| Table J-21. Studies evaluating independent predictive value of NT-proBNP for the composite outcome of all-cause mortality and morbidity – admission and discharge (all time periods) in patients with decompensated heart failure | | | | | | | | |
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| **Author**  **Year** | **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,)** |
| Bettencourt45  2004 | Cohort  Decompensated HF, NT-proBNP change<30% | n=49  mean age:  73.4y (NR)  49.0% males | ADM mean: NR  D/C mean: NR  Cutpoint: NA | NT-proBNP change <30%, NT-proBNP Increase >=30%, Volume overload at D/C | 6m  Death or hospital reADM  (NR) | Multivariable cox regression | Volume overload at D/C | Change <30%: HR=2.03 (1.14-3.64) |
| Cohort  Decompensated HF, NT-proBNP Increase >=30% | n=25  mean age:  74.4y (NR)  44.0% males | ADM mean: NR  D/C mean: NR  Cutpoint: NA | NT-proBNP increase >=30%, NT-proBNP change <30%, volume overload at D/C | 6m  death or hospital reADM  (NR) | Multivariable cox regression | Volume overload at D/C | Increase >35%: HR=5.96 (3.23-11.01) |
| Bettencourt47  2006 | Cohort  Decompensated HF patients | n=224  mean age:  depressed SF=70.7y (12.6)  preserved SF=74.6y (10.5)  48.21% male | ADM mean:  depressed SF= 7,685 (3,664-15,280)\*\*  preserved SF= 4,512 (1,773-9,290)\*\*  D/C mean:  depressed SF= 5,403 (2,160-10,408)\*\*  preserved SF= 2,285 (1,030-4,030)\*\*  Cutpoint: NR | NT-proBNP at D/C, change in NT-proBNP, serum creatinine, Hb | 6m  Composite (death or hospitalizations)  (95, 224) | Multivariable cox regression | Change in NT-proBNP, serum creatinine, Hb | D/C HR=NR |
| Cohort  Cecompensated HF patients with depressed systolic function | n=161  mean age:  70.7y (12.6)  54.0% male | ADM mean: 7,685 (3,664–15,280)\*\*  D/C mean: 5,403 (2,160–10,408)\*\*  Cutpoint: >5,403 | NT-proBNP at D/C, change in NT-proBNP, serum creatinine, Hb | 6m  Composite (death or hospitalizations)  (68, 161) | Multivariable cox regression | Change in NT-proBNP, serum creatinine, Hb | D/C: HR=NS |

| Table J-21. Studies evaluating independent predictive value of NT-proBNP for the composite outcome of all-cause mortality and morbidity - admission and discharge (all time periods) in patients with decompensated heart failure (continued) | | | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Author**  **Year** | **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,)** |
| Bettencourt47  2006  (cont’d) | Cohort  Decompensated HF patients with depressed systolic function, grp 2 vs. grp 1 | n=NR  mean age:  NR  % male: NR | ADM mean: NR  D/C mean: NR  Cutpoint: less than 30 % change from baseline | Change in NT-proBNP, NT-proBNP at D/C, serum creatinine, Hb | 6m  Composite (death or HF hospitalizations or ED visits)  (NR) | Multivariable cox regression | NT-proBNP at D/C, serum creatinine, Hb | Change <30 %: HR=3.88 (0.94, 15.98) |
| Cohort  Decompensated HF patients with depressed systolic function, grp 3 vs. grp 1 | n=NR  mean age:  NR  % male: NR | ADM mean: NR  D/C mean: NR  Cutpoint: More than 30 % increase from baseline | Change in NT-proBNP, NT-proBNP at D/C, serum creatinine, Hb | 6m  Composite (death or hospitalizations)  (NR) | Multivariable cox regression | NT-proBNP at D/C, serum creatinine, Hb | Change >30%: HR=7.79 (2.03, 29.86) |
| Cohort  Decompensated HF patients with preserved systolic function | n=63  mean age:  74.6y (10.5)  33.3% male | ADM mean: 4512 (1,773–9,290)\*\*  D/C mean: 2,285 (1,030–4,030)\*\*  Cutpoint: >2,285 | NT-proBNP at D/C, change in NT-proBNP, serum creatinine, Hb | 6m  Composite (eath or hospitalizations)  (27, 63) | Multivariable cox regression | change in NT-proBNP, gender, preserved, ACE inhibitor | D/C above the median: HR=2.71 (1.49, 4.92) |
| Cohort  Decompensated HF patients with preserved systolic function, grp 2 vs. grp 1 | n=NR  mean age:  NR  % male: NR | ADM mean: NR  D/C mean: NR  Cutpoint: less than 30 % change from baseline | Change in NT-proBNP, NT-proBNP at D/C, gender, preserved, ACE inhibitor | 6m  Composite (death or HF hospitalizations or ED visits)  (NR) | Multivariable cox regression | NT-proBNP at D/C, gender, preserved, ACE inhibitor | D/C: HR= 2.12 (1.17-3.82) |
| Cohort  Decompensated HF patients with preserved systolic function, grp 3 vs. grp 1 | n=NR  mean age:  NR  % male: NR | ADM mean: NR  D/C mean: NR  Cutpoint: More than 30% increase from baseline | Change in NT-proBNP, NT-proBNP at D/C, gender, preserved, ACE inhibitor | 6m  Composite (death or HF hospitalizations or ED visits)  (NR) | Multivariable cox regression | NT-proBNP at D/C, gender, preserved, ACE inhibitor | Change increase 30%: HR=3.18 (1.57-6.46) |
| Ferreira55  2007 | Cohort  Decompensated HF patients | n=304  mean age:  72.7y (11.6)  54% male | ADM mean: 7,006 (2,816-13,788)\*\*  D/C mean: 3,796 (1,618-9,620)\*\*  Cutpoint: >3,796 | NT-proBNP at D/C, age, LVEF, NYHA class, pulse, renal failure, anemia, ACE inhibitors | 6m  Composite  (all-cause mortality or reADM)  (131, 304) | Multivariable cox regression | Age, LVEF, NYHA class, pulse, renal failure, anemia, ACE inhibitors | D/C: HR=2.02 (1.28, 3.2) |
| Cohort  Decompensated HF patients, grp 2 vs. grp 1 | n=257  mean age:  NR  % male: NR | ADM mean: NR  D/C mean: NR  Cutpoint: Decreasing by at least 30% from baseline,grp 1 | Change in NT-proBNP, LVEF, NYHA class, pulse, renal failure, anemia, ACE inhibitors | 6m  Composite  (all-cause mortality or reADM)  (NR) | Multivariable cox regression | Age, LVEF, NYHA class, pulse, renal failure, anemia, ACE inhibitors | Change >30% decrease: HR=2.24 (1.37, 3.66) |
| Cohort  Decompensated HF patients, grp 3 vs. grp 1 | n=209  mean age:  NR  % male: NR | ADM mean: NR  D/C mean: NR  Cutpoint: More than 30% increase from baseline,grp 3 | Change in NT-proBNP, age, LVEF, NYHA class, pulse, renal failure, anemia, ACE inhibitors | 6m  Composite  (all-cause mortality or reADM)  (NR) | Multivariable cox regression | Age, LVEF, NYHA class, pulse, renal failure, anemia, ACE inhibitors | Change increase >30%: HR=3.85 (2.24, 6.63) |
| Siswanto57  2006 | Cohort  Patients hospitalized through the ED with HF | n=97  mean age:  55.2y (10.3)  % males: 53 | ADM mean: 10.283.76 (10210.61)  D/C mean: 6.681.44 (7.64137)  Cutpoint: decrease in NT-proBNP >35% during hospitalization | Decrease in NT-proBNP >35% during hospitalization, BMI, acute lung edema, NYHA class IV, LV wall thickness, not using BB, Hb <12 g/dL, Na <130mmol/L | 6m  Composite (rehospitalization and mortality)  (NR) | Cox proportional hazards | BMI, acute lung edema, NYHA class IV, LV wall thickness, not using BB, Hb<12 g/dL, Na <130mmol/L | Decrease >35%: HR=0.42(0.12-0.76) p=0.010 |
| Pimenta56  2007 | Cohort  Acute HF patients | n=283  mean age:  72.8y (11.7)  48.0% male | ADM mean: NR  D/C mean: NR  Cutpoint: NR | NT-proBNP at D/C, age, sex, Hb, serum Na, LVEF, systolic BP, heart rate, NYHA class | 182d\*\*  Composite  (all-cause mortality or reADM)  (125, 283) | Multivariable cox regression | Age, sex, Hb, serum Na, LVEF, systolic BP, heart rate, NYHA class | D/C: HR=NR |
| Cohort  Acute HF patients with normal eGFR (≥90 mL/min) | n=164  mean age:  70.4y (12.4)  61.58% male | ADM mean: 4,807 (2,089-9,847)\*\*  D/C mean: 2,575 (1,232, 6,454)  Cutpoint: >2,575 | NT-proBNP at D/C above median, age, sex, Hb, serum Na, LVEF, systolic BP, heart rate, NYHA class | 182d\*\*  Composite (all-cause mortality or reADM)  (61, 164) | Multivariable cox regression | Age, sex, Hb, serum Na, LVEF, systolic BP, heart rate, NYHA class | D/C above median: HR=1.64 (0.98, 2.76) |
| Change in NT-proBNP (decrease by 30%), age, sex, Hb, serum Na, LVEF, systolic BP, heart rate, NYHA class | 182d\*\*  Composite (all-cause mortality or reADM)  (61, 164) | Multivariable cox regression | Age, sex, Hb, serum Na, LVEF, systolic BP, heart rate, NYHA class | Change decrease <30%: HR=2.68 (1.54, 4.68) |
| Cohort  Acute HF patients with reduced eGFR (RF) | n=119  mean age:  mild RF= 75.6y (90.9)  moderate RF = 77.9y (8.6)  severe RF= 72.5y (11.9)  27.0% male | ADM mean:  mild RF=10578 (4,538-20,416)\*\*  moderate RF=10,776 (5,342-31,264)\*\*  severe RF=17,789 (10,639-43,691)\*\*  D/C mean:  mild RF=5,512 (2,223-11,002)\*\*  moderate RF=7,504 (4,120-17,592)\*\*  severe RF=25,010 (2,785-37,747)\*\*  Cutpoint: Above median | NT-proBNP at D/C, age, sex, Hb, serum Na, LVEF, systolic BP, heart rate, NYHA class | 182d\*\*  Composite (all-cause mortality or reADM)  (61, 164) | Multivariable cox regression | Age, sex, Hb, serum Na, LVEF, systolic BP, heart rate, NYHA class | D/C above median: HR=2.53 (1.27, 5.03) |
| Pimenta56  2007  (cont’d) | Cohort  Acute HF patients with reduced eGFR (RF) | n=119  mean age:  mild RF=75.6y (90.9)  moderate RF=77.9y (8.6)  severe RF=72.5y (11.9)  % male: 27 | ADM mean:  mild RF=10578 (4538-20416)\*\*  moderate RF=10776 (5342-31264)\*\*  severe RF=17789 (10639-43691)\*\*  D/C mean:  mild RF=5512 (2223-11002)\*\*  moderate RF=7504 (4120-17592)\*\*  severe RF=25010 (2,785-37,747)\*\*  Cutpoint: Above median | Change in NT-proBNP, age, sex, Hb, serum Na, LVEF, systolic BP, heart rate, NYHA class | 182d\*\*  Composite (all-cause mortality or reADM)  (61, 119) | Multivariable cox regression | Age, sex, Hb, serum Na, LVEF, systolic BP, heart rate, NYHA class | Change decrease <30% : HR=2.54 (1.49, 4.33) |
| Carrasco-Sanchez73  2011 | Cohort  Patients admitted with HF and preserved EF (LVEF >45%) | n=218  mean age:  75.6y (8.7)  % male: 39.9 | ADM mean: 3606 (1824-7123)\*\*  D/C mean: NR  Cutpoint: >3606 | NT-proBNP\*, cystatin C, age, creatinine\*, BUN\*, eGFR\*, Hb\*, hyponatraemia, NYHA class\* | 12m  composite (all-cause mortality and reADM)  (126, 218) | Multivariable cox regression and ROC analysis | Cystatin C, age, creatinine\*, BUN\*, eGFR\*, Hb\*, hyponatraemia, NYHA class\* | ADM: HR=NR, p=NS, |
| Michtalik76  2011 | Cohort  Patients With HF | n=217  mean age:  63.3y (14.4)  % male: 50 | ADM mean: 5913 (1831-10989)\*\*  D/C mean: NR  Cutpoint: >50 % change | NT-proBNP, age, gender, race, and ADM creatinine level, LVEF, length of ADM | 12m  Composite (all-cause mortality or hospital ADM)  (134, 217) | Multivariable cox regression | Age, gender, race, and ADM creatinine level, LVEF, length of ADM | Change >50%: HR=1.54 (1.05, 2.27) |

**Abbreviations:** ACE = angiotensin converting enzyme; ADM = admission; BMI = body mass index; BNP = B-type natriuretic peptide; BP = blood pressure; BUN=blood urea nitrogen; CA125 = carbohydrate antigen 125; 95% CI, = confidence interval; CMP = cardiomyopathy; CRP = C-reactive protein; CV = cardiovascular; d = day(s); D/C = discharge; DM = diabetes mellitus; ED = emergency department; EF = ejection fraction; eGFR = estimated glomerular filtration rate; GFR = glomerular filtration rate; grp = group; Hb = hemoglobin; HF = heart failure; HR = hazard ratio; HT = hypertension; ICU = intensive care unit; IL-6=interleukin-6; ln=natural log; LV = left ventricular; LVEF = left ventricular ejection fraction; m = month(s); mL/min=milliliters per minute; MI = myocardial infarction; n=number; Na = sodium; NR = not reported; NS = non-significant; NT-proBNP = N-terminal pro-B-type natriuretic peptide; NYHA = New York Heart Association; OR = odds ratio; pg/mL = picograms per milliliter; RF = renal failure; ROC = receiver operating characteristic; RR = relative risk; SD = standard deviation; vs. = versus; y = year(s)