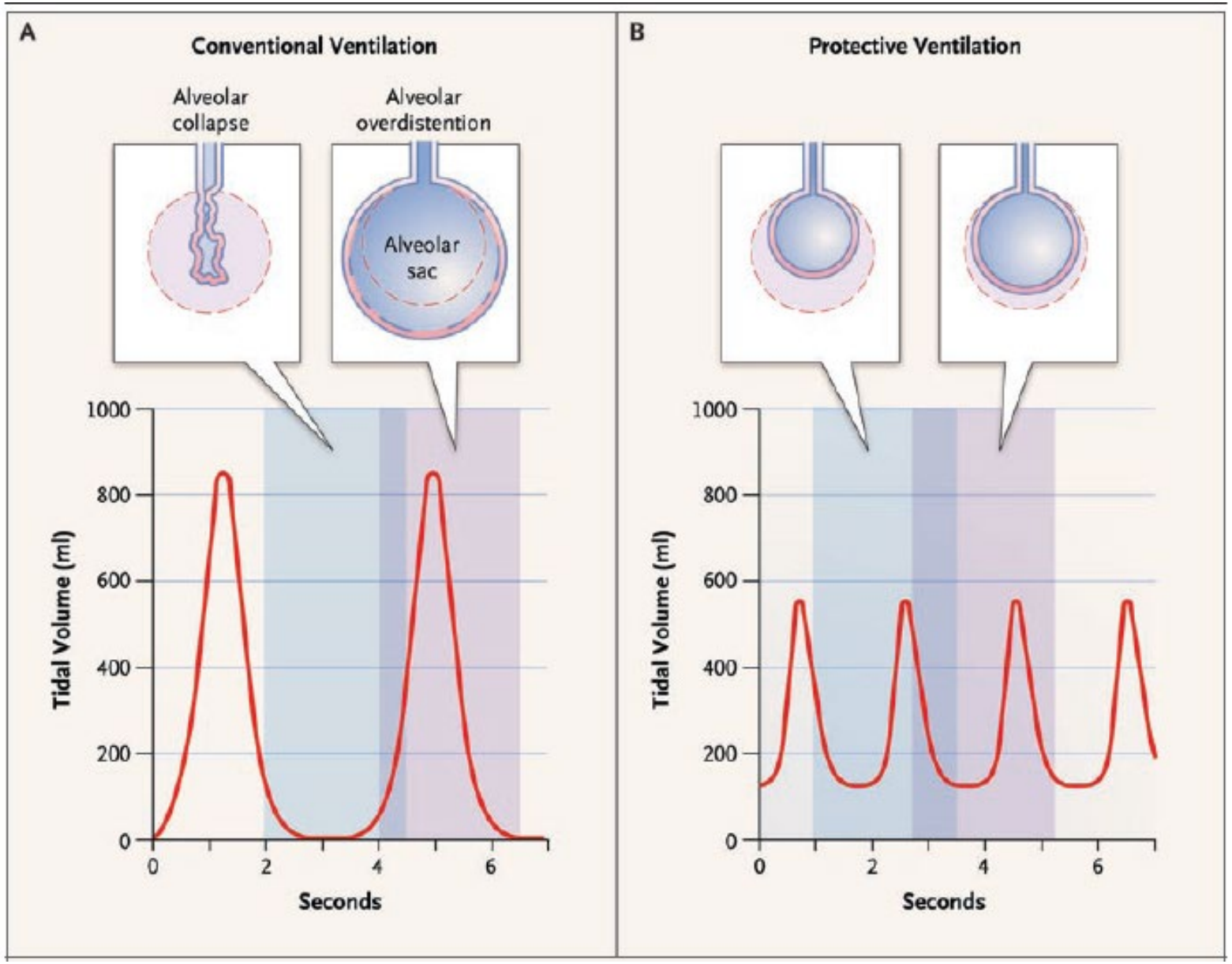
Table 3. End Points by Conventional and Protective Ventilatory Strategies

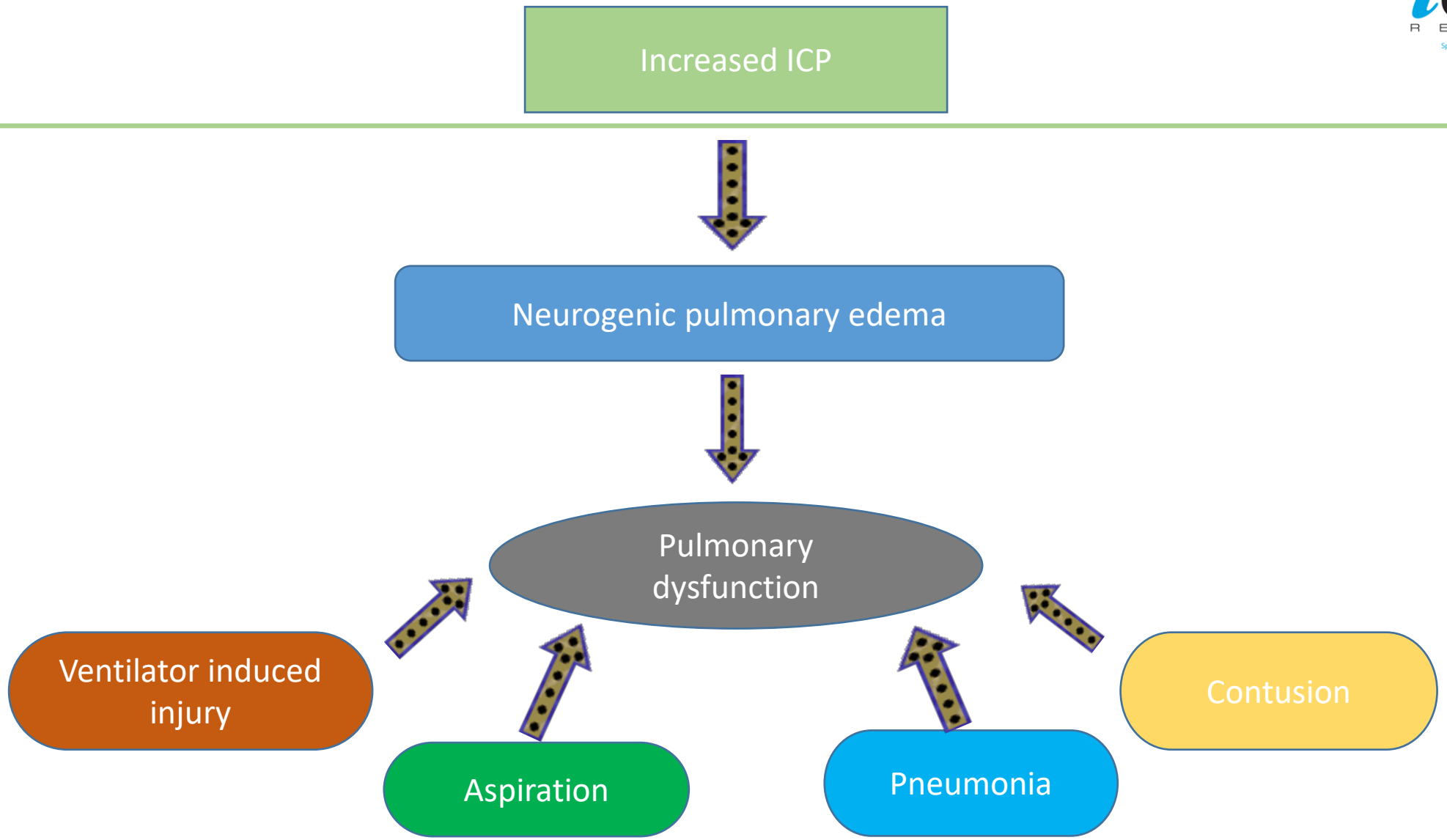
	Ventilatory Strategy, No. (%)		
	Conventional (n = 59)	Protective (n = 59)	Difference of Percentage (95% CI)
Met lung donor eligibility criteria			
At study inclusion	49 (83)	51 (86)	3 (–4.0 to 24.4)
6 h after randomization	32 (54)[a]	56 (95)[b]	41 (26.5 to 54.8)
Lungs harvested			
Yes	16 (27)	32 (54)[c]	27 (10.0 to 44.5)
No	16/32 (50)[d]	24/56 (43)[d]	7 (0 to 29.3)
Reasons lungs not harvested			
Functional	4 (25)	7 (29)	
Infectious	3 (19)	4 (17)	
Inspection	3 (19)	5 (21)	
Donor-recepient incompatibility	4 (25)	5 (21)	
Logistical	2 (12)	3 (12)	

Abbreviation: CI, confidence interval.
[a] $P<.001$ using the McNemar test at study inclusion compared with 6 hours after randomization.
[b] $P=.001$ for comparison with conventional ventilatory strategy using the Fisher exact test.
[c] $P=.004$ for comparison with conventional ventilatory strategy using the χ^2 test.
[d] Values expressed as number/total (percentage).

Preventing Overdistention and Under-Recruitment Injury




A
Conventional Ventilation
Alveolar collapse
Alveolar overdistention
Alveolar sac
1000
800
600
400
200
0
Tidal Volume (ml)
0
2
4
6
Seconds
B
Protective Ventilation
1000
800
600
400
200
0
Tidal Volume (ml)
0
2
4
6
Seconds


Increased ICP
Neurogenic pulmonary edema
Pulmonary dysfunction
Ventilator induced injury
Aspiration
Pneumonia
Contusion

Management of NPE

- Protective lung strategy and adequate PEEP
- Diuretic therapy
- Alfa adrenergic antagonists:
  - Phentolamine
- Beta-adrenergic agonists:
  - Dobutamine
  - Dopamine (avoid high doses)
- Narcan 8 mg IVP x1Controversial

Conclusion: Mechanical Ventilation Targets

- Tidal volume 6–8 ml/kg (lower in NPE)
- PIP <30
- Optimal PEEP to allow minimum FIO2; at least 10 cm H_2O
- FiO_2-adjust keeping SaO_2 >96%, PaO2 >100. Keep FiO_2 at lowest setting
- Recruitment maneuvers initially, and repeated after apnea testing or tracheal suction.
- Closed circuit suctioning
- Maintain tracheal cuff pressure at 25 cm H2O
- Head of the bed elevated to reduce the risk of aspiration.
- Avoid the administration of excessive i.v. fluids.
- Consider diuretics if marked fluid overload

Thank You