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# Provoking conditions, management and outcomes of type 2 myocardial infarction and myocardial necrosis ☆

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ABSTRACT

*Background:* Type 2 myocardial infarction (MI) is defined as myocardial necrosis (myonecrosis) due to an imbalance in supply and demand with clinical evidence of ischemia. Some clinical scenarios of supply–demand mismatch predispose to myonecrosis but limit the identification of symptoms and ECG changes referable to ischemia; therefore, the MI definition may not be met. Factors that predispose to type 2 MI and myonecrosis without definite MI, approaches to treatment, and outcomes remain poorly characterized.
*Methods:* Patients admitted to an academic medical center with an ICD-9 diagnosis of secondary myocardial ischemia or non-primary diagnosis of non-ST-elevation MI were retrospectively reviewed. Cases were classified as either MI ($n = 255$) or myonecrosis without definite MI ($n = 220$) based on reported symptoms, ischemic ECG changes, and new wall motion abnormalities.
*Results:* Conditions associated with type 2 MI or myonecrosis included non-cardiac surgery (38%), anemia or bleeding requiring transfusion (32%), sepsis (31%), tachyarrhythmia (23%), hypotension (22%), respiratory failure (23%), and severe hypertension (8%). Inpatient mortality was 5%, with no difference between patients with MI and those with myonecrosis (6% vs. 5%, $p = 0.41$). At discharge, only 43% of patients received aspirin and statin therapy.
*Conclusions:* Type 2 MI and myonecrosis occur frequently in the setting of supply–demand mismatch due to non-cardiac surgery, sepsis, or anemia. Myonecrosis without definite MI is associated with similar in-hospital mortality as type 2 MI; both groups warrant further workup for cardiovascular disease. Antiplatelet and statin prescriptions were infrequent at discharge, reflecting physician uncertainty about the role of secondary prevention in these patients.



## 1. Introduction

The 2007 Task Force for the Universal Definition of Myocardial Infarction (MI) introduced five subtypes of MI requiring a rise and/or fall of cardiac biomarkers consistent with myocardial necrosis (myonecrosis) and clinical evidence of ischemia, including symptoms, electrocardiogram (ECG) changes, or new regional wall motion abnormalities [1,2]. Type 1 MI results from plaque rupture, erosion, ulceration, fissuring, or dissection in the setting of unstable atherosclerotic coronary artery disease (CAD) [2]. In contrast, type 2 MI addresses the clinical scenario of infarction due to an imbalance in oxygen supply and demand that is attributed to a condition other than unstable CAD or recent coronary revascularization [2]. This definition includes supply demand mismatch in the setting of fixed, stable atherosclerotic CAD [2]. Type 2 MI has been reported in 3% to 25% of acute MI, with variations in incidence based on the population studied [3–6]. Clinical evidence of ischemia (e.g. symptoms or ECG changes) can be difficult to obtain in the setting of provoking conditions such as surgery or sepsis and may be underreported. The clinical relevance of distinctions between type 2 MI fulfilling the Universal Definition criteria and myocardial necrosis without definite MI has not been established [6–9]. We investigated patient characteristics, provoking conditions, management, and in-hospital outcomes of type 2 MI and myonecrosis without definite MI in a large, retrospective, single-center study of patients admitted to an academic tertiary care institution.

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## 2. Methods

Patients admitted to NYU Langone Medical Center from January 2013 to December 2013 with ≥1 abnormal laboratory value of cardiac troponin were identified and International Classification of Diseases, Ninth Revision (ICD-9) diagnosis codes were obtained. Medical records with a principal or secondary diagnosis code of secondary myocardial ischemia (ICD-9411.89) or a secondary diagnosis of non-ST-elevation MI (ICD-9410.71) were retrospectively reviewed. At our institution, these codes are assigned by clinical documentation specialists using a standardized approach that requires provider documentation of the troponin elevation in addition to a positive laboratory result. Cases with admission for heart failure exacerbation, pulmonary embolism, myocarditis, or aortic dissection were excluded. Cases with only one troponin value were excluded, as were cases without either ≥10% rise and fall of troponin or ≥10% fall in troponin if the first value was the highest value. Cases were also excluded when the documented clinical impression of the cardiology consultant was type 1, type 4 (PCI-related) MI, or type 5 (cardiac surgery-related) MI; or complete data were not available from the electronic medical record. Plasma cardiac troponin I (cTnI) was measured using the VITROS cTnI ES assay (Ortho-Clinical Diagnostics, Rochester, NY) or the ST AIA-PACK 2nd generation cTnI assay (Tosoh Bioscience, Tokyo, Japan). The study was approved by the New York University School of Medicine Institutional Review Board with a waiver of informed consent.

Type 2 MI was defined according to the Universal Definition of MI, with a rise and fall (or a fall alone, when the first measured troponin was also the peak value) of serum troponin above the 99% upper reference limit and clinical evidence of ischemia as defined by at least one of the following: (a) symptoms of ischemia; (b) ECG changes with new significant ST-segment–T wave changes, new left bundle branch block (LBBB), or development of pathological Q waves in the ECG; or (c) imaging evidence of a new regional wall motion abnormality [1,2]. Cases with a rise and/or fall in serum troponin but without clinical evidence of ischemia were classified as myonecrosis without definite MI, likely due to supply–demand imbalance.

Patient characteristics were ascertained from hospital administrative and laboratory datasets and retrospective review of the medical record. Conditions associated with and possibly provoking type 2 MI and myonecrosis without definite MI were recorded. Anemia was defined as hemoglobin ≤8 g/dL, GI bleeding, or red blood cell transfusion prior to or within 24 h following the peak serum troponin. Hypotension was defined as a mean arterial pressure (MAP) <65 mm Hg. Severe hypertension was defined as a systolic blood pressure >180 mm Hg or a diastolic blood pressure >110 mm Hg. Respiratory failure was defined as the need for high flow oxygen by facemask, non-invasive positive pressure ventilation, or endotracheal intubation and mechanical ventilation. Sepsis was defined as illness meeting systemic inflammatory response syndrome criteria with an infectious source. Tachycardia and bradycardia were recorded as a provoking condition when the dysrhythmia was suspected as an etiology of myocardial ischemia per the treating physician; threshold heart rates for tachycardia or bradycardia were not specified. All ECGs obtained within 48 h of the peak troponin were retrospectively reviewed for dynamic changes consistent with ischemia. Any cardiovascular testing (echocardiography, stress testing, coronary angiography, coronary CT or cardiac MRI) or ischemic evaluation (stress testing or coronary angiography only) performed during hospital admission or 180 days following hospital discharge were recorded. Medication use was defined from hospital discharge regimens. Subgroup analyses were performed by age, sex, and quartile of peak serum troponin.

Normally distributed continuous data were displayed as means ± standard deviation (SD) and were compared between type 2 MI and myonecrosis without definite MI groups using the two-sided independent sample t test. Skewed continuous data were presented as median [interquartile range] and compared between groups using the Mann–Whitney test. Categorical variables were displayed as n (proportions) and compared by Chi-square or Fisher exact tests. Statistical analyses were performed using SPSS 20 (IBM SPSS Statistics, Armonk, NY). Statistical significance was defined using a two-sided alpha level of 0.05 for all tests.

## 3. Results

Among 34,333 admissions to NYU Langone Medical Center in 2013, 3053 (8.9%) had ≥1 abnormal troponin I value. Of these, 614 admissions (20.1%) had a diagnosis of secondary myocardial ischemia (ICD-9411.89) and 75 (2.5%) had a secondary diagnosis of non-ST-elevation

**Table 1**
Baseline characteristics of patients with type 2 myocardial infarction or necrosis.

| | Total cohort (n = 475) | Type 2 MI (n = 255) | Myonecrosis without definite MI (n = 220) | p-Value |
|---|---|---|---|---|
| Age (years), mean ± SD | 76.2 ± 12.7 | 76.0 ± 13.2 | 76.5 ± 12.1 | 0.70 |
| Age ≥ 65 | 387 (81%) | 208 (82%) | 178 (81%) | 0.85 |
| Male sex, n (%) | 254 (53%) | 132 (52%) | 122 (56%) | 0.42 |
| Race | | | | |
| White | 354 (75%) | 189 (74%) | 165 (75%) | 0.74 |
| Black | 43 (9%) | 26 (10%) | 17 (8%) | |
| Asian | 31 (7%) | 17 (7%) | 14 (6%) | |
| Other | 47 (10%) | 23 (9%) | 24 (10%) | |
| Hispanic ethnicity | 39 (8%) | 20 (8%) | 19 (9%) | 0.73 |
| BMI (kg/m2), mean ± SD | 25.7 ± 6.2 | 25.6 ± 6.1 | 25.9 ± 6.4 | 0.62 |
| Hypertension | 379 (80%) | 213 (84%) | 166 (76%) | 0.03 |
| Hyperlipidemia | 235 (49%) | 126 (49%) | 109 (50%) | 0.94 |
| Diabetes mellitus | 166 (35%) | 101 (40%) | 65 (30%) | 0.02 |
| Kidney disease (eGFR <60) | 198 (42%) | 108 (46%) | 75 (38%) | 0.09 |
| ESRD | 54 (11%) | 32 (13%) | 22 (10%) | 0.38 |
| Atrial fibrillation | 176 (37%) | 98 (38%) | 78 (36%) | 0.52 |
| Coronary artery disease | 215 (45%) | 128 (50%) | 87 (40%) | 0.02 |
| Prior myocardial infarction | 127 (27%) | 76 (30%) | 51 (23%) | 0.10 |
| Prior revascularization | 155 (32%) | 98 (38%) | 57 (26%) | 0.004 |
| Prior PCI | 99 (21%) | 61 (24%) | 38 (17%) | 0.08 |
| Prior CABG | 85 (18%) | 53 (21%) | 32 (15%) | 0.08 |
| History of heart failure | 97 (20%) | 54 (21%) | 43 (20%) | 0.66 |
| History of malignancy | 134 (28%) | 57 (22%) | 76 (35%) | 0.003 |

BMI: body mass index; CABG: coronary artery bypass graft; eGFR: estimated glomerular filtration rate; ESRD: end stage renal disease; MI: myocardial infarction; PCI: percutaneous coronary intervention.