Perioperative Assessment and Management of Cardiac Ischemia

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Objectives

1. Evaluate cardiac risk preoperatively, including for one-day surgery
2. Propose an investigation plan and treatment when MINS is diagnosed

Disclosure

- Research grant for investigator-initiated project from Roche Diagnostics
- Research grant for investigator-initiated project from Abbott Laboratories

Background

- Almost everyone undergoes surgery during lifetime
  - In Western countries, average 7 surgeries over life span
- Hundreds of millions of noncardiac surgeries annually worldwide
  - Includes older population and more comorbidities
- Goals to
  - Improve function
  - Relieve symptoms
  - Prolong longevity
- Despite advances in surgical and anesthetic techniques
  - Comes at price of increased risks

Complications after noncardiac surgery

In-hospital surgery

- Intraop mortality <1/10,000
- 30-day mortality = 1/60

- Most common complications after noncardiac surgery that impact mortality
  - Bleeding
  - Sepsis
  - **Cardiovascular**

VISION investigators. CMAJ. 2019 Jul 29;191(30):E830-E837.

Postop cardiovascular complications: incidence

VISION Study (n=40,004)

- Systematic troponin measurement (TnT or hsTnT) up to postop day 3

Cardiovascular complications	30-day incidence	Association with 30-day mortality Adjusted Hazard ratio
Myocardial injury after noncardiac surgery (« MINS »)	**13%**	2.2 (95% CI, 1.9-2.6)
Stroke	0.3%	3.7 (95% CI, 2.5-5.7)
Heart failure	0.9%	2.4 (95% CI, 1.7-3.2)
New atrial fibrillation	0.9%	1.4 (95% CI, 1.0-2.0)

CMAJ. 2019 Jul 29;191(30):E830-E837.

MINS: incidence

- Systematic review by Smilowitz et al. (2019)
  - 169 studies – 530,867 patients
  - Incidence
    - Without systematic trop surveillance: **9.9%** (95% CI, 8.4–11.5%)
    - With systematic trop surveillance: **19.6%** (95% CI, 17.8–21.4%)

TABLE 2. Short- and Long-Term Postoperative Outcomes in Patients With and Without MINS

	MINS	No MINS	Relative Risk	P-value
In-hospital mortality (n = 25 studies)	8.1% (4.4–12.7%)	0.4% (0.2%–0.7%)	8.3 (4.2–16.6)	<0.001
30-day mortality (n = 24 studies)	8.5% (6.2–11.0%)	1.2% (0.9–1.6%)	5.6 (4.1–7.7)	<0.001
1-yr mortality (n = 18 studies)	20.6% (15.9–25.7%)	5.1% (3.2–7.4%)	4.1 (3.0–5.6)	<0.001
Long-term mortality (n = 11 studies)	42.7% (33.8–51.8%)	19.7% (10.6–30.9%)	2.4 (1.8–3.4)	<0.001

MINS indicates myocardial injury after noncardiac surgery.

Cardiology in Review 2019;27: 267–273

Preoperative cardiac risk assessment

Case 1

An **81-year**-old male seen in preop clinic prior to **elective aorto-bifemoral bypass**.

He has well-controlled **diabetes**, **hypertension**, and a history of **smoking**. Despite his claudication, the patient walks daily and denies shortness of breath or chest pain on exertion.

Physical examination: unremarkable.

Laboratory values:

- **creatinine 117** umol/L
- **NT-proBNP 807** ng/L (ULN = 125 ng/L)

ECG: nonspecific lateral T wave changes

Case 1 – How will you proceed?

1. Proceed with surgery, ward + postop troponin screening
2. Proceed with surgery, step down unit + postop troponin screening
3. Preop echocardiogram
4. Preop cardiac stress test
5. Cancel surgery

Case 1 - continued

Persantine MIBI cardiac stress test:

- normal EF at rest
- reduced EF 35% on persantine
- no focal wall motion abnormalities

Case 1 continued – how will you proceed?

1. Proceed with surgery, ward + postop troponin screening
2. Proceed with surgery, step down unit + postop troponin screening
3. Preop coronary angiography
4. Postop coronary angiography
5. Cancel surgery

Case 1 – continued part 2

Surgery postponed, cardiology consulted

Cath: Severe 3VD with proximal left main stenosis

Patient advanced for and **underwent CABG**, which was complicated by mild AKI and postop delirium.

After 3 months, underwent vascular surgery, without complications.

Cardiac risk evaluation

- Risk scores
- Biomarkers
- ECG
- Echocardiogram
- Cardiac stress test
- Coronary angiogram/PCI

Cardiac risk score : RCRI

Variables	Pts
Hx of IHD	1
Hx of CHF	1
Hx of CVA/TIA	1
Insulin for diabetes	1
Creat >177 μmol/L	1
High-risk surgery	1

Total RCRI points	Original risk estimates Lee 1999*	Risk estimates CCS 2017**	Risk estimates VISION study** (n=35,815)
0	0.4%	3.9%	**1.6%**
1	0.9%	6.0%	**4.0%**
2	7.0%	10.1%	**7.9%**
≥3	11.0%	15.0%	**12.9%**

* MI, pulmonary edema, ventricular fibrillation or primary cardiac arrest, and complete heart block
** MI, cardiac arrest, or death

Circulation 1999 Sep 7;100(10):1043-9
Can J Cardiol 2017 Jan;33(1):17-32
Can J Cardiol 37 (2021) 1215-1224

Cardiac risk score: NSQIP

- **Gupta/NSQIP-MICA calculator**
  - Age, functional status, ASA class, creatinine, type of procedure
  - Requires online calculator
  - Predicts MI or cardiac arrest

- **ACS NSQIP calculator**
  - Age, sex, functional status, emergency case, ASA, steroid, Ascites, recent sepsis, ventilator, cancer, diabetes, HTN, CHF, SOB, smoking, COPD, dialysis, AKI, BMI
  - Requires online calculator
  - Predicts various outcomes

Circulation. 2011;124(4):381-7
J Am Coll Surg 2013;217:833e842

Comparison between RCRI and NSQIP-based scores

Systematic review – 52 studies comparing RCRI to other model

- **RCRI vs NSQIP-MICA**
  - MACE: 3 studies (n = 1567; 95 MACE)
  - MICA: 6 studies (n = 243,896; unknown MICAs)
  - mortality : 1 study (n = 24; 17 deaths)

- **RCRI vs ACS-NSQIP**
  - MACE: 2 studies (n = 1087; 26 MACE)
  - MICA: 2 studies (n = 9678; 94 MICA)
  - Mortality: 3 studies (n = 2461; 155 deaths)

Cochrane Database Syst Rev 2021 Dec 21;12(12):CD013139

Comparison between RCRI and NSQIP-based scores

- **MACE**
  - **no difference** discrimination between RCRI and NSQIP-based scores
- **MI and cardiac arrest**
  - **NSQIP-MICA better** discrimination than RCRI, but RCRI better calibration
    - median **delta c-statistic 0.11**, range -0.05 to 0.39
- **All-cause mortality**
  - **ACS-NSQIP better** discrimination than RCRI
    - median **delta c-statistic 0.14**, range 0.11 to 0.15

Cochrane Database Syst Rev 2021 Dec 21;12(12):CD013139

Which cardiac risk score to use?

- RCRI has undergone more extensive validation in various settings
- RCRI easier to calculate
- RCRI can be combined with cardiac biomarkers
- All scores have limitations, and no clear winner

Preoperative biomarkers

- BNP / NT-proBNP
- Troponin

BNP/NT-proBNP for preop risk stratification

- Alternative to cardiac imaging as first test
  - Less expensive
  - Quicker
  - Good negative predictive value
- Recommended by national guidelines
- Supported by evidence
  - ~60 studies including ~20,000 patients

Summary - Causes of ↑ BNP/NT-proBNP

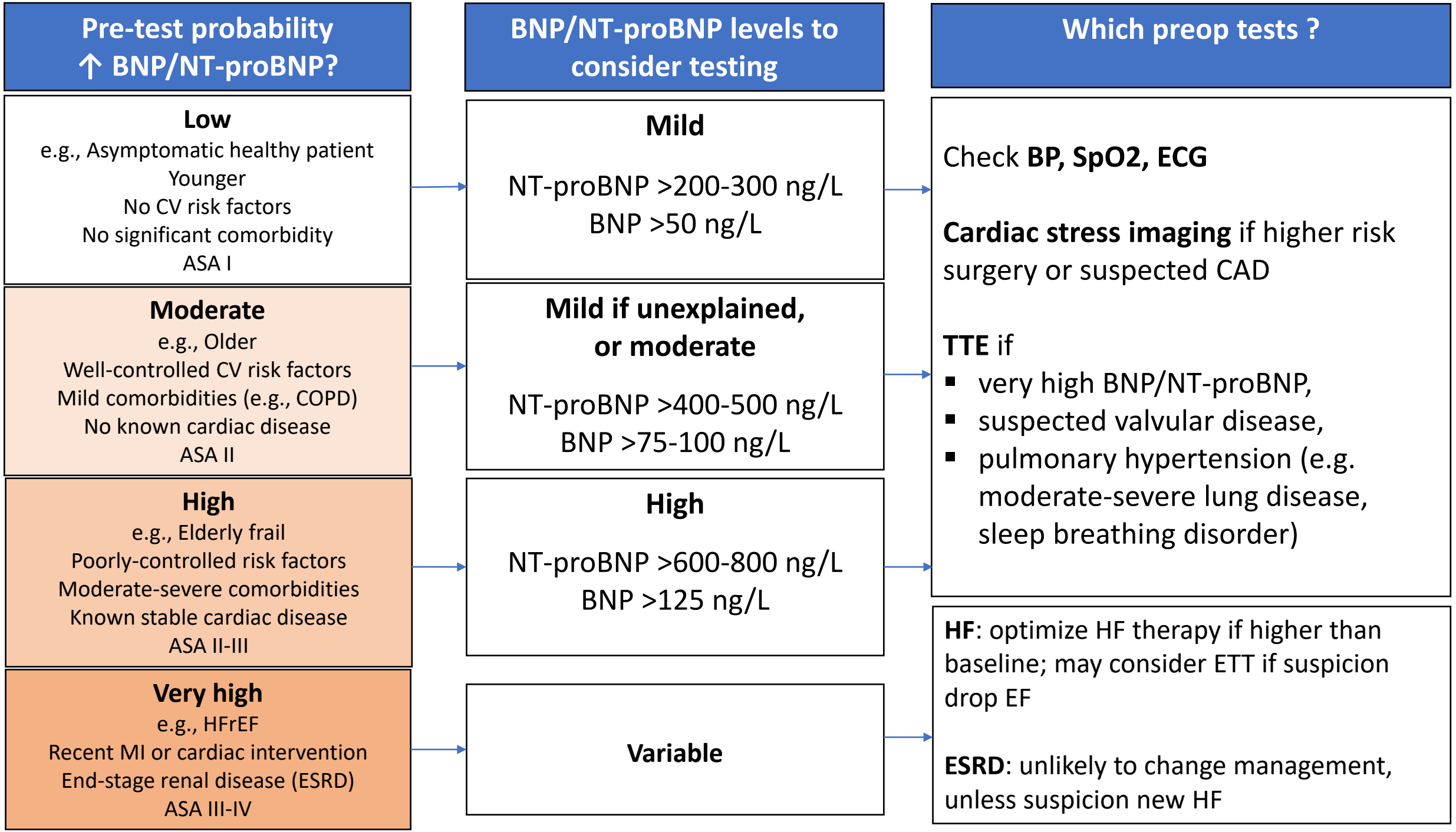
Disease	↑ BNP/NT-proBNP
Uncontrolled hypertension	↑
Left ventricular hypertrophy	↑
Clinical hyperthyroidism without ventricular dysfct	↑
Ischemic heart disease	↑-↑↑
Atrial fibrillation	↑-↑↑
Carcinoid heart disease	↑-↑↑
Primary and secondary pulmonary hypertension	↑-↑↑
Diastolic dysfunction	↑-↑↑
Cirrhosis	↑-↑↑
Cor pulmonale	↑↑-↑↑↑
Chronic heart failure and cardiomyopathy	↑↑-↑↑↑↑
End-stage renal disease	↑↑↑-↑↑↑↑

↑ = ≤2-3x upper limit of normal, ↑↑ = 4-5x upper limit of normal, ↑↑↑ = 5-10x upper limit of normal, ↑↑↑↑ = ≥10x upper limit of normal.

Can Journ Gen Int Med. 2021 Mar. 16

BNP/NT-proBNP for preop risk stratification

- BNP / NT-proBNP in most diseases where ↑:
  - Correlates with severity
  - Good “rule out” test
- Useful in patients without known disease and new findings
  - shortness of breath on exertion
  - heart murmur
  - ECG findings
- Useful to detect undiagnosed disease in patients with risk factors
  - e.g., pulmonary hypertension in COPD/sleep apnea patients


Pre-test probability
↑ BNP/NT-proBNP?
BNP/NT-proBNP levels to consider testing
Which preop tests ?
Low
e.g., Asymptomatic healthy patient
Younger
No CV risk factors
No significant comorbidity
ASA I
Mild
NT-proBNP >200-300 ng/L
BNP >50 ng/L
Check BP, SpO2, ECG
Cardiac stress imaging if higher risk surgery or suspected CAD
TTE if
very high BNP/NT-proBNP,
suspected valvular disease,
pulmonary hypertension (e.g. moderate-severe lung disease, sleep breathing disorder)
Moderate
e.g., Older
Well-controlled CV risk factors
Mild comorbidities (e.g., COPD)
No known cardiac disease
ASA II
Mild if unexplained, or moderate
NT-proBNP >400-500 ng/L
BNP >75-100 ng/L
High
e.g., Elderly frail
Poorly-controlled risk factors
Moderate-severe comorbidities
Known stable cardiac disease
ASA II-III
High
NT-proBNP >600-800 ng/L
BNP >125 ng/L
HF: optimize HF therapy if higher than baseline; may consider ETT if suspicion drop EF
Very high
e.g., HFrEF
Recent MI or cardiac intervention
End-stage renal disease (ESRD)
ASA III-IV
Variable
ESRD: unlikely to change management, unless suspicion new HF

Troponin for preop risk stratification

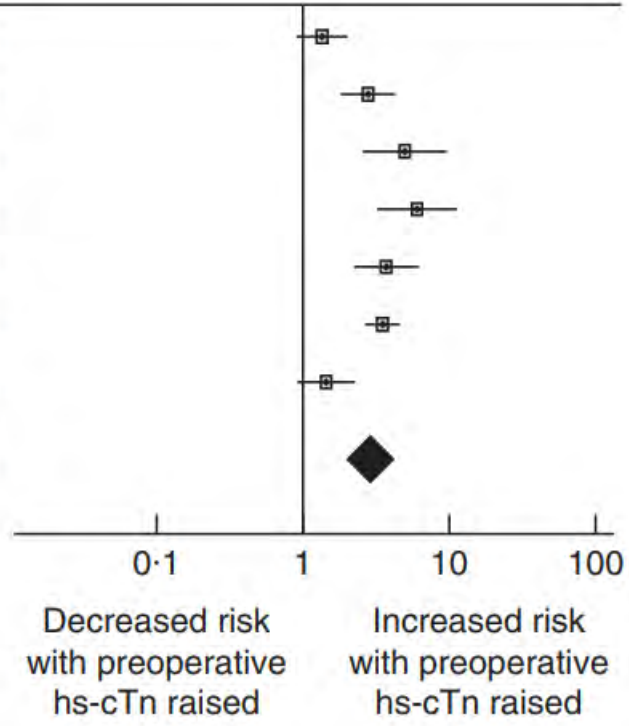
- Less costly and more widely available than BNP / NT-proBNP
- Allows for comparison with postop troponin
- Less evidence than BNP / NT-proBNP

Troponin for preop risk stratification

- Systematic review – 7 studies (n=4836)

Reference	Assay type	Cut-off (ng/l)	Short-term MACE: Preoperative hs-cTn raised	Short-term MACE: Preoperative hs-cTn not raised	Weight (%)	Risk ratio
Alcock *et al.*[26]	hs-cTnT	14	30 of 109	49 of 243	15·26	1·36 (0·92, 2·02)
Nagele *et al.*[21]	hs-cTnT	14	54 of 247	28 of 361	14·89	2·82 (1·84, 4·32)
Weber *et al.*[23]	hs-cTnT	14	22 of 233	14 of 746	12·14	5·03 (2·62, 9·67)
Gillmann *et al.*[24]	hs-cTnT	17·8	28 of 119	13 of 336	12·50	6·08 (3·26, 11·35)
Kim *et al.*[20]	hs-cTnT	6·5	44 of 107	17 of 155	13·98	3·75 (2·27, 6·20)
Puelacher *et al.*[19]	hs-cTnT	14	206 of 931	63 of 1006	16·58	3·53 (2·70, 4·62)
Gualandro *et al.*[25]	hs-cTnT	14	26 of 87	32 of 156	14·66	1·46 (0·93, 2·28)
Total			410 of 1833	216 of 3003	100·00	2·92 (1·96, 4·37)

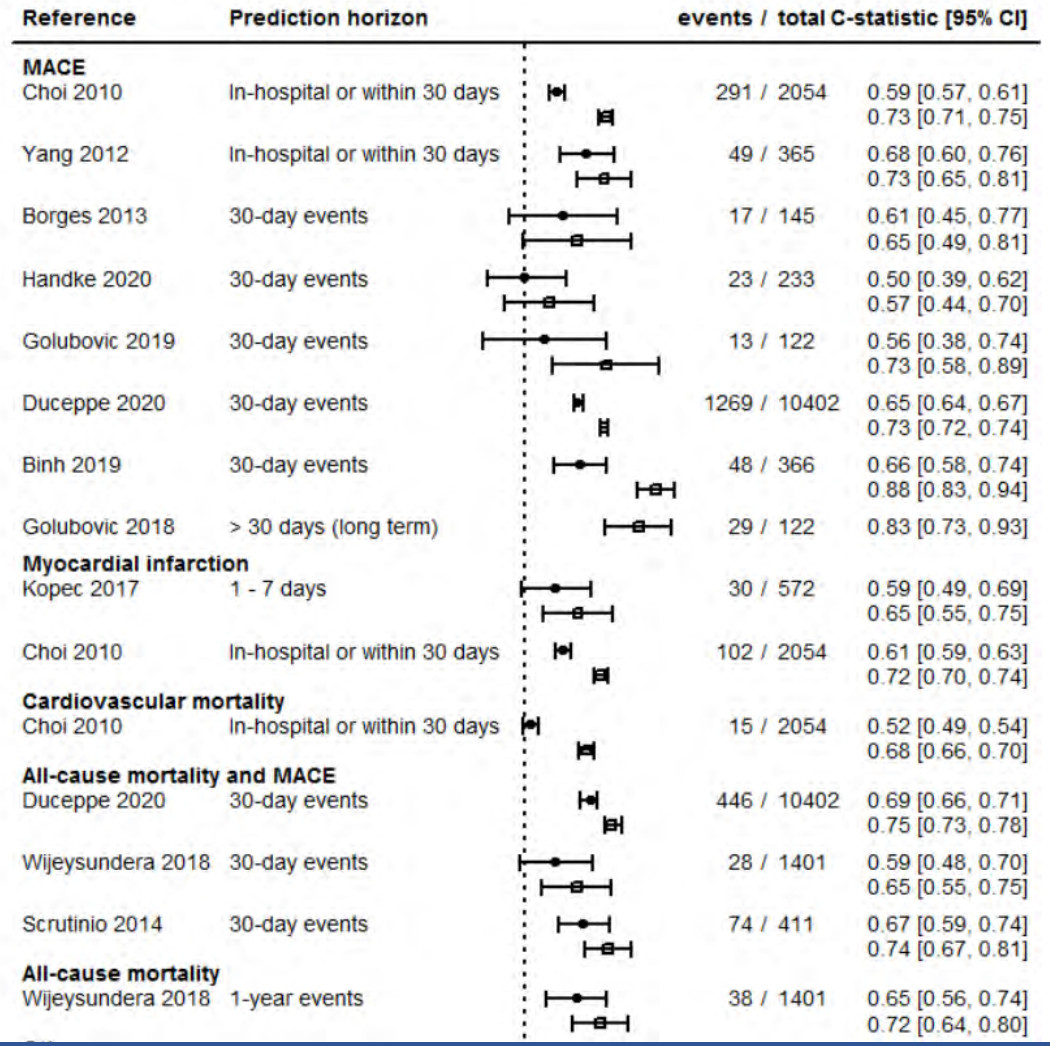
Heterogeneity: $\tau^2 = 0{\cdot}23$; $\chi^2 = 34{\cdot}56$, 6 d.f., $P < 0{\cdot}001$; $I^2 = 82{\cdot}6\%$
Test for overall effect: $Z = 5{\cdot}24$, $P < 0{\cdot}001$



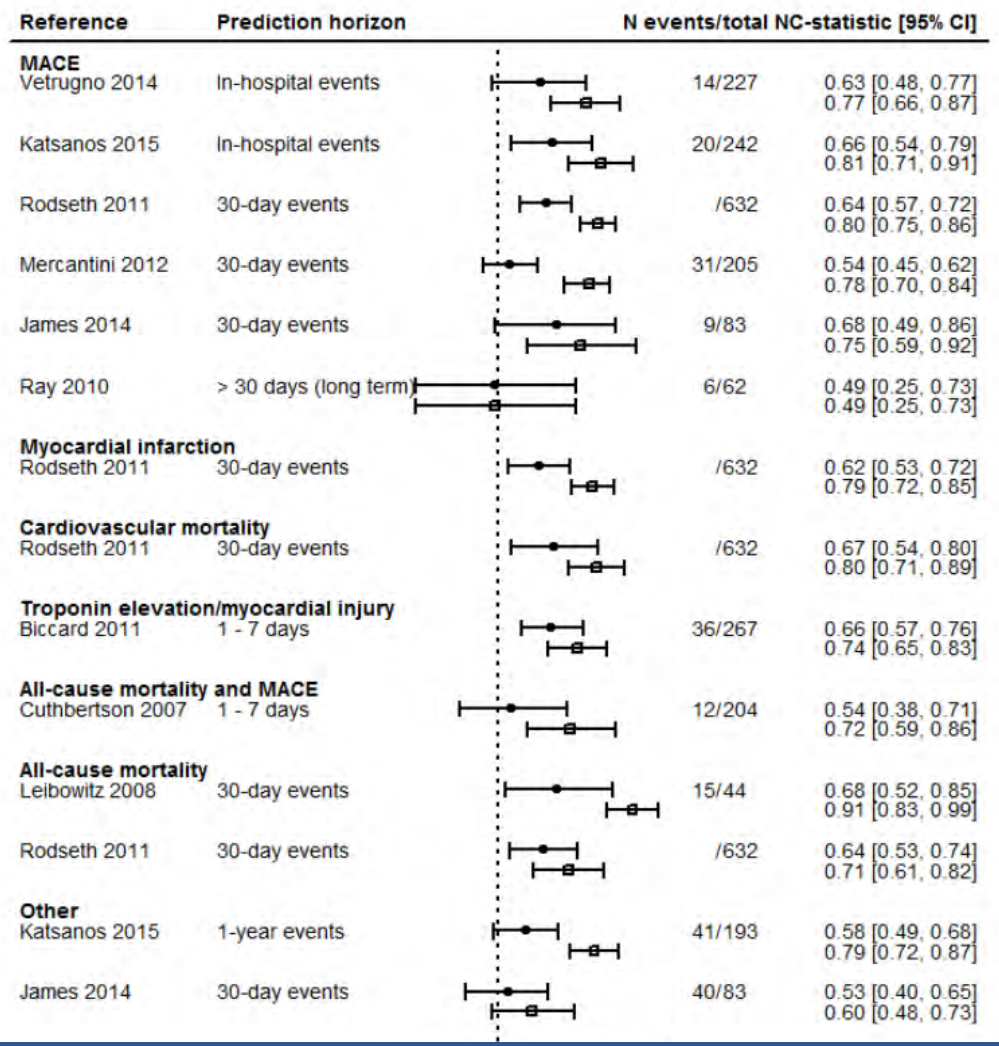
BJS 2020; 107: e81–e90

Added value of biomarkers in addition to risk scores

RCRI vs RCRI+**NT-proBNP**



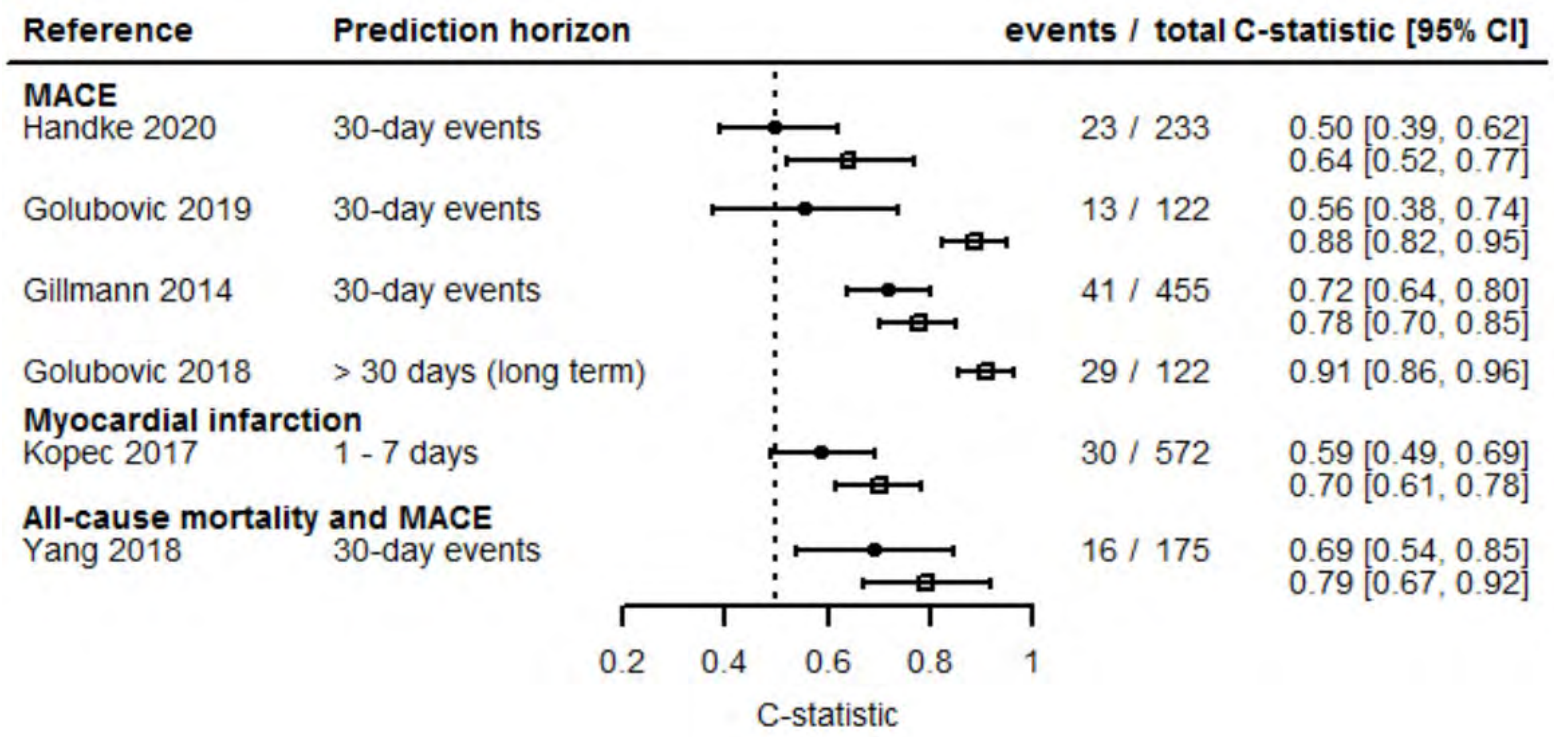
RCRI vs RCRI+**BNP**



Cochrane Database Syst Rev 2021 Dec 21;12(12):CD013139

Added value of biomarkers in addition to risk scores

RCRI vs
RCRI+troponin



Cochrane Database Syst Rev 2021 Dec 21;12(12):CD013139

Which biomarkers to use?

- Preop NT-proBNP, BNP, and troponin all provide additional prognostic information when added to RCRI
- NT-proBNP / BNP has undergone more extensive validation
- NT-proBNP / BNP have established prognostic thresholds for preop cardiac risk evaluation
- Troponin more widely available and less costly

ECG

- Often done routinely
- Low quality evidence and heterogeneous results
  - Mostly small or outdated studies (1980s)
- No specific ECG finding has been shown systematically to predict postop outcomes
- Incremental predictive value not demonstrated
- High-rate false positive, lead to testing/consultation

Order preop ECG?

- Not routinely in same-day surgery/low-risk surgery
- Similar cost to biomarkers
  - Biomarkers largely superior for risk prediction
- Useful for comparison with postop ECGs
  - In higher risk patients undergoing in-hospital surgery
  - If clinically indicated based on signs/symptoms

Preop echocardiogram

- Studies show inconsistent association between echocardiogram findings and perioperative ischemic events

- Park 2011
  - 1923 pts prospective cohort
  - echocardiogram within 2 weeks before surgery
  - several echocardiogram measurements predictors of major CV events
  - all echocardiogram parameters inferior to NT-proBNP for predicting major CV events ($p<0.001$)

Korean Circ J 2011;41:505-511

When to consider preop echocardiogram ?

- Large database study show that 1 in 4 preop echocardiogram “rarely appropriate”
- Not done routinely
- In selected patients with suspicion
  - cardiomyopathy
  - moderate to severe valvulopathy
  - pulmonary hypertension
  - NOT for suspicion of ischemic heart disease

Anesthesiology November 2021, Vol. 135, 854–863.

Preop cardiac stress tests

- Not routinely
- In selected patients with suspicion of ischemic heart disease
- If it will change management, consider
  - Urgency of surgery
  - Risk, duration of surgery
  - Patients risk factors
- Can impact
  - Intraop monitoring
  - Hemodynamic management
  - Transfusion threshold
  - Medication management
  - Timing of surgery

Preop coronary angiography/PCI

- In patients with high-risk findings on stress test
  - Suspicion 3VD, left main disease

- Balance risk of delaying surgery + bleeding risk vs cardiac risk
  - 1 month post PCI dual = surgery with dual antiplatelet therapy, then ASA only

What about same-day surgery?

- Very limited evidence in same-day surgery
  - Despite ≥50% of all procedures
- Many « low-risk » surgeries performed as same-day surgery included in earlier studies
  - VISION study (2007-2013): 9.3% MINS in low-risk surgery subgroup
- No guidelines on cardiac risk assesment for same-day surgery
- No systematic surveillance

What about same-day surgery?

- Risk scores
  - No validation in same-day surgery
  - Tend to underestimate risk in low-risk categories
  - Can be used as guidance but not risk estimates
- Biomarkers
  - Not recommended routinely
  - Useful to guide further investigation if clinical uncertainty
- ECG
  - Not routinely
- Cardiac testing
  - Only in selected population with clinical uncertainty/appropriateness for same-day surgery

Investigation plan and treatment for MINS

Case 2 – Postop consultation

- 74 yo female underwent whipple for pancreatic cancer
- Past medical Hx: HTN, type 2 diabetes, smoking history, mild COPD
- POD 1:
  - Well-controlled pain with epidural
  - BP 121/74 HR 88 Sat 95%
  - Hb 124
  - Creat 85
  - Hs-TnI 54 (ULN 14)
  - ECG: normal, same as preop

Case 2 – How will you proceed?

- Look at anesthetic record for precipitating factor (eg. hypotension)
- Continue measuring troponin + ECG daily for 2 days
- Echocardiogram
- Cardiac stress test
- Prescribe ASA + statin
- All of the above
- None of the above

MINS: How to define?

2021 AHA statement on MINS

Diagnostic criteria for MINS

≥1 postop cTn above 99th percentile, with rise/fall pattern
Within first 30 days postop (and typically within 72 h)
Attributable to presumed ischemic mechanism (ie, supply-demand mismatch or atherothrombosis) in absence of overt nonischemic cause (eg, pulmonary embolism)
Ischemic feature not required, as clinical symptoms may be masked by postop sedation/analgesia

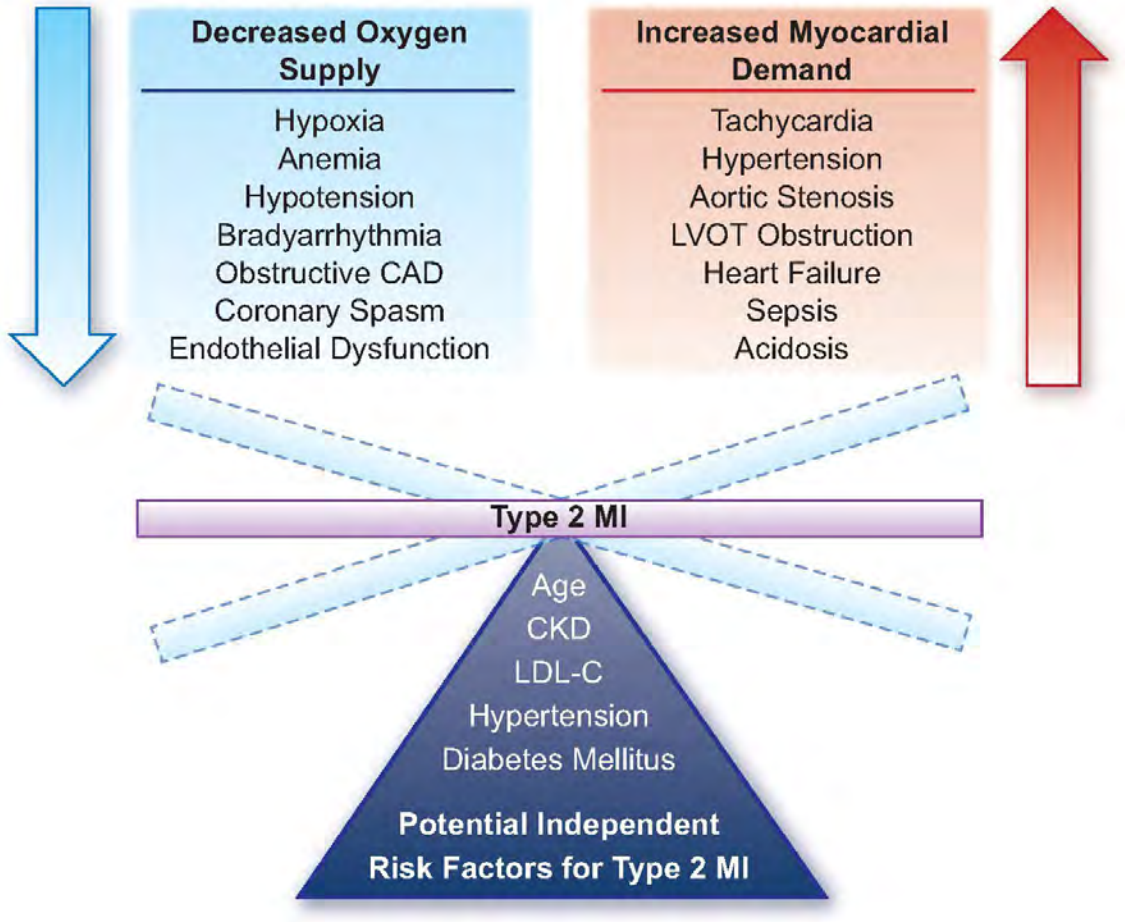
Circulation. 2021;144:e287–e305

MINS etiology

- Myocardial injury vs myocardial infarction
  - Type I vs Type II

Type 2 myocardial injury/infarction

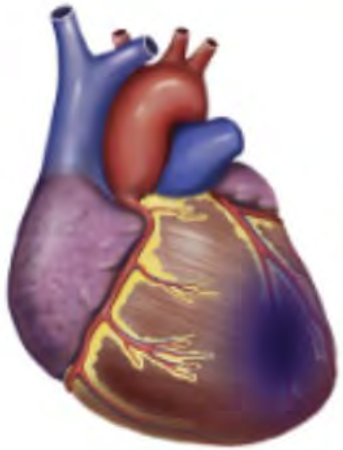
Surgery itself does not make a type II MI

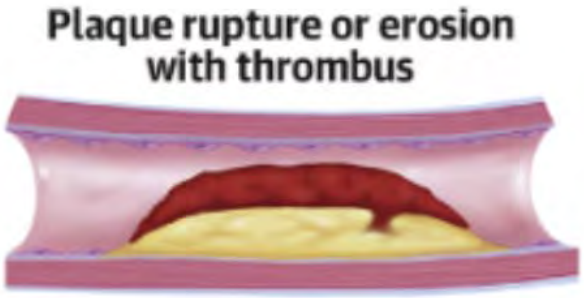


Eur Heart J, Volume 43, Issue 2, 7 January 2022, Pages 136–137, https://doi.org/10.1093/eurheartj/ehab707

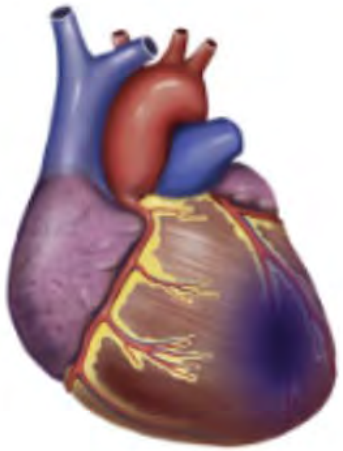
Is there underlying CAD?

Type 1 Myocardial Infarction

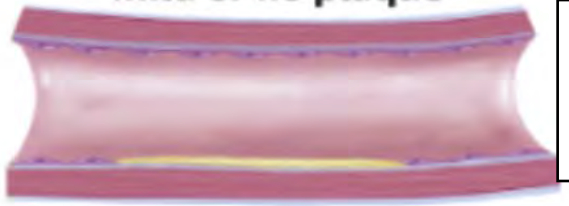




Type 2 Myocardial Infarction



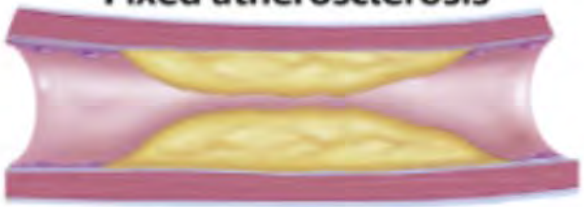
Mild or no plaque



↓↓↓ supply
and/or
↑↑↑ demand

OR

Fixed atherosclerosis



↓ supply
and/or
↑ demand

J Am Coll Cardiol 2021;77:848–5

MINS etiology: type 2 events

DEMAND-MI study

Prospective cohort

- 100 pts with type 2 MI enrolled
  - underwent coronary imaging: coronary angiogram or CCTA

Results

- Coronary imaging:
  - **60%** had findings of **unrecognized CAD**
  - **30%** had **obstructive CAD**
  - only **19%** had **normal coronary** imaging with no atherosclerosis or other coronary abnormalities

Circulation 2022 Apr 19;145(16):1188-1200

MINS etiology

VISION CCTA study

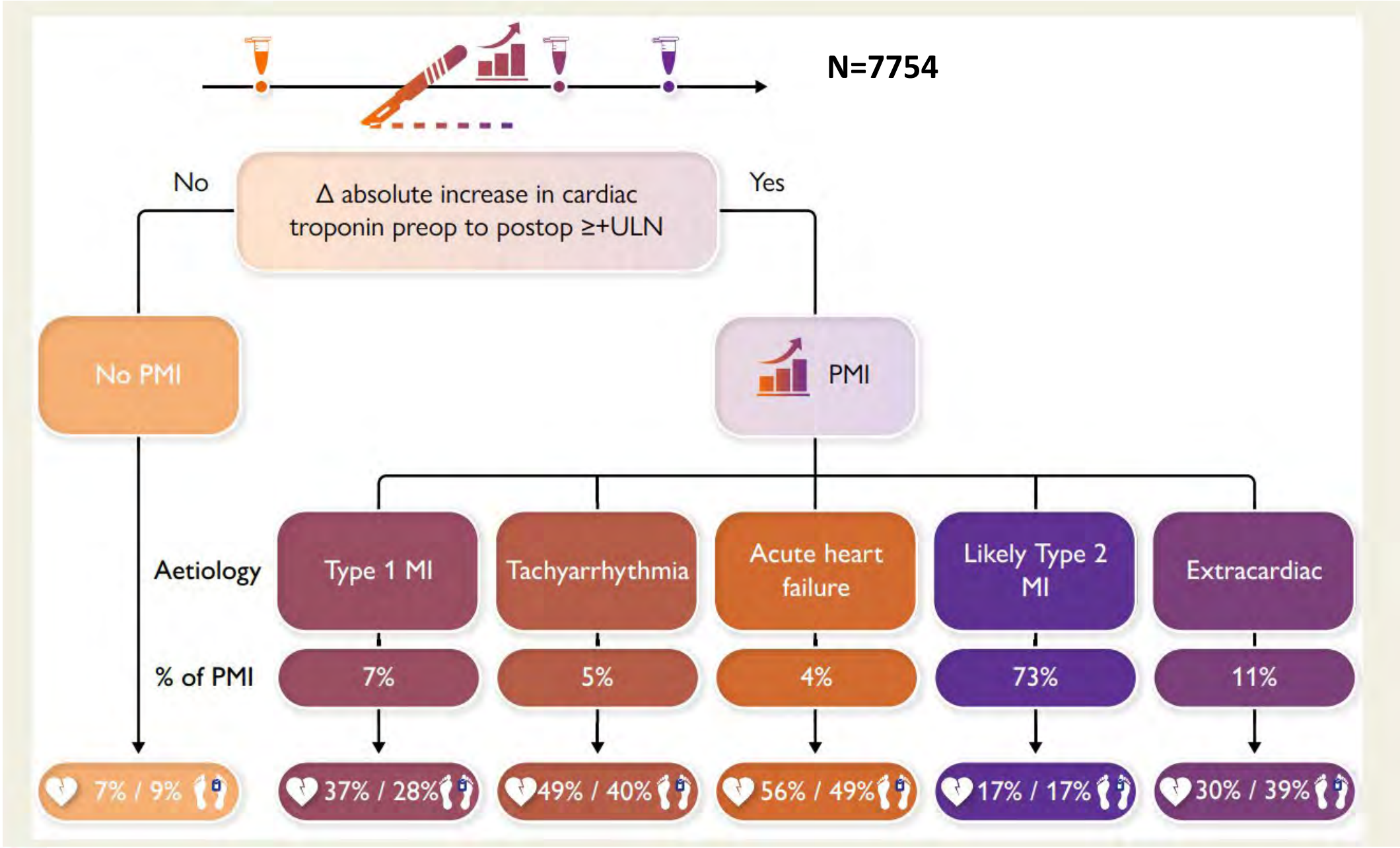
- 955 patients noncardiac surgery
- blinded preop coronary computed tomographic angiography (CCTA)

- among patients with postop MI, only **4% had no CAD**
  - 31% showed extensive obstructive CAD
  - 41% obstructive CAD
  - 24% non-obstructive CAD

Prognosis according to etiology

BASEL PMI study

- Prospective cohort study
  - 7754 patients
  - 3 hospitals (Switzerland, Brazil)
- Population
  - ≥65 years of age, OR
  - ≥45 years with history of CAD, PAD, or stroke
  - undergoing inpatient non-cardiac surgery with overnight hospital stay
- High-sensitivity troponin
  - Preop
  - POD 1, POD 2
- 1 year follow-up



MACE Mortality

MACE = acute myocardial infarction, AHF, life-threatening arrhythmia, and cardiovascular death

Puelacher et al. European Heart Journal (2022) 00, 1–12

MINS etiology

- Majority of patients with MINS have underlying CAD
  - Most type 2 MIs
- Evaluation should include looking for precipitating factor
- Based on current evidence, default should be to consider underlying CAD predisposing to MINS
  - unless clear supply/demand mechanism

MINS: investigation plan

Additional testing after MINS diagnosis

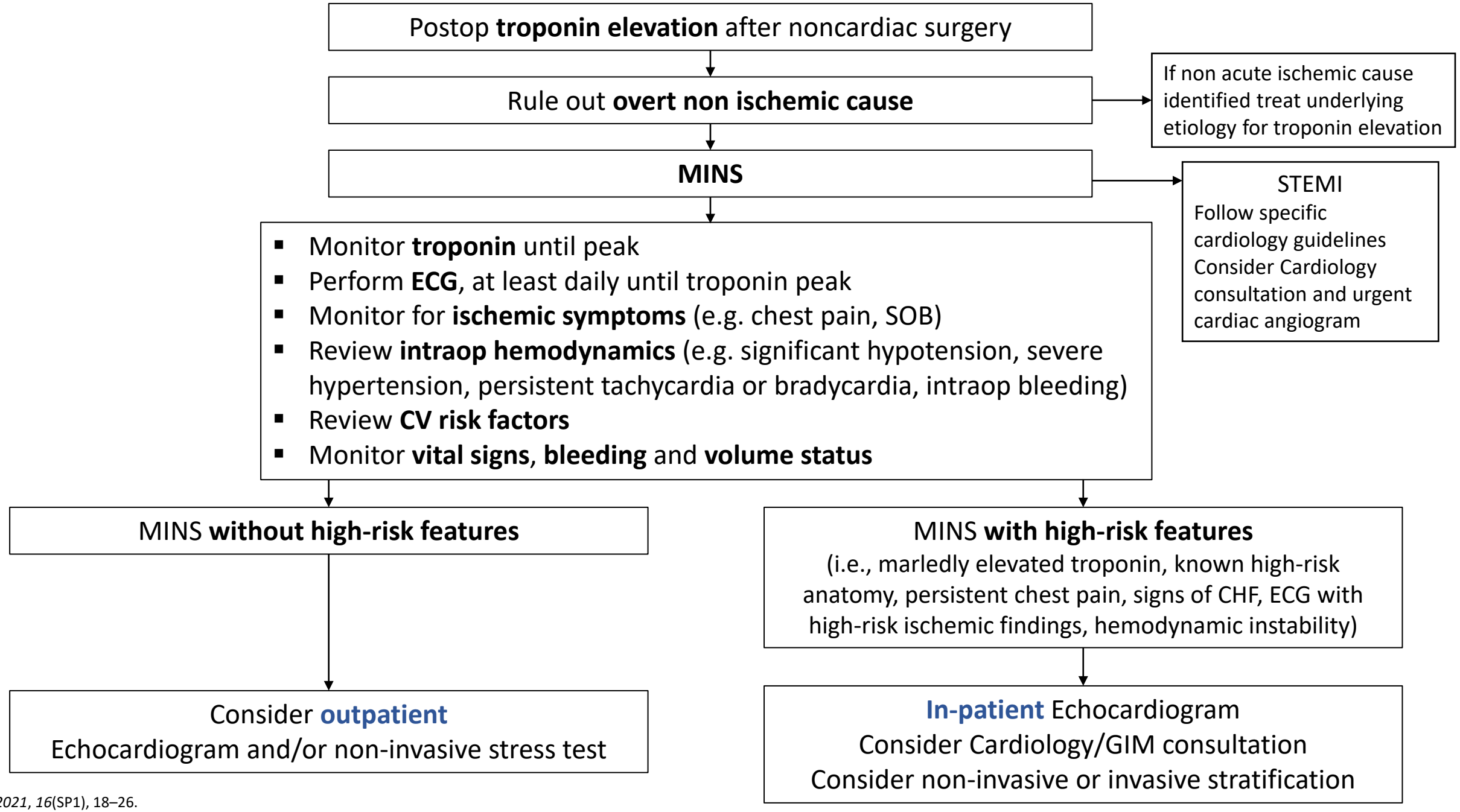
What should be done:

- **Serial troponin** → Identify peak cTn
  - *Higher Tn have worse prognosis*
- **Serial ECGs** → ischemic changes?
  - *MINS with ischemic features have worse prognosis*

What should be considered:

- **Echocardiogram** → assess cardiac structure and function, regional wall motion abnormalities?
  - *1 in 4 MINS meet definition of MI*
- **Non-invasive cardiac stress test** → underlying ischemia?
  - *Coronary angiography studies show that ≥2/3 have significant CAD, but only 4% have no CAD*
- **Coronary angiography** → if high risk ischemic features

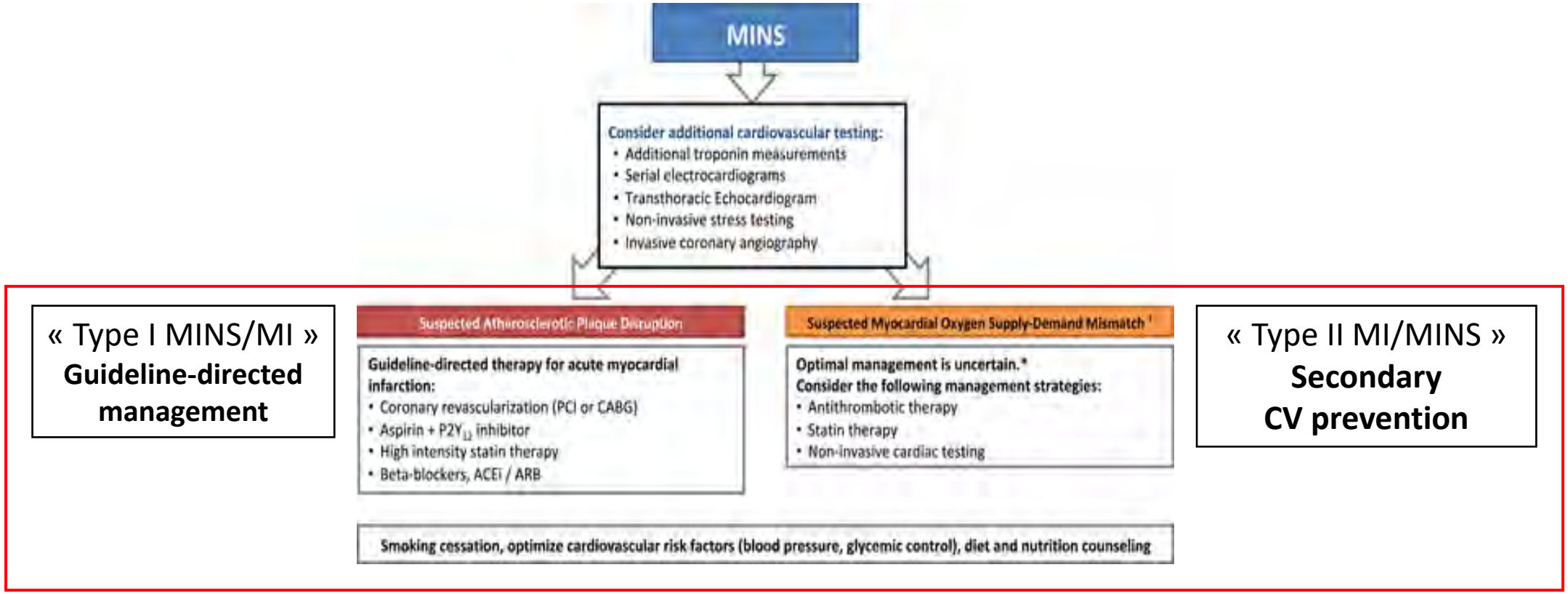
J Am Coll Cardiol. 2016 Jul 26;68(4):329-38
CMAJ. 2019 Jul 29;191(30):E830-E837
JAMA. 2017;317(16):1642-1651.



CJGIM 2021, *16*(SP1), 18–26.

MINS: treatment options

2021 AHA statement on MINS



Kurt Ruetzler. Circulation. Diagnosis and Management of Patients With Myocardial Injury After Noncardiac Surgery: A Scientific Statement From the American Heart Association, Volume: 144, Issue: 19, Pages: e287-e305, DOI: (10.1161/CIR.0000000000001024)

MINS: treatment options for secondary CV prevention

Therapy	Summary of Evidence	References
ASA	▪ Cohort 415 pts with postop MI : **aOR 0.54** (95% CI, 0.29-0.99) in **30d mortality** ▪ Cohort 3818 pts with MINS: **aOR 0.48** (95% CI, 0.39-0.73) in **1y mortality**	Ann Intern Med. 2011;154:523-528 Open Heart 2023;10
Statin	▪ Cohort 5109 pts with MINS: **aHR 0.55** (95% CI, 0.41–0.74) for **1y mortality** ▪ Cohort 415 pts with postop MI : **aOR 0.26** (95% CI, 0.13-0.54) in **30d mortality** ▪ Cohort 2793 pts with MINS: **aHR 0.60 for ACS** and **aHR 0.46 for HF** at 6 mth	Sci Rep. 2020 Jul 15;10(1):11616 Ann Intern Med. 2011;154:523-528 Can J Card 37 (2021) 57-65
ACEI/ARB	▪ Cohort 2793 pts with MINS: **aHR 0.53 for ACS** and **aHR 0.26 for HF** at 6mth	Can J Card 37 (2021) 57-65
Beta-blocker	▪ Cohort 2793 pts with MINS: **aHR 0.48 for ACS** and **aHR 0.47 for HF** at 6 mth	Can J Card 37 (2021) 57-65
CV therapy	▪ Cohort machine learning 7629 pts with MINS: **antiplatelet, statin, CCB, ACEI/ARB, and DOAC** associated with **reduced 30-day mortality** ▪ Case-control 667 pts: Pts with MINS who **did not have intensification of CV therapy** HR **2.80** (95% CI, 1.05–24.2) compared with patients who did receive treatment intensification for 1y MACE	JMIR Med Inform 2021;9(10):e32771 Anesth Analg 2014 Nov;119(5):1053-63
DOAC	▪ RCT 1754 pts with MINS **dabigatran** 110 mg BID vs placebo: **HR 0.72** (95%CI 0.55-0.93) for composite vasc death, MI, stroke, peripheral art. thrombosis, amputation, and VTE (MANAGE Trial)	Lancet 2018; 391: 2325–34

MINS: How to manage?

- General consensus in guidelines to intensify CV medication therapy
  - **ASA** and **statin** for secondary prevention
  - potential benefit for **ACEI/ARB** and **beta-blockers**
  - treat other risk factors (HTN, diabetes etc)
  - coronary angiogram/PCI if high risk features

- Uncertainty remains for MINS without high-risk features

- MANAGE Trial only RCT
  - uptake limited for DOAC/dabigatran in clinical practice
  - provides compelling evidence, consistent with coronary angiogram studies, that thrombosis and underlying CAD contribute to MINS and associated prognosis

MINS: outpatient follow-up

- Gouda et al. (Alberta)
  - 2793 pts with MINS
  - follow-up with internal medicine or cardiology after MINS
    - ➢ reduction in 6-month mortality (HR 0.49; p=0.004)

- Oh et al. (South Korea)
  - 1329 patients with MINS
  - propensity score matched analyses
  - outpatient cardiology consultation
    - ➢ reduced 30-day CV mortality (HR 0.58, 95% CI 0.35-0.95)

Gouda et al. Can J Card 37 (2021) 57-65
Oh et al. Diagnostics (Basel) 2021;11. 2229

In summary

- MINS
  - Serial troponin until peak
  - ECG to detect ischemic features
  - Consider cardiac imaging, in particular if high-risk features
  - Initiate secondary cardiovascular prevention
    - ASA and statin, +/- other CV medications
  - Outpatient follow-up, in particular high-risk features