| Table J-34. Studies evaluating independent predictive value of NT-proBNP for the outcome of cardiovascular mortality in patients with stable heart failure  |
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| **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,1632011 | CohortPatients with systolic chronic HF | n=491mean age:63y(11)91.0% male | ADM mean: 875 (347, 2,465)\*\*D/C mean: NRCutpoint: >2,465 | log10NT-proBNP, CT-proET-1 (log), NYHA, LVEF, age, serum creatinine | 12mCV mortality (70, 491) | Multivariable cox regression | CT-proET-1 (log), NYHA, LVEF, age, serum creatinine | HR=3.36 (2.40-4.71) |
| Tziakas,1752012 | CohortPatients with acute decompensation of chronic HF admitted to Coronary Care Unit | n=219mean 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: NRCutpoint: >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 | 12mCV 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,1582007 | CohortChronic HF patients without cachexia referred to institution | n=82mean age:61y(13)74.0% male | ADM mean: 844 (220.2, 2,755.5)\*\*D/C mean: NRCutpoint: per log unit | NT-proBNP, NYHA, heart rate, IGF-I, log IGF-I/GH ratio | 18.4mCV 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 increasep<0.001 |
| ADM mean: 844 (220.2, 2,755.5)\*\*D/C mean: NRCutpoint: >844 | logNT-proBNP, NYHA, heart rate, IGF-I, log IGF-I/GH ratio | 18.4mCV 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,1662011 | CohortPatients with chronic HF | n=106mean age:72y(63, 78.5)\*\*67.3% male | ADM mean: 2,669.8 (3,274.5)D/C mean: NRCutpoint: 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  |
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| **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,1472008 | Case seriesPatients with LVSD (LVEF <45%) | n=75mean 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: NRCutpoint: 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) | 750dCardiac 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: NRCutpoint: 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) | 750dCardiac 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,1252009 | CohortChronic HF patients with LVSD, EF=31(8)% | n=147mean 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: NRCutpoint: 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,1182010Tsutamoto, 2006; 2007 | CohortPatients with systolic chronic HF | n=258mean age:63.8y(12.8)78.7% male | ADM mean: 522 (215-1,240)\*\*D/C mean: NRCutpoint: >627 | NT-proBNP, age, NYHA class, ischemic heart disease, LVEDP, LVEF, cTnT, hs-cTnl | 2.6yCardiac 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,1222009CORONA | Case seriesSecondary analysis of RCT dataChronic HF patients, ≥60 years, with NYHA II-IV, ischemic etiology, and EF<35-40% | n=3,664mean 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/LT2:173(133-220)\*\* pmol/LT3:486(367-776)\*\* pmol/LD/C mean: NRCutpoint: 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,1312009CORONA study | Case seriesSecondary analysis of RCT dataChronic HF patients, ≥60 years, with NYHA II-IV, ischemic etiology, and EF<35-40% | n=3,342mean age:72.5y(7.1)75.0% male | ADM mean: 166 (70-358)\*\*D/C mean: NRCutpoint: 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,1562007MUSIC Study | CohortPatients with HF referred to specialist HF clinics | n=494mean age:63y(11)78.0% male | ADM mean: NRD/C mean: NRCutpoint: >908 | NT-proBNP, indexed LA size >26mm/m2, history of MI, peripheral edema, DM, Hb, NYHA, AF  | 36mSudden 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,1132007 | CohortHF outpatients, EF of ≤40% | n=204mean age:56.8y(12.2)67.3% male | ADM mean:1,477 (1,810)D/C mean: NRCutpoint: 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,1652011 | CohortHF outpatients, age 18+ | n=148mean age:68y(NR)68.9% male | ADM mean: NRD/C mean: NRCutpoint: NR | logNT-proBNP, PTH upper median, 25 OHD, age, vitamin D insufficiency  | 3.5yCardiac mortality(44, 148) | Multivariable cox proportional hazard regression | PTH upper median, 25\_OHD, age, vitamin D insufficiency | HR=NR |
| Vazquez,1282009 | CohortAmbulatory patients with chronic HF, NYHA class II/III | n=992mean age:65y(12)72.4% male | ADM mean: NRD/C mean: NRCutpoint: 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,1372008 | CohortPatients with clinically stable HF recruited from HF clinics (LVEF ≤40%) | n=211mean age:57y(12)69.0% male | ADM mean:1 675 (2 657)D/C mean: NRCutpoint: 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,1692011 | CohortStable outpatients with non-ischemic chronic HF | n=95mean 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,1192009Tsutamoto, 2008 | CohortPatients with systolic chronic HF | n=107mean age:63.6y(13)85.0% male | ADM mean: 600 (233, 1,184)\*\*D/C mean: NRCutpoint: NR | logNT-proBNP, age, sex, NYHA class, ischemic heart disease, LVEDP, LVEF, norepinephrine  | 4.3yCardiac 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,1682011CHS | CohortCommunity-based subjects with HF (aged ≥65 years) | n=208mean age:75.2y(6.1)49.0% male | ADM mean:depression=496 (159, 1,632)\*\*No depression=520 (148, 1,716)\*\*D/C mean: NRCutpoint: >190 | NT-proBNP, age, gender, race, systolic BP, cholesterol, DM, BMI, smoking, reduced physical activity, LVEF, left ventricular hypertrophy, CHD at baseline | 14yCV 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)