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# Long-term prognostic importance of resting heart rate in patients with left ventricular dysfunction in connection with either heart failure or myocardial infarction: The DIAMOND study ☆

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**Abstract**

*Background:* Elevated resting heart rate is associated with increased mortality in a variety of cardiac diseases, but comparisons between different clinical settings are lacking. We investigated the long-term prognostic importance of resting heart rate in patients hospitalized with left ventricular dysfunction in connection with either heart failure (HF) or myocardial infarction (MI).
*Methods:* In the Danish Investigations and Arrhythmia ON Dofetilide (DIAMOND) study; patients with left ventricular dysfunction were randomized to Dofetilide (class III antiarrhythmic drug) or placebo. One part of the study enrolled 1518 patients with HF and another 1510 patients with MI. Mortality analyses were performed using multivariable adjusted Cox proportional hazard models.
*Results:* During 10 years of follow-up, 1076 (72%) patients with MI and 1336 (89%) patients with HF died. In multivariable adjusted models, every increment in baseline heart rate of 10 bpm was associated with an increase in mortality in both MI-patients (hazard ratio, 1.14; 95%-confidence interval (CI): 1.09–1.19; $P<.0001$) and HF-patients (hazard ratio, 1.10; CI: 1.06–1.15; $P<.0001$). The importance of resting heart rate on short-term prognosis was stronger in the MI patients compared to the HF patients ($P<.0001$ for interaction). There was no interaction between heart rate and β-blockade, and inclusion of β-blockade in the model did not change the results.
*Conclusions:* Resting heart rate was independently associated with increased risk of overall mortality. The prognostic importance of resting heart rate is stronger in patients with MI compared to patients with HF, especially in the short term.


*Keywords:* Resting heart rate; Myocardial infarction; Heart failure; Left ventricular dysfunction; Mortality

## 1. Introduction

An elevated heart rate is a known risk factor in the general population and in a variety of diseases and independently predicts early death [1–8]. Heart rate has also been associated with coronary artery disease (CAD) in animal models [9,10]. The importance of resting heart rate on long-term prognosis in hospitalized patients with left ventricular dysfunction is however less clear. In patients with heart failure (HF) and/or acute myocardial infarction (MI); treatment with β-blockers has shown to improve prognosis substantially. Explorative analyses suggest that there is a strong correlation between reduction in heart rate, accomplished with β-blockers after MI and the survival benefit of β-blockade [11]. However, it is unknown whether this effect is directly related to the anti-

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Table 1
Baseline data according to resting heart rate divided into quartiles.

| Heart rate | 40–70 | 71–80 | 81–91 | 92–max | 40–max (all) |
|---|---|---|---|---|---|
| Heart rate | 63 | 76 | 86 | 100 | 80 |
| *n* (All) | 798 (26%) | 710 (24%) | 762 (25%) | 743 (25%) | 3013 (100%) |
| *n* (HF) | 351 (23%) | 331 (22%) | 371 (25%) | 455 (30%) | 1508 (100%) |
| *n* (MI) | 447 (30%) | 379 (25%) | 391 (26%) | 288 (19%) | 1505 (100%) |
| Age, years | | | | | |
| HF, † | 72 (56–84) | 71 (53–85) | 71 (52–83) | 70 (46–83) | 71 (51–84) |
| MI | 70 (48–84) | 70 (48–84) | 71 (49–84) | 70 (50–84) | 70 (49–83) |
| Male gender | | | | | |
| HF | 252 (72%) | 232 (70%) | 286 (77%) | 334 (73%) | 1104 (73%) |
| MI, † | 348 (78%) | 284 (75%) | 272 (70%) | 206 (72%) | 1110 (74%) |
| Smoker | | | | | |
| HF | 115 (33%) | 116 (35%) | 132 (36%) | 155 (34%) | 518 (35%) |
| MI | 206 (46%) | 177 (47%) | 158 (40%) | 120 (42%) | 661 (44%) |
| *History of* | | | | | |
| Diabetes | | | | | |
| HF | 63 (18%) | 67 (20%) | 63 (17%) | 97 (21%) | 290 (19%) |
| MI | 51 (11%) | 44 (12%) | 61 (16%) | 37 (13%) | 193 (13%) |
| Atrial fibrillation | | | | | |
| HF | 75 (21%) | 52 (16%) | 60 (16%) | 108 (24%) | 295 (20%) |
| MI | 23 (5%) | 15 (4%) | 19 (5%) | 21 (7%) | 78 (5%) |
| Angina pectoris | | | | | |
| HF, † | 211 (60%) | 153 (46%) | 162 (44%) | 164 (36%) | 690 (46%) |
| MI, † | 236 (54%) | 174 (46%) | 163 (42%) | 127 (44%) | 700 (47%) |
| Previous myocardial infarction | | | | | |
| HF, ∗ | 224 (64%) | 191 (58%) | 185 (50%) | 175 (38%) | 775 (51%) |
| MI, † | 204 (46%) | 142 (37%) | 110 (28%) | 89 (31%) | 545 (36%) |
| Ischemic heart disease | | | | | |
| HF, † | 283 (81%) | 233 (70%) | 247 (67%) | 247 (54%) | 1010 (67%) |
| MI, † | 287 (64%) | 220 (58%) | 202 (52%) | 160 (56%) | 869 (58%) |
| *Screening* | | | | | |
| QRS duration, ms | | | | | |
| HF, † | 110 (60–180) | 110 (70–160) | 100 (60–160) | 100 (60–160) | 100 (60–160) |
| MI | 92 (60–160) | 100 (60–140) | 100 (60–150) | 100 (60–140) | 100 (60–150) |
| WMI (WMI∗30∼LVEF) | | | | | |
| HF, † | 1.0 (0.5–1.2) | 0.9 (0.5–1.2) | 0.9 (0.5–1.2) | 0.8 (0.5–1.2) | 0.9 (0.5–1.2) |
| MI, † | 1.0 (0.7–1.2) | 1.1 (0.8–1.2) | 1.1 (0.6–1.2) | 1.0 (0.6–1.2) | 1.1 (0.7–1.2) |
| Creatinine clearance in ml/minute | | | | | |
| HF | 53.3 (24.9–93.4) | 52.0 (27.6–95.9) | 53.2 (26.0–104.7) | 53.2 (26.4–110.6) | 52.8 (26.3–101.5) |
| MI | 60.7 (29.0–109.8) | 59.5 (27.8–120.9) | 58.2 (29.2–112.5) | 56.7 (29.4–109.8) | 58.8 (28.9–113.2) |
| BMI, kg/m$^2$ | | | | | |
| HF | 25.3 (19.4–33.1) | 25.3 (18.4–34.0) | 25.0 (19.1–32.6) | 25.2 (19.0–34.9) | 25.2 (19.0–33.8) |
| MI | 25.0 (19.8–32.7) | 25.8 (19.9–31.0) | 25.6 (19.1–32.4) | 25.1 (20.2–33.5) | 25.5 (19.7–32.1) |
| Haemoglobin, mmol/l | | | | | |
| HF | 8.4 (6.7–10.0) | 8.5 (6.5–10.2) | 8.4 (6.8–10.2) | 8.5 (6.8–10.5) | 8.4 (6.7–10.2) |
| MI | 8.4 (6.8–10.0) | 8.3 (6.6–9.8) | 8.3 (6.7–9.8) | 8.4 (6.6–9.8) | 8.3 (6.7–9.9) |
| Clinical HF | | | | | |
| HF | 351 (100%) | 330 (100%) | 370 (100%) | 455 (100%) | 1506 (100%) |
| MI, † | 162 (36%) | 160 (42%) | 167 (43%) | 157 (55%) | 646 (43%) |
| *Medical treatment at screening* | | | | | |
| β-blockers | | | | | |
| HF, † | 77 (22%) | 32 (10%) | 16 (4%) | 25 (5%) | 150 (10%) |
| MI, † | 236 (53%) | 124 (33%) | 112 (29%) | 64 (22%) | 536 (36%) |
| ACEi | | | | | |
| HF, † | 281 (80%) | 242 (73%) | 271 (73%) | 329 (72%) | 1123 (75%) |
| MI | 244 (55%) | 213 (56%) | 221 (56%) | 163 (57%) | 841 (56%) |
| CCB | | | | | |
| HF, † | 104 (30%) | 80 (24%) | 58 (15%) | 77 (17%) | 319 (21%) |
| MI, † | 90 (20%) | 63 (17%) | 56 (14%) | 38 (13%) | 247 (16%) |
| Digoxin | | | | | |
| HF, † | 192 (55%) | 188 (57%) | 240 (65%) | 321 (71%) | 941 (62%) |
| MI, † | 86 (19%) | 88 (23%) | 119 (30%) | 127 (44%) | 420 (28%) |