Multimodal Analgesia Strategies (Opioid Sparing)

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Cardiac Surgical Pain

- **Multiple sites & sources of pain**
  - *Incisional pain, sternotomy, chest retraction, operative positioning*
    - intercostal nerve pain / visceral pain / leg pain (vein graft harvesting)
  - *invasion of chest tubes, endotracheal tube, tracheal suctioning, urinary catheter, IV lines, NG tube*

- **Initial hemodynamic instability**

- **Longer duration of acute postop. recovery**
  - *peaks over the first 2 days*
    - then, declines daily through postoperative day 6
    - pain from coughing continues to be severe throughout the first week

Postoperative Pain Management (1)

- Potential complications associated with acute postoperative pain
  - *Sympathetic response to pain -> increase myocardial oxygen consumption -> predispose to **arrhythmia**, potentially **myocardial injury***
  - *Inadequate respiratory effort -> atelectasis, hypoxemia, **pneumonia***

- ***Increased need for ventilator support, prolonged ICU/hospital stay***

Postoperative Pain Management (2)

- Poorly controlled postoperative pain
  - *nausea, anorexia -> compromising nutritional status & immunosupression*
    - delayed wound healing, predispose to infection
  - *Insomnia, exhaustion -> aggravated delirium*
  - *decreased ambulation -> increase risk of venous thromboembolism*
  - *delay patient recovery*
  - *prolonged outpatient opioid use*

- **Persistent postoperative pain**
  - *Poststernotomy neuralgia for at least 3months duration*

Traditional Opioid Analgesia

- IV / oral opioid
  - *Cornerstone of postoperative pain management*
- Side effects
  - ***nausea, vomiting, constipation, ileus, urinary retention, pruritus***
  - ***sedation, delirium, respiratory depression***
- In cardiac surgery patients: vasodilatation -> hypotension, bradycardia
- Impede quality & timing of patient recovery, prolong hospital stay, increase costs
  - ***development of long-term opioid dependence***

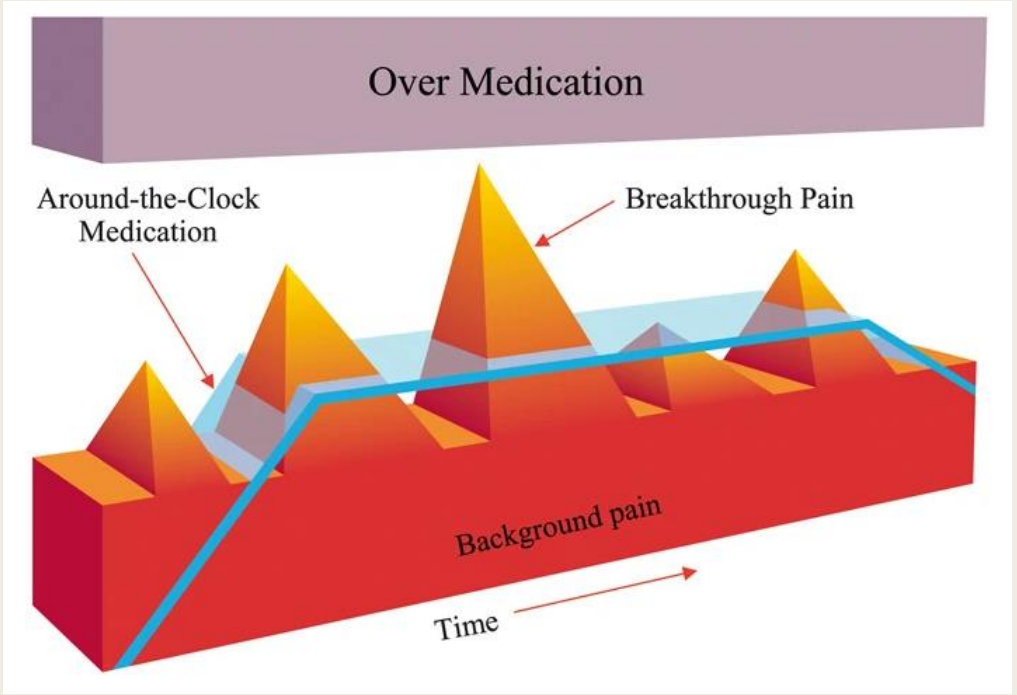
MULTIMODAL ANALGESIA STRATEGY

Analgesic Principles

- Unless contraindicated,

  patients should receive an around-the-clock

  regimen



- Dosing regimens should be administered to optimize efficacy while minimizing the risk of adverse events
- The choice of medication, does, route, and duration of therapy should be individualized

Multimodal Analgesia Strategy

- Use of multiple, simultaneous mechanisms of pain control acting synergistically
- To improve analgesic effect + to reduce the doses of any single agent
- Multiple pathways and mediators involved in nociception
  - *Targeting several mechanisms -> increase analgesic efficacy*
  - *Combination of systematic & regional anesthesia*

The aim of MMA
to improve pain relief while reducing opioid requirements and opioid-related adverse effects

Multimodal analgesia strategy

- Multimodal, opioid-sparing analgesia
  - *Promoted for more than 20 yrs*
  - *Only recently begun to have broad uptake*
    - with increasing adoption of ERAS pathway

ERAS pathway

- With the goal of improving and expediting patients' recovery after surgery

- "Fast Track" protocol
  - *Use of short-acting hypnotic drugs with reduced doses of opioids*

- ***Standardized multimodal analgesic regimen***
- IV, oral, rectal, topical
  - *Transition form IV to oral if possible*
    - Less IV cannula-related complications, encourage mobility

Clinical Review & Education

JAMA Surgery | Special Communication

Guidelines for Perioperative Care in Cardiac Surgery
Enhanced Recovery After Surgery Society Recommendations

Daniel T. Engelman, MD; Walid Ben Ali, MD; Judson B. Williams, MD, MHS; Louis P. Perrault, MD, PhD; V. Seenu Reddy, MD; Rakesh C. Arora, MD, PhD; Eric E. Roselli, MD; Ali Khoynezhad, MD, PhD; Marc Gerdisch, MD; Jerrold H. Levy, MD; Kevin Lobdell, MD; Nick Fletcher, MD, MBBS; Matthias Kirsch, MD; Gregg Nelson, MD; Richard M. Engelman, MD; Alexander J. Gregory, MD; Edward M. Boyle, MD

A multimodal, opioid-sparing, pain management plan is recommended postoperatively.

Class (Strength) of Recommendation	Class I (Strong)
Level (Quality) of Evidence	Level B-NR (Non-randomized)

Pain Management

Until recently, parenteral opioids were the mainstay of postoperative pain management after CS. Opioids are associated with multiple adverse effects, including sedation, respiratory depression, nausea, vomiting, and ileus.[99] There is growing evidence that multimodal opioid-sparing approaches can adequately address pain through the additive or synergistic effects of different types of analgesics, permitting lower opioid doses in the population receiving CS.[100]

Nonsteroidal anti-inflammatory drugs are associated with renal dysfunction after CS.[101] Selective *COX-2* inhibition is associated with a significant risk of thromboembolic events after CS.[102] The safest nonopioid analgesic may be acetaminophen.[103] Intravenous acetaminophen may be better absorbed until gut function has recovered postoperatively.[104] Per a medium-quality meta-analysis, when added to opioids, acetaminophen produces superior analgesia, an opioid-sparing effect, and independent antiemetic actions.[105] Acetaminophen dosing is 1 g every 8 hours. Combination acetaminophen preparations with opioids should be discontinued.

Tramadol has dual opioid and nonopioid effects but with a high delirium risk.[106] Tramadol produces a 25% decrease in morphine consumption, decreased pain scores, and improved patient comfort postoperatively.[107] Pregabalin also decreases opioid consumption and is used in postoperative multimodal analgesia.[108] Pregabalin given 1 hour before surgery and for 2 postoperative days improves pain scores compared with placebo.[109] A 600-mg gabapentin dose, 2 hours before CS, lowers pain scores, opioid requirements, and postoperative nausea and vomiting.[110]

Dexmedetomidine, an intravenous α-2 agonist, reduces opioid requirements.[111] A medium-quality meta-analysis of dexmedetomidine infusion reduced all-cause mortality at 30 days with a lower incidence of postoperative delirium and shorter intubation times.[112,113] Dexmedetomidine may reduce AKI after CS.[114] Ketamine has potential uses in CS owing to its favorable hemodynamic profile, minimal respiratory depression, analgesic properties, and reduced delirium incidence; further studies are needed in the CS setting.[115]

Patients should receive preoperative counseling to establish appropriate expectations of perioperative analgesia targets. Pain assessments must be made in the intubated patient to ensure the lowest effective opioid dose. The Critical Care Pain Observation Tool, Behavioral Pain Scale, and Bispectral Index monitoring may have a role in this setting.[116-119] Although no single pathway exists for multimodal opioid-sparing pain management, there is sufficient evidence to recommend that CS programs use acetaminophen, Tramadol, dexmedetomidine, and pregabalin (or gabapentin) based on formulary availability (class I, level B-NR).

NON-OPIOID ANALGESIA

Acetaminophen (1)

- Analgesic with anti-pyretic properties
- Act predominantly in the central nervous system
  - *increasing pain threshold by inhibiting isoforms of COX, COX-1, Cox-2, COX-3*
  - *not inhibit COX activity in peripheral tissues > no anti-inflammatory property*
- Relatively safe non-opioid analgesia for cardiac surgery patients

ELSEVIER

European Journal of Cardio-thoracic Surgery 32 (2007) 527-

Double-blind, RCT
IV AAP vs. placebo
↓ VAS scores at rest & deep breath

Intravenous paracetamol as adjunctive treatment for postoperative pain after cardiac surgery: a double blind randomized controlled trial

Iolter Cattabriga [a,*], Davide Pacini [b], Gaia Lamazza [a], Francesco Talarico [a], Roberto Di Bartolomeo [b], Giovanni Grillone [a], Letizia Bacchi-Reggiani [c]

[a] Department of Anesthesia and Intensive Care, Sant'Orsola-Malpighi Hospital, University of Bologna, Italy

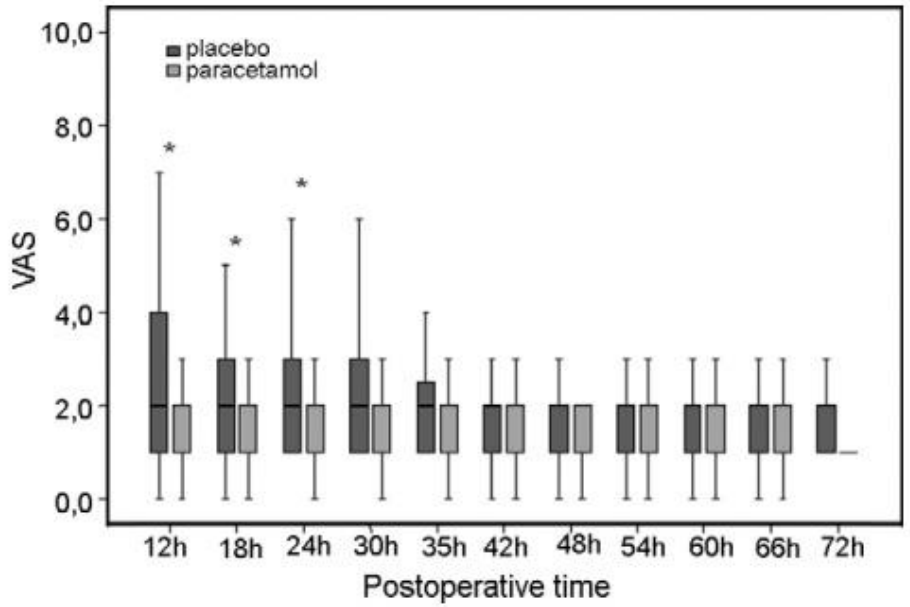


Fig. 1. Time course of visual analog scale (VAS) pain scores at rest. Values are expressed as median. (*) $p < 0.05$.

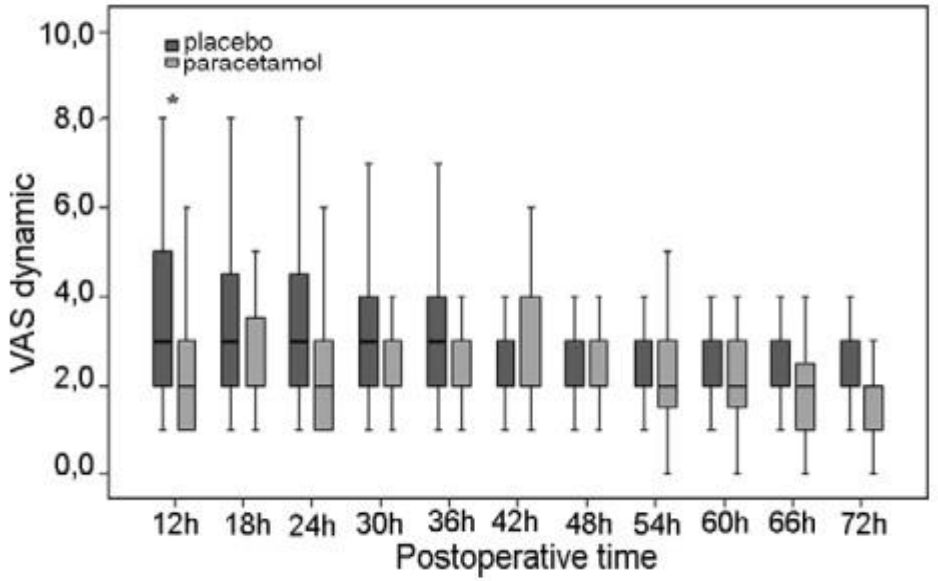


Fig. 2. Time course of visual analog scale (VAS) pain scores during a deep breath. Values are expressed as median. (*) $p < 0.05$.

Intravenous Acetaminophen as an Adjunct Analgesic in Cardiac Surgery Reduces Opioid Consumption But Not Opioid-Related Adverse Effects: A Randomized Controlled Trial

Srdjan Jelacic, MD,* Laurent Bollag, MD,* Andrew Bowdle, MD, PhD,* Cyril Rivat, PhD,* Kevin C. Cain, PhD,† and Philippe Richebe, MD, PhD*

Table 2. Primary and Secondary Outcomes

Variable	Placebo Group (n = 35)*	Acetaminophen Group (n = 33)	p Value	p Value†
24-h opioid consumption in morphine equivalents (mg)	62.3 ± 29.5	45.6 ± 29.5	0.024	0.013
48-h opioid consumption in morphine equivalents (mg)	105.1 ± 42.1	85.1 ± 42.3	0.059	0.020
24-h pain scores at rest	3.9 ± 2.3	3.7 ± 2.3	0.724	0.510
48-h pain scores at rest	2.4 ± 2.2	2.0 ± 1.8	0.397	0.458
24-h pain scores with coughing	6.3 ± 2.5	6.0 ± 2.5	0.600	0.509
48-h pain scores with coughing	5.1 ± 2.9	4.6 ± 2.0	0.399	0.395
24-h extent of wound hyperalgesia (cm)	4.8 ± 4.3	4.5 ± 3.8	0.771	0.927
48-h extent of wound hyperalgesia (cm)	4.6 ± 3.9	5.0 ± 3.5	0.644	0.160
Length of mechanical ventilation (min)	407 ± 683	360 ± 276	0.710	0.475
Length of ICU stay (h)	67 ± 35	61 ± 27	0.508	0.905

NOTE. Data are shown as mean ± SD.

Abbreviation: ICU, intensive care unit.

*The number of patients completing each postoperative assessment varied in the placebo group due to missing data (n = 35 for the length of mechanical ventilation and ICU stay; n = 34 for opioid consumption; n = 33 for 48-hour pain scores and 48-hour extent of secondary hyperalgesia; n = 32 for 24-hour pain scores and 24-hour extent of secondary hyperalgesia).

†p values when controlling for age, sex, and body mass index.

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PAIN®

www.elsevier.com/locate/pain

Intravenous acetaminophen reduces postoperative nausea and vomiting: A systematic review and meta-analysis

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[e] Department of Pharmacology, Temple Un
[f] Department of Anaesthesiology, Ludwig-

Table 2
Efficacy of i.v. acetaminophen to reduce nausea and vomiting.

Comparison	Acetaminophen	Control	Risk ratio	95% CI	*P*-value of effect
Nausea	281/1122	351/1097	0.73	0.60–0.88	0.001
Investigator initiated trials/prophylactic	137/685	228/684	0.63	0.54–0.75	< 0.001
Before surgery	44/217	81/213	0.54	0.40–0.74	<0.001
During or immediately after surgery	93/468	147/471	0.67	0.55–0.83	<0.001
Prophylactic single dose	46/282	96/284	0.50	0.38–0.66	<0.001
Prophylactic repeated doses	91/403	132/400	0.72	0.58–0.89	0.002
Vomiting	125/977	178/954	0.63	0.45–0.88	0.008
Investigator-initiated trials/prophylactic	50/541	129/541	0.42	0.31–0.56	<0.001
Before surgery	9/181	34/178	0.29	0.14–0.57	<0.001
During or immediately after surgery	41/360	95/363	0.46	0.33–0.63	<0.001
Prophylactic single dose	16/236	57/238	0.31	0.19–0.51	<0.001
Prophylactic repeated doses	34/305	72/303	0.49	0.35–0.70	<0.001

i.v., intravenous; CI, confidence interval.

Journal of Cardiothoracic and Vascular Anesthesia
Volume 19, Issue 3, June 2005, Pages 306-309

Original article

Intravenous Acetaminophen Reduced the Use of Opioids Compared With Oral Administration After Coronary Artery Bypass Grafting

Pia Holmér Pettersson CRNA, PhD * †, Jan Jakobsson MD, PhD ‡, Anders Öwall MD, PhD *

Prospective, randomized study
CABG
IV AAP vs. PO AAP
↓ Opioid consumption in IV AAP group

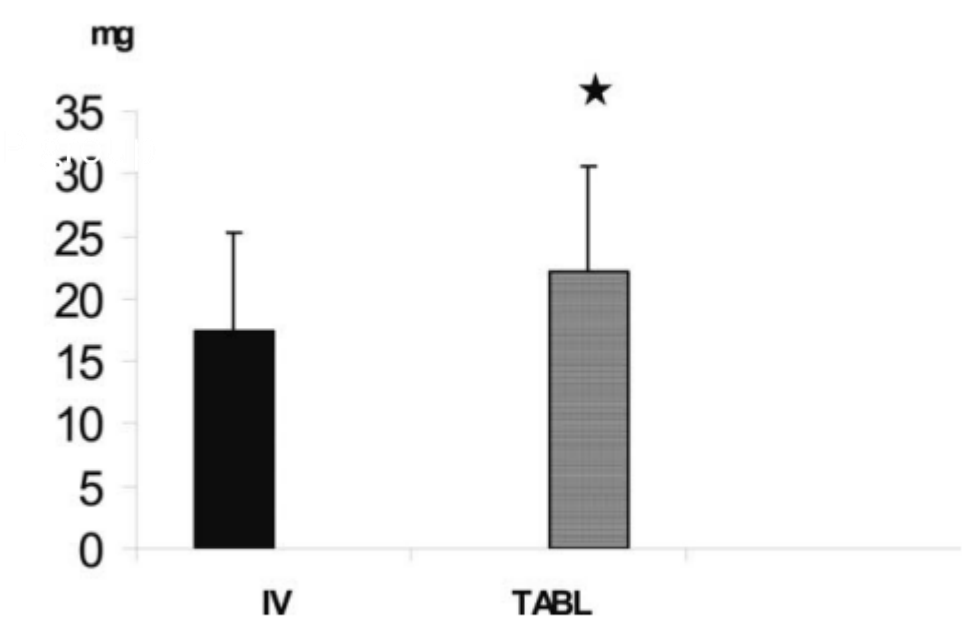


Fig 1. The mean amount of the opioid ketobemidone given during the study period, intravenous and orally treated groups. *$p < 0.05$ significant difference between groups.

REVIEW

Intravenous versus Oral Acetaminophen for Pain: Systematic Review of Current Evidence to Support Clinical Decision-Making

Farah Jibril, Sherif Sharaby, Ahmed Mohamed, and Kyle J Wilby

Systematic review
6 RCTs
IV AAP vs. PO AAP
No strong evidence of superiority of IV over oral

ABSTRACT

Background: Intravenous (IV) acetaminophen is increasingly used around the world for pain control for a variety of indications. However, it is unclear whether IV administration offers advantages over oral administration.

Objective: To identify, summarize, and critically evaluate the literature comparing analgesic efficacy, safety, and pharmacokinetics for IV and oral dosage forms of acetaminophen.

Data Sources: A literature search of the PubMed, Embase, and International Pharmaceutical Abstracts databases was supplemented with keyword searches of Science Direct, Wiley Library Online, and Springer Link databases for the period 1948 to November 2014. The reference lists of identified studies were searched manually.

Study Selection and Data Extraction: Randomized controlled trials comparing IV and oral dosage forms of acetaminophen were included if they assessed an efficacy, safety, or pharmacokinetic outcome. For each study, 2 investigators independently extracted data (study design, population, interventions, follow-up, efficacy outcomes, safety outcomes, pharmacokinetic outcomes, and any other pertinent information) and completed risk-of-bias assessments.

Data Synthesis: Six randomized clinical trials were included. Three of the studies reported outcomes pertaining to efficacy, 4 to safety, and 4 to pharmacokinetics. No clinically significant differences in efficacy were found between the 2 dosage forms. Safety outcomes were not reported consistently enough to allow adequate assessment. No evidence was found to suggest that increased bioavailability of the IV formulation enhances efficacy outcomes. For studies reporting clinical outcomes, the results of risk-of-bias assessments were largely unclear.

Conclusions: For patients who can take an oral dosage form, no clear indication exists for preferential prescribing of IV acetaminophen. Decision-making must take into account the known adverse effects of each dosage form and other considerations such as convenience and cost. Future studies should assess multiple-dose regimens over longer periods for patients with common pain indications such as cancer, trauma, and surgery.

Keywords: acetaminophen, paracetamol, intravenous, analgesia, pain

Acetaminophen (2)

- 15mg/kg, up to 1g, 4 times daily (q 6hr)
- Oral / parenteral forms
- IV form
  - *more often, conveniently used*
  - *produces early, reliable, and higher peak blood and cerebrospinal fluid levels*

- not associated with an increased incidence of respiratory depression, nausea/vomiting
  - *significant derangement of liver function has not been demonstrated*

Research

JAMA | Preliminary Communication | CARING FOR THE CRITICALLY ILL PATIENT

Effect of Intravenous Acetaminophen vs Placebo Combined With Propofol or Dexmedetomidine on Postoperative Delirium Among Older Patients Following Cardiac S

The DEXACET Randomized Clinical Trial

Balachundhar Subramaniam, MD, MPH; Puja Shankar, MD; Shahzad Shaefi, MD, MPH; Ariel Mueller, MA; Brian O'Gara, MD; Valerie Banner-Goodspeed, MPH; Jackie Gallagher, MS; Doris Gasangwa, BS; Melissa Patxot, BS; Senthil Packiasabapathy, MB Matthias Eikermann, MD, PhD; Daniel Talmor, MD, MPH; Edward R. Marcantonio, MD, SM

Randomized, placebo-controlled
IV AAP vs. placebo
↓ total morphine consumption, ↓ delirium

Table 2. Primary and Secondary Outcomes

Outcomes	Analgesic: Acetaminophen (n = 60)	Placebo (n = 60)	Difference (95% CI)	P Value
Delirium				
In-hospital delirium (primary outcome), No. (%)	6 (10.00)	17 (28.33)	−18.3% (−32.0% to −4.6%)	.01
Days with delirium, median (IQR)	1.0 (1.0 to 1.0)	2.0 (1.0 to 3.0)	−1 (−2 to 0)	.03
Worst delirium severity, median (IQR)[a]	9.0 (7.0 to 11.0)	8.0 (6.0 to 11.0)	1.0 (−2.0 to 3.0)	.81
MoCA score[b]				
Baseline, median (IQR)	24.0 (22.0 to 26.0)	23.5 (20.4 to 26.0)	0.5 (−1 to 2)	.39
Discharge, median (IQR)	24.0 (21.0 to 26.0)	24.0 (20.0 to 26.0)	0 (−1 to 2)	.29
Change from baseline, median (IQR)	0.0 (−2.0 to 1.0)	−0.4 (−2.0 to 1.0)	0.4 (−1.0 to 1.0)	.82
Time-related outcomes				
Hospital length of stay, median (IQR), d	8.0 (6.0 to 9.5)	8.5 (6.0 to 11.0)	−0.5 (−2 to 0)	.13
ICU length of stay, median (IQR), h	29.46 (25.07 to 49.43)	46.17 (27.83 to 81.44)	−16.7 (−20.3 to −0.8)	.02
48-h Postoperative				
Total morphine equivalent administered, median (IQR), μg[c]	10 082.5 (7524.0 to 15 090.0)	12 609.0 (10 076.0 to 20 141.5)	−2530 (−5064 to −22)	.03

Nonsteroidal Anti-inflammatory Drugs (1)

- inhibit COX enzymes -> ↓ inflammation, pain, and fever

- **Nonselective agents**: aspirin, ibuprofen, ketorolac, diclofenac
- **COX inhibitor-2 selective agents**: parecoxib, celecoxib
  - *Reducing the risk of peptic ulceration associated with NSAIDs*

- oral, IV, topical, rectal

The NEW ENGLAND JOURNAL of MEDICINE

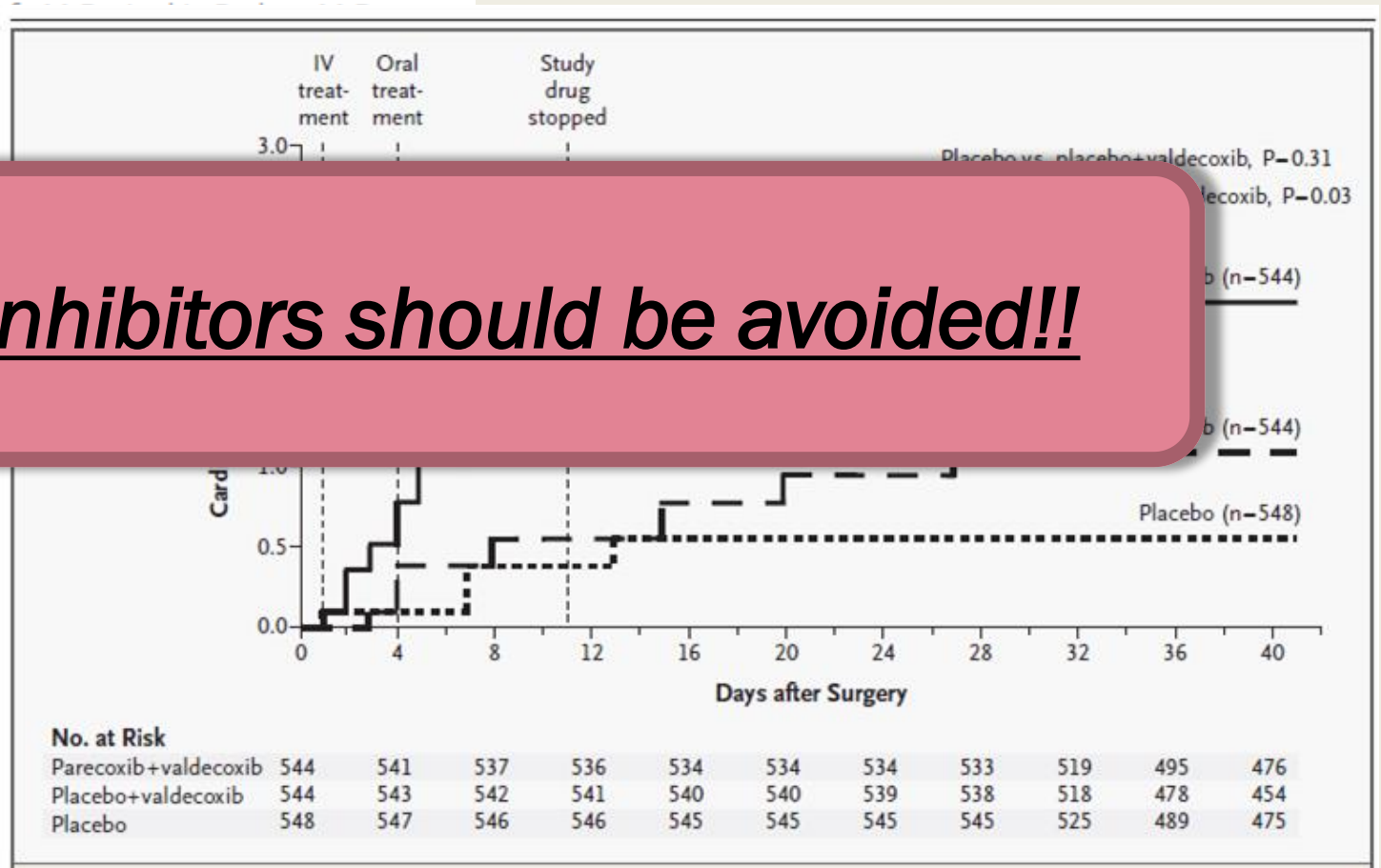
ORIGINAL ARTICLE

Complications of the COX-2 Inhibitors Parecoxib and Valdecoxib after Cardiac Surgery

Nancy A. Nussmeier, M.D., Andrew A. Whelton, M.D., Mark T. Brown, M.D., Richard M. Langford, F.R.C.A., Andreas Ho
Steven W. Boyce, M.D., and Kenne

Multicenter, double-blind, RCT
CABG
valdecoxib/parecoxib vs. placebo
↑ Incidence of cardiovascular events

COX-2 inhibitors should be avoided!!



Nonsteroidal Anti-inflammatory Drugs (2)

- **Renal complications**
  - Non-significant degree in healthy adults
  - *CPB mediated renal ischemia & systemic inflammation*
    - Kidney medullary hypoxia during CPB -> decline in glomerular filtration rate
    - Inflammatory cytokines released

- Caution in patients with **bleeding, thrombotic tendencies, renal insufficiency!!**
- GI inflammation, peptic ulcer

Dexmedetomidine (1)

- selective α2-adrenoceptor agonist
  - *sympatholysis, sedation, anxiolysis, and analgesia*

- Reduction of systemic NE release

  -> improve hemodynamic stability

  -> ↓ myocardial oxygen demand

  -> myocardiac protection

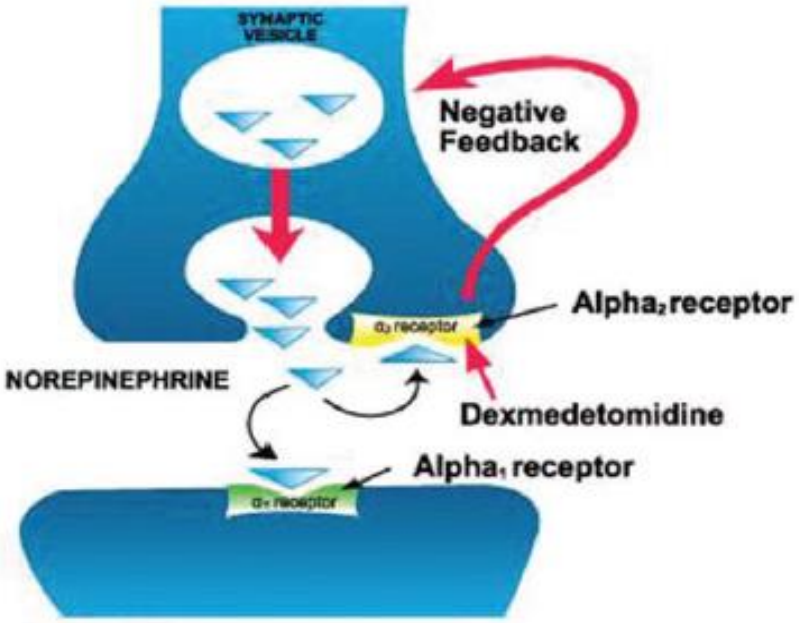
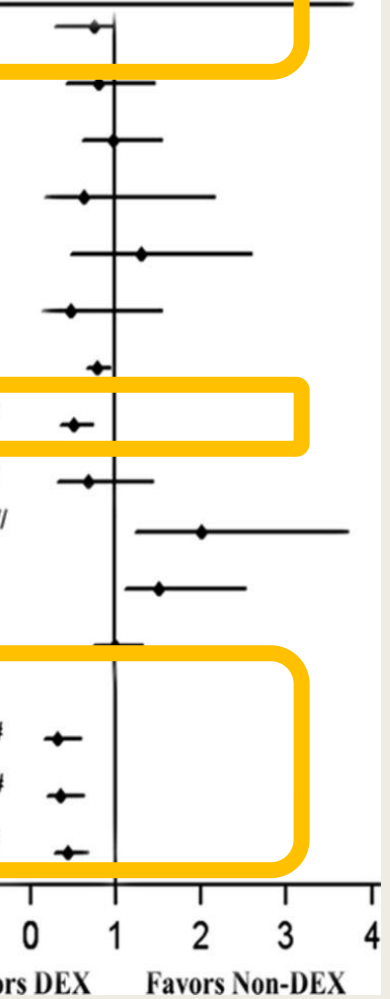


Figure 2. Mechanisms of action: dexmedetomidine is a potent and highly selective α-2 adrenoceptor agonist with sympatholytic, sedative, amnestic, and analgesic properties. The presynaptic sites of action are clinically significant because they modulate the release of norepinephrine and adenosine triphosphate through a negative feedback mechanism. (Part of the figure was adopted from Giovannitti JA Jr, Thoms SM, Crawford JJ. *Anesth Prog*. 2015;62:31–39 published by Allen Press with permission.)

Circulation
Volume 127, Issue 15, 16 April 2013; Pages 1576-1584
https://doi.org/10.1161/CIRCULATIONAHA.112.000936

Outcomes	Dexmedetomidine Yes(n=568) n(%)	Dexmedetomidine No(n=566) n(%)	Univariate OR	Univariate 95% CI	Univariate P Value	Adjusted OR	Adjusted 95% CI	Adjusted P Value	Adjusted OR(95%CI)
MACE	45(7.92)	57(10.07)	0.72	0.30-0.90	0.206	0.75	0.32-0.99	0.089	
Perioprative MI	8 (1.41)	15(2.65)	0.53	0.45-0.76	0.138	0.81	0.45-1.47	0.257	
Heart Block	25(4.40)	24(4.24)	1.04	0.58-1.87	0.891	0.99	0.63-1.55	0.963	
Cardiac Arrest	2(0.35)	9(1.59)	0.22	0.5-1.01	0.034	0.64	0.19-2.14	0.4681 *	
Stroke	8(1.41)	6(1.06)	1.33	0.46-3.87	0.595	1.31	0.50-2.57	0.7677	
Coma	2(0.35)	3(0.53)	0.66	0.11-3.98	0.651	0.49	0.15-1.56	0.2257	
Any Complication	268(47.18)	306(54.06)	0.76	0.60-0.96	0.0205	0.80	0.68-0.96	0.0136 †	
Delirium	31(5.46)	42(7.42)	0.72	0.45-1.16	0.178	0.53	0.37-0.75	0.0030 ‡	
Sepsis	4(0.7)	12(2.12)	0.33	0.11-1.02	0.043	0. 70	0.34-1.45	0.3349 §	
Postoperative RF	27(4.75)	19(3.13)	1.22	0.91-2.22	0.190	1.50	1.12-2.51	0.00945 //	
Postoperative Dialysis	66(11.62)	52(9.19)	1.30	0.88-1.07	0.180	1. 80	1.15-3.68	0.1011	
30-day Readmission	27 (4.78)	24(4.28)	1.26	0.73-2.18	0.416	1.00	0.76-1.33	0.980	
Mortality									
In-hospital	7(1.23)	26(4.59)	0.26	0.11-0.60	0.0008	0.34	0.19 -0.61	<0.0001 #	
30-day	10(1.76)	29(5.12)	0.33	0.16-0.67	0.002	0.3 9	0.23-0.66	<0.0001 #	
1-year	18(3.17)	45(7.95)	0.38	0.22-0.66	0.0004	0.4 7	0.31 -0.70	0.0002 #	



Dexmedetomidine (2)

- IV infusion 0.2-0.6 mcg/kg/hr
  - *Initiated after CPB in OR & continued for <24 hrs postoperatively in ICU*
- No respiratory depression -> as sedative drug
- Synergistic effect with opioids
  - *resulting in reduced analgesic requirement*
    both intraoperatively and postoperatively

Journal of Cardiothoracic and Vascular Anesthesia
Volume 17, Issue 5, October 2003, Pages 576-584

Original article

ICU sedation after coronary artery bypass graft surgery: dexmedetomidine-based versus propofol-based sedation regimens ☆

Daniel L Herr MD (FCCM) *, S.T.John Sum-Ping MD †, Michael England MD ‡

Multicenter, randomized trial
CABG
Dexmedetomidine vs. propofol
↓ morphine consumption

Table 3. Morphine (mg/h)

	Dexmedetomidine	Propofol-based	*p* Value*
Sternal closure to extubation			
n†	144	145	
Morphine‡	0.16 (0.04)	0.61 (0.08)	<0.001
Extubation to 1 hour postextubation			
n	132	141	
Morphine	0.36 (0.10)	1.16 (0.10)	0.002
Hour 1-2 postextubation			
n	132	141	
Morphine	0.41 (0.11)	0.82 (0.14)	0.033
Hour 2-3 postextubation			
n	132	141	
Morphine	0.27 (0.09)	0.88 (0.14)	0.009
Hour 3-4 postextubation			
n	132	141	
Morphine	0.10 (0.05)	0.74 (0.13)	0.002
Hour 4-5 postextubation			
n	132	141	
Morphine	0.20 (0.06)	0.81 (0.13)	0.015
Hour 5-6 postextubation			
n	132	141	
Morphine	0.10 (0.05)	0.74 (0.13)	<0.001
Extubation to 6 hours postextubation			
n	132	141	
Morphine	1.43 (0.25)	5.18 (0.13)	0.005
Sternal closure to 6 hours postextubation			
n	132	140	
Morphine	0.23 (0.03)	0.84 (0.03)	<0.001

Gabapentin (1)

- Gabapentinoids : gabapentin and pregabalin

- Analogue of the neurotransmitter γ-aminobutyric acid
- analgesic, anticonvulsant, anxiolytic effects

- S/E: dizziness, drowsiness, fatigue
  - *careful monitoring for central nervous system adverse events,*
  - *especially in elderly patients*

Journal of Cardiothoracic and Vascular Anesthesia
Volume 24, Issue 5, October 2010, Pages 808-813

Original article

Effects of Single-Dose Gabapentin on Postoperative Pain and Morphine Consumption After Cardiac Surgery

Ferdi Menda MD *, Özge Köner MD *, Murat Sayın MD *,
Mehmet Ergenoğlu MD †, Süha Küçükaksu MD †, Bora Aykaç MD *

Double-blind, RCT
CABG
Gabapentin vs. placebo
↓ morphine consumption, ↓ postop. pain

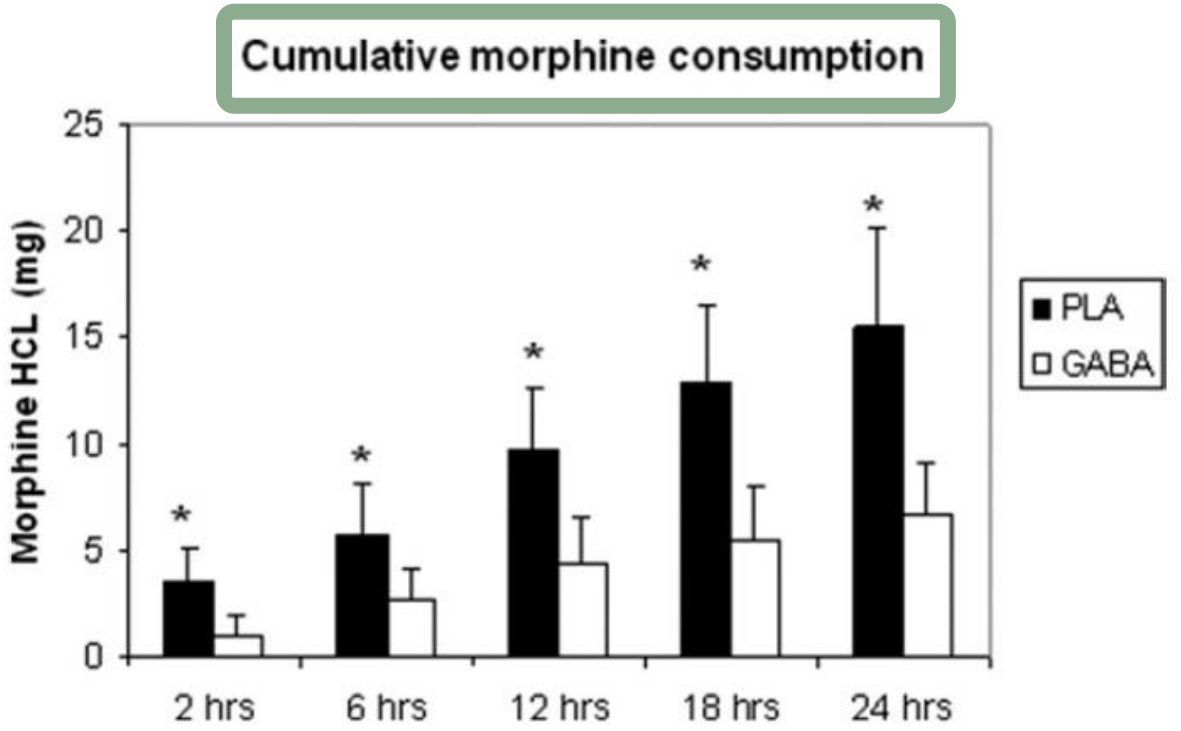


Fig 1. Cumulative morphine consumption of the groups during the study period; *$p < 0.01$ between the groups.

Gabapentin (2)

- **Gabapentin**
  - *Preop.: 1200mg PO once (2hr before incision)*
  - *Postop.: 300mg PO TID*

- **Pregabalin**
  - *Preop.: 300mg PO once (2hr before incision)*
  - *Postop.: 150mg PO BID*

Tramadol

- Central analgesic effect through μ-opioid receptors
- Dual opioid & non-opioid effects

- not result in respiratory depression and causes less dizziness and drowsiness
- *High delirium risk*

- oral, rectal, and IV form

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The effects of single-dose tramadol on post-operative pain and morphine requirements after coronary artery bypass surgery

A. K. But, F. Erdil, A. Yucel, E. Gedik, M. Durmus, M. O. Ersoy

First publ | Citat

RCT
CABG
IV tramadol vs. placebo
↓ morphine consumption, ↓ VAS score

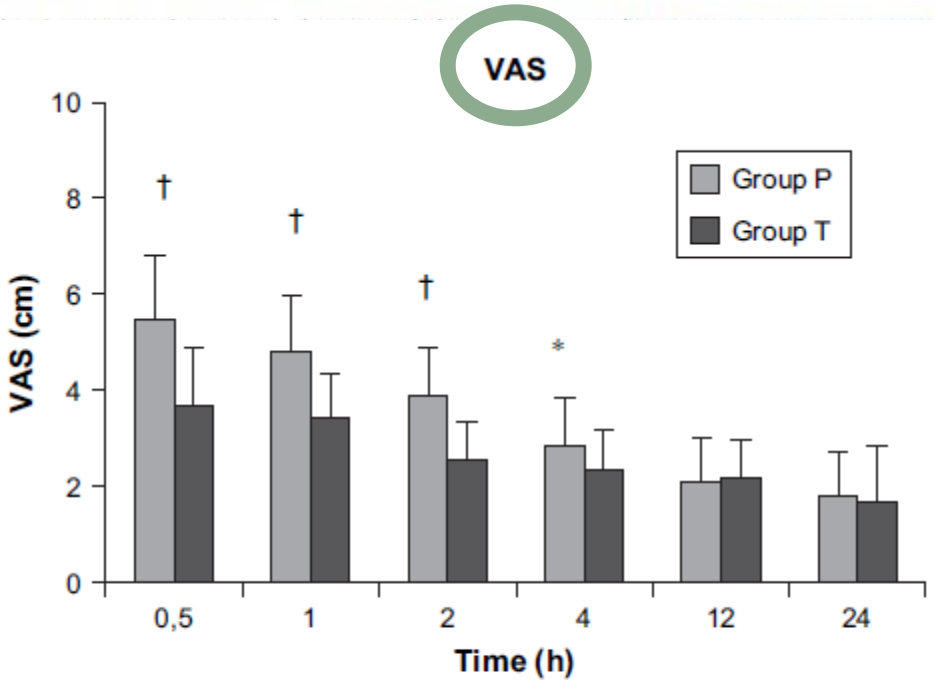

*Fig. 1. Post-operative pain scores. Scores were measured with a visual analogue scale (VAS) (0–10 cm; 0, no pain; 10, worst possible pain). Pain scores are expressed as the mean ± standard deviation for each group. *P < 0.05, group P vs. T. †P < 0.01, group P vs. T. Group P, saline; group T, tramadol.*

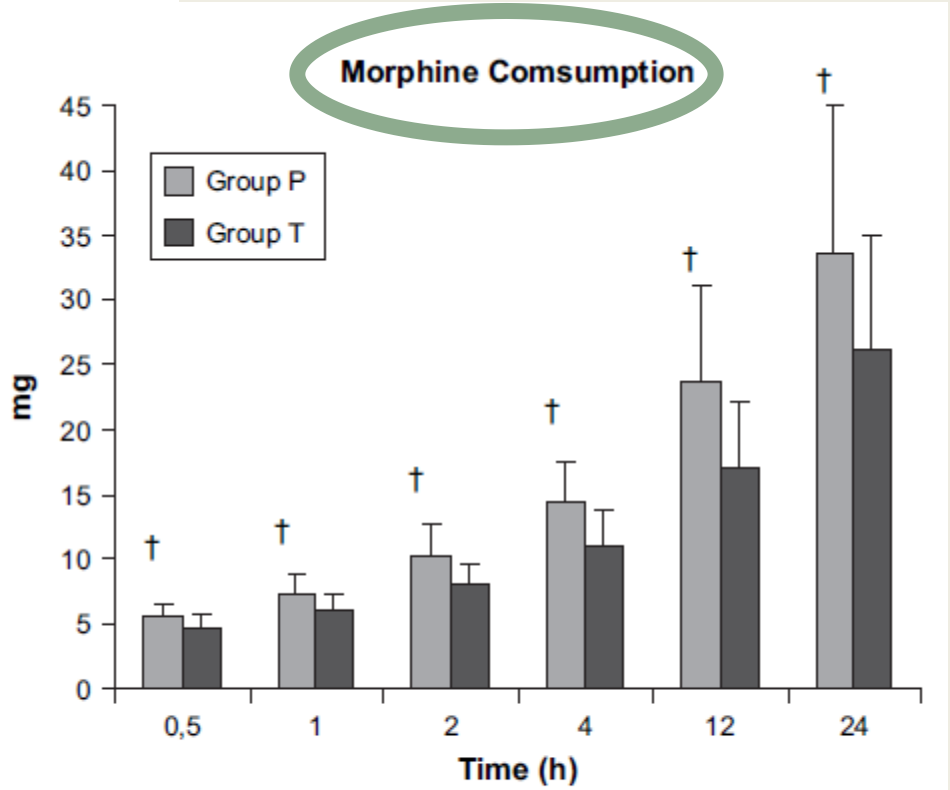

Fig. 4. Cumulative doses of morphine in the post-operative period. Results are expressed as the mean ± standard deviation for each group. †P < 0.01, group P vs. T. Group P, saline; group T, tramadol.

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Table 3
Number of PCA demands/boluses, requirement of additional analgesics, total morphine consumption

	Group T (n = 25; morphine + tramadol)	Group P (n = 25; morphine + placebo)	*P*
PCA demand[a] (mg), median (range)	40.48 ± 13.6 (34)	96.24 ± 16.5 (95)	.001
PCA given[a] (mg), median (range)	29.64 ± 10.25 (25)	58.24 ± 9.54 (58)	.001
Rescue analgesia[a] (mg), median (range)	2.37 ± 0.52 (2)	5.06 ± 1.0 (5)	.001
Total morphine consumption[a] (mg)	30.40 ± 9.92 (26)	61.72 ± 8.83 (62)	.001

PCA = patient-controlled analgesia.
[a] Mann-Whitney *U* test.

[b] Department of Cardiovascular Surgery, Baskent University Istanbul Training and Medical Research Center, Istanbul, Turkey

Table 4
MV time, CICU stay time, patient satisfaction, and adverse effects

	Group T (n = 25; morphine + tramadol)	Group P (n = 25; morphine + placebo)	*P*
MV time[a] (h), median (range)	6.2 ± 1.5 (6)	10.16 ± 2.4 (10)	.001**
Intensive care unit discharge time[a] (h), median (range)	49.4 ± 10.4 (48)	63.08 ± 10.7 (62)	.001**
Patient satisfaction[a], median (range)	3.76 ± 0.83 (4)	3.56 ± 0.65 (4)	.194
Adverse effects[b], n (%)			
Yes	7 (28)		.023*
No	18 (72)		

MV = mechanical ventilation; CICU = cardiac intensive care unit.
[a] Mann-Whitney *U* test.
[b] Continuity (Yates) correction.
* $P < .05$.
** $P < .01$.

Double-blind, RCT
CABG
PO Tramadol vs. placebo
↓ cumulative morphine requirements, ↓ VAS score

Opiates

- Morphine, diamorphine, synthetic opioids (fentanyl, alfentanil, remifentanil)
- Recommends *short-acting* (fentanyl, alfentanil), *ultrashort-acting* (remifentanil infusion) instead of morphine
  - *Less side effects (respiratory depression, nausea)*
- Routes: IV, intrathecal, epidural
- Used as adjuncts with local anesthesia in field blocks
- Patches used predominantly in chronic pain

REGIONAL ANESTHETICS

Regional anesthesia techniques

Table 2. Common Regional Analgesic Techniques

Techniques	Advantages	Disadvantages
Neuraxial		
Epidural	Less pain (vs systemic opioids); reduced cardiac/pulmonary morbidity; earlier return of GI tract function; catheter use can continue into the postoperative period	Epidural LA: hypotension; sensory deficits; motor weakness; urinary retention
		Epidural opioids: nausea; vomiting; pruritus; respiratory depression
		Technique related: backache; PDPH (spinal); neurologic injury; epidural hematoma
Spinal/intrathecal	Less pain; reduced systemic opioid requirements	Nausea; vomiting; pruritus; respiratory depression
Peripheral		
TAP block	Less pain; reduced systemic opioid requirements in the immediate postoperative period; typically performed under ultrasonographic guidance	Visceral pain; LA toxicity; perforation of the peritoneum with possible damage to visceral structures
Paravertebral block	Less pain; reduced systemic opioid requirements; lower risk of pulmonary complications for patients undergoing thoracotomy; catheter use can continue into the postoperative period; comparable levels of analgesia as epidural analgesia; less hypotension	Possible hypotension; vascular or pleural puncture; possible pneumothorax
Brachial plexus, sciatic/femoral nerve block	Less pain (vs systemic opioids); reduced systemic opioid requirements; catheter use can continue into the postoperative period	Not useful for abdominal or thoracic surgery; LA toxicity
Wound infiltration	Less pain and morphine consumption within the first few hours after surgery; easily administered by the surgeon	Uncertain long-term (≥24 h) analgesic efficacy

uctures

ravertebral block, or

ion -> paraplegia

CARDIOVASCULAR ANESTHESIA
SECTION EDITOR
KENNETH J. TUMAN

SOCIETY OF CARDIOVASCULAR ANESTHESIOLOGISTS

A Prospective Randomized Study of the Potential Benefits of Thoracic Epidural Anesthesia and Analgesia in Patients Undergoing Coronary Artery Bypass Grafting

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Adarsh B. Lal, FRCA*, John Norrie, MSc†, Werner J. B. Nagels, MD*, and
G. Pradeep Ramayya, FRCA*

Prospective, RCT
CABG
TEA vs. G/A only
↓postop. complications

Table 4. Unadjusted and Adjusted Odds Ratios for GA Versus TEA for Various Outcomes

Outcome	TEA (n = 206), n (%)	GA (n = 202), n (%)	Unadjusted		Adjusted[a]	
			OR (95% CI)	P value	OR (95% CI)	P value
Supraventricular arrhythmia	21 (10.2)	45 (22.3)	2.53 (1.44–4.42)	0.0012	2.56 (1.41–4.66)	0.0020
Lower respiratory tract infection	31 (15.3)	59 (29.2)	2.33 (1.43–3.79)	0.0007	2.06 (1.22–3.47)	0.0065
[illegible]	[illegible]	[illegible]	[illegible]	[illegible][b]	[illegible]	
CVA	2 (1.0)	6 (3.0)	3.12 (0.62–15.7)	0.17[b]	Not fitted[c]	
[illegible]	[illegible]	[illegible]	[illegible]	[illegible][b]	[illegible]	
Significant bleeding	35	23	0.63 (0.36–1.11)	0.11	0.52 (0.28–0.96)	0.035
Any complications	84	108	1.67 (1.13–2.47)	0.011	1.44 (0.95–2.19)	0.089

TEA = thoracic epidural analgesia; GA = general anesthesia; OR = odds ratio; CVA = cerebrovascular accident; CI = confidence interval.
[a] Data missing on some of the adjusted covariates for nine subjects.
[b] Fisher's exact tests.
[c] Adjusted model not fitted because of sparsity of events.

Journal of *Clinical Medicine*

MDPI

Article

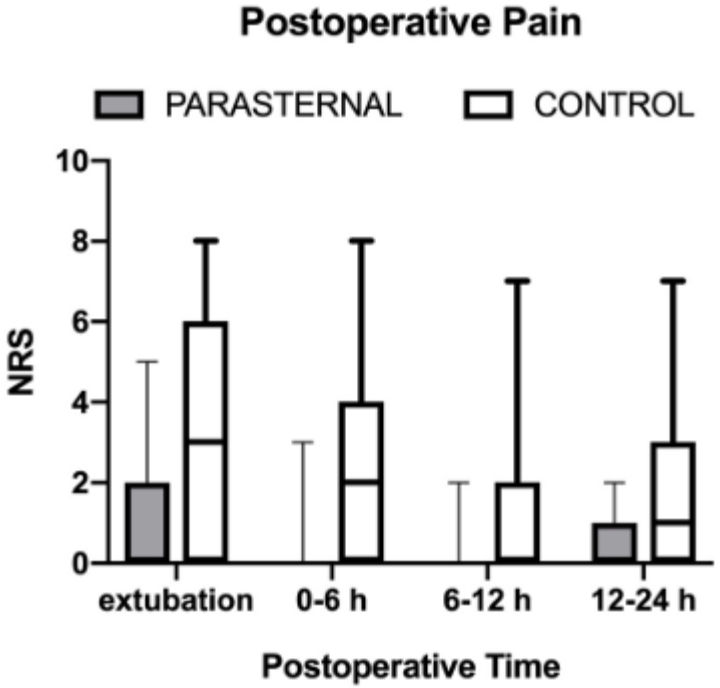
Ultrasound Guided Parasternal Block for Perioperative Analgesia in Cardiac Surgery: A Prospective Study

Giuseppe Pascarella [1], Fabio Costa [1], Giulia Nonnis [2], Alessandro Strumia [1,*], Domenico Sarubbi [1], Lorenzo Schiavoni [1], Annalaura Di Pumpo [1], Lara Mortini [1], Stefania Grande [1], Andrea Attanasio [3], Giovanni Gadotti [4], Alessandro De Cassai [5], Alessia Mattei [1], Antonio Nenna [6], Massimo Chello [6],

Table 2. Main Outcomes.

	Parasternal	Control	*p*-Value
Intraoperative fentanyl (γ)	406.3 ± 81.6	864.3 ± 154.4	**<0.001**
Postoperative pain (NRS max 0–10)			
Extubation	2 (0–4.5)	3 (0–6)	0.07
0–6 h	0 (0–3)	2 (0–4)	0.46
6–12 h	0 (0–2)	0 (0–2)	0.57
12–24 h	1 (0–2)	2 (0–3)	0.69
Postoperative opiates consumption			
Yes	19 (30%)	18 (29%)	0.8
No	44 (70%)	45 (71%)	
Time to first opioid (min)	30 (10–45)	30 (11–60)	0.6
Morphine consumption 0–24 h (mg)	0 (0–2)	0 (0–2)	>0.9

Values are expressed in mean ± standard deviation; median (interquartile range); number of patients (%); NRS (numeric rating scale).



SUCCESS WITH MULTIMODAL THERAPY

Key to Success with MMA

Education & Planning	1. Education of front-line providers and allied staff 2. Education of patients and families 3. Set realistic, specific goals 4. Quantitative pain assessments
Interventions	1. Multimodal analgesic strategy that targets different parts of pain pathways 2. Use of preemptive, scheduled non-opioid analgesics 3. Reginal anesthetic techniques 4. Minimize opioids 5. Nausea prophylaxis 6. Remove lines and tubes as soon as possible 7. Early extubation / early mobilization 8. Integration of pain management and recovery pathways into discharge planning
Continuous Improvement	1. Longitudinal data capture for program assessment 2. Obtain feedback from providers and patients to modify program

Take-Home Messages

- ***Optimizing postoperative pain*** control accelerates normalization of ***quality of life and functionality*** for patients.
- Inadequately treated acute pain can contribute to the ***development of chronic pain***
  - *in 20% of patients*
- ***Opioids*** are associated with the undesirable side effects of sedation, respiratory depression, nausea, vomiting, and ileus.
- ***Multimodal analgesia*** has emerged as an essential component of ***ERAS pathways***
  - *concurrent use of primarily* ***non-opioid analgesics***
  - *additive or synergistic, analgesic effect.*


Thank You
For Your Attention