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| **Variable** | **Missing** | **Heart Failure and Atrial Fibrillation (1164)** | **Heart Failure and Sinus Rhythm (2406)** | **p** | **HFrEF in Sinus Rhythm**  **(1372)** | **HFpEF in Sinus Rhythm**  **(1034)** | **p** |
| **Demographics** | | | | | | | |
| **Age (Years)** | 0 | 76 (70-82) | 73 (65-79) | <0.001 | 71 (63-77) | 76 (70-82) | <0.001 |
| **Men** | 0 | 774 (67%) | 1483 (62%) | 0.005 | 1002 (73%) | 481 (47%) | <0.001 |
| **Body Mass Index (kg/m2)** | 11 | 28 (25-32) | 28 (25-32) | 0.07 | 28 (24-31) | 28 (25-32) | <0.001 |
| **Systolic Blood Pressure (mmHg)** | 11 | 136 (25) | 139 (26) | <0.001 | 132 (24) | 149 (26) | <0.001 |
| **Diastolic Blood Pressure (mmHg)** | 10 | 80 (16) | 77 (14) | <0.001 | 76 (13) | 78 (14) | <0.001 |
| **Heart Rate (bpm)** | 10 | 81 (20) | 71 (15) | <0.001 | 72 (15) | 70 (15) | <0.001 |
| **Diabetes Mellitus** | 0 | 278 (24%) | 603 (25%) | 0.444 | 326 (24%) | 277 (27%) | 0.090 |
| **Hypertension** | 0 | 629 (54%) | 1238 (52%) | 0.147 | 563 (41%) | 675 (65%) | <0.001 |
| **Valvular Disease** | 0 | 192 (17%) | 181 (8%) | <0.001 | 75 (6%) | 106 (10%) | <0.001 |
| **Ischemic Heart Disease** | 0 | 483 (42%) | 1425 (59%) | <0.001 | 956 (70%) | 469 (45%) | <0.001 |
| **Previous TIA/Stroke** | 0 | 144 (12%) | 163 (7%) | <0.001 | 103 (8%) | 60 (6%) | 0.100 |
| **Peripheral Vascular Disease** | 0 | 76 (7%) | 179 (7%) | 0.322 | 113 (8%) | 66 (6%) | 0.086 |
| **Paroxysmal Atrial Fibrillation** | 0 | Not applicable | 190 (8%) | Not applicable | 116 (9%) | 74 (7%) | 0.242 |
| **NYHA Class I** | 0 | 174 (15%) | 583 (24%) | <0.001 | 268 (20%) | 315 (31%) | <0.001 |
| **NYHA Class II** | 571 (49%) | 1156 (48%) | 682 (50%) | 474 (46%) |
| **NYHA Class III** | 399 (34%) | 618 (26%) | 386 (28%) | 232 (22%) |
| **NYHA Class IV** | 20 (2%) | 49 (2%) | 36 (2%) | 13 (1%) |
| **Blood results** | | | | | | | |
| **NT-proBNP (ng/L)** | 11 | 1936 (1057-3607) | 833 (372-2119) | <0.001 | 1165 (474-3012) | 587 (326-1288) | <0.001 |
| **Albumin (g/L)** | 233 | 37 (4) | 38 (4) | 0.001 | 38 (4) | 37 (4) | 0.002 |
| **Bilirubin (µmol/L)** | 243 | 16 (13-21) | 13 (11-17) | <0.001 | 14 (12-18) | 13 (10-15) | <0.001 |
| **Creatinine (µmol/L)** | 153 | 104 (86-130) | 100 (82-128) | 0.002 | 102 (86-128) | 96 (79-125) | <0.001 |
| **Haemoglobin (g/dL)** | 157 | 13.4 (1.9) | 13.1 (1.7) | <0.001 | 13.4 (1.7) | 12.8 (1.7) | <0.001 |
| **K (mmol/L)** | 171 | 4.3 (4.0-4.6) | 4.4 (4.1-4.7) | <0.001 | 4.4 (4.1-4.7) | 4.3 (4.1-4.7) | 0.001 |
| **Na (mmol/L)** | 151 | 138 (3) | 138 (3) | 0.894 | 138 (3) | 138 (3) | 0.584 |
| **Urea (mmol/L)** | 151 | 7.1 (5.4-9.8) | 6.8 (5.2-9.2) | 0.003 | 6.8 (5.3-9.2) | 6.8 (5.2-9.2) | 0.640 |
| **Thyroid-Stimulating Hormone (mU/L)** | 408 | 1.8 (1.2-2.8) | 1.7 (1.1-2.5) | 0.002 | 1.6 (1.0-2.5) | 1.7 (1.1-2.6) | 0.151 |
| **Medications#** | | | | | | | |
| **Loop diuretic** | 0 | 860 (74%) | 1505 (63%) | <0.001 | 959 (70%) | 546 (53%) | <0.001 |
| **Mineralocorticoid receptor antagonist** | 0 | 227 (20%) | 525 (22%) | 0.111 | 417 (30%) | 108 (10%) | <0.001 |
| **ACE-I or ARB** | 0 | 812 (70%) | 1743 (72%) | 0.096 | 1115 (81%) | 628 (61%) | <0.001 |
| **Beta-blockers** | 0 | 660 (57%) | 1429 (59%) | 0.126 | 906 (66%) | 523 (51%) | <0.001 |
| **Echocardiography\*** | | | | | | | |
| **Left Ventricular Ejection Fraction >55%** | 0 | 403 (35%) | 618 (26%) | <0.001 | 0 | 618 (60%) | Not applicable |
| **Left Ventricular Ejection Fraction: 46-54%** | 283 (24%) | 416 (17%) | 0 | 416 (40%) |
| **Left Ventricular Ejection Fraction: 36-45%** | 242 (21%) | 658 (27%) | 658 (48%) | 0 |
| **Left Ventricular Ejection Fraction: <35%** | 236 (20%) | 714 (30%) | 714 (52%) | 0 |
| **Left Atrial Diameter (cm)** | 431 | 4.7 (0.8) | 4.0 (0.7) | <0.001 | 4.2 (1.7) | 3.9 (0.7) | <0.001 |
| **Events** | | | | | | | |
| **Incident Atrial Fibrillation** | 0 | Not applicable | 291 (12%) | Not applicable | 205 (15%) | 86 (8%) | Not applicable |
| **Incident Atrial Fibrillation at 1 year** | 0 | Not applicable | 62 (3%) | Not applicable | 34 (3%) | 28 (3%) | 0.73 |

**Table 1:** Baseline characteristics of patients with HF, by diagnostic category and by heart rhythm. \*Left Ventricular Ejection Fraction was measured (n=2013) or visually estimated. # Medications recorded at baseline prior to changes subsequent to initial referral.

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| **Variable** | **Univariable analysis** | | | **Multivariable analysis**  **LA included**  **LA excluded** | | |
|  | **HR (95% CI)** | **χ2** | **p-value** | **HR (95% CI)** | **χ2** | **p-value** |
| Age (1 Year increase) | 1.03 (1.01-1.05) | 17.69 | <0.001 | 1.04 (1.02-1.05)  1.03 (1.02-1.05) | 17.75  16.90 | <0.001  <0.001 |
| Male sex (vs female) | 1.70 (1.31-2.21) | 15.59 | <0.001 | 1.64 (1.17-2.30)  1.98 (1.45-2.70) | 8.29  18.75 | 0.004  <0.001 |
| Body Mass Index (kg/m2) | 0.99 (0.98-1.02) | 0.014 | 0.91 |  |  |  |
| Systolic Blood Pressure (mmHg) | 0.99 (0.99-1.00) | 6.34 | 0.012 |  |  |  |
| Diastolic Blood Pressure (mmHg) | 0.99 (0.98-1.00) | 6.23 | 0.013 |  |  |  |
| Heart Rate (bpm) | 1.00 (1.00-1.01) | 0.19 | 0.66 |  |  |  |
| Diabetes Mellitus (yes vs not) | 1.12 (0.85-1.48) | 0.68 | 0.41 |  |  |  |
| Hypertension (yes vs not) | 0.89 (0.71-1.12) | 0.99 | 0.32 |  |  |  |
| Valvular Disease (yes vs not) | 1.13 (0.73-1.76) | 0.29 | 0.59 |  |  |  |
| Ischemic Heart Disease (yes vs not) | 1.40 (1.10-1.80) | 7.16 | 0.007 |  |  |  |
| Previous TIA/Stroke (yes vs not) | 0.95 (0.59-1.53) | 0.05 | 0.95 |  |  |  |
| Peripheral Vascular Disease (yes vs not) | 1.11 (0.71-1.75) | 0.21 | 0.65 |  |  |  |
| Paroxysmal Atrial Fibrillation (yes vs not) | 3.06 (2.26-4.13) | 53.20 | <0.001 | 2.52 (1.78-3.57)  2.62 (1.89-3.64) | 27.18  33.28 | <0.001  <0.001 |
| NYHA class (III/IV vs I/II) | 1.40 (1.08-1.81) | 6.54 | 0.010 |  |  |  |
| LogNT-proBNP (ng/L) | 2.39 (1.94-2.96) | 64.69 | <0.001 | 1.80 (1.34-2.42)  1.91 (1.46-2.50) | 15.19  22.04 | <0.001  <0.001 |
| Albumin (g/l) | 0.97 (0.94-1.00) | 3.58 | 0.057 |  |  |  |
| Bilirubin (µmol/L) | 1.03 (1.01-1.05) | 13.53 | <0.001 |  |  |  |
| Creatinine (µmol/L) | 1.01 (1.00-1.01) | 7.32 | 0.007 |  |  |  |
| Haemoglobin (g/dL) | 0.94 (0.87-1.00) | 3.28 | 0.070 |  |  |  |
| K (mmol/L) | 1.03 (0.81-1.31) | 0.06 | 0.81 |  |  |  |
| Na (mmol/L) | 1.01 (0.97-1.05) | 0.11 | 0.74 |  |  |  |
| Urea (mmol/L) | 1.04 (1.02-1.06) | 15.67 | <0.001 |  |  |  |
| Thyroid-Stimulating Hormone (mU/L) | 1.02 (0.99-1.04) | 1.83 | 0.18 |  |  |  |
| HFrEF vs HFpEF | 1.63 (1.27-2.09) | 14.33 | <0.001 | 1.44 (1.02-2.04)  - | 4.36  - | 0.037  - |
| Left Atrial Diameter (cm) | 1.78 (1.50-2.12) | 42.86 | <0.001 | 1.56 (1.28-1.89)  - | 20.17  - | <0.001  - |

**Table 2:** Univariable and multivariable analysis for the incidence of atrial fibrillation in the overall population with heart failure. Two models were constructed, one including and one excluding left atrial diameter (available for 2085 patients, 87%). Variable included in the multivariable models were: age, sex, systolic blood pressure, diastolic blood pressure, ischaemic heart disease, paroxysmal atrial fibrillation, LogNT-proBNP, albumin, bilirubin, haemoglobin, urea, diagnostic category (HFrEF vs HFpEF) and left atrial diameter.

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| **Quintile of NT-proBNP (range, ng/L)** | **Patients with HFrEF with incident AF**  **(per 1000 person-years), n** | **Hazard ratio (95% CI), p (vs Q1)** |
| Q1 (9-363) | 14.44 | 1 |
| Q2 (364-832) | 25.51 | 1.80 (1.12-2.92); 0.016 |
| Q3 (835-1652) | 39.85 | 2.89 (1.82-4.58);<0.001 |
| Q4 (1667-3780) | 41.94 | 3.11 (1.93-4.99); <0.001 |
| Q5 (3781-61888) | 42.53 | 3.18 (1.93-5.25); <0.001 |
| **Quintile of NT-proBNP (range, ng/L)** | **Patients with** **HFpEF with incident AF**  **(per 1000 person-years), n** | **Hazard ratio (95% CI), p (vs Q1)** |
| Q1 (221-309) | 8.95 | 1 |
| Q2 (310-448) | 9.22 | 1.03 (0.44-2.42); 0.948 |
| Q3 (449-762) | 15.28 | 1.64 (0.74-3.62); 0.223 |
| Q4 (763-1573) | 30.71 | 3.26 (1.59-6.69);0.001 |
| Q5 (1575-35000) | 41.57 | 4.29 (2.12-8.70);<0.001 |

**Table 3.** Risk of developing AF during follow-up according to NTproBNP quintiles in patients with HFrEF and HFpEF.