

**Table 1 of the supplementary data.** Baseline characteristics of the study population by primary endpoint (3-year all-cause death or nonfatal myocardial infarction).

| Variable   | All patients<br>(N = 377) | 3-year death or MI       |                        | P      |
|--|---------------------------|--------------------------|------------------------|--------|
|  |                           | No (n = 318)             | Yes (n = 59)           |        |
| <b>Demographics</b>                              |                           |                          |                        |        |
| Age, y   | 61.5 ± 12.9               | 60.1 ± 12.2              | 69.6 ± 13.7            | < .001 |
| Sex, female                                      | 78 (20.7)                 | 62 (19.5)                | 16 (27.1)              | .184   |
| BMI, kg/m <sup>2</sup>                           | 27.0 [24.9-29.8]          | 26.8 [24.9-29.7]         | 27.9 [24.8-30.5]       | .414   |
| <b>History</b>                                   |                           |                          |                        |        |
| Smoking  |                           |                          |                        | .009   |
| Never  | 90 (23.9)                 | 71 (22.3)                | 19 (32.2)              |        |
| Former   | 103 (27.3)                | 81 (25.5)                | 22 (37.3)              |        |
| Active   | 184 (48.8)                | 166 (52.2)               | 18 (30.5)              |        |
| Hypertension                                     | 202 (53.6)                | 158 (49.7)               | 44 (74.6)              | < .001 |
| Diabetes mellitus                                |                           |                          |                        | .004   |
| No   | 278 (73.7)                | 242 (76.1)               | 36 (61.0)              |        |
| Noninsulin treatment                             | 64 (17.0)                 | 53 (16.7)                | 11 (18.6)              |        |
| Insulin treatment                                | 35 (9.3)                  | 23 (7.2)                 | 12 (20.3)              |        |
| Dyslipidemia                                     | 201 (53.3)                | 167 (52.5)               | 34 (57.6)              | .470   |
| Cerebrovascular disease                          | 20 (5.3)                  | 12 (3.8)                 | 8 (13.6)               | .002   |
| Peripheral arterial disease                      | 21 (5.6)                  | 16 (5.0)                 | 5 (8.5)                | .290   |
| End-stage chronic kidney disease                 | 4 (1.1)                   | 3 (0.9)                  | 1 (1.7)                | .495   |
| Previous heart failure                           | 3 (0.8)                   | 0                        | 3 (5.1)                | < .001 |
| Previous MI                                      | 35 (9.3)                  | 25 (7.9)                 | 10 (16.9)              | .027   |
| Previous PCI                                     | 32 (8.5)                  | 21 (6.6)                 | 11 (18.6)              | .002   |
| Previous CABG                                    | 1 (0.3)                   | 0                        | 1 (1.7)                | .156   |
| <b>Clinical presentation</b>                     |                           |                          |                        |        |
| GRACE score                                      | 149.1 ± 39.4              | 142.4 ± 32.9             | 185.2 ± 50.8           | < .001 |
| Anterior infarct location                        | 159 (42.2)                | 133 (41.8)               | 26 (44.1)              | .749   |
| Killip-Kimball class                             |                           |                          |                        | < .001 |
| I  | 308 (81.7)                | 273 (85.5)               | 35 (59.3)              |        |
| II   | 38 (10.1)                 | 29 (9.1)                 | 9 (15.3)               |        |
| III  | 7 (1.9)                   | 4 (1.3)                  | 3 (5.1)                |        |
| IV   | 24 (6.4)                  | 12 (3.8)                 | 12 (20.3)              |        |
| Right ventricular infarction                     | 14 (3.7)                  | 11 (3.5)                 | 3 (5.1)                | .467   |
| Cardiac arrest                                   | 24 (6.4)                  | 14 (4.4)                 | 10 (16.9)              | < .001 |
| Primary VF                                       | 18 (4.8)                  | 11 (3.5)                 | 7 (11.9)               | .005   |
| 2nd/3rd degree atrioventricular block            | 18 (4.8)                  | 16 (5.0)                 | 2 (3.4)                | .750   |
| Atrial fibrillation                              | 23 (6.1)                  | 15 (4.7)                 | 8 (13.6)               | .009   |
| Main epicardial coronary arteries ≥ 70% stenosis |                           |                          |                        | .336   |
| 1  | 190 (50.5)                | 164 (51.6)               | 26 (44.8)              |        |
| 2  | 109 (29.0)                | 93 (29.2)                | 16 (27.6)              |        |
| 3  | 77 (20.5)                 | 61 (19.2)                | 16 (27.6)              |        |
| Left main ≥ 50% stenosis                         | 15 (4.0)                  | 11 (3.5)                 | 4 (6.9)                | .264   |
| Successful primary PCI                           | 365 (96.8)                | 308 (96.9)               | 57 (96.6)              | .922   |
| Symptom onset-to-balloon, min                    | 180 [122-295]             | 178 [119-285]            | 237 [134-372]          | .049   |
| LVEF, %  | 51.1 ± 10.6               | 52.2 ± 9.8               | 45.0 ± 12.9            | < .001 |
| <b>Laboratory results</b>                        |                           |                          |                        |        |
| Hemoglobin on admission, g/dL                    | 13.0 ± 1.8                | 13.2 ± 1.6               | 12.0 ± 2.5             | .001   |
| Creatinine clearance on admission, mL/min*       | 89.1 ± 37.7               | 92.0 ± 36.3              | 73.6 ± 41.9            | .001   |
| LDL-cholesterol, mg/dL                           | 105.3 ± 34.9              | 107.8 ± 34.7             | 90.8 ± 32.6            | .001   |
| CK-MB peak, ng/mL                                | 176.0 [73.2-332.9]        | 175.4 [71.9-287.4]       | 219.9 [74.6-500.8]     | .066   |
| hs-Troponin T at 12h, pg/mL                      | 3714.5 [1,190.3-7,146.3]  | 3536.1 [1,196.6-6,556.7] | 4092.2 [1094.1-9726.7] | .192   |
| NT-proBNP at 12h, pg/mL                          | 573.4 [253.8-1535.2]      | 525.7 [243.3-1160.9]     | 2648.6 [430.0-5562.4]  | < .001 |
| Meteorin-like protein at 12 h, pg/mL             | 415.5 [321.6-563.8]       | 400.4 [315.0-526.2]      | 599.0 [402.4-826.5]    | < .001 |

BMI, body mass index; GRACE, CK-MB, creatine kinase-MB; Global Registry of Acute Coronary Events; HDL, high density lipoprotein; HR, heart rate; LDL, low density lipoprotein; LVEF, left ventricular ejection fraction; NT-proBNP, inactive proform of natriuretic peptide B; SBP, systolic blood pressure.

Data are presented as No. (%), mean  $\pm$  standard deviation, or median [(interquartile range: Q1-Q3)].

\*Estimated with the Cockcroft-Gault formula.

**Table 2 of the supplementary data.** STEMI complications by median circulating Metrnl levels

| Complication                             | All patients<br>(N = 381) | Metrnl<br>< 413.2 pg/mL | Metrnl<br>> 413.2 pg/mL | P      |
|--|---------------------------|-------------------------|-------------------------|--------|
| Postinfarction angina                    | 11 (2.9)                  | 5 (2.6)                 | 6 (3.1)                 | .766   |
| Reinfarction                             | 4 (1.0)                   | 2 (1.1)                 | 2 (1.0)                 | 1.000  |
| Pericarditis                             | 8 (2.1)                   | 4 (2.1)                 | 4 (2.1)                 | 1.000  |
| Primary VF                               | 19 (5.0)                  | 9 (4.7)                 | 10 (5.2)                | .823   |
| Sustained VT                             | 21 (5.5)                  | 5 (2.6)                 | 16 (8.4)                | .014   |
| 2nd/3rd degree atrioventricular block    | 18 (4.7)                  | 6 (3.2)                 | 12 (6.3)                | .151   |
| Atrial fibrillation                      | 23 (6.0)                  | 9 (4.7)                 | 14 (7.3)                | .288   |
| Intraventricular conduction disturbances | 6 (1.6)                   | 1 (0.5)                 | 5 (2.6)                 | .215   |
| Mechanical complications                 | 3 (0.8)                   | 1 (0.5)                 | 2 (1.0)                 | 1.000  |
| Right ventricular infarction             | 14 (3.7)                  | 3 (1.6)                 | 11 (5.8)                | .053   |
| Heart failure                            | 37 (9.7)                  | 10 (5.3)                | 27 (14.1)               | .003   |
| Shock                                    | 20 (5.2)                  | 1 (0.5)                 | 19 (9.9)                | < .001 |
| Cardiac arrest                           | 25 (6.6)                  | 9 (4.7)                 | 16 (8.4)                | .151   |
| In-hospital death                        | 16 (4.2)                  | 2 (1.1)                 | 14 (7.3)                | .003   |

VF, ventricular fibrillation; VT, ventricular tachycardia.

Data are expressed as No. (%).

**Table 3 of the supplementary data.** Sensitivity analysis of Cox regression outcomes including hs-Troponin T and NT-proBNP

| <i>3-year all-cause death or nonfatal MI</i> |                   |        |                    |        |
|--|-------------------|--------|--------------------|--------|
|  | Univariable       |        | Multivariable      |        |
|  | HR (95%CI)        | P      | HR (95%CI)         | P      |
| MetrnI                                       | 2.18 (1.53-3.11)  | < .001 | 1.85 (1.23-2.79)   | .003   |
| Age  | 1.06 (1.04-1.09)  | < .001 | 1.06 (1.03-1.09)   | < .001 |
| Cardiac arrest                               | 3.98 (1.78-8.90)  | .001   | 4.67 (1.91-11.46)  | .001   |
| Killip-Kimball III/IV class                  | 5.11 (2.60-10.05) | < .001 | -                  | -      |
| LVEF   | 0.94 (0.92-0.96)  | < .001 | 0.95 (0.93-0.98)   | < .001 |
| hs-Troponin T                                | 1.16 (0.98-1.37)  | .090   | -                  | -      |
| NT-proBNP                                    | 1.41 (1.24-1.60)  | < .001 | -                  | -      |
| <i>3-year all cause-death</i>                |                   |        |                    |        |
|  | Univariable       |        | Multivariable      |        |
|  | HR (95%CI)        | P      | HR (95%CI)         | P      |
| MetrnI                                       | 2.67 (1.75-4.07)  | < .001 | 2.00 (1.11-3.60)   | .020   |
| Age  | 1.13 (1.09-1.18)  | < .001 | 1.13 (1.07-1.18)   | < .001 |
| Cardiac arrest                               | 4.17 (1.60-10.90) | .004   | 10.15 (3.05-33.78) | < .001 |
| Killip-Kimball III/IV class                  | 9.52 (4.52-20.06) | < .001 | 2.43 (1.01-5.86)   | .048   |
| LVEF   | 0.92 (0.89-0.94)  | < .001 | 0.95 (0.92-0.99)   | .006   |
| hs-Troponin T                                | 1.40 (1.11-1.76)  | .004   | -                  | -      |
| NT-proBNP                                    | 1.71 (1.48-1.98)  | < .001 | -                  | -      |

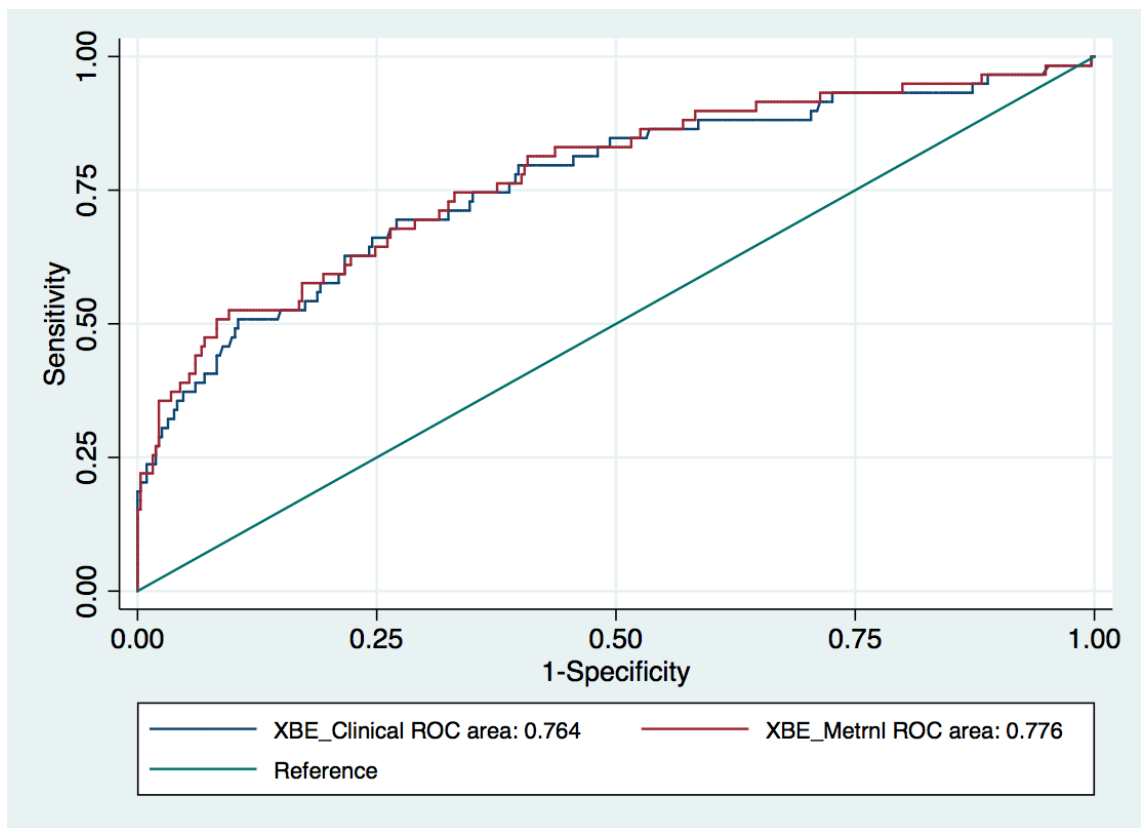
MI, myocardial infarction; HR, hazard ratio; CI, confidence interval; LVEF, left ventricular ejection fraction; NT-proBNP, inactive proform of natriuretic peptide B.

\* Analyses included only the 305 patients with complete data on all variables.

**Figure 1 of the supplementary data.** Dispersion plot showing the association between the admission GRACE score and circulating Metrnl levels at 12 hours after STEMI onset.

The GRACE score for prediction of in-hospital death includes the following variables: age, systolic blood pressure, heart rate, initial serum creatinine level, Killip-Kimball class, ST-segment deviation, elevated cardiac enzyme levels and cardiac arrest at admission.

**Figure 2 of the supplementary data.** Receiver operating characteristic (ROC) curves showing the accuracy of Metrnl for predicting 3-year all cause-death and nonfatal myocardial infarction when added to the clinical model.



The Harrel c-index or area under the curve (AUC) for each plot is provided. The clinical model includes age, cardiac arrest at admission, Killip-Kimball III/IV class and left ventricular ejection fraction.