| 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,)** |
| Bettencourt452004  | CohortDecompensated HF, NT-proBNP change<30% | n=49mean age:73.4y (NR)49.0% males  | ADM mean: NRD/C mean: NRCutpoint: NA | NT-proBNP change <30%, NT-proBNP Increase >=30%, Volume overload at D/C | 6mDeath or hospital reADM(NR) | Multivariable cox regression | Volume overload at D/C | Change <30%: HR=2.03 (1.14-3.64) |
| CohortDecompensated HF, NT-proBNP Increase >=30% | n=25mean age:74.4y (NR)44.0% males  | ADM mean: NRD/C mean: NRCutpoint: NA | NT-proBNP increase >=30%, NT-proBNP change <30%, volume overload at D/C | 6mdeath or hospital reADM(NR) | Multivariable cox regression | Volume overload at D/C | Increase >35%: HR=5.96 (3.23-11.01) |
| Bettencourt472006  | CohortDecompensated HF patients | n=224mean 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  | 6mComposite (death or hospitalizations)(95, 224) | Multivariable cox regression | Change in NT-proBNP, serum creatinine, Hb | D/C HR=NR  |
| CohortCecompensated HF patients with depressed systolic function | n=161mean 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  | 6mComposite (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) |
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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,)** |
| Bettencourt472006(cont’d)   | CohortDecompensated HF patients with depressed systolic function, grp 2 vs. grp 1  | n=NRmean age:NR% male: NR | ADM mean: NRD/C mean: NRCutpoint: less than 30 % change from baseline | Change in NT-proBNP, NT-proBNP at D/C, serum creatinine, Hb  | 6mComposite (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) |
| CohortDecompensated HF patients with depressed systolic function, grp 3 vs. grp 1  | n=NRmean age:NR% male: NR | ADM mean: NRD/C mean: NRCutpoint: More than 30 % increase from baseline | Change in NT-proBNP, NT-proBNP at D/C, serum creatinine, Hb  | 6mComposite (death or hospitalizations)(NR) | Multivariable cox regression | NT-proBNP at D/C, serum creatinine, Hb  | Change >30%: HR=7.79 (2.03, 29.86) |
| CohortDecompensated HF patients with preserved systolic function | n=63mean 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 | 6mComposite (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) |
| CohortDecompensated HF patients with preserved systolic function, grp 2 vs. grp 1  | n=NRmean age:NR% male: NR | ADM mean: NRD/C mean: NRCutpoint: less than 30 % change from baseline | Change in NT-proBNP, NT-proBNP at D/C, gender, preserved, ACE inhibitor  | 6mComposite (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) |
| CohortDecompensated HF patients with preserved systolic function, grp 3 vs. grp 1  | n=NRmean age:NR% male: NR | ADM mean: NRD/C mean: NRCutpoint: More than 30% increase from baseline | Change in NT-proBNP, NT-proBNP at D/C, gender, preserved, ACE inhibitor  | 6mComposite (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) |
| Ferreira552007  | CohortDecompensated HF patients | n=304mean 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 | 6mComposite(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) |
| CohortDecompensated HF patients, grp 2 vs. grp 1  | n=257mean age:NR% male: NR | ADM mean: NRD/C mean: NRCutpoint: Decreasing by at least 30% from baseline,grp 1 | Change in NT-proBNP, LVEF, NYHA class, pulse, renal failure, anemia, ACE inhibitors | 6mComposite(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) |
| CohortDecompensated HF patients, grp 3 vs. grp 1  | n=209mean age:NR% male: NR | ADM mean: NRD/C mean: NRCutpoint: More than 30% increase from baseline,grp 3 | Change in NT-proBNP, age, LVEF, NYHA class, pulse, renal failure, anemia, ACE inhibitors | 6mComposite(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) |
| Siswanto572006 | CohortPatients hospitalized through the ED with HF | n=97mean 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  | 6mComposite (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 |
| Pimenta562007  | CohortAcute HF patients | n=283mean age:72.8y (11.7)48.0% male  | ADM mean: NRD/C mean: NRCutpoint: 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 |
| CohortAcute HF patients with normal eGFR (≥90 mL/min) | n=164mean 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) |
| CohortAcute HF patients with reduced eGFR (RF)  | n=119mean 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) |
| Pimenta562007(cont’d) | CohortAcute HF patients with reduced eGFR (RF)  | n=119mean 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-Sanchez732011  | CohortPatients admitted with HF and preserved EF (LVEF >45%) | n=218mean age:75.6y (8.7)% male: 39.9 | ADM mean: 3606 (1824-7123)\*\*D/C mean: NRCutpoint: >3606 | NT-proBNP\*, cystatin C, age, creatinine\*, BUN\*, eGFR\*, Hb\*, hyponatraemia, NYHA class\* | 12mcomposite (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, |
| Michtalik762011 | CohortPatients With HF | n=217mean age:63.3y (14.4)% male: 50 | ADM mean: 5913 (1831-10989)\*\*D/C mean: NRCutpoint: >50 % change  | NT-proBNP, age, gender, race, and ADM creatinine level, LVEF, length of ADM | 12mComposite (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)