

## **Sensitive Troponin Assay and the Classification of Myocardial Infarction**

**Purpose:** Lowering the diagnostic threshold for troponin is controversial because it may disproportionately increase the diagnosis of myocardial infarction in patients without acute coronary syndrome. We assessed the impact of lowering the diagnostic threshold of troponin on the incidence, management and outcome of patients with myocardial infarction or myocardial injury.

**Methods:** Consecutive patients with elevated plasma troponin I concentrations ( $\geq 50$  ng/L;  $n=2,929$ ) were classified as type 1 (54%) myocardial infarction, type 2 myocardial infarction (20%) or myocardial injury (24%) and type 3-5 myocardial infarction (2%) before and after lowering the diagnostic threshold from 200 to 50 ng/L with a sensitive assay (table). Event-free survival from death and recurrent myocardial infarction at one year was evaluated.

**Results:** Lowering the threshold increased the diagnosis of type 2 myocardial infarction or myocardial injury more than type 1 myocardial infarction (574 *versus* 257 additional patients,  $P<0.001$ ). Patients with myocardial injury or type 2 myocardial infarction were at higher risk of death compared to type 1 myocardial infarction (16% *versus* 34%; HR 1.76, 95%CI 1.46-2.11), but had fewer recurrent myocardial infarctions (12% *versus* 4%; HR 0.31, 0.22-0.45). In patients with troponin concentrations 50-199 ng/L, lowering the diagnostic threshold was associated with increased healthcare resource utilization ( $P<0.05$ , figure) that reduced recurrent myocardial infarction and death for patients with type 1 myocardial infarction (31% *versus* 20%; RR 0.64, 0.41-0.99), but not type 2 myocardial infarction or myocardial injury (37% *versus* 30%; RR 0.82, 0.65-1.04).

**Conclusion:** Following implementation of a sensitive troponin assay, the incidence of type 2 myocardial infarction and myocardial injury disproportionately increased, and is now as frequent as type 1 myocardial infarction. Outcomes of patients with type 1 myocardial infarction improved, but despite increases in healthcare resource utilization, outcomes of patients with type 2 myocardial infarction and myocardial injury were unchanged and remained poor.

**Key Words:** troponin, myocardial infarction, myocardial injury

**Table:** Baseline characteristics of patients with type 1 myocardial infarction, type 2 myocardial infarction and myocardial injury

|  | Type 1 MI<br>(n=1,171) | Type 2 MI<br>(n=429) | Myocardial Injury<br>(n = 522) |
|--|------------------------|----------------------|--------------------------------|
| Age                                    | 68 (14)                | 75 (14)              | 76 (13)                        |
| Male sex, (%)                          | 709 (61%)              | 222 (52%)            | 260 (50%)                      |
| <b>Presenting symptom, n (%)</b>       |                        |                      |                                |
| Ischaemic chest pain                   | 1,041 (89%)            | 217 (51%)            | 0 (0%)                         |
| Dyspnoea                               | 45 (4%)                | 80 (19%)             | 172 (33%)                      |
| Collapse/Syncope                       | 21 (2%)                | 31 (7%)              | 94 (18%)                       |
| Falls                                  | 18 (2%)                | 40 (9%)              | 86 (17%)                       |
| Confusion                              | 2 (0%)                 | 15 (4%)              | 23 (4%)                        |
| Palpitations                           | 2 (0%)                 | 4 (1%)               | 18 (3%)                        |
| Abdominal pain                         | 6 (1%)                 | 6 (1%)               | 12 (2.3%)                      |
| Cardiac arrest                         | 14 (1%)                | 0 (0%)               | 3 (1%)                         |
| <b>Past medical history, n (%)</b>     |                        |                      |                                |
| Ischemic heart disease                 | 497 (45%)              | 191 (45%)            | 186 (36%)                      |
| Myocardial infarction                  | 231 (24%)              | 109 (26%)            | 107 (21%)                      |
| Stroke                                 | 92 (8%)                | 48 (11%)             | 86 (17%)                       |
| Peripheral vascular disease            | 85 (8%)                | 29 (7%)              | 39 (8%)                        |
| Previous PCI                           | 153 (15%)              | 17 (4%)              | 23 (5%)                        |
| Previous CABG                          | 62 (6%)                | 30 (7%)              | 32 (6%)                        |
| <b>Risk factors, n (%)</b>             |                        |                      |                                |
| Current smoker                         | 380 (34%)              | 62 (15%)             | 73 (14%)                       |
| Hypertension                           | 533 (48%)              | 254 (59%)            | 303 (59%)                      |
| Hyperlipidemia                         | 539 (49%)              | 177 (42%)            | 202 (39%)                      |
| Diabetes mellitus                      | 185 (17%)              | 93 (22%)             | 96 (19%)                       |
| <b>Biochemistry</b>                    |                        |                      |                                |
| Hemoglobin, mg/dL                      | 13.3 (2.0)             | 12.1 (2.5)           | 12.0 (2.2)                     |
| Creatinine, mg/dL                      | 1.2 (0.7)              | 1.5 (1.2)            | 1.4 (1.4)                      |
| GFR, ml/min                            | 69 (26)                | 56 (30)              | 52 (33)                        |
| GFR < 30ml/min, %                      | 89 (8%)                | 67 (16%)             | 125 (24%)                      |
| Cholesterol, mg/dL                     | 185 (50)               | 166 (51)             | 171 (53)                       |
| Troponin, ng/L                         | 2,420 (270 – 15,230)   | 140 (70 – 660)       | 130 (60 – 390)                 |
| Change in troponin ≥ 20%               | 432 (86%)              | 41 (65%)             | 41 (79%)                       |
| <b>Electrocardiography, no (%)</b>     |                        |                      |                                |
| ST elevation                           | 427 (38%)              | 40 (10%)             | 3 (1%)                         |
| ST depression                          | 207 (18%)              | 152 (36%)            | 0 (0%)                         |
| T-wave inversion                       | 125 (11%)              | 97 (23%)             | 13 (3%)                        |
| <b>Medication on admission, no (%)</b> |                        |                      |                                |
| Aspirin                                | 418 (50%)              | 222 (56%)            | 244 (54%)                      |
| Clopidogrel                            | 100 (12%)              | 25 (63%)             | 26 (6%)                        |
| β-blockers                             | 257 (31%)              | 101 (26%)            | 111 (25%)                      |
| ACE-inhibitors                         | 300 (36%)              | 136 (34%)            | 158 (35%)                      |
| Statins                                | 384 (47%)              | 156 (40%)            | 191 (42%)                      |
| Warfarin                               | 35 (4%)                | 38 (10%)             | 52 (12%)                       |
| Proton pump inhibitors                 | 188 (24%)              | 127 (33%)            | 135 (30%)                      |

Values are mean (standard deviation), median (interquartile range) and counts (%). Abbreviations: PCI – Percutaneous Coronary Intervention, CABG – Coronary Artery Bypass Grafting, TIMI – Thrombolysis in Myocardial Infarction, GFR = Glomerular Filtration Rate, ACE – Angiotensin Converting Enzyme. Conversion factor to SI Units as follows: Hemoglobin = 10, Creatinine = 88.4, Cholesterol = 0.0259).

**Figure 3. Change in the investigation, management and clinical outcome of patients with type 1 myocardial infarction and type 2 myocardial infarction / myocardial injury following implementation of a sensitive troponin assay**

In patients with plasma troponin concentrations of 50-199 ng/L and type 1 myocardial infarction, lowering the diagnostic threshold increased referrals for a specialist opinion, further investigation and treatments for myocardial infarction ( $P < 0.01$  for all). For type 2 myocardial infarction / myocardial injury similar patterns were seen although the absolute magnitude was smaller. In patients with type 1 myocardial infarction, lowering the diagnostic threshold was associated with a significant reduction in recurrent myocardial infarction (absolute risk reduction 12%, 95% CI 3 to 23%) whereas outcomes in patients with type 2 myocardial infarction / myocardial injury remained unchanged. PCI = percutaneous coronary intervention; DAPT = dual anti-platelet therapy. \* $P < 0.05$ , \*\*  $P < 0.01$ , \*\*\* $P < 0.001$

