Prognostic variables in heart failure
- Risk stratification -

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Risk stratification

? Why

? When

? How

Role of the Cardiologists in HF Evaluation

- ?Why -

- Confirm or dispute the diagnosis
- Rule out treatable causes
- Ensure that patient is on appropriate evidence-based therapy

- **Provide better information for patients and their families to help them appropriately plan for their futures**

- **Identifies patients in whom cardiac transplantation or mechanical device therapy should be considered**

?When

- Acute stage
  - Guide immediate decision
- Chronic stable stage
  - Predict destabilization and death

- Evaluation point
  - At initial presentation
  - After maximal treatment

?How

- Clinical variables
- Chest X-ray, ECG, Echo
- Functional findings
- Blood
- Hemodynamic findings

Myocardial damage vs Compensation
Causes vs Results

- ?Genomics and Proteomics

How to obtain the prognostic variables?

- HF trials
- Patients referred for transplantation
- Registries

Acute Decompensated HF

ADHERE

(Acute Decompensated Heart Failure Registry)

	Derivation cohort (n=33046)	Validation cohort (n=32229)
Deaths, No(%)	**1383 (4.2)**	**1302 (4.0)**
Length of stay, day		
Total	**5.9 ± 5.7**	**5.8 ± 5.2**
ICU	**4.0 ± 5.8**	**3.7 ± 4.5**

Fonarow GC JAMA 2005

ADHERE Mortality Analysis

- Two primary analyses of in-hospital mortality using
  - Classification and regression tree (CART) methodology
  - Multivariate regression

CART analysis: Variables analyzed

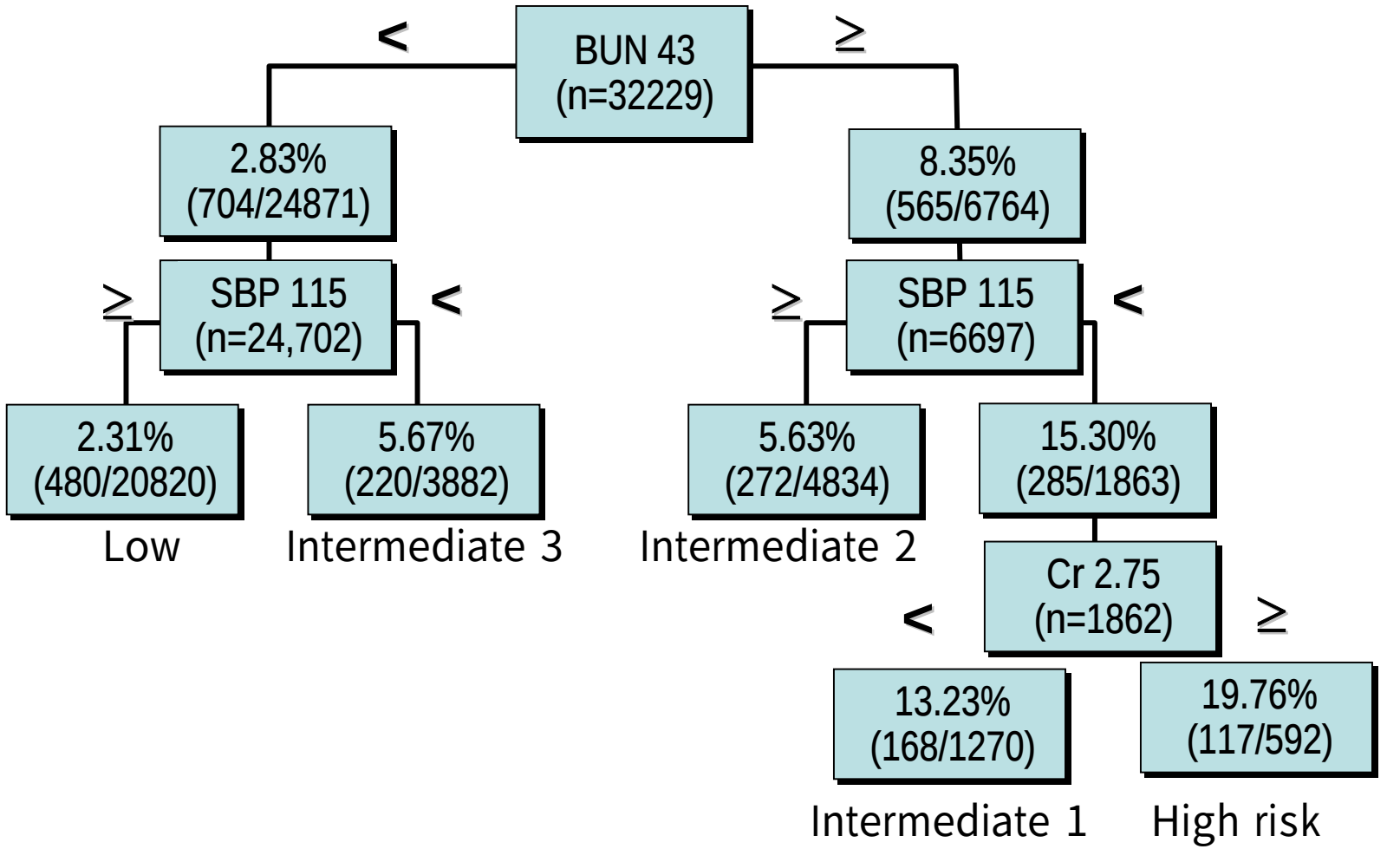
Age
AF
BNP
BUN
BUN/Cr ratio
CAD
Prior MI
Prior revascul
Cardiac enzymes
Congest/1st X-ray
Creatinine
Diabetes
Duration of Sx
Dyspnea category
Dyspnea type
Ever smoked
Fatigue
First DBP
First height
First SBP
First weight
Gender
HBG < 12
Heart rate
Hemoglobin
HF: baseline NYHA cl
HF: pre-hospital
Hyperlipidemia
Hypertension
Hypertensive-SBP>140
Ischemic etiology
UNC HF score
LOS-inpatient
NYHA cl IV/Pres
Peripheral edema
Primary insurance
QRS >120ms
Qualitative LVEF
Race/ethnicity
Rales
Sodium
Stroke / TIA
Tachycardia >100
Time in care

Fonarow et al. JAMA 2005

CART analysis

- Among 39 variables
  - High admission BUN (≥43 mg/dL)
    - Low admission SBP (<115 mmHg)
      - High serum Cr (≥2.75 mg/dL)

Inpatient Mortality From ADHERE Registry Based on Admission BUN, Creatinine and BP (Validation cohort)



Analysis of patients in the National Acute Decompensated Heart Failure National Registry (ADHERE)
BUN=blood urea nitrogen, Cr=serum creatinine, SBP-systolic blood pressure
Fonarow GC et al. *J Cardiac Fail* 2003;9(suppl 1):S79.

Multivariate logistic regression model

Log odds of mortality =

(0.0212 x BUN)

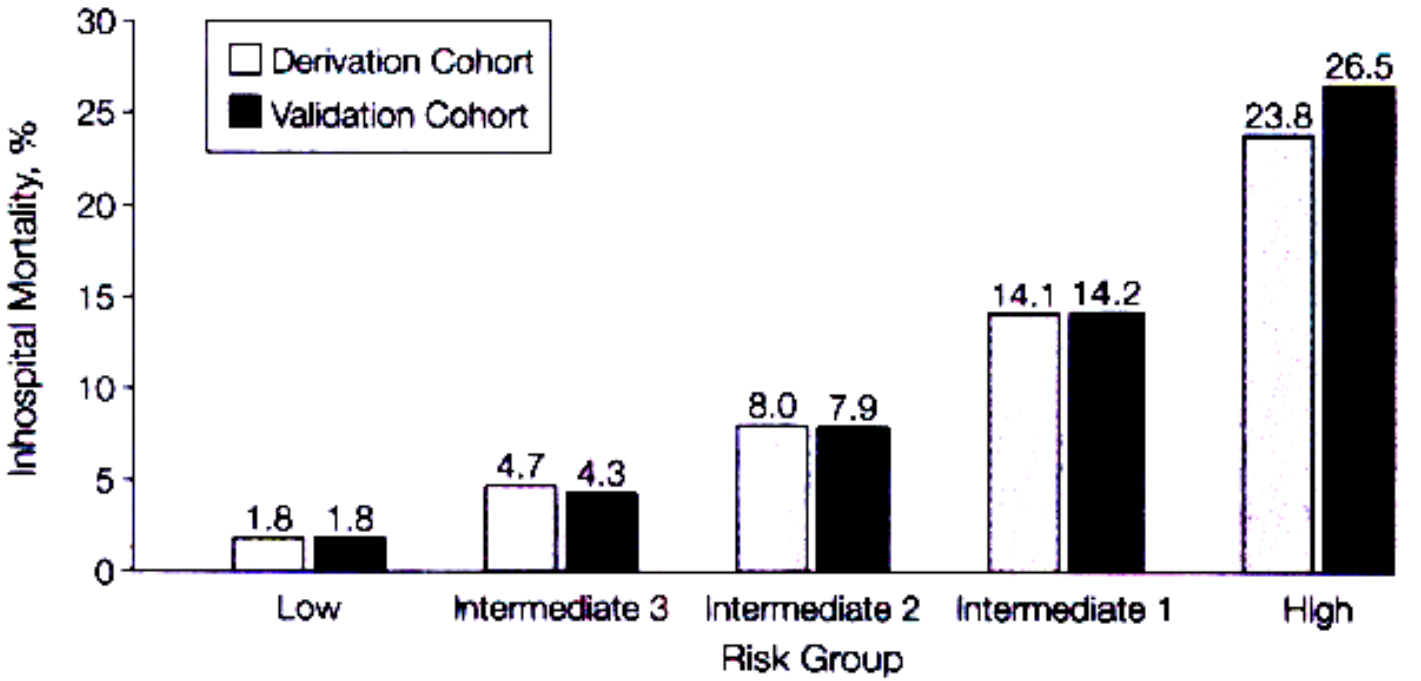
– (0.0192 x SBP)

+ (0.0131 x HR)

+ (0.0288 x Age)

– 4.72

In-hospital mortality based on the Logistic regression model



No. of Patients					
Derivation Cohort	20764	4087	5087	1419	617
Validation Cohort	20518	4010	4919	1370	471

Log odds of mortality was calculated for all records in the derivation cohort and risk group cut points established at percentile rankings equivalent to those of the classification and regression tree model (65th, 78th, 94th, and 98th percentiles).

ROC
Area under the curve

- CART
  - Derivation cohort 68.7%
  - Validation cohort 66.8%
- Logistic regression
  - Derivation cohort 75.9%
  - Validation cohort 75.7%

Chronic stabilized HF

Prognostic variables

Demographic and historical	Clinical	Electrophysiologic	Functional/exertional	Blood	Central hemodynamic
Advanced age*	High heart rate	Broad QRS	**VO_2 max* (mL/kg per min <10-14)**	**High serum BNP***	**Low LVEF***
Coronary etiology	**Persistent low BP***	Low heart rate variability	High VE/VCO_2 ratio	High serum norepinephrine	Increased left ventricular volumes
Diabetes	**NYHA functional Class III-IV***	Complex ventricular rhythms	Low 6 min walking ability	**Low serum sodium***	Low cardiac index
Resuscitated sudden death*	Involuntary weight loss	T-wave alternans		**High serum creatinine***	High left ventricular filling pressure
Race	Ventilatory rhythm and rate disturbances			**High serum bilirubine***	Restrictive mitral filling pattern
				Anemia	**Impaired right ventricular function***
				High serum troponin High serum uric acid	Cardiothoracic ratio

CHF = chronic heart failure; BP = blood pressure; NYHA = New York heart Association; VE = ventilation volume per min; VCO2 = ventilation of CO2; BNP = brain natriuretic peptide; LVEF = left ventricular ejection fraction.
*Strong

Val-HeFT trial

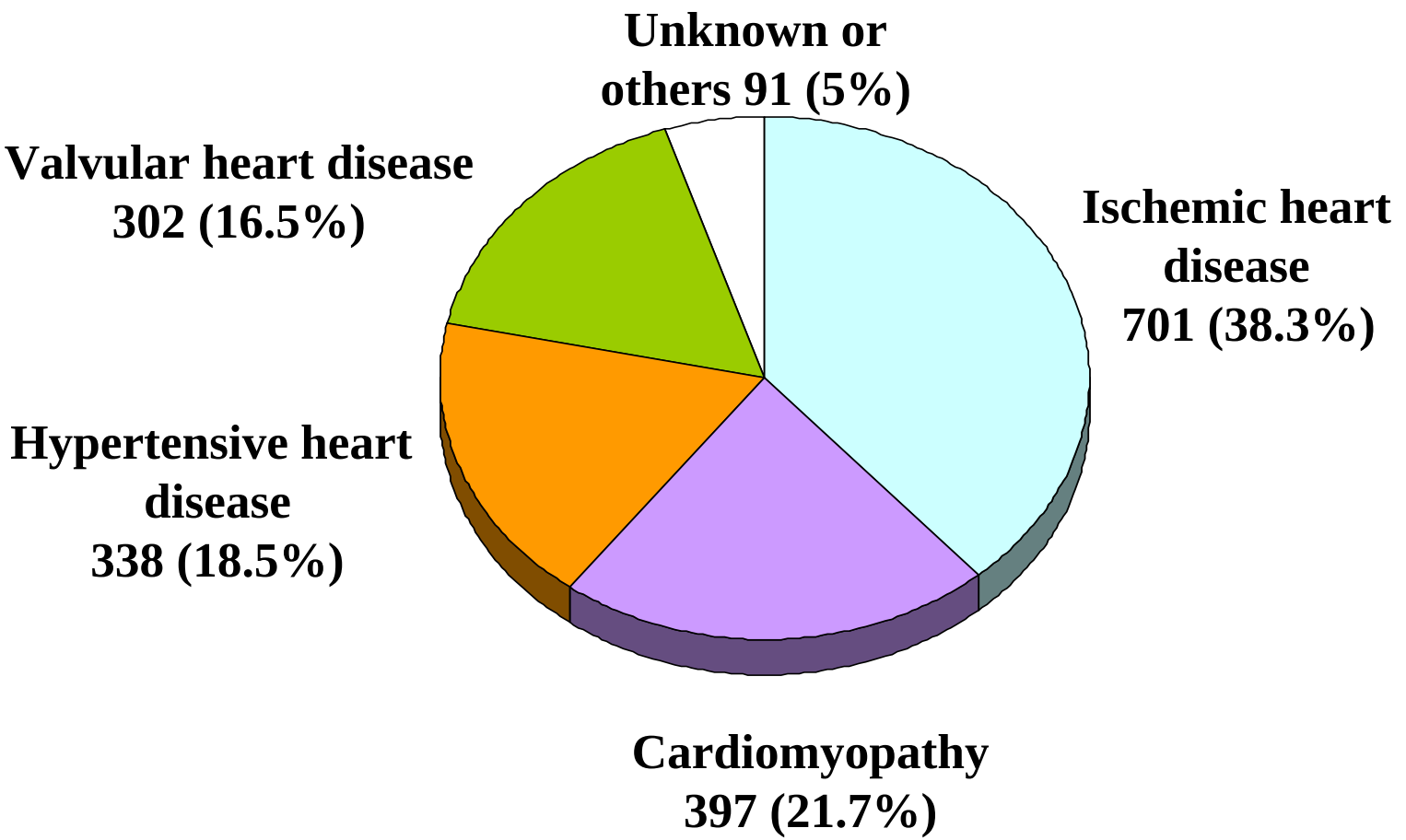
	Mortality				First Morbid Event			
		95% CI				95% CI		
Variables	HR	Lower	Upper	*P*	HR	Lower	Upper	*P*
BNP, pg/mL†	1.010	1.007	1.012	<0.001	1.009	1.007	1.011	<0.001
LVIDd/BSA, cm/m²	1.60	1.39	1.84	<0.001	1.52	1.36	1.70	<0.001
Nonischemic/ischemic	0.71	0.60	0.85	<0.001	0.81	0.71	0.93	0.003
NYHA class I+II/III+IV	1.34	1.15	1.57	<0.001	1.52	1.34	1.72	<0.001
CRP quartile 4 vs quartile 1	1.51	1.20	1.90	<0.001	1.53	1.28	1.84	<0.001
β-Blocker use, yes/no	0.76	0.64	0.90	0.001	0.79	0.69	0.90	<0.001
Male/female	1.46	1.16	1.84	0.001	1.17	0.99	1.39	0.07
Uric acid, μmol/L‡	1.02	1.01	1.03	0.002	1.02	1.01	1.03	<0.001
GFR, mL·min^{-1}·1.73 m^{-2}	0.991	0.984	0.997	0.005	0.99	0.986	0.996	<0.001
CRP quartile 3 vs quartile 1	1.24	0.99	1.57	0.07	1.33	1.10	1.59	0.003
LVEF, %*	0.95	0.90	1.01	0.08	0.95	0.914	0.997	0.04
Hemoglobin, g/dL	0.95	0.90	1.01	0.10	0.96	0.92	1.001	0.06
CRP quartile 2 vs quartile 1	1.21	0.96	1.53	0.11	1.28	1.06	1.54	0.01
Plasma renin activity, ng·mL^{-1}·h^{-1}†	1.02	0.99	1.05	0.15	1.02	0.99	1.04	0.14
Aldosterone, pg/mL†	1.004	0.999	1.009	0.15	1.003	0.999	1.007	0.12
Statin use, yes/no	0.89	0.75	1.05	0.18	0.97	0.85	1.11	0.62
Age, y	1.006	0.996	1.014	0.19	1.003	0.996	1.009	0.40
Norepinephrine, pg/mL‡	1.002	0.992	1.009	0.39	1.001	0.997	1.005	0.50
Aspirin use, yes/no	0.98	0.84	1.14	0.77	0.94	0.83	1.06	0.29
Treatment, valsartan vs placebo	0.98	0.85	1.14	0.79	0.85	0.76	0.96	0.008

LVIDd/BSA indicates left ventricular internal diastolic diameter/body surface area; GFR, glomerular filtration rate; and LVEF, left ventricular ejection fraction.

*For every 5-unit increase; †for every 10-unit increase; ‡for every 20-unit increase.

(*Circulation*. 2005;112:1428-1434)

Underlying Heart Disease



A Multicenter Survey of Heart Failure in Korean 11 University

Prognostic Factors

	Odd ratio	95% CI	p value
Male sex	1.221	0.893-1.673	NS
Hypertension	0.982	0.812-2.233	NS
Diabetes*	1.983	1.245-2.745	<0.01
Smoking	1.122	0.756-1.562	NS
Previous MI*	2.312	1.843-4.325	<0.001
Atrial fibrillation	1.316	1.001-2.002	<0.05
Stroke	2.020	1.166-3.101	<0.01
Hyponatremia*	3.214	1.243-6.320	<0.05
Azotemia*	1.254	1.001-1.984	<0.05
CLBBB	1.452	1.239-2.873	<0.01
Chronic lung disease	1.893	0.895-2.673	NS

* $p < 0.05$ by multivariated analysis

A Multicenter Survey of Heart Failure in Korean 11 University

EFFECT study

- 4031 community based hospitalized patients in Ontario, Canada
  - 2624 in derivation cohort
  - 1407 in validation cohort
- All cause 30-day and 1-year mortality

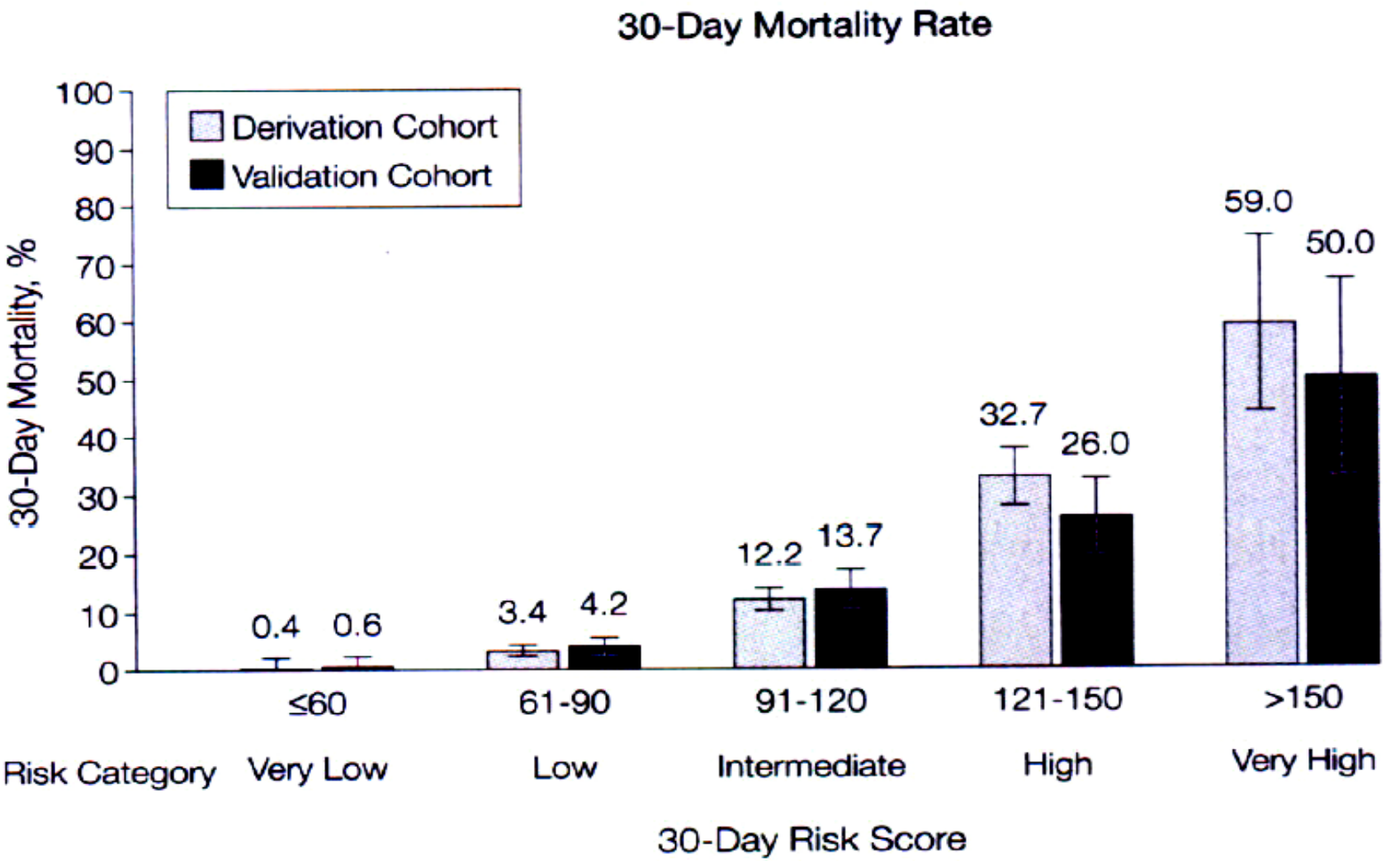
Multivariable predictors of mortality

Variable	30-Day Model		1-Year Model	
	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value
Age, y (per 10-unit increase)	1.70 (1.45-1.99)	<.001	1.61 (1.46-1.77)	<.001
Vital sign				
Systolic blood pressure, mm Hg (per 10-unit increase)	0.84 (0.80-0.88)	<.001	0.88 (0.85-0.90)	<.001
Respiratory rate, breaths/min (per 5-unit increase)	1.23 (1.12-1.36)	<.001	1.15 (1.08-1.24)	<.001
Serum concentration				
Sodium <136 mEq/L	1.53 (1.14-2.05)	.005	1.46 (1.19-1.80)	<.001
Hemoglobin <10.0 g/dL	NA	NA	1.37 (1.05-1.78)	.02
Urea nitrogen, mg/dL (per 10-unit increase)	1.55 (1.42-1.71)	<.001	1.49 (1.39-1.60)	<.001
Comorbid condition				
Cerebrovascular disease	1.43 (1.03-1.98)	.03	1.36 (1.08-1.71)	.01
Dementia	2.54 (1.77-3.65)	<.001	2.00 (1.47-2.72)	<.001
Chronic obstructive pulmonary disease	1.66 (1.22-2.27)	.002	1.41 (1.13-1.75)	.003
Hepatic cirrhosis	3.22 (1.08-9.65)	.04	5.80 (2.23-15.11)	<.001
Cancer	1.86 (1.28-2.70)	.001	1.85 (1.40-2.43)	<.001

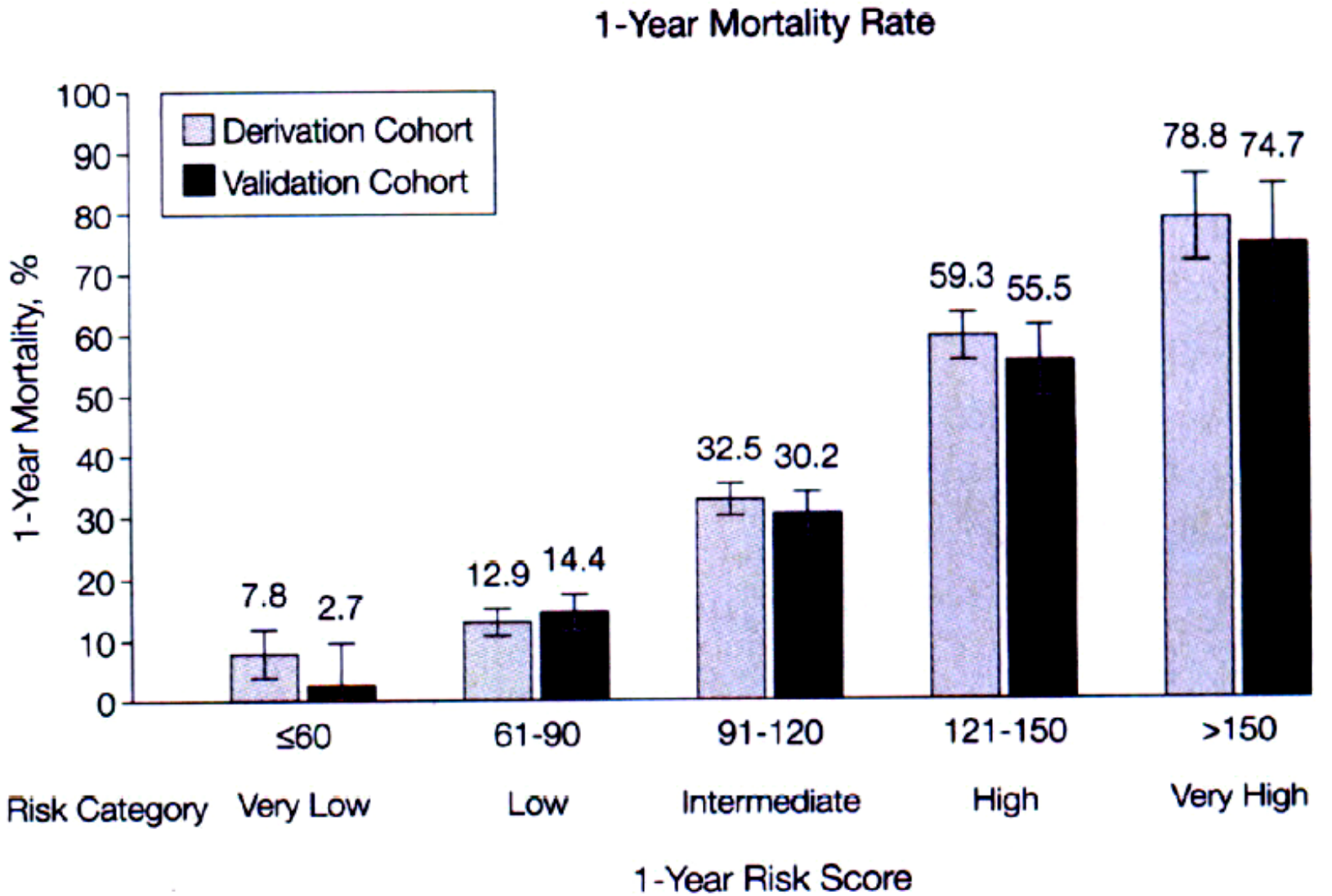
Heart Failure Risk Scoring System

Variable	No. of Points	
	30-Day Score†	1-Year Score‡
Age, y	+Age (in years)	+Age (in years)
Respiratory rate, min (minimal 20; maximum 45)§	+Rate (in breaths/min)	+Rate (in breaths/min)
Systolic blood pressure, mm Hg‖		
≥180	−60	−50
160-179	−55	−45
140-159	−50	−40
120-139	−45	−35
100-119	−40	−30
90-99	−35	−25
<90	−30	−20
Urea nitrogen (maximum, 60 mg/dL)§¶	+Level (in mg/dL)	+Level (in mg/dL)
Sodium concentration <136 mEq/L	+10	+10
Cerebrovascular disease	+10	+10
Dementia	+20	+15
Chronic obstructive pulmonary disease	+10	+10
Hepatic cirrhosis	+25	+35
Cancer	+15	+15
Hemoglobin <10.0 g/dL (<100 g/L)	NA	+10

Mortality rates stratified by 30-day risk scores



Mortality rates stratified by 1-year risk scores



Canadian Cardiovascular Outcomes Research Team

CCORT

A Canadian Institutes of Health Research - Heart and Stroke Foundation Interdisciplinary Health Research Team

act on Risk-Treatment Mismatch in the Pharmacotherapy of Heart Failure Risk-Tre

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EFFECT Heart Failure Mortality Prediction

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This prediction score is a method to stratify the risk of death in heart failure patients that can be applied using clinical information available at the bedside. Using the heart failure risk index, one can predict the risk of death at 30 days and one year. The component risk variables are categorized into the following: age, vital signs, laboratory tests, and comorbidities. The risk prediction method is intended to be applied to patients presenting with heart failure in a hospital-based setting, and can be used to stratify risk within hours of hospital presentation. Reference: JAMA 2003; 290(19):2581-2587.

The following is a step-by-step guide to use the electronic heart failure risk predictor:

1. Select conventional or SI units of measurement.
2. Enter age in years.
3. Enter respiratory rate at hospital presentation.
4. Select systolic blood pressure at hospital presentation.
5. Enter blood urea nitrogen laboratory value.
6. Select "Yes" if serum sodium concentration <136 mEq/L, and "No" if not.
7. Select "Yes" for the following comorbidities (if present): Cerebrovascular disease, Dementia, Chronic obstructive pulmonary disease, Hepatic cirrhosis, Cancer, and Anemia.
8. Click "Calculate" to calculate the 30-day and one-year scores.

>150 points = very high risk

Mortality risk at 30 days:

30-Day Score	30-Day Mortality Rate (%)
≤ 60	0.4
61-90	3.4
91-120	12.2
121-150	32.7
>150	59.0

Mortality risk at one year:

One-Year Score	One-Year Mortality Rate (%)
≤ 60	7.8
61-90	12.9
91-120	32.5
121-150	59.3
>150	78.8

We are interested in your comments and feedback on the prognosis system. Please send comments by e-mail to: doug.lee@ices.on.ca

Heart Failure Survival Score

Noninvasive Model (n=268) and Invasive Model (n=231) Obtained From the Derivation Sample

Variable	Model Coefficient	Adjusted Hazard Ratio (95% CI)	Wald x^2	P
Noninvasive model				
Ischemic cardiomyopathy	0.6931	2.00 (1.35, 2.97)	11.71	.0006
Resting heart rate (bpm)	0.0216	1.02 (1.01, 1.04)	11.45	.0007
LVEF (%)	–0.0464	0.96 (0.93, 0.98)	10.65	.0011
Mean blood pressure (mm Hg)	–0.0255	0.98 (0.96, 0.99)	8.94	.0028
IVCD	0.6083	1.84 (1.22, 2.76)	8.55	.0035
Peak $\dot{V}O_2$ (mL · kg^{-1} · min^{-1})	–0.0546	0.95 (0.91, 0.99)	6.76	.0093
Serum sodium (mmol/L)	–0.0470	0.95 (0.92, 1.00)	4.76	.0292
Invasive model				
Mean blood pressure (mm Hg)	–0.0289	0.97 (0.96, 0.99)	10.51	.0012
Resting heart rate (bpm)	0.0218	1.02 (1.01, 1.04)	9.32	.0023
IVCD	0.5931	1.81 (1.17, 2.80)	7.12	.0076
Peak $\dot{V}O_2$ (mL · kg^{-1} · min^{-1})	–0.0621	0.94 (0.90, 0.99)	6.81	.0091
Ischemic cardiomyopathy	0.5654	1.76 (1.15, 2.70)	6.75	.0094
LVEF (%)	–0.0396	0.96 (0.93, 0.99)	6.70	.0096
Mean PCWP (mm Hg)	0.0285	1.03 (1.01, 1.05)	5.77	.0163
Serum sodium (mmol/L)	–0.0462	0.96 (0.91, 0.997)	4.32	.0376

Aaronson KD, et al. *Circulation.* 1997;95:2660-2667.

HFSS:1-year event free survival

	HFSS	Derivation sample	Validation sample
Low	$\geq$ 8.10	93$\pm$2%	88$\pm$4%
Medium	7.20 to 8.09	72$\pm$5%	60$\pm$6%
High	$\leq$ 7.19	43$\pm$7%	35$\pm$10%

German Transplantation Society Score

building. Therefore, the calculation of the GTS score is as follows: (GTS=0 [if residence=home] and 0.79 [if residence=general ward and if no IV inotropes] and 0.87 [if residence=general ward and if IV inotropes] and 0.89 (if residence=ICU and if no MCSD implant and if no hemodialysis and if no hemofiltration) and 1.96 [if residence=ICU and a MCSD implant or hemodialysis or hemofiltration] $-0.0055\times[(CI/0.022) + (LVEF/0.25)-186.12])\times100$.

original continuous score. This grouping led to the following cut-off points for the GTS score: low-risk patients yielded a score below 82, high-risk patients above 118. The same cut-off points were retained for the 1998 cohort. Results of the

Issues

- Data derived from Population, not a patient
- How will we identify patients at an earlier stage?
- How do we identify patients with the greatest

Korean
Acute Decompensated Heart Failure
Registry

- **?Application in Korean patients**

Above all, what do we have to do is…

- Intensive investigations to prevent this cardiac plague…
  - **the control of hypertension and vascular risk factors.**