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Cardiac

What is the problem

Cancer patients are a high cardiovascular risk cohort. Both cancer and cardiovascular disease have interlinked risk factors in common such as increasing age, obesity and smoking. Many oncological therapies also have associated cardiovascular side effects which further increase the cardiovascular risk profile of cancer patients.

Cancer therapy related cardiovascular toxicity (CTR-CVT) refers to any cancer treatment related effects that cause injury to the cardiovascular system. This injury can lead to both structural and/or functional injury to the myocardium.

Commonly encountered oncological therapies which cause cardiotoxicity

High dose chest radiotherapy

- May include heart within radiation field
- Induces inflammation and subsequent scarring to the myocardium, conduction system, coronary vessels, valves, and pericardium
- Can affect contractility, cardiac conduction, coronary perfusion, valvular stenosis, and ventricular filling.

Anthracyclines e.g. doxorubicin

- Used to treat solid organ tumours e.g. breast, lung or haematological malignancies
- Cardiotoxicity likely arises from the formation of reactive oxygen species that trigger myocardial dysfunction and apoptosis
- Dose related risk especially if cumulative dose exceeds >400mg/m^2.

HER 2 receptor monoclonal antibodies e.g. trastuzumab

- Used in combination with anthracyclines for HER 2 positive breast cancer
- Improves cancer survival by 33% and reduces recurrence rates by 50%
- Thought to interfere with myocyte remodelling and healing.

Antimetabolites e.g. 5 fluorouracil

- Used in solid organ tumours e.g. colon
- Capecitabine is oral version of 5-FU
- Patients can develop chest pain, ECG changes and elevated troponins (acute coronary syndrome picture) from associated coronary vasospasm.

Immune checkpoint inhibitors e.g. ipilimumab

- New developing field of oncology enhancing T cell mediated tumour destruction
- Autoimmune side effects are fairly common
- Myocarditis is rare (1%), but usual fatal if develops.

Cardio-oncology

Cardio-oncology services arose in response to the identification of CTR-CVT and an increasing number of long-term cancer survivors affected by cardiovascular disease. The overarching aim is to allow patients with cancer to receive the best possible cancer treatment safely[1]. This involves a baseline cardiovascular risk assessment, surveillance and management of acute CTR-CVT during cancer treatment and guidance on management of long-term cardiovascular complications on completion of treatment.

The CTR-CVT graph (figure. 1) shows the timing of highest cardiovascular toxicity risk during cancer treatment. This often coincides with perioperative patients undergoing neoadjuvant therapy prior to cancer surgery. The cardio-oncology goals to minimise CTR-CVT and overall cardiovascular risk profile conveniently align with the period of perioperative optimisation of cardiac risk factors during prehabilitation.

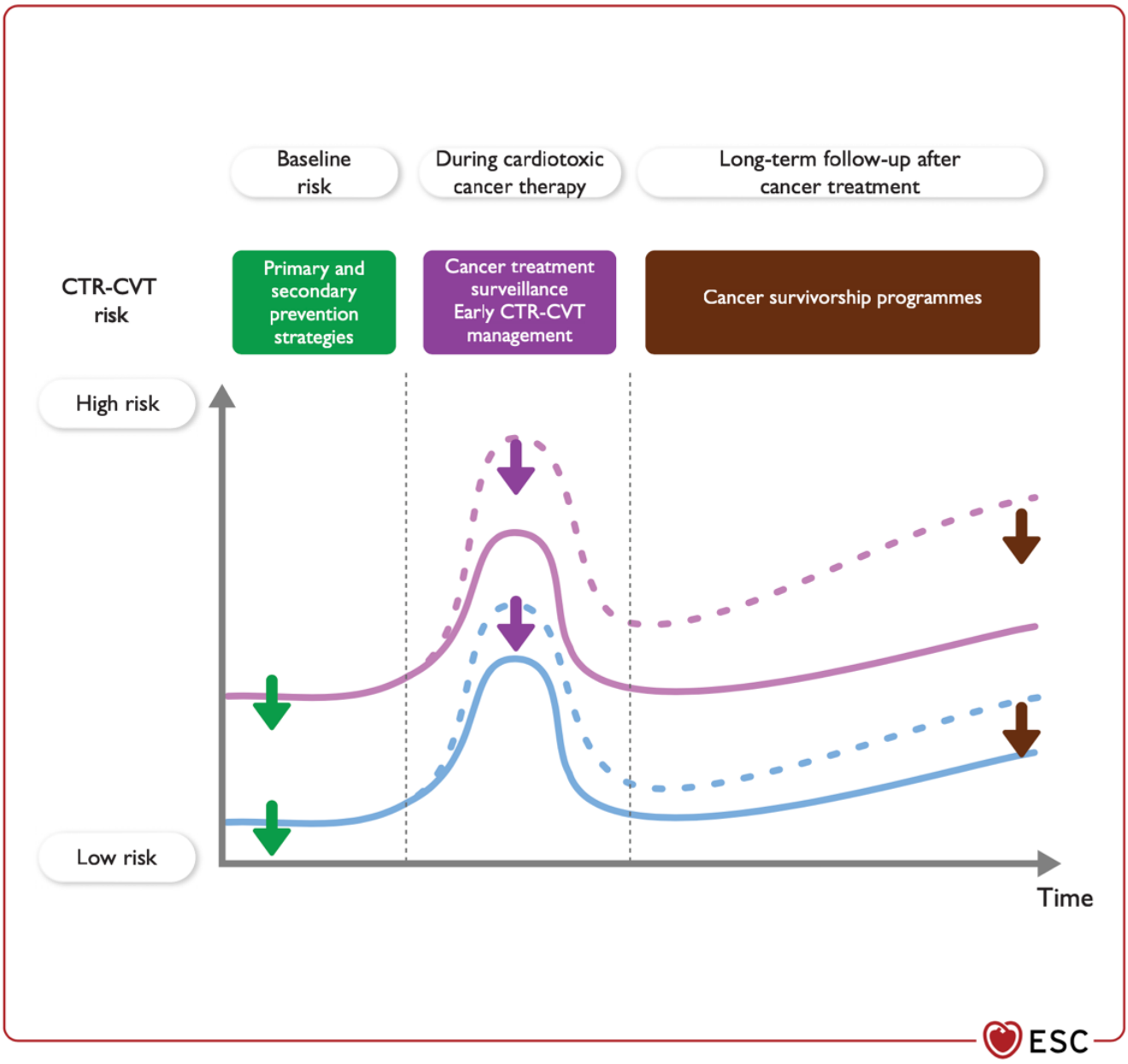


Figure 1: Cardiovascular toxicity risk of patients over time, with the potential effect of cardioprotective strategies to reduce risk (arrows)[2].

The majority of cardiotoxicity syndromes manifest within the first year of oncological treatment, which forms the majority of patients presenting for cancer surgery. The oncological factors that increase the risk of cardiotoxicity can be grouped into three categories[3]:

Patient factors

- Female
- Age > 50 years
- Presence of cardiovascular risk factors: hypertension, smoking, obesity dyslipidaemia, insulin resistance
- Pre-existing cardiac disease, reduced LVEF 50-54% pre-treatment

Oncological factors

- Doxorubicin lifetime dose >250mg/m2 or equivalent
- Prior chemotherapy related cardiotoxicity
- High dose radiation to central chest including heart in radiation field >30Gy

Objective biomarkers

- Elevated baseline troponin or NT-proBNP
- Elevated troponin or NT-proBNP during cancer therapy
- eGFR < 78mL/min/1.73m2

Delayed cardiotoxicity occurring 12 months or more after completion of oncological care is less likely to be encountered in the prehabilitation setting. A history of previous cancer therapies should be enquired for in a patient presenting with features of heart failure in the perioperative period.

Screening and assessment

The initial assessment of cardiovascular toxicity risk involves:

1. Evaluation of the patient's baseline cardiac risk factors
2. Understanding the cardiovascular implications of a specific tumour aetiology
3. Identification and treatment of unwanted cardiac side effects of oncological treatment.

This framework aims to reduce long term cardiovascular risk in cancer patients.

Routine perioperative cardiovascular risk evaluation utilising history, examination and investigations forms the foundation of a baseline cardiovascular toxicity risk assessment[2].

- History of smoking, alcohol intake, diabetes, hypertension, dyslipidaemia, obesity, renal impairment and presence of existing cardiac disease
- Enquiry should be made for symptoms of exertional dyspnoea, chest pain, palpitations, pre-syncope/syncope, orthopnoea, paroxysmal nocturnal dyspnoea and peripheral oedema
- Evaluation of functional status through the Duke Activity Status Index (DASI) with a score ≤34 indicating increased risk of perioperative complications
- Cardiovascular examination including pulse, BP, SpO2, presence of murmurs, JVP, peripheral oedema
- Baseline cardiac investigations: ECG, FBC, U&E, HbA1c and BNP and troponin if appropriate (see section on biomarkers below).

Biomarkers

A combination risk assessment includes clinical history and assessment of functional capacity as above, and measurement of biomarkers:

- B-type natriuretic peptide (BNP) or N-terminal pro-B-type natriuretic peptide (NT-proBNP)

and/or

- high-sensitivity cardiac troponins I or T (cTn I or cTn T).

Cardiac biomarkers can be measured in patients with cardiac risk factors, known/suspected cardiac disease or cardiotoxicity who are scheduled to undergo intermediate or major surgery[2,4,5,6,7,8].

These tests may be used to risk stratify, guide the need for further cardiac testing pre-operatively, advise shared decision making and inform perioperative management such as the level of postoperative care/monitoring (eg HDU or ward) or pre-operative referral to perioperative medicine services for shared post-operative care.

High sensitivity cardiac troponins I and T (cTn I and cTn T)

- Consider measurement before and for 48 to 72 hours after intermediate and high-risk surgery in patients aged ≥ 65 years, or those < 65 years with significant cardiovascular disease risk
- Facilitates differentiation between acute postoperative changes and chronic elevations
- Associated with 30-day all-cause mortality, 1-year mortality and 30-day major adverse cardiac events (MACE)
- In patients who suffer myocardial injury after non-cardiac surgery (MINS), consider inpatient referral to cardiology for aggressive cardiac risk factor modification and need for further investigation

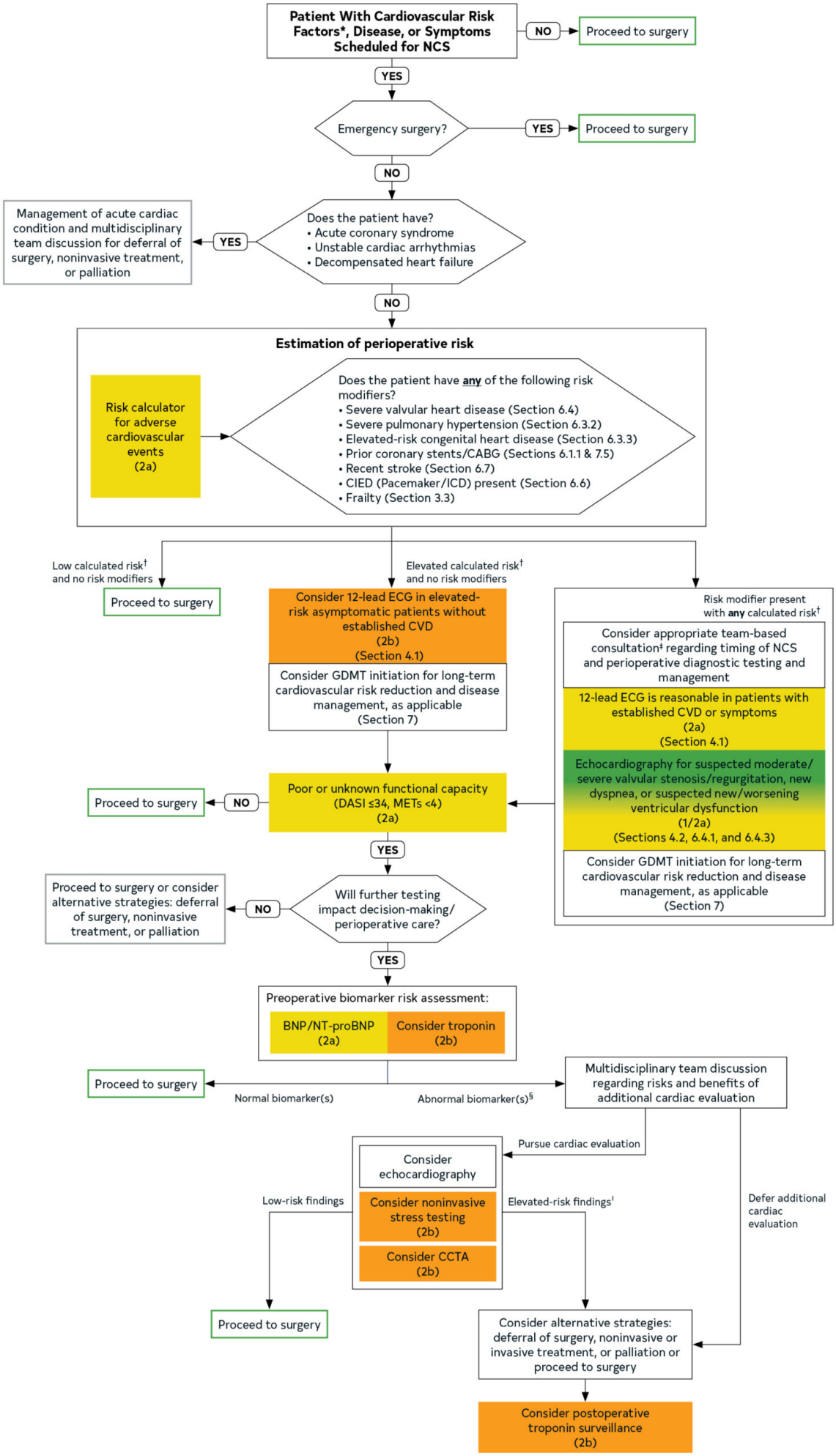
B-type natriuretic peptide (BNP) and N-terminal pro-B-type natriuretic peptide (NT-proBNP)

- Consider measurement before intermediate and high-risk surgery in patients aged ≥ 65 years, or those < 65 years with significant cardiovascular disease risk
- May be used to help evaluate risk of 30-day MACE, 30-day mortality & myocardial infarction (MI)
- It is worth noting that BNP cut offs for elevated perioperative risk may be less than those required for a diagnosis of heart failure (particularly in elderly patients).

NT-proBNP Measurement and Perioperative risk of MACE or MINS (Adapted from Duceppe et al 2020) (8)

NT-proBNP level	HR for MACE or MINS	30 Day mortality (Incidence)
100-200ng/ml	2.27 (95% CI 1.90-2.70)	0.7%
200-1500ng/ml	3.63 (3.13-4.12)	1.4%
>1500ng/ml	5.82 (4.81 to 7.05)	4%

Figure 2. 2024 AHA/ACC/ACS/ASNC/HRS/SCA/SCCT/SCMR/SVM Guideline[6] – One potential approach to perioperative cardiovascular risk assessment


Patient With Cardiovascular Risk Factors*, Disease, or Symptoms Scheduled for NCS
NO
Proceed to surgery
YES
Emergency surgery?
YES
Proceed to surgery
NO
Does the patient have?
• Acute coronary syndrome
• Unstable cardiac arrhythmias
• Decompensated heart failure
YES
Management of acute cardiac condition and multidisciplinary team discussion for deferral of surgery, noninvasive treatment, or palliation
NO
Estimation of perioperative risk
Risk calculator for adverse cardiovascular events (2a)
Does the patient have any of the following risk modifiers?
• Severe valvular heart disease (Section 6.4)
• Severe pulmonary hypertension (Section 6.3.2)
• Elevated-risk congenital heart disease (Section 6.3.3)
• Prior coronary stents/CABG (Sections 6.1.1 & 7.5)
• Recent stroke (Section 6.7)
• CIED (Pacemaker/ICD) present (Section 6.6)
• Frailty (Section 3.3)
Low calculated risk† and no risk modifiers
Proceed to surgery
Elevated calculated risk† and no risk modifiers
Consider 12-lead ECG in elevated-risk asymptomatic patients without established CVD (2b) (Section 4.1)
Consider GDMT initiation for long-term cardiovascular risk reduction and disease management, as applicable (Section 7)
Risk modifier present with any calculated risk†
Consider appropriate team-based consultation‡ regarding timing of NCS and perioperative diagnostic testing and management
12-lead ECG is reasonable in patients with established CVD or symptoms (2a) (Section 4.1)
Echocardiography for suspected moderate/severe valvular stenosis/regurgitation, new dyspnea, or suspected new/worsening ventricular dysfunction (1/2a) (Sections 4.2, 6.4.1, and 6.4.3)
Consider GDMT initiation for long-term cardiovascular risk reduction and disease management, as applicable (Section 7)
Poor or unknown functional capacity (DASI ≤34, METs <4) (2a)
NO
Proceed to surgery
YES
Will further testing impact decision-making/perioperative care?
NO
Proceed to surgery or consider alternative strategies: deferral of surgery, noninvasive treatment, or palliation
YES
Preoperative biomarker risk assessment:
BNP/NT-proBNP (2a)
Consider troponin (2b)
Normal biomarker(s)
Proceed to surgery
Abnormal biomarker(s)§
Multidisciplinary team discussion regarding risks and benefits of additional cardiac evaluation
Pursue cardiac evaluation
Consider echocardiography
Consider noninvasive stress testing (2b)
Consider CCTA (2b)
Low-risk findings
Proceed to surgery
Elevated-risk findings‖
Consider alternative strategies: deferral of surgery, noninvasive or invasive treatment, or palliation or proceed to surgery
Defer additional cardiac evaluation
Consider postoperative troponin surveillance (2b)

Referral and specialised cardiac investigations

The choice of cardiac investigation to answer a specific clinical question is influenced by availability, cost and level of accuracy required. Each investigation will have specific advantages and disadvantages (see table below).

A referral to a cardiologist is recommended prior to arranging any specific investigation.

MUGA

Advantages	Disadvantages
Accessible Cheap Reproducible result	Inaccurate (often by >10%) Significant radiation exposure Cannot evaluate dynamic cardiac function e.g. valvular function, diastology

Echocardiogram

Advantages	Disadvantages
Accessible Cheap Moderately accurate LVEF Ability to assess right ventricle and valves	LVEF can have 5-10% inaccuracy Difficult in obese

Advanced echocardiogram

Advantages	Disadvantages
3D LVEF and GLS is more accurate and reproducible Provides ‘early warning’ for reduced LV function	Not always accessible

Cardiac CT

Advantages	Disadvantages
Allows for calcium scoring Can exclude obstruction coronary artery disease Can measure left and right ejection fraction	Radiation and contrast exposure Need for beta-blockersCost Not always accessible

Cardiac MRI

Advantages	Disadvantages

Gold standard for evaluating left and right ventricular ejection fraction Able to visualise myocardial scar tissue	Poor accessibility CostNot suitable for some patients e.g. claustrophobia, pacemakers

Carcinoid heart disease

Carcinoid heart disease can occur in patients with carcinoid syndrome secretory neuroendocrine tumours. Cardiac involvement is present in 37% of patients with carcinoid syndrome and typically leads to tricuspid regurgitation, pulmonary stenosis and/or pulmonary hypertension. An echocardiogram is required to determine the presence of valvular disease, pulmonary hypertension and left and right ventricular function. 5-HIAA levels can be useful as carcinoid heart disease is almost never seen if 5-HIAA levels are below 50mg/24 hours[9].

Hepatic resection of metastatic carcinoid cancer can prolong survival and control symptomatic endocrinopathy[10]. The increased central venous pressure associated with tricuspid regurgitation significantly increases surgical risk due to increased blood loss during liver resection. Valve replacement should be considered if transpulmonary gradient is ≥10mmHg. It is safe and is association with similar outcomes as patients without carcinoid heart disease undergoing hepatic resection for carcinoid syndrome[11].

Resources

Guidelines

- 2024 ACC/AHA Guideline for Perioperative Cardiovascular Management for Noncardiac Surgery
- 2023 ESAIC focused guideline for the use of cardiac biomarkers in perioperative risk evaluation
- 2022 ESC Guidelines on cardiovascular assessment and management of patients undergoing non-cardiac surgery
- 2017 Canadian Cardiovascular Society Guidelines on Perioperative Cardiac Risk Assessment and Management for Patients Who Undergo Noncardiac Surgery

Example of local guideline (Northern Health)

Northern Preoperative Cardiac Testing Guideline

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