EVIDENCE TABELLEN

UITGANGSVRAAG: Welke factoren bepalen de levensverwachting van patiënten met hartfalen NYHA klasse III-IV?

Systematic reviews

Study ID	Method	Patient characteristics	Results	Critical appraisal of review quality
Alba 2013	• SR • Funding/CoI: Vanier Canada Graduate Scholarship, administered by the Canadian Institutes of Health Research, Ottawa, ON, Canada; no CoI • Search date: May 2012 • Databases: Medline, Embase, Cinahl, references • Study designs: no restrictions	• Eligibility criteria: Eligible articles enrolled adults (>19 years) who were ambulatory patients with heart failure; used multivariable analysis (≥2 independent variables) to predict mortality or a composite outcome including mortality; reported >30 deaths; reported results as a score, a prediction rule, or as a set of regression coefficients sufficient to make predictions for individual patients; and reported a measure of discrimination or calibration. They also included	5 externally validated models (independent cohort): - <u>Heart Failure Survival Score</u>: • 7 variables: ischemic cardiomyopathy, presence of intraventricular conduction delay (QRS >120 ms), LVEF, resting heart rate, mean blood pressure, peak oxygen consumption, and serum sodium • Composite outcome of death, urgent heart transplantation and ventricular assist device implantation • 3 risk scores: high, medium, low • Derived from single-centre cohort (N=268) • Validated in 8 independent single-centre cohorts (N=2240) • c-statistic at 1y: range 0.56-0.79 - <u>Seattle Heart Failure Model</u>: • 10 continuous variables: age, LVEF, NYHA class, systolic blood pressure, diuretic dose adjusted by weight, lymphocyte count, hemoglobin, serum sodium, total cholesterol, and uric acid; 10 categorical variables: sex, ischemic cardiomyopathy, QRS>120 ms, use of β-blockers, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, potassium-sparing diuretic, statins and allopurinol, and ICD/CRT status • Composite outcome of death, urgent heart transplantation, and ventricular assist device • Continuous risk score, expressed as predicted mean life expectancy or event-free survival at 1, 2, and 5 years • Derived from RCT (N=1125)	• High-quality review • Duplicate study selection, but unclear if duplicate data extraction

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	• N included studies: 32 (20 models, of which 5 were validated)	studies evaluating the performance of an existing score in a different population to the one from which it was developed, and reported model discrimination and calibration • No restrictions on study design, left ventricular ejection fraction (LVEF), language, or date of publication • They excluded studies that enrolled patients during hospital admission or duplicate studies providing no new relevant data	• Validated in 14 independent cohorts (N=16057) • c-statistic: range 0.63-0.81 - <u>Frankenstein et al's model</u>: • 2 variables: brain natriuretic peptide and 6-minute walk test with different cutoffs depending on sex and use of β-blockers • Outcome: all-cause mortality • 3 risk score: 0, 1 or 2 • Derived from single cohort (N=636) • Validated in independent cohort (N=676) • c-statistic: range 0.66-0.68 - <u>PACE Risk Score</u>: • 4 variables: presence of peripheral vascular disease, age >70 years, creatinine >2 mg/dL, and LVEF <20% • Outcome: all-cause mortality • Continuous risk score from 0-5 • Derived from single ICD cohort (N=905) • Validated in independent ICD cohort (N=1812) • c-statistic: 0.69 at 1y - <u>SHOCKED Predictors</u>: • 7 variables: age >75 years, NYHA class >II, atrial fibrillation, chronic obstructive pulmonary disease, chronic kidney disease, LVEF <20%, and diabetes mellitus • Outcome: 1-, 2-, 3- and 4-year survival (nomogram) • Continuous risk score from 0-400 • Derived and validated from Medicare ICD cohort (N=27893) • c-statistic: 0.74 at 1y	

Primaire studies

Study ID	Method	Patient characteristics	Model	Results	Critical appraisal of study quality
Scrutinio 2014	• Design: cohort study • Funding/CoI: no CoI • Setting: unclear • Sample size: N=445 • Duration: unclear	• Eligibility criteria: current hospitalization for worsening of chronic established HF, history of heart failure for at least 1 year, receiving chronic treatment with standard therapies, NYHA Class III/IV symptoms and evidence of severe left ventricular systolic dysfunction (left ventricular ejection fraction <= 0.30 as measured by two-dimensional echocardiography) at admission, and need for intravenous diuretic and/or inotropic treatment • Exclusion criteria: acute coronary syndromes or angina pectoris, recent cardiac surgical or percutaneous procedures, planned coronary revascularization, congenital heart disease, and valvular heart disease regardless of whether surgically	ADHF/NT-proBNP score - 8 variables: chronic obstructive pulmonary disease, systolic blood pressure, estimated glomerular filtration rate, serum sodium, hemoglobin concentration, NT-proBNP concentration, LVEF, moderate-to-severe tricuspid regurgitation - Outcome: cumulative mortality, 1y-mortality	c-statistic: Cumulative mortality: - 0.738 in overall cohort - 0.771 in patients aged 70 or less Post-discharge mortality: - 0.741 in overall cohort - 0.751 in patients aged 70 or less Adding prior (<=6 months) hospitalizations for HF to the score increased the c-statistic for post-discharge mortality to 0.759 in the overall cohort and to 0.774 in patients aged 70 or less	Level of evidence: high risk of bias • 9 patients lost-to-follow-up from 454 eligible patients • 364 patients were included in original study (179 in derivation cohort, 185 in validation cohort)

Study ID	Method	Patient characteristics	Model	Results	Critical appraisal of study quality
		corrected • *A priori* patient characteristics: ○ Mean age: 62y ○ Male: 84.7% ○ NYHA IV: 44.7% ○ LVEF <= 20%: 38%			
Scrutinio 2015	• Design: cohort study • Funding/CoI: no CoI • Setting: multicentre • Sample size: N=701 • Duration: Apr 2006 – Apr 2014	• Eligibility criteria: patients admitted for acute decompensation of chronic, established HF with NYHA III/IV symptoms and evidence of severe LV systolic dysfunction (LVEF ≤0.30 on 2-D echocardiography) at admission • *A priori* patient characteristics: ○ Mean age: 63 ○ Male: 83.7% ○ NYHA IV: 46% ○ LVEF <= 20%: 37.1%	Updated ADHF/NT-proBNP score - 8 variables: chronic obstructive pulmonary disease, systolic blood pressure, estimated glomerular filtration rate, serum sodium, hemoglobin concentration, NT-proBNP concentration, LVEF, moderate-to-severe	c-statistic: 90-day mortality: 0.81 in-hospital mortality: 0.815	Level of evidence: high risk of bias • 33 patients incomplete follow-up

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			tricuspid regurgitation, - Adjusted for age and hospitalization for HF within the 6 months preceding the index admission - Outcome: all-cause mortality within 90d of admission		
Uszko - Lencer 2017	• Design: cohort study • Funding/CoI: clearly reported in article, many grants from pharmaceutical companies • Setting: university centre, Germany	• Eligibility criteria: patients diagnosed with heart failure • *A priori* patient characteristics: ○ Mean age: 63.3y ○ Male: 72% ○ NYHA III/IV: 51.3% ○ LVEF <= 45%: 88.1%	BARDICHE index - 8 variables: BMI, age, resting systolic blood pressure, NYHA classification, NT-proBNP, eGFR, resting	Significant differences between BARDICHE-risk groups for mortality (HR 3.63 per BARDICHE-group, 95%CI 3.10-4.25) Almost identical AUCs were shown between the BARDICHE and the MAGGIC-score regarding 2-year mortality (0.736 vs 0.738, p>0.9)	Level of evidence: high risk of bias • Model theoretically developed • Validated in dataset of 1811 patients: 602 from the TIME-CHF study and 1209 from a local cohort

Study ID	Method	Patient characteristics	Model	Results	Critical appraisal of study quality
	• Sample size: N=1811 • Duration: median follow-up 887d		heart rate, and 6-min walk test - Outcome: 5y all-cause survival - 3 risk categories: low, medium, high		
Salah 2014	• Design: 7 prospective cohort studies • Funding/CoI: competing interests reported • Setting: 7 cohort studies • Sample size: N=1301 (derivation cohort) • Duration: unclear	• Eligibility criteria: (1) admitted because of clinically validated ADHF, (2) discharged alive and (3) NT-proBNP measurements available at admission and at discharge • *A priori* patient characteristics: ○ Median age: 74y ○ Male: 60% ○ NYHA IV: 0.3% ○ LVEF <25%: 28%	ELAN-HF score - 8 variables: NT-proBNP reduction, NT-proBNP discharge value, age, peripheral oedema at admission, systolic blood pressure, hyponatremia at admission, serum urea	Derivation cohort: c-statistic 0.76 Validation cohort (N=325): 1y all-cause mortality, low risk 7%, intermediate risk 13%, high risk 24%, very high risk 52% (p<0.001)	Level of evidence: high risk of bias

Study ID	Method	Patient characteristics	Model	Results	Critical appraisal of study quality
			at discharge, NYHA class at discharge - Outcome: all-cause mortality within 180d of admission - 4 risk categories: low, intermediate, high, very high		
Pocock 2013	• Design: 30 studies, individual patient data • Funding/CoI: grants fromthe New Zealand National Heart Foundation, the University of Auckland, and the	• Eligibility criteria: patients with heart failure • *A priori* patient characteristics: alive vs. died ○ Mean age: 64.3 vs. 71.9y ○ Male: 69% vs. 65.1% ○ NYHA IV: 4.1% vs. 13.4% ○ Mean LVEF: 36.6% vs. 33.6%	MAGGIC - 13 variables: age, lower EF, NYHA class, serum creatinine, diabetes, not prescribed beta-blocker, lower systolic	No c-statistic reported Model goodness-of-fit: only reported in figure, no data reported 3y-mortality probability for score 10, 20, 30 and 40: 0.101, 0.256, 0.525, and 0.842, respectively	Level of evidence: low risk of bias

Study ID	Method	Patient characteristics	Model	Results	Critical appraisal of study quality
	University of Glasgow; no CoI • Setting: • Sample size: N=39372 • Duration: median follow-up 2.5y		BP, lower body mass, time since diagnosis, current smoker, chronic obstructive pulmonary disease, male gender, and not prescribed ACE-inhibitor or angiotensin -receptor blockers - Outcome: 3y mortality - Integer score		
Sartip y 2014	• Design: cohort study • Funding/CoI: Swedish • Heart Lung Foundation (grant nos 20080409 and	• Eligibility criteria: patients with clinician-judged heart failure • *A priori* patient characteristics: alive vs. died ○ Mean age: 71.3 vs. 80.0y ○ Male: 62% vs. 58%	MAGGIC - 13 variables: age, lower LVEF, NYHA class, serum creatinine,	Overall 3y mortality: 39.4% Predicted mortality: 36.4% c-statistic: 0.741	Level of evidence: low risk of bias

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	20100419 to L.H.L.) and the Stockholm County Council (grant no. 00556-2009 to L.H.L.); no CoI • Setting: nationwide, Sweden • Sample size: N=51043 • Duration: May 2000 – Nov 2012	○ NYHA IV: 2% vs. 9% ○ LVEF <30%: 28% vs. 29%	diabetes, not prescribed beta-blocker, lower systolic BP, lower body mass, time since diagnosis, current smoker, chronic obstructive pulmonary disease, male gender, and not prescribed ACE-inhibitor or angiotensin -receptor blockers - Outcome: 3y mortality - Integer score		
Bjurman	• Design: prospective	• Eligibility criteria: patients with heart failure and	Multimarker score	High risk scores were associated with both all-cause	Level of evidence: high

Study ID	Method	Patient characteristics	Model	Results	Critical appraisal of study quality
2015	cohort study • Funding/CoI: supported by the Heart and Lung Foundation; no CoI • Setting: single university centre, Sweden • Sample size: N=124 • Duration: 2010; 3y follow-up	reduced LVEF <50% • *A priori* patient characteristics: survived vs. died ○ Mean age: 72 vs. 78y ○ Male: 72% vs. 73% ○ Mean LVEF: 35% vs. 33%	- 3 variables: age, serum troponin T, and serum cystatin C - Outcome: all-cause mortality, cardiovascular mortality - 3 risk groups: low, medium, high	mortality (HR 4.2, 95%CI 2.2-8.1, p<0.001) and CV mortality (HR 3.6, 95%CI 1.7-8.0, p = 0.0015)	risk of bias • Validation cohort
Hussain 2014	• Design: cohort study • Funding/CoI: not reported • Setting: single centre, Pakistan • Sample size: N=118 • Duration: 1y follow-up	• Eligibility criteria: patients with systolic heart failure, LVEF <40% • *A priori* patient characteristics: intervention vs. control ○ Mean age: 41.6y ○ Male: 73.7% ○ NYHA III/IV: 97.5% ○ Mean LVEF: 23%	Seattle Heart Failure Model - 10 continuous variables: age, LVEF, NYHA class, systolic blood pressure, diuretic dose adjusted by weight,	AUC for 1y mortality: 0.802	Level of evidence: high risk of bias

Study ID	Method	Patient characteristics	Model	Results	Critical appraisal of study quality
			lymphocyte count, hemoglobin, serum sodium, total cholesterol, and uric acid; 10 categorical variables: sex, ischemic cardiomyopathy, QRS>120 ms, use of β-blockers, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, potassium-sparing diuretic, statins and allopurinol, and ICD/CRT		

Study ID	Method	Patient characteristics	Model	Results	Critical appraisal of study quality
			status - Outcome: 1y, 2y and 3y mortality		
Shiraishi 2016	• Design: cohort study • Funding/CoI: supported by JPSS KAKENHI Grant Number 23591062; one author with links with Pfizer and Bayer Pharmaceutical Co. • Setting: single university centre, Japan • Sample size: N=504 • Duration: Apr 2006 – Aug 2014; mean follow-up 763d	• Eligibility criteria: patients hospitalised because of acute heart failure • *A priori* patient characteristics: ○ Mean age: 68y ○ Male: 68% ○ Mean NYHA class: 2.2 ○ Median LVEF: 35%	Seattle Heart Failure Model - 10 continuous variables: age, LVEF, NYHA class, systolic blood pressure, diuretic dose adjusted by weight, lymphocyte count, hemoglobin, serum sodium, total cholesterol, and uric acid; 10 categorical variables: sex, ischemic	c-statistic: - 1y post-discharge survival: 0.666 - 2y post-discharge survival: 0.721	Level of evidence: high risk of bias • 12 patients died during hospitalisation (excluded)

Study ID	Method	Patient characteristics	Model	Results	Critical appraisal of study quality
			cardiomyopathy, QRS>120 ms, use of β-blockers, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, potassium-sparing diuretic, statins and allopurinol, and ICD/CRT status - Outcome: 1y, 2y and 3y mortality		

Abbreviations: 95%CI: 95% confidence interval; AUC: area under the curve; CoI: conflicts of interest; CRT: cardiac resynchronization therapy; ICD: implantable cardioverter-defibrillator; LVEF: left ventricular ejection fraction; MA: meta-analysis; MD: mean difference; NS: not significant; NYHA: New York Heart Association; QOL: quality of life; RCT: randomized controlled trial; SR: systematic review.

Referenties

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