ACADEMIA
ANESTESIA & ANALGESIA
VETERINARIA

ANESTESIA EN CX ONCOLOGICA

- CURSO -
ANESTESIA PACIENTES
ESPECIALES

Paulo Mallea V.
Medico Veterinario

OBJETIVOS ANESTÉSICOS

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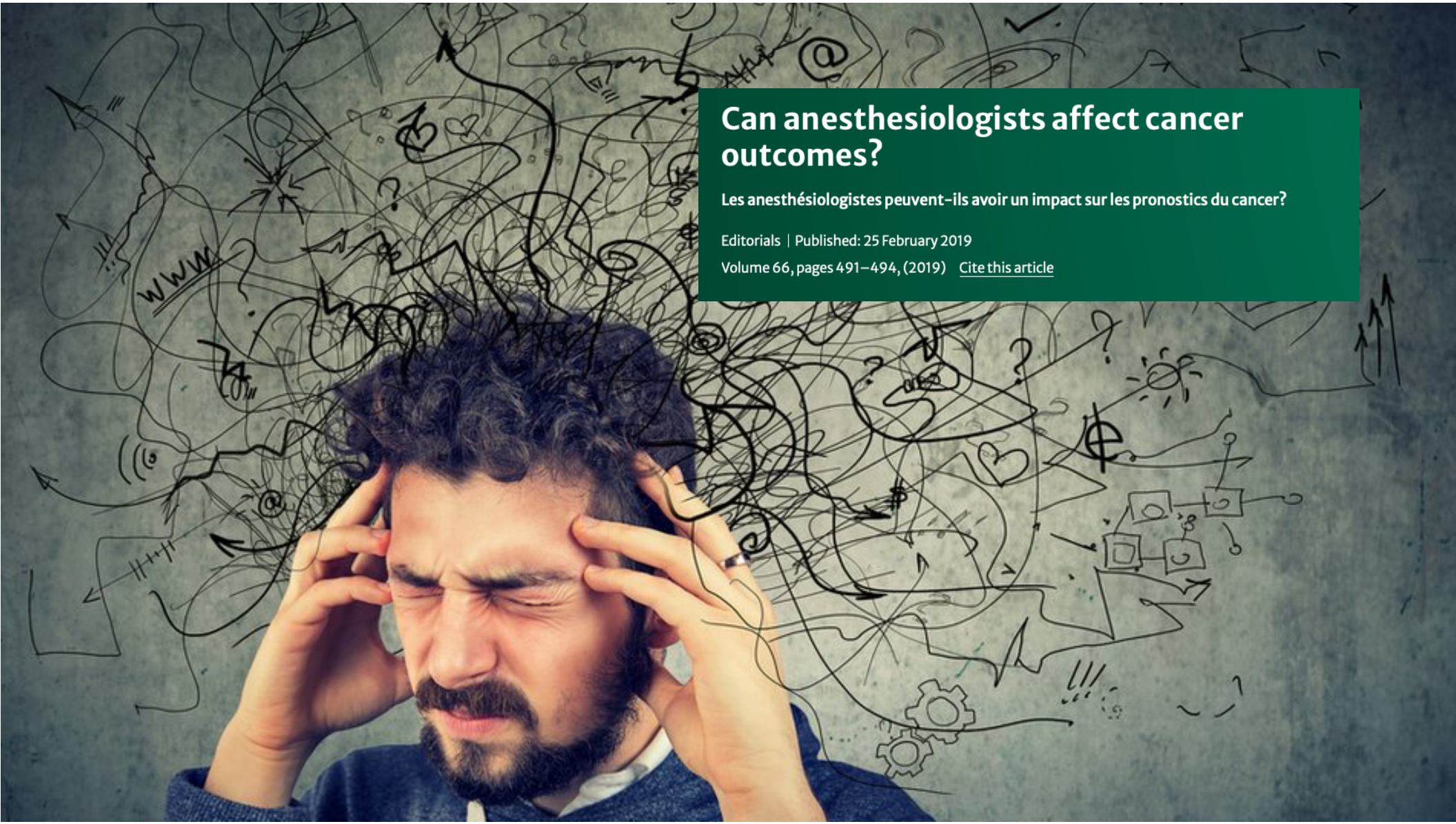


Can anesthesiologists affect cancer outcomes?

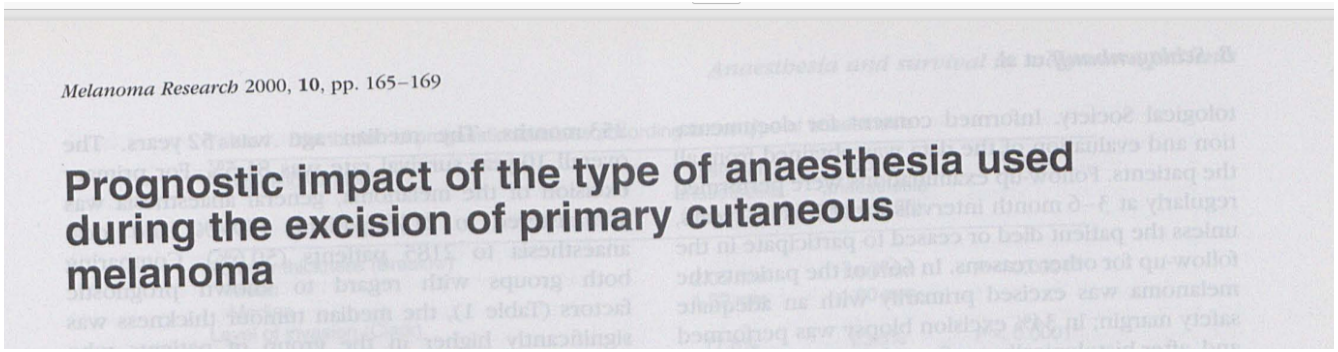
Les anesthésiologistes peuvent-ils avoir un impact sur les pronostics du cancer?

Editorials | Published: 25 February 2019
Volume 66, pages 491–494, (2019) Cite this article

CONTEXTO

- Controversia hace 2 décadas respecto al impacto de la Anestesia en la Recurrencia Cáncer.

- Stress Quirúrgico/Anestesia afectan inmunidad paciente



Melanoma Research 2000, **10**, pp. 165–169

Prognostic impact of the type of anaesthesia used during the excision of primary cutaneous melanoma

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Se sugiere que la **ANESTESIA LOCAL** posee beneficio (menor recurrencia) respecto la **ANESTESIA GENERAL** (Inhalada)

REFLEJO de los efectos de la **ANESTESIA GENERAL** en la respuesta inmune del paciente

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REVIEWS

Perioperative events influence cancer recurrence risk after surgery

Jonathan G. Hiller[1,2,3,4], Nicholas J. Perry[5]*, George Poulogiannis[5,6], Bernhard Riedel[1–3] and Erica K. Sloan[1,3,7]*

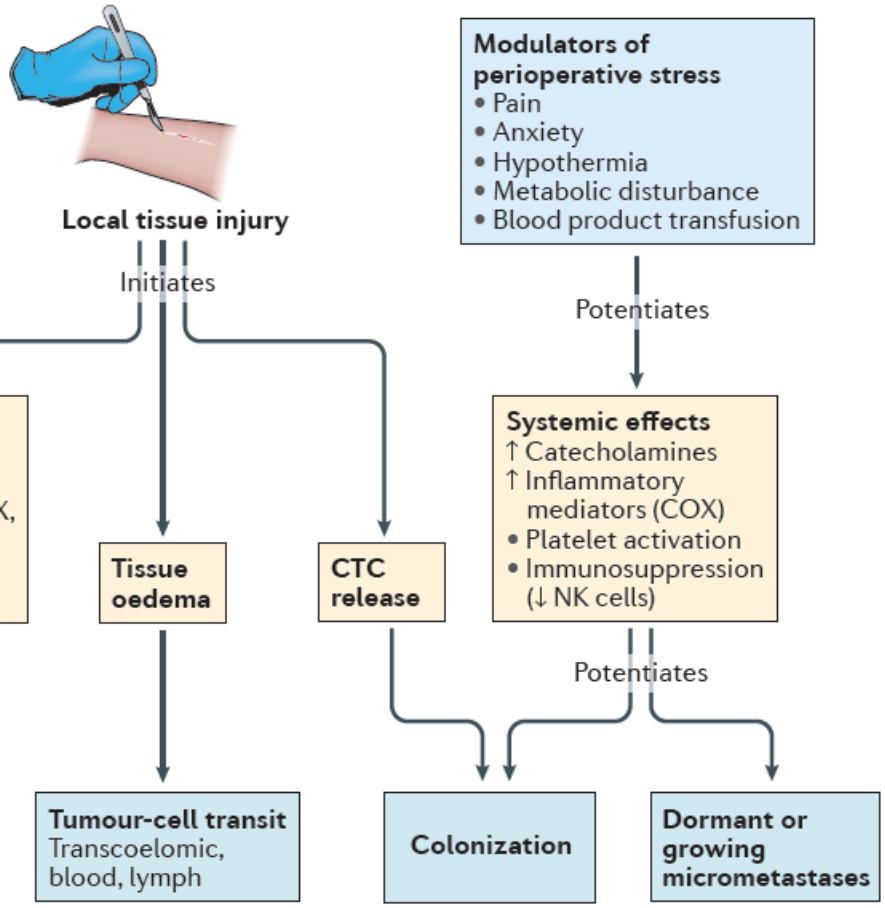
NATURE REVIEWS | CLINICAL ONCOLOGY VOLUME 15 | APRIL 2018 | 205

STEPHEN PAGET, M.A., F.R.C.S.
(Founder of the Research Defence Society).

Analogía "**Semilla y Suelo**"

Perioperative events influence cancer recurrence risk after surgery

Jonathan G. Hiller[1,2,3,4], Nicholas J. Perry[5]*, George Poulogiannis[5,6], Bernhard Riedel[1–3] and Erica K. Sloan[1,3,7]*



OPIODES EN EL PROTOCOLO

State-of-the-Art-Review

Journal of Veterinary Emergency and Critical Care **20**(4) 2010, pp 376–385
doi: 10.1111/j.1476-4431.2010.00561.x

Immunomodulatory effects of opioids

Adesola Odunayo, DVM, MS; John R. Dodam, DVM, MS, PhD, DACVA;
Marie E. Kerl, DVM, DACVIM, DACVECC and Amy E. DeClue, DVM, MS, DACVIM

Receptores Opioides entre las **mas conservadas** en el reino animal y no solo en vertebrados

Fundamentales en **Respuesta Inmune** post injuria

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OPIODES EN EL PROTOCOLO

Table 3: Immunomodulating properties of selected opioids

Opioid	Primary receptor activity	HPA axis	Corticosteroid secretion	NK cell activity	Additional information
Morphine	OP_3 agonist	Stimulates[31,34]	Increases[31,34]	Decrease[28,31,35]	Generally upregulates production of pro-inflammatory mediators and suppresses the production of anti-inflammatory mediators. Suppresses immune cell proliferation[31,33]
Fentanyl	OP_3 agonist	Stimulates[34]	Increases[34]	Decreases, has also been reported to increase. May be dose dependent[29,36,37]	Does not stimulate the release of nitric oxide.[38] Suppresses T cell proliferation, IFN-γ and IL-2 production[29,39]
Hydromorphone	OP_3 agonist	No known reported effect	No known reported effect	No effect[33]	Has no effect on immune cell proliferation or IL-2 production
Buprenorphine	OP_3 partial agonist	No effect[31,34]	No effect, decreases[29,31]	No effect[29,31]	No effects on immune cell proliferation or cytokine activity[29]
Naloxone	OP_3 antagonist	Variable and dose dependent[40]	Variable[40]	Increase, decrease, or no effect[41,42]	Not well studied. Decreases IL-4 Increases the production of IL-2 and IFN-γ. Increases T lymphocyte proliferation[42]
Naltrexone	OP_3 antagonist	Variable and dose[40] dependent	Variable[40]	Increase, decrease, or no effect[41]	Not well studied. Effects likely similar to naloxone

HPA, hypothalamo-pituitary axis; NK, natural killer; IL, interleukin; IFN, interferon.

QUE SABEMOS

- Parecen haber algunos **Efectos Inmunológicos**
- **Control del Dolor bien demostrado**

OPIOIDES CONTROL DEL DOLOR

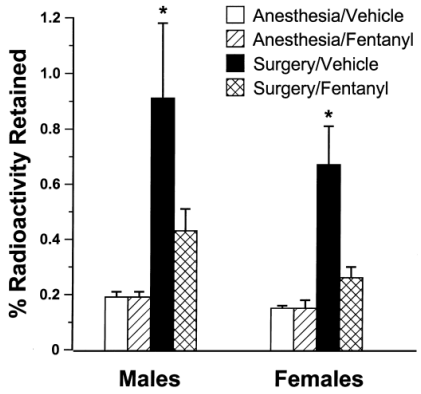
Evidence that postoperative pain is a mediator of the tumor-promoting effects of surgery in rats ☆

Gayle Giboney Page[a,*], Wendy P. Blakely[a], Shamgar Ben-Eliyahu[b]

[a]*School of Nursing, Johns Hopkins University, 525 North Wolfe Street, Baltimore, MD 21205, USA*
[b]*Department of Psychology, Tel Aviv University, Tel Aviv 69978, Israel*

Received 11 April 2000; received in revised form 31 July 2000; accepted 9 August 2000

Pain 90 (2001) 191–199



Review Article

Perioperative Immunosuppression and Risk of Cancer Progression: The Impact of Opioids on Pain Management

Renata Zajączkowska,[1] Wojciech Leppert,[2] Joanna Mika,[3] Magdalena Kocot-Kępska,[4] Jarosław Woroń,[1] Anna Wrzosek,[1] and Jerzy Wordliczek[1]

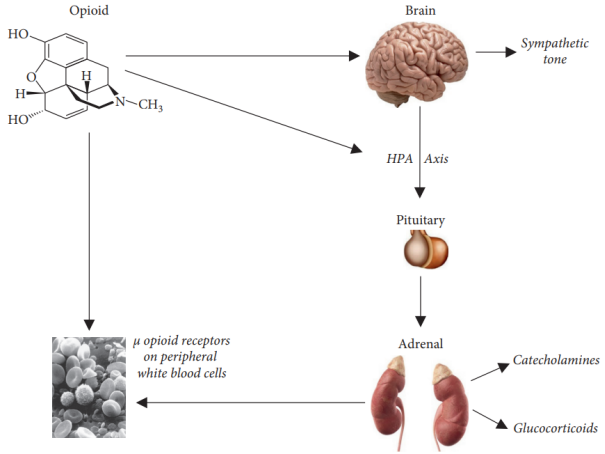


FIGURE 1: Potential mechanisms of immunosuppressive effects of opioids [13].

Control Intraoperatorio **define post operatorio y riesgo de dolor crónico post operatorio**

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SE DEBE TRABAJAR SIN OPIOIDES?
Opioid Free Anestesia

Es posible hacer OFA ?

Es necesario hacer OFA?

Hay beneficio demostrado al hacer OFA ?

SOFA
The Society for Opioid Free Anesthesia

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ES POSIBLE HACER OFA ?

Original Article

Comparison of opioid-based and opioid-free TIVA for laparoscopic urological procedures in obese patients

Shaman Bhardwaj, Kamakshi Garg[1], Sumeet Devgan[2]

Departments of Anaesthesiology and Critical Care and [2]Urology and Kidney Transplant, Grecian Super Specialty Hospital, Mohali, [1]Department of Anaesthesiology, Dayanand Medical College and Hospital, Ludhiana, Punjab, India

Submitted: 11/12/2016 Accepted: 25/04/2017 Published: 10/05/2017

Opioid-free anaesthesia in three dogs

Donna M. White*, Alastair R. Mair and Fernando Martinez-Taboada

Department of Anaesthesia and Analgesia, Veterinary Teaching Hospital, University of Sydney, Evelyn Williams Building B10, 65 Parramatta Road, Camperdown, NSW. 2050. Australia

A randomized, prospective, masked clinical trial comparing an opioid-free vs. opioid-sparing anesthetic technique in adult cats undergoing ovariohysterectomy

Maxime Rufiange[1], Helene L. M. Ruel[1], Beatriz P. Monteiro[1], Ryota Watanabe[1], Inga-Catalina Cruz Benedetti[1], Javier Benito[1] and Paulo V. M. Steagall[1,2]*

Vet Record CaseReports

CASE REPORT

Companion or pet animals

An opioid-free anaesthesia (OFA) technique for dorsal laminectomy in a dog subsequent to severe bradycardia and hypothermia after previous subcutaneous methadone administration

Natalia Libera[1,2] | William McFadzean[2]

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ES NECESARIO HACER OFA ?
HAY BENEFICIO DEMOSTRADO?

- Existe **racionalidad** para intentar evitar los opioides en especial cuando se utiliza anestesia regional
- Se **desconoce efectos a largo plazo** (ej: dolor persistente crónico, outcomes de sobrevivencia)
- **Poca info del postCX** – ALGUNOS ESTUDIOS OPIOIDE POST
- Algunos **sin diferencia opioide postcx**
- Necesidad de **equipos de infusión**
- Info de **seguridad de variadas infusiones conjuntas**

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ANESTHESIOLOGY

Perioperative Opioid Administration

A Critical Review of Opioid-free *versus* Opioid-sparing Approaches

Anesthesiology 2021; 134:645–59

Do Opioid-free Strategies Have Benefits beyond and above Opioid-sparing Strategies?

To date, there is no evidence. Multimodal analgesia can lead to significant opioid sparing.

BJA

British Journal of Anaesthesia, 123 (2): 135–150 (2019)

doi: 10.1016/j.bja.2019.04.062
Advance Access Publication Date: 27 June 2019
Review Article

CLINICAL PRACTICE

Influence of perioperative anaesthetic and analgesic interventions on oncological outcomes: a narrative review

T. Wall[1,2,*], A. Sherwin[1,2], D. Ma[2,3] and D. J. Buggy[1,2,4]

[1]Department of Anaesthesiology and Perioperative Medicine, Mater University Hospital, School of Medicine, University College Dublin, Dublin, Ireland, [2]EU-COST Action 15204, Euro-Periscope, Avenue Louise 149, 1050 Brussels, Belgium, [3]Department of Anaesthesia, Imperial College School of Medicine, London, UK and [4]Outcomes Research, Cleveland Clinic, Cleveland, OH, USA

*Corresponding author. E-mail: tom.p.wall@gmail.com

In our opinion, the balance of evidence suggests a signal that opioids may facilitate metastasis in certain conditions, but, as with every anaesthetic intervention discussed in this review, the hypothesis must be tested in a prospective RCT before any major change in practice is justified.

frontiers in Oncology

MINI REVIEW
published: 23 December 2021
doi: 10.3389/fonc.2021.803266

Anesthesia and Cancer, Friend or Foe? A Narrative Review

Julio Montejano * *and Vesna Jevtovic-Todorovic*

. Frustratingly, opioid sparing techniques do not seem to affect short term survival as noted in one study that randomized patients to receive remifentanil infusions (47). Thus, the question becomes whether there is a balance of pharmacologic effects between anesthetic and analgesic agents that could be found to improve patient disease free survival.

The Benefits of Opioid Free Anesthesia and the Precautions Necessary When Employing It

Christian Bohringer, MD, **Carlos Astorga, MD**, **Hong Liu, MD, FASE**
Department of Anesthesiology and Pain Medicine, University of California Davis Health, Sacramento, California, USA

DOI: 10.23937/2377-4630/1410104 ISSN:

Figure 1: Specific populations that benefit from the use

- **Obesidad, Apnea del sueño, COPD**
- **Cx con alta incidencia de Falla Respiratoria postcx**
- **Cx intestinal (íleo ⇢ Fuga por anastomosis)**
- **Opioides liberalmente ⇢ Distención Abdominal ⇢ Fx Resp/Dehiscencia sutura**
- **Cx oftálmica, GI alta, Cabeza/cuello, Neurocirugía ⇢ PONV**
- **Retención Urinaria**

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Opioid-free Anesthesia: Time to Regain Our Balance

Evan D. Kharasch, M.D., Ph.D., J. David Clark, M.D., Ph.D.

ANESTHESIOLOGY, V 134 • NO 4 APRIL 2021

ANESTHESIOLOGY

Balanced Opioid-free Anesthesia with Dexmedetomidine *versus* Balanced Anesthesia with Remifentanil for Major or Intermediate Noncardiac Surgery

Table 1. Description of the Five Cases of Profound Bradycardia in Dexmedetomidine Group

Baseline Characteristics	Dex Dosage	Description	Comments
Female, 44 kg, scheduled for pancreatic surgery; no noticeable preoperative condition	1 μg · kg^{-1} · h^{-1}	40 min after induction and before surgical incision: Profound bradycardia (heart rate, 15 beats/min) and asystolia Resuscitation including atropine and epinephrine to restore a rhythm; dexmedetomidine administration was stopped Because of the administration of IV lidocaine, IV intralipids were administered Patient transferred in intensive care unit without surgery No complication, no sequalae, and surgery rescheduled 1 week later	The weight was overestimated by the investigator; low weight of the patient was not considered
Male, 85 kg, scheduled for robot-assisted laparoscopic prostatectomy; no noticeable preoperative condition	0.6 μg · kg^{-1} · h^{-1}	During surgical carbon dioxide insufflation: bradycardia (heart rate, 38 beats/min) followed by asystolia for 15 s Dexmedetomidine administration and insufflation were temporarily stopped; atropine was administered Normal hemodynamic restored and surgery completed No complication, no sequalae	Diagnosis: bradycardia secondary to vagal stimulation during carbon dioxide insufflation
Male, 76 kg, scheduled for robot-assisted laparoscopic prostatectomy; no noticeable preoperative condition	0.53 μg · kg^{-1} · h^{-1}	During surgical carbon dioxide insufflation: bradycardia (heart rate, 42 beats/min) followed by asystolia for 15 s Dexmedetomidine administration and insufflation were stopped; ephedrine and resuscitation maneuvers were administered Normal hemodynamic restored and surgery completed No complication, no sequalae	Diagnosis: bradycardia secondary to vagal stimulation during carbon dioxide insufflation
Female, 124 kg, scheduled for laparoscopic gastrectomy; no noticeable preoperative condition	0.9 μg · kg^{-1} · h^{-1}	15 min after carbon dioxide insufflation: bradycardia (heart rate, 10 beats/min) Dexmedetomidine administration was stopped; atropine was administered Normal hemodynamic restored and surgery completed No complication, no sequalae	Diagnosis not clear
Male, 84 kg, scheduled for laparoscopic prostatectomy. No noticeable preoperative condition.	0.48 μg · kg^{-1} · h^{-1}	During surgical carbon dioxide insufflation: bradycardia (heart rate, 30 beats/min): Dexmedetomidine dosage was lowered and insufflation is stopped; atropine and resuscitation maneuvers were administered Normal hemodynamic restored and surgery completed	Diagnosis: bradycardia secondary to vagal stimulation during carbon dioxide insufflation

Balanced Opioid-free Anesthesia with Dexmedetomidine *versus* Balanced Anesthesia with Remifentanil for Major or Intermediate Noncardiac Surgery

Prospective, randomized, multicenter, parallel-group, single-blind and controlled study in adults in 10 centers in France

- Randomization (1:1) to dexmedetomidine (opioid-free) or remifentanil groups
- Standardized anesthetic plan for both groups

Primary outcome: Composite postop opioid-related adverse events within 48 h after extubation

- Hypoxemia
- Ileus
- Cognitive dysfunction

Stopped study prematurely because of 5 cases of severe bradycardia in dexmedetomidine group

	Dexmedetomidine	Remifentanil	Relative Risk
Primary composite outcome	122 of 156 (78%)	105 of 156 (67%)	1.2; $P = 0.03$

- Opioid-free anesthesia with dexmedetomidine, compared with remifentanil, did not result in fewer postoperative opioid-related adverse events
- Dexmedetomidine resulted in greater incidence of serious adverse events, especially hypoxemia and bradycardia

Beloeil H, *et al.* ANEST

ANESTH

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Parece haber **variaciones en efectividad** con los manejos multimodales, por tanto se requiere **mayor investigación** para establecer recomendaciones **procedimiento-especificas** y **refinamiento** de las técnicas opioid free/ opioid sparing

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HIPERALGESIA POR OPIOIDES

Focused Review

A Comprehensive Review of Opioid-Induced Hyperalgesia

Marion Lee, MD[1], Sanford Silverman, MD[2], Hans Hansen, MD[3], Vikram Patel,MD[4], and Laxmaiah Manchikanti, MD[5]

Journal Pre-proof

Determination of acute tolerance and hyperalgesia to remifentanil constant rate infusion in dogs undergoing sevoflurane anaesthesia

Patricia Ruíz-López, Rocío Navarrete-Calvo, Juan Morgaz, Juan Manuel Domínguez, Setefilla Quirós-Carmona, Pilar Muñoz-Rascón, Rafael Jesús Gómez-Villamandos, José Andrés Fernández-Sarmiento, María del Mar Granados

Mechanisms, diagnosis, prevention and management of perioperative opioid-induced hyperalgesia

Pain Manag. (2021) 11(4), 405–417

Sylvia H Wilson*,[1], Kevin M Hellman[2], Dominika James[3], Adam C Adler[4,5] & Arvinc

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HIPERALGESIA POR OPIOIDES

- Analgesics
  - Administration of the lowest possible opioid infusion doses (remifentanil <0.2 μg/kg/min), which are tapered before infusion cessation, in operations requiring short-term exposure to high potency opioids;
  - Administer a combination of ketamine and α-2 agonists as administration of more than one non-opioid adjunct likely has a synergistic effect and may have a greater ability to mollify or prevent OIH;
  - Utilize perioperative regional anesthesia to decrease acute inflammation, cytokine production, and central markers of pain sensitization.

Preoperative	Intraoperative	Postoperative

Day of surgery
• Consider regional analgesia
• Non-opioid analgesics
  • NSAIDs
  • Acetaminophen
	Opioid minimization
	• NMDA antagonist
	• α-2 agonist
	• β-blockers
	• NSAIDs
	• Regional analgesia
	
	Opioids
	• Supplemental analgesia (not first line)
	• Lowest possible infusion doses when needed
	• Consider methadone
		Opioid minimization
		• Nonpharmacologic strategies
		  • Early mobilization
		  • Caloric intake
		  • Education
		  • Social support
		  • Psychological support
		  • Relaxation techniques
		• Non-opioid analgesics
		  • NSAIDs
		  • Acetaminophen
		  • NMDA antagonists
		  • α-2 agonist
		• Regional analgesia
		• Opioids
		  • S
		  (

ENTONCES ?

No existe evidencia clara de que OFA es mejor que Opioid Sparing

Existe **Racionalidad Teórica** sobre algún Beneficio Inmunológico, siempre y cuando la analgesia del paciente sea adecuada.

Particularmente cuando va acompañada de **Anestesia Regional**

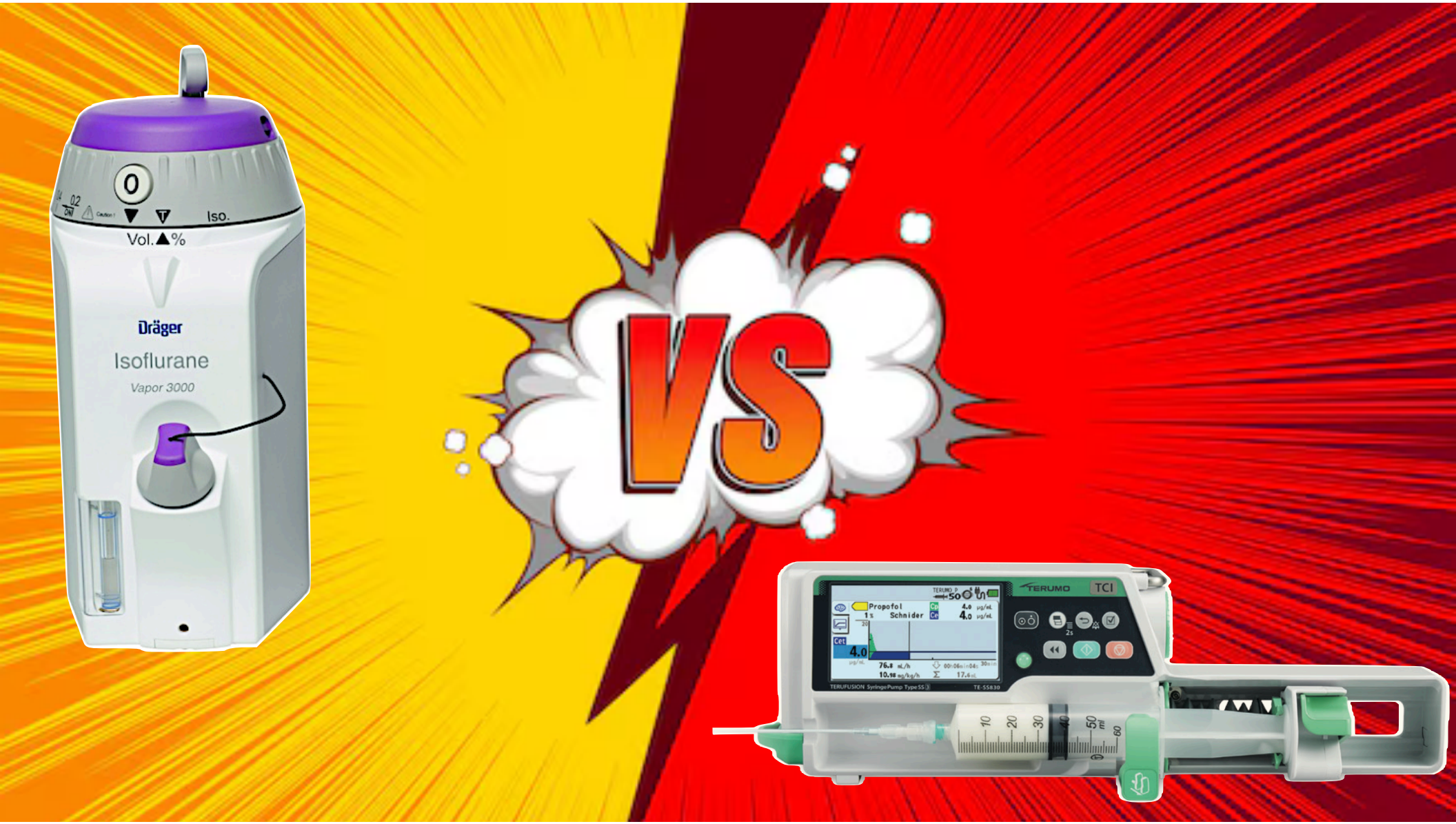
PREOCUPESE de las necesidades del paciente

ANESTESIA REGIONAL

- Menor Escalas de dolor postcx
- Menos PONV
- Reducción de otros analgésicos
- Menos inflamación – rpta stress

- Puede ser piedra angular de protocolos OFA
- Disminuye riesgo de dolor persistente post operatorio (Cx mamaria, toracotomía y cesárea)

- No ha demostrado ser universalmente mejor que opioides sistémicos en prevenir recurrencia o afectar el outcome en cirugía de Cáncer


Dräger
Isoflurane
Vapor 3000
Vol.▲%
Iso.
VS
TERUMO
TCI
Propofol
Schnider
4.0
TERUFUSION SyringePump TypeSS
TE-SS830

El Propofol es **irrefutablemente mejor** que los halogenados para Anestesia de Cirugía Oncológica.

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INHALATORIA / PROPOFOL

Brogi and Forfori *J Anesth Analg Crit Care* (2022) 2:33
https://doi.org/10.1186/s44158-022-00060-9

SIAARTI
PRO VITA CONTRA DOLOREM SEMPER

Journal of Anesthesia, Analgesia and Critical Care

REVIEW Open Access

Anesthesia and cancer recurrence: an overview

Etrusca Brogi* and Francesco Forfori

Effects of anesthetics on cancer recurrence

Type of anesthetics	*Effects*
Volatile anesthetics	-Pro-inflammatory and immunosuppressive action -Reduces Th1/Th2 ratio -Impairs NK cell activity -Induces T cell and B cell apoptosis -Upregulation of hypoxia-inducible factors (HIF-1α, HIF-2α,) -Increase transcription of pro-metastatic factors (VEGF, angiopoietin-1, proteases MMP-2, and MMP-9) -Enhanced tumor cell proliferation -Increase angiogenesis, and cell migration
Intravenous anesthetics	-Anti-inflammatory and immunosuppression properties -Suppression of prostaglandin and inflammatory cytokine production -Inhibition of cyclooxygenase (COX) activity -Stimulate the proliferation of NK cells -Increase expression of granzyme B and IFNγ -Increase cytotoxic T lymphocyte activity -Does not affect the Th1/Th2 ratio -Modulate genetic signaling pathways -Inhibits histone acetylation

[Sin título]

gery

A comparison of the immunological effects of propofol and isoflurane for maintenance of anesthesia in healthy dogs

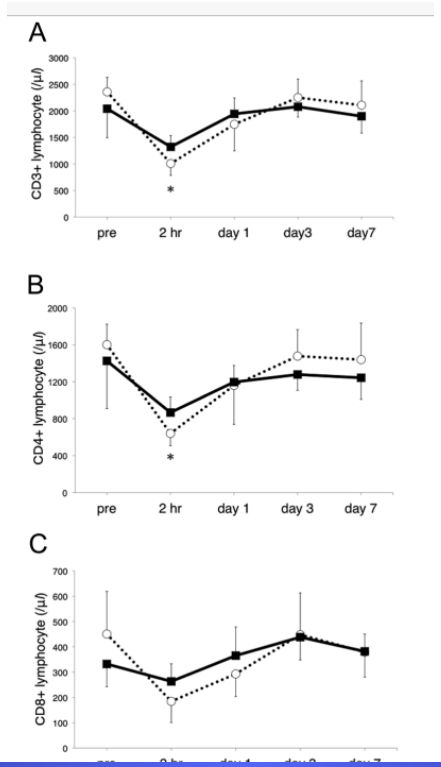
Mizuki TOMIHARI[1)]*, Akira NISHIHARA[1)], Terumasa SHIMADA[2)], Masashi YANAGAWA[1)], Masafumi MIYOSHI[1)], Kazurou MIYAHARA[1)] and Akihiro OISHI[1)]

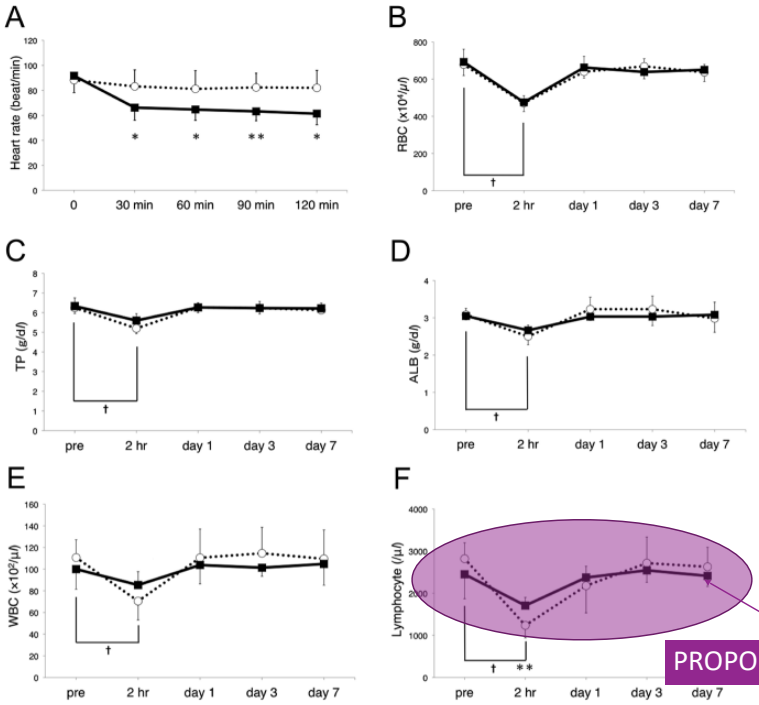
[1)]*Department of Applied Veterinary Medicine, Obihiro University of Agriculture and Veterinary Medicine, Nishi 2-sen 11 Inada-cho, Obihiro, Hokkaido 080–8555, Japan*
[2)]*Veterinary Medical Center, Graduate School of Life and Environmental Sciences, Osaka Prefecture University, 1–58 Rinku Ourai Kita, Izumisano, Osaka 598–8531, Japan*

Midazolam 0,3 mg kg

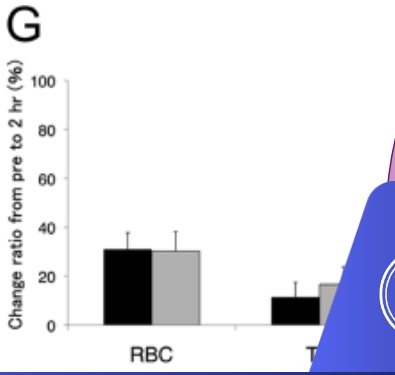
Fentanilo 10 ug Kg h

PROPOFOL VS ISOFLURANO





PROPOFOL



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INHALATORIA / PROPOFOL

Can J Anesth/J Can Anesth
https://doi.org/10.1007/s12630-019-01330-x

REVIEW ARTICLE/BRIEF REVIEW

Anesthetic technique and cancer outcomes: a meta-analysis of total intravenous *versus* volatile anesthesia

Technique d'anesthésie et pronostics de cancer : une méta-analyse analyse comparant l'anesthésie intraveineuse totale et l'anesthésie par inhalation

Andrea Yap, FANZCA · Maria A. Lopez-Olivo, PhD · Julia Dubowitz, MBBS · Jonathan Hiller, FANZCA · Bernhard Riedel, PhD · the Global Onco-Anesthesia Research Collaboration Group

META-ANALISIS 6 ESTUDIOS (5 retrospectivos) – 7800 PACIENTES

Cancer Mamario, esófago, NSCLC

TIVA → Mayor intervalo libre de recurrencia

Gran heterogeneidad de extensión de CX, tipo de Ca y pacientes.

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CLINICAL PRACTICE

Inhalation or total intravenous anaesthesia and recurrence after colorectal cancer surgery: a propensity score matched Danish registry-based study

Rune P. Hasselager[1,*], Jesper Hallas[2] and Ismail Gögenur[1]

[1]Center for Surgical Science, Zealand University Hospital, Koege, Denmark and [2]Clinical Pharmacology and Pharmacy, Odense University Hospital, Odense, Denmark

*Corresponding author. E-mail: rubh@regionsjaelland.dk

An abstract of this study has been submitted as an oral presentation at the Danish Surgical Society's annual conference 2020.

Estudio Retrospectivo – 8600 pacientes

Ca Colorectal

Pequeño aumento en Recurrencia en Inhalatoria
Sin diferencia en sobrevida Total

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INHALATORIA / PROPOFOL

PROPOFOL + RA VS INHALATORIA

Paravertebral block in regional anesthesia with propofol sedation reduces locoregional recurrence in patients with breast cancer receiving breast conservative surgery compared with volatile inhalational without propofol in general anesthesia

Jiaqiang Zhang [a,1], Chia-Lun Chang [b,c,1], Chang-Yun Lu [d,1], Ho-Min Chen [e], Szu-Yuan Wu [e,f,g,h,i,j,*,2,3,4]

Table 1
Demographics of propensity score–matched patients with breast cancer receiving breast-conserving surgery under PB-RA with propofol or INHA-GA without propofol.

		INHA-GA without propofol N = 1395		PB-RA with propofol N = 1395		
		n	(%)	n	(%)	P value
Follow-up time, months	Mean (SD)	61.2	(25.2)	62.1	(28.1)	0.8135
All-cause death		114	(8.2)	93	(6.7)	0.1291
Local recurrence		90	(6.5)	60	(4.3)	0.0120
Distant metastasis		150	(10.8)	118	(8.5)	

Current Status and Prospects of Anesthesia and Breast Cancer: Does Anesthetic Technique Affect Recurrence and Survival Rates in Breast Cancer Surgery?

Ryungsa Kim[1], Ami Kawai[1], Megumi Wakisaka[1] and Takanori Kin[2]*

[1] Department of Breast Surgery, Hiroshima Mark Clinic, Hiroshima, Japan, [2] Department of Breast Surgery, Hiroshima City Hospital, Hiroshima, Japan

February 2022 | Volume 12 | Article 795864

CONCLUDING REMARKS

At this time, RCTs have not provided sufficient evidence that the anesthetic technique is associated with the recurrence rate or long-term outcomes in patients undergoing breast cancer surgery.

Indicaciones para TIVA

Oncologia

Current Oncology

MDPI

Review

Anaesthetic Techniques and Strategies: Do They Influence Oncological Outcomes?

Liam Murphy [1,*], John Shaker [1] and Donal J. Buggy [1,2,3]

Curr. Oncol. **2023**, *30*(6), 5309-5321; https://doi.org/10.3390/curroncol30060403

Abstract: Background: With the global disease burden of cancer increasing, and with at least 60% of cancer patients requiring surgery and, hence, anaesthesia over their disease course, the question of whether anaesthetic and analgesia techniques during primary cancer resection surgery might influence long term oncological outcomes assumes high priority. Methods: We searched the available literature linking anaesthetic-analgesic techniques and strategies during tumour resection surgery to oncological outcomes and synthesised this narrative review, predominantly using studies published since 2019. Current evidence is presented around opioids, regional anaesthesia, propofol total intravenous anaesthesia (TIVA) and volatile anaesthesia, dexamethasone, dexmedetomidine, non-steroidal anti-inflammatory medications and beta-blockers. Conclusions: The research base in onco-anaesthesia is expanding. There continue to be few sufficiently powered RCTs, which are necessary to confirm a causal link between any perioperative intervention and long-term oncologic outcome. In the absence of any convincing Level 1 recommending a change in [illegible] oncologic benefit should not be part of the decision on choice of anaesthetic te[illegible] resection surgery.

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Volatiles vs. TIVA – Is there a difference in cancer patients

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Table 1
Overview of studies on overall and recurrence-free survival in patients undergoing IA vs. TIVA in oncological surgery.

Author	Study type	Recurrence free survival	Overall survival
Enlund 2023 [24]	Randomised controlled trial	/	=
Cao 2023 [25]	Randomised controlled trial	=	=
Che 2023 [27]	Retrospective cohort study	=	TIVA
Seo 2023 [28]	Retrospective cohort study	TIVA	TIVA
Oh 2023 [29]	Retrospective cohort study	/	TIVA
Ma 2023 [25]	Retrospective cohort study	=	=
Karami 2022 [30]	Retrospective cohort study	IA	=
Sun 2022 [31]	Retrospective cohort study	TIVA	TIVA
Gao 2022 [32]	Retrospective cohort study	=	=
Yoon 2022 [33]	Retrospective cohort study	/	=
Ren 2022 [34]	Retrospective cohort study	=	=
Miao 2022 [35]	Retrospective cohort study	=	=
Lee 2022 [36]	Retrospective cohort study	=	=
Ishiyama 2022 [37]	Retrospective cohort study	/	=
Enlund 2022 [38]	Retrospective cohort study	=	=
Zhang 2022 [39]	Retrospective cohort study	/	=
De la Motte Watson 2021 [40]	Retrospective cohort study	/	=
Ttseng 2021 [41]	Retrospective cohort study	TIVA	TIVA
Pfail 2021 [42]	Retrospective cohort study	TIVA	TIVA
Wu 2021 [43]	Retrospective cohort study	/	=
Huang 2021 [44]	Retrospective cohort study	TIVA	TIVA
Hayasaka 2021 [45]	Retrospective cohort study	TIVA	TIVA
Hasselager 2021 [46]	Retrospective cohort study	TIVA	=
Makito 2020 [47]	Retrospective cohort study	=	=
Meng 2020 [48]	Retrospective cohort study	TIVA	TIVA
Shiono 2020 [49]	Retrospective cohort study	=	/
Schmoch 2021 [50]	Retrospective cohort study	=	=
Takeyama 2021 [51]	Retrospective cohort study	TIVA	TIVA
Koo 2020 [52]	Retrospective cohort study	TIVA	/
Lai 2020 [53]	Retrospective cohort study	TIVA	TIVA
Enlund 2020 [54]	Retrospective cohort study	/	=
Huang 2020 [55]	Retrospective cohort study	TIVA	TIVA
Dong 2020 [56]	Retrospective cohort study	/	=
Orriach 2020 [57]	Prospective	TIVA	/
Hong 2019 [58]	Retrospective cohort study	/	=
Huang 2019 [59]	Retrospective cohort study	=	=
Sung 2019 [60]	Retrospective cohort study	=	=
Yoo 2019 [61]	Retrospective cohort study	=	=
Oh 2019 [62]	Retrospective cohort study	/	=
Lai 2019 [63]	Retrospective cohort study	TIVA	TIVA
Sessler 2019 [26]	Randomised controlled trial	=	/
Yan 2019 [64]	Randomised controlled trial	=	=
Yan 2018 [65]	Randomised controlled trial	=	=
Zheng 2018 [66]	Retrospective cohort study	/	TIVA
Wu 2018 [67]	Retrospective cohort study	/	TIVA
Oh 2018 [68]	Retrospective cohort study	=	=
Kim 2017 [69]	Retrospective cohort study	=	=
Jun 2017 [70]	Retrospective cohort study	TIVA	TIVA
Wigmore 2016 [11]	Retrospective cohort study	/	TIVA
Lee 2016 [13]	Retrospective cohort study	TIVA	
Enlund 2014 [12] **(Breast cancer)**	Retrospective cohort study	/	
Enlund 2014 [12] **(Colon cancer)**	Retrospective cohort study	/	
Enlund 2014 [12] **(Rectal cancer)**	Retrospective cohort study	/	

(/) = not reported, **(TIVA)** = statistical significant benefit of TIVA, (IA) = statistical significant be
between TIVA and IA

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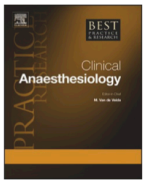

Volatiles vs. TIVA – Is there a difference in cancer patients

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Currently, there is no strong evidence that TIVA or IA has a meaningful impact on cancer-free survival. This review critically examines the available research and presents an alternative perspective on this controversial topic.

cancers

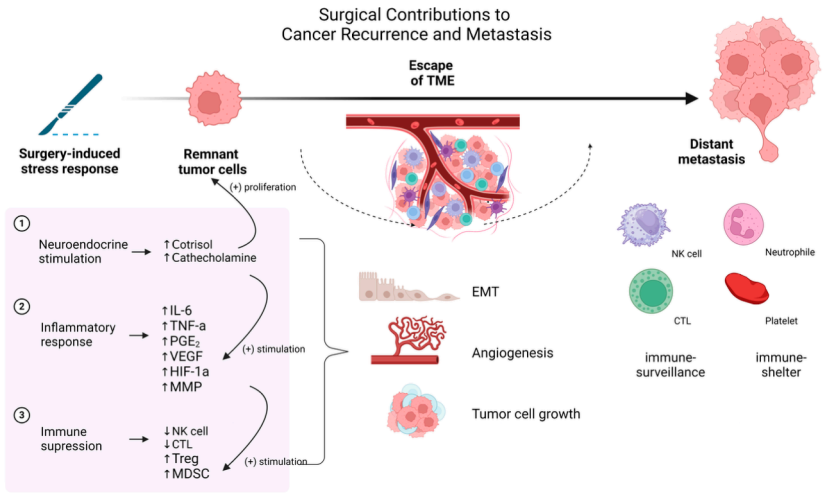
MDPI

Review

Anesthetic Approaches and Their Impact on Cancer Recurrence and Metastasis: A Comprehensive Review

Hoon Choi and Wonjung Hwang *

Cancers **2024**, *16*, 4269. https://doi.org/10.3390/cancers16244269



Anesthetic Technique	Mechanisms Affected	Molecular Markers	Impact on Cancer Progression	References (Related Impacts on Cancer Progression)
Inhaled anesthetics	↑ Stress response, ↑ inflammatory response, ↓ immune function	↑ IL-6, ↑ TNF-α, ↓ NK cells, ↑ VEGF, ↑ HIF-1α, ↑ MMPs, ↑ CTCs	↑ CTC survival, ↑ angiogenesis, ↑ tumor cell migration	[7,44], [45,46], [47–52]
Propofol-based TIVA	↓ Stress response, ↓ inflammatory imbalance, ↑ immune function	↓ IL-6, ↓ PGE_2, ↑ NK cells, ↓ VEGF, ↓ HIF-1α, ↓ MMPs, ↓ CTCs	↓ CTC survival, ↓ angiogenesis, ↓ tumor cell migration	[53], [45,53,54], [53,55–57]
Opioids	↑ Stress response, ↑ inflammatory response, ↓ immune function, ↑ MOR activation	↑ IL-6, ↓ NK cells, ↓ CTLs ↑ VEGF	↑ Tumor proliferation, ↑ angiogenesis, ↑ tumor cell mig	[9,58,59],

Anesthetic Technique	Mechanisms Affected	Molecular Markers	Impact on Cancer Progression	References (Related Impacts on Cancer Progression)
NSAIDS	↓ Inflammatory response	↓ COX2, ↓ PGE_2, ↓ IL-10, ↓ VEGF, ↓ MMPs, ↓ MDSCs	↓ Tumor proliferation, ↓ angiogenesis, ↓ tumor cell migration	[63–65], [63,64], [63,64,66,67]
Dexmedetomidine	↓ Stress response, ↓ inflammatory imbalance,	↑ VEGF, ↑ HIF-1α, ↑ MMPs, ↓ EGFR, ↑ MDSCs	↓ Tumor growth, (dual effects based on dose and context) ↑ angiogenesis, ↑ tumor cell migration	[68,69], [70–72], [73–76]
Ketamine	↓ Inflammatory response, modulates NMDA receptors	↓ IL-6, ↓ TNF-α, ↓ NK cells, ↓ VEGF, ↑ ROS	↓ Tumor growth (mixed impact)	[77–81], [82]
Local anesthetics	↓ Stress response, ↓ inflammatory response, ↑ immune function, blocks sodium channels, direct cytotoxicity	↓ IL-6, ↓ TNF-α, ↓ NK cells, ↓ VEGF, ↓ MMPs, ↓ CTCs	↑ Apoptosis, ↓ angiogenesis, ↓ tumor cell migration	[83–88], [89], [89–96]
Regional anesthesia	↓ Systemic stress response	↓ IL-6, ↓ NK cells, ↓ VEGF, ↓ CTCs	↓ CTC survival, ↓ angiogenesis, ↓ tumor cell migration	[97], [97,98], [97,98]

Cancer Type	Anesthetic Techniques	Findings	Study Type	References
Breast	TIVA (vs. Inhaled)	Improved OS	Retrospective	[99]
		Improved RFS	Retrospective	[100]
		No difference in OS and RFS	Retrospective	[101–103]
		Decreased locoregional recurrence	Retrospective	[104]
	Regional (vs. General)	No difference in recurrence rate	RCT	[105]
		No difference in recurrence rate and OS	RCT	[106]
	Dexmedetomidine	No difference in recurrence rate	Retrospective	[107]
Lung	TIVA (vs. Inhaled)	No difference in OS and RFS	Retrospective	[108]
	Opioid	Decreased OS and RFS (in stage I)	Retrospective	[109]
		Increase in recurrence rate	Retrospective	[110]
		No difference in recurrence rate and OS	Retrospective	[111]
	Regional (vs. General)	No difference in OS and RFS	RCT	[112]
	Dexmedetomidine	Decreased OS and no difference in RFS	Retrospective	[113]

TIVA: total intravenous anesthesia; OS: overall survival; RFS: recurrence-free survival; RCT: randomiz
trial.

Cancer Type	Anesthetic Techniques	Findings	Study Type	References
Gastro-intestinal	TIVA (vs. Inhaled)	No difference in OS and RFS (in overall)	Retrospective	[114]
		Improved OS (in gastric)	Retrospective	[115]
		Improved OS (in colorectal)	Retrospective	[116]
		Improved OS and RFS (in esophageal)	Retrospective	[117]
		Improved OS (in hepatic)	Retrospective	[118]
	Opioid	Improved OS (in esophageal)	Retrospective	[119]
		No difference in OS and RFS (in esophageal)	Retrospective	[120]
		Decreased RFS and no difference in OS (in esophageal)	Retrospective	[121]
	Local anesthetics	Improved OS (in pancreas)	Retrospective	[122]
Urologic	Opioid	Decreased OS and RFS (in prostate)	Retrospective	[60]
	Regional (vs. General)	Improved OS and no difference in RFS (in prostate)	Meta-analysis	[123]
		No difference in disease-free survival (in prostate)	RCT	[124]
		No difference in OS and RFS (in bladder)	Retrospective	[125]
		Improved RFS (in bladder, esp. high-risk patients)	Retrospective	[126]
Brain	TIVA (vs. Inhaled)	No difference in OS and RFS	Retrospective	[127]
		No difference in OS and progression-free survival	Retrospective	[128]
Overall	TIVA (vs. Inhaled)	Improved OS (esp. gastrointestinal)	Retrospective	[129]
		Improved OS and no difference in RFS	Meta-analysis	[130]
		Improved OS and RFS	Meta-analysis	[131]
	Regional (vs. General)	Improved OS (esp. colorectal)	Meta-analysis	

TIVA: total intravenous anesthesia; OS: overall survival; RFS: recurrence-free survival; RCT: randomi
trial.

OTRAS DROGAS ?

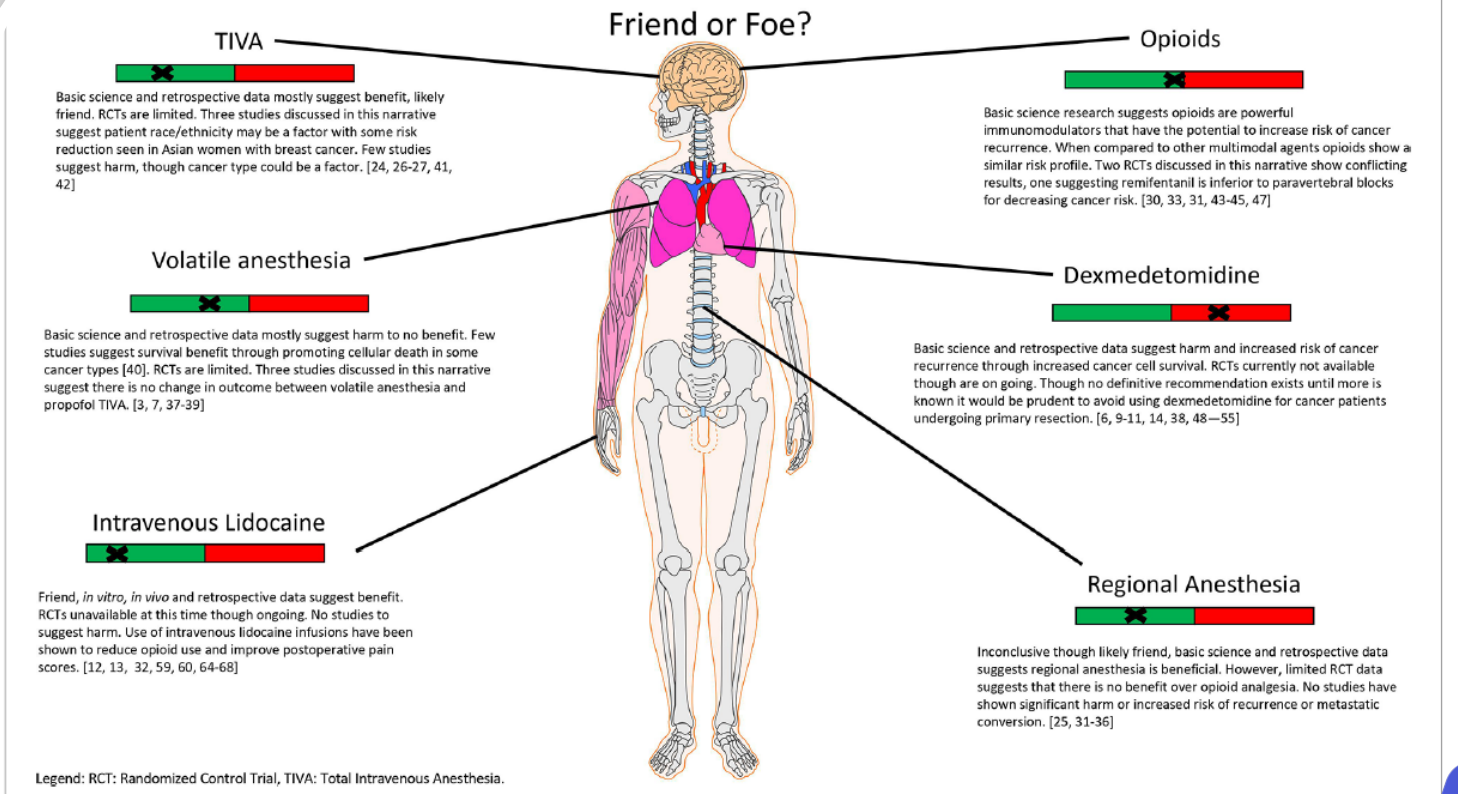
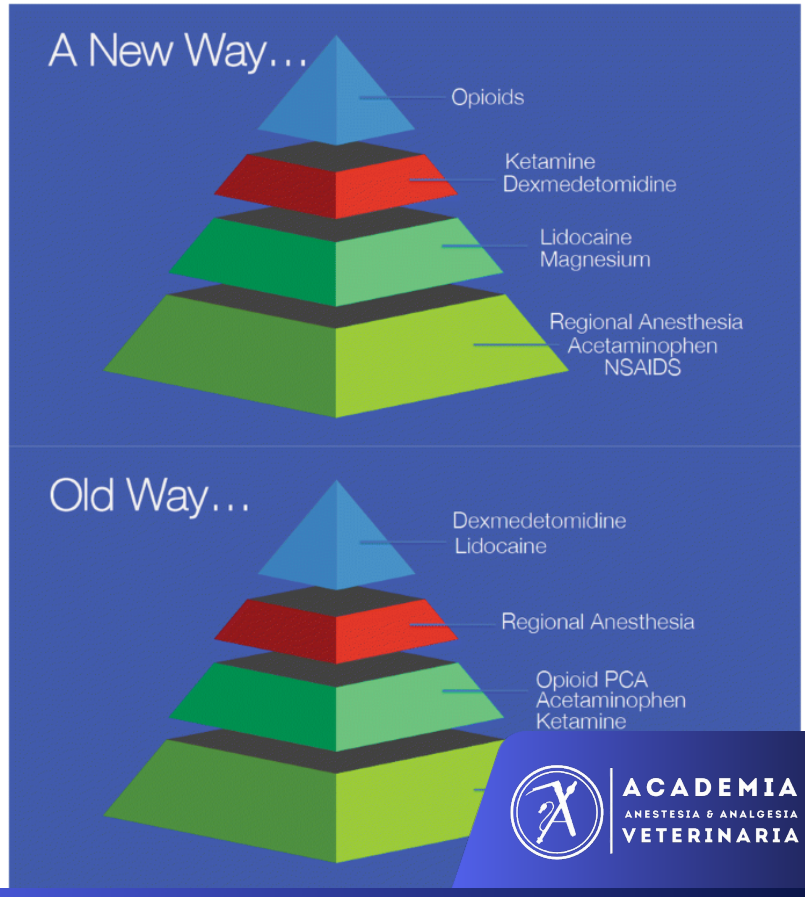


FIGURE 1 | A summary of findings depicted in this narrative review.

MESAJES FINALES

- Control **Stress Perioperatorio**
- **No esta claro el beneficio** OFA vs Opioid Sparing
- Privilegiar **abordaje Multimodal**
- **Anestesia Regional**
- **No esta claro el beneficio del Propofol** respecto a recurrencia y metástasis
- **Otras Drogas ?**



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MESAJES FINALES

No existe información a la fecha que permita establecer recomendaciones **que cambien la práctica clínica actual**.

Existe cierta **racionalidad** para **preferir** alguna técnica sin embargo **no se puede afirmar beneficios** en términos de sobrevida o recurrencia

Muchas Gracias
por su atención

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