**Cardiac troponin I is associated with prothrombotic alterations in atrial fibrillation**

**Running title: Biomarkers and thrombin generation in AF**

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**Supplementary Table 1 Patient characteristics by** **high-sensitivity cardiac troponin I tertiles.**

|  |  |  |  |
| --- | --- | --- | --- |
| **Variable** | **Whole group, n=65** | **High-sensitivity cardiac troponin I tertiles** | ***P*-value** |
| **T1 (2.9-5.6 ng/l, n=21)** | **T2 (5.7-7.3 ng/l, n=22)** | **T3 (7.5-13.****7 ng/l, n=22)** |
| **Demographics** |
|  **Age (years)** | 70.0 (65.0-76.5) | 65.0 (57.0-69.5) | 69.5 (65.8-74.3) | 78.0 (72.0-82.5) | <0.0001 |
|  **Male sex, n (%)** | 38 (58.5) | 13 (61.9) | 13 (59.1) | 12 (54.5) | 0.89 |
|  **BMI (kg/m2)** | 29.1 ± 4.8 | 28.8 ± 4.2 | 29.9 ± 6.2 | 28.6 ± 3.8 | 0.69 |
| **Type of AF** |
|  **Paroxysmal AF, n (%)** | 20 (30.8) | 9 (42.9) | 7 (31.8) | 4 (18.2) | 0.17 |
|  **Persistent AF, n (%)** | 10 (15.4) | 5 (23.8) | 2 (9.1) | 3 (13.6) |
|  **Permanent AF, n (%)** | 35 (53.8) | 7 (33.3) | 13 (59.1) | 15 (68.2) |
| **AF on the day of blood collection, n (%)** | 48 (73.8) | 13 (61.9) | 16 (72.7) | 19 (86.4) | 0.19 |
| **Comorbidities and CVD risk factors** |
|  **Hypertension, n (%)** | 54 (83.1) | 15 (71.4) | 20 (90.9) | 19 (86.4) | 0.24 |
|  **Diabetes mellitus, n (%)** | 27 (41.5) | 6 (28.6) | 10 (45.5) | 11 (50.0) | 0.33 |
|  **Dyslipidemia, n (%)** | 56 (86.2) | 17 (81.0) | 19 (86.4) | 20 (90.9) | 0.61 |
|  **Smoking history, n (%)** | 6 (9.2) | 3 (14.3) | 1 (4.5) | 2 (9.1) | 0.50 |
|  **CAD, n (%)** | 36 (55.4) | 9 (42.9) | 12 (54.5) | 15 (68.2) | 0.25 |
|  **Previous MI, n (%)** | 16 (24.6) | 6 (28.6) | 2 (9.1) | 8 (36.4) | 0.10 |
|  **Previous stroke, n (%)** | 9 (13.8) | 1 (4.8) | 5 (22.7) | 3 (13.6) | 0.27 |
|  **CKD stage 3 or 4, n (%)** | 20 (30.8) | 3 (14.3) | 4 (18.2) | 13 (59.1) | 0.002 |
|  **COPD, n (%)** | 6 (9.2) | 1 (4.8) | 3 (13.6) | 2 (9.1) | 0.86 |
|  **CHA2DS2-VASc score** | 4.5 ± 1.8 | 3.4 ± 1.6 | 4.7 ± 1.8 | 5.5 ± 1.6 | 0.0005 |
| **Medications, n (%)** |
|  **Beta-blocker** | 52 (80.0) | 17 (81.0) | 17 (77.3) | 18 (81.8) | 1.00 |
|  **ACE-I** | 37 (56.9) | 12 (57.1) | 12 (54.5) | 13 (59.1) | 0.95 |
|  **ARB** | 12 (18.5) | 3 (14.3) | 5 (22.7) | 4 (18.2) | 0.92 |
|  **CCB** | 14 (21.5) | 3 (14.3) | 4 (18.2) | 7 (31.8) | 0.40 |
|  **Aspirin** | 12 (18.5) | 6 (28.6) | 2 (9.1) | 4 (18.2) | 0.24 |
|  **Clopidogrel** | 2 (3.1) | 2 (9.5) | 0 (0.0) | 0 (0.0) | 0.10 |
|  **Statin** | 43 (66.2) | 11 (52.4) | 15 (68.2) | 17 (77.3) | 0.22 |
|  **Digoxin** | 13 (20.0) | 2 (9.5) | 4 (18.2) | 7 (31.8) | 0.20 |
|  **Aldosterone antagonist** | 20 (30.8) | 10 (47.6) | 4 (18.2) | 6 (27.3) | 0.10 |
|  **Furosemide** | 14 (21.5) | 5 (23.8) | 4 (18.2) | 5 (22.7) | 0.93 |
|  **Torasemide** | 24 (36.9) | 7 (33.3) | 9 (40.9) | 8 (36.4) | 0.87 |
|  **Hydrochlorothiazide** | 8 (12.3) | 4 (19.0) | 1 (4.5) | 3 (13.6) | 0.32 |
|  **Indapamide** | 8 (12.3) | 2 (9.5) | 2 (9.1) | 4 (18.2) | 0.71 |
|  **Amiodarone** | 6 (9.2) | 2 (9.5) | 1 (4.5) | 3 (13.6) | 0.67 |
|  **Propafenone** | 7 (10.8) | 2 (9.5) | 3 (13.6) | 2 (9.1) | 1.0 |
| **Echocardiographic parameters** |
|  **LVEF (%)** | 49.1 ± 15.3 | 51.2 ± 14.0 | 47.0 ± 19.0 | 49.1 ± 12.5 | 0.67 |
|  **LA diameter (cm)** | 4.5 ± 0.6 | 4.6 ± 0.7 | 4.5 ± 0.7 | 4.5 ± 0.6 | 0.77 |

ACE-I, angiotensin-converting enzyme inhibitor; AF, atrial fibrillation; ARB, angiotensin II receptor blocker; BMI, body mass index; CAD, coronary artery disease; CCB, calcium channel blocker; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CVD, cardiovascular disease; LA, left atrial; LVEF, left ventricular ejection fraction; MI, myocardial infarction; n, number; NT-proBNP, N-terminal pro-B-type natriuretic peptide. Values are presented as mean ± standard deviation or median (interquartile range) or number (percentage).

**Supplementary Table 2 Laboratory parameters by high-sensitivity cardiac troponin I tertiles.**

|  |  |  |  |
| --- | --- | --- | --- |
| **Variable** | **Whole group, n=65** | **High-sensitivity cardiac troponin I tertiles** | ***P*-value** |
| **T1 (2.9-5.6 ng/l, n=21)** | **T2 (5.7-7.3 ng/l, n=22)** | **T3 (7.5-13.7 ng/l, n=22)** |
| **Laboratory tests results**  |
|  **WBC (x1000/µl)** | 6.2 (5.1-7.4) | 6.1 (4.9-7.9) | 6.1 (5.1-7.0) | 6.4 (5.8-7.5) | 0.41 |
|  **Hgb (g/dl)** | 13.8 ± 1.5 | 14.3 ± 1.7 | 13.9 ± 1.1 | 13.2 ± 1.4 | 0.02 |
|  **Platelets (x1000/µl)** | 201.9 ± 50.4 | 205.7 ± 57.3 | 201.6 ± 38.8 | 198.6 ± 55.5 | 0.90 |
|  **Glucose (mmol/l)** | 6.0 (5.5-6.6) | 5.7 (5.3-6.4) | 5.9 (5.5-6.5) | 6.2 (5.5-6.9) | 0.47 |
|  **GFR (****ml/min)** | 70.0 (55.0-83.0) | 83.0 (72.0-95.0) | 69.0 (62.3-78.5) | 51.5 (41.8-72.5) | <0.0001 |
|  **Cystatin C (mg/l)** | 1.0 ± 0.2 | 0.9 ± 0.1 | 1.0 ± 0.1 | 1.0 ± 0.2 | 0.15 |
|  **cTnI-hs (ng/l)** | 6.4 (5.2-7.9) | 4.7 (3.6-5.2) | 6.4 (5.9-7.0) | 10.1 (7.9-11.7) | - |
|  **CRP (mg/l) #** | 2.0 (1.0-4.0) | 2.6 (1.2-5.2) | 1.8 (1.0-3.0) | 2.0 (1.0-5.8) | 0.45 |
|  **NT-proBNP**  **(pg/ml)** | 772.0 (395.5-1537.0) | 495.0 (235.5-995.5) | 714.0 (459.5-1539.0) | 1180.5 (703.8-1993.8) | 0.02 |
|  **TC (mmol/l)** | 4.0 (3.6-4.5) | 4.2 (3.5-5.3) | 4.0 (3.7-4.6) | 3.9 (3.5-4.3) | 0.43 |
|  **LDL-C (mmol/l)** | 2.3 (2.0-2.8) | 2.4 (1.9-3.1) | 2.4 (2.0-2.8) | 2.3 (2.1-2.6) | 0.85 |
|  **HDL-C (mmol/l)** | 1.4 (1.1-1.6) | 1.5 (1.1-1.7) | 1.2 (1.0-1.6) | 1.4 (1.2-1.5) | 0.71 |
|  **Triglyceride (mmol/l)** | 1.2 (0.8-1.5) | 1.1 (0.8-1.6) | 1.2 (0.8-1.4) | 1.2 (0.8-1.5) | 0.86 |
| **Coagulation parameters** |
|  **APTT (seconds)** | 26.1 ± 3.3 | 26.2 ± 3.4 | 26.0 ± 3.2 | 26.2 ± 3.4 | 0.98 |
|  **INR** | 1.1 (1.0-1.1) | 1.1 (1.0-1.1) | 1.0 (1.0-1.1) | 1.1 (1.0-1.1) | 0.41 |
|  **Fibrinogen (g/l) #** | 3.7 (3.1-4.1) | 3.7 (3.1-4.2) | 3.6 (3.1-4.0) | 3.6 (3.1-4.3) | 0.88 |
|  **vWF:Ag (%)** | 179.0 (146.0-212.0) | 179.0 (159.5-196.0) | 190.5 (152.3-226.0) | 161.5 (133.5-239.8) | 0.58 |
| **Thrombin generation** |
|  **Lag time (seconds)** | 1636.0 ± 715.9 | 1668.9 ± 545.2 | 1771.8 ± 671.2 | 1452.2 ± 896.4 | 0.35 |
|  **Time to peak thrombin generation (seconds)** | 2067.4 ± 856.5 | 2256.0 ± 740.8 | 2163.6 ± 792.9 | 1791.3 ± 979.3 | 0.17 |
|  **Peak thrombin concentration (n**M**)** | 82.4 (49.9-119.2) | 63.4 (40.6-115.1) | 63.3 (44.5-96.3) | 117.0 (85.5-298.4) | 0.006 |
|  **ETP (nM x seconds)** | 60454.0 (40606.2-85327.6) | 59827.2 (37549.3-85156.7) | 57894.9 (37040.8-75422.3) | 75359.5 (50823.8-134016.7) | 0.12 |

Ag, antigen; APTT, activated partial thromboplastin time; CRP, C-reactive protein; cTnI-hs, high-sensitivity cardiac troponin I; ETP, endogenous thrombin potential; GFR, glomerular filtration rate; HDL-C, high-density lipoprotein cholesterol; Hgb, hemoglobin concentration; INR, international normalized ratio; LDL-C, low-density lipoprotein cholesterol; TC, total cholesterol; vWF, von Willebrand factor; WBC, white blood cell; for other abbreviations see the description of Supplementary Table 1. Values are presented as mean ± standard deviation or median (interquartile range). #The data for fibrinogen, lag time and ETP were available for 63, 63 and 60 patients, respectively.