

Prognostic Scores for Risk Stratification in Patients with Acute Heart Failure

Escalas de estratificación del pronóstico en pacientes con falla cardíaca aguda

JOHN J. SPROCKEL, LAURA ALFARO, JENNIFER CIFUENTES, MÓNICA JIMÉNEZ, RAFAEL A. BARON, WALTER G. CHAVES

ABSTRACT

Background: Heart failure is a common, progressive and potentially lethal condition. An adequate risk assessment in acute cases might optimize care and resources.

Objective: The aim of this study was to apply three of the existent risk scores to predict in-hospital mortality in patients with acute heart failure in order to understand their performance.

Methods: This prognostic study included patients hospitalized by the department of internal medicine with diagnosis of decompensated heart failure between February 2010 and March 2013. Three risk scores were used to evaluate in-hospital mortality: the ADHERE decision tree, the OPTIMIZE-HF score and the GWTG-HF score. Contingency tables were constructed using the performance of the different cutoff points and the ROC curves of each score; then, the areas under the curve were calculated.

Results: Score results were calculated in 379 patients. Mean age was 75 years, 54% were women, 79% had hypertension, and 24% were diabetics. The area under the curve for the three risk scores was 0.63 (95% CI, 0.53-0.73) for OPTIMIZE-HF, 0.57 (95% CI, 0.49-0.65) for GWTG-HF and 0.58 (95% CI, 0.47-0.68) for ADHERE.

Conclusion: In a population of patients hospitalized for decompensated heart failure, the ADHERE, OPTIMIZE and GWTG-HF risk scores showed poor discrimination ability to predict in-hospital mortality.

Key words: Heart Failure - Risk - Prognosis - Mortality

RESUMEN

Introducción: La insuficiencia cardíaca es una condición frecuente, progresiva y potencialmente mortal. La evaluación correcta del riesgo de los desenlaces en los casos agudos permitiría la optimización de la atención y de los recursos.

Objetivo: Aplicar tres de las escalas existentes para la evaluación del riesgo de muerte intrahospitalaria en pacientes con falla cardíaca aguda a fin de conocer su desempeño.

Material y métodos: Estudio con diseño de pronóstico en el que se incluyeron pacientes hospitalizados por el servicio de medicina interna con diagnóstico de falla cardíaca descompensada entre febrero de 2010 y marzo de 2013. Se aplicaron tres escalas de riesgo para evaluar la mortalidad intrahospitalaria: árbol de decisiones ADHERE, OPTIMIZE-HF y GWTG-HF. Se construyeron tablas de contingencia mediante el cálculo del desempeño para los diferentes puntos de corte, así como las curvas ROC de cada escala y luego se calcularon las áreas bajo la curva.

Resultados: Se calculó el resultado de las escalas en 379 pacientes, de los cuales el 54% eran mujeres; la mediana de edad fue de 75 años, el 79% eran hipertensos y el 24% eran diabéticos. El área bajo la curva del OPTIMIZE-HF fue de 0,63 (IC 95% 0,53-0,73), la del GWTG-HF fue de 0,57 (IC 95% 0,49-0,65) y la del ADHERE fue de 0,58 (IC 95% 0,47-0,68).

Conclusión: En una población de pacientes hospitalizados por falla cardíaca descompensada, las escalas de riesgo ADHERE, OPTIMIZE y GWTG-HF mostraron una pobre capacidad de discriminación del riesgo de muerte intrahospitalaria.

Palabras clave: Falla cardíaca - Riesgo - Pronóstico - Mortalidad

Abbreviations

AUC	Area under the curve	LVEF	Left ventricular ejection fraction
IQR	Interquartile range	NT-proBNP	N-terminal pro B-type natriuretic peptide

REV ARGENT CARDIOL 2016;84:550-555. <http://dx.doi.org/10.7775/rac.v84.i6.9823>

Received: 10/07/2016 – Accepted: 10/30/2016

Address for reprints: John Sprockel Díaz - Hospital de San José- Fundación Universitaria de Ciencias de la Salud - Cra. 19 No. 8ª - 32 Pbx: 3538100 - e-mail: jjsprockel@fucsahud.edu.co

Hospital de San José - Fundación Universitaria de Ciencias de la Salud. Bogotá, Colombia

INTRODUCTION

Heart failure is a common, progressive and potentially lethal condition. As Gheorghiadu et al. noted, the incidence of acute heart failure is very similar to that of acute myocardial infarction (the clinical condition with the highest mortality worldwide), with similar in-hospital mortality. Yet, after discharge, heart failure-related mortality is between four and five times greater. (1) A registry performed by the Hospital de San José during a 4-year period (2010-2013), including data of 462 patients, reported an in-hospital mortality of 8.9% and 30-day mortality of 13.8% for decompensated heart failure, (2) while in-hospital mortality of ST-segment elevation myocardial infarction was 6.7% in a review of acute coronary syndromes performed between 2009 and 2010 and 9.5% in another study carried out in 2012. (4)

United States data indicate that mortality rates at 30 days, 1 year and 5 years after hospitalization for heart failure are 10.4%, 22 % and 42.3%, respectively; (5) adjusted mortality at 1 year decreased from 31.7% in 1999 to 29.6% in 2008 ($p < 0.001$). (6) Recent data of the cohort in Olmsted County, Minnesota, reveal that although the age- and sex-adjusted incidence of heart failure declined from 316 per 100,000 in 2000 to 219 per 100,000 in 2010 (a rate reduction of 37.5%), mortality among the new cases of heart failure remained constant at 5 years after the diagnosis, around 52.6%, and was frequently ascribed to noncardiovascular causes (54.3%). (7) Over the past years, length of hospital stay has decreased, but has been associated with greater 30-day mortality after hospitalization and greater readmission rates due to heart failure. (8) By 2012, the total cost attributable to heart failure was estimated in 30.7 billion dollars, and 68% was due to direct medical costs. (9)

Several prognostic markers have been evaluated in decompensated heart failure. Clinical markers are: hypertension, (10), elevated heart rate, (11), third heart sound and elevated jugular venous pressure (12, 13); lab tests: renal function, (14) hyponatremia, (15), anemia, (16) cardiac troponins, (10, 17) natriuretic peptides; (18) imaging tests: cardiothoracic ratio, (19) ejection fraction, (20), pulmonary hypertension; (21) functional class: 6-minute walk test, (22), peak exercise oxygen consumption, (23); hemodynamic parameters: pulmonary capillary wedge pressure; and use of neuro-modulating drugs, among others. Despite these correlations, individual predictors are rarely sufficient to provide accurate risk estimation. (24)

Because heart failure is a complex syndrome, patients with this condition have a wide spectrum of mortality risk. Patients at high risk of mortality should receive high rates of drug treatment to maximize the benefit, while interventions should be limited and out-patient care should be considered in those at low risk. More than 64 prediction scores have been developed to help risk assessment. (25) Nevertheless, the use of these tools in clinical practice is still very

low. The most often stated barriers to apply these instruments are doubts concerning over-simplification of risk assessment, potential risk of over-treatment, or the fact that the numerical information resulting from prediction directives is often not helpful for decision-making. (26)

The aim of the present study is to evaluate the correlation of the three main risk scores to predict the risk of mortality in patients with acute heart failure: the ADHERE risk tree, (27), the OPTIMIZE-HF score, (28) and the GWTG-HF score (29) in the population of patients hospitalized in a tertiary care center in Bogotá, Colombia.

METHODS

A prognostic evaluation study was performed from a prospective cohort of patients admitted to the emergency department of Hospital San José in Bogotá, Colombia, from February 2010 to March 2013, (2) which included patients >18 years with decompensated heart failure according to the Framingham cohort diagnostic criteria, hospitalized by the department of internal medicine.

Major criteria were: paroxysmal nocturnal dyspnea, neck vein distention, pulmonary rales, cardiomegaly, acute pulmonary edema, third heart sound and hepatojugular reflux. Minor criteria were: lower limb edema, nocturnal cough, dyspnea on exertion, hepatomegaly, pleural effusion and tachycardia > 120 bpm. Presence of at least 2 major criteria or 1 major criterion and 2 minor criteria was required to enter the study. (30)

Patients with the following conditions were excluded: decompensated diabetes mellitus, urgent dialysis, diagnosis of Child class C cirrhosis, acute liver failure, nephrotic syndrome, hypovolemic shock secondary to upper gastrointestinal bleeding, septic shock, or end-stage cancer documented

Table 1. Demographic characteristics of the population

	n	%
Age in years, median (IQR)	75	(65-82)
Female sex	205	(54)
Comorbidities		
COPD	162	(42)
Hypertension	301	(79)
Coronary artery disease	76	(20)
Type 2 diabetes mellitus	94	(24)
Chronic kidney failure	55	(14)
Laboratory tests		
Creatinine levels, median (IQR) mg/dL	1	(0.8-1.4)
Sodium, median (IQR) mg/dL	139	(135-142)
BUN, median (IQR) mg/dL	24	(18-35)
Troponin I, median (IQR) µg/dL	0,04	(0.015-0.09)
Hemoglobin, median (IQR) mg/dL	13,9	(11.7-15.5)
NT-ProBNP >4,630	197	(51)
LVEF, <40%	176	(46.4)

IQR: Interquartile range COPD: Chronic obstructive pulmonary disease. BUN: Blood urea nitrogen. NT-pro BNP: N-terminal pro B-type natriuretic peptide. LVEF: Left ventricular ejection fraction.

in the clinical record or subsequently confirmed.

The information was entered into a specially designed data collection form and the socio-demographic variables, clinical variables, concomitant conditions, history of hospitalizations and physical examination data were recorded. Blood samples were obtained to measure blood urea nitrogen, creatinine levels, N-terminal pro B-type natriuretic peptide (NT-proBNP) (5600 Integrated Immunodiagnostic System), hemoglobin levels, sodium and troponin I (VITROS Immunodiagnostic System). An electrocardiogram was taken to all the patients at admission. Left ventricular ejection fraction (LVEF) was calculated from the echocardiograms performed at the department of cardiology of the institution or from previous studies performed within 3 months. All the patients were followed up until discharge. In-hospital mortality was documented and 30-day mortality was investigated by telephone calls or by consulting the Affiliate Unique Registry (RUAF).

Statistical analysis

All the calculations were performed using STATA 13 software package. Continuous variables are expressed as mean ± standard deviation and categorical variables as absolute and relative frequencies. Data for the calculation of the dif-

ferent scores was available in 379 patients of the original cohort of 462. A nonparametric estimation of the area under the ROC curve (AUC) was performed for each of the scores evaluated as well as the calculation of the receiver operation characteristics for the different cutoff points according to the percentiles (OPTIMIZE and GWTG-HF) or risk classification (ADHERE decision tree). A p value < 0.05 was considered statistically significant.

The number of in-hospital deaths was divided by the best cutoff point for NT pro-BNP (4630 pg/dL) found in the original paper. (2)

Ethical considerations

This study was approved by the Human Research Ethics Committee of the *Fundación Universitaria de Ciencias de la Salud and the Hospital San José*. As the study was considered to be of negligible risk, an informed consent was not necessary. The original study received funding from the internal call for proposals N 4-2009.

RESULTS

Between February 2010 and March 2013, 485 patients with diagnosis of decompensated heart failure un-

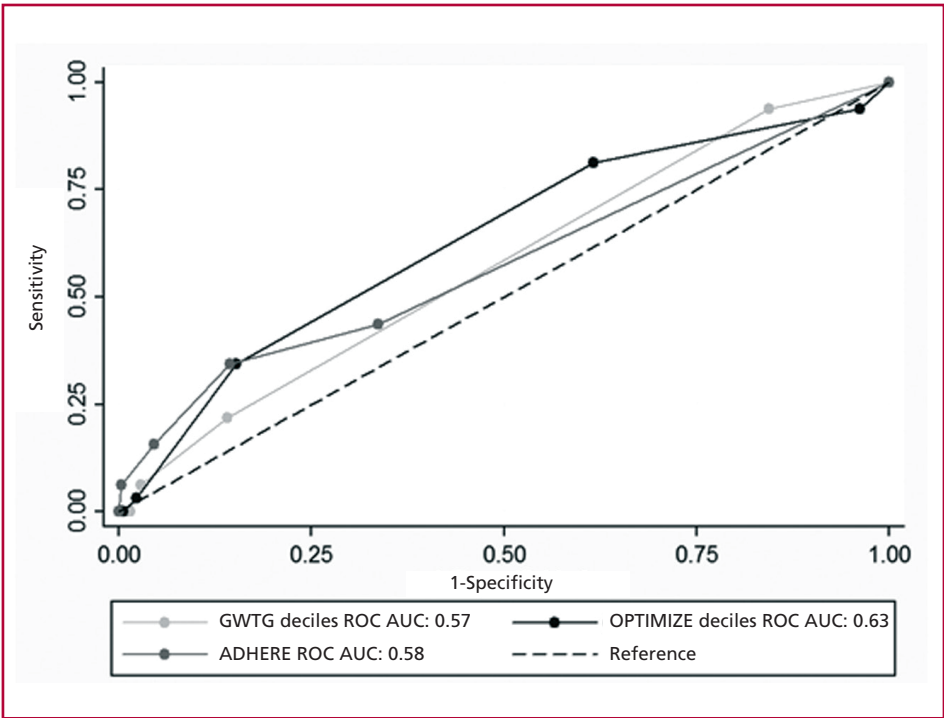


Fig. 1. Diagram of the area under the receiver operating characteristic curve (AUC) of the different risk scores for in-hospital mortality in patients with acute heart failure.

Cutoff point	Sensitivity	Specificity	LR+	LR-
1	100%	0.0%	1.00	-
2	93.8%	3.8%	0.97	1.67
3	81.3%	38.3%	1.32	0.49
4	34.4%	84.7%	2.25	0.77
5	3.1%	97.7%	1.35	0.99
6	0.0%	99.4%	0.00	1.01
7	0.0%	99.7%	0.00	1.00
> 7	0.0%	100%	-	1.00

Table 2. Discrimination of the OPTIMIZE score performance for in-hospital mortality according to the different cutoff points in the scoring deciles

Table 3. Performance of in-hospital deaths according to the best cutoff point for natriuretic peptide in the OPTIMIZE score

Percentiles of the OPTIMIZE score	NT-proBNP <4,630 pg/dl	NT-proBNP ≥4,630 pg/dl
<3, n (%)	2 (33.3)	4 (66.7)
≥3, n (%)	8 (30.8)	18 (69.2)

NT-pro BNP: N-terminal pro B-type natriuretic peptide.

derwent screening, and data from 379 patients was available to calculate the scores. Demographics of the series are depicted in Table 1. Median age was 75 [interquartile range (IQR: 65-82)] years, 54% of patients were women, 79% had hypertension, 42% chronic obstructive pulmonary disease and 20% coronary artery disease. Less than half of the patients (46%) had LVEF <40%.

Lab tests showed median creatinine level of 1mg/

Author and date	Model evaluated	Outcome	Database	Number of patients	Number of deaths	Deaths %	C (or AUC)
Development							
Fonarow, 2005 (27)	ADHERE CARD	In-hospital mortality	ADHERE	Development: 33,046	NA	NA	0.687
				Validation: 32,229	NA	NA	0.668
Abraham, 2008 (28)	OPTIMIZE-HF risk score	In-hospital mortality	OPTIMIZE-HF	Development: 37,548	1,217	3.24	0.753
			OPTIME CHF trial	Validation: 937	28	2.99	0.756
			ADHERE	Validation: 181,830	4,649	2.56	0.746
Peterson, 2010 (29)	GWTG-HF risk score	In-hospital mortality	GWTG-HF	39,783	1,139	2.86	0.75
Validation							
Auble, 2007 (34)	ADHERE CARD	In-hospital mortality (and at 30 days)	Pennsylvania Health Care Cost Containment Council database of demographic and administrative variables and	32,160	1,432	4.45	0.68 (0.66)
	EFFECT		Cardinal Health Information Companies-MediQual Systems	33,533	1,498	4.47	0.74 (0.73)
	BWH		Atlas Severity of Illness System database	33,533	1,498	4.47	0.61 (0.59)
Austin, 2010 (35)	EFFECT-HF mortality model	In-hospital mortality	EFFECT HF	15,844	NA	NA	0.772
	ADHERE Logistic regression model						0.747
	ADHERE CARD						0.651
Scrutinio, 2015 (36)	ADHF/NT-proBNP	In-hospital mortality (and at 90 days)	Multicenter	701	53	7.60	0.815 (0.81)
	ADHERE Logistic regression model						0.758
	OPTIMIZE-HF risk score						0.771
	GWTG-HF risk score						0.776
Shiraishi, 2016 (37)	GWTG-HF risk score	In-hospital mortality	West Tokyo Heart Failure (WET-HF) registry	1876	68	3.62	0.763
Present study	ADHERE CARD	In-hospital mortality	Hospital San José	379	32	8.44	0.58
	OPTIMIZE-HF risk score						0.63
	GWTG-HF risk score						0.57

dL (IQR 0.8-1.4) with 10% of patients presenting creatinine levels >2 mg/dL; median blood urea nitrogen of 24 mg/dL (IQR 18-35) and sodium 139 mEq/L (IQR 135-142), with hyponatremia (sodium <135 mEq/L) in 21% and hemoglobin <12 mg/dL in 29 % of the patients.

Most of the population evaluated could be classified as low risk according to the three scores evaluated. According to the ADHERE risk tree, 83.9% of the population had low risk or intermediate-low risk; 96.8% of the population was within the first three deciles of the GWTG score and 86.1% was within the first three deciles of the OPTIMIZE score.

The AUC evaluating the discrimination of each score to predict in-hospital mortality was as follows: 0.63 (95% CI, 0.53-0.73) for the OPTIMIZE score, 0.57 (95% CI, 0.49-0.65) for the GWTG-HF score and 0.58 (95% CI, 0.47-0.68) for the ADHERE decision tree (Figure 1).

The analysis of each decile of the OPTIMIZE-HF score showed that decile 3 had the highest discrimination capacity, with a sensitivity of 81%, a specificity of 38% and an accuracy of 41% (Table 2). For the GWTG-HF score, the second decile had the highest discrimination ability, with a sensitivity of 94% and a specificity of 16%.

The AUC for NT pro-BNP was 0.63 (95% CI, 0.54-0.73), and after dividing the number of deaths by the best cutoff point for NT pro-BNP (4,630 pg/dL) the likelihood of death was two times higher, independently of the result of the OPTIMIZE score (Table 3).

DISCUSSION

Risk assessment is essential in patients with heart failure for an adequate management of this population. A study performed in 2002 documented that physicians overestimated the probability of severe complications in patients with acute heart failure, which might be related with the overutilization of resources. (31) A survey performed in 2008 among 1,450 geriatricians, cardiologists, internists and family practitioners revealed that less than 25% of respondents believed that they could accurately predict death in heart failure patients. (32)

In another study, over half of the patients admitted for heart failure to an acute care facility were low risk, (33) a finding that is similar and even higher in our results ($> 80\%$). For this reason, the cases with the highest scores may be underrepresented, affecting the possibility of obtaining reliable information about the performance of scores in our population.

Table 4 presents the results of the studies that developed the risk scores evaluated (27-29) and of the validation studies (34-37). In most cases, the performance is hardly acceptable, while in the present study it was very poor. The ADHERE decision tree was the model most commonly evaluated. (34-36) In two cases, when natriuretic peptide levels are added to the risk score, the ability of the score to predict risk in-

creases significantly. (36, 37)

Although the results seem to indicate that the OPTIMIZE score has a better performance, the AUC overlaps with the other two scores evaluated and, thus, we cannot confirm that this score was the best. In any case, the AUC range obtained would mean that the use of any of these scores would not be useful in practice. Yet, it is not possible to know if it would be useful for the negative cases or if the addition of natriuretic peptide would improve discrimination.

It is highly possible that our setting might have factors different from those explored in the different scores that would affect mortality, probably making mortality of the lower scores higher than the mortality found in the studies in which the scores were developed or validated.

Limitations

Among the limitations of this study, we must mention the low number of events, which prevents considering our study as a real validation of these scores. The intermediate and high score levels are underrepresented, a fact that contrasts with the higher mortality compared with other trials, except for the study by Scrutinio (36) who reported a mortality rate similar to our findings.

CONCLUSION

In a population of patients hospitalized for decompensated heart failure, the ADHERE, OPTIMIZE and GWTG-HF risk scores showed poor discrimination to predict in-hospital mortality. The population of patients with decompensated heart failure gathers around the lower risk scores. The results obtained seem to indicate that use of these scores in our environment would provide little information for decision-making.

Conflicts of interest

None declared.

(See authors' conflicts of interest forms in the website/Supplementary material).

REFERENCES

1. Gheorghiade M, Zannad F, Sopko G, Klein L, Pina IL, Konstam MA, et al. Acute heart failure syndromes: current state and framework for future research. *Circulation* 2005;112:3958-68. <http://doi.org/fg4v42>
2. Chaves WG, Diaztagle JJ, Sprockel JJ, Hernández JJ, Benavidez J, Henao D y cols. Factores asociados a mortalidad en pacientes con falla cardíaca descompensada. *Acta Med Colomb* 2014;39:314-20. <http://www.scielo.org.co/pdf/amc/v39n4/v39n4a03.pdf>
3. Sprockel JJ, Diaztagle JJ, Filizola V, Uribe L, Alfonso C. Descripción clínica y tratamiento de los pacientes con síndrome coronario agudo en el hospital San José de Bogotá. *Acta Med Colomb* 2014;39:124-30. <http://www.scielo.org.co/pdf/amc/v39n2/v39n2a07.pdf>
4. Sprockel JJ, Diaztagle JJ, Chaves WG, Heras JC, Simon CJ, Afanador D y cols. Calidad de la atención de los síndromes coronarios agudos: implementación de una ruta crítica. *Rev Colomb Cardiol* 2015;22:119-26. <http://www.scielo.org.co/pdf/rcca/v22n3/v22n3a02.pdf>

5. Mozaffarian D, Benjamin EJ, Go AS, Arnett DK, Blaha MJ, Cushman M, et al. Heart Disease and Stroke Statistics- 2016 Update A Report From the American Heart Association. *Circulation* 2016;133:e38-e360. <http://doi.org/bvft>
6. Chen J, Normand ST, Wang Y, Krumholz HM. National and regional trends in heart failure hospitalization and mortality rates for medicare beneficiaries, 1998-2008. *JAMA* 2011;306:1669-78. <http://doi.org/bq84z9>
7. Gerber Y, Weston SA, Redfield MM, Chamberlain AM, Manemann SM, Jiang R, et al. A contemporary appraisal of the heart failure epidemic in Olmsted County, Minnesota, 2000 to 2010. *JAMA Intern Med* 2015;175:996-1004.
8. Bueno H, Ross JS, Wang Y, Chen J, Vidán MT, Normand SL, et al. Trends in length of stay and short-term outcomes among Medicare patients hospitalized for heart failure, 1993-2006. *JAMA* 2010;303:2141-7. <http://dx.doi.org/http://doi.org/bjgntz>
9. Heidenreich PA, Albert NM, Allen LA, Blumke DA, Butler J, Fonarow GC, et al. Forecasting the impact of heart failure in the United States: a policy statement from the American Heart Association. *Circ Heart Fail* 2013;6:606-19. <http://doi.org/bvfw>
10. Diercks DB, Peacock WF, Kirk JD, Weber JE. ED patients with heart failure: identification of an observational unit-appropriate cohort. *Am J Emerg Med* 2006;24:319-24. <http://doi.org/b3hpkk>
11. Takada T, Sakata Y, Miyata S, Takahashi J, Nochioka K, Miura M, et al. Impact of elevated heart rate on clinical outcomes in patients with heart failure with reduced and preserved ejection fraction: a report from the CHART-2 Study. *Eur J Heart Fail* 2014;16:309-16. <http://doi.org/bvfx>
12. Rame JE, Dries DL, Drazner MH. The prognostic value of the physical examination in patients with chronic heart failure. *Congest Heart Fail* 2003;9:170-5.
13. Drazner MH, Rame JE, Stevenson LW, Dries DL. Prognostic importance of elevated jugular venous pressure and a third heart sound in patients with heart failure. *N Engl J Med* 2001;345:574-81. <http://doi.org/d3c49d>
14. Damman K, Valente MAE, Voors AA, O'Connor CM, van Veldhuisen DJ, Hillege HL. Renal impairment, worsening renal function, and outcome in patients with heart failure: an updated meta-analysis. *Eur Heart J* 2014;35:455-69. <http://doi.org/d3c49d>
15. Gheorghiade M, Rossi JS, Cotts W, Shin DD, Hellkamp AS, Piña IL, et al. Characterization and prognostic value of persistent hyponatremia in patients with severe heart failure in the ESCAPE Trial. *Arch Intern Med* 2007;167:1998-2005. <http://doi.org/cv5zd6>
16. Felker GM, Gattis WA, Leimberger JD, Adams KF, Cuffe MS, Gheorghiade M, et al. Usefulness of anemia as a predictor of death and rehospitalization in patients with decompensated heart failure. *Am J Cardiol* 2003;92:625-8. <http://doi.org/fgdp6v>
17. Horwich TB, Patel J, MacLellan WR, Fonarow GC. Cardiac troponin I is associated with impaired hemodynamics, progressive left ventricular dysfunction, and increased mortality rates in advanced heart failure. *Circulation* 2003;108:833-8. <http://doi.org/ch38pw>
18. Van Kimmenade RRJ, Pinto YM, Bayes-Genis A, Lainchbury JG, Richards AM, Januzzi J. Usefulness of intermediate aminoterminal pro-brain natriuretic peptide concentrations for diagnosis and prognosis of acute heart failure. *Am J Cardiol* 2006;98:386-90. <http://doi.org/d72kpw>
19. Kearney MT, Fox KAA, Lee AJ, Prescott RJ, Shah AM, Batin PD, et al. Predicting death due to progressive heart failure in patients with mild-to-moderate chronic heart failure. *J Am Coll Cardiol* 2002;40:1801-8. <http://doi.org/dt6vv9>
20. Solomon SD, Anavekar N, Skali H, McMurray JJV, Swedberg K, Yusuf S, et al. Influence of ejection fraction on cardiovascular outcomes in a broad spectrum of heart failure patients. *Circulation* 2005;112:3738-44. <http://doi.org/bvdzck9>
21. Miller WL, Mahoney DW, Enriquez-Sarano M. Quantitative Doppler-echocardiographic imaging and clinical outcomes with left ventricular systolic dysfunction: independent effect of pulmonary hypertension. *Circ Cardiovasc Imaging* 2014;7:330-6. <http://doi.org/bvfvz>
22. Ingle L, Cleland JG, Clark AL. The long-term prognostic significance of 6-minute walk test distance in patients with chronic heart failure. *Biomed Res Int* 2014;2014:505969. <http://doi.org/bvfvz>
23. Cohn JN, Johnson GR, Shabetai R, Loeb H, Tristani F, Rector T, et al. Ejection fraction, peak exercise oxygen consumption, cardiothoracic ratio, ventricular arrhythmias, and plasma norepinephrine as determinants of prognosis in heart failure. The V-HeFT VA Cooperation Studies Group. *Circulation* 1993;87(6 Suppl):VI5-16.
24. Moons KGM, Kengne AP, Woodward M, Royston P, Vergouwe Y, Altman DG, et al. Risk prediction models: I. Development, internal validation, and assessing the incremental value of a new (bio)marker. *Heart* 2012;98:683-90. <http://doi.org/bvfvz>
25. Rahimi K, Bennett D, Conrad N, Williams TM, Basu J, Dwight J, et al. Risk prediction in patients with heart failure: a systematic review and analysis. *JACC Heart Fail* 2014;2:440-6. <http://doi.org/bvfvz>
26. Eichler K, Zoller M, Tschudi P, Steurer J. Barriers to apply cardiovascular prediction rules in primary care: a postal survey. *BMC Fam Pract* 2007;8:1. <http://doi.org/bfssvd>
27. Fonarow GC, Adams KF, Abraham WT, Yancy CW, Boscardin WJ, ADHERE Scientific Advisory Committee, Study Group, and Investigators. Risk stratification for in-hospital mortality in acutely decompensated heart failure: classification and regression tree analysis. *JAMA* 2005;293:572-80. <http://doi.org/dnzcgv>
28. Abraham WT, Fonarow GC, Albert NM, Stough WG, Gheorghiade M, Greenberg BH, et al. Predictors of in-hospital mortality in patients hospitalized for heart failure: insights from the Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure (OPTIMIZE-HF). *J Am Coll Cardiol* 2008;52:347-56. <http://doi.org/cqn86f>
29. Peterson PN, Rumsfeld JS, Liang L, Albert NM, Hernandez AF, Peterson ED, et al. A validated risk score for in-hospital mortality in patients with heart failure from the American Heart Association get with the guidelines program. *Circ Cardiovasc Qual Outcomes* 2010;3:25-32. <http://doi.org/dpv3cd>
30. McKee PA, Castelli WP, McNamara PM, Kannel WB. The natural history of congestive heart failure: the Framingham study. *N Engl J Med* 1971;285:1441-6. <http://doi.org/fpg62f>
31. Smith WR, Poses RM, McClish DK, Huber EC, Clemons FLW, Alexander D, et al. Prognostic judgments and triage decisions for patients with acute congestive heart failure. *Chest* 2002;121:1610-7. <http://doi.org/fqc69d>
32. Hauptman PJ, Swindle J, Hussain Z, Biener L, Burroughs TE. Physician attitudes toward end-stage heart failure: a national survey. *Am J Med* 2008;121:127-35. <http://doi.org/cbwtmp>
33. Butler J, Hanumanthu S, Chomsky D, Wilson JR. Frequency of low-risk hospital admissions for heart failure. *Am J Cardiol* 1998;81:41-4. <http://doi.org/d48r3g>
34. Auble TE, Hsieh M, McCausland JB, Yealy DM. Comparison of four clinical prediction rules for estimating risk in heart failure. *Ann Emerg Med* 2007;50:127-35. <http://doi.org/c7mcts>
35. Austin PC, Tu JV, Lee DS. Logistic regression had superior performance compared with regression trees for predicting in-hospital mortality in patients hospitalized with heart failure. *J Clin Epidemiol* 2010;63:1145-55. <http://doi.org/drhct4>
36. Scrutinio D, Ammirati E, Passantino A, Guida P, D'Angelo L, Oliva F, et al. Predicting short-term mortality in advanced decompensated heart failure- role of the updated acute decompensated heart failure/N-terminal pro-B-type natriuretic Peptide risk score. *Circ J* 2015;79:1076-83. <http://doi.org/bvfvz>
37. Shiraishi Y, Kohsaka S, Abe T, Mizuno A, Goda A, Izumi Y, et al. Validation of the Get With The Guideline- Heart Failure risk score in Japanese patients and the potential improvement of its discrimination ability by the inclusion of B-type natriuretic peptide level. *Am Heart J* 2016;171:33-9. <http://doi.org/bvfvz>