



Intravenöz veya İnhalasyon Anestezikleri: Kanıt ve Klinisyenin Tercih Nedir?

Doç.Dr. Mustafa Kemal Arslantaş

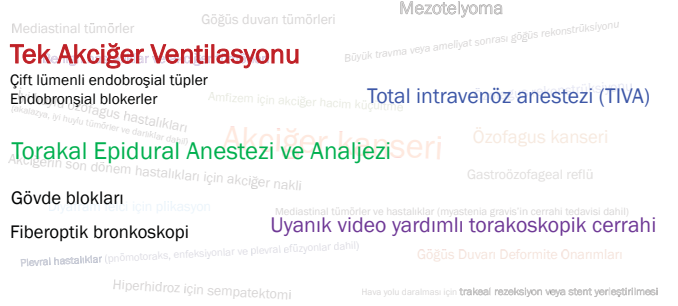


Bu konu ile ilgili herhangi bir kurum veya firma ile
çıkarcı ilişkim yoktur

Toraks Cerrahisi



Toraks Cerrahisi Anestezisi



Sunum Planı

- Toraks cerrahisinde anestezi uygulamaları
- Akciğer hasarı ve inflamasyon
- Kanıtlar ne diyor?
 - İnflamasyon
 - Oksijenizasyon
 - İntraoperatif hemodinami
 - Morbidite & Mortalite
 - Postoperatif pulmoner komplikasyonlar
 - Maligniteler ve kanser gelişimi
- Klinisyenlerin tercihi ne?



Akciğer Hasarı

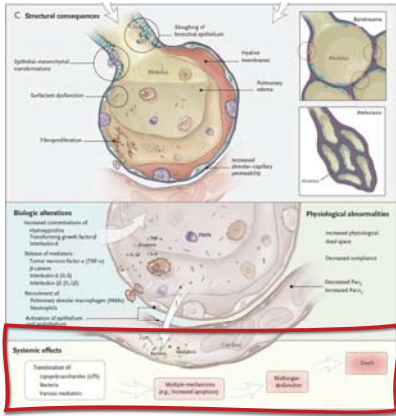
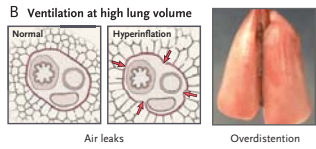
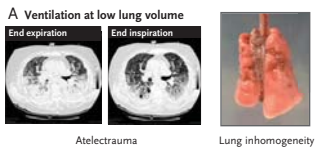
Ventile olmayan akciğer

- Reventilasyon ve reekspansiyon nedeniyle **alveollerde mekanik stres ve inflamasyon**
- Reventilasyonun ardından HPV'nin tersine çevrilmesi nedeniyle inflamasyona daha fazla katkıda bulunan **iskemi-reperfüzyon**
- Ameliyat sırasında sönmüş akciğerin manipülasyonundan kaynaklanan **inflamasyon**



Ventile olan akciğer

- Yüksek tidal volüm ve yüksek havayolu basıncı uygulaması nedeniyle **hiperinflamasyon**
- Ventile olmayan akciğerde gelişen HPV nedeniyle hiperperfüzyon
- Hiperoksinin yol açtığı **oksidatif stres**



Stability, A. S., & Ranieri, V. M. (2013). Ventilator-Induced Lung Injury. *New England Journal of Medicine*, 369(21), 2120-2130.

Anestezik ilaç seçimini etkileyen faktörler

Farmakolojik Nedenler

- Farmakokinetik
- Farmakodinamik

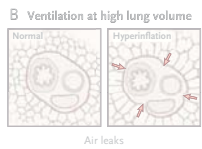
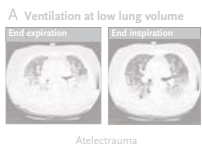


Farmakolojik olmayan nedenler

- Cerrahi tipi ve yeri
- Alışkanlık ve kişisel tercihler
- Lojistik koşullar
- Maliyet



Müst et al. Anaesthetic Drug Choices of Senior Anaesthetists. *Türk J Anaesthesiol Reanim* 2018; 46(5): 348-53

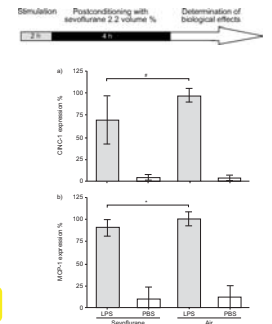


Stability, A. S., & Ranieri, V. M. (2013). Ventilator-Induced Lung Injury. *New England Journal of Medicine*, 369(21), 2120-2130.

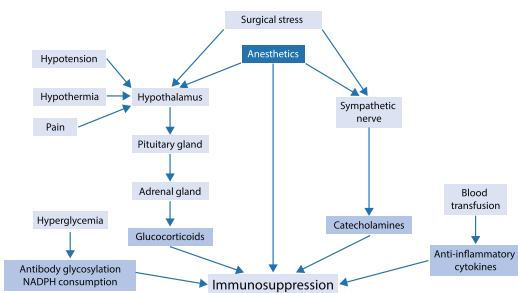
inflamasyon

Postconditioning with a volatile anaesthetic in alveolar epithelial cells *in vitro*

ABSTRACT: Acute lung injury is a common complication in critically ill patients. The present study examined possible immunomodulating effects of the volatile anaesthetic sevoflurane on lipopolysaccharide (LPS)-stimulated alveolar epithelial cells (AEC) *in vitro*. Sevoflurane was applied after the onset of injury, simulating a 'preconditioning' scenario. Rat AEC were stimulated with LPS for 2 h, followed by a 4 h co-exposure to a CO₂/air mixture with sevoflurane 2.2 volume %; control cells were exposed to the CO₂/air mixture only. Cytokine-induced neutrophil chemoattractant-1, monocyte chemoattractant protein-1, intercellular adhesion molecule-1, as well as the potential protective mediators inducible nitric oxide synthase (iNOS) and heat shock protein (HSP-27), were analysed. Additionally, functional assays (chemotaxis, adherence and cytotoxicity assays) were performed. A significant reduction of inflammatory mediators in LPS-stimulated, sevoflurane-exposed AEC was found, leading to reduced chemotaxis, neutrophil adherence and neutrophil-induced AEC killing. While iNOS was increased in the sevoflurane group, blocking experiments with iNOS2 inhibitor did not affect sevoflurane-induced decrease of inflammatory mediators and AEC killing. Interestingly, sevoflurane treatment also resulted in an enhanced expression of HSP-27. The data presented in the current study provide strong evidence that anaesthetic postconditioning with sevoflurane mediates cytoprotection in the respiratory compartment in an *in vitro* model of acute lung injury.



Cruz, F. F., Russo, P. F. M., & Pádua, P. Anti-inflammatory properties of anesthetic agents. *Crit Care* 21, 67 (2017).



inflamasyon

Effects of propofol and desflurane anaesthesia on the alveolar inflammatory response to one-lung ventilation

T. Schilling¹, A. Kuehn¹, M. Kretschmar¹, C. Halk¹, T. Witke¹, F. Böhling¹, G. Holmström¹ and T. Hahnshöjjer¹

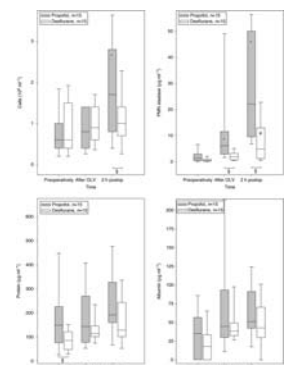
Background: One-lung ventilation (OLV) induces a pro-inflammatory response including cytokine release and leukocyte recruitment in the ventilated lung. Whether volatile or i.v. anaesthetic differentially modulates the alveolar inflammatory response to OLV is unclear.

Methods: Thirty patients, ASA II or III, undergoing open thoracic surgery were randomized to receive either propofol 4 mg kg⁻¹ h⁻¹ (n=15) or 1 MAC desflurane in air (n=15) during thoracic surgery. Analysis was provided by iv infusion of remifentanyl (0.25 µg kg⁻¹ min⁻¹) in both groups. The patients were mechanically ventilated according to a standard protocol during one-lung ventilation and OLV. Flow cytometric bronchoalveolar lavage (BAL) of the ventilated lung was performed before and after OLV and 2 h postoperatively. Alveolar cells, protein, tumor necrosis factor-α (TNF-α), interleukin (IL)-6, soluble intercellular adhesion molecule-1 (sICAM-1), IL-10, and polymorphonuclear (PMN) elastase were determined in the BAL fluid. Data were analysed by parametric or non-parametric tests, as indicated.

Results: In both groups, an increase in pro-inflammatory markers was found after OLV and 2 h postoperatively; however, the fraction of alveolar granulocytes (median 63.7 vs 31.1%, P<0.05) was significantly higher in the propofol group compared with the desflurane group. The time course of alveolar elastase, IL-6, and IL-10 differed between groups, and alveolar TNF-α (7.4 vs 21.6 ng ml⁻¹, P<0.05) and sICAM-1 (52.3 vs 26.3 ng ml⁻¹, P<0.05) were significantly higher in the propofol group.

Conclusions: These data indicate that pro-inflammatory reactions during OLV were influenced by the type of general anaesthesia. Different patterns of alveolar cytokines may be a result of increased granulocyte recruitment during propofol anaesthesia.

Br J Anaesth 2007; 99: 346-75



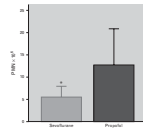
Inflamasyon

ORIGINAL ARTICLE

Sevoflurane, but not propofol, reduces the lung inflammatory response and improves oxygenation in an acute respiratory distress syndrome model
A randomised laboratory study

Conclusion

In an experimental model of ARDS, sevoflurane exerts a greater immunomodulatory effect than propofol, alters the permeability of the alveolar capillary membrane to a lesser extent and results in a lower EVLWI, which may explain the better maintenance of oxygenation observed. Further experimental studies are required to confirm these results.

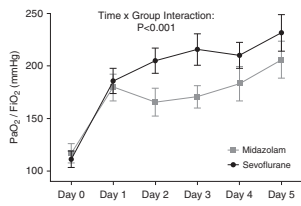
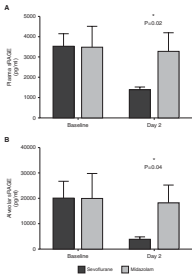


Parameter	Anaesthetic	T ₁	T ₂	T ₃	T ₄
PaO ₂ /FIO ₂ (kPa)	Sevoflurane	16.5 ± 4.8	23.5 ± 2.7	22.9 ± 5.3	22.3 ± 5.7
	Propofol	17.2 ± 5.5	20.7 ± 2.4	18.5 ± 2.8	17.5 ± 2.5*
EVLWI (ml kg ⁻¹)	Sevoflurane	14 ± 2	13 ± 1	14 ± 1	16 ± 3
	Propofol	16 ± 2	17 ± 3*	19 ± 5*	22 ± 7*

Inflamasyon

ORIGINAL ARTICLE

Sevoflurane for Sedation in Acute Respiratory Distress Syndrome
A Randomized Controlled Pilot Study



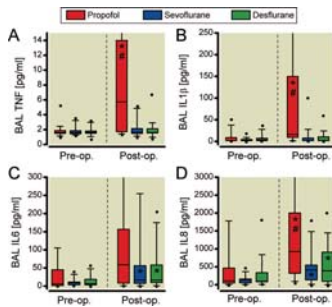
In patients with ARDS, use of inhaled sevoflurane improved oxygenation and decreased levels of a marker of epithelial injury and of some inflammatory markers, compared with midazolam.

Jabaudon M et al. Am J Respir Crit Care Med Vol 185, Iss 6, pp 792-800, Mar 15, 2017

Inflamasyon

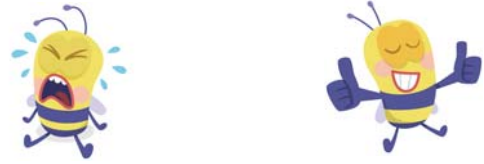
Effects of Volatile and Intravenous Anesthesia on the Alveolar and Systemic Inflammatory Response in Thoracic Surgical Patients

The alveolar cytokine release in the ventilated lung was decreased in patients undergoing elective open thoracic surgery when sevoflurane and desflurane were administered compared with the administration of propofol as the anesthetic



Schilling et al. Anesthesiology 2012; 115:651-74

Inflamasyon



intravenöz

inhalasyon

Oksijenizasyon

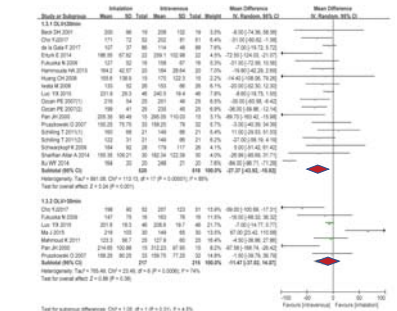
Oksijenizasyon İndeksi

Inhalasyon anesteziikleri oksijenizasyon indeksini anlamlı şekilde azaltır

FiO₂ x Ort. Havayolu Basıncı
PaO₂

- OI < 25 İyi prognosis
- OI 25-40 >40% Mortalite
- OI > 40 ECMO aday

Pang Q, Y. et al. Minerva Anestesiol 84(11):2287-2297, 2018.



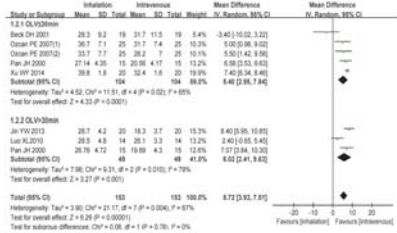
Test for heterogeneity: Chi² = 1.08, df = 1, P = 0.301, I² = 4.8%

Inflamasyon

Oksijenizasyon

Pulmoner şant fraksiyonu

Inhalasyon anesteziikleri Pulmoner şant fraksiyonunu (Qs/Qt) anlamlı şekilde arttırır



Test for heterogeneity: Chi² = 0.08, df = 1, P = 0.78, I² = 0%

Pang Q, Y. et al. Minerva Anestesiol 84(11):2287-2297, 2018.

Oksijenizasyon Pulmoner şant fraksiyonu

Effect of One-Lung Ventilation on Blood Sevoflurane and Desflurane Concentrations

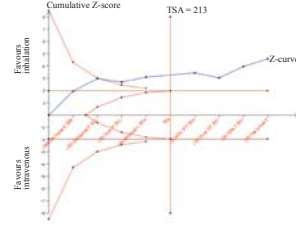
Ebru Biricik, MD¹, Feride Karacaer, MD², Yasemin Güneş, MD³,
Nebile Dağlıoğlu, MD⁴, Pınar Efeoğlu, MD⁵, Murat Iğnel, MD⁶,
Alper Avcı, MD⁷, Dilek Özcengiz, MD⁸

Tek akciğer ventilasyonu prosedürü sevofluran ve desfluranın hem arteriyel hem de venöz kan konsantrasyonlarında bir azalmaya neden olur.

Bu azalmanın ventilasyon-perfüzyon uyumsuzluğundan kaynaklandığına inanılmaktadır.

J Cardiothorac Vasc Anesth. 2019 Feb;33(2):432-440

Morbidite & Mortalite Postoperatif pulmoner komplikasyonlar



Pulmoner komplikasyon insidansı inhalasyon grubunda daha az

Pang Q, Y, et al. Minerva Anestesiol 84(11):1287-1297, 2018.

Oksijenizasyon



Intravenöz Inhalasyon

Morbidite & Mortalite Malignite gelişimi ve prognoz

BJA

TRANSLATIONAL STUDIES

Differential effects of sevoflurane on the metastatic potential and chemosensitivity of non-small-cell lung adenocarcinoma and renal cell carcinoma in vitro

Sevoflurane promotes the metastatic potential of renal carcinoma, but not of non-small cell lung cancer. This may be associated with its differential effect on cellular signalling including TGF- β . Our findings indicate that sevoflurane may have different effects on the metastatic potential and chemosensitivity of different tumour types.

S. Cechinewicz, et al. Br J Anaesth 120(2):268-275, 2018.

ANESTHESIOLOGY

Total Intravenous Anesthesia versus Inhalation Anesthesia for Breast Cancer Surgery

A Retrospective Cohort Study

The authors found no association between type of anesthesia used and the long-term prognosis of breast cancer. The results of this retrospective cohort study do not suggest specific selection of IV or inhalation anesthesia for breast cancer surgery.

Sehara Y et al. Anesthesiology 130(3):40, 2019.

Hemodinami

Study or Subgroup	Inhalation		Intravenous		Weight	Mean Difference, IV, Random, 95% CI	Mean Difference, IV, Random, 95% CI	
	Mean	SD	Mean	SD				
Beck CH 2001 ¹⁴	2.8	0.8	1.9	2.7	0.6	1.9	4.1%	0.10 [-0.35, 0.55]
Cho Y 2017 ¹⁷	2.9	0.7	5.2	2.8	0.9	51	8.5%	0.10 [-0.21, 0.41]
de W Saif F 2017 ¹⁸	3.9	4.1	8.6	2.8	1.1	68	1.0%	0.10 [-0.95, 1.05]
Xu WY 2014 ¹³	3.6	0.1	2.0	3.4	0.2	20	86.3%	0.20 [-0.15, 0.30]
Total (95% CI)	177		178		100.0%	0.19		[0.10, 0.28]

Heterogeneity: Tau² = 0.00; Chi² = 0.55, df = 3 (P = 0.91), I² = 0%
Test for overall effect: Z = 4.01 (P < 0.0001)

Kardiyak indeks tek akciğer ventilasyonu sırasında inhalasyon anestezisinde daha yüksek

Kardiyak advers olaylar (kardiyak disfonksiyon, aritmi, miyokardiyal iskemi, v.b) açısından gruplar arası anlamlı bir fark yok

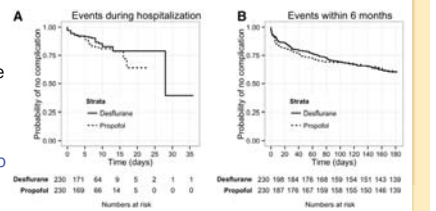
Pang Q, Y, et al. Minerva Anestesiol 84(11):1287-1297, 2018.

Morbidite & Mortalite

Which Anesthesia Regimen Is Best to Reduce Morbidity and Mortality in Lung Surgery?

A Multicenter Randomized Controlled Trial

Four hundred and sixty patients (five centers) undergoing one-lung ventilation during thoracic surgery were randomized to receive either propofol or desflurane. There was no difference in major complications between the two groups.



Beck-Schimmer et al. Anesthesiology 2016; 125:213-221

Morbidite & Mortalite



Trusted evidence.
Informed decisions.
Better health.

Cochrane Database of Systematic Reviews

Intravenous versus inhalation anaesthesia for one-lung ventilation

850 hastayla yapılan 20 çalışmanın Cochrane incelemesi, inhalasyon anestezi tekniğiyle karşılaştırıldığında tek akciğer ventilasyonu sırasında TIVA tekniğinin kullanılması olguların sonuçlarını etkilememiştir.

Madsen NSP, et al. Intravenous versus inhalation anaesthesia for one-lung ventilation. Cochrane Database of Systematic Reviews 2013, Issue 7. Art.No. CD009313.

Klinisyenlerin tercihi ÇİN

A Survey of Thoracic Anesthesia Practice in Chongqing City, China

The majority of respondents preferred intravenous and inhalation combined anesthesia (45 [77.6%]).

Total intravenous anesthesia was the first choice in 11 hospitals (19%), and only 2 hospitals (3.4%) routinely used inhalation anesthesia.

There was a significant difference between intravenous combined with inhalation anesthesia and the other anesthesia methods ($p < 0.001$).

© Veimage.com

H. Liu, B. Yang and E. Chen: A Survey of Thoracic Anesthesia Practice in Chongqing City, China. J Cardiothorac Vasc Anesth 33(3):884-885, 2019.

Morbidite & Mortalite



intravenöz

inhalasyon

Klinisyenlerin tercihi İTALYA

Survey of Thoracic Anesthetic Practice in Italy

Nineteen centers (40%) only maintained anesthesia with an inhalation agent, while 16 centers (34%) reported the sole use of intravenous anesthesia (total intravenous anesthetic technique and target-controlled infusion technique).

Twelve centers (26%) used either a volatile anesthetic agent or intravenous anesthesia.

G. Della Rocca et al.: Survey of thoracic anesthetic practice in Italy. Journal of cardiothoracic and vascular anesthesia 27(6):1321-1329, 2013.

Klinisyenin Tercihi?



Klinisyenlerin tercihi HİNDİSTAN

A Survey of Practice of Thoracic Anesthesia in India

Significantly higher number of anesthesiologists preferred inhalational anesthetics over total intravenous anesthesia during OLV (131/162 i.e. 80.8% versus 7/162 i.e. 4.3%, $p < 0.001$).

Among the inhalational anesthetic agents, sevoflurane (51%) and isoflurane (43.3%) were the most commonly preferred agents.

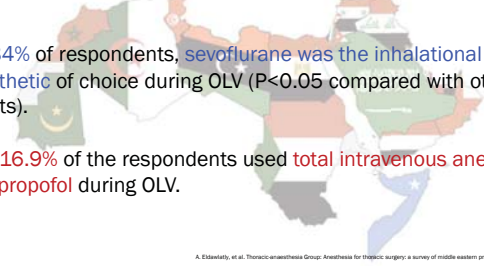
S. V. Parth, et al.: A Survey of Practice of Thoracic Anesthesia in India. Journal of Cardiothoracic and Vascular Anesthesia, 2020.

Klinisyenlerin tercihi ORTA DOĞU

Anesthesia for thoracic surgery:
A survey of middle eastern practice

For 84% of respondents, sevoflurane was the inhalational anesthetic of choice during OLV (P<0.05 compared with other agents).

Only 16.9% of the respondents used total intravenous anesthesia with propofol during OLV.



A. Elshewity, et al. Thoracic-anesthesia Group. Anesthesia for thoracic surgery: a survey of middle eastern practice. Saudi J Anaesth 6(3):152-6, 2012.

Sonuç olarak...

- Toraks cerrahisi sırasında inhalasyon anesteziikleri intravenöz anesteziiklere göre avantajlı görünse de morbidite ve mortalite açısından olguların sonuçları üzerine etkileri gösterilememiştir
- Klinisyenler en çok inhalasyon anesteziiklerini tercih etmektedir

Klinisyenlerin tercihi



Intravenöz



Inhalasyon

*Her insan seçiminde özgürdür
fakat her seçiminde bir bedeli vardır*

Teşekkür ederim...

Sonuç olarak...

- Tek akciğer ventilasyonu nedeniyle oluşan fizyolojik değişiklikler ve inflamatuvar yanıt postoperatif akciğer hasarı için risk oluşturur
- **Inhalasyon anesteziikleri,**
 - Antiinflamatuvar etkiye sahiptir
 - İntraoperatif kardiyak fonksiyonu koruyabilir ve postoperatif pulmoner komplikasyonları azaltabilir
 - İntraoperatif pulmoner fonksiyonu azaltmasına rağmen, toraks cerrahisinde intravenöz anesteziiden üstün olabilir