

Perioperative assessment and management of cardiovascular risk

Have we reached a consensus?

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DISCLOSURE STATEMENT

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Edwards Lifesciences
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Laboratoire Aggretant

Perioperative cardiac events are common

Incidence and predictors of major perioperative adverse cardiac and cerebrovascular events in non-cardiac surgery

Sabate S et al.

British Journal of Anaesthesia **107** (6): 879–90 (2011)

4.3%
MACCE

Effects of extended-release metoprolol succinate in patients undergoing non-cardiac surgery (POISE trial): a randomised controlled trial

POISE Study Group*

Lancet 2008; 371: 1839–47

≈6.5%
CV death/MICA

Aspirin in Patients Undergoing Noncardiac Surgery

Devereaux PJ et al.

N Engl J Med 2014;370:1494-503.

≈7%
Death or MI

Myocardial Injury after Noncardiac Surgery

The Vascular events In noncardiac Surgery patients cOhort evaluation (VISION) Writing Group, on behalf of The Vascular events In noncardiac Surgery patients cOhort evaluation (VISION) Investigators

(ANESTHESIOLOGY 2014; 120:564-78)

8% MINS
3.6% MACE

ISOS

International Surgical Outcomes Study



British Journal Of Anaesthesia, 117 (5): 601–9 (2016)

BJA

The International Surgical Outcomes Study group

- Cardiovascular complications 4.5%
- 3rd most common
- Mortality in this group 6.9% (0.5% in whole cohort)

Perioperative myocardial injury and MINS

Myocardial Injury after Noncardiac Surgery

A Large, International, Prospective Cohort Study Establishing Diagnostic Criteria, Characteristics, Predictors, and 30-day Outcomes
[ANESTHESIOLOGY 2014; 120:564-78](#)

The Vascular events In noncardiac Surgery patients cOhort evaluation (VISION) Writing Group, on behalf of The Vascular events In noncardiac Surgery patients cOhort evaluation (VISION) Investigators

JAMA | **Original Investigation**

Association of Postoperative High-Sensitivity Troponin Levels With Myocardial Injury and 30-Day Mortality Among Patients Undergoing Noncardiac Surgery

Writing Committee for the VISION Study Investigators

[JAMA. 2017;317\(16\):1642-1651. doi:10.1001/jama.2017.4360](#)

ORIGINAL RESEARCH ARTICLE

Perioperative Myocardial Injury After Noncardiac Surgery

Incidence, Mortality, and Characterization

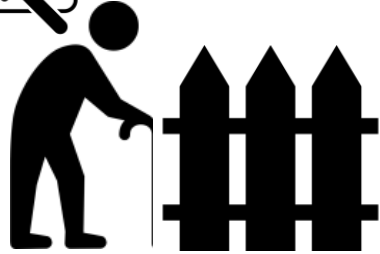
Puelacher C et al. *Circulation*. 2018;137:1221–1232.

MINS and PMI

- Previously unrecognised cardiovascular complication
- Occurs commonly (up to approx. 20%)
- Does not require ischaemic feature
- Largely asymptomatic:
 - VISION (2014) study: 85% of patients without ischaemic symptoms
 - Puelacher (2018): 82% without ischaemic symptoms
 - Chew (2021): >90% asymptomatic
- Independently associated with short- and long-term mortality, short-term complications, short- and long-term MACE

How to protect the heart?

What is the risk?
Risk of what?



Informed consent, shared decision-making
Tailored perioperative management



Risk re-assessment
Early detection
Management of complications



Prevent/detect

- Perioperative myocardial injury/infarction
- Acute heart failure
- Arrhythmias
- Stroke



Avoidance of
failure to rescue

Recognition of high-risk patients

Revised Cardiac Risk Index

NSQIP-MICA

Risk Factors	Points
History of ischemic heart disease	1
High-risk type of surgery	1
History of congestive heart failure	1
History of cerebrovascular disease	1
Preoperative treatment with insulin	1
Preoperative serum creatinine >2.0 mg/dL	1

Table 2. Total RCRI score and corresponding risk of myocardial infarction, cardiac arrest, or death at 30 days after noncardiac surgery*

Total RCRI points	Risk estimate, %	95% CI for the risk estimate
0	3.9	2.8%-5.4%
1	6.0	4.9%-7.4%
2	10.1	8.1%-12.6%
≥3	15.0	11.1%-20.0%

Gupta Perioperative Risk for Myocardial Infarction or Cardiac Arrest (MICA) ☆

Predicts risk of MI or cardiac arrest after surgery.

INSTRUCTIONS

Use within 30 days of surgery (pre- or postoperatively). May be used in cardiac or noncardiac procedures.

When to Use ▾

Pearls/Pitfalls ▾

Why Use ▾

Age

65

years

Functional status

Independent

Partially dependent

Totally dependent

ASA class

1: normal healthy patient

2: mild systemic disease

3: severe systemic disease

4: severe systemic disease that is a constant threat to life (i.e., patient could die acutely without intervention)

5: moribund, not expected to survive without surgery

Creatinine

Normal (≤1.5 mg/dL, 133 μmol/L)

Elevated (>1.5 mg/dL, 133 μmol/L)

Unknown

Type of procedure

Intestinal ▾

0.8 %

Risk of myocardial infarction or cardiac arrest, intraoperatively or up to 30 days post-op

Copy Results 📄

Next Steps ➡️



Do biomarkers add to risk stratification?

GUIDELINES

Pre-operative evaluation of adults undergoing elective noncardiac surgery

Updated guideline from the European Society of Anaesthesiology

Eur J Anaesthesiol 2018; **35**:407–465

We recommend that pre-operative measurements of natriuretic peptides be used for risk stratification in intermediate or high-risk patients undergoing vascular or major thoracic surgery (1C)

Annals of Internal Medicine®

Preoperative *N*-Terminal Pro-B-Type Natriuretic Peptide and Cardiovascular Events After Noncardiac Surgery: A Cohort Study

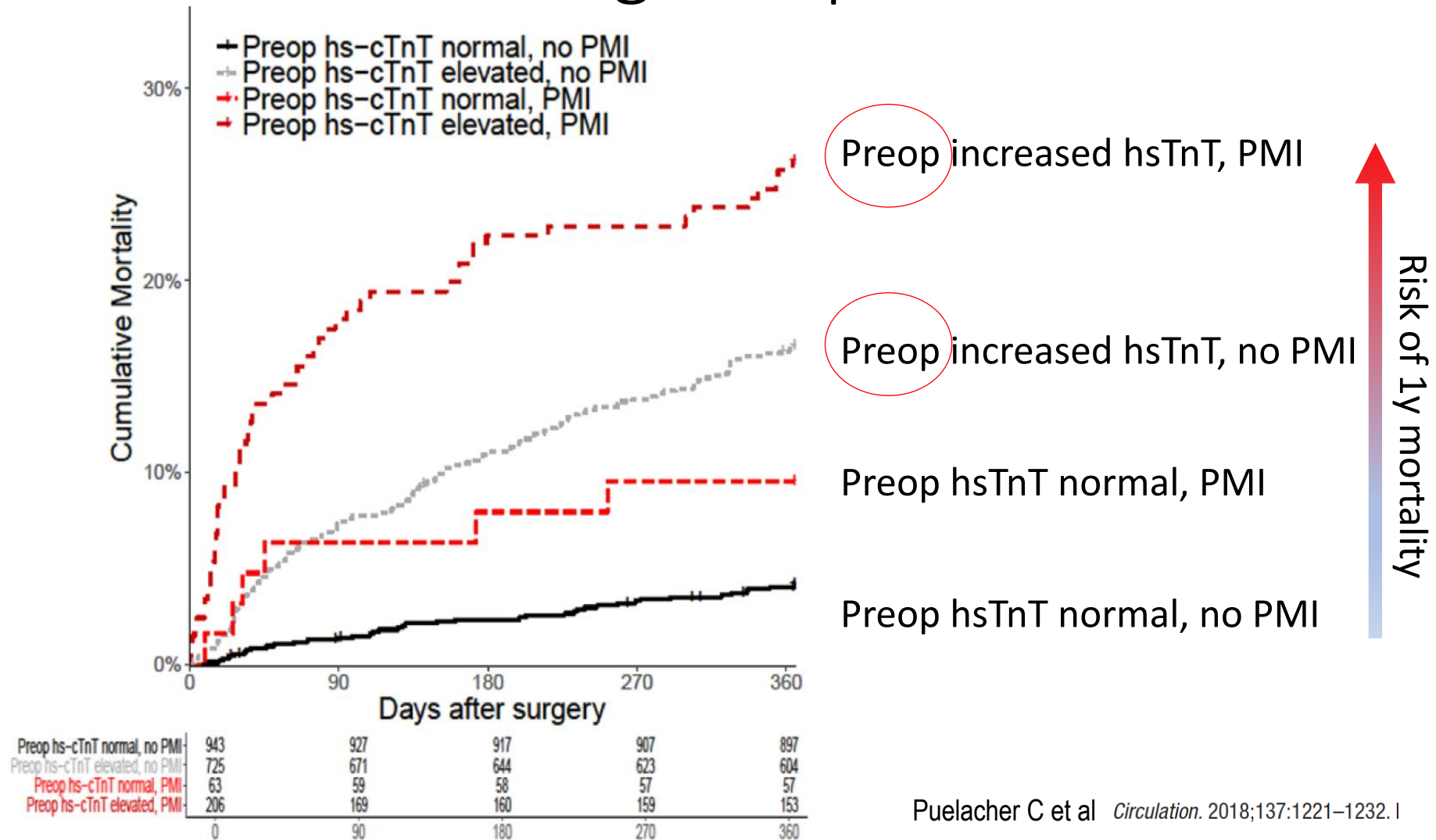
Duceppe et al *Ann Intern Med.* 2020;172:96-104.

- Pre-planned subgroup of VISION study population
- Exposure was preoperative NT-proBNP at various cutoffs
- Compared to RCRI (known to underestimate morbidity)
- Primary outcome MINS + vascular death at 30d

Variable	All Patients (<i>n</i> = 10 402)	Preoperative NT-proBNP Threshold			
		<100 pg/mL (<i>n</i> = 5356)	100 to <200 pg/mL (<i>n</i> = 1843)	200 to <1500 pg/mL (<i>n</i> = 2608)	≥1500 pg/mL (<i>n</i> = 595)
Composite of vascular death or MINS					
Events, <i>n</i> (incidence [95% CI], %) [†]	1269 (12.2 [11.6–12.8])	278 (5.2 [4.6–5.8])	226 (12.3 [10.8–13.8])	542 (20.8 [19.2–22.3])	223 (37.5 [33.5–41.3])
Adjusted HR (95% CI)	–	1.00	2.27 (1.90–2.70)	3.63 (3.13–4.21)	5.82 (4.81–7.05)
Composite of all-cause mortality or MI					
Events, <i>n</i> (incidence [95% CI], %) [†]	446 (4.3 [3.9–4.7])	92 (1.7 [1.4–2.1])	55 (3.0 [2.2–3.8])	205 (7.9 [6.8–8.9])	94 (15.8 [12.8–18.7])
Adjusted HR (95% CI)	–	1.00	1.57 (1.12–2.19)	3.64 (2.83–4.69)	5.35 (3.91–7.34)

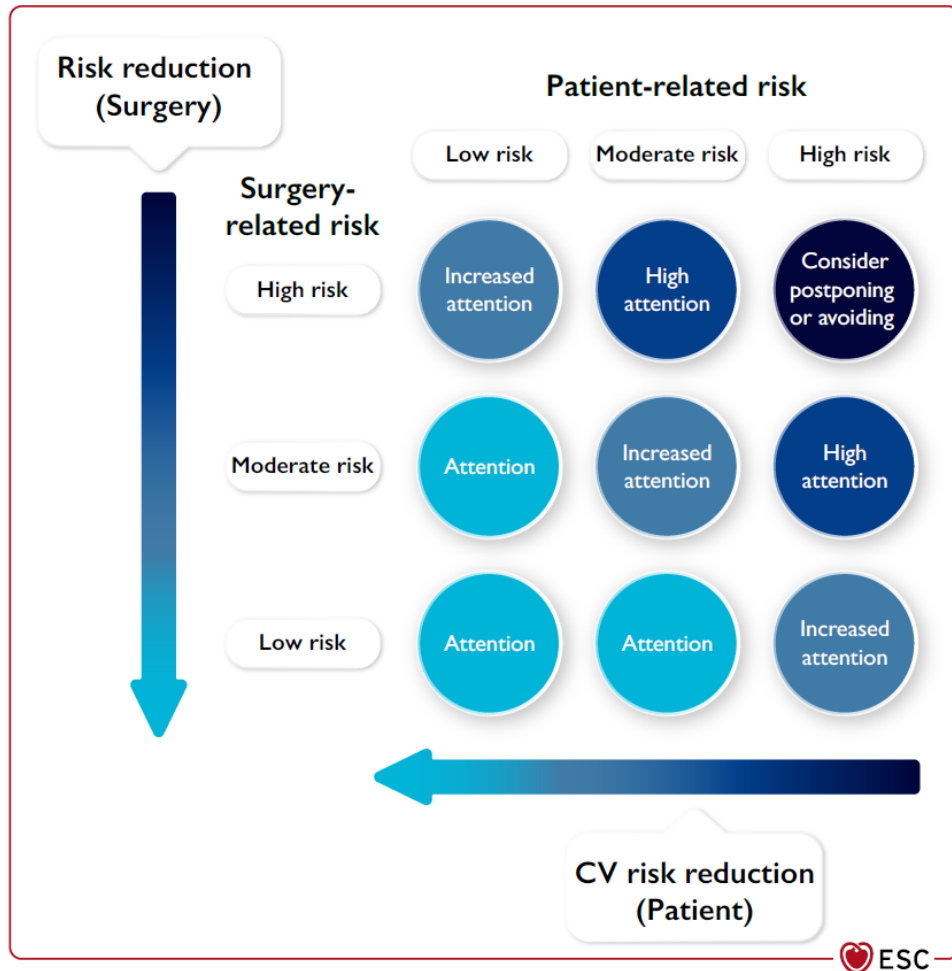
- ↑Preoperative NTproBNP increased risk of primary outcome
- Concentration-dependent effect
- Improved risk classification by 25%
- AUCs increased from 0.65 (CI 0.64-0.67) to 0.75 (CI 0.73-0.78)
- Supports previous IPDMA and SR/MA (Rodseth JACC 2014, Lurati Buse AA 2011)

Perioperative biomarker surveillance- timing is important



Puelacher C et al *Circulation*. 2018;137:1221–1232. |

What do the ESC guidelines recommend?



- History and examination focus on CV risk
- Hb and renal function
 - intermediate – high-risk surgery
- ECG
- Functional capacity
- Risk Scores
- Biomarkers
- Echocardiography



ESC

European Society
of Cardiology

European Heart Journal (2022) 00, 1–99
<https://doi.org/10.1093/eurheartj/ehac270>

**2022 ESC Guidelines on cardiovascular
assessment and management of patients
undergoing non-cardiac surgery**



ESC

2022 ESC Guidelines on cardiovascular assessment and management of patients undergoing non-cardiac surgery

Developed by the task force for cardiovascular assessment and management of patients undergoing non-cardiac surgery of the European Society of Cardiology (ESC)

Endorsed by the European Society of Anaesthesiology and Intensive Care (ESAIC)

Asymptomatic patients,
high risk surgery

Patients with known CVD or
patients with CV risk factors
or patients >65yo
Intermediate or high risk
surgery

Clinical risk evaluation—Section 3

In patients aged 45–65 years without signs, symptoms, or history of CVD, ECG and biomarkers should be considered before high-risk NCS.

Ila

In patients who have known CVD, CV risk factors (including age ≥ 65 years), or symptoms suggestive of CVD, it is recommended to measure hs-cTn T or hs-cTn I before intermediate- and high-risk NCS, and at 24 h and 48 h afterwards.

I

In patients who have known CVD, CV risk factors (including age ≥ 65 years), or symptoms suggestive of CVD, it should be considered to measure BNP or NT-proBNP before intermediate- and high-risk NCS.

Ila

Class 1 or Ila recommendations for pre and postoperative cardiac biomarkers in the majority of our patients at PMI Karolinska

Downloaded from https://academic.oup.com/ehj/advance-article/doi/10.1093/eurheartj/ehac270/6544441 by University of Cambridge user on 11 September 2022

2022 ESC Guidelines on cardiovascular assessment and management of patients undergoing non-cardiac surgery

Developed by the task force for cardiovascular assessment and management of patients undergoing non-cardiac surgery of the European Society of Cardiology (ESC)

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Downloaded from <https://academic.oup.com/ehj/advance-article/doi/10.1093/eurheartj/ehac270/6588881>

Perioperative cardiovascular complications—Section 8

It is recommended to have high awareness of peri-operative CV complications combined with surveillance for PMI in patients undergoing intermediate- or high-risk NCS.

I

Systematic PMI work-up is recommended to identify the underlying pathophysiology and to define therapy.

I

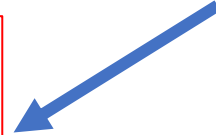
Surveillance for PMI = pre and postoperative hs-cTn
Systematic PMI workup => How to do this? Who will do it?

2022 ESC Guidelines on cardiovascular assessment and management of patients undergoing non-cardiac surgery

Developed by the task force for cardiovascular assessment and management of patients undergoing non-cardiac surgery of the European Society of Cardiology (ESC)

Endorsed by the European Society of Anaesthesiology and Intensive Care (ESAIC)

Patients with known CVD or patients with CV risk factors or patients >65yo
Intermediate or high risk surgery



Transthoracic echocardiography

TTE is recommended in patients with poor functional capacity and/or high NT-proBNP/BNP, or if murmurs are detected before high-risk NCS, in order to undertake risk-reduction strategies.

I

TTE should be considered in patients with suspected new CVD or unexplained signs or symptoms before high-risk NCS.

IIa

TTE may be considered in patients with poor functional capacity, abnormal ECG, high NT-proBNP/BNP, or >1 clinical risk factor before intermediate-risk NCS.

IIb

To avoid delaying surgery, a FOCUS exam performed by trained specialists may be considered as an alternative to TTE for pre-operative triage.

IIb

‘updated recommendations did not improve the yield of pathological findings compared with the 2014 guidelines in a sample of patients at elevated cardiovascular risk. For example, in presence of a class I recommendation for TTE, even in a selected population, the probability of detecting a severe reduction in EF amounts to less than 10%.’
Stroda et al. British Journal of Anaesthesia, 132 (4): 675e684 (2024)

ESAIC focused BM guidelines recommendations

Preoperative biomarkers may have some prognostic value but little data to support that they can discriminate patients with and without adverse outcome.

No evidence for preoperative BM-led management

Prognosis: Should I routinely measure cardiac biomarkers before surgery in order to assess if my patient might have increased risk for postoperative events?		
cTn	"We suggest measuring cardiac troponins preoperatively to assess prognosis" See why	Quality of evidence ☆☆☆☆ Very low
B-Type NP	"We suggest measuring B-type natriuretic peptides preoperatively to assess prognosis" See why	Quality of evidence ☆☆☆☆ Moderate
Prediction: Should I routinely measure and add preoperative cardiac biomarkers to clinical risk scores to predict postoperative events?		
cTn	"No recommendation due to very low quality data, use in research only" See why	Quality of evidence ☆☆☆☆ Very low
B-Type NP	"We suggest measuring B-type natriuretic peptides preoperatively to improve prediction of postoperative events" See why	Quality of evidence ☆☆☆☆ Very low
Management: Should I routinely use preoperative cardiac biomarkers to change my patient's postoperative care and improve outcome?		
cTn	"No recommendation due to lack of data, use in research only"	Quality of evidence No data
B-Type NP	"No recommendation due to lack of data, use in research only"	Quality of evidence No data

EJA

INFOGRAPHIC

GUIDELINES

Lurati Buse G et al. ESAIC focused guideline for the use of cardiac biomarkers in perioperative risk evaluation.

EJA 2023;40:888-927

Current ESAIC guidelines say?

Cardiovascular assessment

What kind of tools could we use to assess the cardiovascular system preoperatively?

R3.1: We suggest using the Revised Cardiac Risk Index (RCRI) score in preoperative patient risk stratification. (2C)

R3.2: When ordering preoperative blood tests, we suggest using natriuretic peptides as biological markers in high-risk patients (RCRI > 2) undergoing high-risk surgery. (2C)

R3.3: We discourage using METs as a subjective measurement of the patient's functional capacity before medical decision-making. The preoperative patient-subjective estimate of METs correlates poorly with the METs measured by exercise stress testing. Nonetheless, in selected individuals, the preoperative assessment of patient-subjective METs is used as a surrogate marker of preoperative performance even if this is not seen as a substitute for preoperative cardiopulmonary testing. (1A)

R3.4: We recommend combining natriuretic peptides and Duke Activity Status Index questionnaires to evaluate cardiac reserve in high-risk patients undergoing high-risk surgery. (1C)

R3.5: We recommend completing the WHO Disability Assessment Schedule 2.0 in high-risk patients before surgery as this could be useful to inform the patients about the risks of postoperative disability. (1C)

Use of Point-of-Care Ultrasound (POCUS)

Should POCUS of the heart and lung be an integral part of the preoperative assessment in all patients with heart disease who are about to undergo high-risk surgery?

R4.1: We suggest using a focused POCUS examination of the heart and lung, performed by a trained anaesthetist, in patients with any concerns regarding cardiovascular comorbidity before urgent or emergency surgery to address significant cardiac abnormalities and request a cardiology consultation and trigger more thorough cardiovascular monitoring, but it should not delay surgery. (2B)

R4.2: There is no compelling evidence that a preoperative focused cardiac POCUS exam in patients with or without known chronic heart failure or coronary artery disease before elective high-risk surgery could reduce postoperative morbidity. (2B)

EJA

Eur J Anaesthesiol 2025; **42**:1–35

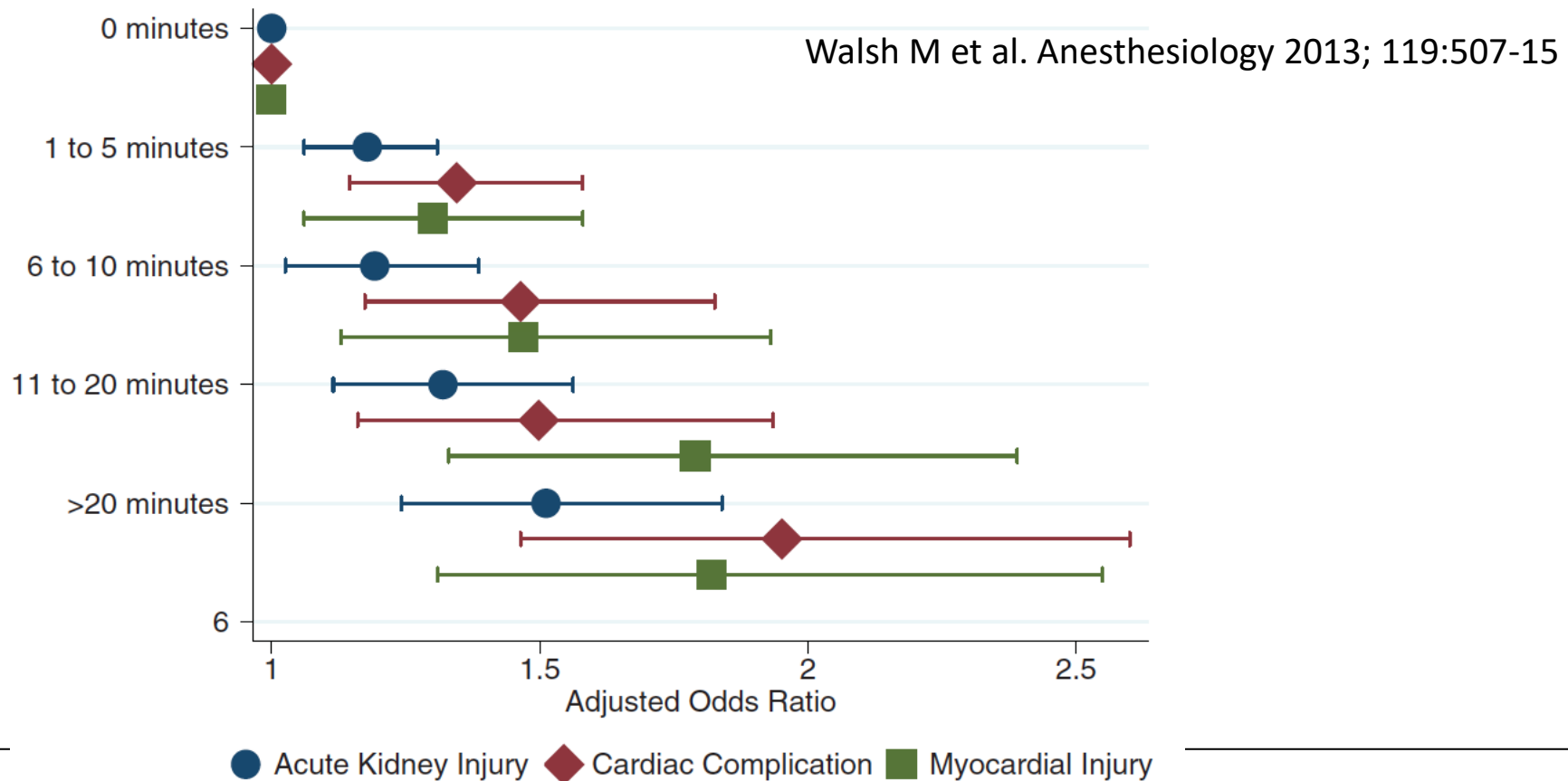
GUIDELINES

Preoperative assessment of adults undergoing elective noncardiac surgery

Recognition and minimization of intra- and postoperative risk

Intraoperative hypotension (IOH) and morbidity

Initial studies were inconclusive but now a large body of evidence show the deleterious effects of IOH regardless of definition



IOH is associated with myocardial injury

Association between Intraoperative Hypotension and Myocardial Injury after Vascular Surgery

Judith A. R. van Waes, M.D., Wilton A. van Klei, M.D., Ph.D., Duminda N. Wijeyesundera, M.D., Ph.D., Leo van Wolfswinkel, M.D., Ph.D., Thomas F. Lindsay, M.D., Ph.D., W. Scott Beattie, M.D., Ph.D.

([ANESTHESIOLOGY 2016; 124:35-44](#))

Association of Intraoperative Hypotension with Acute Kidney Injury after Elective Noncardiac Surgery

Louise Y. Sun, M.D., S.M., Duminda N. Wijeyesundera, M.D., Ph.D., Gordon A. Tait, Ph.D., W. Scott Beattie, M.D., Ph.D.

([ANESTHESIOLOGY 2015; 123:515-23](#))

Relationship between Intraoperative Hypotension, Defined by Either Reduction from Baseline or Absolute Thresholds, and Acute Kidney and Myocardial Injury after Noncardiac Surgery

Vafi Salmasi, M.D., Kamal Maheshwari, M.D., M.P.H., Dongsheng Yang, M.A., Edward J. Mascha, Ph.D., Asha Singh, M.D., Daniel I. Sessler, M.D., Andrea Kurz, M.D.

([ANESTHESIOLOGY 2017; 126:47-65](#))

[Eur J Anaesthesiol. 2018 Apr;35\(4\):273-279.](#)

Linn Hallqvist ¹, Fredrik Granath, Elin Huldt, Max Bell



How low can I safely go?

Relationship between Intraoperative Hypotension, Defined by Either Reduction from Baseline or Absolute Thresholds, and Acute Kidney and Myocardial Injury after Noncardiac Surgery

A Retrospective Cohort Analysis

Vafi Salmasi, M.D., Kamal Maheshwari, M.D., M.P.H., Dongsheng Yang, M.A.,
Edward J. Mascha, Ph.D., Asha Singh, M.D., Daniel I. Sessler, M.D., Andrea Kurz, M.D.

(ANESTHESIOLOGY 2017; 126:47-65)

Pressures that are often considered clinically acceptable (MAP 65 mmHg) were associated with both myocardial and renal injuries.

Postoperative hypotension

Period-dependent Associations between Hypotension during and for Four Days after Noncardiac Surgery and a Composite of Myocardial Infarction and Death

A Substudy of the POISE-2 Trial

(*ANESTHESIOLOGY* 2018; 128:317-27)

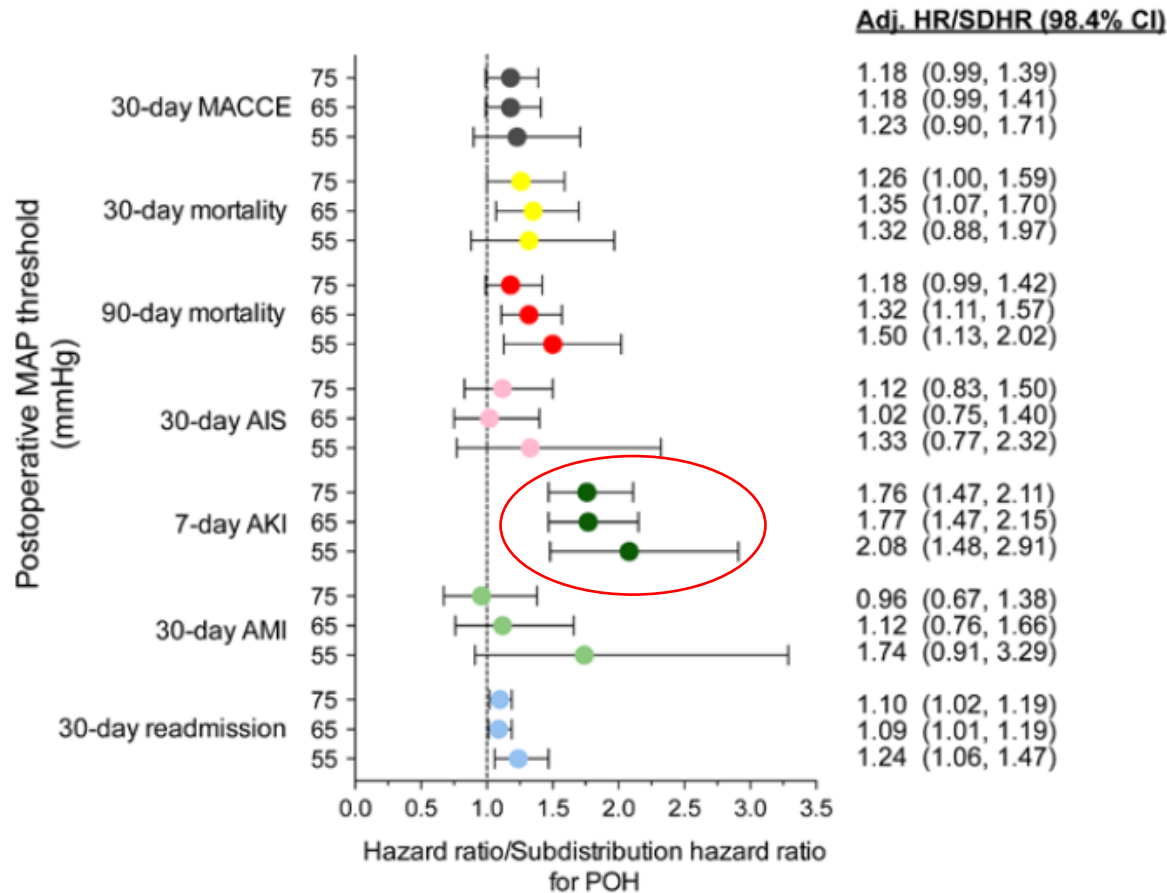
Table 3. Primary Analysis: The Association between Clinically Important Hypotension and the Composite Outcome of 30-day Myocardial Infarction and Mortality

Period	Average Relative Effect OR (98.3% CI)*	P Value ²	
10-min increase in hypotension			
Intraoperative (N = 9,765)	1.08 (1.03, 1.12)	< 0.001‡	
Remaining day of surgery (N = 9,592)	1.03 (1.01, 1.05)	< 0.001‡	← PACU
Hypotension vs. nonhypotension: PODs 1 to 4 (N = 9,186)	2.83 (1.26, 6.35)	0.002‡	← Ward

Deleterious effect of POH on kidney outcomes - even without antecedent IOH

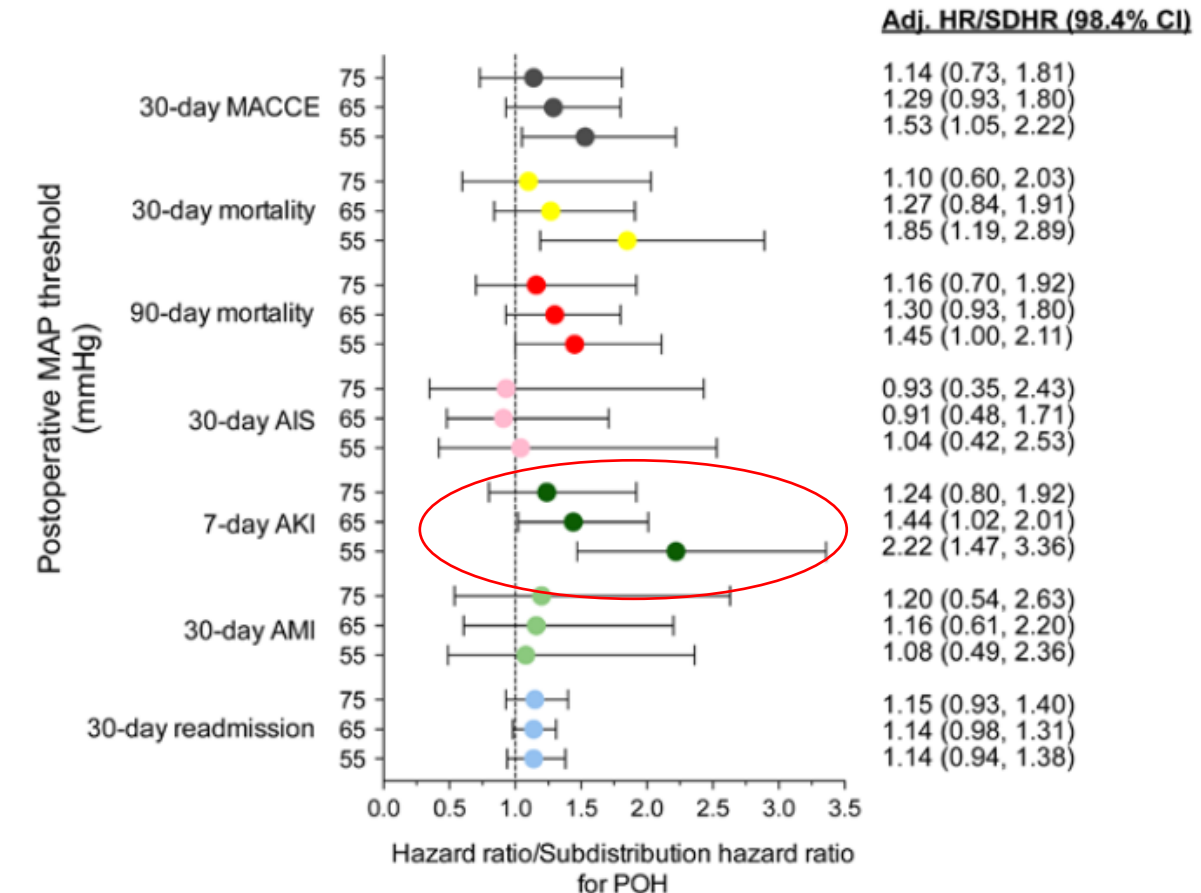
A

Hazards of POH in patients without IOH



B

Hazards of POH in patients with IOH



Perioperative BP management

JAMA | **Original Investigation** | CARING FOR THE CRITICALLY ILL PATIENT

Effect of Individualized vs Standard Blood Pressure Management Strategies on Postoperative Organ Dysfunction Among High-Risk Patients Undergoing Major Surgery

A Randomized Clinical Trial

Futier E et al

JAMA. 2017;318(14):1346-1357.

- SBP within 10% of the patient's normal resting value vs. standard practice intra + up to 4h postoperatively
- Composite of systemic inflammatory response syndrome and least 1 organ dysfunction at day 7 postsurgery

Perioperative BP management

Primary outcome:

38.1 vs 51.7% (RR 0.73, 95%CI 0.56 to 0.94, P=0.02)

Complications within 30 d							
Use of renal replacement therapy, No. (%)	6 (4.1)	7 (4.8)	0 (-5 to 4)	0.85 (0.29 to 2.46)	.76	0.85 (0.29 to 2.48)	.77
Pneumonia, No. (%)	6 (4.1)	16 (11.0)	-7 (-13 to -1)	0.37 (0.15 to 0.92)	.03	0.38 (0.15 to 0.93)	.03
ARDS, No. (%)	9 (6.1)	8 (5.5)	1 (-5 to 6)	1.11 (0.44 to 2.80)	.83	1.10 (0.44 to 2.75)	.84
Reintubation, No. (%) ^g	16 (10.9)	20 (13.8)	-3 (-10 to 5)	0.79 (0.43 to 1.46)	.45	0.79 (0.43 to 1.46)	.46
Need for noninvasive or invasive ventilation, No. (%)	28 (19.1)	40 (27.6)	-9 (-18 to 1)	0.69 (0.45 to 1.06)	.09	0.73 (0.48 to 1.11)	.14
Sepsis, No. (%)	22 (15.0)	38 (26.2)	-11 (-20 to -2)	0.57 (0.36 to 0.92)	.02	0.54 (0.34 to 0.86)	.009
Severe sepsis or septic shock, No. (%)	18 (12.2)	22 (15.2)	-3 (-11 to 5)	0.81 (0.45 to 1.44)	.47	0.81 (0.46 to 1.43)	.47
Acute heart failure, No. (%)	3 (2.0)	1 (0.7)	1 (-1 to 4)	2.96 (0.31 to 28.12)	.35	2.53 (0.25 to 25.08)	.43
Myocardial ischemia or infarction, No. (%)	0	1 (0.7)					
Stroke, No. (%)	0	0					
Surgical complications, No. (%)							
Surgical site infection	23 (15.7)	36 (24.8)	-9 (-18 to 0)	0.63 (0.39 to 1.00)	.05	0.63 (0.40 to 0.98)	.04
Surgical reoperation	23 (15.7)	29 (20.0)	-4 (-13 to 4)	0.78 (0.48 to 1.29)	.33	0.77 (0.47 to 1.26)	.30
Anastomotic leakage ^h	24 (16.3)	25 (17.2)	-1 (-9 to 8)	0.95 (0.57 to 1.58)	.83	0.92 (0.57 to 1.50)	.74
Death at day 30, No. (%)	9 (6.1)	8 (5.5)	1 (-4 to 6)	1.11 (0.44 to 2.80)	.83	1.11 (0.44 to 2.81)	.82

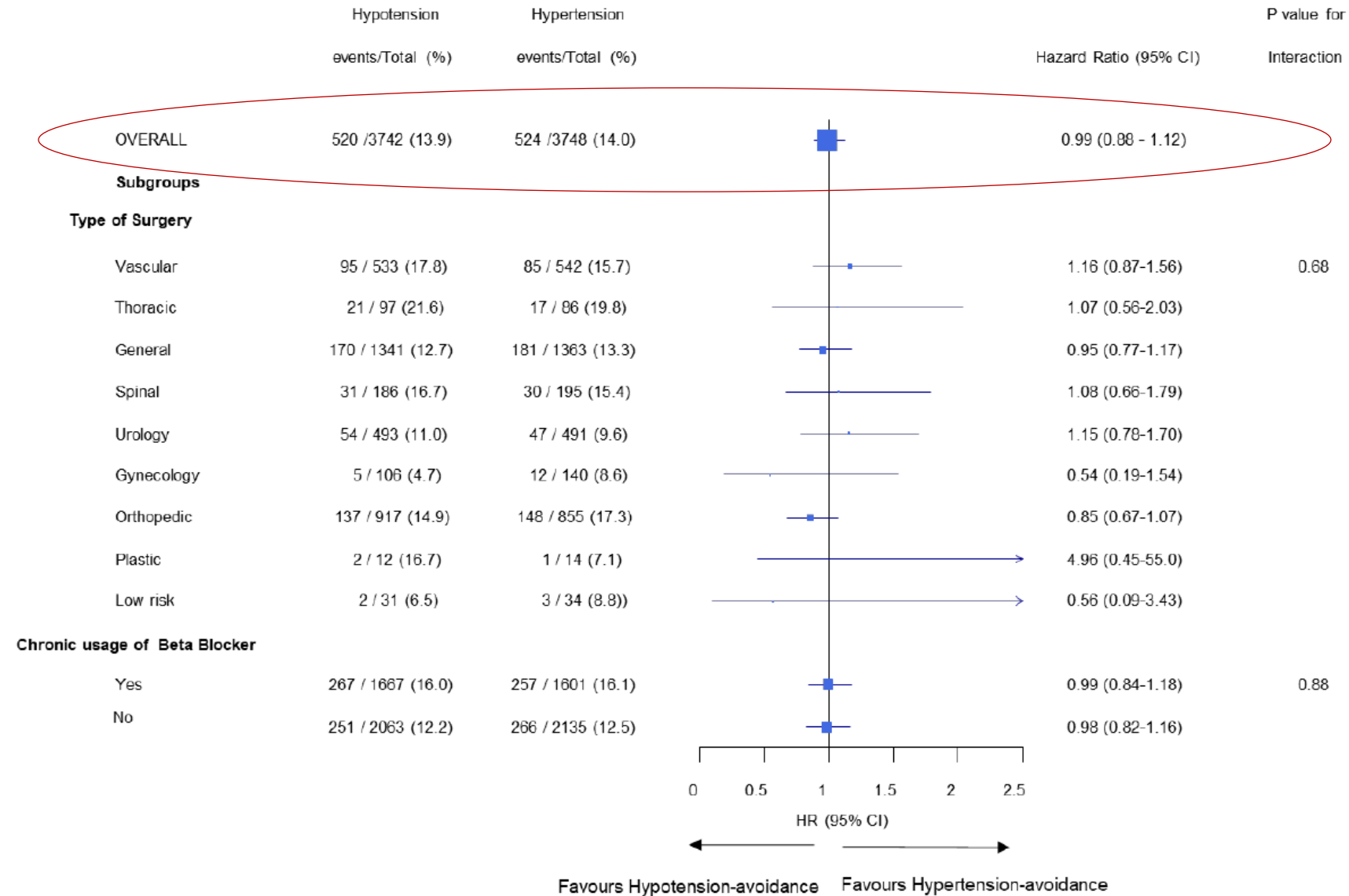
Targeting Higher Intraoperative Blood Pressures Does Not Reduce Adverse Cardiovascular Events Following Noncardiac Surgery

Patrick M. Wanner, MD,^{a,*} Dirk U. Wulff, PhD,^b Mirjana Djurdjevic,^a Wolfgang Korte, MD,^c Thomas W. Schnider, MD,^d Miodrag Filipovic, MD^a

<https://doi.org/10.1016/j.jacc.2021.08.048>

**No reduction in acute myocardial injury
or 30d MACE and/or AKI**

POISE-3 BP arm



Personalised BT?

Effect of personalized perioperative blood pressure management on postoperative complications and mortality in high-risk patients having major abdominal surgery: protocol for a multicenter randomized trial (IMPROVE-multi)

[Alina Bergholz](#),¹ [Agnes S. Meidert](#),² [Moritz Flick](#),¹ [Linda Krause](#),³ [Eik Vettorazzi](#),³ [Antonia Zapf](#),³
[Frank M. Brunkhorst](#),^{4,5} [Patrick Meybohm](#),⁶ [Kai Zacharowski](#),⁷ [Alexander Zarbock](#),⁸ [Daniel I. Sessler](#),^{9,10}
[Karim Kouz](#),^{#1} and [Bernd Sauge](#)^{#1,10}

**Personalised BP based on mean BP on the
night prior to op vs. control**

Intraoperative hypotension and postoperative outcomes: a meta-analysis of randomised trials

Filippo D'Amico¹, Evgeny V. Fominskiy¹, Stefano Turi¹, Alessandro Pruna¹, Stefano Fresilli¹, Margherita Triulzi¹, Alberto Zangrillo^{1,2} and Giovanni Landoni^{1,2,*}

¹Department of Anesthesia and Intensive Care, IRCCS San Raffaele Scientific Institute, Milan, Italy and ²School of Medicine, Vita-Salute San Raffaele University, Milan, Italy

Outcomes	Number of studies	Hypotensive target (N=4680) No. of patients/ total no. (%)	Normotensive target (N=4379) No. of patients/ total no. (%)	Odds ratio	I ² (%)	P-value
Primary outcome						
All-cause mortality	9	89/4644 (1.9)	99/4643 (2.1)	0.88 (0.65–1.18)	0	P=0.38
Secondary outcomes						
Atrial fibrillation	3	102/3894 (2.6)	130/3883 (3.4)	0.71 (0.52–0.96)	0	P=0.02
Acute kidney injury	9	161/807 (19)	171/811 (22)	0.89 (0.68–1.17)	43	P=0.39
Delirium	3	49/290 (18)	28/300 (9)	1.92 (0.54–6.83)	71	P=0.31
Stroke	6	30/4305 (0.6)	30/4288 (0.7)	0.98 (0.59–1.63)	45	P=0.95
Myocardial infarction	5	71/4283 (1.7)	75/4272 (1.8)	0.94 (0.68–1.31)	0	P=0.73
Patients requiring transfusion	3	65/336 (19)	82/346 (24)	0.68 (0.46–1.02)	41	P=0.07
				Mean difference		
Length hospital stay	6			−0.20 (−0.26; −0.13)	0	P<0.001
Time on mechanical ventilation	3			−1.74 (−4.66; 1.19)	97	P=0.24

Can MINS be treated?

Dabigatran in patients with myocardial injury after non-cardiac surgery (MANAGE): an international, randomised, placebo-controlled trial

*P J Devereaux, Emmanuelle Duceppe, Gordon Guyatt, Vikas Tandon, Reitze Rodseth, Bruce M Bickard, Denis Xavier, Wojciech Szczeklik, Christian S Meyhoff, Jessica Vincent, Maria Grazia Franzosi, Sadeesh K Srinathan, Jason Erb, Patrick Magloire, John Neary, Mangala Rao, Prashant V Rahate, Navneet K Chaudhry, Bongani Mayosi, Miriam de Nadal, Pilar Paniagua Iglesias, Otavio Berwanger, Juan Carlos Villar, Fernando Botto, John W Eikelboom, Daniel I Sessler, Clive Kearon, Shirley Pettit, Mukul Sharma, Stuart J Connolly, Shrikant I Bangdiwala, Purnima Rao-Melacini, Andreas Hoeft, Salim Yusuf, on behalf of the MANAGE Investigators**

Interpretation Among patients who had MINS, dabigatran 110 mg twice daily lowered the risk of major vascular complications, with no significant increase in major bleeding. Lancet 2019;10137:2325-2334

Funding Boehringer Ingelheim and Canadian Institutes of Health Research.

Risk-reduction interventions

Indirect evidence (risk adjusted observational data) for early cardiology consultation, initiation of long-term ASA and statins in patients suffering from MINS

Foucrier A, et al. Anesth Analg 2014;119:1053-63, Devereaux PJ, et al. Ann Intern Med 2011;154:523-8. Hua A, et al. J Thorac Dis 2016; 8:920–924. Park J, et al. Heart 2022;108:695–702.

Specific interventions to reduce cardiovascular risk

POISE: beta blockers

Effects of extended-release metoprolol succinate in patients undergoing non-cardiac surgery (POISE trial): a randomised controlled trial

POISE Study Group*

Lancet 2008; 371: 1839-47

- 8351 patients with /at risk of atherosclerotic disease
- Metoprolol 2-4 h prior to surgery and continuing 30d post surgery
- Primary end point composite of cardiovascular death, non-fatal myocardial infarction, and non-fatal cardiac arrest

Fewer with primary end point BUT more deaths and stroke, clinically significant hypotension and bradycardia

POISE-2: aspirin

The NEW ENGLAND JOURNAL of MEDICINE

Aspirin in Patients Undergoing Noncardiac Surgery

N Engl J Med 2014;370:1494-503.

- 10010 patients with CV risk factors undergoing noncardiac surgery
- Aspirin prior to surgery and continuing 30d post surgery
- Primary end point composite of death and non-fatal myocardial infarction
- No difference in primary end point
- Increased risk of life-threatening and major bleeding

POISE-2: clonidine

The NEW ENGLAND JOURNAL of MEDICINE

Clonidine in Patients Undergoing Noncardiac Surgery

N Engl J Med 2014;370:1504-13.

- 10010 patients with CV risk factors undergoing noncardiac surgery
- Clonidine 200ug prior to surgery and continuing 30d post surgery
- Primary end point composite of death and non-fatal myocardial infarction
- No difference in primary end point
- Increased risk of other catastrophic events

ENIGMA-II

Nitrous Oxide and Serious Long-term Morbidity and Mortality in the Evaluation of Nitrous Oxide in the Gas Mixture for Anaesthesia (ENIGMA)-II Trial

ANESTHESIOLOGY 2015; 123:1267–80

- ENIGMA-I suggested an increase in the incidence of MI during long-term follow up that was not evident at 30 days
- 7112 patients at risk of CV complications undergoing NCS
- 70%/30% N₂O/O₂ or no N₂O
- Primary outcome: composite of death and CV events
- Secondary: disability (Katz ADL <8)

NO DIFFERENCE IN PRIMARY OR ANY SECONDARY OUTCOMES

How do I manage this patient with CV risk factors requiring noncardiac surgery?

- History and examination focus on CV risk ✓
- Hb and renal function ✓
- ECG ✓
- Functional capacity ✓
- Risk Scores ✓
- Biomarkers ✓
- Invasive BP and flow monitoring ✓
- Extended PACU or Intermediate Care ✓

Perioperative assessment and management of cardiovascular risk

Have we reached a consensus?

**European study on perioperative management and
outcome following Preoperative Transthoracic
Echocardiography in noncardiac surgery patients**



Incidence, phenotypes, determinants and outcomes of Acute Heart Failure after non-cardiac surgery (pAHF)

9 164 Patients
11 262 Surgeries



≥ 65y or
≥ 45y+ CAD, PAD, CVD

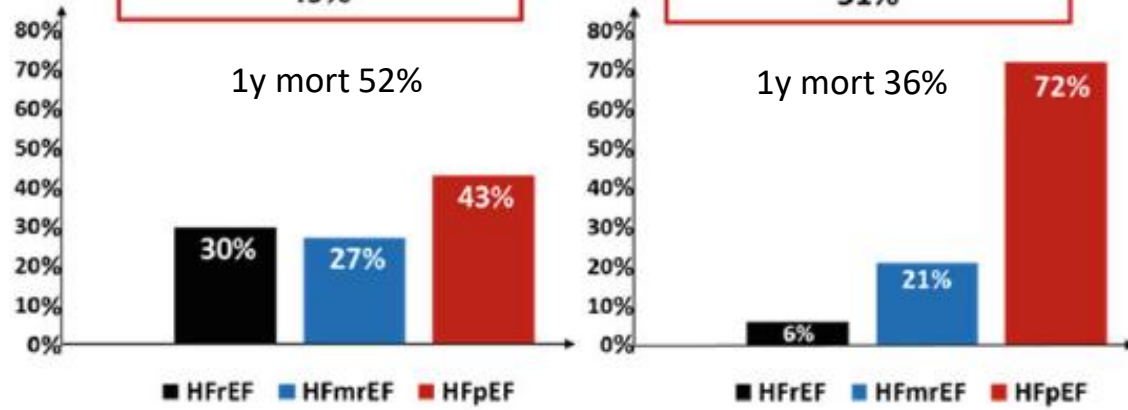
Independent predictors of pAHF

Chronic HF	COPD
Diabetes	Anemia
Urgent/emergent surgery	PAD
Atrial fibrillation	Age
Cardiac troponin elevation	CAD

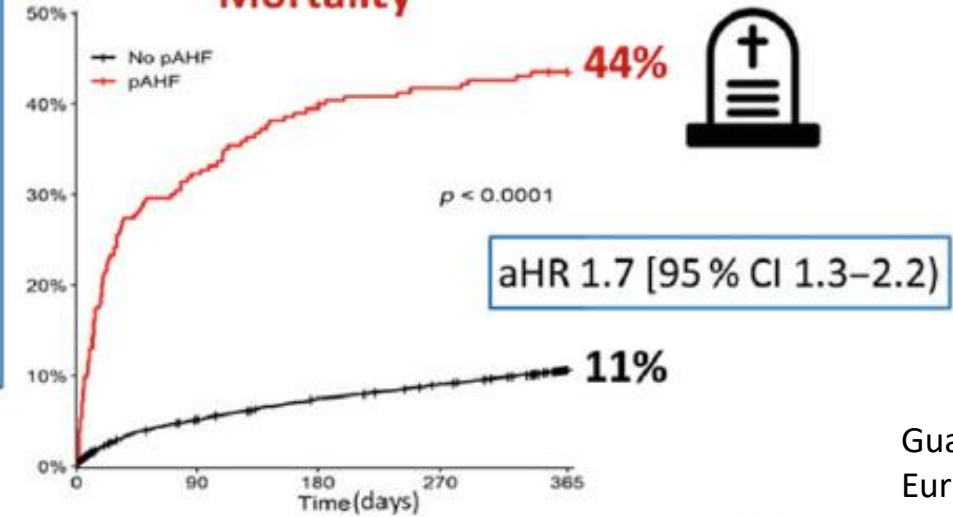
283 cases of pAHF (incidence 2.5%)

139 pAHF in chronic HF
49%

144 *de novo* pAHF
51%

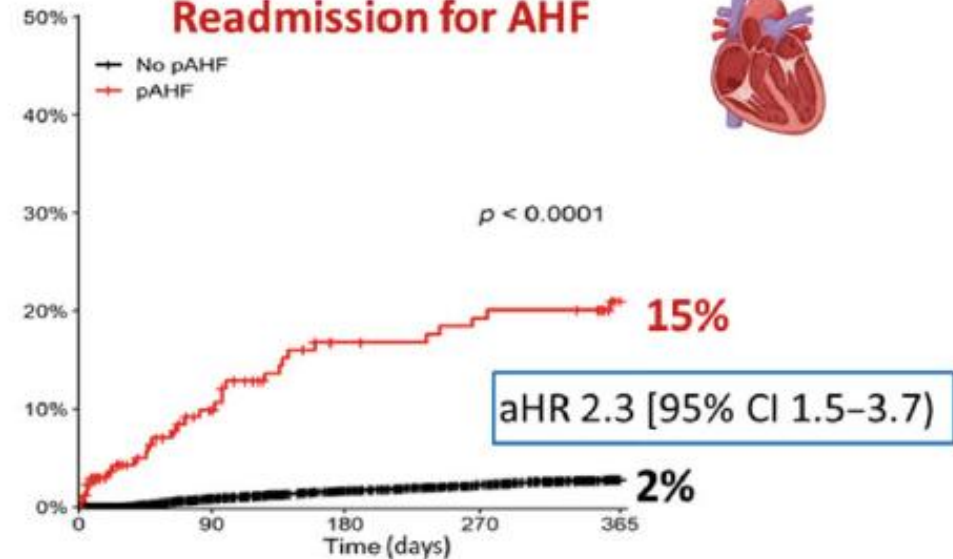


Mortality



Gualandro et al.
Eur J Heart Fail
2023;25:347-57

Readmission for AHF



Prediction of IOH

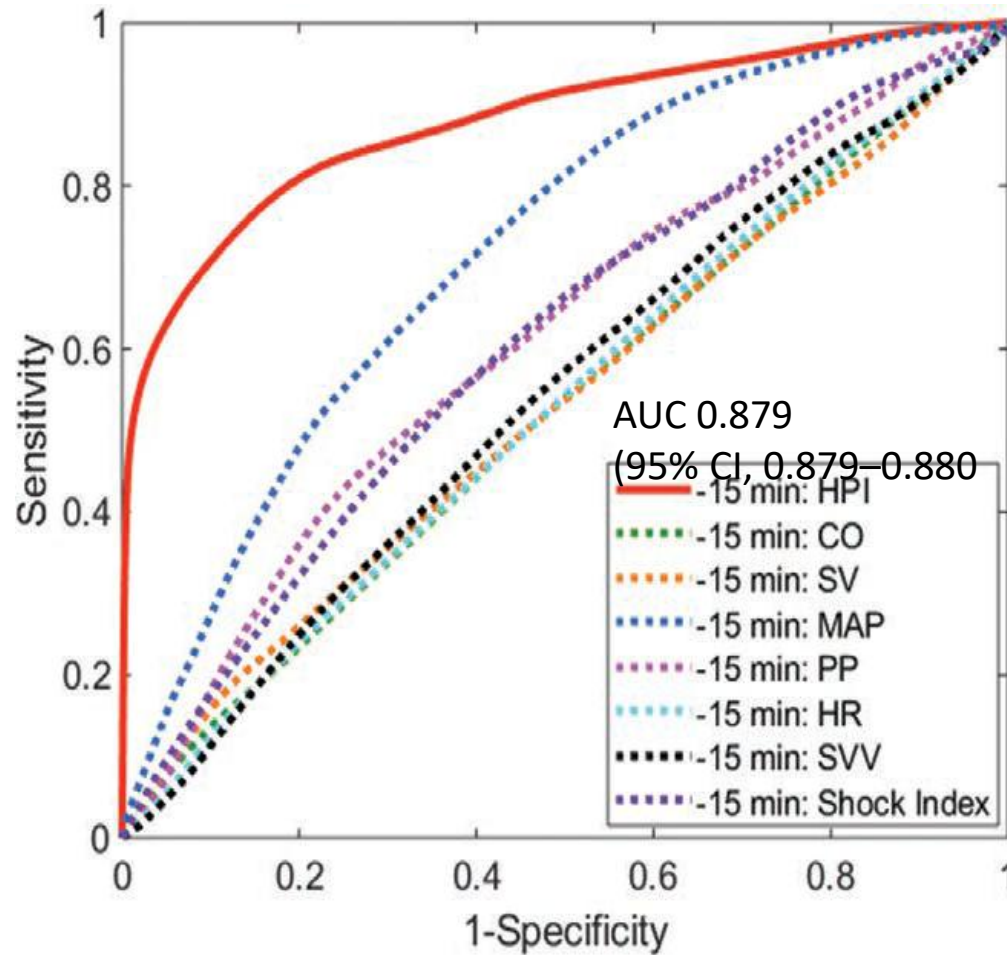
- Machine learning algorithms now available that can predict the occurrence of IOH up to 15 prior to its occurrence

Ability of an Arterial Waveform Analysis–Derived Hypotension Prediction Index to Predict Future Hypotensive Events in Surgical Patients

Simon James Davies, MD, PhD,* Simon Tilma Vistisen, PhD,† Zhongping Jian, PhD,‡
Feras Hatib, PhD,‡ and Thomas W. L. Scheeren, PhD§

Anest Analg 2020;130:352-359

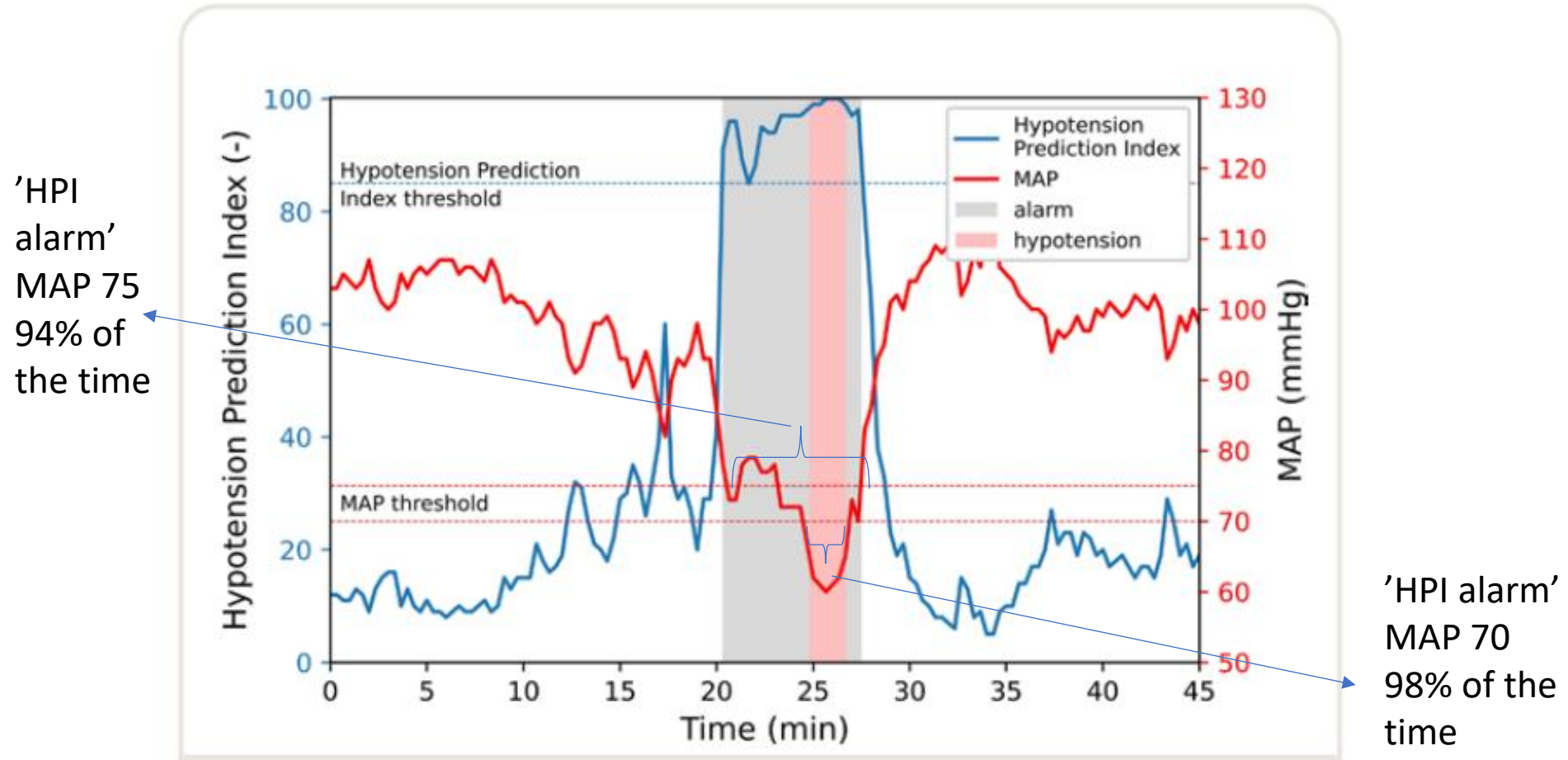
Preemptive treatment of IOH?



Performed better than commonly measured clinical variables eg. SV, SVV, Δ MAP and HR

Anest Analg 2020;130:352-359

Continuous Mean Arterial Pressure vs. Hypotension Prediction Index?



Mulder M et al. Anesthesiology 2023; 138:657–69

Hemodynamic Management Guided by the Hypotension Prediction Index in Abdominal Surgery

A multicenter randomized clinical trial (28 hospitals, 917 patients) age >65 yr or age >18 yr with ASA II or greater

Can goal-directed care guided with the proprietary Hypotension Prediction Index (HPI) reduce AKI within 7 days after elective surgery?



Primary outcome:
KDIGO criteria for moderate or severe AKI



- Urine output < 0.5 ml/kg/h for 12+ h



- Serum creatinine more than 2x baseline



The incidence of moderate-to-severe AKI was not significantly lower in the HPI group

	 HPI group (n=459)	 Standard care group (n=458)
Median age (IQR)	71 yr (65–77 yr)	70 yr (63–76 yr)
ASA III / IV (%)	58.3%	57.9%
AKI	6.1%	7.0%

Goal-directed hemodynamic management based on Hypotension Prediction Index did not reduce postoperative incidence of moderate-to-severe acute kidney injury compared to standard of care

ANESTHESIOLOGY

Ripollés-Melchor J, *et al.* ANESTHESIOLOGY, 2025.
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Risk scores

Predictive performance is generally comparable between scores
Some scoring systems are better validated
Only RCRI, NSQIP MICA and AUB-HAS2 specifically predict cardiovascular outcomes

	Revised Cardiac Risk Index (RCRI) (1999) ^a	Surgical Risk Calculator (2011)	The American College of Surgery National Surgical Quality Improvement Program (ACS NSQIP) (2013)	Surgical Outcome Risk Tool (SORT) (2014)	The American University of Beirut (AUB)-HAS2 Cardiovascular Risk Index (2019) ^b
Variables	Ischaemic heart disease Cerebrovascular disease History of congestive heart failure Insulin therapy for diabetes Serum creatinine level ≥ 2 mg/dL High-risk surgery (each assigned 1 point)	Age ASA-PS grade Pre-operative dependent functional status Creatinine >1.5 mg/dL Type of surgery	Age Sex Functional status Emergency case ASA class Current steroid use Ascites within 30 days Systemic sepsis within 48 h Ventilator dependence Disseminated cancer Diabetes Hypertension on treatment Congestive HF Dyspnoea Current smoker History of severe COPD Dialysis Acute renal failure Body mass index Surgery code	ASA-PS grade Urgency of surgery High-risk surgical specialty Surgical severity (from minor to complex major) Cancer Age ≥ 65 years or over	History of Heart disease Symptoms of Heart disease (angina or dyspnoea) Age ≥ 75 years Anaemia (haemoglobin <12 g/dL) Vascular Surgery Emergency Surgery (2 H, 2 A and 2 S) (each assigned 1 point)

Functional capacity

CARDIOVASCULAR

Risk assessment for major adverse cardiovascular events after noncardiac surgery using self-reported functional capacity: international prospective cohort study

Giovanna A. Lurati Buse^{1,*} , Eckhard Mauermann², Daniela Ionescu³, Wojciech Szczeklik⁴, Stefan De Hert⁵, Miodrag Filipovic⁶, Beatrice Beck-Schimmer⁷, Savino Spadaro⁸, Purificación Matute⁹, Daniel Bolliger², Sanem Cakar Turhan¹⁰, Judith van Waes¹¹, Filipa Lagarto¹², Kassiani Theodoraki¹³ , Anil Gupta¹⁴ , Hans-Jörg Gillmann¹⁵ , Luca Guzzetti¹⁶ , Katarzyna Kotfis¹⁷, Hinnerk Wulf¹⁸, Jan Larmann¹⁹, Dan Corneci²⁰, Frederique Chammartin-Basnet²¹, Simon J. Howell²², and the MET: Reevaluation for Perioperative Cardiac Risk investigators[†], European Society of Anaesthesiology and Intensive Care[†]

British Journal of Anaesthesia, 130 (6): 655e665 (2023)

- Patient reported functional capacity is prognostic of MACE and non-MACE complications
- Did not add predictive value to a model based on clinical factors alone

Do

	CCSG2017	AHA2021	ESC2022	ESAIC2023
Who	≥45 yo OR 18-44 yo with known significant CV disease requiring overnight hospitalization	Acute/elective not specified ≥65 yo OR ≥45 with established coronary or peripheral atherosclerotic disease	≥65 yo OR known CVD (any age) OR <65 y + CV risk factors AND Undergoing elective intermediate and high risk surgery	≥18 yo undergoing noncardiac surgery excluding transplantation (not renal) and obstetric surgery
What and When	Preoperative BNP or NT-proBNP	Preoperative baseline	Preoperative and 24- 48h postoperative: Hs-cTn (class I, class IIa for asymptomatic, >45yo + CV risk factors) Preoperative: NT-proBNP (class IIa)	Preoperative BNP/NT-proBNP, cTn

i?

Unlikely that preoperative biomarkers can be measured in most patients undergoing emergency surgery

Prognosis: Should I routinely measure cardiac biomarkers before surgery in order to assess if my patient might have increased risk for postoperative events?		
cTn	"We suggest measuring cardiac troponins preoperatively to assess prognosis" See why	Quality of evidence ☆☆☆☆ Very low
B-Type NP	"We suggest measuring B-type natriuretic peptides preoperatively to assess prognosis" See why	Quality of evidence ★★★★ Moderate
Prediction: Should I routinely measure and add preoperative cardiac biomarkers to clinical risk scores to predict postoperative events?		
cTn	"No recommendation due to very low quality data, use in research only" See why	Quality of evidence ☆☆☆☆ Very low
B-Type NP	"We suggest measuring B-type natriuretic peptides preoperatively to improve prediction of postoperative events" See why	Quality of evidence ☆☆☆☆ Very low
Management: Should I routinely use preoperative cardiac biomarkers to change my patient's postoperative care and improve outcome?		
cTn	"No recommendation due to lack of data, use in research only"	Quality of evidence No data
B-Type NP	"No recommendation due to lack of data, use in research only"	Quality of evidence No data

EJA

INFOGRAPHIC

GUIDELINES

Lurati Buse G et al. ESAIC focused guideline for the use of cardiac biomarkers in perioperative risk evaluation. EJA 2023;40:888-927

Biomarkers after emergency surgery?

	CCSG2017	AHA2021	ESC2022	ESAIC2023
Who	<p>≥45 yo OR 18-44 yo with known significant CV disease requiring overnight hospitalization</p>	<p>Acute/elective not specified ≥65 yo OR ≥45 with established coronary or peripheral atherosclerotic disease</p>	<p>≥65 yo OR known CVD (any age) OR <65 y + CV risk factors AND Undergoing elective intermediate and high risk surgery</p>	<p>≥18 yo undergoing noncardiac surgery excluding transplantation (not renal) and obstetric surgery</p>
What and When	<p>Preoperative BNP or NT-proBNP Postoperative cTn if 1) acute surgery 2) NT-proBNP ≥300 mg/L or BNP ≥92 mg/ 3) NT-proBNP n/a</p>	<p>Preoperative baseline, Repeat within 48-72h of surgery IF results of testing would modify clinical management</p>	<p>Preoperative and 24-48h postoperative: Hs-cTn (class I, class IIa for asymptomatic, >45yo + CV risk factors) Preoperative: NT-proBNP (class IIa)</p>	<p>Preoperative BNP/NT-proBNP, cTn Perioperative cTn Postoperative cTn Recommendations differ depending on intention (prognosis/prediction/management)</p>

Myocardial injury is largely silent and cannot be detected without surveillance
 Biomarkers should be used in their 'conventional' sense e.g. for diagnosis of AMI, acute heart failure

Prognosis: Should I routinely measure cardiac biomarkers after surgery in order to assess if my patient might have increased risk for postoperative events?		
cTn	"We suggest measuring cardiac troponins postoperatively to assess prognosis" See why	Quality of evidence ★ ★ ★ ☆ Moderate
B-Type NP	"No recommendation due to lack of data, use in research only"	Quality of evidence ★ ☆ ☆ ☆ Very low

Prediction: Should I routinely measure and add postoperative cardiac biomarkers to collect scores to predict postoperative events?		
cTn	"We suggest measuring cardiac troponins postoperatively to improve prediction of postoperative events" See why	Quality of evidence ★ ★ ☆ ☆ Low
B-Type NP	"No recommendation due to lack of data, use in research only"	Quality of evidence ★ ☆ ☆ ☆ Very low

Management: Should I routinely use postoperative cardiac biomarkers to change my patient's postoperative care and improve outcome?		
cTn	"No recommendation due to lack of data, use in research only"	Quality of evidence ★ ☆ ☆ ☆ Very low
B-Type NP	"No recommendation due to lack of data, use in research only"	Quality of evidence No data

EJA

INFOGRAPHIC

GUIDELINES

Lurati Buse G et al. ESAIC focused guideline for the use of cardiac biomarkers in perioperative risk evaluation. EJA 2023;40:888-927

	CCSG2017	AHA2021	ESC2022	ESAIC2023
How increased risk is defined by biomarker	Preop risk: Preop NT-proBNP ≥ 300 mg/L or BNP ≥ 92 mg/L	Postop risk: Absolute change ≥ 5 ng/L if values are between 20 and 65 ng/L OR Any absolute value ≥ 65 ng/L OR Any absolute change ≥ 14 ng/L	Preop risk: hs-cTn > URL NT-proBNP ≥ 125 pg/ml Postop risk: change > 1 URL of any hs-cTn assay	No cutoffs specified due to interassay variations and different thresholds used from study to study. Absolute increase of > 1 URL of any cTn assay may be pragmatic
Management	Explicit communication of periop risk (event rate and 95% CI of the risk estimate) Add cTn if preop NT-proBNP ≥ 300 mg/L .	Smoking cessation, diet and nutrition counseling, stress reduction, cardiac rehabilitation, optimize management of CV risk factors.	Preop risk: TTE +/- stress imaging Postop risk: determine aetiology incl. diagnostic workup with ECG/TTE/CCTA/ICA. Rx includes aspirin/statins for IT2MI and missed T1MI.	For communicating prognosis and shared decision-making. No routine use for risk prediction. No evidence for biomarker-led management strategies.

ESAIC focused guideline for the use of cardiac biomarkers in perioperative risk evaluation

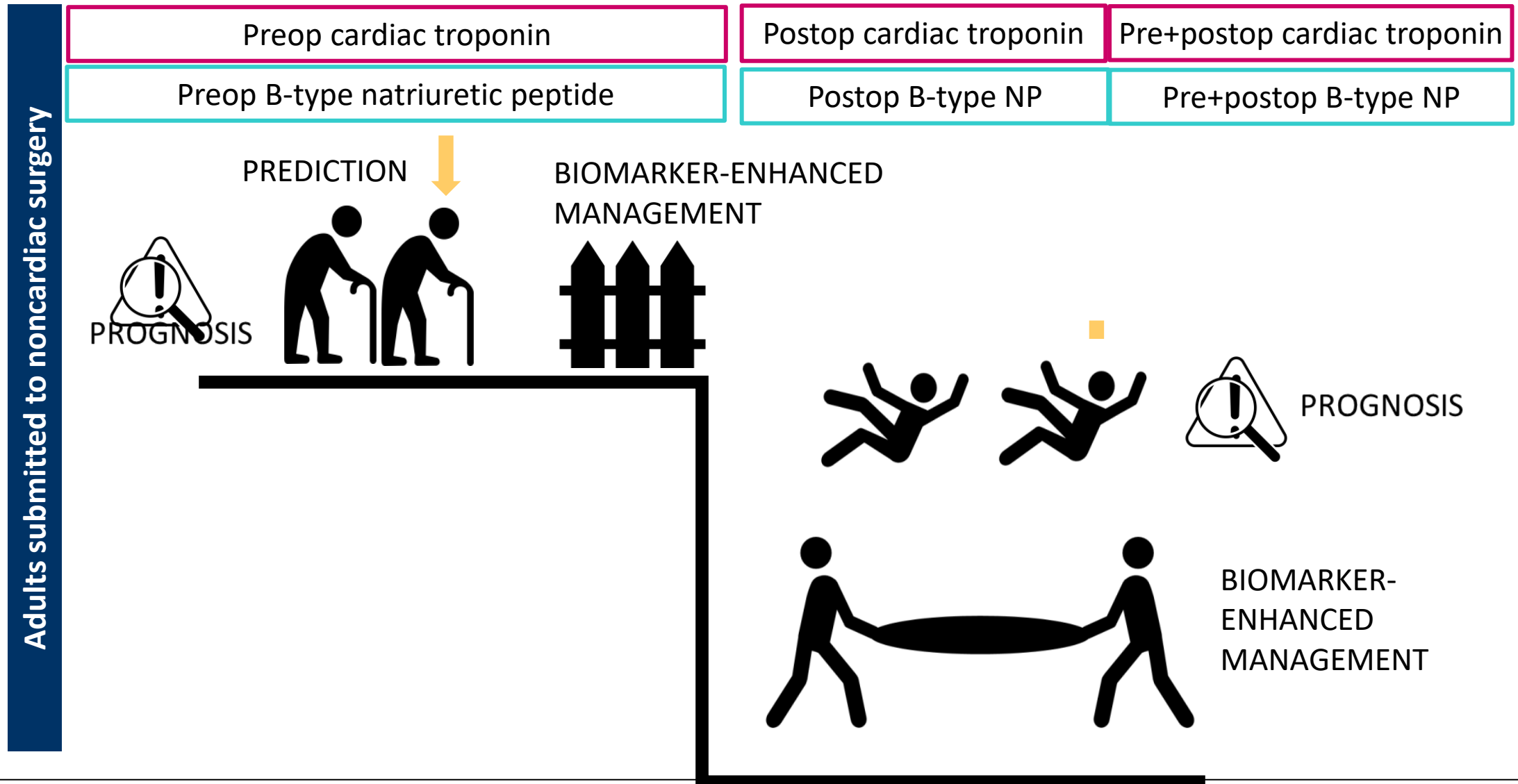
EJA

Eur J Anaesthesiol 2023; 40:888–927

12 critical
outcomes

- All cause mortality up to 30d after surgery
- All cause mortality up to 1y after surgery
- Cardiac mortality up to 30d after surgery
- Death or MI up to 30d after surgery
- Death or MI up to 1y after surgery
- MACE up to 30d after surgery
- MACE up to 1y after surgery
- Cardiac complications (any severity) up to 30d after surgery
- Myocardial injury up to 30d after surgery
- Complications (cardiac + noncardiac) up to 30d after surgery
- Short term disability
- Short term QoL (up to 90d after surgery)

The 3 separate questions addressed



ESAIC focused guideline for the use of cardiac biomarkers in perioperative risk evaluation

PROGNOSIS: How do elevated biomarker concentrations influence the risk of specific outcomes?				PREDICTION: How does the biomarker contribute to the differentiation of patients at risk ?				BIOMARKER-LED MANAGEMENT: Does adaptation of periop managment triggered by biomarkers results improve outcome?			
Recommendations on use for prognosis				Recommendations on use for prediction				Recommendations on biomarker-led management			
Preop Tn	Research	Weak-2D	Strong for	Research	Weak for	Strong for		Research	Weak for	Strong for	
Comb Tn	Research	Weak-2B	Strong for	Research	Weak -2D	Strong for		No recommendation (no consensus)			
Postop Tn	Research	Weak-2B	Strong for	Research	Weak -2C	Strong for		Research	Weak for	Strong for	
Preop BNP	Research	Weak-2B	Strong for	Research	Weak -2D	Strong for		Research	Weak for	Strong for	
Post BNP	Research	Weak for	Strong for	Research	Weak for	Strong for		Research	Weak for	Strong for	
Variation in incidence of outcome over time in a population of interest.				Ability to discriminate disease from non-disease cases				Any management pathway based on ROUTINE surveillance			

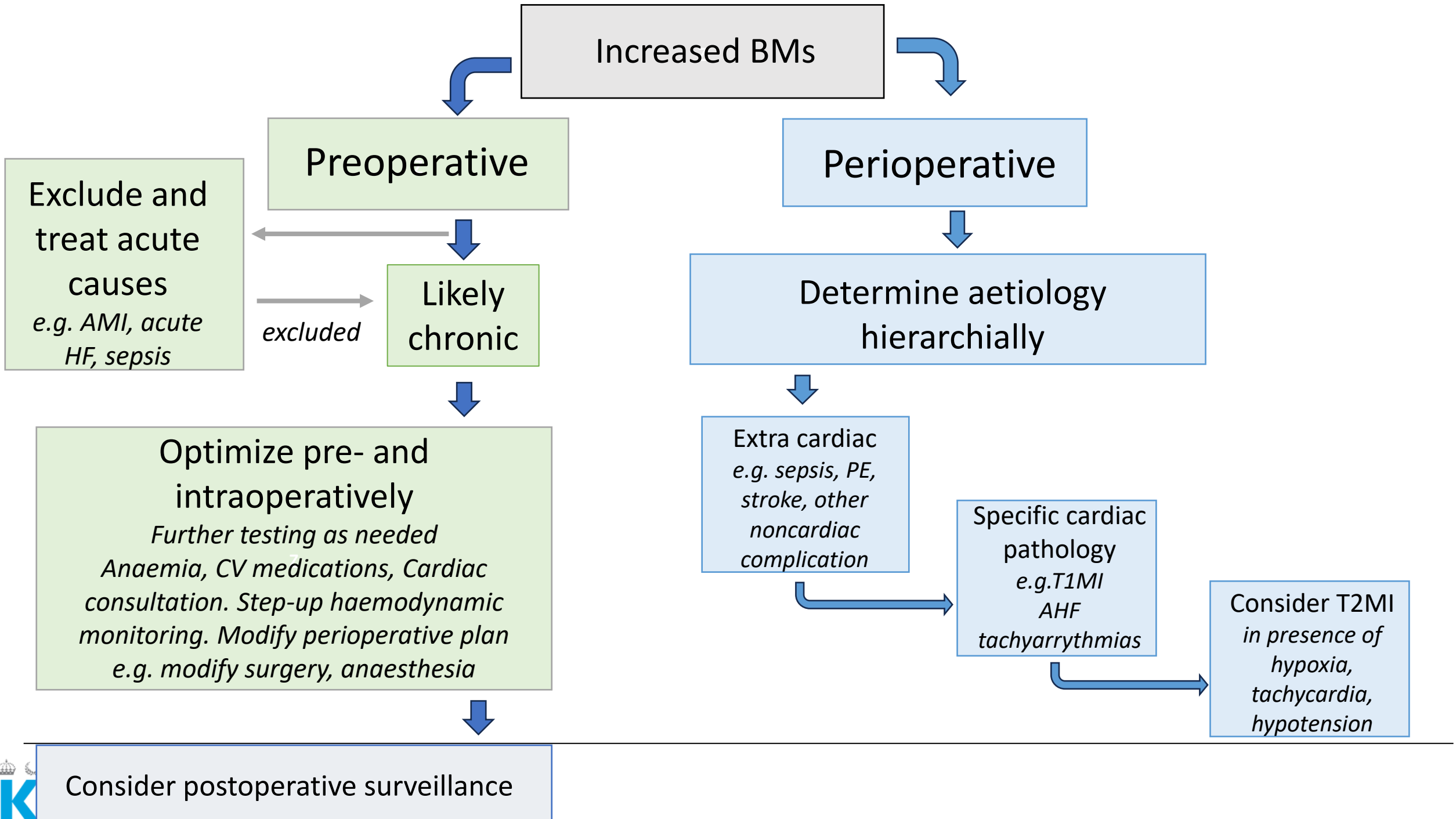
Can MINS be treated?

Dabigatran in patients with myocardial injury after non-cardiac surgery (MANAGE): an international, randomised, placebo-controlled trial

*P J Devereaux, Emmanuelle Duceppe, Gordon Guyatt, Vikas Tandon, Reitze Rodseth, Bruce M Bickard, Denis Xavier, Wojciech Szczeklik, Christian S Meyhoff, Jessica Vincent, Maria Grazia Franzosi, Sadeesh K Srinathan, Jason Erb, Patrick Magloire, John Neary, Mangala Rao, Prashant V Rahate, Navneet K Chaudhry, Bongani Mayosi, Miriam de Nadal, Pilar Paniagua Iglesias, Otavio Berwanger, Juan Carlos Villar, Fernando Botto, John W Eikelboom, Daniel I Sessler, Clive Kearon, Shirley Pettit, Mukul Sharma, Stuart J Connolly, Shrikant I Bangdiwala, Purnima Rao-Melacini, Andreas Hoefft, Salim Yusuf, on behalf of the MANAGE Investigators**

Interpretation Among patients who had MINS, dabigatran 110 mg twice daily lowered the risk of major vascular complications, with no significant increase in major bleeding.

Funding Boehringer Ingelheim and Canadian Institutes of Health Research.





WHEN USING CARDIAC BIOMARKERS CLINICALLY, CONSIDER:



Myocardial injury is largely undetectable without biomarker surveillance



All elevations prognostically important, but risk predictive value still not established



One RCT for Rx of MINS, reduction of *vascular complications*



No trial has been effective in preventing myocardial injury



Added value?



For prognosis, detection of unfavourable events



Unnecessary expense?



For prediction, BM-led management

Have a good day

