| Table J-34. Studies evaluating independent predictive value of NT-proBNP for the outcome of cardiovascular mortality in patients with stable heart failure | | | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Author**  **Year**  **Companion** | **Study Design**  **Population** | **n**  **Mean Age (SD)**  **% male** | **BNP Levels (pg/mL)** | **Prognostic Markers** | **Followup**  **Outcomes**  **(#events, #risk)** | **Model** | **Adjusted/Non-**  **adjusted**  **Covariates** | **Measure(s) of Risk**  **(95% CI,)** |
| Jankowska,163  2011 | Cohort  Patients with systolic chronic HF | n=491  mean age:  63y(11)  91.0% male | ADM mean: 875 (347, 2,465)\*\*  D/C mean: NR  Cutpoint: >2,465 | log10NT-proBNP, CT-proET-1 (log), NYHA, LVEF, age, serum creatinine | 12m  CV mortality (70, 491) | Multivariable cox regression | CT-proET-1 (log), NYHA, LVEF, age, serum creatinine | HR=3.36 (2.40-4.71) |
| Tziakas,175  2012 | Cohort  Patients with acute decompensation of chronic HF admitted to Coronary Care Unit | n=219  mean age:  cardiac event:  68.5y(11)  No cardiac event:  69.5y(13)  64.3% male | ADM mean:  cardiac event: 4,241.5 (6,130)  No cardiac event:1,213( 2,438)  D/C mean: NR  Cutpoint: >3,357 | D/C NT-proBNP, age, sex, systolic BP, heart rate, BMI, NYHA, underlying etiologies, accompanying disease, echocardiographic data, mediation during followup, laboratory results | 12m  CV mortality (56, 196) | Multivariable cox regression | Age, sex, systolic BP, heart rate, BMI, NYHA, Underlying etiologies, accompanying disease, echocardiographic data, mediation during followup, laboratory results. | HR=0.43 (0.23-0.79), p=0.007 |
| Petretta,158  2007 | Cohort  Chronic HF patients without cachexia referred to institution | n=82  mean age:  61y(13)  74.0% male | ADM mean: 844 (220.2, 2,755.5)\*\*  D/C mean: NR  Cutpoint: per log unit | NT-proBNP, NYHA, heart rate, IGF-I, log IGF-I/GH ratio | 18.4m  CV mortality (70, 491) | Multivariable cox regression | NYHA, heart rate, IGF-I, log IGF-I/GH ratio | HR=1.02 (1.01 - 1.03) per unit increase  p<0.001 |
| ADM mean: 844 (220.2, 2,755.5)\*\*  D/C mean: NR  Cutpoint: >844 | logNT-proBNP, NYHA, heart rate, IGF-I, log IGF-I/GH ratio | 18.4m  CV mortality (70, 491) | Multivariable cox regression | NYHA, heart rate, IGF-I, log IGF-I/GH ratio | HR = 9.79 (3.02 - 31.8)  p<0.001 |
| Raposeiras-Roubin,166  2011 | Cohort  Patients with chronic HF | n=106  mean age:  72y  (63, 78.5)\*\*  67.3% male | ADM mean: 2,669.8 (3,274.5)  D/C mean: NR  Cutpoint: NR | NT-proBNP, sRAGE, SHFS, HDL, Hb, creatinine, GFR | 1.3y\*\*  Cardiac mortality  (11, 106) | Multivariable cox regression | sRAGE, SHFS, HDL, Hb, creatinine, GFR | HR=1.039 (1.014 - 1.065) per 100 pg/mL |

| Table J-34. Studies evaluating independent predictive value of NT-proBNP for the outcome of cardiovascular mortality in patients with stable heart failure | | | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Author**  **Year**  **Companion** | **Study Design**  **Population** | **n**  **Mean Age (SD)**  **% male** | **BNP Levels (pg/mL)** | **Prognostic Markers** | **Followup**  **Outcomes**  **(#events, #risk)** | **Model** | **Adjusted/Non-**  **adjusted**  **Covariates** | **Measure(s) of Risk**  **(95% CI,)** |
| Koc,147  2008 | Case series  Patients with LVSD (LVEF <45%) | n=75  mean age:  53.4 (8.8)  67.3% male | ADM mean:  NYHA 1: 266(233)  NYHA 2: 979(841)  NYHA 3: 3,845(2,094)  D/C mean: NR  Cutpoint: NT-proBNP at rest for each 50 pg/mL | NT-proBNP at rest (for each 50 pg/mL), absolute change of NT-proBNP (for each 20 pg/mL), LVEDV (for each 10 mL), LVESV (for each 10 mL) | 750d  Cardiac mortality  (14, 75) | Multivariable logistic regression | Absolute change of NT–BNP (for each 20 pg/mL), LVEDV (for each 10 mL), LVESV (for each 10 mL) | OR=0.912 (0.656-1.269) |
| ADM mean:  NYHA1: 266(233)  NYHA2: 979(841)  NYHA3:  3,845(2,094)  D/C mean: NR  Cutpoint: NT-proBNP at rest for each 20 pg/mL | NT-proBNP at rest (for each 20 pg/mL), absolute change of NT–BNP (for each 20 pg/mL), LVEDV (for each 10 mL), LVESV (for each 10 mL) | 750d  Cardiac mortality  (14, 75) | Multivariable logistic regression | Absolute change of NT–BNP (for each 20 pg/mL), LVEDV (for each 10 mL), LVESV (for each 10 mL) | OR=1.106 (1.022-1.197) |
| Poletti,125  2009 | Cohort  Chronic HF patients with LVSD, EF=31(8)% | n=147  mean age:  64y(12)  80.5% male | ADM mean:  Normal breathing: 448.5(147-1,599)\*\*  Cheyne-Stokes: 2,575(814-3,320)\*\*  D/C mean: NR  Cutpoint: NR | Increased NT-proBNP, daytime CS, age, AF, higher NYHA, EF | 30m\*\*  CV mortality  (17,147) | Multivariable cox regression | Daytime CS, age, AF, higher NYHA, EF | HR=2.98 (1.35-6.56) |
| Tsutamoto,118  2010  Tsutamoto, 2006; 2007 | Cohort  Patients with systolic chronic HF | n=258  mean age:  63.8y(12.8)  78.7% male | ADM mean: 522 (215-1,240)\*\*  D/C mean: NR  Cutpoint: >627 | NT-proBNP, age, NYHA class, ischemic heart disease, LVEDP, LVEF, cTnT, hs-cTnl | 2.6y  Cardiac mortality  (20, 258) | Multivariable cox regression | Age, NYHA class, Ischemic heart disease, LVEDP, LVEF, cTnT, hs-cTnl | HR=4.7 (1.5-14.4) |
| Cleland,122  2009  CORONA | Case series  Secondary analysis of RCT data  Chronic HF patients, ≥60 years, with NYHA II-IV, ischemic etiology, and EF<35-40% | n=3,664  mean age:  T1:70.8y(6.7)  T2: 72.7y(7)  T3:74.5y(7.2)  67.7% male | ADM mean:  T1:47(26-78)\*\* pmol/L  T2:173(133-220)\*\* pmol/L  T3:486(367-776)\*\* pmol/L  D/C mean: NR  Cutpoint: per log unit | logNT-proBNP, age, AF, diabetes, NYHA, claudication, APO A-I, EF, systolic BP/10, creatinine, BMI, heart rate, gender, triglycerides | 32m\*\*  Worsening HF death  (230, 3664) | Multivariable cox proportional hazard regression | Age, AF, diabetes, NYHA, claudication, APO A-I, EF, systolic BP/10, creatinine, BMI, heart rate, gender, triglycerides | HR=1.986 (NR) |
| Wedel,131  2009  CORONA study | Case series  Secondary analysis of RCT data  Chronic HF patients, ≥60 years, with NYHA II-IV, ischemic etiology, and EF<35-40% | n=3,342  mean age:  72.5y(7.1)  75.0% male | ADM mean: 166 (70-358)\*\*  D/C mean: NR  Cutpoint: per log unit | log NT-proBNP, NYHA, intermittent claudication, diabetes, heart rate | 32m\*\*  Death from HF  (230, 3,342) | Multivariable cox proportional hazard regression | NYHA, intermittent claudication, diabetes, heart rate | HR=1.99 (1.71-2.30) |
| 32m\*\*  CV mortality  (725, 3,342) | Multivariable cox proportional hazard regression | NYHA, intermittent claudication, diabetes, heart rate | HR=1.74 (1.60-1.88) |
| Bayes-Genis,156  2007  MUSIC Study | Cohort  Patients with HF referred to specialist HF clinics | n=494  mean age:  63y(11)  78.0% male | ADM mean: NR  D/C mean: NR  Cutpoint: >908 | NT-proBNP, indexed LA size >26mm/m2, history of MI, peripheral edema, DM, Hb, NYHA, AF | 36m  Sudden cardiac death  (50, 494) | Multivariable cox proportional hazard regression | Indexed LA size >26mm/m2, history of MI, peripheral edema, DM, Hb, NYHA, AF | HR=3.1 (1.5 - 6.7) |
| Sherwood,113  2007 | Cohort  HF outpatients, EF of ≤40% | n=204  mean age:  56.8y(12.2)  67.3% male | ADM mean:  1,477 (1,810)  D/C mean: NR  Cutpoint: 1,000 | NT-proBNP, age, HF etiology, LVEF, BDI score, antidepressant | 3y\*\*  CV mortality  (54,204) | Multivariable cox proportional hazard regression | Age, HF etiology, LVEF, BDI score, antidepressant | HR=1.42 (1.42-1.24) |
| Schierbeck,165  2011 | Cohort  HF outpatients, age 18+ | n=148  mean age:  68y(NR)  68.9% male | ADM mean: NR  D/C mean: NR  Cutpoint: NR | logNT-proBNP, PTH upper median, 25 OHD, age, vitamin D insufficiency | 3.5y  Cardiac mortality  (44, 148) | Multivariable cox proportional hazard regression | PTH upper median, 25\_OHD, age, vitamin D insufficiency | HR=NR |
| Vazquez,128  2009 | Cohort  Ambulatory patients with chronic HF, NYHA class II/III | n=992  mean age:  65y(12)  72.4% male | ADM mean: NR  D/C mean: NR  Cutpoint: 1,000 | NT-proBNP>1.000 ng/L, prior AVE, LA size, LVEDD, grade 3/4 MR, LVEF≤35%, restrictive filling pattern, AF, LBBB or IVCD, non-sustained VT and frequent VPBs, eGFR, troponin-positive | 44m\*\*  Cardiac mortality  (213, 992) | Multivariable cox proportional hazard regression | Prior AVE, LA size, LVEDD, grade 3/4 MR, LVEF≤35%, restrictive filling pattern, AF, LBBB or IVCD, non-sustained VT and frequent VPBs, eGFR, troponin-positive | HR=2.15 (1.54-3.01) |
| 44m\*\*  Pump-failure death  (123, 992) | Multivariable cox proportional hazard regression | prior AVE, LA size, LVEDD, grade 3/4 MR, LVEF≤35%, restrictive filling pattern, AF, LBBB or IVCD, non-sustained VT and frequent VPBs, eGFR, troponin-positive | HR=2.87 (1.80-4.57) |
| Hinderliter,137  2008 | Cohort  Patients with clinically stable HF recruited from HF clinics (LVEF ≤40%) | n=211  mean age:  57y(12)  69.0% male | ADM mean:  1 675 (2 657)  D/C mean: NR  Cutpoint: NR | change in NT-proBNP, age, LVEF, LVEDV, deceleration time, MR area, LA volume index, tricuspid annular excursion, TR area, RA volume index | 4y\*\*  Progressive HF mortality  (23, 211) | Multivariable cox proportional hazard regression | Age, LVEF, LVEDV, deceleration time, MR area, LA volume index, tricuspid annular excursion, TR area, RA volume index | HR=NR |
| 4y\*\*  Sudden cardiac death (31, 211) | Multivariable cox proportional hazard regression | Age, LVEF, LVEDV, deceleration time, MR area, LA volume index, tricuspid annular excursion, TR area, RA volume index | HR=NR |
| Kawahara,169  2011 | Cohort  Stable outpatients with non-ischemic chronic HF | n=95  mean age:  62.3y(9.9)  84.2% male | ADM mean: 603.9 (154, 1,257)\*\*  D/C mean: 596.9 (182, 1,006)\*\*  Cutpoint: >711 | Baseline NT-proBNP, discharge NT-proBNP, hs-cTnl, age, NYHA class, creatinine, gender, LVEF | 4.25y\*\*  Cardiac mortality (27, 95) | Multivariable cox proportional hazard regression | Discharge NT-proBNP, hs-cTnl, age, NYHA class, creatinine, gender, LVEF | HR=6.8 (2.2 - 20.9) |
| Nishiyama,119  2009  Tsutamoto, 2008 | Cohort  Patients with systolic chronic HF | n=107  mean age:  63.6y(13)  85.0% male | ADM mean: 600 (233, 1,184)\*\*  D/C mean: NR  Cutpoint: NR | logNT-proBNP, age, sex, NYHA class, ischemic heart disease, LVEDP, LVEF, norepinephrine | 4.3y  Cardiac mortality  (13,107) | Multivariable cox proportional hazard regression | Age, sex, NYHA class, ischemic heart disease, LVEDP, LVEF, norepinephrine | HR=5.3 (1.31–18.02) |
| Broek,168  2011  CHS | Cohort  Community-based subjects with HF (aged ≥65 years) | n=208  mean age:  75.2y(6.1)  49.0% male | ADM mean:  depression=496 (159, 1,632)\*\*  No depression=520 (148, 1,716)\*\*  D/C mean: NR  Cutpoint: >190 | NT-proBNP, age, gender, race, systolic BP, cholesterol, DM, BMI, smoking, reduced physical activity, LVEF, left ventricular hypertrophy, CHD at baseline | 14y  CV mortality  (97, 208) | Multivariable cox proportional hazard regression | Age, gender, race, SBP, cholesterol, DM, BMI, smoking, reduced physical activity, LVEF, left ventricular hypertrophy, CHD at baseline | HR=2.70 (1.47-4.95) |

**Abbreviations:** 25\_OHD = 25-hydroxyvitamin D; AF = atrial fibrillation; ADM = admission; APO A-I = apolipoprotein A1; AVE = atherosclerotic vascular event; BDI = Beck Depression Inventory; BMI = body mass index; BP = blood pressure; CHD = chronic heart disease; 95% CI, = confidence interval; CS = Cheyne-Stokes; cTnT = cardiac troponin T; CT-proET-1 = C-terminal pro-endothelian-1 precursor fragment; CV = cardiovascular; d = day(s); D/C = discharge; DM = diabetes mellitus; EF = ejection fraction; eGFR = estimated glomerular filtration rate; GFR = glomerular filtration rate; GH = growth hormone; Hb = hemoglobin; HDL = high-density lipoprotein; HF = heart failure; HR = hazard ratio; hs-cTnT = high-sensitivity cardiac troponin T; IGF-I = insulin-like growth factor-I; IVCD = intraventricular conduction delay; LA = left atrial; LBBB = left bundle branch block; LVESV = left ventricular end-systolic volume; LVEDD = left ventricular end-diastolic diameter; LVEDP = left ventricular end-diastolic pressure; LVEDV = left ventricular end-diastolic volume; LVEF = left ventricular ejection fraction; LVSD = left ventricular systolic dysfunction; m = month(s); mm/m2 = millimeter per meter squared; MI = myocardial infarction; MR = mitral regurgitation; n=number; ng/L = nanograms per liter; NR = not reported; NT-proBNP = N-terminal pro-B-type natriuretic peptide; NYHA = New York Heart Association; OR = odds ratio; pmol/L = picomol per liter; pg/mL = picograms per milliliter; PTH = parathyroid hormone; RA = right atrial; SD = standard deviation; SHFS = Seattle Heart Failure Score; sRAGE = soluble receptor for advanced glycogen end products; TR = tricuspid regurgitation; VPBs = ventricular premature beats; VT = ventricular tachycardia; y = year(s)