Supplemental Digital Content 1

Methods:

<u>Rule Set for Classifying Heart Failure Death</u>

- a. If IMMEDIATE cause of death is due to heart failure or congestive heart failure, then = HEART FAILURE DEATH
- b. If IMMEDIATE cause of death is Respiratory Failure and secondary cause of death is heart failure, congestive heart failure, diastolic heart failure, systolic heart failure, or pulmonary edema then = HEART FAILURE DEATH
- c. If IMMEDIATE cause of death is an arrhythmia or "cardiac arrest," with secondary cause of death listed as heart failure (all kinds systolic, diastolic, congestive), cardiomyopathy (dilated, hypertrophic, idiopathic, etcetera), then = HEART FAILURE DEATH
- d. If IMMEDIATE cause is multisystem organ failure and secondary cause is heart failure without other precipitating factor such as sepsis/infection/postoperative state, could be HEART FAILURE DEATH, but not if seems sepsis/infection of inflammatory postoperative state is the precipitating cause of multisystem organ failure.
- e. If IMMEDIATE cause of death is any kind of cardiovascular/hemodynamic "collapse" or cardiac arrest with the secondary contributing cause being sepsis/infection, then NOT HEART FAILURE DEATH
- f. If IMMEDIATE cause of death is infection (i.e. pneumonia or influenza) and secondary cause of death is heart failure, then NOT HEART FAILURE DEATH

Rule Set for Classifying Heart Failure Hospitalizations

All subject questionnaire responses as of 5/7/2009 were reviewed for hospitalizations during the 5 years after coronary artery bypass graft surgery. Any overnight hospitalization that involved pulmonary problems, hemodynamic instability (including syncope and aortic dissection), chest pain, myocardial infarction, heart failure, arrhythmia, need for implantable cardioverter-defibrillator or pacemaker implant or replacement was noted and the discharge summaries and other hospital records such as chest x-rays, echocardiogram reports, electrocardiogram reports, and laboratories for these hospitalizations were obtained from respective hospitals. If reason for hospitalization was unknown or uncertain, then hospital records were obtained for these admissions as well.

We did not pursue obtaining hospital records for clearly non-cardiac overnight hospitalizations such as those for knee replacements, gallbladder surgery or complications from cancer.

Classifying Heart Failure Hospitalizations:

- If discharge summary states that the subject developed pulmonary edema, or was admitted for diuresis, or was admitted for heart failure (congestive, diastolic, dilated), then = HEART FAILURE HOSPITALIZATION
- 2. If the subject was admitted for placement of a biventricular pacemaker or an ICD upgrade to a biventricular pacemaker, then = HEART FAILURE HOSPITALIZATION
- If chest x-ray revealed pulmonary edema during admission, then = HEART FAILURE HOSPITALIZATION
- 4. If patient develops pulmonary edema in the setting of renal failure, still = HEART FAILURE HOSPITALIZATION

If patient develops pulmonary edema in the setting of acute coronary syndrome or arrhythmia, then still = HEART FAILURE HOSPITALIZATION

 Table 1: Multivariable Clinical Cox Proportional Hazards Regression Model of Time to Heart Failure Hospitalization or Mortality after

 Primary Coronary Artery Bypass Graft Surgery.*

Demographic and Perioperative Clinical Variables	Hazard Ratio (95% CI)	P value
$n=947^{\dagger}$; 99 subjects with heart failure events		
AIC = 1196.90		
Age ≥ 65 years	1.77 (1.13, 2.77)	0.01
Gender (female)	1.69 (1.09, 2.63)	0.02
Institution	1.89 (0.85, 4.17)	0.12
Preoperative left ventricular ejection fraction (per 1% increase)	0.980 (0.964, 0.996)	0.02
Diabetes mellitus	1.76 (1.17, 2.63)	0.006
> 30 pack year history of smoking	1.99 (1.30, 3.03)	0.002
Past arrhythmia	3.09 (1.92, 4.98)	< 0.001
Preoperative anemia	1.99 (1.29, 3.08)	0.002
Preoperative diuretic	1.89 (1.24, 2.90)	0.003
Postoperative ventricular dysfunction	1.73 (1.05, 2.87)	0.03
Postoperative creatinine clearance $< 30 \text{ mL/min}/1.73 \text{m}^2$	3.14 (1.63, 6.02)	<0.001

* Multivariable clinical model includes demographic and clinical risk factors and was created before incorporating BNP into the model.

[†]78 subjects missing one or more of the model's variables are not included in the multivariable analysis

AIC = Akaike information criterion; BNP = B-type natriuretic peptide; CI = Confidence interval

Clinical Variables	Mean or Proportion
Age ≥ 65 years	77 (66.7%)
Female gender	32 (30.5%)
Ethnicity (minority)	14 (13.3%)
Obesity (BMI >30 kg/m ²)	49 (46.7%)
Diabetes mellitus	50 (47.6%)
Hypertension	89 (84.8%)
Hypercholesterolemia	77 (73.3%)
Smoking, >30 pack year history (n=101)	45 (44.6%)
Preoperative creatinine clearance (mL/min/1.73m ²)	63.6 (SD: 21.1)
Myocardial infarction ≤2 weeks preoperatively	27 (25.7%)
Left ventricular ejection fraction (%) (n=102)	47 (SD: 14)
Coronary artery regions with >50% stenosis	

 Table 2: Clinical and Surgical Characteristics of the 105 Primary CABG Subjects Who Experienced Postoperative HF Events

0-1 Region	8 (7.6%)
2 regions	37 (35.2%)
3 regions	60 (57.2%)
Mitral insufficiency (moderate or severe; n=101)	7 (6.9%)
History of preoperative arrhythmia treatment	24 (22.9%)
Anemia (n=104)	64 (61.5%)
Preoperative cTnI >0.1µg/L	19 (18.1%)
ACE-inhibitor	59 (56.2%)
Diuretic	44 (41.9%)
Statin	86 (81.9%)
Digoxin	6 (5.7%)
Beta blocker	87 (82.9%)
Calcium channel blocker	22 (21.0%)
Aspirin	76 (72.4%)
Non-aspirin platelet inhibitor	29 (27.6%)
Nitroglycerin intravenous	10 (9.5%)

Heparin intravenous	37 (35.2%)
Urgent surgery	72 (68.6%)
Cardiopulmonary bypass time >120 minutes	23 (21.9%)
Number of coronary grafts (n=104)	
<3 grafts	20 (19.2%)
3 grafts	54 (51.9%)
>3 grafts	30 (28.9%)
Ventricular dysfunction*	26 (24.8%)
New onset atrial fibrillation	44 (41.9%)
Postoperative creatinine clearance (mL/min/1.73m ²)	54.8 (SD: 22.5)
Postoperative creatinine clearance <30 mL/min/1.73m ²	13 (12.4%)
Peak postoperative cTnI (µg/L)	5.64 (SD: 12.31)

Data are shown as n (%) for categorical variables and mean \pm standard deviation for continuous variables.

* defined as new postoperative need for ≥ 2 inotropes or an intra-aortic balloon pump

ACE = angiotensin converting enzyme; BMI = body mass index; CABG = coronary artery bypass graft; cTnI = cardiac troponin I;

HF = heart failure; SD = standard deviation