

Separation from Cardiopulmonary Bypass

Intraoperative teaching · CA-3

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.

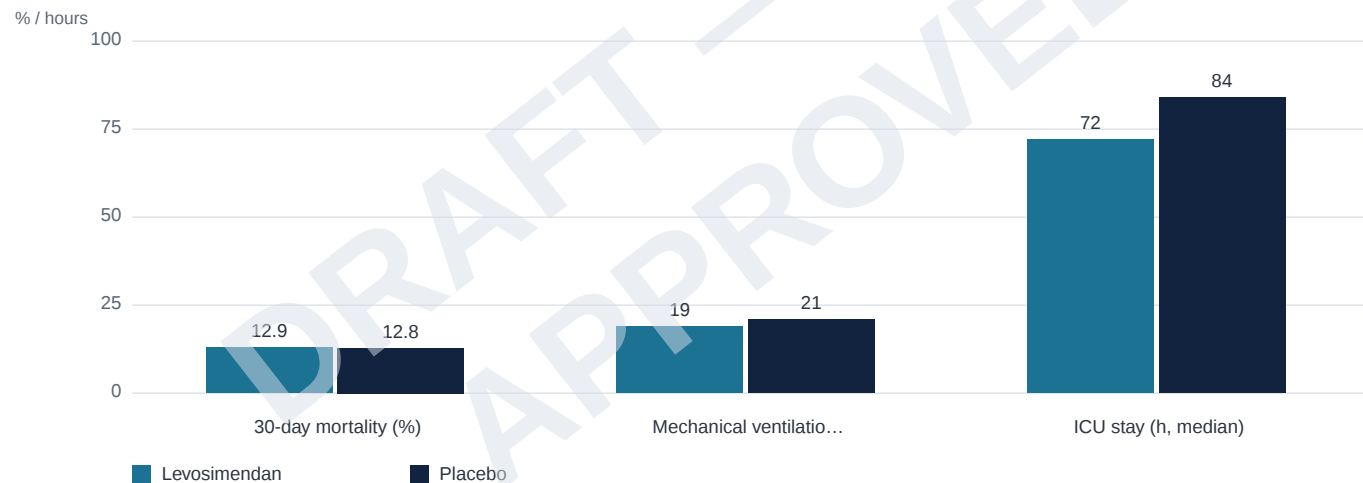
Design	Year	Journal	What it found
Other	2020	Journal of cardiothoracic and vasc	Complex CPB separation needs prompt diagnosis/treatment
Other	1997	Journal of anesthesia	Pre-CPB RWMA predicts post-CPB inotrope need

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

THE NUMBERS

Levosimendan did not buy a mortality advantage over standard support

Reach for it to come off bypass, not to change how the patient does at 30 days.



Stopped for futility at 506 patients. Mortality was identical; ventilation and ICU time were not significantly different either. It is a weaning drug, not an outcome drug.

CHEETAH, NEJM 2017 · PMID 28320259

IN PRACTICE

What the cohorts and reviews add

2 findings, each on the slide that follows.

JOURNAL OF CARDIOTHORACIC AND VASCULAR ANESTHESIA 2020

Complex CPB separation needs prompt diagnosis/treatment

Complex CPB separation, potentially leading to poor outcomes if untreated, requires prompt diagnosis and therapeutic decisions within minutes.

Pre-CPB RWMA predicts post-CPB inotrope need

Pre-CPB left ventricular regional wall motion abnormalities (RWMA) predict the need for inotropic support during weaning from CPB in CABG patients.

IN PRACTICE

Complex CPB separation needs prompt diagnosis/treatment

Other · Journal of cardiothoracic and vasc

Complex CPB separation, potentially leading to poor outcomes if untreated, requires prompt diagnosis and therapeutic decisions within minutes.

Management of Challenging Cardiopulmonary Bypass Separation, Journal of cardiothoracic and vascular anesthesia 2020 · PMID 32276758

IN PRACTICE

Pre-CPB RWMA predicts post-CPB inotrope need

Other · Journal of anesthesia

Pre-CPB left ventricular regional wall motion abnormalities (RWMA) predict the need for inotropic support during weaning from CPB in CABG patients.

Predictors of inotropic support during weaning from cardiopulmonary bypass in coronary artery bypass grafting surgery, Journal of anesthesia 1997 · PMID 28921261

INDICATIONS

When this is the right block

MANAGEMENT OF CHALLENGING CARDIOPULMONARY BYPASS SEPARATION, J CARDIOTHORAC VASC ANESTH 2020

Transoesophageal echocardiography as the instrument of the decision

Separation from bypass is a progressive transition from full mechanical support back to the patient's own heart and lungs, and measurements of cardiac performance by transoesophageal echocardiography provide the rationale behind the diagnostic and therapeutic decisions taken in those minutes.

PREDICTORS OF INOTROPE USE DURING SEPARATION FROM CPB, J CARDIOTHORAC VASC ANESTH 2004

Predict the difficult separation before the clamp comes off

In 1009 patients having coronary bypass or combined coronary and valve surgery with pre-bypass transoesophageal echocardiography, inotropic support was used at separation in 39%, and six independent predictors emerged: wall motion score index, combined bypass and mitral surgery, ejection fraction below 35%, reoperation, moderate-to-severe mitral regurgitation, and aortic cross-clamp time.

ACUTE RIGHT VENTRICULAR FAILURE DURING CPB SEPARATION, J CARDIOTHORAC VASC ANESTH 2019

Right ventricular failure at separation, treated as its own emergency

In 176 patients treated with a 5 mg intratracheal milrinone bolus for unexpected acute right ventricular failure during separation, the failure improved in 61.9% and persisted in 38.1%; severely reduced left ventricular ejection fraction below 35% (adjusted OR 3.72), longer bypass time and elevated postoperative fluid balance predicted persistence.

CONTRAINDICATIONS

When it is not

HEMODYNAMIC CHANGES AFTER PROTAMINE AND MORTALITY AFTER CABG, ANESTHESIOLOGY 2005

Dismissing a protamine reaction as a transient wobble

Across 6921 coronary bypass patients, the degree and duration of systemic hypotension and pulmonary hypertension in the 30 minutes after protamine were independently associated with in-hospital mortality — odds ratios of 1.28 and 1.27 per 150 mmHg·min increment — and the association held even at the lowest observed range of values.

PERIOPERATIVE PROTAMINE REACTIONS IN PATIENTS WITH FISH ALLERGIES, J CARDIOTHORAC VASC ANESTH 2024

Withholding protamine because of a fish allergy

Among 214 adults with documented fish allergy who received protamine — median heparin dose 46,000 IU, median protamine dose 310 mg — two cases (under 1%) of anaphylaxis or protamine reaction occurred. Cross-reactivity is unlikely, and the authors do not recommend avoiding protamine on the basis of fish allergy alone when heparin reversal is required.

INHALED MILRINONE IN HIGH-RISK CARDIAC SURGERY RCT, CAN J ANAESTH 2016

Expecting prophylactic inhaled milrinone to make the separation easy

In 124 high-risk cardiac surgical patients with pulmonary hypertension, inhaled milrinone before bypass raised cardiac output and lowered systolic pulmonary artery pressure without systemic hypotension, but did not change the combined incidence of difficult or complex separation (30% versus 28%) or right ventricular failure (15% versus 14%). Mortality was 22% in patients with right ventricular failure versus 2% without.

Treating methylene blue for vasoplegia as established therapy

A meta-analysis of 11 randomised trials in 556 critically ill and perioperative patients found lower mortality with methylene blue (RR 0.60, 95% CI 0.43 to 0.84), higher mean arterial pressure (+8.4 mmHg) and higher systemic vascular resistance, with no change in cardiac output — on a total sample small enough that the authors call for adequately powered trials before the finding is relied on.

PEARLS

What experience adds

ANTIBODIES TO PROTAMINE AND PROTAMINE/HEPARIN COMPLEXES, BLOOD 2013

Most bypass patients make antibodies to protamine

In specimens from a 500-patient prospective trial, 29% of cardiopulmonary bypass patients developed antibodies to protamine/heparin complexes. They were high-titre, showed heparin-dependent binding, activated platelets in the presence of protamine, and cross-reacted with protamine-containing insulin preparations — though with no circulating antigen at day 30 there were no thrombocytopenic or thrombotic complications.

MANAGEMENT OF CHALLENGING CARDIOPULMONARY BYPASS SEPARATION, J CARDIOTHORAC VASC ANESTH 2020

There is no guideline for this

No specific criteria defining a complex separation from bypass and no management guidelines currently exist, which is why the review that names the common scenarios also had to describe the routine strategies of 17 large cardiac centres across 14 countries and five continents to say what usual practice is.

Say the separation plan out loud before the clamp comes off

Rhythm, rate, filling, contractility, who is on the echo, who is on the pressure, and what each of you will call out. The minutes after separation are the wrong time for anyone in the room to be inferring the plan from what you happen to be doing.

IN THE ROOM

What this changes about the next case

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

- 1**
Complex CPB separation, potentially leading to poor outcomes if untreated, requires prompt diagnosis and therapeutic decisions within minutes.
- 2**
Pre-CPB left ventricular regional wall motion abnormalities (RWMA) predict the need for inotropic support during weaning from CPB in CABG patients.

KEY TAKEAWAYS

What to carry into the next case

Complex CPB separation needs prompt diagnosis/treatment

Journal of cardiothoracic and vascular anesthesia 2020

Pre-CPB RWMA predicts post-CPB inotrope need

Journal of anesthesia 1997

Recognize pre-CPB RWMA as a predictor for post-CPB hemodynamic instability; address complex separations rapidly.

QUESTIONS I'LL ASK YOU IN THE ROOM

1. What are the key hemodynamic changes expected immediately after CPB separation?
2. How does the patient's acid-base status influence post-CPB management?
3. What strategies can be employed to manage potential arrhythmias following CPB weaning?
4. How do you assess and address potential myocardial dysfunction after coming off bypass?

ORAL BOARDS STEM

A 71-year-old is being weaned from bypass after three-vessel CABG. The heart is slow to eject, and TEE shows a dilated, poorly contracting left ventricle.

BOARD QUESTIONS

1. In the CHEETAH trial of low-dose levosimendan for patients requiring perioperative haemodynamic support after cardiac surgery, what happened to 30-day mortality?
 - A. No significant difference: 12.9% versus 12.8%
 - B. A significant reduction: 8.1% versus 12.8%
 - C. A significant increase: 18.4% versus 12.8%
 - D. The trial was too small to report mortality
2. CHEETAH was stopped for futility. What does that specifically mean, and how is it different from a trial stopped for harm or one that simply reports a negative result?
3. Besides mortality, which secondary outcomes did CHEETAH examine, and what did they show?

ANSWER KEY

1. A. No significant difference: 12.9% versus 12.8%

The trial was stopped for futility after 506 patients, and duration of mechanical ventilation, ICU stay and hospital stay showed no significant differences either. CHEETAH failed to demonstrate improved outcomes; that is not the same as proving levosimendan has no effect.

CHEETAH trial, NEJM 2017 · PMID 28320259

2. Stopping for futility means a preplanned interim analysis showed that continuing to the planned sample size was very unlikely to demonstrate the hypothesised benefit — so further enrolment would expose patients to an intervention and a trial burden with no realistic prospect of a positive answer. It is not a finding of harm; CHEETAH found no significant difference in rates of hypotension or cardiac arrhythmias either. It differs from an ordinary negative trial in that the confidence intervals are wider than planned, so it is better read as failing to demonstrate benefit than as proving equivalence.

Futility stopping limits what you can conclude in both directions. It is evidence against a large benefit, not proof of no effect.

CHEETAH trial, NEJM 2017 · PMID 28320259

3. Duration of mechanical ventilation (median 19 hours with levosimendan versus 21 with placebo), ICU stay (median 72 versus 84 hours) and hospital stay (median 14 versus 14 days). None reached statistical significance, although the ICU stay difference of -12 hours had a confidence interval of -21 to 2 hours and a P value of 0.09, which is the kind of near-miss that gets over-quoted.

A P of 0.09 on a secondary outcome in a trial stopped for futility is a hypothesis, not a finding.

CHEETAH trial, NEJM 2017 · PMID 28320259

Recognize pre-CPB RWMA as a predictor for post-CPB hemodynamic instability; address complex separations rapidly.

SOURCES

- [1] Management of Challenging Cardiopulmonary Bypass Separation, Journal of cardiothoracic and vascular anesthesia 2020 · PMID 32276758
- [2] Predictors of inotropic support during weaning from cardiopulmonary bypass in coronary artery bypass grafting surgery, Journal of anesthesia 1997 · PMID 28921261
- [3] CHEETAH, NEJM 2017 · PMID 28320259
- [4] Predictors of inotrope use during separation from CPB, J Cardiothorac Vasc Anesth 2004 · PMID 15365918
- [5] Acute right ventricular failure during CPB separation, J Cardiothorac Vasc Anesth 2019 · PMID 30683595
- [6] Hemodynamic changes after protamine and mortality after CABG, Anesthesiology 2005 · PMID 15681944
- [7] Perioperative protamine reactions in patients with fish allergies, J Cardiothorac Vasc Anesth 2024 · PMID 39261207
- [8] Inhaled milrinone in high-risk cardiac surgery RCT, Can J Anaesth 2016 · PMID 27470232
- [9] Methylene blue in critically ill and perioperative patients meta-analysis, J Cardiothorac Vasc Anesth 2024 · PMID 37880041
- [10] Antibodies to protamine and protamine/heparin complexes, Blood 2013 · PMID 23422751