

**SUPPLEMENTARY DATA****Table 1 of the supplementary data**

Characteristics of different CA125 commercial assays

| Supplier                           | Name   | Assay     | Reference    | Cut-off (U/mL) | Analytical Sensitivity (U/mL) | Assay Range (U/mL) |
|------------------------------------|--|-----------|--------------|----------------|-------------------------------|--------------------|
| Abbott Diagnostic                  | ARCHITECT CA 125 II assay                      | Automated | 2K45         | 35             | ≤ 1.0                         | 1.0-1000           |
| Roche Diagnostics                  | Elecsys CA 125 II                              | Automated | 11776223 190 | 35             | -                             | 0.6-5000           |
| Siemens Healthcare Diagnostics     | ADVIA Centaur CA 125II Assay                   | Automated | 09427226     | 35             | 2.0                           | 2.0-600            |
| Beckman Coulter                    | Access OV Monitor (Cancer Antigen 125)         | Automated | 386357       | 35             | 0.5                           | 0.5-5,000          |
| Ortho-Clinical Diagnostics         | CA 125 II                                      | Automated | 6800038      | 35             | -                             | 5.5-1000           |
| DiaSorin                           | LIAISON CA 125 IITM                            | Automated | 314211       | 35             | 0.3                           | 0-1000             |
| LDN Labor Diagnostika Nord GmbH&Co | CA125 ELISA                                    | ELISA     | TM E-4300    | 35-65          | 0.25                          | 0.25-600           |
| DRG Diagnostics                    | DRG TM-CA 125 ELISA                            | ELISA     | EIA-5072     | 35-65          | 0.25                          | 0.25-600           |
| IBL International                  | CA125 ELISA                                    | ELISA     | CA511201     | 35             | -                             | 1.5-500            |
| Invitrogen                         | MUCIN 16/CA125 Human ELISA Kit                 | ELISA     | EHMUC16      | -              | 0.6                           | 0.55-400           |
| LSBio LifeSpan BioSciences         | Human MUC16 / CA125 (Sandwich ELISA) ELISA Kit | ELISA     | LS-F428-1    | -              | 0.549                         | 0.549-133.3        |

|             |  |       |          |    |       |          |
|-------------|--|-------|----------|----|-------|----------|
| Abcam       | Human CA125 ELISA Kit (MUC16)          | ELISA | ab195213 | -  | 0.07  | 1.56-100 |
| R&D Systems | Human CA125/MUC16 Quantikine ELISA Kit | ELISA | DCA125   | 35 | 0.099 | 0.5-32   |

CA125, carbohydrate antigen 125; ELISA, enzyme-linked immunosorbent assay.

Table 2 of the supplementary data

Baseline characteristics among CA125 categories. Validation cohort

| Variables                               | CA125<br>< 23 U/mL<br>(n = 432) | CA125<br>23-34.9 U/mL<br>(n = 149) | CA125<br>35-64.9 U/mL<br>(n = 216) | CA125<br>≥ 65 U/mL<br>(n = 786) | P      | P for trend |
|---|---------------------------------|------------------------------------|------------------------------------|---------------------------------|--------|-------------|
| <b>Epidemiology and medical history</b> |                                 |                                    |                                    |                                 |        |             |
| Age, y                                  | 68.5 ± 12.0                     | 69.3 ± 13.3                        | 71.0 ± 11.6                        | 68.7 ± 12.4                     | .469   | .589        |
| Sex, male                               | 312 (72.2)                      | 109 (73.1)                         | 154 (71.3)                         | 566 (72.0)                      | .984   | .883        |
| Hypertension                            | 291 (67.4)                      | 99 (66.4)                          | 150 (69.4)                         | 462 (58.8)                      | .003   | .002        |
| Diabetes                                | 143 (33.1)                      | 52 (34.9)                          | 74 (34.3)                          | 271 (34.5)                      | .963   | .668        |
| Smoker                                  | 70 (16.2)                       | 18 (12.1)                          | 35 (16.2)                          | 137 (17.4)                      | .449   | .856        |
| Former smoker                           | 214 (49.6)                      | 69 (43.6)                          | 107 (49.5)                         | 356 (45.3)                      | .455   | .184        |
| Prior valve surgery                     | 24 (5.6)                        | 14 (9.4)                           | 14 (6.5)                           | 64 (8.1)                        | .269   | .163        |
| Prior HF admission                      | 116 (26.8)                      | 45 (30.2)                          | 51 (23.6)                          | 213 (27.1)                      | .566   | .893        |
| IHD                                     | 251 (59.1)                      | 84 (57.5)                          | 116 (54.5)                         | 399 (51.7)                      | .092   | .011        |
| Coronary<br>revascularization           | 149 (34.5)                      | 52 (34.9)                          | 69 (31.9)                          | 246 (31.3)                      | .635   | .212        |
| COPD                                    | 72 (16.7)                       | 35 (23.5)                          | 36 (16.7)                          | 141 (17.9)                      | .280   | .890        |
| Stroke                                  | 33 (7.6)                        | 13 (8.7)                           | 31 (14.3)                          | 74 (9.4)                        | .052   | .269        |
| PAD                                     | 45 (10.4)                       | 16 (10.7)                          | 35 (16.2)                          | 94 (12)                         | .182   | .361        |
| <b>Signs</b>                            |                                 |                                    |                                    |                                 |        |             |
| Heart rate, bpm <sup>a</sup>            | 79 ± 20                         | 80 ± 18                            | 83 ± 22                            | 84 ± 21                         | .031   | < .001      |
| SBP, mmHg <sup>a</sup>                  | 125 ± 23                        | 122 ± 20                           | 128 ± 24                           | 122 ± 23                        | .081   | .023        |
| DBP, mmHg <sup>a</sup>                  | 74 ± 13                         | 73 ± 12                            | 74 ± 17                            | 74 ± 14                         | < .001 | .837        |
| Peripheral edema <sup>a</sup>           | 176 (51.5)                      | 72 (56.7)                          | 131 (72.8)                         | 517 (75.0)                      | < .001 | < .001      |
| <b>ECG</b>                              |                                 |                                    |                                    |                                 |        |             |
| Atrial fibrillation                     | 183 (42.4)                      | 67 (45.0)                          | 108 (50.0)                         | 371 (47.2)                      | .239   | .096        |
| BBB <sup>b</sup>                        | 122 (28.6)                      | 48 (32.4)                          | 59 (27.3)                          | 249 (32.0)                      | .411   | .282        |

| <b>Echocardiography</b>                           |                  |                  |                  |                     |        |        |
|---|------------------|------------------|------------------|---------------------|--------|--------|
| LVEF, % <sup>c</sup>                              | 32.0 ± 9.8       | 31.5 ± 11.9      | 34.3 ± 12.7      | 30.1 ± 11.9         | < .001 | < .001 |
| LVEF categories                                   |                  |                  |                  |                     | .004   | .157   |
| < 40%   |                  |                  |                  |                     |        |        |
| 40-49%  | 350 (89.1)       | 115 (87.1)       | 144 (77.4)       | 587 (86.4)          |        |        |
| ≥ 50%   | 21 (5.3)         | 5 (3.8)          | 20 (10.7)        | 32 (4.7)            |        |        |
|   | 22 (5.6)         | 12 (9.1)         | 22 (11.8)        | 60 (8.8)            |        |        |
| LVEDD, mm <sup>d</sup>                            | 61 ± 10          | 59 ± 10          | 60 ± 11          | 60 ± 9              | .020   | .852   |
| LVESD, mm <sup>e</sup>                            | 49 ± 12          | 48 ± 11          | 49 ± 13          | 50 ± 12             | .387   | .088   |
| LA diameter, m <sup>f</sup>                       | 46 ± 8           | 46 ± 9           | 47 ± 8           | 48 ± 8              | .281   | < .001 |
| <b>Laboratory</b>                                 |                  |                  |                  |                     |        |        |
| Hemoglobin, g/dL <sup>g</sup>                     | 13.1 ± 1.9       | 13.1 ± 1.8       | 12.8 ± 2.0       | 13.1 ± 2.0          | .720   | .266   |
| Serum creatinine, mg/dL <sup>h</sup>              | 1.28 ± 0.59      | 1.27 ± 0.48      | 1.32 ± 0.65      | 1.35 ± 0.62         | .001   | .082   |
| eGFR (MDRD formula), mg/dL/1.73 m <sup>2h</sup>   | 64.4 ± 6.6       | 63.5 ± 23.0      | 63.0 ± 25.5      | 61.6 ± 24.7         | .124   | .070   |
| BUN, mg/dL <sup>i</sup>                           | 36.6 [22.7-59.2] | 34.8 [22.2-52.2] | 29 [19.1-50.9]   | 33.1 [21.9-54.6]    | < .001 | .060   |
| Sodium, mmol/L <sup>h</sup>                       | 140 ± 3          | 139 ± 4          | 139 ± 4          | 138 ± 4             | < .001 | < .001 |
| Potassium, mmol/L <sup>h</sup>                    | 4.2 ± 0.6        | 4.3 ± 0.7        | 4.2 ± 0.5        | 4.2 ± 0.6           | < .001 | .288   |
| NT-proBNP, pg/dL <sup>j</sup>                     | 1524 [755-3682]  | 2578 [1007-5478] | 3371 [1520-6073] | 4623 [2384-8656]    | < .001 | < .001 |
| CA125, U/mL                                       | 13.2 [9.1-17.5]  | 28.2 [24.8-31.8] | 48.3 [39.3-56.3] | 170.1 [103.6-312.2] | < .001 | < .001 |
| <b>Medical treatment at discharge<sup>k</sup></b> |                  |                  |                  |                     |        |        |
| Diuretics   | 431 (99.8)       | 148 (99.3)       | 216 (100)        | 786 (100)           | .161   | .137   |
| Aldosterone antagonists                           | 235 (54.4)       | 87 (58.4)        | 100 (46.3)       | 427 (54.3)          | .099   | .747   |
| Beta-blockers                                     | 350 (81.0)       | 126 (84.6)       | 166 (76.8)       | 625 (79.5)          | .299   | .346   |
| ACEI/ARB  | 303 (70.1)       | 96 (64.4)        | 152 (70.4)       | 542 (69.0)          | .592   | .890   |
| <b>Endpoints</b>                                  |                  |                  |                  |                     |        |        |
| 1-month death                                     | 5 (1.1)          | 2 (1.34)         | 5 (2.3)          | 30 (3.8)            | .027   | .005   |
| 1-month death or HF-readmission                   | 17 (3.9)         | 8 (5.4)          | 14 (6.5)         | 81 (10.3)           | < .001 | < .001 |

|  |           |           |           |            |        |        |
|--|-----------|-----------|-----------|------------|--------|--------|
| <i>6-month death</i>                   | 26 (6)    | 12 (8.1)  | 25 (11.6) | 120 (15.3) | < .001 | < .001 |
| <i>6-month death or HF-readmission</i> | 65 (15.1) | 29 (19.5) | 49 (22.7) | 228 (29)   | < .001 | < .001 |

ACEI, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blockers; BBB, bundle branch block; BUN, blood urea nitrogen; CA125, carbohydrate antigen 125; COPD, chronic obstructive pulmonary disease; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; HF, heart failure; IHD, ischemic heart disease; LA, left atrial LVEDD, left ventricle end-diastolic diameter; LVEF, left ventricle ejection fraction; LVESD, left ventricle end-systolic diameter; MDRD, Modification of Diet in Renal Disease; NT-proBNP, N-terminal pro-B-type natriuretic peptide; PAD, peripheral artery disease; SBP, systolic blood pressure.

Variables are expressed as No. (%), mean  $\pm$  standard deviation, or median [interquartile range].

<sup>a</sup>Data available in 1577 patients

<sup>b</sup>Data available in 1569 patients

<sup>c</sup>Data available in 1390 patients

<sup>d</sup>Data available in 1320 patients

<sup>e</sup>Data available in 897 patients

<sup>f</sup>Data available in 1128 patients

<sup>g</sup>Data available in 1553 patients

<sup>h</sup>Data available in 1568 patients

<sup>i</sup>Data available in 1419 patients

<sup>j</sup>Data available in 1548 patients

<sup>k</sup>Treatment received at discharge or on admission in patients with in-hospital mortality.

**Figure 1 of the supplementary data**

All-cause mortality risk among the prespecified subgroups. eGFR, estimated glomerular filtration rate; LVEF, left ventricle ejection fraction; NT-proBNP, N-terminal pro-B-type natriuretic peptide.

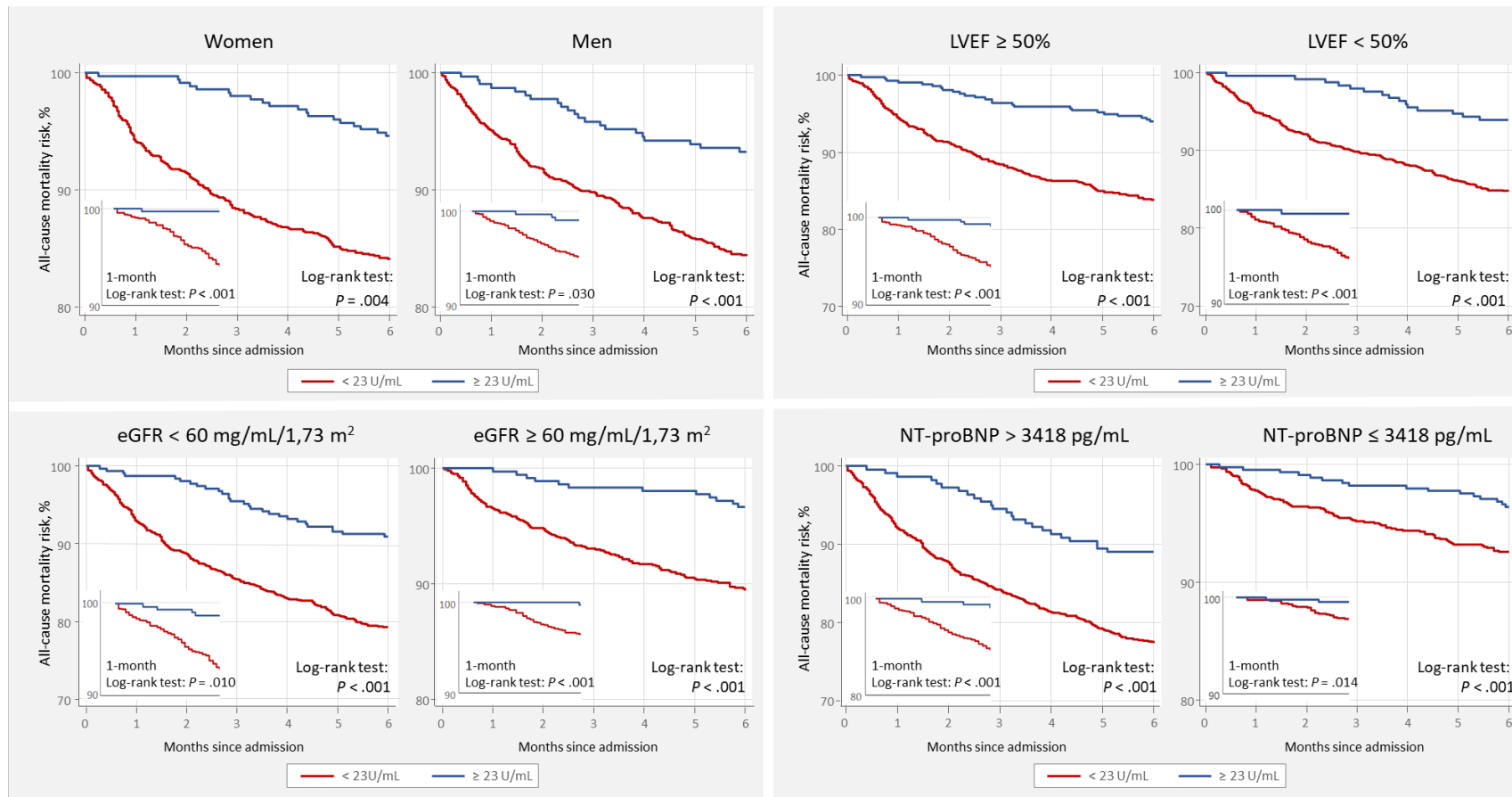


Figure 2 of the supplementary data

Death/HF-hospitalization risk among the prespecified subgroups. eGFR, estimated glomerular filtration rate; LVEF, left ventricle ejection fraction; NT-proBNP, N-terminal pro-B-type natriuretic peptide.

