

The effect of perioperative multimodal adjunct analgesics on postoperative pulmonary complications and opioid requirements: A retrospective cohort study

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INTRODUCTION

BACKGROUND

- Postoperative pain is a strong predictor of patient dissatisfaction, has been linked to prolonged hospitalization and higher risks of postoperative pulmonary complications (PPC) [1]
- Multimodal adjunct analgesics (MAA) target various nociceptive pathways, reducing opioid use, possibly lowering PPC risk [2,3]

HYPOTHESIS

- The use of perioperative MAA is associated with a lower risk of PPC, possibly mediated by lower perioperative opioid requirements.

METHODS

SETTING AND STUDY POPULATION

- 62,265 adults** undergoing non-ambulatory, non-emergent, non-cardiac surgery under **general anesthesia** with PACU admission (2014–2024, Beth Israel Deaconess Medical Center, Boston, Figure 1)

EXPOSURE

- MAA defined as ≥2 non-opioid analgesics** given perioperatively in preoperative holding area or operating room

OUTCOMES

- Primary: PPC**; composite of reintubation, emergency non-invasive ventilation and pneumonia ≤7 days
- Secondary: opioid requirements** intraoperatively and in PACU (presented in oral morphine equivalents OME) and **postextubation desaturation**

STATISTICAL ANALYSIS

- Multivariable logistic** and **zero-inflated negative binomial regression**, adjusted for patient, procedural, and anesthetic factors (Table 1)

67,154 Adult patients undergoing non-ambulatory, non-emergent, non-cardiac surgical or interventional procedures under general anesthesia with postoperative admission to the PACU at BIDMC between 2014 and 2024

4,409 Excluded for exclusion criteria *
2,712 ICU admission 7 days prior
1,692 Pneumonia 1 month prior
5 ASA > 4

480 Excluded for missing confounders *
358 Body mass index
61 Work relative value units
50 Hypotension below MAP 55
6 Sex
3 Reversal agent use
2 SPORC

Final study cohort (n = 62,265)

Figure 1. Study flow diagram

* multiple criteria may apply

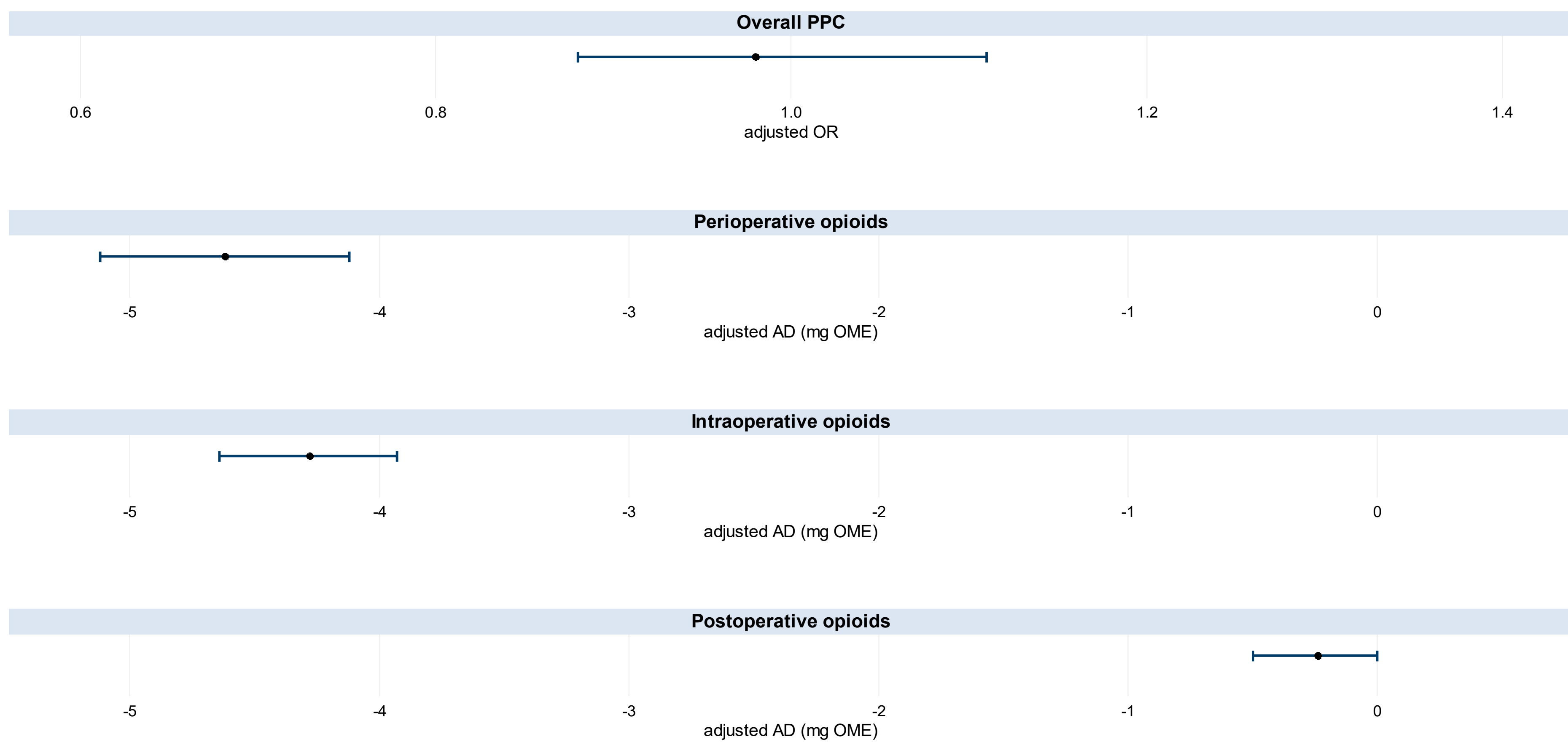


Figure 2. Primary and secondary results

Effect modifier	n	Adjusted AD (mg OME)	p
Age, years			
<65	36,654	-5.89 (-6.53 to -5.24)	< 0.001
≥65	25,611	-2.36 (-3.05 to -1.67)	< 0.001
ASA physical status classification			
ASA I - II	27,774	-6.72 (-7.48 to -5.95)	< 0.001
ASA III - IV	34,491	-3.10 (-3.71 to -2.50)	< 0.001
Elixhauser comorbidity score			
<5	3 (1- 5)	-5.61 (-6.27 to -4.95)	< 0.001
≥5	214 (0.6%)	-3.54 (-4.22 to -2.86)	< 0.001
Duration of surgery			
≥180 minutes	29,554	-5.84 (-6.53 to -5.14)	< 0.001
<180 minutes	32,711	-3.04 (-3.70 to -2.39)	< 0.001
Work relative value units			
≥17.4	31,155	-6.48 (-7.14 to -5.82)	< 0.001
<17.4	31,110	-2.66 (-3.34 to -1.97)	< 0.001

Table 2. Effect modification and linear combination analyses

CONCLUSION

MAA was associated with **reduced perioperative opioid requirements** and a decreased risk of **postextubation desaturation**, but not with overall PPC risk reduction. These effects were more pronounced in **selected procedures** and patient **subgroups**.

	No multimodal adjunct analgesia use (n=37,046)	Multimodal adjunct analgesia use (n=25,219)	Max. absolute standardized difference
Patient demographics and comorbidities			
Age, years	60.9 ± 16.4	56.9 ± 14.7	0.257
Sex, female	19,141 (51.7%)	15,157 (60.1%)	0.170
Body mass index, kg/m²	28.9 ± 6.9	29.4 ± 7	0.069
ASA physical status classification			0.268
ASA I - II	14,540 (39.2%)	13,234 (52.5%)	
ASA III - IV	22,506 (60.8%)	11,985 (47.5%)	
Elixhauser comorbidity score	6 (0 - 16)	4 (0 - 11)	0.245
SPORC	3 (1 - 5)	2 (0 - 4)	0.342
Covid19-Infection 1 month prior	214 (0.6%)	155 (0.6%)	0.005
Supplemental oxygen at home	3,689 (10.0%)	1,407 (5.6%)	0.164
Preoperative prescription of			
Opioids	8,103 (21.9%)	6,193 (24.6%)	0.064
Benzodiazepines	4,638 (12.5%)	3,727 (14.8%)	0.066
Antidepressants	13,576 (36.6%)	10,352 (41%)	0.090
Procedural characteristics			
Admission type			0.728
Sameday	23,310 (62.9%)	23,103 (91.6%)	
Inpatient	13,736 (37.1%)	2,116 (8.4%)	
Surgical Service			0.262
Robotic surgery	1,820 (4.9%)	3,044 (12.1%)	0.259
Laparoscopic surgery	6,591 (17.8%)	6,982 (27.7%)	0.238
Epidural anesthesia	2,300 (6.2%)	1,560 (6.2%)	0.001
Spinal anesthesia	53 (0.1%)	82 (0.3%)	0.038
Regional anesthesia	5,216 (14.1%)	4,534 (18.0%)	0.106
Use of perioperative benzodiazepines	20,750 (56%)	17,957 (71.2%)	0.320
High baseline pain score	8,282 (22.4%)	4,859 (19.3%)	0.076

Data are presented as n (%), median (interquartile range), or mean (standard deviation). Abbreviations: ASA, American Society of Anesthesiologists. SPORC, Score for Prediction of Postoperative Respiratory Complications

Table 1. Patient characteristics and distribution of variables

RESULTS

- No overall risk reduction of PPC (ORadj 0.98; 95%CI 0.88-1.11, p=0.79, Figure 2)
- Reduced requirements of perioperative opioids (excluding remifentanyl, Figure 2)
- Benefits were especially pronounced in younger and healthier patients as well as longer and more complex procedures (Table 2)
- Lower risk of postextubation desaturation (n= 46,061, ORadj 0.82; 95%CI 0.75 - 0.90; p< 0.001)

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REFERENCES

[1] Anesthesiology. 2024;140(4):657-667.

[2] Anesth Analg. 1991; 72(1):58-61.

[3] J Med Primatol. 2012;41(4):251-5.

