

1 **Effect of a Proposed Modification of the Type 1 and Type 2 Myocardial**
2 **Infarction Definition on Incidence and Prognosis**

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33 The 4th Universal Definition of Myocardial Infarction (UDMI) classifies myocardial
34 infarction (MI) into 5 subtypes, of which types 1 and 2 MI are the most common.^{1,2} Type
35 1 MI (T1MI) is defined as MI caused by acute coronary atherothrombosis including
36 plaque rupture and erosion. In contrast, type 2 MI (T2MI) is defined as MI resulting
37 from myocardial oxygen supply/demand mismatch including central hemodynamic de-
38 arrangements such as tachyarrhythmia, hypotension, hypertension, anemia, and
39 hypoxemia, as well as acute coronary pathologies that obstruct coronary blood flow
40 such as spontaneous coronary artery dissection (SCAD), coronary embolism, and
41 coronary vasospasm.^{1,2} As from pathophysiological, diagnostic, and management
42 perspectives the latter are similar to T1MI and have little in common with other T2MI
43 etiologies, modest revision of the UDMI has recently been proposed by a group of
44 experts to reclassify SCAD, coronary embolism, and coronary vasospasm from T2MI
45 to T1MI.¹⁻³ In addition, it was proposed to further subclassify T2MI into those patients
46 with or without coronary artery disease (CAD).³ The impact of this proposed revision
47 on the incidence and prognosis of T1MI and T2MI is largely unknown.

48 Therefore, the aim of this study was to evaluate the impact of this proposed
49 reclassification on the incidence and prognosis of T1MI and T2MI in a large,
50 international multicenter diagnostic study enrolling patients with acute chest discomfort
51 using central adjudication by two independent cardiologists according to the UDMI in
52 five European countries (NCT00470587).⁴ The study has been approved by local
53 ethics committee. Written informed consent was obtained from all patients.

54 Among 6145 patients, 1364 (22.2%) had MI, 1116 patients (81.8% of all MIs) had T1MI
55 and 248 (18.2% of all MIs) T2MI. The proposed revision resulted in 17 (6.8% of all
56 T2MI) patients with SCAD, coronary embolism, and coronary vasospasm being
57 reclassified from T2MI to T1MI_{new} (Figure 1). Among the remaining 231 T2MI_{new}

58 patients, CAD was present in 104 (45% of all T2MI_{new}) T2AMI patients and absent in
59 127 (55% of all T2MI_{new}) T2BMI patients.

60 Due to the relatively small number of reclassified patients, the overall number (1116
61 versus 1133), and 30-day (3.6% (40/1116) versus 3.5% (40/1133) and 2-year all-cause
62 mortality (12.0% (134/1116) versus 11.8% (134/1133)) were comparable between
63 T1MI versus T1MI_{new}. The same finding emerged for recurrent MI and hospitalization
64 for acute heart failure (AHF, all p=ns, using the bootstrap resampling method with 1000
65 iterations).

66 Two-year outcomes differed substantially among the categories of T2MI_{new}. Two-year
67 all-cause mortality was 25.0% (95% confidence interval (CI), 17.7-34.1%, calculated
68 with the Wilson score interval) in T2AMI versus 7.9% (95%CI, 4.3-13.9%) in T2BMI
69 (p<0.001, p-values were calculated with Fisher's Exact test and Pearson's Chi-squared
70 test with Yates' continuity correction respectively when required). Similarly, the rate of
71 recurrent MI within two years was 10.6% (95%CI, 6.0-18.0%) in T2AMI versus 2.4%
72 (95%CI, 0.8-7.6%) in T2BMI (p=0.01).

73 During 2-years, T1MI_{new} and T2MI_{new} had comparable all-cause mortality (11.8%
74 (134/1133) versus 15.6% (36/231), p=ns) and hospitalizations for AHF (5.7% (95%CI,
75 4.5-7.3%) versus 5.6% (95%CI, 3.3-9.4%) in T2MI_{new} (p=ns)).

76 Some limitations warrant consideration when interpreting the findings of this study.
77 **First**, the study was conducted in emergency department patients with symptoms
78 suggestive of MI. Further research is required in the perioperative setting, in critically
79 ill patients or patients directly transferred to the catheterization laboratory. **Second**,
80 despite using the most stringent methodology to adjudicate T2MI, including central
81 adjudication by experienced cardiologists, misclassification may have occurred in a

82 small number of patients. **Third**, in some patients with T2_BMI, the presence of CAD
83 may have been missed as coronary angiography and/or functional cardiac imaging
84 was not systematically performed in all patients. Additional limitations were the lack of
85 sites in the US, the relatively low number of some T2MI subtypes, and the inability to
86 comment on patients on chronic dialysis, as they were excluded.

87 In conclusion, the suggested possible reclassification from T2MI to T1MI_{new} would
88 affect about 7% of all T2MI, and nearly half of the remaining T2MI have underlying
89 CAD (T2_AMI). Two-year all-cause mortality in T2_AMI is more than three times higher
90 than in T2_BMI.

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117 **Disclosures**

118 The authors designed the study, gathered and analyzed the data, vouch for the data
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4th universal definition of T1MI: n=1116

4th universal definition of T2MI: n=248

Proposed redefinition of T1MI: n=1133

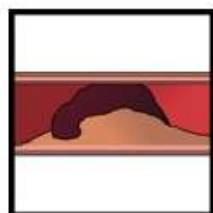
Proposed redefinition of T2MI: n=231

MI with acute coronary obstruction

MI due to O₂ supply/demand mismatch without acute coronary obstruction

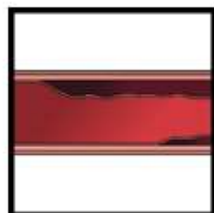
SCAD
Embolism
Vasospasm or
Microvasc. dysfunct.
n=17 (6.9%)

TYPE 1A



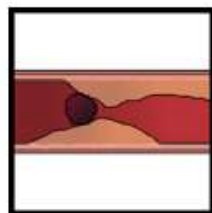
Plaque rupture/erosion with thrombus

TYPE 1B



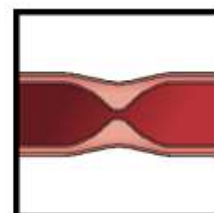
Spontaneous coronary artery dissection

TYPE 1C



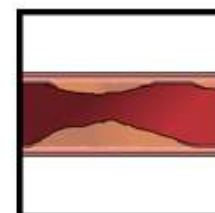
Coronary embolism

TYPE 1D



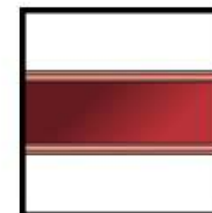
Vasospasm or Microvascular dysfunction

TYPE 2A



With fixed obstructive CAD

TYPE 2B



Without fixed obstructive CAD

Count (n, %)	TYPE 1A	TYPE 1B	TYPE 1C	TYPE 1D	TYPE 2A	TYPE 2B
	1116 (98.5%)	2 (0.2%)	2 (0.2%)	13 (1.1%)	104 (45.0%)	127 (55.0%)

All cause death at 30d (n, %)	40 (3.6%)	0 (0%)	0 (0%)	0 (0%)	3 (2.9%)	0 (0%)
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All cause death at 2y (n, %)	134 (12.0%)	0 (0%)	0 (0%)	0 (0%)	26 (25.0%)	10 (7.9%)
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New MI within 30d (n, %)	35 (3.1%)	0 (0%)	0 (0%)	2 (15.4%)	4 (3.8%)	0 (0%)
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New MI within at 2y (n, %)	112 (10.0%)	0 (0%)	0 (0%)	4 (30.8%)	11 (10.6%)	3 (2.4%)
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Rehosp. for AHF within 30d (n, %)	2 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
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Rehosp. for AHF within 2y (n, %)	64 (5.7%)	0 (0%)	0 (0%)	0 (0%)	9 (8.7%)	4 (3.1%)
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Figure 1: Flowchart showing the placement of myocardial infarction patients following the proposed modification of the 4th Universal Definition of Myocardial Infarction. T1MI: Type 1 myocardial infarction. T2MI: Type 2 myocardial infarction. n: sample size. SCAD: Spontaneous coronary artery dissection. Microvasc. dysfunct: Microvascular dysfunction. CAD: Coronary artery disease. d: days. y: years. Rehosp. for AHF: Rehospitalization for acute heart failure. The percentages of “Count” are given for the total number of cases of redefined T1MI (T1MI_{new}) and redefined T2MI (T2MI_{new}) respectively. The percentages of all-cause death, new MI and AHF are given for the respective sub-category.