

Manitoba Troponin Guideline

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Note: This document was originally prepared for use within the WRHA that uses Troponin T only, due to differences in laboratory instrumentation. As most of the content is the same for either TnT or TnI this document has been modified to reflect the assays in use in other parts of Manitoba. Troponin I and T are of equivalent diagnostic use. Values reported by different Troponin assays will not be identical.

Abbreviations:

AMI	acute myocardial infarction
AUC	area under the curve
CAD	coronary artery disease
CRF	chronic renal failure
CV	coefficient of variation
ED	emergency department
ESC/ACC	European Society of Cardiology / American College of Cardiology
LOS	length-of-stay
MR	mitral regurgitation
NLR	negative likelihood ratio
NPV	negative predictive value
NSTEMI	non-ST segment elevation MI
ROC	receiver operating curve
STEMI	ST segment elevation MI
th ile	percentile
TnI	troponin I
TnT	troponin T

OVERVIEW

1. In patients with a low likelihood of ACS:

- ⇒ Troponin must be measured at least six (6) hours after the onset of chest pain.
- ⇒ Troponin measurement may be deferred until six (6) hours after the onset of pain.
- ⇒ Troponin samples may be measured two (2) hours apart when measured at least 6 - 9 hours after the onset of chest pain (e.g. sample one at 6 hours after the onset of pain, sample two at 8 hours).
- ⇒ If Troponin measured ≥ 9 (nine) hours is negative, AMI may be safely ruled-out in patients with a low likelihood of ACS.

2. Troponin is considered negative: (when measured $\geq 6 - 9$ hours after the onset of chest pain)

i-STAT Tnl	Dade Tnl	Bayer Tnl ultra	Roche TnT	
< 0.08 µg/L	< 0.07 µg/L	<0.04 µg/L	< 0.01 µg/L	
≥ 0.08 µg/L	≥ 0.07 µg/L	≥ 0.04 µg/L	≥ 0.01 µg/L	<u>and</u> not rising on 2 samples measured at least 2 hours apart <u>and</u> in context of alternate etiology for elevated troponin

3. A rising troponin level is required in order to diagnose AMI.

4. In patients with background elevations of troponin (e.g. patients with CRF), two (2) measurements are required to demonstrate a rising pattern.

5. No single serum marker used alone has sufficient sensitivity or specificity to reliably identify or exclude AMI within 6 hours after symptom onset.

6. Discontinue the use of myoglobin, CK, and CK-MB as cardiac markers for the rule-out of AMI in the ED.

7. Do not utilize cardiac serum marker tests to exclude unstable angina.

8. Document the time of onset of chest pain on all patients.

Recommended Troponin testing protocol for a patient with a low likelihood of ACS

- ⇒ **Do not utilize cardiac serum marker tests to exclude unstable angina.**
(ACEP NSTEMI Clinical Policy, 2006)
- For the definition of unstable angina, see appendix A
- ⇒ **Document the time of onset of chest pain on all patients.**
- ⇒ If the time of onset of chest pain is not known, then the time of presentation must be utilized for cardiac marker interpretation.

Assess Likelihood of ACS:

Low Likelihood (e.g. 1% - 14% likelihood)

- chest pain, “probably not angina” in patients with one or no risk factors for CAD, but not diabetes
- T-wave flat or inverted < 1 mm
- normal ECG

Intermediate Likelihood (e.g. 15% - 84% likelihood)

- “definite angina” in patients with no risk factors
- “probable angina” in patients with one or more risk factors
- “probably not angina” in patients with diabetes or with two or three other risk factors
- patients with extracardiac vascular disease
- ST depression 0.5 – 1 mm
- T-wave inversion ≥ 1 mm

High Likelihood (e.g. 85% - 99% likelihood)

- known history of prior AMI or CAD
- “definite angina” in males ≥ 60 or females ≥ 70
- transient hemodynamic or ECG changes during pain
- ST elevation or depression ≥ 1 mm
- Marked symmetrical T-wave inversion in multiple leads

UCLA 2005 Chest Pain and ACS Patient Management Guideline

See Appendix B: *WRHA algorithm for the management of patients with suspected ACS in the ED*

See Appendix C: *Likelihood that signs and symptoms represent an ACS*

ESC/ACC Diagnostic Criteria for Acute Myocardial Infarction

Diagnostic Criteria for AMI

Typical rise and/or fall of biochemical markers (preferably troponin) with at least one value above the 99th percentile of the upper reference limit together with evidence of myocardial ischemia with at least one of the following:

- Symptoms of ischemia
- ECG changes indicative of new ischaemia [new ST-T changes or new left bundle branch block (LBBB)]
- Development of pathologic Q waves in the ECG
- Imaging evidence of loss of viable myocardium or NEW regional wall motion abnormality

*Myocardial infarction redefined – J Am Coll Cardiol 2000
Universal Definition of Myocardial Infarction – Circulation 2007*

See Appendix D

- Troponins are more specific than other biomarkers in detecting myocardial injury with associated skeletal muscle injury and have a higher sensitivity, allowing detection of small amounts of myocardial necrosis that would have gone undetected by creatine kinase and its MB fraction (Roger, 2006).
- The criteria acknowledge that elevations in biomarkers are fundamental to the diagnosis of AMI because symptoms may be atypical or nonexistent and ECG changes may be absent or nonspecific (Babuin, 2005).
- Troponins have replaced CK-MB as the preferred biochemical markers for the diagnosis of AMI (Roger, 2006; Korff, 2006).
- An indepth document outlining the new Universal definitoin of acute myocardial infarctions along with its subcategories is provided in Circulation 2007; 116: 2634 – 53..

Algorithm for risk stratification of patients with unstable angina and NSTEMI

	<i>non-cardiac chest pain</i>	<i>stable angina</i>	<i>unstable angina</i>	<i>NSTEMI</i>	<i>STEMI</i>
Clinical finding	atypical pain	exertional pain	rest pain, post-AMI, diabetes	ongoing pain	
ECG	negative		ST-T wave changes	ST elevation	
TnT	negative		positive		
Risk assessment	low probability	low risk	medium - high risk	STEMI	

How do you interpret Troponin results?

Interpretation of Troponin values						
Troponin value	i-STAT Tnl µg/L	Dade Tnl µg/L	Bayer Tnl ultra	Roche TnT µg/L	Comment	Interpretation
Below 99 th ile	<0.08	<0.07	<0.04	< 0.01	Below 99 th ile.	No myocardial necrosis, if > 6 hrs after onset of symptoms.
Between (99 th ile) and functional sensitivity (10% CV)	0.08 to 0.10	0.07 to 0.21	0.04 to 0.07	0.01 to 0.03	Troponin present and can be distinguished from background but cannot be quantified repeatedly at this level	Possible myocardial injury, in the context of suspected ACS, repeat after two (2) hours (must be > 6 hrs after onset of symptoms)
Above functional sensitivity (10% CV or less)	>0.10	>0.21	>0.07	> 0.03	Definite myocardial necrosis, measurements are repeatable	NSTEMI when seen in the context of suspected ACS

- The fact that any troponin elevation exceeding the 99th ile is associated with an increased cardiac risk (Venge, 2002; Lindahl, 2001) is reflected by the recommendation of this cutoff for diagnostic purposes (ESC/ACC diagnostic criteria for AMI).
- It is important to realize that no troponin assays currently available has a CV less than 10% for values less than the 99th percentile of a normal reference population. Values between the 99th ile and the level at which a 10% CV are reached have low positive predictive values, resulting in a considerable risk for diagnostic misclassification.
- A rising troponin level is required in order to diagnose AMI.
- In patients with background elevations of troponin (e.g. patients with CRF), two (2) measurements are required to demonstrate a rising pattern.
- Troponin is specific for heart cell damage - any detectable level indicates myocardial damage. However, the etiology may be other than ACS
- See Appendix E for the differential diagnoses of an elevated troponin.

In order to rule-out AMI in a patient with a low likelihood of ACS:

- **Tnl must be measured at least 6 hours after the onset of chest pain.**

i-STAT Tnl µg/L	Dade Tnl µg/L	Bayer Tnl µg/L	Roche Tnl (ug/L)	Interpretation
<0.08	<0.07	<0.04	< 0.01	Below 99th ile. AMI can be ruled out
0.08 to 0.10	0.07 to 0.21	0.04 to 0.07	0.01 to 0.03	repeat TnT at least two (2) hours after previous sample ⇒ if not rising, consider alternate etiology for elevated troponin (see Appendix E)
>0.10	>0.21	>0.07	> 0.03	Myocardial necrosis - probable NSTEMI in setting of ACS

- **If the repeat is less than the 99th ile - AMI is unlikely. But if clinical suspicion remains high, a third Tnl may be considered.**

No

Should Troponin *always* be performed at the time of ED presentation?

- For patients with low likelihood of ACS, the diagnostic value of a Troponin drawn at the time of ED presentation (which is often less than 2 hours after the onset of chest pain) is very low and very unlikely to permit earlier consultation and/or admission decisions, or to improve ED throughput. The Troponin measurement may be deferred until six hours after the onset of chest pain, when a negative Troponin test result may be most helpful.
- In patients with recurrent chest pain, ECG abnormalities, or intermediate to high clinical suspicion, immediate treatment for presumed ACS should take place, including prompt consultation when appropriate. In these cases, performing Troponin earlier than six hours may be permissible.

What is the rationale for two hour intervals between Troponin samples?

- A recent study (MacRae, 2006) provided support for measuring TnT at six (6) hours after onset of chest pain and for two (2) hour intervals between TnT samples:
 - ⇒ A troponin (TnI) assay in specimen sets having one specimen > 6 hours after the onset of chest pain gave an AMI prevalence equivalent to the AHA definition.
 - ⇒ When the time from onset of symptoms was included in the specimen selection algorithm, a *one hour interval* between troponin samples was sufficient provided that at least one specimen was collected > 6 hours after the onset of chest pain.

Consider discharge of patients with low likelihood of ACS if all of the following are met:

- no recurrent chest pain
- no ECG changes
- negative Troponin measured six (6) hrs after the onset of chest pain

3. Troponin is considered negative: (when measured ≥ 6 hours after the onset of chest pain)

i-STAT TnI	Dade TnI	Bayer TnI ultra	Roche TnT	
< 0.08 µg/L	< 0.07 µg/L	< 0.04 µg/L	< 0.01 µg/L	
≥ 0.08 µg/L	≥ 0.07 µg/L	≥ 0.04 µg/L	≥ 0.01 µg/L	<u>and</u> not rising on 2 samples measured at least 2 hours apart <u>and</u> in context of alternate etiology for elevated troponin

No**Can single markers be utilized to safely rule out AMI *less than 6 hours* after the onset of chest pain?**

- No single serum marker used alone has sufficient sensitivity or specificity to reliably identify or exclude AMI within 6 hours after symptom onset (ACEP 2006 NSTEMI Clinical Policy).
- The ACEP 2006 NSTEMI Clinical Policy refers only to an option of performing myoglobin in conjunction with a more definitive cardiac marker (a level B recommendation).
- Use of a single marker such as myoglobin for the evaluation of chest pain should be avoided – a positive result only leads to additional lab testing because confirmation by a more definitive cardiac marker (troponin) will be needed (Eggers, 2004).

YES**Can TnT be utilized to safely rule out AMI ≥ 6 hours after the onset of pain?****Collinson P - Annal Clin Biochem 2006**

- TnT sample 1 was drawn at the time of presentation;
 - TnT sample 2 was drawn at six (6) hours from the onset of chest pain *and* at least two (2) hours after sample 1.
 - In this study, the optimal decision threshold from the ROC curves for TnT was 0.02 ug/L.
- ⇒ The sensitivity of TnT (0.02ug/L cutoff) exceeds 98% if measured at least six (6) hours after the onset of chest pain, with a negative predictive value (NPV) $\geq 99.9\%$ and a negative likelihood ratio (NLR) of 0.02.

6 hour Troponin T measurement (TnT 0.02 ug/L)					
TnT sample 2 was drawn:	Sensitivity % (95%CI)	Specificity % (95%CI)	Negative Likelihood Ratio	Negative Predictive Value %	AUC (95%CI)
only between 6 to 12 hrs after the onset of chest pain	100 (90.7 - 100)	98.2 (96.6 – 99.2)	< 0.001	100	1.000 (0.966 – 1.000)
all times after 6 hrs	98 (89.4-99.9)	98.3 (97.1 – 99.1)	0.02	99.9	0.989 (0.999 – 1.000)

Interpretation:

If TnT measured ≥ 6 hours is negative, AMI may be safely ruled-out in patients with a low likelihood of ACS.

Maybe

Can Tnl be utilized to safely rule out AMI ≥ 6 hours after the onset of pain?

Due to the variety of Tnl assays on the market, and the fact that they are not all calibrated the same way and have different specifications for the 99th percentile of a normal population and 10% cv, a more conservative approach may be warranted. The 2007 "National Academy of Clinical Biochemistry Laboratory Medicine Practice Guidelines: Clinical Characteristics and Utilization of Biomchemical Markers in Acute Coronary Syndromes" state:

"Given the improvements in the analytic performance assay, testing up to 6 – 9 h after symptom onset is expected to deliver optimal sensitivity in most patients. However, in patients for whom these initial samples are negative and there is an intermediate or high clinical index of suspicion, or in whom plausibly ischemic symptoms have recurred, repeat testing at 12 – 24 h should be considered."

No

Does the measurement of CK provide any additional information?

Numerous studies have demonstrated that measurement of CK and its isoforms does not improve diagnostic accuracy for AMI or facilitate more rapid decision-making than Tnl or TnT alone.

No

Does the measurement of myoglobin provide any additional value?

The first three studies below are widely quoted as supporting the use of myoglobin:

McCord - Ann Emerg Med 2003

- The authors report that using myoglobin in combination with Tnl at 0 and 90 minutes had a sensitivity of 84.4% (NLR 0.25).
- The maximum sensitivity at 94% was reached at nine hours using a combination of Tnl, CK-MB, and myoglobin (*the likely reason for the low sensitivity is that an insensitive Tnl assay was used in this study*).

Interpretation: the maximum sensitivity attained is not sufficient

Sallach - Am J Cardio 2004

- This is the same study of population as McCord, suggesting a post-hoc analysis.
- Their results for a change of ≥ 20 ng/ml of myoglobin at 90 minutes after presentation produced 83.3% sensitivity and 86.6% specificity, 99.5% NPV and an NLR of 0.19 for AMI.
- The combined sensitivity of Tnl and myoglobin at 90 minutes after presentation was 97.3%.
- However, in both McCord and Sallach studies, the median time of presentation after the onset of chest pain was 4.3 hours, meaning that most of the delta measurements were performed at six hours or more after the onset of chest pain.

Interpretation: delta myoglobin performed at six hours after onset of chest pain has a lower sensitivity and NLR than a TnT performed at six hours

Ng - Am J Cardio 2001

- This study looked at using a combination of delta myoglobin, CK-MB, and Tnl in concert with clinical history and ECG.
- All AMI's were diagnosed within 90 minutes of presentation: 100% sensitivity, 94% specificity, 100% NPV.

- Over 50% of patients presented more than six hours after onset of pain, 98% of patients were male, and 40% of patients were discharged without complete recording of outcome.
Interpretation: unlikely to be applicable given reservations about methods

Eggers - Am Heart J 2004

- Multi-marker strategies using TnI and myoglobin did not provide a superior overall diagnostic performance as compared to TnI alone.
- Even in patients with an onset of chest pain less than four hours before presentation, low TnI cutoffs demonstrated higher early sensitivities than myoglobin.

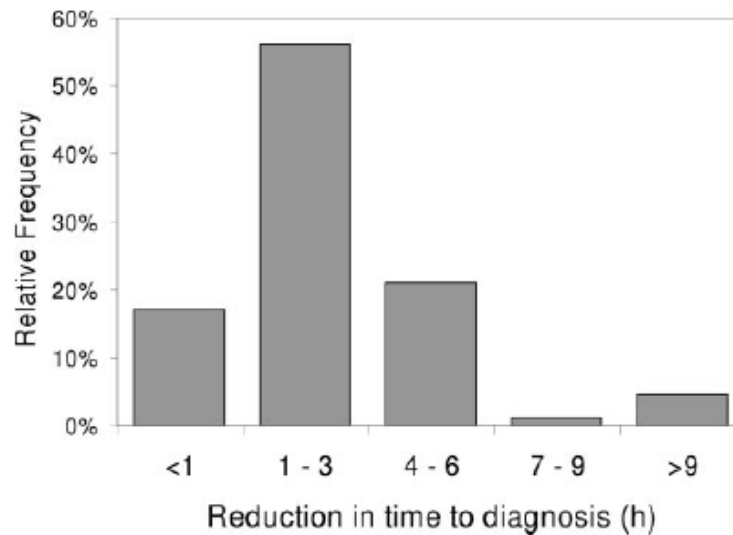
Interpretation: performance of myoglobin does not improve sensitivity or NLR

Recommendation: discontinue use of myoglobin as a cardiac marker.

- At six hours after the onset of chest pain, TnT alone has a sensitivity for the detection of AMI of >98%, which exceeds the sensitivity of other single markers or combinations of markers.
- Based on the above studies, there is insufficient evidence to justify the use of myoglobin as a cardiac marker.
- We found no studies that looked at the use of myoglobin alone for the rule-out of AMI.
- Therefore, the potential use of myoglobin as an early marker for rule-out of AMI is not supported.

Implications for ED throughput

Potential Reduction in the time to Diagnosis



Patient distribution in terms of the reduction in time (h) to achieve a diagnosis with the ≥ 6 h from onset protocol compared with the AHA case definition.

MacRae - Clin Chem 2006

The AHA Scientific Statement previously defined an adequate set of biomarkers as at least two measurements of the same marker taken at least six hours apart. The “AHA adequate set” was a set of markers measured over a six hour interval *from the time of ED presentation*, whereas in the study protocol the interval was timed *from the onset of chest pain*. For each of these sets, the required time to diagnosis was calculated as the time from the presentation specimen to the time of the second specimen in the set, without incorporating an assay turnaround time. The time to diagnosis for the candidate time-from onset specimen sets were subtracted from the identically calculated interval in the AHA-adequate sets to estimate the reduction in time to diagnosis afforded by the time-from-onset protocols.

For more detailed discussions of the cardiac markers, please refer to the following:

- Lippi, 2006
 - Jaffe, 2005
 - Carreiro-Lewandowski, 2006
 - Aviles, 2005
- } *reviews of markers of necrosis and ischemia*
- Collison, 2003
 - Korff, 2006
- } *reviews of troponins*
- Innes, 2006
- } *discussion of the clinical utility of new cardiac markers*

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Appendix A

Presentations of Unstable Angina

Table 3. Three Principal Presentations of UA

Rest angina*	Angina occurring at rest and prolonged, usually >20 minutes
New-onset angina	New-onset angina of at least CCS Class III severity
Increasing angina	Previously diagnosed angina that has become distinctly more frequent, longer in duration, or lower in threshold (i.e., increased by greater than or equal to 1 CCS class to at least CCS Class III severity)

CCS Grading of Angina

Table 4. Grading of Angina Pectoris According to CCS Classification

Class	Description of Stage
I	“Ordinary physical activity does not cause . . . angina,” such as walking or climbing stairs. Angina occurs with strenuous, rapid, or prolonged exertion at work or recreation.
II	“Slight limitation of ordinary activity.” Angina occurs on walking or climbing stairs rapidly; walking uphill; walking or stair climbing after meals; in cold, in wind, or under emotional stress; or only during the few hours after awakening. Angina occurs on walking >2 blocks on the level and climbing >1 flight of ordinary stairs at a normal pace and under normal conditions.
III	“Marked limitations of ordinary physical activity.” Angina occurs on walking 1 to 2 blocks on the level and climbing 1 flight of stairs under normal conditions and at a normal pace.
IV	“Inability to carry on any physical activity without discomfort—anginal symptoms may be present at rest.”

ACC/AHA 2002 Unstable angina / NSTEMI guideline update

Appendix B

The WRHA algorithm for the management of patients with suspected ACS in the ED is under revision by WRHA ER and Cardiology Programs and will be circulated when available.

Appendix C

Likelihood that signs and symptoms represent an ACS

Table 5. Likelihood That Signs and Symptoms Represent an ACS Secondary to CAD

Feature	High Likelihood <i>Any of the following:</i>	Intermediate Likelihood <i>Absence of high-likelihood features and presence of any of the following:</i>	Low Likelihood <i>Absence of high- or intermediate-likelihood features but may have:</i>
History	Chest or left arm pain or discomfort as chief symptom reproducing prior documented angina Known history of CAD, including MI	Chest or left arm pain or discomfort as chief symptom Age >70 years Male sex Diabetes mellitus	Probable ischemic symptoms in absence of any of the intermediate likelihood characteristics Recent cocaine use
Examination	Transient MR, hypotension, diaphoresis, pulmonary edema, or rales	Extracardiac vascular disease	Chest discomfort reproduced by palpation
ECG	New, or presumably new, transient ST-segment deviation (≥ 0.05 mV) or T-wave inversion (≥ 0.2 mV) with symptoms	Fixed Q waves Abnormal ST segments or T waves not documented to be new	T-wave flattening or inversion in leads with dominant R waves Normal ECG
Cardiac markers	Elevated cardiac TnI, TnT, or CK-MB	Normal	Normal

Braunwald E, Mark DB, Jones RH, et al. Unstable angina: diagnosis and management. Rockville, MD: Agency for Health Care Policy and Research and the National Heart, Lung, and Blood Institute, US Public Health Service, US Department of Health and Human Services; 1994; AHCPR Publication No. 94-0602.

Braunwald – AHCPR Publication No. 94-0602
ACC/AHA 2002 Unstable angina / NSTEMI guideline update

Appendix D

Definition of Myocardial Infarction by Joint ESC/ACCF/AHA/WHF Task Force for the Redefinition of Myocardial Infarction as reported in Thygesen 2007

Definition of myocardial infarction

Criteria for acute myocardial infarction

The term myocardial infarction should be used when there is evidence of myocardial necrosis in a clinical setting consistent with myocardial ischaemia. Under these conditions any one of the following criteria meets the diagnosis for myocardial infarction:

- Detection of rise and/or fall of cardiac biomarkers (preferably troponin) with at least one value above the 99th percentile of the upper reference limit (URL) together with evidence of myocardial ischaemia with at least one of the following:
 - Symptoms of ischaemia;
 - ECG changes indicative of new ischaemia [new ST-T changes or new left bundle branch block (LBBB)];
 - Development of pathological Q waves in the ECG;
 - Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality.
- Sudden, unexpected cardiac death, involving cardiac arrest, often with symptoms suggestive of myocardial ischaemia, and accompanied by presumably new ST elevation, or new LBBB, and/or evidence of fresh thrombus by coronary angiography and/or at autopsy, but death occurring before blood samples could be obtained, or at a time before the appearance of cardiac biomarkers in the blood.
- For percutaneous coronary interventions (PCI) in patients with normal baseline troponin values, elevations of cardiac biomarkers above the 99th percentile URL are indicative of peri-procedural myocardial necrosis. By convention, increases of biomarkers greater than 3 × 99th percentile URL have been designated as defining PCI-related myocardial infarction. A subtype related to a documented stent thrombosis is recognized.
- For coronary artery bypass grafting (CABG) in patients with normal baseline troponin values, elevations of cardiac biomarkers above the 99th percentile URL are indicative of peri-procedural myocardial necrosis. By convention, increases of biomarkers greater than 5 × 99th percentile URL plus either new pathological Q waves or new LBBB, or angiographically documented new graft or native coronary artery occlusion, or imaging evidence of new loss of viable myocardium have been designated as defining CABG-related myocardial infarction.
- Pathological findings of an acute myocardial infarction.

Criteria for prior myocardial infarction

Any one of the following criteria meets the diagnosis for prior myocardial infarction:

- Development of new pathological Q waves with or without symptoms.
- Imaging evidence of a region of loss of viable myocardium that is thinned and fails to contract, in the absence of a non-ischaemic cause.
- Pathological findings of a healed or healing myocardial infarction.

Appendix E

Differential Diagnosis of Elevated Troponin

Table 1 Examples of reported elevations of cardiac troponin

Primary ischaemic cardiac injury		
Thrombotic coronary artery occlusion caused by platelets/fibrin	ST elevation MI Non-ST elevation MI (previously non-Q wave AMI plus troponin positive unstable angina)	
Secondary ischaemic cardiac injury		
Coronary intervention	Primary PTCA	Distal embolisation from clot or atheroma; side branch occlusion
	Elective PTCA	Distal embolisation from atheroma or debris; side branch occlusion
	CABG	Global ischaemia from inadequate perfusion, myocardial cell protection or anoxia
Sympathomimetics	Cocaine Catecholamine storm	Head injury, stroke, intracerebral bleed
Pulmonary embolus	Presumed right heart strain or hypoxia	
Coronary artery spasm	Small percentage of patients only	
Coronary artery embolisation	Clot	
	Air	
	CABG	
Coronary artery inflammation with microvascular occlusion	Vasculitides	
	Connective tissue disease	
	SLE	
End stage renal failure	More severe CAD but 50% have normal coronaries	
Rhythm disturbances	Prolonged tachyarrhythmia or bradyarrhythmia with IHD	
Acute heart failure	Only if caused by IHD	
Direct coronary artery trauma		
Extreme endurance exercise	Extreme marathons	Wall motion abnormalities
	Extreme training	cTn +ve deaths presumed caused by extreme oxygen debt producing ischaemia
Non-ischaemic cardiac injury		
Known causes of myocarditis	Infection	Bacterial
		Viral
	Inflammation	Polymyositis
		Scleroderma
		Sarcoid
	Auto-immune	Alcohol
Chemotherapy		
Drugs		
Cardiac trauma	Inflammation	
	Direct	RTA Stabbing
Metabolic/toxic	Cardiac surgery	
	Renal failure	
	Multiple organ failure	

AMI, acute myocardial infarction; CABG, coronary artery bypass graft; CAD, coronary artery disease; IHD, ischaemic heart disease; MI, myocardial infarction; PTCA, percutaneous transluminal coronary angioplasty; RTA, road traffic accident; SLE, systemic lupus erythematosus.