| Table J-10. Studies evaluating independent predictive value of BNP for the composite outcome of all-cause mortality and cardiovascular morbidity |
| --- |
| **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,)** |
| Maisel362011 | CohortAcute HF patients admitted for decompensation | n=186,mean age:67y (13.2)98.6 % male  | ADM mean:with events= 837 (500–1,465)\*\*no events= 672 (359–1,350)\*\*D/C mean:with events= 585 (375–1,380)\*\*no events= 84 (172–818)\*\*Cutpoint: per log unit | logBNP, NGAL, eGFR | 1m (30d)composite (all-cause mortality and HF hospitalization)(29, 186) | Multivariable cox regression | NGAL, eGFR | ADM: HR=2.47 (0.99, 6.14), p=0.052 |
| ADM mean:with events= 837 (500–1,465)\*\*no events= 672 (359–1,350)\*\*D/C mean:with events= 585 (375–1,380)\*\*no events= 84 (172–818)\*\*Cutpoint: per log unit | logBNP, NGAL, creatinine | 1m (30d)composite (all-cause mortality and HF hospitalization)(29, 186) | Multivariable cox regression | NGAL, creatinine | ADM: HR=2.327 (0.934, 5.795), p=0.07 |
| Pimenta292010 | CohortPatients admitted for acute HF | n=163,mean age:73y (61-80)\*\*70.0% male  | ADM mean: 1,129.90 (681.35 - 2,094.50)\*\*D/C mean: 659.30 (253 – 1,474)\*\*Cutpoint: per 10 pg/mL | BNP (D/C), albumin, serum Na, renal failure, stroke index, thoracic fluid content, age, NYHA class, LVEF, hemoglobin | 2mComposite (all-cause mortality and HF hospitalization)(45, 163) | Multivariable cox regression | Albumin, serum Na, renal failure, stroke index, thoracic fluid content, age, NYHA class, LVEF, Hb | D/C: HR=1.002 (1.001, 1.004) per 10 pg/mL |
| Maisel12004 REDHOT study | CohortPatients presenting in ED with CHF | n=464mean age:64y (51-76)\*\*53.9% male  | ADM mean: 766D/C mean: 976Cutpoint: 200 | logBNP, NYHA, ED disposition (initial intent, actual disposition) | 90 daysComposite (mortality or cardiac-related reADM or ED visit)(129, 452) | Multivariable logistic regression  | NYHA, ED disposition (initial intent, actual disposition) | logOR=0.708 (SE=0.254), OR=2.030 |

| Table J-10. Studies evaluating independent predictive value of BNP for the composite outcome of all-cause mortality and cardiovascular morbidity (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,)** |
| Xue302011 | CohortAcute HF patients admitted for decompensation | n=144mean age:67y (13.2)98.6 % male  | ADM mean: NRD/C mean: NRCutpoint: >360 | BNP (D/C), cTnI, BUN, history of MI, cardiac murmurs, chronic renal insufficiency, pleural effusions on X-ray, cardiomegaly on X-ray | 3m (90d)composite (all-cause mortality and HF hospitalization)(38, 144) | Multivariable cox regression | cTnI, BUN, history of MI, cardiac murmurs, chronic renal insufficiency, pleural effusions on X-ray, cardiomegaly on X-ray | D/C: HR=1.8 (p=0.12) |
| ADM mean: NRD/C mean: NRCutpoint: per unit increase | BNP (D/C), troponin I, Tnl, Blood urea nitrogen, History of MI, cardiac murmurs, Chronic renal insufficiency, Pleural effusions on X-ray, Cardiomegaly on X-ray | 3m (90 days)Composite (all-cause mortality and HF hospitalization)(38, 144) | Multivariable cox regression | troponin I, Tnl, Blood urea nitrogen, History of MI, cardiac murmurs, Chronic renal insufficiency, Pleural effusions on X-ray, Cardiomegaly on X-ray | D/C: HR=2.066 (p=0.051) |
| Aspromonte32007 | CohortAmbulatory patients with CHF and diabetes | n=145mean age:72y (9)60.0% male  | ADM mean: NRD/C mean: 186\*\* (75-348)Cutpoint: NR | D/C BNP, LVEF, NYHA, creatinine, restrictive pattern, age, AF, ischemic etiology | 6mComposite (all-cause mortality or HF reADM)(41, 145) | Multivariable cox regression | LVEF, NYHA, creatinine, restrictive pattern, age, AF, ischemic etiology | D/C: HR=NR |
| BNP, 201-499 vs. BNP ≤200 | n=118,mean age:NR% male: NR | ADM mean: NRD/C mean: NRCutpoint: 201-499 | D/C BNP, LVEF, NYHA, creatinine, restrictive pattern\* | 6mComposite (all-cause mortality or HF reADM)(NR) | Multivariable cox regression | LVEF, NYHA, creatinine, restrictive pattern, age, AF, ischemic etiology | D/C: HR=3.82 (1.1379-12.8339) |
| BNP ≥500 vs. BNP ≤200 | n=102mean age:NR% male: NR | ADM mean: NRD/C mean: NRCutpoint: ≥ 500 | D/C BNP, LVEF, NYHA, creatinine, restrictive pattern | 6mComposite (all-cause mortality or HF reADM) (NR) | Multivariable cox regression | LVEF, NYHA, creatinine, restrictive pattern | D/C: HR=7.7 (2.2192-26.7696) |
| Faggiano142010 | CohortPatients with acute worsening of chronic HF | n=150mean age:69y (12)100% male  | ADM mean: 1,000 (684)D/C mean: NRCutpoint: ≥250 | BNP at D/C, age, sex, LVEF, NYHA class, creatinine, restrictive pattern | 6mComposite (all-cause mortality and HF hospitalization)(59, 150) | Multivariable cox regression | Age, sex, LVEF, NYHA class, creatinine, restrictive pattern | D/C: HR=4.5 (2.0, 10.3) |
| Feola222008  | CohortCHF patients enrolled at hospital D/C after an acute decompensation | n=250mean age:73y (12)66.0% male  | ADM mean: NRD/C mean: 643 (566)Cutpoint: per unit increase | BNP (D/C), age, serum creatinine, NYHA class, LVEF, DT, AF, ischemic etiology | 6mComposite (all-cause mortality and HF hospitalization)(141, 250) | Multivariable cox regression | Age, serum creatinine, NYHA class, LVEF, DT, AF, ischemic etiology | D/C: HR=1.0006 (1.0004, 1.0009) per unit increase, p<0.00001 |
| Valle242008 | CohortPatients admitted for HF | n=166mean age:77y (9)48.0% male  | ADM mean: 764D/C mean: 456Cutpoint: 250 | D/C BNP, LVEF, age\*, NYHA\*, restrictive mitral pattern\*, creatinine | 6mMortality and HF reADM(60, 166) | Multivariable cox regression | Age, NYHA, restrictive mitral pattern\*, creatinine | D/C: HR=0.2717 (0.1412, 0.5227) P=0.0001 |
| Valle262008 | CohortPatients admitted for acute HF | n=186,mean age:77y (10)50.0% male  | ADM mean: 716 (567)D/C mean: 404 (607)Cutpoint: >250 | BNP (D/C), restrictive mitral pattern, age, serum creatinine, NYHA class, LVEF, serum creatinine | 6mComposite (all-cause mortality and HF hospitalization)(65, 186) | Multivariable cox regression | Restrictive mitral pattern, age, serum creatinine, NYHA class, LVEF, serum creatinine | D/C HR=3.2 (1.6, 5.8), p=0.004 |
| Farmakis152010 | Non-randomizedPatients with acutely decompensated chronic HF  | n=98mean age:64y (10)90.8% male  | ADM mean:Levosimendan grp=1,043 (644)standard therapy grp=919 (605)D/C mean: NRCutpoint: NR | BNP, systolic BP, serum Na, NYHA class, LVEF, age | 6mComposite (all-cause mortality and HF re-hospitalization)(88, 98) | Multivariable cox regression | Systolic BP, serum Na, NYHA class, LVEF, age | ADM: OR=NS |
| Farmakis152010(cont’d) | Non-randomizedPatients with acutely decompensated chronic HF treated with Levosimendan | n=69mean age:65y (9)93.0% male  | ADM mean: 1,043 (644)D/C mean: NRCutpoint: <58% change | Change in BNP, systolic BP, serum Na, NYHA class, LVEF, age | 6mComposite (all-cause mortality and HF re-hospitalization)(62, 69) | Multivariable cox regression | Systolic BP, serum Na, NYHA class, LVEF, age | Change <58%: OR=0.970 (0.954, 0.986), p<0.001 |
| Logeart22004 | CohortDecompensated patients with chronic HF | n=114mean age:69.4y (14.4)44.0% male | ADM mean: 1,015 (604)D/C mean: 457 (451)Cutpoint: per unit increase | BNP (preD/C), % change in BNP level, age, gender, LVEF, ischemic etiology, use of inotropes  | 6mAll-cause mortality or chronic HF rehospitalization(51, 114) | Multivariable cox regression | % change in BNP level, age, gender, LVEF, ischemic etiology, use of inotropes  | D/C: HR=1.14(1.02, 1.28) per unit increase |
| BNP (preD/C), % change in BNP level, age, gender, LVEF, ischemic etiology, use of inotropes  | 6m1m mortality or chronic HF rehospitalization(15, 114) | Multivariable cox regression | % change in BNP level, age, gender, LVEF, ischemic etiology, use of inotropes  | D/C: HR=1.17 (1.06 to 1.28), per unit increase |
| BNP (preD/C), % change in BNP level, age, gender, LVEF, ischemic etiology, use of inotropes  | 6mAll-cause mortality or chronic HF rehospitalization(39, 114) | Multivariable cox regression | % change in BNP level, age, gender, LVEF, ischemic etiology, use of inotropes  | D/C: HR=1.25 (1.16to 1.34) per unit increase |
| Logeart22004(cont’d) | CohortDecompensated patients with chronic HF  | n=223,mean age:derivation Cohort= 69.4y (14.4)validation Cohort= 70.9y (13.3)43.5% male  | ADM mean:derivation cohort= 1,015 (604)validation cohort= 941 (526)D/C mean:derivation cohort= 457 (451)validation cohort= 441 (501)Cutpoint: >350 (subgroup) | BNP (preD/C), % change in BNP level, age, gender, LVEF, ischemic etiology, use of inotropes  | 6mAll-cause mortality or chronic HF rehospitalization(86, 223) | Multivariable cox regression | % change in BNP level, age, gender, LVEF, ischemic etiology, use of inotropes  | D/C: HR=5.1 (2.8, 9.1) |
| BNP (preD/C), % change in BNP level, age, gender, LVEF, ischemic etiology, use of inotropes  | 6mAll-cause mortality or chronic HF rehospitalization(86, 223) | Multivariable cox regression | % change in BNP level, age, gender, LVEF, ischemic etiology, use of inotropes  | D/C: HR=15.2 (8.5 to 27) |
| Parissis182009 | CohortPatients hospitalized due to chronic HF | n=300mean age:65y (12)83.0% male  | ADM mean:depression=735 (737)no depression=455 (334)D/C mean: NRCutpoint: 290 | BNP, age, sex, NYHA class, 6MWT, LVEF, sIAM-1, IL-6, IL-10, TN factor-α | 12mComposite (All-cause mortality and HF hospitalization)(NR, 300) | Multivariable logistic regression | Age, sex, NYHA class, 6MWT, LVEF, sIAM-1, IL-6, IL-10, TN factor-α | OR=NR |
| Dhaliwal202009 | CohortPatients with decompensated HF  | n=203mean age:67.2y (10.7)99.0% male  | ADM mean: 1,107.3 (868.4)D/C mean: 646.6 (674.3)Cutpoint: Tertiles  | BNP (F/U=last available measurement in hospital or 30d from D/C), age, race, BB, LVEF, prior HF hospitalization, NYHA class, presence of renal insufficiency, ACE inhibitor or ARB,  | 392d\*\*Composite (all-cause mortality and HF hospitalization)(126, 203) | Multivariable cox regression | Age, race, LVEF, history of prior HF hospitalization, presence of renal insufficiency, BB, ACE inhibitor or ARB, and NYHA class | Post ADM up to 30d post D/C: HR=1.4 (1.1, 1.8), p=0.003 |
| ADM mean: 1,107.3 (868.4)D/C mean: 646.6 (674.3)Cutpoint: % reduction in BNP | BNP (% reduction), age, race, LVEF, BB, prior HF hospitalization, NYHA class, presence of renal insufficiency, ACE inhibitor or ARB,  | 392d\*\*Composite (all-cause mortality and HF hospitalization)(126, 203) | Multivariable cox regression | Age, race, LVEF, history of prior HF hospitalization, presence of renal insufficiency, BB, ACE inhibitor or ARB, and NYHA class | Change % reduction: HR=0.7 (0.6, 0.9),p= 0.006 |
|  |   |   | ADM mean: 1,107.3 (868.4)D/C mean: 646.6 (674.3)Cutpoint: % reduction in BNP | BNP (% reduction), age, race, LVEF, BB, prior HF hospitalization, presence of renal insufficiency, ACE inhibitor or ARB, NYHA class | 392d\*\*Composite (all-cause mortality and HF hospitalization)(126, 203) | Multivariable cox regression | Age, race, LVEF, history of prior HF hospitalization, presence of renal insufficiency, BB, ACE inhibitor or ARB, and NYHA class | Change % reduction: HR=0.7 (0.6, 0.9),p= 0.006 |
| Stoiser42006 | CohortPatients diagnosed with chronic HF admitted to hospital | n=268mean age:71y (13)67.0% male  | ADM mean: 699 (811)D/C mean: NRCutpoint: 448 | D/C BNP, copeptin, age, history of diabetes, HT, CAD, kidney dysfunction\*, gender | 24mComposite (mortality or chronic HF reADM)(145, 268) | Multivariable cox regression | Age, history of diabetes, HT, CAD, kidney dysfunction\*, gender | D/C: Chi-square 4.9, p=0.0002 |

Abbreviations: 6MWT = 6 minute walk test; ACE = angiotensin converting enzyme; ADM = admission; AF = atrial fibrillation; ARB = angiotensin receptor blockers; BNP = B-type natriuretic peptide; BUN=blood urea nitrogen; CAD = coronary artery disease; CHF = congestive heart failure; 95% CI, = confidence interval; cTnI = cardiac troponin I;d = day(s); D/C = discharge; DT=deceleration time; ED = emergency department; eGFR = estimated glomerular filtration rate; grp = group; Hb = hemoglobin; HF = heart failure; HR = hazard ratio; HT = hypertension; IL-6=interleukin-6; IL-10=interleukin-10; LVEF = left ventricular ejection fraction; m = month(s); MI = myocardial infarction; n=number; Na = sodium; NGAL-neutral gelatinase-associated lipocalin; NR = not reported; NS = non-significant; NYHA = New York Heart Association; OR = odds ratio; pg/mL = picograms per milliliter; RR = relative risk; SD = standard deviation; sIAM-1=soluble intercellular adhesion molecule-1; TN factor-α = tumor necrosis factor-alpha; vs. = versus; w = week(s); y = year(s)