| 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,)** |
| Maisel36  2011 | Cohort  Acute 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 |
| Pimenta29  2010 | Cohort  Patients 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 | 2m  Composite (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 |
| Maisel1  2004  REDHOT study | Cohort  Patients presenting in ED with CHF | n=464  mean age:  64y (51-76)\*\*  53.9% male | ADM mean: 766  D/C mean: 976  Cutpoint: 200 | logBNP, NYHA, ED disposition (initial intent, actual disposition) | 90 days  Composite (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,)** |
| Xue30  2011 | Cohort  Acute HF patients admitted for decompensation | n=144  mean age:  67y (13.2)  98.6 % male | ADM mean: NR  D/C mean: NR  Cutpoint: >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: NR  D/C mean: NR  Cutpoint: 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) |
| Aspromonte3  2007 | Cohort  Ambulatory patients with CHF and diabetes | n=145  mean age:  72y (9)  60.0% male | ADM mean: NR  D/C mean: 186\*\* (75-348)  Cutpoint: NR | D/C BNP, LVEF, NYHA, creatinine, restrictive pattern, age, AF, ischemic etiology | 6m  Composite (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: NR  D/C mean: NR  Cutpoint: 201-499 | D/C BNP, LVEF, NYHA, creatinine, restrictive pattern\* | 6m  Composite (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=102  mean age:  NR  % male: NR | ADM mean: NR  D/C mean: NR  Cutpoint: ≥ 500 | D/C BNP, LVEF, NYHA, creatinine, restrictive pattern | 6m  Composite (all-cause mortality or HF reADM) (NR) | Multivariable cox regression | LVEF, NYHA, creatinine, restrictive pattern | D/C: HR=7.7 (2.2192-26.7696) |
| Faggiano14  2010 | Cohort  Patients with acute worsening of chronic HF | n=150  mean age:  69y (12)  100% male | ADM mean: 1,000 (684)  D/C mean: NR  Cutpoint: ≥250 | BNP at D/C, age, sex, LVEF, NYHA class, creatinine, restrictive pattern | 6m  Composite (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) |
| Feola22  2008 | Cohort  CHF patients enrolled at hospital D/C after an acute decompensation | n=250  mean age:  73y (12)  66.0% male | ADM mean: NR  D/C mean: 643 (566)  Cutpoint: per unit increase | BNP (D/C), age, serum creatinine, NYHA class, LVEF, DT, AF, ischemic etiology | 6m  Composite (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 |
| Valle24  2008 | Cohort  Patients admitted for HF | n=166  mean age:  77y (9)  48.0% male | ADM mean: 764  D/C mean: 456  Cutpoint: 250 | D/C BNP, LVEF, age\*, NYHA\*, restrictive mitral pattern\*, creatinine | 6m  Mortality 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 |
| Valle26  2008 | Cohort  Patients 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 | 6m  Composite (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 |
| Farmakis15  2010 | Non-randomized  Patients with acutely decompensated chronic HF | n=98  mean age:  64y (10)  90.8% male | ADM mean:  Levosimendan grp=1,043 (644)  standard therapy grp=919 (605)  D/C mean: NR  Cutpoint: NR | BNP, systolic BP, serum Na, NYHA class, LVEF, age | 6m  Composite (all-cause mortality and HF re-hospitalization)  (88, 98) | Multivariable cox regression | Systolic BP, serum Na, NYHA class, LVEF, age | ADM: OR=NS |
| Farmakis15  2010  (cont’d) | Non-randomized  Patients with acutely decompensated chronic HF treated with Levosimendan | n=69  mean age:  65y (9)  93.0% male | ADM mean: 1,043 (644)  D/C mean: NR  Cutpoint: <58% change | Change in BNP, systolic BP, serum Na, NYHA class, LVEF, age | 6m  Composite (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 |
| Logeart2  2004 | Cohort  Decompensated patients with chronic HF | n=114  mean 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 | 6m  All-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 | 6m  1m 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 | 6m  All-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 (1.16  to 1.34) per unit increase |
| Logeart2  2004  (cont’d) | Cohort  Decompensated 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 | 6m  All-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 | 6m  All-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) |
| Parissis18  2009 | Cohort  Patients hospitalized due to chronic HF | n=300  mean age:  65y (12)  83.0% male | ADM mean:  depression=735 (737)  no depression=455 (334)  D/C mean: NR  Cutpoint: 290 | BNP, age, sex, NYHA class, 6MWT, LVEF, sIAM-1, IL-6, IL-10, TN factor-α | 12m  Composite (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 |
| Dhaliwal20  2009 | Cohort  Patients with decompensated HF | n=203  mean 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 |
| Stoiser4  2006 | Cohort  Patients diagnosed with chronic HF admitted to hospital | n=268  mean age:  71y (13)  67.0% male | ADM mean: 699 (811)  D/C mean: NR  Cutpoint: 448 | D/C BNP, copeptin, age, history of diabetes, HT, CAD, kidney dysfunction\*, gender | 24m  Composite (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)