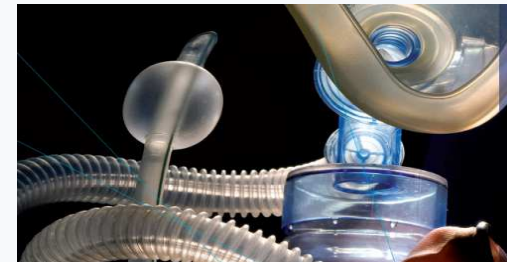


25e Journées d'Anesthésie- Réanimation Chirurgicale d'Aquitaine

Use of volatile anesthetics in ICU
When, why and how?

La sédation par halogénés
Pourquoi? Qui? Quand?



Prof. Dr. F. Kehl
Klinik für Anästhesie und Intensivmedizin
Städtisches Klinikum Karlsruhe
Direktor: Prof. Dr. Franz Kehl



ICU-Analgo-Sedation

Skylia: PAIN, Agitation & Self-extubation

Charybdis: VAP & LOS



Daily interruption of sedative infusions in critically ill patients undergoing mechanical ventilation

- Reduction of mechanical ventilation
from 7 to 5 days
- Reduction of ICU-stay (LOS)
from 10 to 6.5 days



Unwarranted deep sedation harms

- 1x daily awakening trial increases survival
- Deep sedation within first 48 hours increased mortality

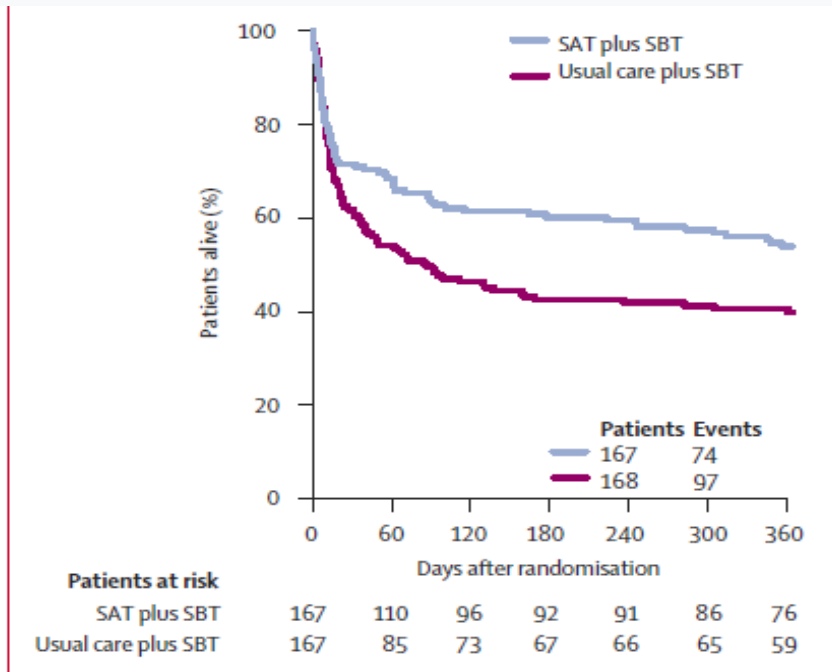
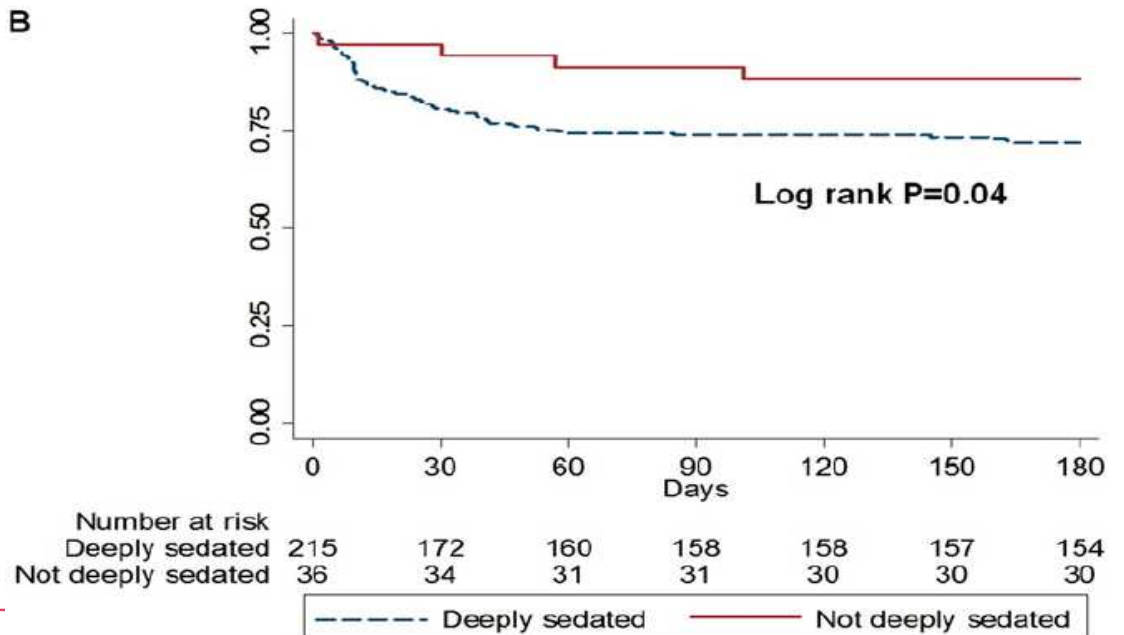


Figure 4: Survival at 1 year
Events indicate the number of deaths in each group in the year after enrolment.

Girard et al, Lancet 2008; 371:126-34

B



Shehebi et al, Am J Respir Crit Care Med
2012; 186, 724-31

Pharmacological Options for Sedation

- **Benzodiazepine (midazolam & lorazepam)**
- Barbiturate (methohexital & pentobarbital & thiopentone)
- **Major tranquilizers (haloperidol)**
- Propofol
- **Gammahydroxybutyric acid**
- **Gabapentin**
- **Ketamin**
- Volatile Anesthetics
- Dexmedetomidin / Clonidin

Thus there is only the choice of:

**Propofol und Dexmedetomidine/Clonidine
and Volatile Anesthetics and Barbiturates**

Barbiturates

KI: Porphyria

I: Intracranial Hypertension
 EEG burst suppression

only in combination

Inhalational Sedation

KI: Malignant Hyperthermia
TBI/SHT (w/o ICP-measurement)

I: When i.v. Sedation is problematic
(3-4 different agents needed)
Asthma bronchiale
Cardiovascular patients at risk

Sedation protocol at my institution

- Predicted sedation duration < 7d
 - Fentanyl/Propofol
 - Fentanyl/Isoflurane
- Predicted sedation duration > 7d
 - Fentanyl/Midazolam or
 - Fentanyl/Isoflurane

Inhalation Sedation: When? Isoflurane/Fentanyl

- Breaking Status asthmaticus
- Postresuscitation
- All cardiovascular high-risk patients

- For short or long-term sedation
- When iv is not sufficient

Inhalation Sedation: When? Isoflurane/Fentanyl

- In septic patients (meeting the above criteria)
- Neurological patients requiring repeated neurological exams
- Cardiovascular patients at risk (aortic and vascular surgery)
- Patients with difficult airway
- 2nd line in severe intracranial hypertension

Ideal Sedative I

- Efficacious sedation with short onset and short duration ✓
- No accumulation ✓
- No active metabolites ✓
- Easy titration ✓

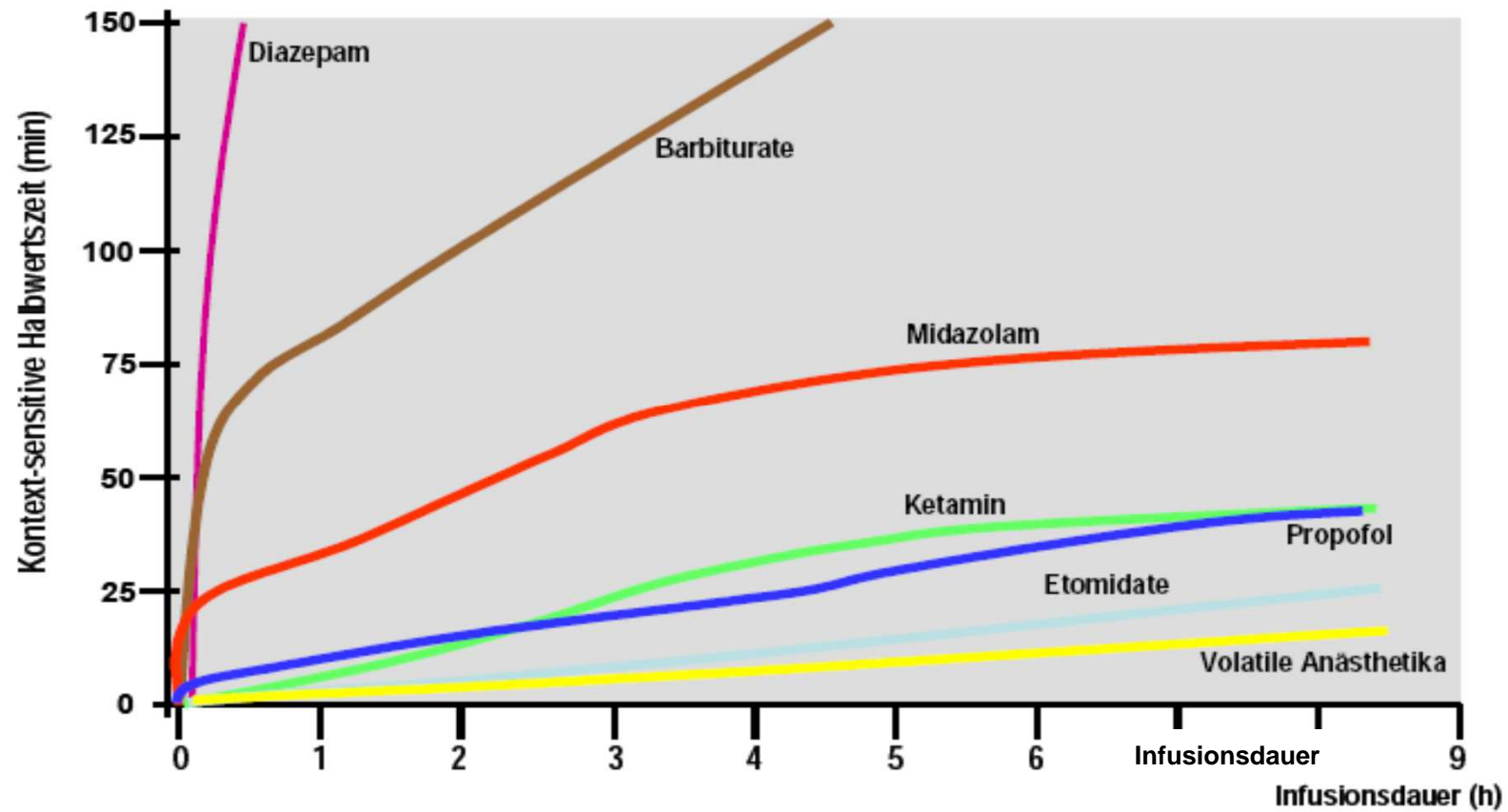
Ideal Sedative II

- No serious cardiopulmonary depression ✓
- Metabolism not affected by organinsufficiencies ✓
- No tolerance or addictive development for the drug in the patient ✓

Ideal Sedative
=
Volatile Anesthetic

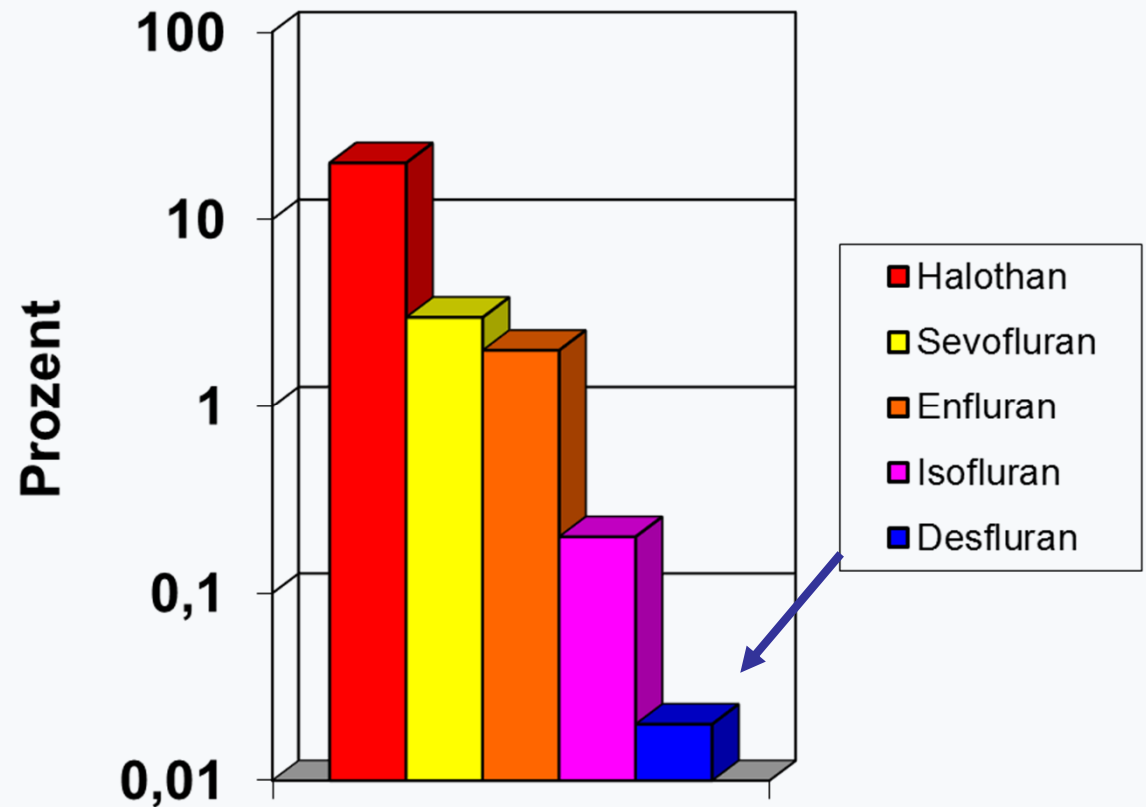
Why? 3 reasons

1. reason: context-sensitive halftime



Basically no metabolism

Halothan	10 - 20%
Sevofluran	3 - 5%
Enfluran	2 - 3%
Isofluran	0,2%
Desfluran	0,02%



Before the advent of the ANACONDA

- Technical Problems with application need for anesthesia machines
- Room air contamination with open system as in ICU-ventilators and lack of gas scavenging systems



Clinical studies I

- **Kong KL et al.: Isoflurane compared with midazolam for sedation in the intensive care unit.** BMJ. 1989 May 13;298(6683):1277-80
- **Millane TA et al.: Isoflurane and propofol for long-term sedation in the intensive care unit. A crossover study.** Anaesthesia. 1992 Sep;47(9):768-74
- **Spencer EM et al.: Isoflurane for prolonged sedation in the intensive care unit; efficacy and safety.** Intensive Care Med. 1992;18(7):415-21
- **Haraguchi N et al.: Inhalation sedation with Sevoflurane: a comparative study with nitrous oxide.** J Oral Maxillofac Surg. 1995 Jan;53(1):24-6
- **Meiser A et al.: Desflurane compared with propofol for postoperative sedation in the intensive care unit.** Br J Anaesth. 2003 Mar;90(3):273-80.

2. reason: control



? ? ? ? ? ? ? ?

?

Intravenous Sedation

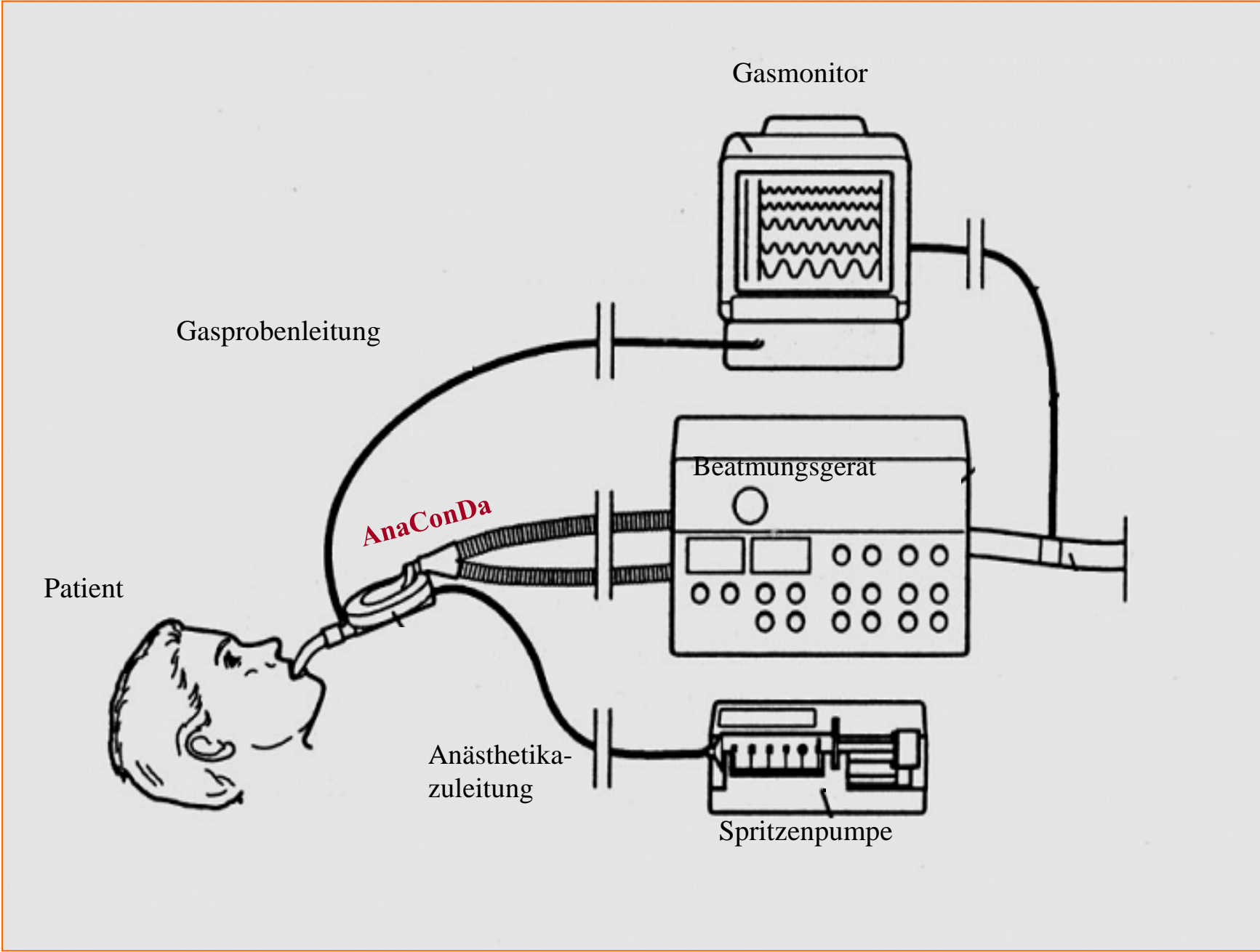


2. reason: control, endtidal measurement

Inhalational Sedation

!

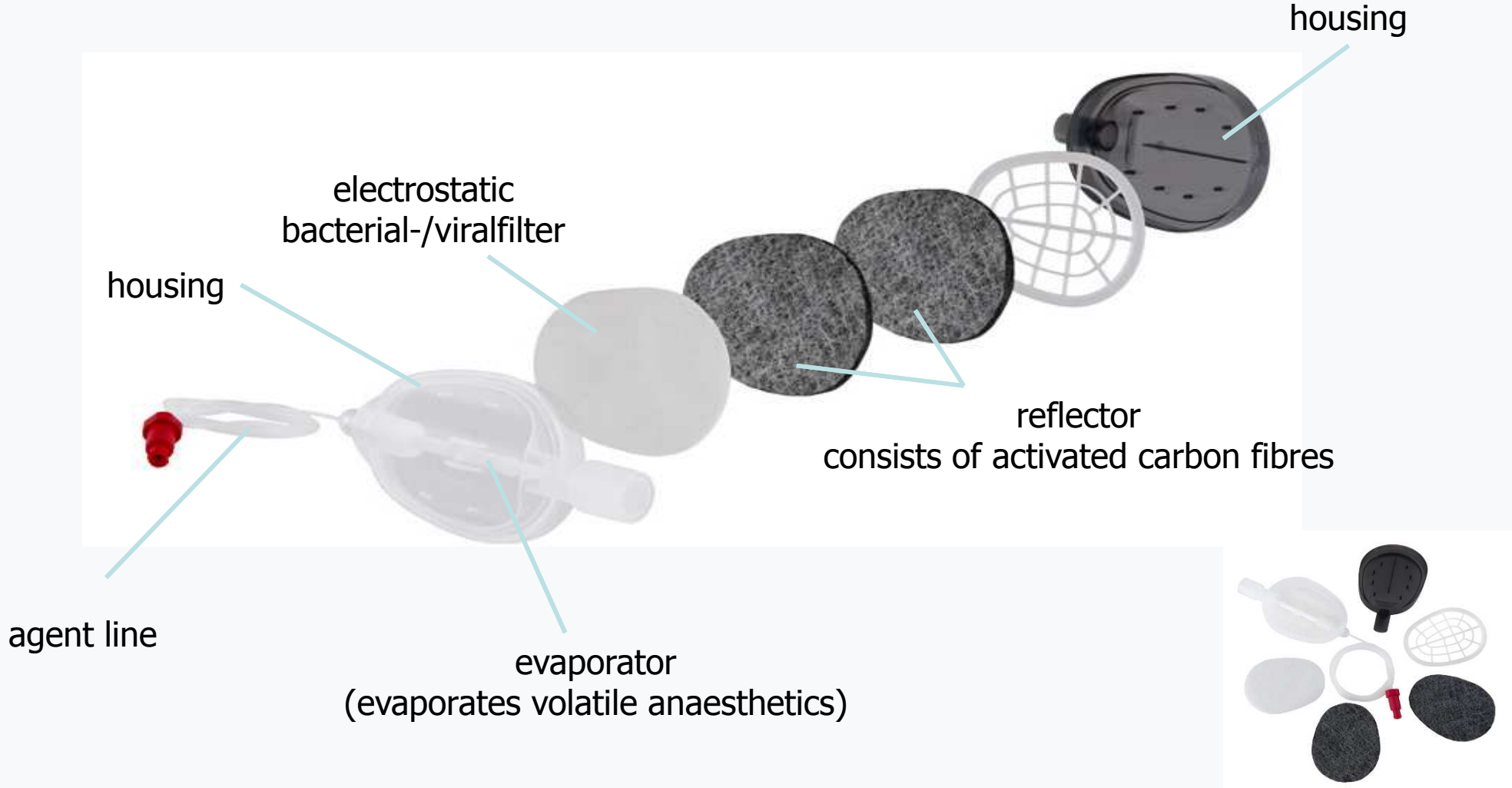




AnaConDa™ Anesthetic Conserving Device



What is AnaConDa



All in One !



Vapor



**Circlesystem
Low Flow**



Bakteria-/Virusfilter

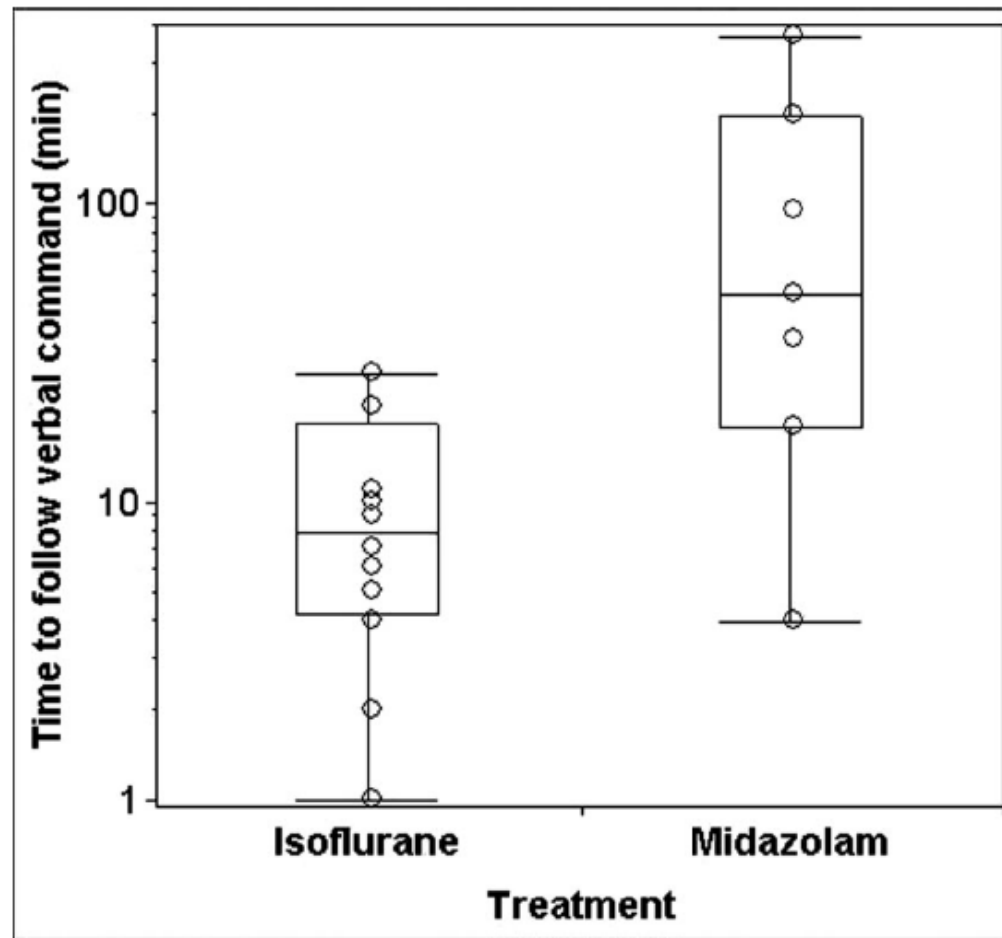


**HME
(passive humidifier)**

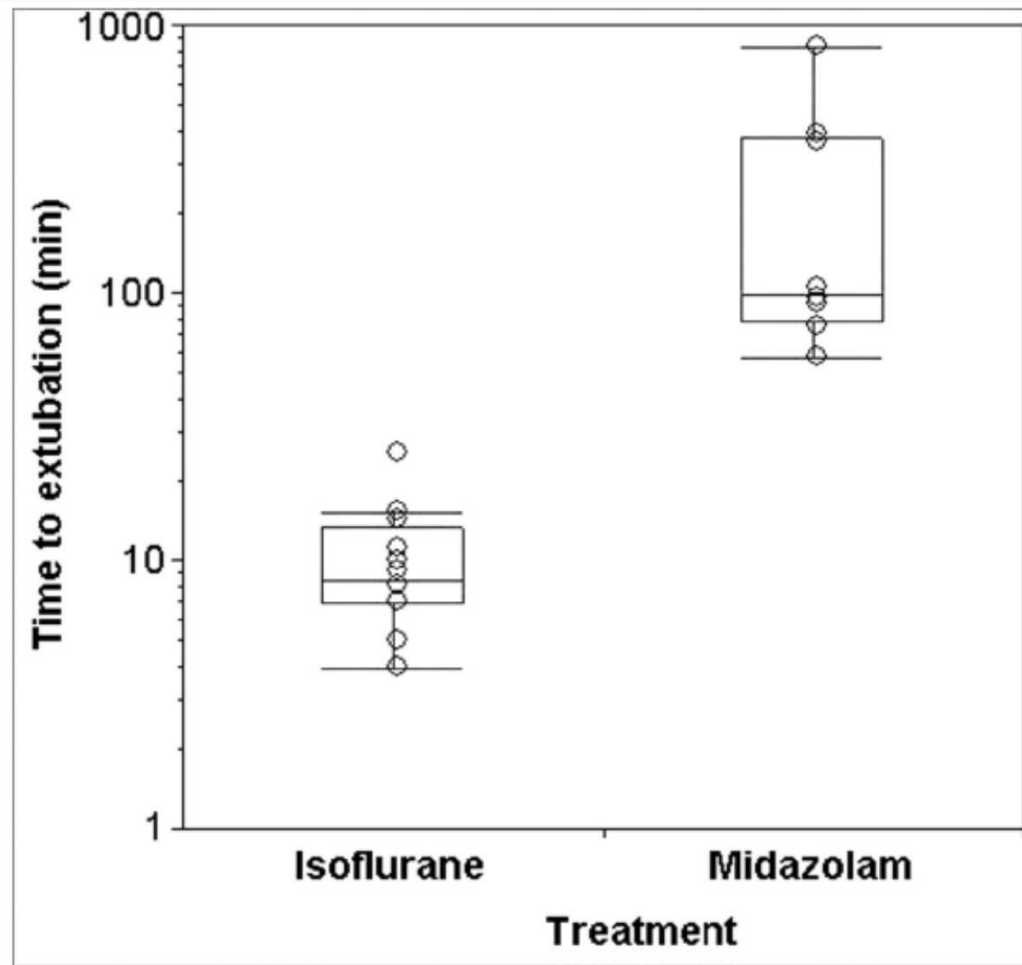
Clinical studies II

- **Sackey PV et al.: Three cases of PICU sedation with isoflurane delivered by the 'AnaConDa'. Paediatr Anaesth. 2005 Oct;15(10):879-85**
- **Hanafy MA et al.: Clinical evaluation of inhalational sedation following coronary artery bypass grafting. Eg J Anaesth. 2005;21:237-42**
- **Sackey PV et al.: Ambient isoflurane pollution and isoflurane consumption during intensive care unit sedation with the Anesthetic Conserving Device. Crit Care Med. 2005 Mar;33(3):585-90**
- **Sackey PV et al.: Prolonged isoflurane sedation of intensive care unit patients with the Anesthetic Conserving Device. Crit Care Med. 2004 Nov;32(11):2241-6**
- **Hellström J et al.: Cardiac outcome after sevoflurane versus propofol sedation following coronary bypass surgery: a pilot study. Acta Anaesthesiol Scand. 2011; 55: 460-467**

10 vs 110 min



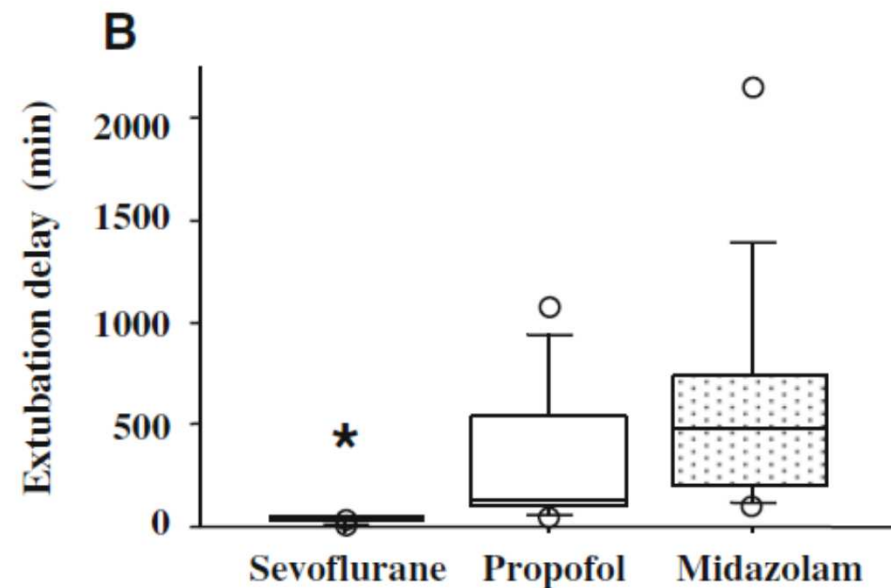
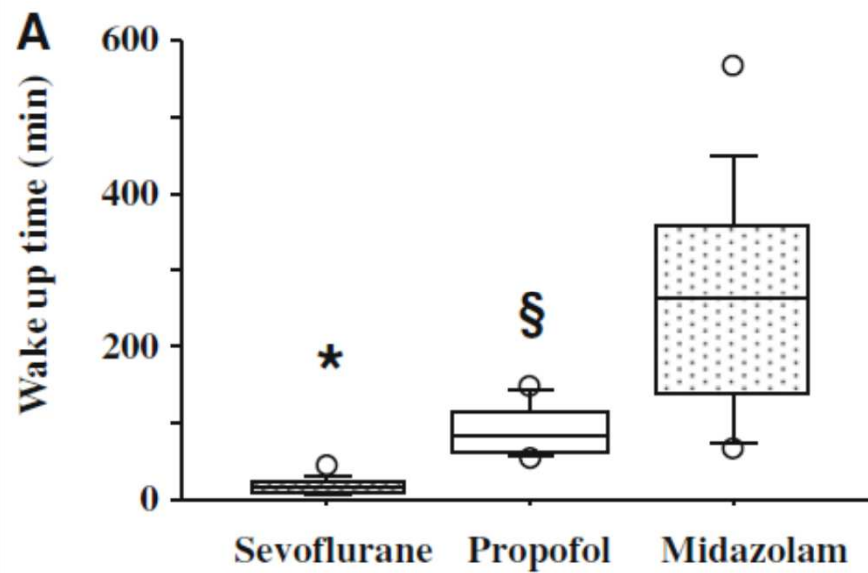
10 vs 252 min

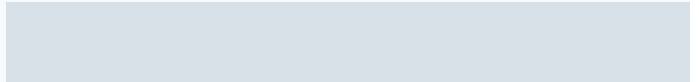


Malcie Mesnil
Xavier Capdevila
Sophie Bringuier
Pierre-Olivier Trine
Yoan Falquet
Jonathan Charbit
Jean-Paul Roustan
Gerald Chanques
Samir Jaber

Long-term sedation in intensive care unit: a randomized comparison between inhaled sevoflurane and intravenous propofol or midazolam

After 50 hrs of sedation





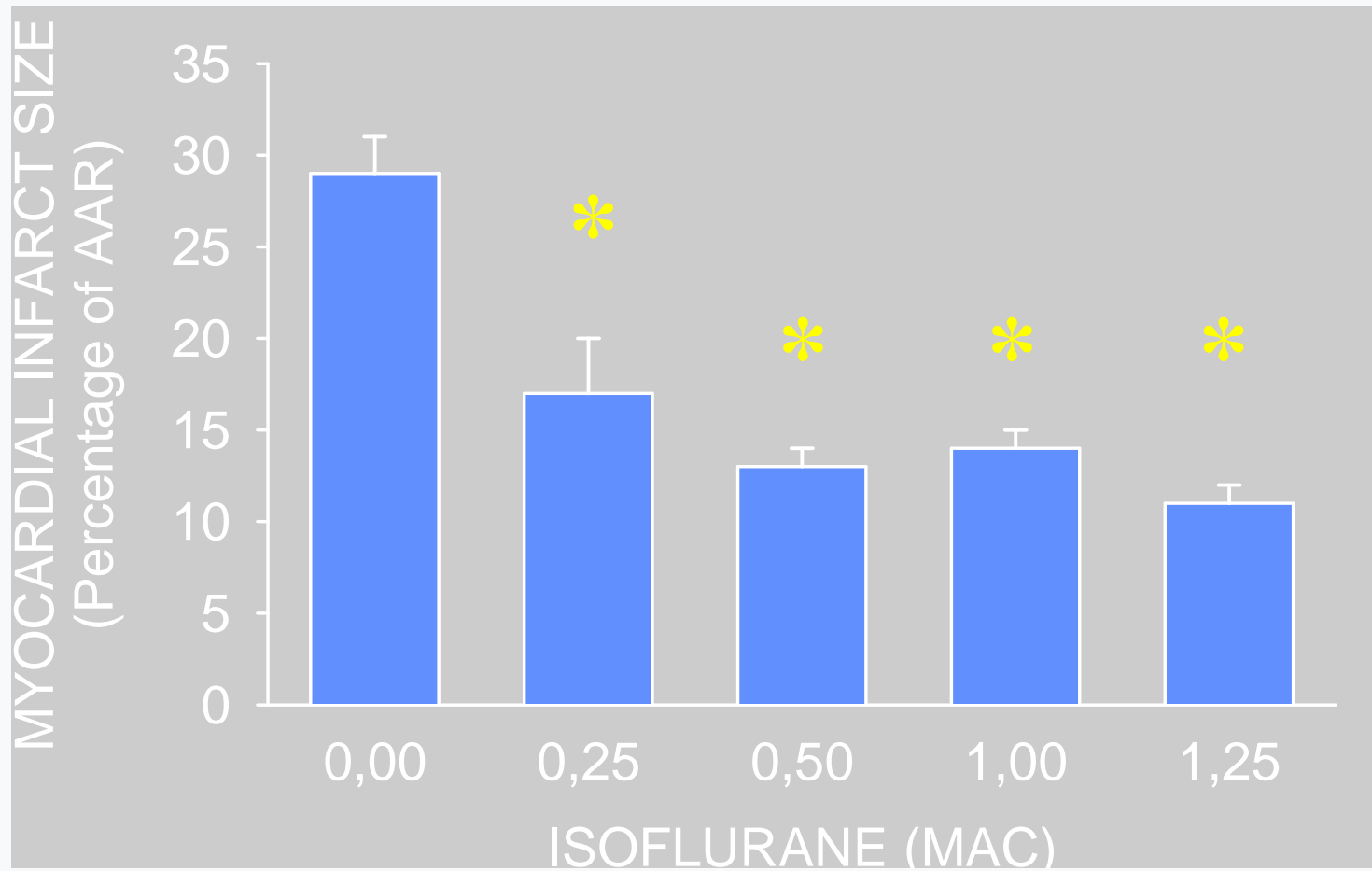
3. reason: Organprotection



Volatile anesthetic-induced cardiac protection: molecular mechanisms, clinical aspects, and interactions with nonvolatile agents.

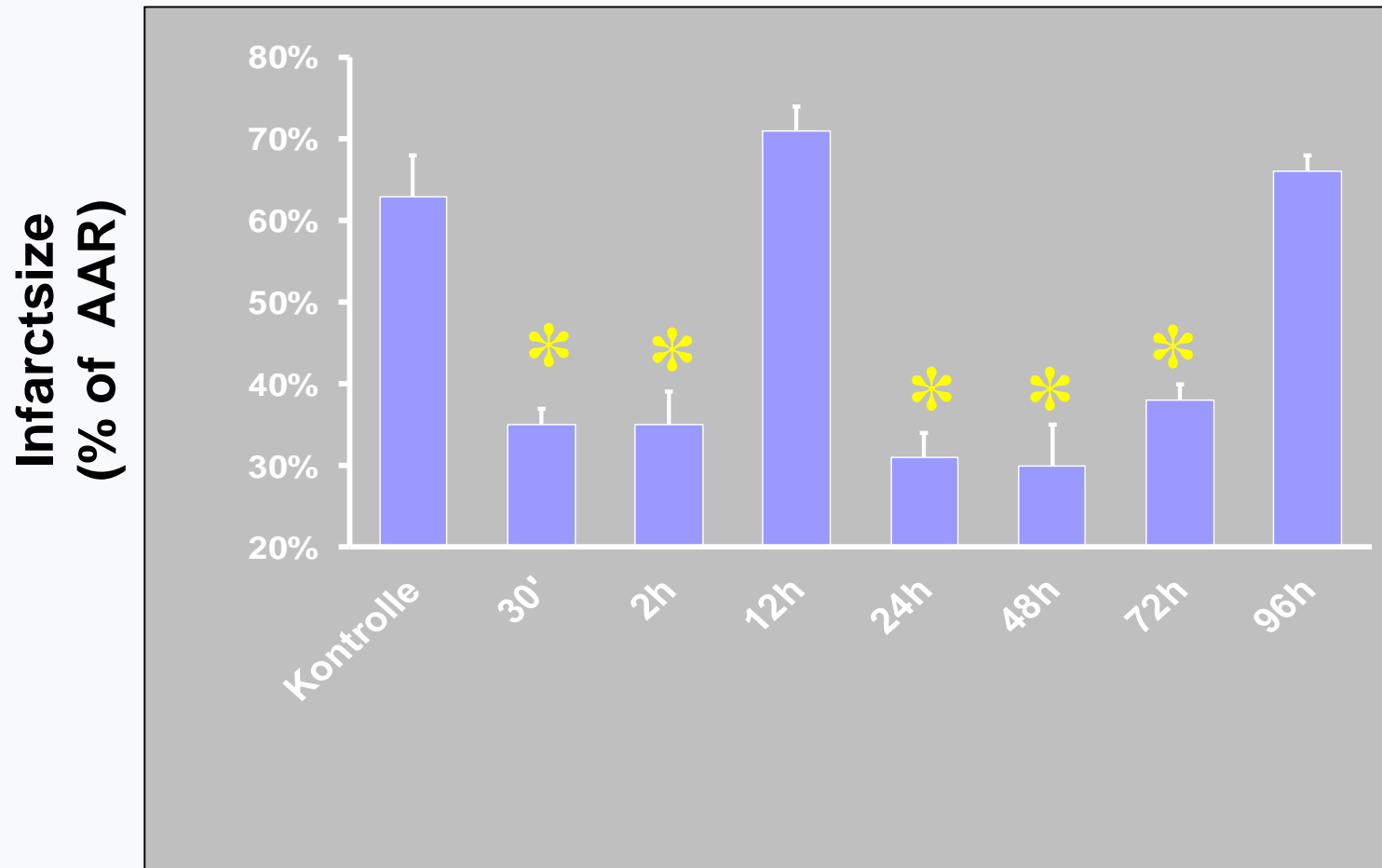
Lotz C, Kehl F., J Cardiothorac Vasc Anesth. 2015;29:749-60

Isoflurane Cardioprotection from 0.25

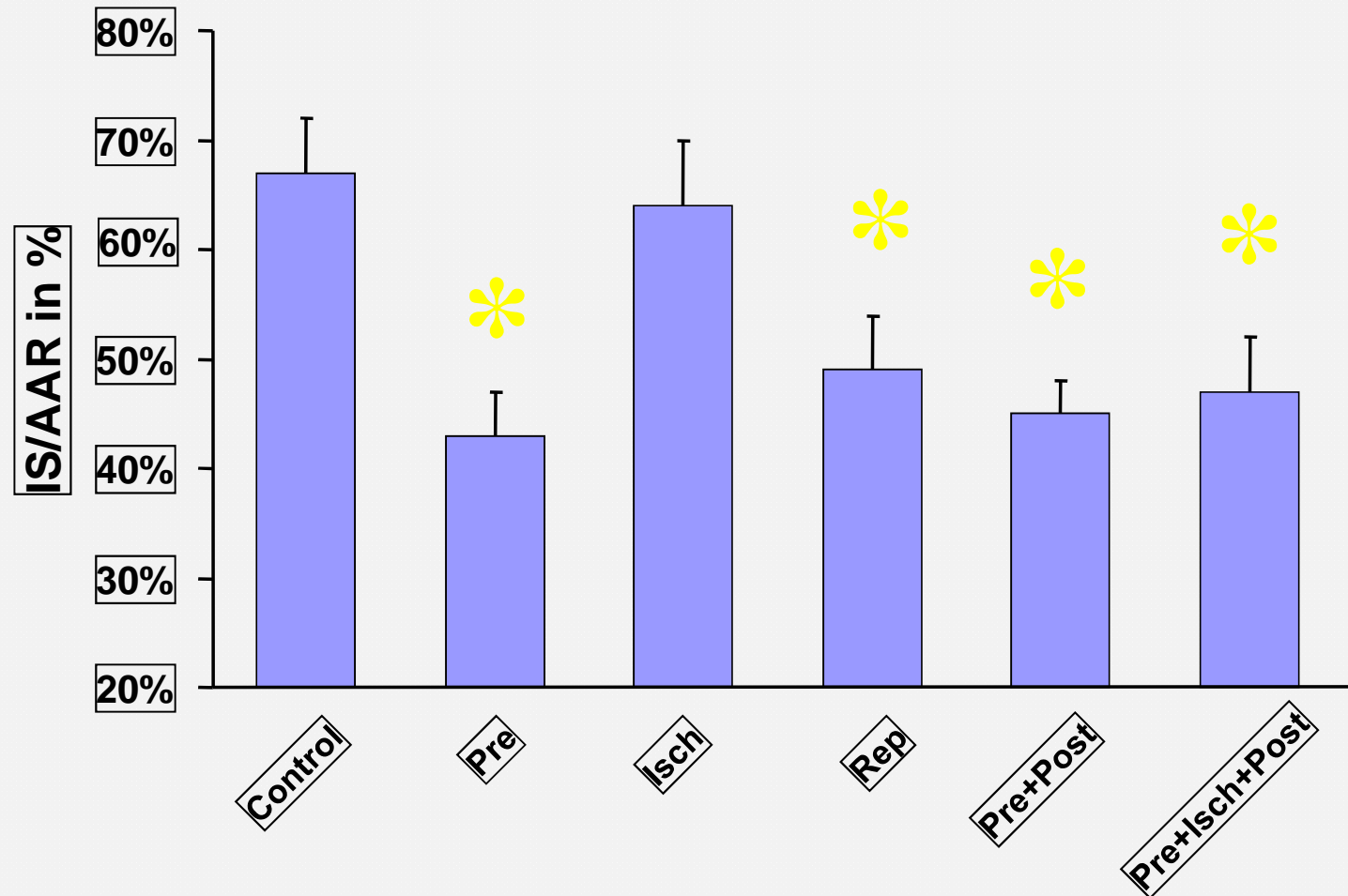


Kehl et al., Anesthesiology 96:675-680, 2002

Desflurane 1. & 2. Window of Protection

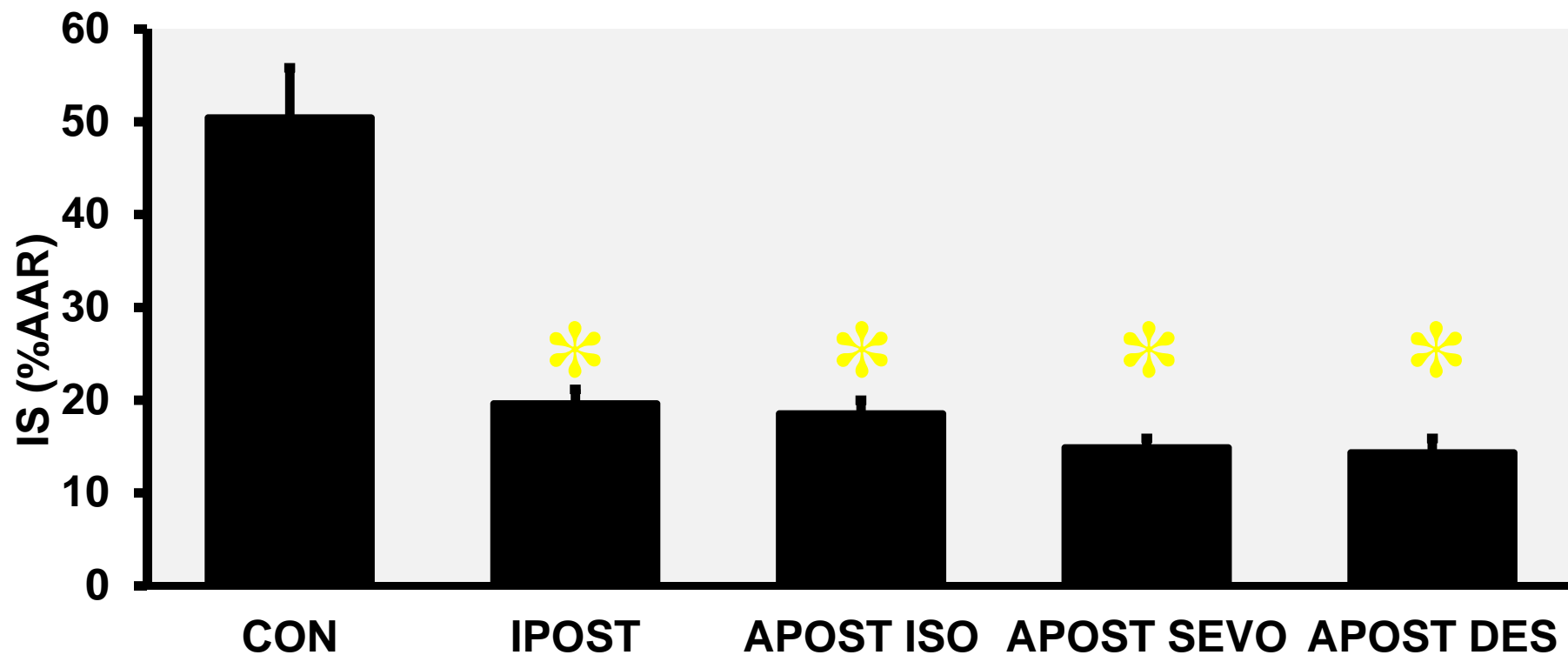


Pre- and Postconditioning!



Smul et al., J Cardiothor Vasc Anesth 23:600-6, 2009

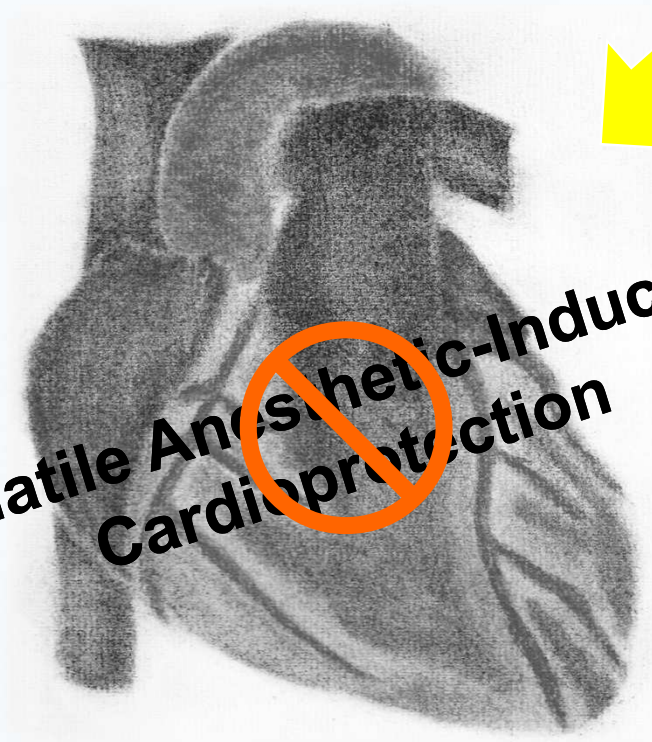
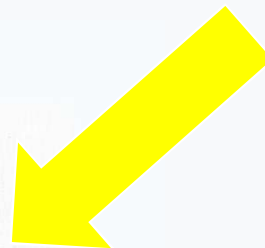
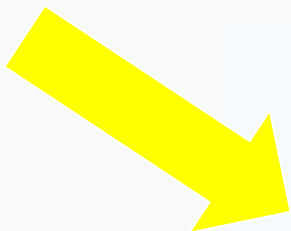
All Volatile Anesthetics confer Anesthetic-induced Postconditioning



Redel et al., Exp Biol Med (Maywood);234(10):1186-91, 2009

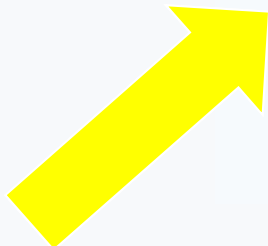
Propofol

β -adrenergic Receptor Blockers



**Volatile Anesthetic-Induced
Cardioprotection**

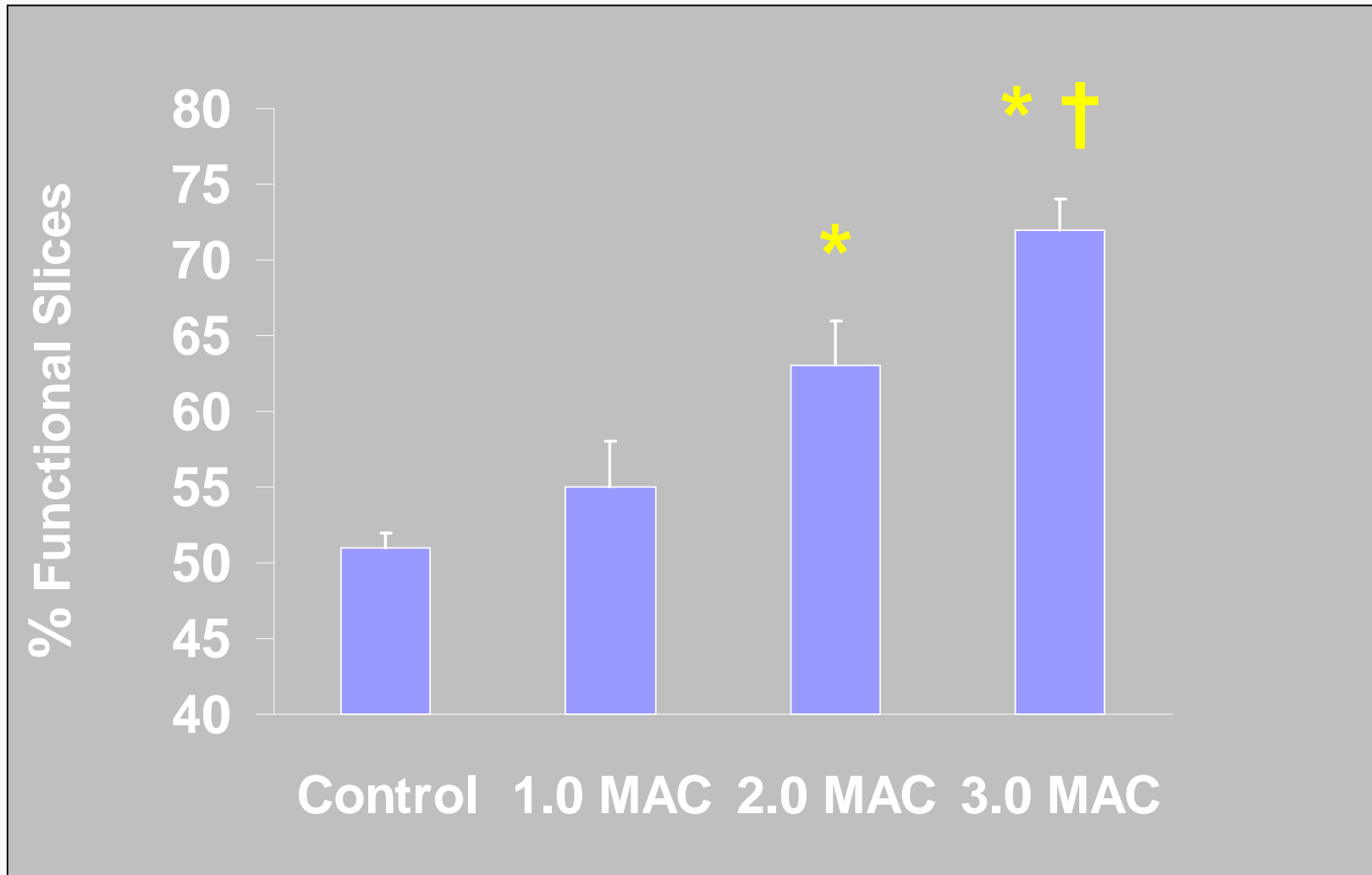
Advanced Age



Hyperglycaemia
Diabetes Mellitus

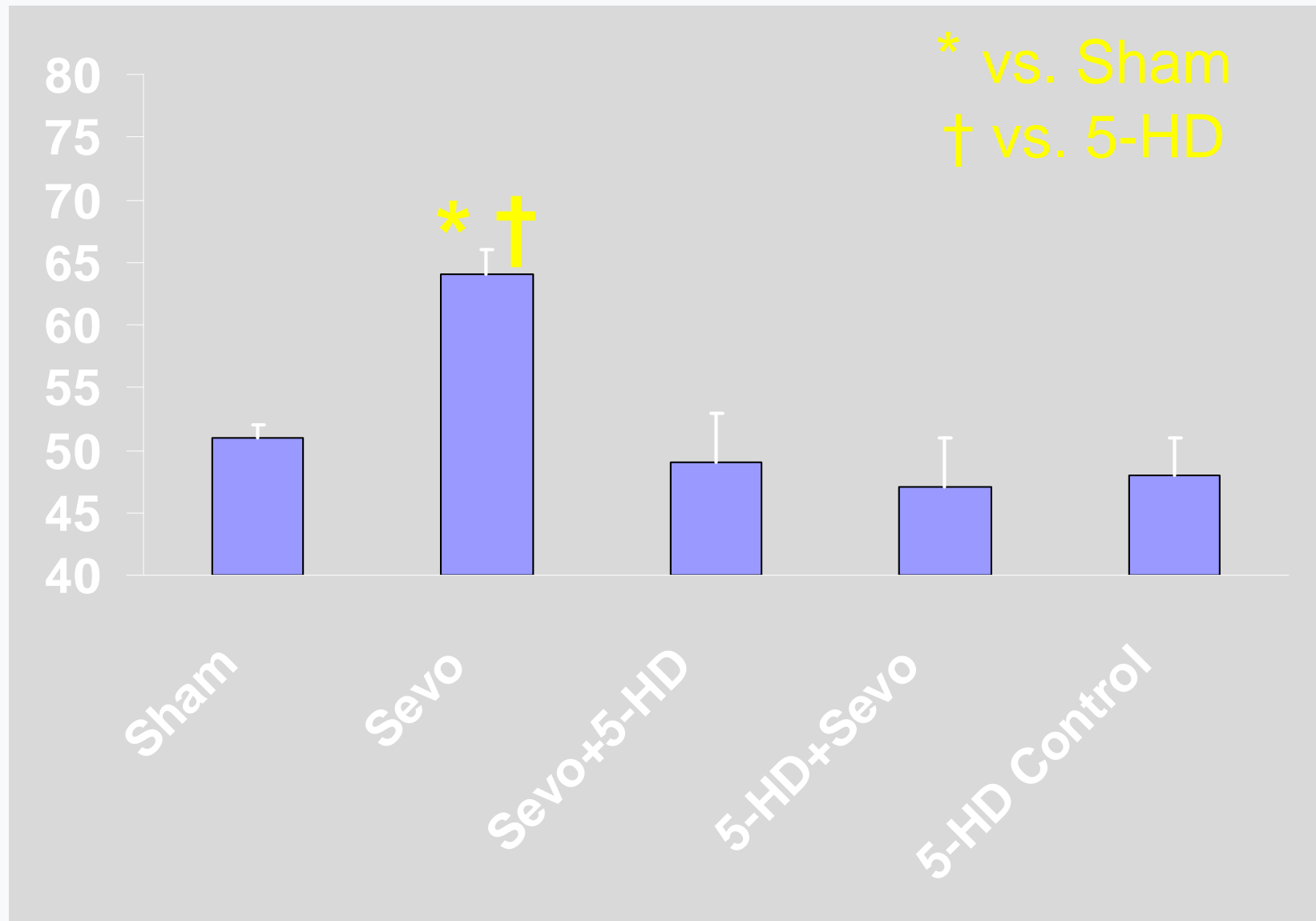


Cerebroprotection *in vitro*

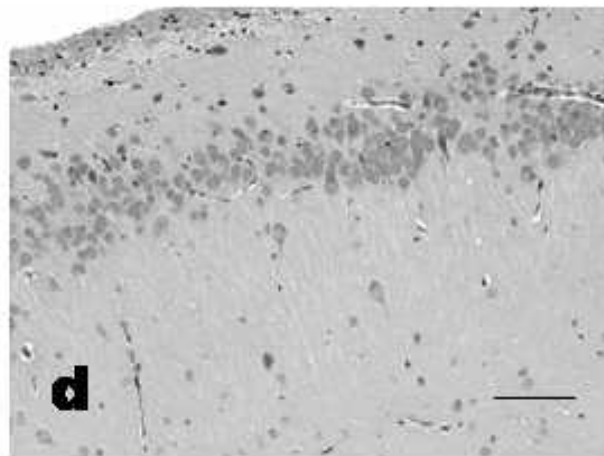
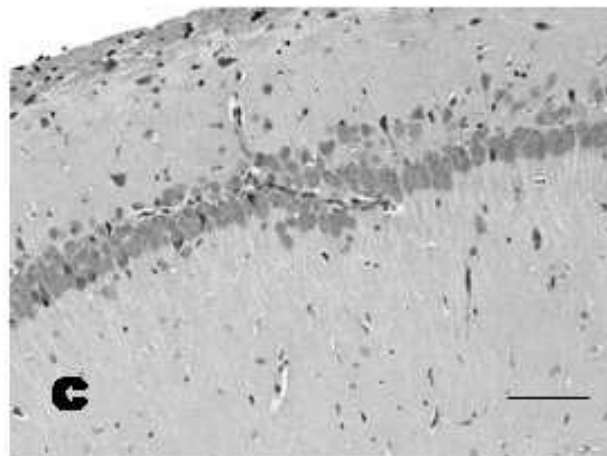
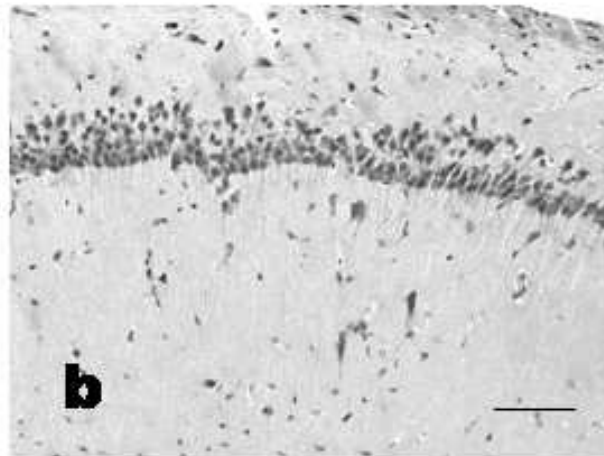
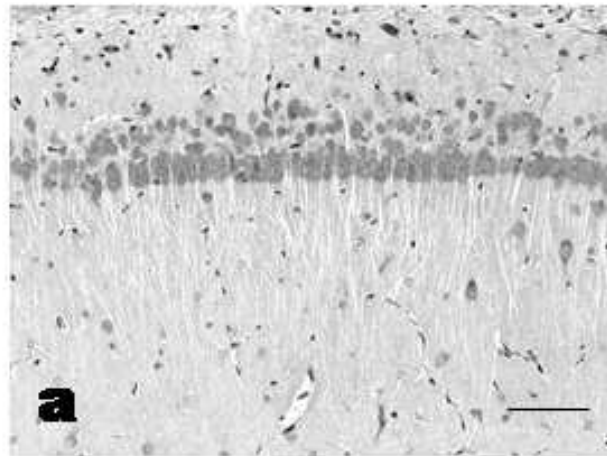


Cerebroprotection *in vivo*

% Functional Slices



Cerebroprotection *in vivo*



Julian Bösel
Jan C. Purrucker
Frank Nowak
Julian Renzland
Petra Schiller
Eva Benveniste Pérez
Sven Poli
Benjamin Brunn
Werner Hacke
Thorsten Steiner

Volatile isoflurane sedation in cerebrovascular intensive care patients using AnaConDa®: effects on cerebral oxygenation, circulation, and pressure

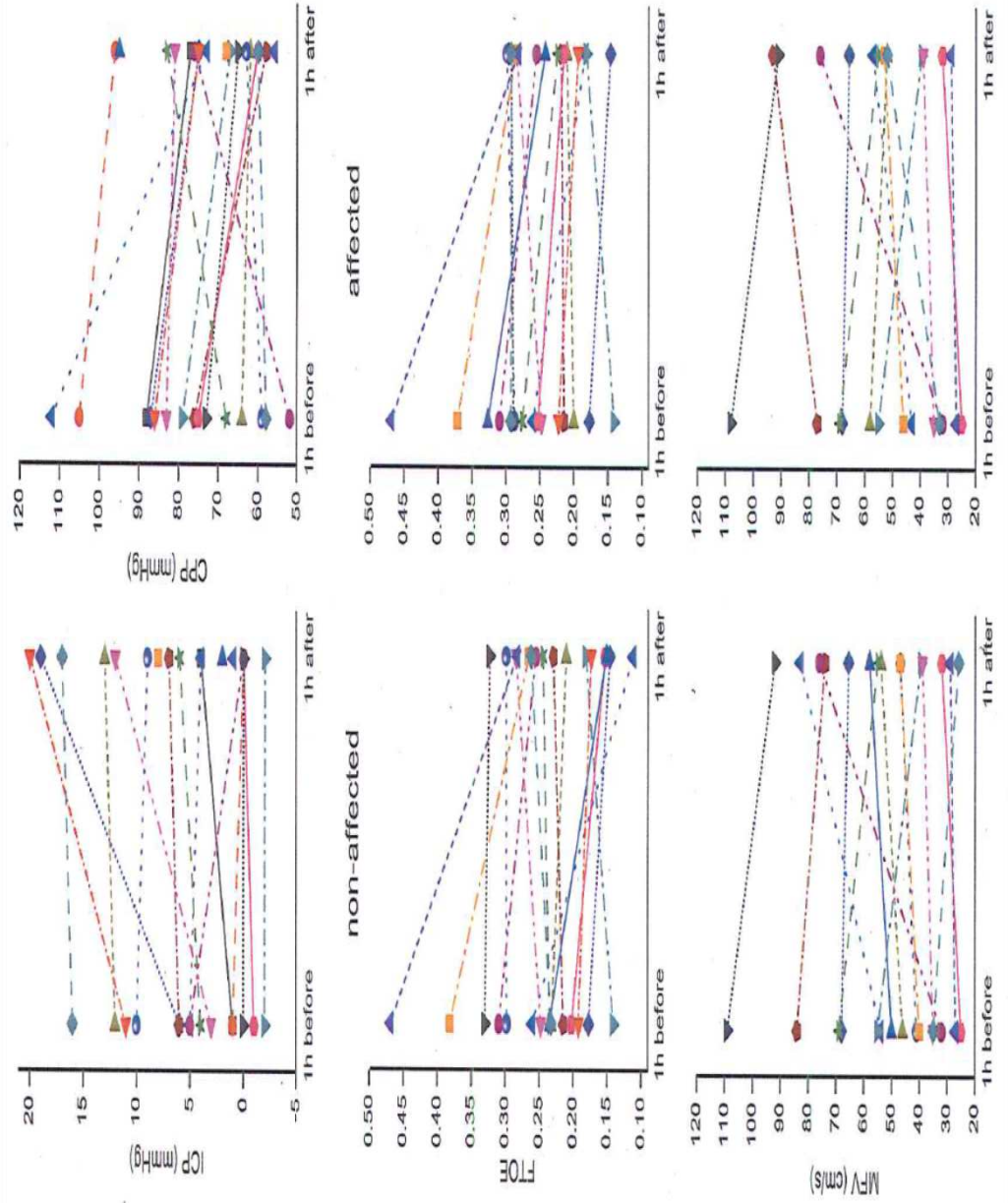


Fig. 1 Individual changes in ICP, CPP, MFV and FTOE 1 h before and 1 h after the sedation switch to isoflurane for each non-affected and affected hemisphere (for FTOE and MFV). A full dataset was obtained in 16 patients, data were missing for ICP (and thus CPP) in 1 patient, MFV in 2 patients, and FTOE in 2 patients (partially overlapping) for various technical reasons

British Journal of Anaesthesia **111** (6): 886–96 (2013)
Advance Access publication 12 July 2013 · doi:10.1093/bja/aet231

BJA

Anaesthetic drugs and survival: a Bayesian network meta-analysis of randomized trials in cardiac surgery

G. Landoni^{1*}, T. Greco¹, G. Biondi-Zoccai², C. Nigro Neto^{3,4}, D. Febres¹, M. Pintaudi¹, L. Pasin¹, L. Cabrini¹, G. Finco⁵ and A. Zangrillo¹

¹ Anesthesia and Intensive Care Department, San Raffaele Scientific Institute, Milan, Italy

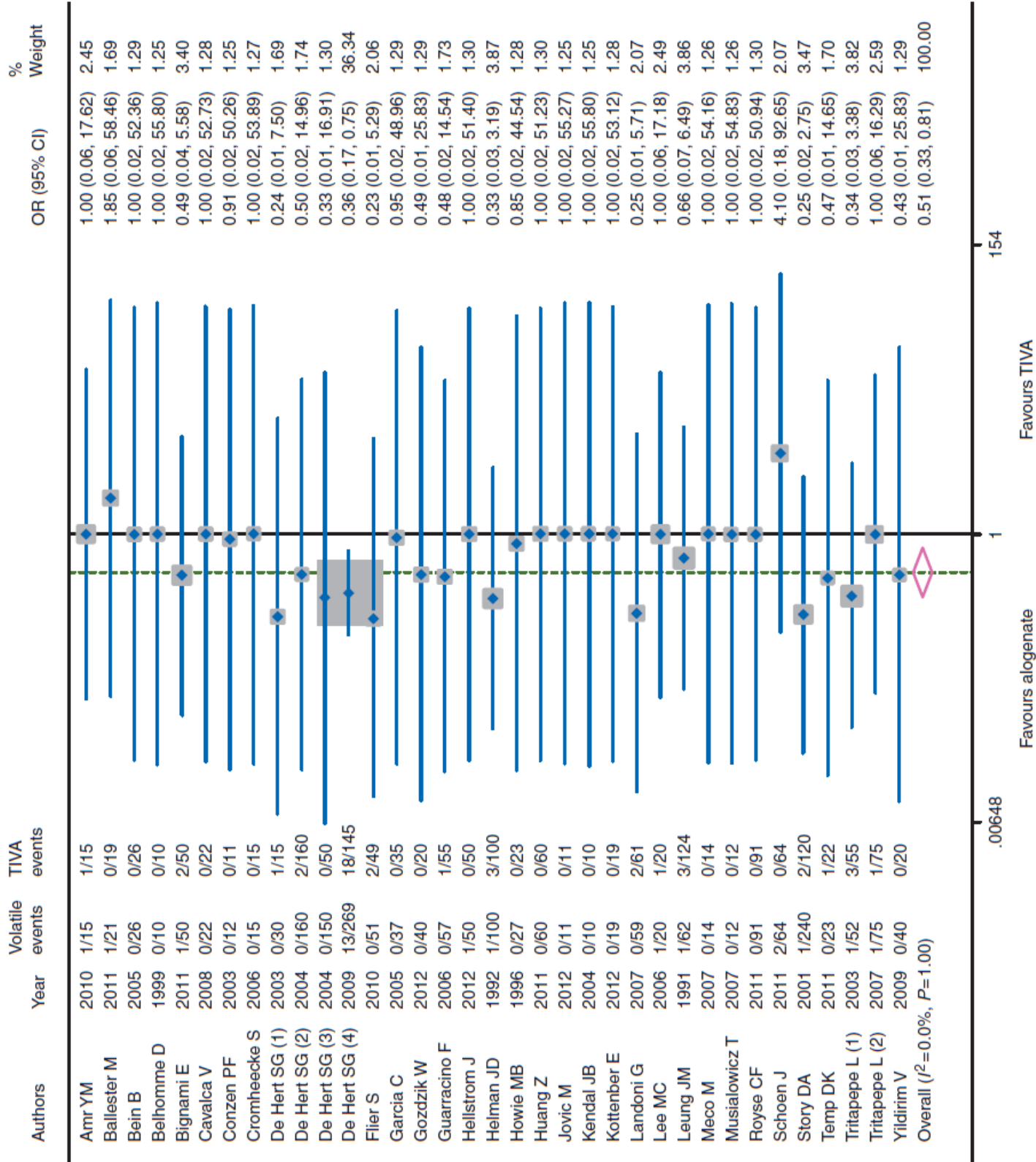
² Department of Medico-Surgical Sciences and Biotechnologies, Sapienza University of Rome, Latina, Italy

³ Anaesthesia and Intensive Care Department, Federal University of São Paulo, São Paulo, Brazil

⁴ Dante Pazzanese Institute of Cardiology, São Paulo, Brazil

⁵ Department of Medical Sciences “M. Aresu”, University of Cagliari, Italy

* Corresponding author. E-mail: landoni.giovanni@hsr.it



.00648

154

Favours allogenate

Favours TIVA

Mortality reduced by 50% in CABG

Table 2 Secondary and sensitivity analyses to evaluate the effect on mortality of volatile vs TIVA regimen in 35 studies. For these analyses (volatile vs TIVA), the three studies comparing a volatile anaesthetic with another volatile anaesthetic were not included. TIVA, total i.v. anaesthesia; NNT, number needed to treat; CABG, coronary artery bypass graft; CPB, cardiopulmonary bypass; ICU, intensive care unit

	Number of included studies	Events in the volatile group	Events in the TIVA group	OR (all in favour of volatile agents)	95% CI	P-value for effect	NNT	I ²
Mortality								
Overall analysis	35	25/1994 (1.3%)	43/1648 (2.6%)	0.51	0.33–0.81	0.004	74	0%
Sensitivity analysis on mortality								
Low risk of bias studies	18	17/1380 (1.2%)	32/998 (3.2%)	0.42	0.24–0.73	0.002	50	0%
Without the largest study (6)	34	12/1725 (0.7%)	25/1503 (1.7%)	0.63	0.36–1.11	0.11		
More than 100 patients	16	22/1590 (1.4%)	39/1309 (3.0%)	0.43	0.25–0.72	0.002	63	0%
CABG surgery studies	28	22/1746 (1.3%)	39/1402 (2.8%)	0.48	0.30–0.78	0.003	66	0%
CPB-CABG surgery	22	21/1597 (1.3%)	37/1259 (2.9%)	0.45	0.27–0.75	0.002	62	0%
OPCABG surgery	6	1/149 (0.7%)	2/143 (1.4%)	0.83	0.19–3.74	0.8		
Non-CABG surgery	7	3/248(1.2%)	4/246 (1.6%)	0.82	0.23–2.89	0.8		
Myocardial infarction	27	44/1879 (2.3%)	74/1560 (4.7%)	0.56	0.38–0.82	0.003	42	0%
Inotropes use	21	309/1186 (26%)	426/1115 (38%)	0.42	0.31–0.59	<0.001	8	45%

Effects of Volatile Anesthetics on Mortality and Postoperative Pulmonary and Other Complications in Patients Undergoing Surgery

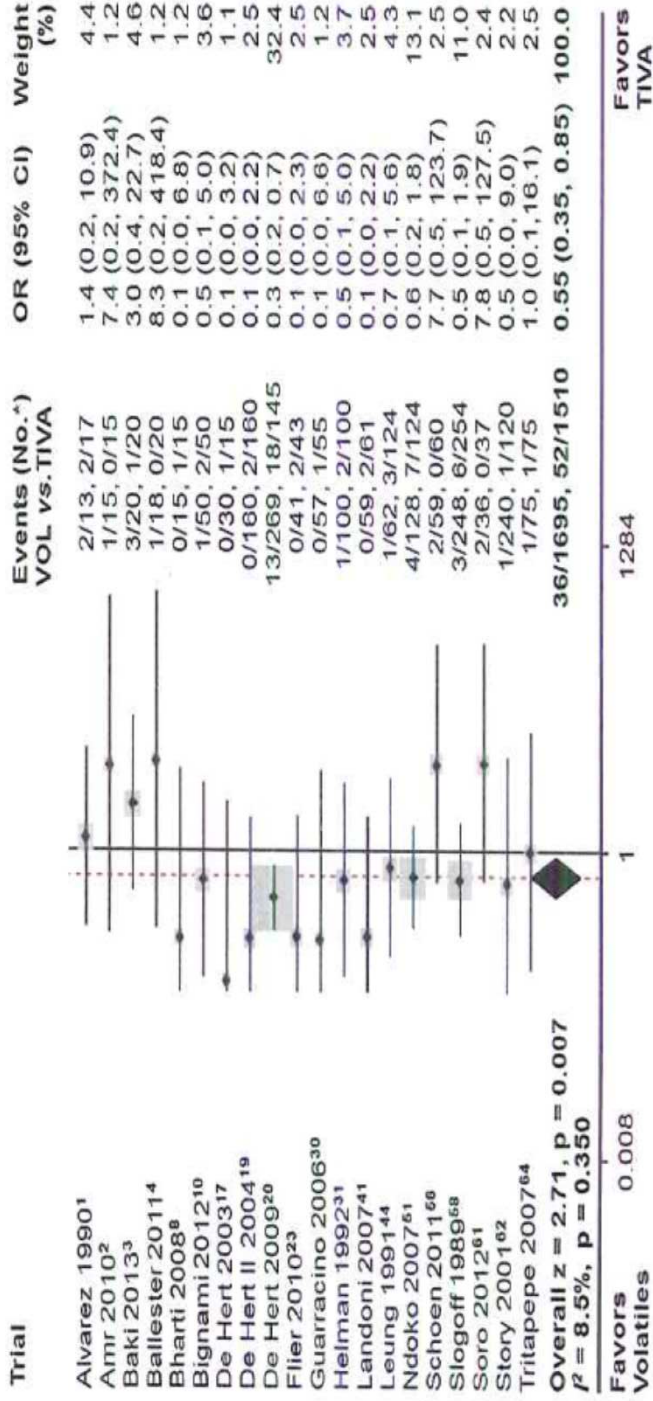
A Systematic Review and Meta-analysis

Christopher Uhlig, M.D., Thomas Bluth, M.D., Kristin Schwarz, M.Sc., Stefanie Deckert, M.Sc., Luise Heinrich, M.Sc., Stefan De Hert, M.D., Ph.D., Giovanni Landoni, M.D., Ary Serpa Neto, M.D., Ph.D., Marcus J. Schultz, M.D., Ph.D., Paolo Pelosi, M.D., F.E.R.S., Jochen Schmitt, M.D., Ph.D., Marcelo Gama de Abreu, M.D., M.Sc., Ph.D., D.E.S.A.

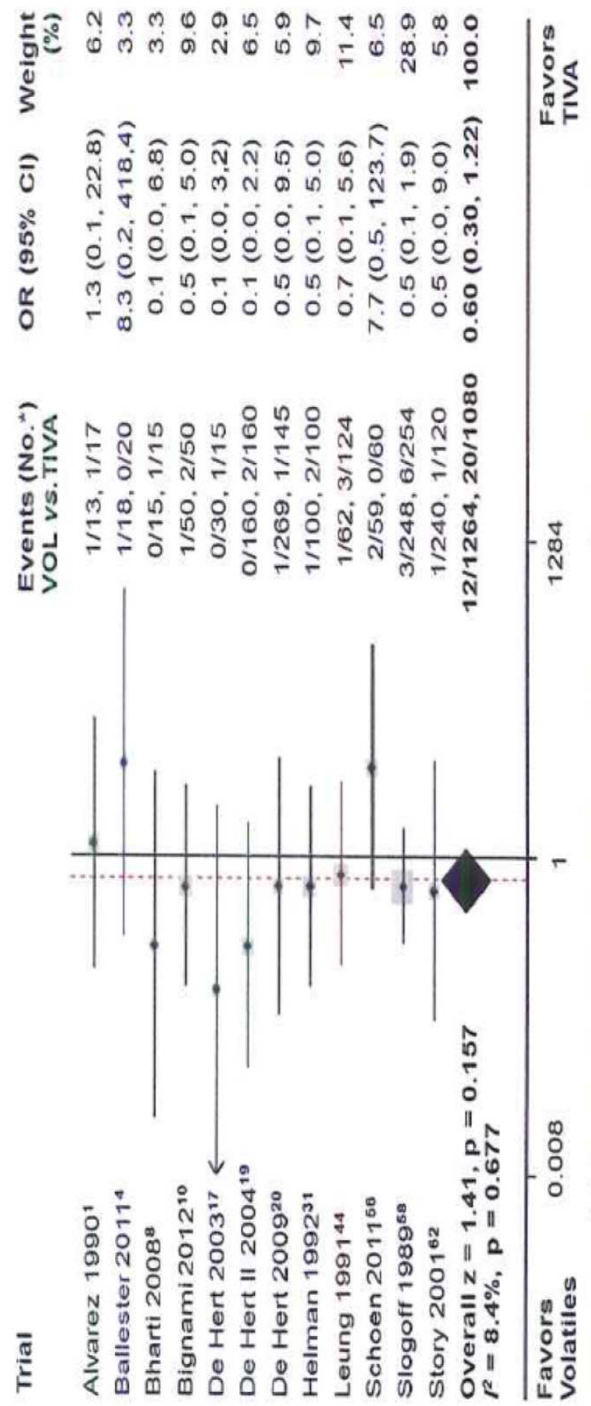


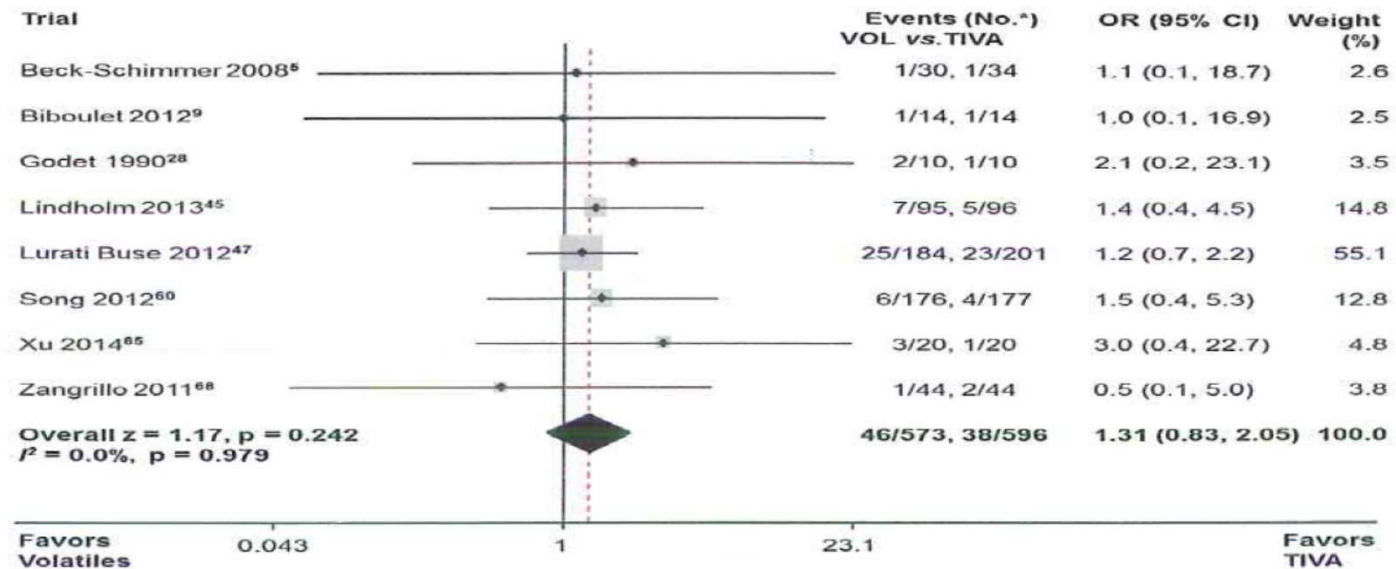
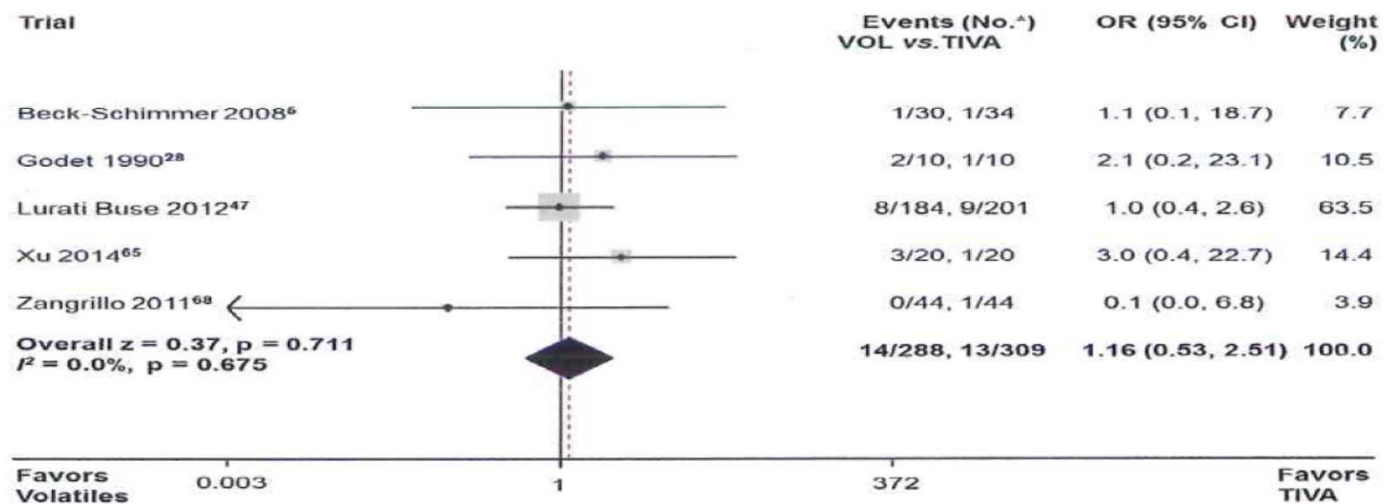
This article has been selected for the ANESTHESIOLOGY CME Program. Learning objectives and disclosure and ordering information can be found in the CME section at the front of this issue.

A Overall Mortality – Cardiac Surgery

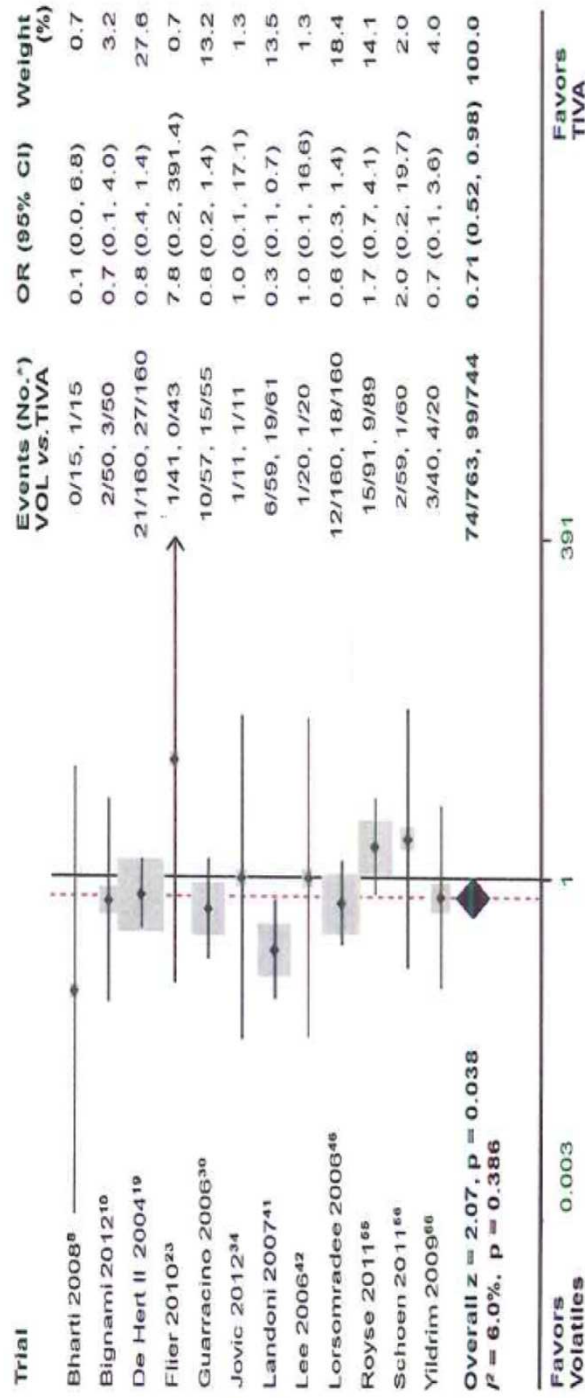


B In-hospital Mortality – Cardiac Surgery

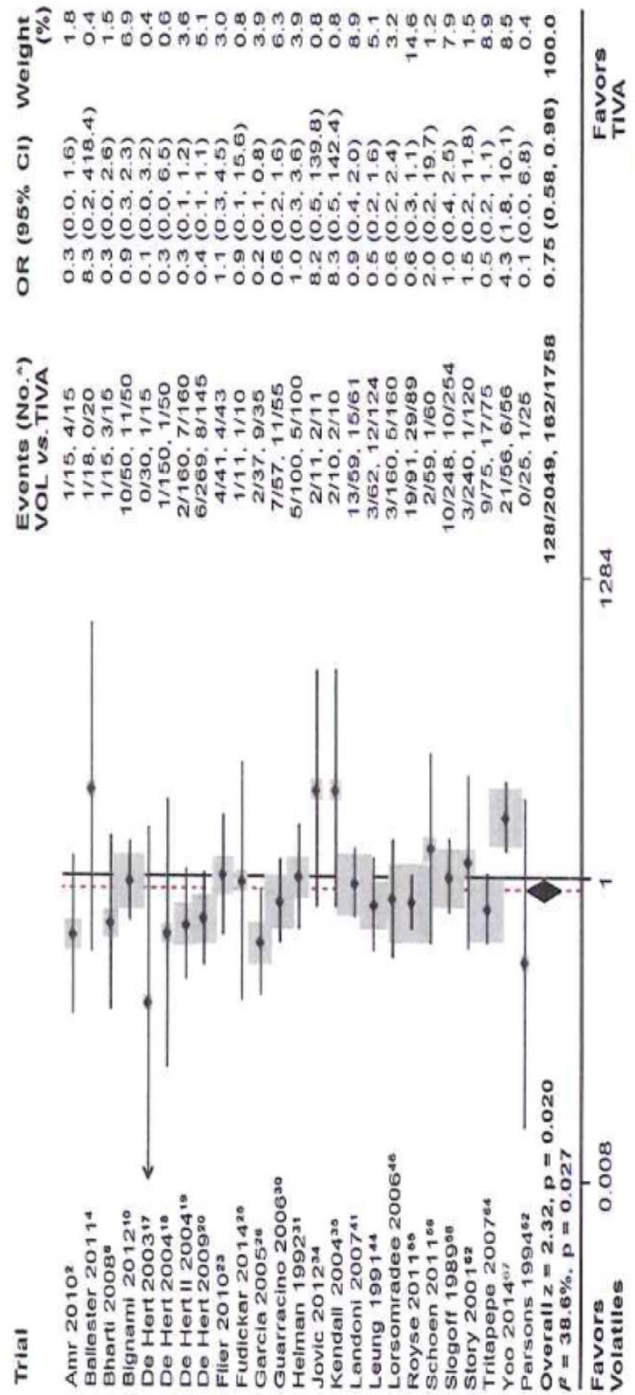


A**Overall Mortality – Non-cardiac Surgery****B****In-hospital Mortality – Non-cardiac Surgery**

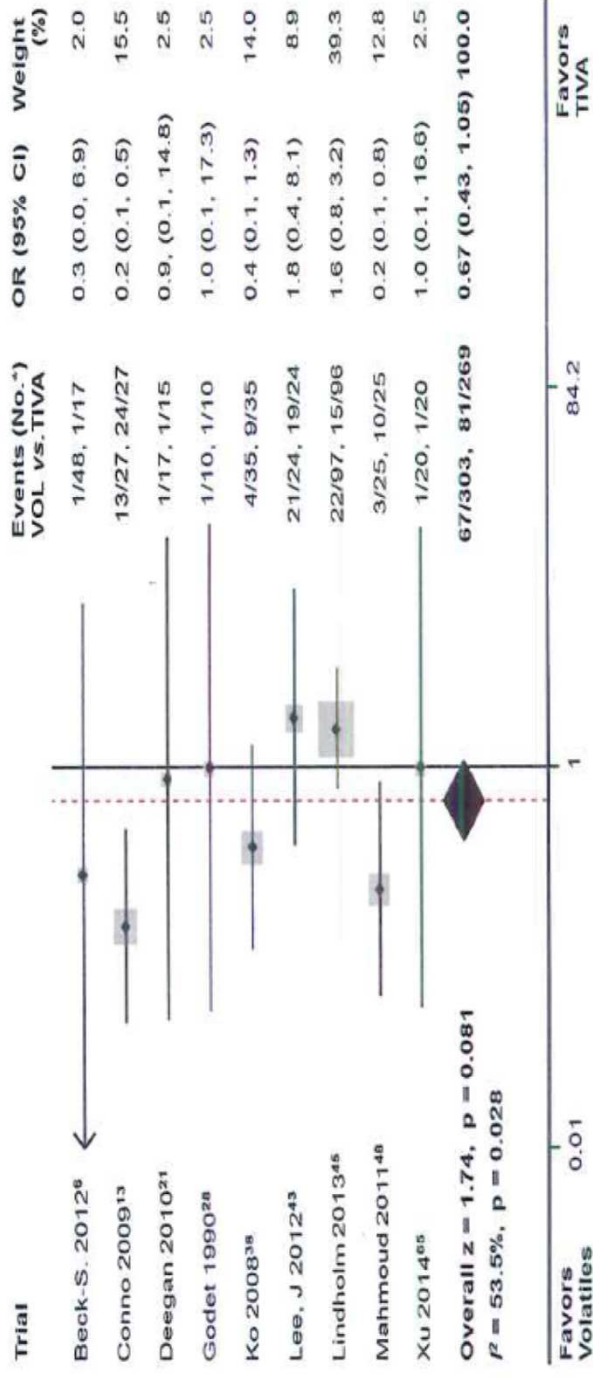
A Pulmonary Complications – Cardiac Surgery



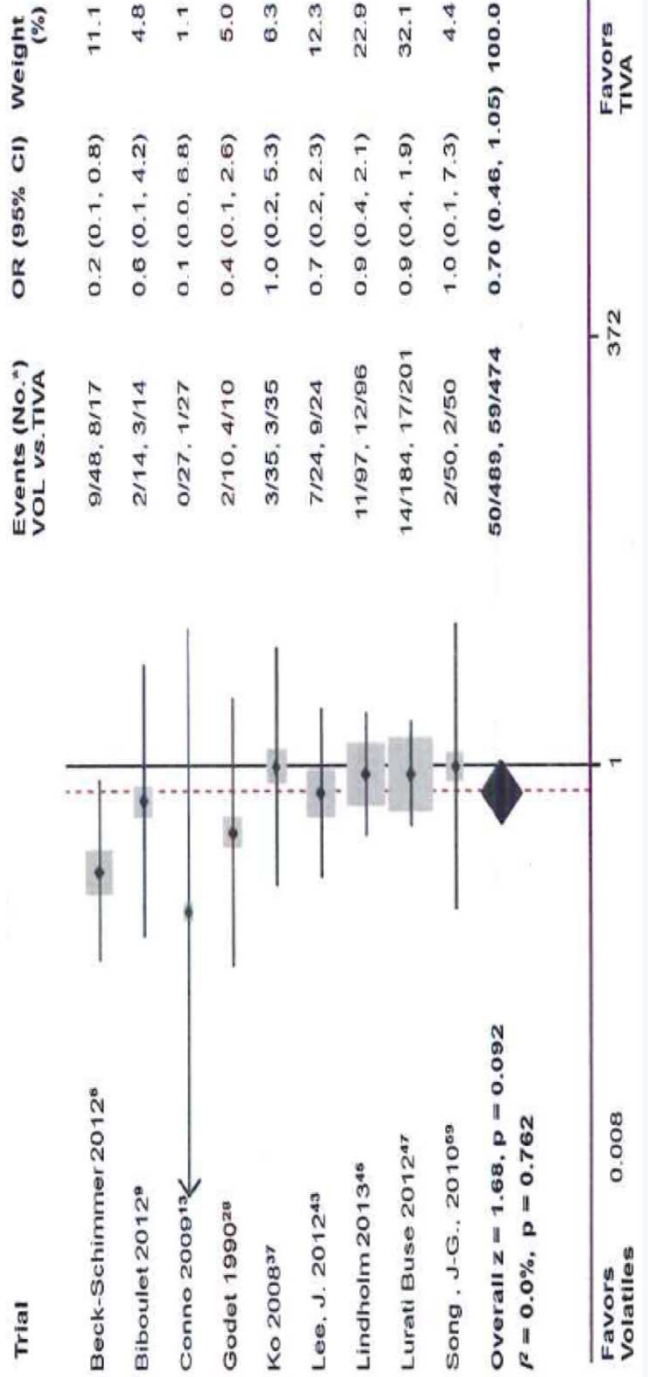
B Other Complications – Cardiac Surgery



A Pulmonary complications – Non-cardiac Surgery



B Other complications – Non-cardiac Surgery



Prolonged sevoflurane administration in the off-pump coronary artery bypass graft surgery: Beneficial effects☆☆☆

Jose L. Guerrero Orriach MD*, M. Galán Ortega MD, M. Ramirez Aliaga MD, P. Iglesias MD, M. Rubio Navarro MD, J. Cruz Mañas MD

Department of Anaesthesia, Hospital Virgen de la Victoria, Málaga, Spain

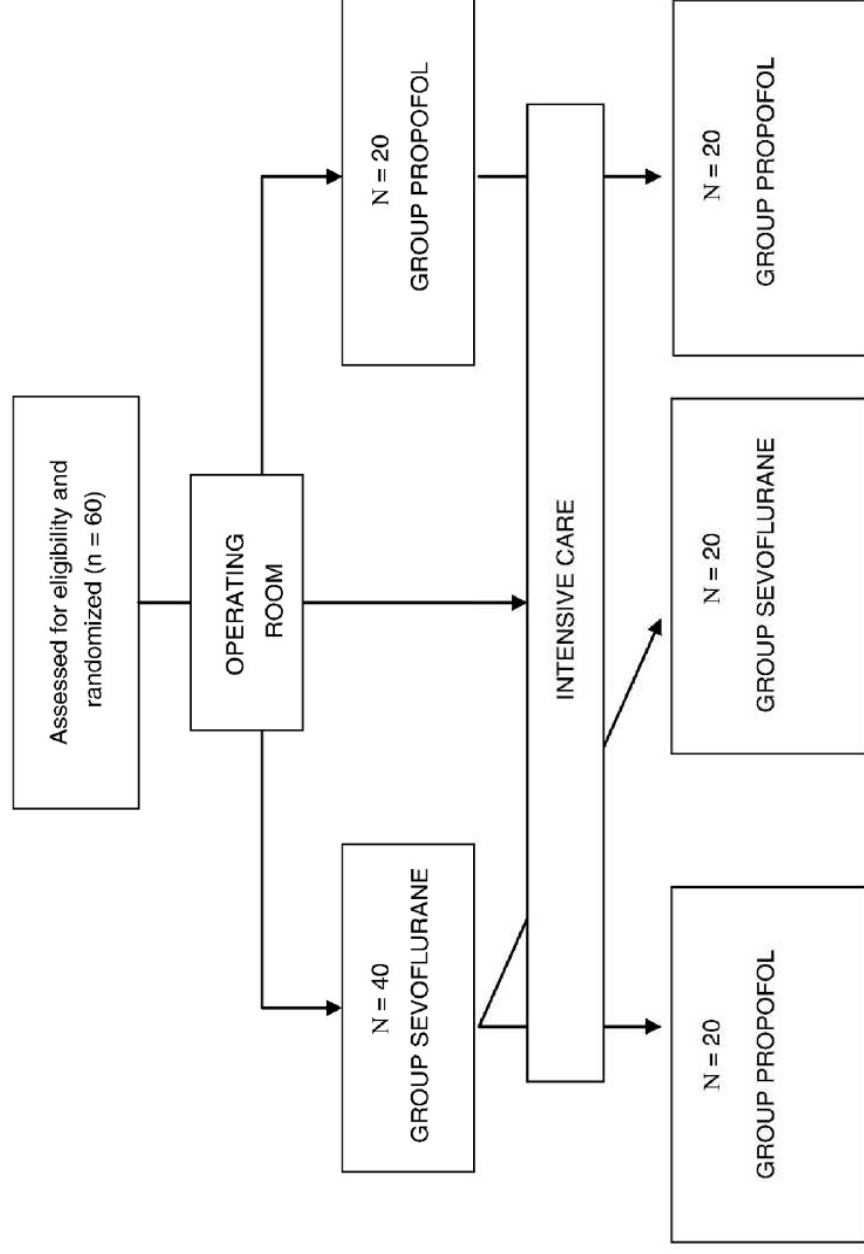


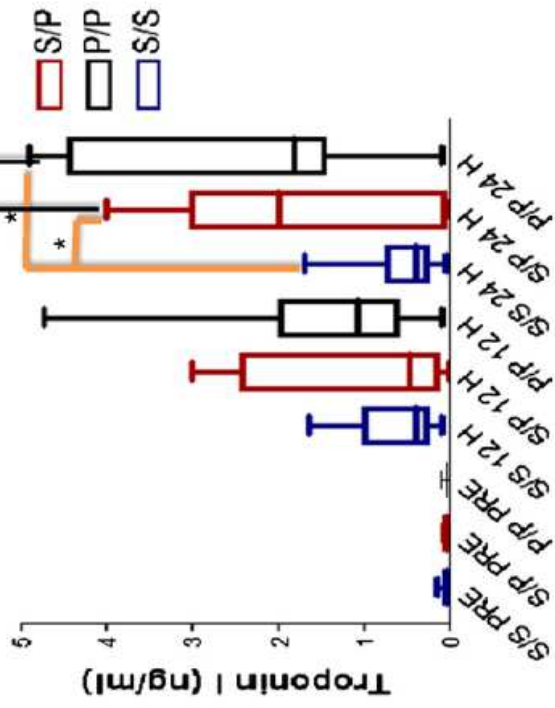
Fig. 1 Distribution of patients in our study.



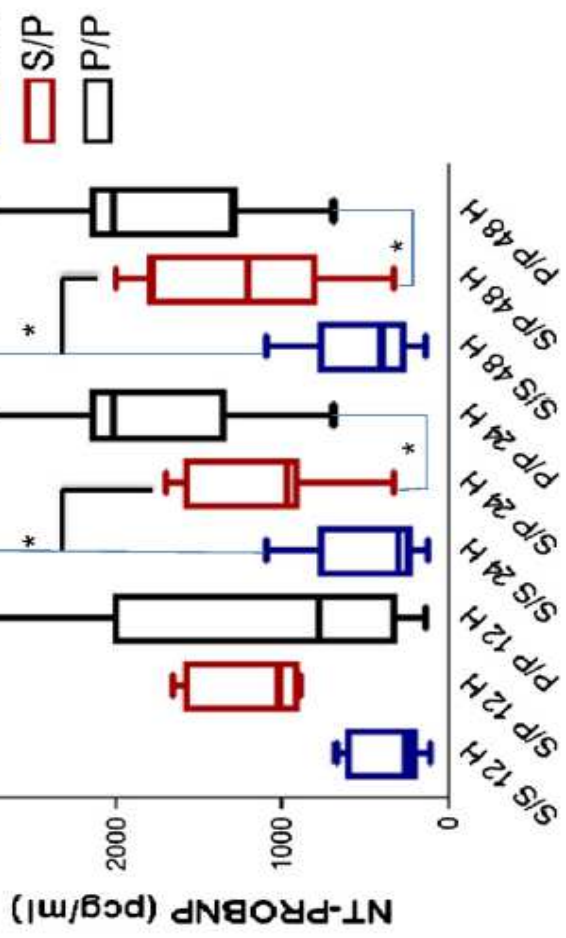
Prolonged sevoflurane administration in the off-pump coronary artery bypass graft surgery: Beneficial effects ☆, ☆ ☆

Jose L. Guerrero Orriach MD*, M. Galán Ortega MD, M. Ramirez Aliaga MD, P. Iglesias MD, M. Rubio Navarro MD, J. Cruz Mañas MD

Department of Anesthesia, Hospital Virgen de la Victoria, Málaga, Spain



Points during the first 48 hours after intervention



Points during the first 48 hours after intervention

Which Anesthetics in cardiac risk?

8.1. Choice of Anesthetic Technique and Agent

Recommendations for Use of Volatile Anesthetic Agents

CLASS IIa

1. It can be beneficial to use volatile anesthetic agents during noncardiac surgery for the maintenance of general anesthesia in hemodynamically stable patients at risk for myocardial ischemia.
(*Level of Evidence: B*)

Volatiles: what else!

Inhalational Sedation as a new therapeutic option

- Superior Control of level of sedation without tolerance development
- Organprotection

ORIGINAL ARTICLE**Survival after long-term isoflurane sedation as opposed to intravenous sedation in critically ill surgical patients**

Martin Bellgardt, Hagen Bomberg, Jenny Herzog-Niescery, Burkhard Dasch, Heike Vogelsang, Thomas P. Weber, Claudia Steinfort, Waldemar Uhl, Stefan Wagenpfeil, Thomas Volk and Andreas Meiser

Patients from the departments of General Surgery, Vascular Surgery and Orthopedic and Trauma Surgery.

In 86 patients from the primary cohort, isoflurane sedation was started within 72 h of commencing ventilation (group ISO).

A further 237 patients received only intravenous drugs for sedation (group Prop/Mida).

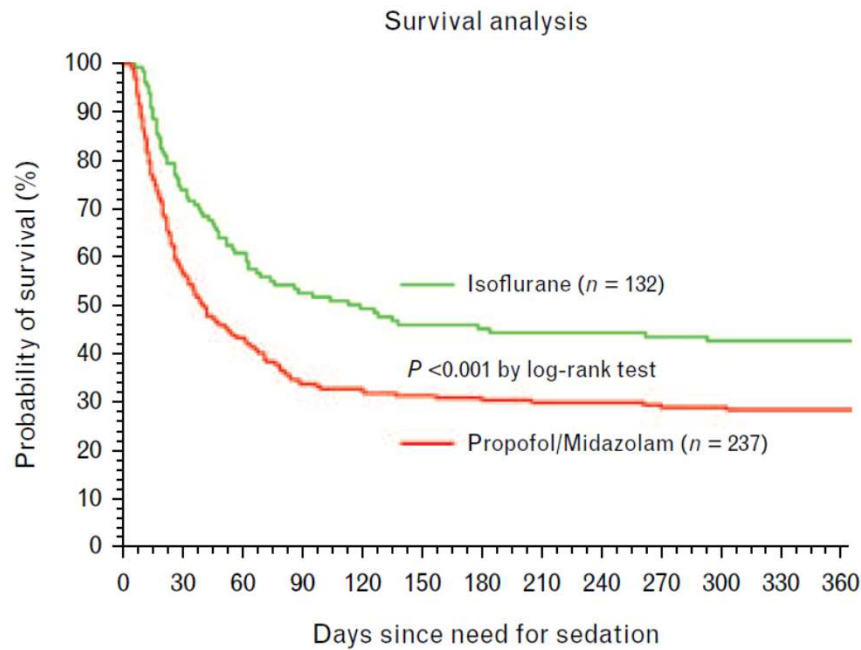
In 46 patients, isoflurane was given late in the course of ventilation after a period of sedation with propofol or midazolam (mixed group).

Table 1 General characteristics of the patients

	Isoflurane (<i>n</i> = 72)	Propofol/Midazolam (<i>n</i> = 128)	<i>P</i>
Preoperative			
Sex male	33 (46)	48 (38)	0.29
Age (years)	66.4 ± 13	67.7 ± 9	0.38
COPD	18 (25)	28 (22)	0.61
Liver metastases	4 (6)	11 (9)	0.58
Coronary heart disease	38 (53)	67 (52)	1
Peripheral arterial disease	7 (10)	24 (19)	0.11
Operative procedures			
Lung surgery	8 (11)	3 (2)	0.02
Colon surgery	26 (36)	51 (40)	0.65
Pancreatic surgery	18 (25)	29 (23)	0.73
Peripheral bypass	5 (7)	19 (15)	0.12
Liver, bile duct surgery	6 (8)	13 (10)	0.80
Stomach surgery	3 (4)	11 (9)	0.39
Hip/femur surgery	6 (8)	10 (8)	1
Skin, soft tissue surgery	3 (4)	4 (3)	0.70
Ruptured aortic aneurysm	4 (6)	5 (4)	0.73
Oesophageal surgery	4 (6)	5 (4)	0.73
Necrotizing fasciitis	2 (3)	5 (4)	1

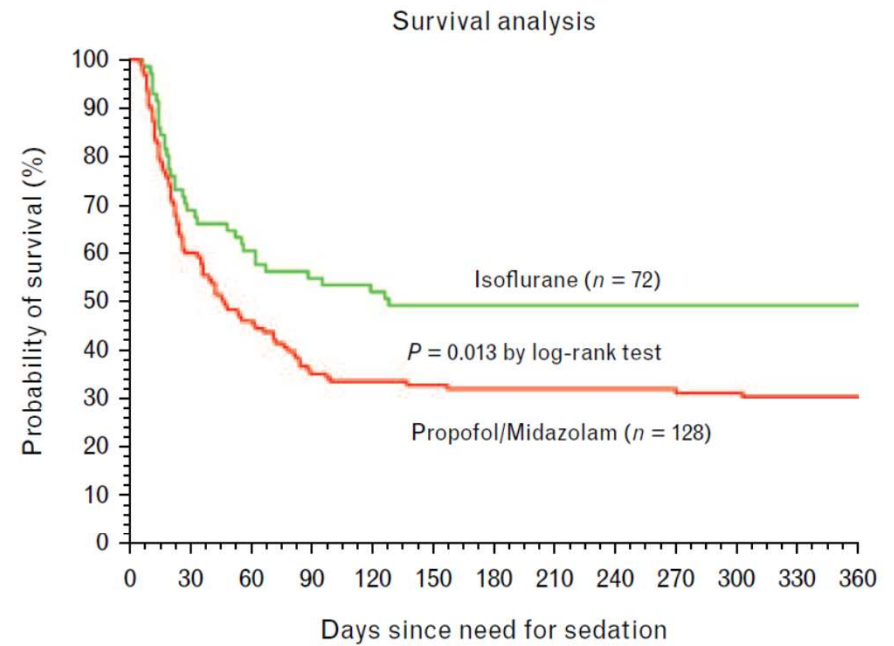
Data are presented as number (%), or for quantitative data, mean ± standard deviation. A *P* value <0.05 was considered as statistically significant. COPD, chronic obstructive pulmonary disease.

Fig. 2



Kaplan–Meier survival curves of all 369 patients who underwent long-term sedation and ventilation. Green curve, all patients who received isoflurane; red curve, patients who never received isoflurane. P values were calculated with the use of the log-rank test.

Fig. 3



Kaplan–Meier survival curves for the 200 patients in the finally selected cohort of patients who underwent long-term sedation and ventilation. P values were calculated with the use of the log-rank test.

Summary

- Superior Control with volatile Anesthetic Sedation
- Protection presumably in all organ systems
- Isoflurane or Sevoflurane with AnaConDa

- Standard of the future?

Je vous remercie pour votre attention

Vielen Dank für Ihre Aufmerksamkeit

Thank you for your attention

