INTRAOPERATIVE TEACHING

ACE Inhibitors and ARBs Before Surgery

Intraoperative teaching · CA-1

THE QUESTION

Where the evidence disagrees

This topic was selected because an evidence synthesis beats a textbook on it: the trials disagree, or the guidance has moved recently.

THE EVIDENCE

What each source contributes, and how strong it is

Study design first — a cohort and a randomised trial do not carry the same weight.

Design	Year	Journal	What it found
Meta-analysis	2025	Annals of medicine	Pooling 14 randomised trials, withholding ACE inhibitors or ARBs cut intraoperative
Randomised trial	2024	JAMA	Continuing renin-angiotensin system inhibitors to the day of surgery gave the same
Cohort	2017	Anesthesiology	In a 4,802-patient cohort, withholding an ACE inhibitor or ARB in the 24 hours
Review	1992	Journal of cardiovascular pharmaco	ACE inhibitors attenuate sympathetic neurotransmission, particularly when endogenous
Meta-analysis	2024	Journal of clinical anesthesia	Across 16 studies and 59,105 patients, withholding RAAS inhibitors lowered
Randomised trial	2024	British journal of anaesthesia	In patients whose preoperative NT-proBNP was below 100 pg/mL, stopping RAS

6 resolved citations behind this deck; every point above traces to one of them.

WHERE THE GUIDANCE SITS

What the guidelines and pooled evidence say

2 findings, each on the slide that follows.

ANNALS OF MEDICINE 2025

Pooling 14 randomised trials, withholding ACE inhibitors or ARBs cut intraoperative

Pooling 14 randomised trials, withholding ACE inhibitors or ARBs cut intraoperative hypotension from 48% to 36% and reduced vasopressor use

JOURNAL OF CLINICAL ANESTHESIA 2024

Across 16 studies and 59,105 patients, withholding RAAS inhibitors lowered

Across 16 studies and 59,105 patients, withholding RAAS inhibitors lowered intraoperative hypotension and acute kidney injury but made no significant…

WHERE THE GUIDANCE SITS

Pooling 14 randomised trials, withholding ACE inhibitors or ARBs cut intraoperative

Meta-analysis · Annals of medicine

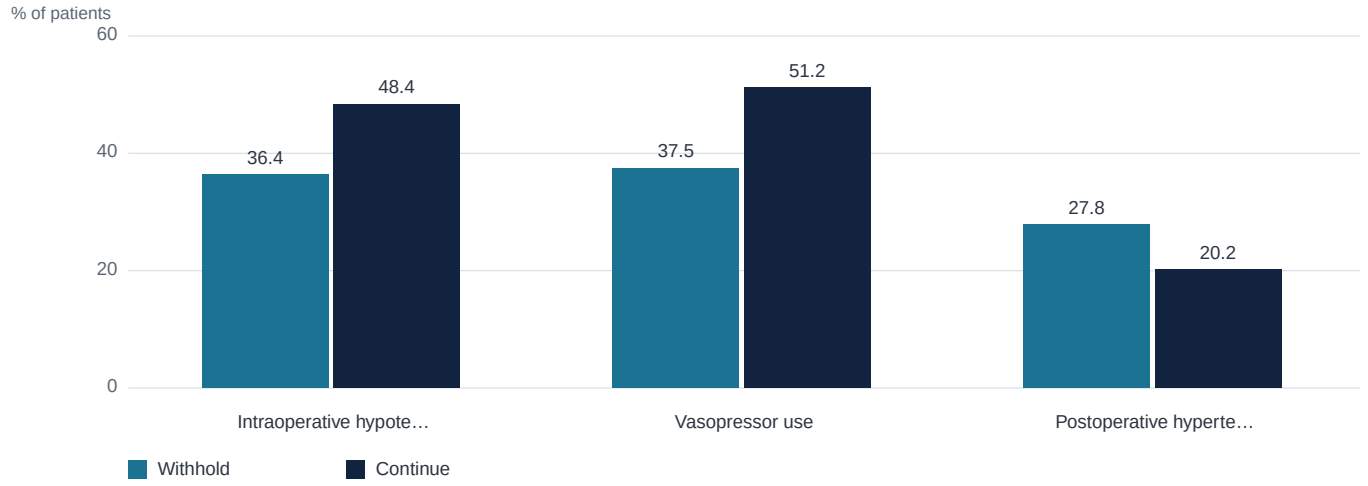
Pooling 14 randomised trials, withholding ACE inhibitors or ARBs cut intraoperative hypotension from 48% to 36% and reduced vasopressor use, but raised postoperative hypertension from 20% to 28%, on very low certainty evidence.

Withholding vs. Continuing Angiotensin-Converting Enzyme Inhibitors or Angiotensin Receptor Blockers Before Surgery: A Systematic Review and Meta-Analysis of Randomized Controlled Trials, Annals of medicine 2025 · PMID 41017370

THE NUMBERS

Withholding reduces hypotension but raises rebound hypertension

Pooled across 14 randomised trials, 4,063 patients.



Withholding buys a calmer induction and costs a higher postoperative pressure.

Withholding vs. Continuing Angiotensin-Converting Enzyme Inhibitors or Angiotensin Receptor Blockers Before Surgery: A Systematic Review and Meta-Analysis of Randomized Controlled Trials, Annals of medicine 2025 · PMID 41017370

WHERE THE GUIDANCE SITS

Across 16 studies and 59,105 patients, withholding RAAS inhibitors lowered

Meta-analysis · Journal of clinical anesthesia

Across 16 studies and 59,105 patients, withholding RAAS inhibitors lowered intraoperative hypotension and acute kidney injury but made no significant difference to mortality, major cardiac events, infarction or stroke.

Continuation Versus Discontinuation of Renin-Angiotensin Aldosterone System Inhibitors Before Non-Cardiac Surgery: A Systematic Review and Meta-Analysis, Journal of clinical anesthesia 2024 · PMID 39531998

WHAT THE TRIALS FOUND

Where randomised evidence moved the question

2 findings, each on the slide that follows.

JAMA 2024

Continuing renin-angiotensin system inhibitors to the day of surgery gave the same

Continuing renin-angiotensin system inhibitors to the day of surgery gave the same rate of death and major complications at 28 days as stopping them…

BRITISH JOURNAL OF ANAESTHESIA 2024

In patients whose preoperative NT-proBNP was below 100 pg/mL, stopping RAS

In patients whose preoperative NT-proBNP was below 100 pg/mL, stopping RAS inhibitors before surgery raised myocardial injury from 23% to 40% — the…

WHAT THE TRIALS FOUND

Continuing renin-angiotensin system inhibitors to the day of surgery gave the same

Randomised trial · JAMA

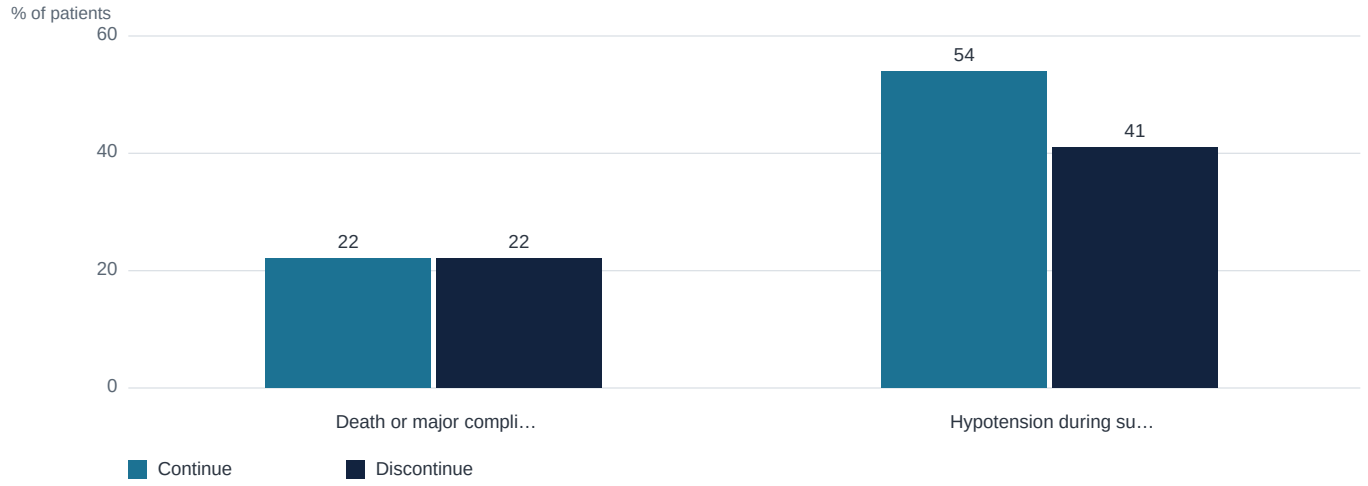
Continuing renin-angiotensin system inhibitors to the day of surgery gave the same rate of death and major complications at 28 days as stopping them 48 hours before (22% in each arm), but hypotension during surgery rose from 41% to 54%.

Continuation vs Discontinuation of Renin-Angiotensin System Inhibitors Before Major Noncardiac Surgery, JAMA 2024 · PMID 39212270

THE NUMBERS

STOP-or-NOT: same outcomes, more hypotension

Continuing versus stopping 48 hours before major noncardiac surgery.



Outcomes were identical; only intraoperative hypotension differed. That is the whole result.

Continuation vs Discontinuation of Renin-Angiotensin System Inhibitors Before Major Noncardiac Surgery, JAMA 2024 · PMID 39212270

WHAT THE TRIALS FOUND

In patients whose preoperative NT-proBNP was below 100 pg/mL, stopping RAS

Randomised trial · British journal of anaesthesia

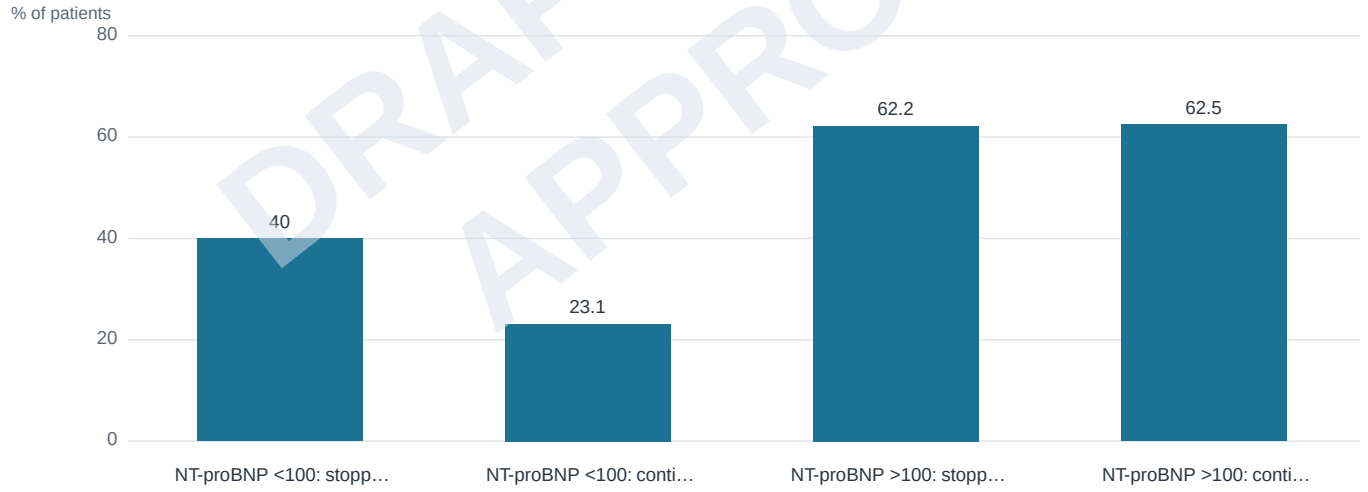
In patients whose preoperative NT-proBNP was below 100 pg/mL, stopping RAS inhibitors before surgery raised myocardial injury from 23% to 40% — the harm of stopping is not uniform across risk groups.

Preoperative N-Terminal Pro-B-Type Natriuretic Peptide and Myocardial Injury After Stopping or Continuing Renin-Angiotensin System Inhibitors in Noncardiac Surgery: A Prespecified Analysis of a Phase 2 Randomised Controlled Multicentre Trial, British journal of anaesthesia 2024 · PMID 38341283

THE NUMBERS

In lower-risk patients, stopping caused the harm

Myocardial injury by preoperative NT-proBNP stratum.



The direction reverses by risk stratum — in the low-NT-proBNP group, stopping nearly doubled myocardial injury.

Preoperative N-Terminal Pro-B-Type Natriuretic Peptide and Myocardial Injury After Stopping or Continuing Renin-Angiotensin System Inhibitors in Noncardiac Surgery: A Prespecified Analysis of a Phase 2 Randomised Controlled Multicentre Trial, British journal of anaesthesia 2024 · PMID 38341283

IN PRACTICE

What the cohorts and reviews add

2 findings, each on the slide that follows.

ANESTHESIOLOGY 2017

In a 4,802-patient cohort, withholding an ACE inhibitor or ARB in the 24 hours

In a 4,802-patient cohort, withholding an ACE inhibitor or ARB in the 24 hours before noncardiac surgery was associated with a lower risk of the…

JOURNAL OF CARDIOVASCULAR PHARMACOLOGY 1992

ACE inhibitors attenuate sympathetic neurotransmission, particularly when endogenous

ACE inhibitors attenuate sympathetic neurotransmission, particularly when endogenous renin-angiotensin activity is high.

IN PRACTICE

In a 4,802-patient cohort, withholding an ACE inhibitor or ARB in the 24 hours

Cohort · Anesthesiology

In a 4,802-patient cohort, withholding an ACE inhibitor or ARB in the 24 hours before noncardiac surgery was associated with a lower risk of the composite of death, stroke or myocardial injury at 30 days.

Withholding Versus Continuing Angiotensin-Converting Enzyme Inhibitors or Angiotensin II Receptor Blockers Before Noncardiac Surgery: An Analysis of the Vascular Events in Noncardiac Surgery patIents cOhort evaluatioN Prospective Cohort, Anesthesiology 2017 · PMID 27775997

IN PRACTICE

ACE inhibitors attenuate sympathetic neurotransmission, particularly when endogenous

Review · Journal of cardiovascular pharmaco

ACE inhibitors attenuate sympathetic neurotransmission, particularly when endogenous renin-angiotensin activity is high.

Interaction Between the Renin-Angiotensin-Aldosterone and Sympathetic Nervous Systems, Journal of cardiovascular pharmacology 1992 · PMID 1382170

IN THE ROOM

What this changes about the next case

Colour is the strength of the evidence behind each step, not the urgency.

1. **1**
   Pooling 14 randomised trials, withholding ACE inhibitors or ARBs cut intraoperative hypotension from 48% to 36% and reduced vasopressor use, but raised postoperative hypertension from 20% to 28%, on very low certainty evidence.
2. **2**
   Across 16 studies and 59,105 patients, withholding RAAS inhibitors lowered intraoperative hypotension and acute kidney injury but made no significant difference to mortality, major cardiac events, infarction or stroke.
3. **3**
   Continuing renin-angiotensin system inhibitors to the day of surgery gave the same rate of death and major complications at 28 days as stopping them 48 hours before (22% in each arm), but hypotension during surgery rose from 41% to 54%.
4. **4**
   In patients whose preoperative NT-proBNP was below 100 pg/mL, stopping RAS inhibitors before surgery raised myocardial injury from 23% to 40% — the harm of stopping is not uniform across risk groups.
5. **5**
   In a 4,802-patient cohort, withholding an ACE inhibitor or ARB in the 24 hours before noncardiac surgery was associated with a lower risk of the composite of death, stroke or myocardial injury at 30 days.

KEY TAKEAWAYS

What to carry into the next case

Pooling 14 randomised trials, withholding ACE inhibitors or ARBs cut intraoperative
Annals of medicine 2025

Continuing renin-angiotensin system inhibitors to the day of surgery gave the same
JAMA 2024

In a 4,802-patient cohort, withholding an ACE inhibitor or ARB in the 24 hours
Anesthesiology 2017

ACE inhibitors attenuate sympathetic neurotransmission, particularly when endogenous
Journal of cardiovascular pharmacology 1992

Pooling 14 randomised trials, withholding ACE inhibitors or ARBs cut intraoperative

QUESTIONS I'LL ASK YOU IN THE ROOM

1. Walk me through your setup for this before we start.
2. What are you watching on the monitor that would tell you this is going wrong?
3. What is your first move if it does?
4. What would you want ready in the room before induction?

ORAL BOARDS STEM

> *A 61-year-old on lisinopril for hypertension arrives for laparoscopic cholecystectomy having taken her morning dose. After induction the MAP falls to 52 mmHg and responds poorly to phenylephrine.*

BOARD QUESTIONS

1. In the randomised trial comparing continuing renin-angiotensin system inhibitors up to the day of major noncardiac surgery against stopping them 48 hours beforehand, what happened to the 28-day rate of death and major complications, and what happened to the rate of intraoperative hypotension? Give the approximate numbers for each arm.

2. A meta-analysis of randomised trials examined withholding versus continuing ACE inhibitors or ARBs before surgery. Withholding them reduces intraoperative hypotension. State the price you pay postoperatively for that benefit, with approximate rates, and say how confident the pooled evidence lets you be.

3. Beyond blocking angiotensin II formation, ACE inhibitors have an effect on sympathetic neurotransmission. Describe that effect and name the circumstance in which it is most pronounced.

4. A prospective cohort of 4,802 patients found that withholding an ACE inhibitor or ARB in the 24 hours before noncardiac surgery was associated with a lower risk of the 30-day composite of death, stroke or myocardial injury. Explain to a junior resident what this study design does NOT establish, and how you would phrase the finding accurately.

ANSWER KEY

1. Death and major complications at 28 days were the same in both arms, about 22% each. Intraoperative hypotension differed: it rose from 41% in the discontinuation arm to 54% when the inhibitor was continued to the day of surgery.

The trial shows continuing these drugs buys you more intraoperative hypotension without changing 28-day death or major complications.

Continuation vs Discontinuation of Renin-Angiotensin System Inhibitors Before Major Noncardiac Surgery, JAMA 2024 · PMID 39212270

2. Withholding cut intraoperative hypotension from about 48% to 36% and reduced vasopressor use, but the trade-off is more postoperative hypertension, rising from about 20% to 28%. The pooled evidence across those 14 randomised trials was rated very low certainty, so the estimates are weak and should not be treated as settled.

Withholding trades an intraoperative problem for a postoperative one, and at very low certainty the size of both effects is uncertain.

Withholding vs. Continuing Angiotensin-Converting Enzyme Inhibitors or Angiotensin Receptor Blockers Before Surgery: A Systematic Review and Meta-Analysis of Randomized Controlled Trials, Annals of medicine 2025 · PMID 41017370

3. ACE inhibitors attenuate sympathetic neurotransmission, and this attenuation is particularly evident when endogenous renin-angiotensin activity is high.

That is why the hypovolaemic, high-renin patient on an ACE inhibitor loses not just angiotensin support but sympathetic support as well.

Interaction Between the Renin-Angiotensin-Aldosterone and Sympathetic Nervous Systems, Journal of cardiovascular pharmacology 1992 · PMID 1382170

4. It is a cohort analysis, so the finding is an association between withholding and a lower risk of the 30-day composite of death, stroke or myocardial injury, not a demonstration that withholding causes the improvement. Patients whose drug was withheld may differ systematically from those whose drug was continued, and the design cannot exclude that. The accurate phrasing is that withholding was associated with a lower risk of that composite at 30 days, not that withholding reduces it or should be routinely done.

Say the word association out loud when you quote this cohort, because that is exactly as far as the design will carry you.

Withholding Versus Continuing Angiotensin-Converting Enzyme Inhibitors or Angiotensin II Receptor Blockers Before Noncardiac Surgery: An Analysis of the Vascular Events in Noncardiac Surgery patIents cOhort evaluatioN Prospective Cohort, Anesthesiology 2017 · PMID 27775997

Pooling 14 randomised trials, withholding ACE inhibitors or ARBs cut intraoperative

SOURCES

[1] Withholding vs. Continuing Angiotensin-Converting Enzyme Inhibitors or Angiotensin Receptor Blockers Before Surgery: A Systematic Review and Meta-Analysis of Randomized Controlled Trials, Annals of medicine 2025 · PMID 41017370

[2] Continuation vs Discontinuation of Renin-Angiotensin System Inhibitors Before Major Noncardiac Surgery, JAMA 2024 · PMID 39212270
[3] Withholding Versus Continuing Angiotensin-Converting Enzyme Inhibitors or Angiotensin II Receptor Blockers Before Noncardiac Surgery: An Analysis of the Vascular Events in Noncardiac Surgery patIents cOhort evaluatioN Prospective Cohort, Anesthesiology 2017 · PMID 27775997
[4] Interaction Between the Renin-Angiotensin-Aldosterone and Sympathetic Nervous Systems, Journal of cardiovascular pharmacology 1992 · PMID 1382170
[5] Continuation Versus Discontinuation of Renin-Angiotensin Aldosterone System Inhibitors Before Non-Cardiac Surgery: A Systematic Review and Meta-Analysis, Journal of clinical anesthesia 2024 · PMID 39531998
[6] Preoperative N-Terminal Pro-B-Type Natriuretic Peptide and Myocardial Injury After Stopping or Continuing Renin-Angiotensin System Inhibitors in Noncardiac Surgery: A Prespecified Analysis of a Phase 2 Randomised Controlled Multicentre Trial, British journal of anaesthesia 2024 · PMID 38341283