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

Study ID	Method	Patient characteristics	Results	Critical appraisal of review quality
	• 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

Study ID	Method	Patient characteristics	Model	Results	Critical appraisal of study quality
			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

Study ID	Method	Patient characteristics	Model	Results	Critical appraisal of study quality
	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

Alba AC, Agoritsas T, Jankowski M, et al. Risk prediction models for mortality in ambulatory patients with heart failure: a systematic review. Circ. Heart fail. 2013;6(5):881-9.

Bjurman C, Holmstrom A, Petzold M, et al. Assessment of a multi-marker risk score for predicting cause-specific mortality at three years in older patients with heart failure and reduced ejection fraction. Cardiol J. 2015;22(1):31-6.

Hussain S, Kayani AM, Munir R, et al. Validation of the Seattle Heart Failure Model (SHFM) in heart failure population. J Coll Physicians Surg Pak. 2014;24(3):153-6.
Pocock SJ, Ariti CA, McMurray JJ, et al. Predicting survival in heart failure: a risk score based on 39 372 patients from 30 studies. Eur Heart J. 2013;34(19):1404-13.
Salah K, Kok WE, Eurlings LW, et al. A novel discharge risk model for patients hospitalised for acute decompensated heart failure incorporating N-terminal pro-B-type natriuretic peptide levels: a European coLlaboration on Acute decompeNsated Heart Failure: ELAN-HF Score. Heart. 2014;100(2):115-25.
Sartipy U, Dahlstrom U, Edner M, et al. Predicting survival in heart failure: validation of the MAGGIC heart failure risk score in 51,043 patients from the Swedish heart failure registry. Eur J Heart Fail. 2014;16(2):173-9.
Scrutinio D, Ammirati E, Guida P, et al. The ADHF/NT-proBNP risk score to predict 1-year mortality in hospitalized patients with advanced decompensated heart failure. J Heart Lung Transplant. 2014;33(4):404-11.
Scrutinio D, Ammirati E, Passantino A, 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(5):1076-83.
Shiraishi Y, Sawano M, Kohno T, et al. Validation of the Seattle Heart Failure Model in Japanese heart failure patients. International Journal of Cardiology. 2016;203:87-9.
Uszko-Lencer NH, Frankenstein L, Spruit MA, et al. TIME-CHF Investigators. Int J Cardiol. 2017 Jan 15;227:901-907. doi: 10.1016/j.ijcard.2016.11.122. Epub 2016 Nov 9. Predicting hospitalization and mortality in patients with heart failure: The BARDICHE-index.

UITGANGSVRAAG: Leidt advance care planning bij patiënten met hartfalen (NYHA-klasse III-IV) tot een betere kwaliteit van leven en/of hogere tevredenheid van de patiënt en de familieleden?

Systematic reviews

Study ID	Method	Patient characteristics	Intervention(s)	Results	Critical appraisal of review quality
Kirlos 2014	• SR • Funding/CoI: no CoI • Search date: Apr 2013 • Databases: Medline; bibliographies • Study designs: controlled studies, before-after studies • N included studies: N=6	• Eligibility criteria: studies with a well-defined intervention, that identified as outcome either hospice referral or hospice enrollment, and quantitatively compared the outcome variable between the intervention group and a control group, or between time periods before and after the intervention was implemented; patients at the end of their lives	Interventions to increase hospice referral/ enrollment	One study evaluated ACP in heart failure patients: Schellinger 2011: • The intervention included the process of referral and enrollment into disease specific advanced care planning (DS ACP), and encompassed 5 steps: (1) referral to DS ACP (through discharge orders, direct referral from medical provider, or referral request sent by facilitators to primary care physicians; (2) referral coordinators explained to patients the ACP process and scheduled a visit with program facilitators (registered nurses, and social workers); (3) Facilitators and patients discuss end-of-life wishes; (4) facilitators include needs and wishes in the EMR; and (5) the facilitators follow-up with the patients' providers • DS-ACP participants were more likely to have used hospice compared to nonparticipants (56% versus 37%, p=0.002) • 94.3% of those completing the DS-ACP process, had a health directive compared to 24.8% of noncompleters (p<0.001)	• Low-quality review • English literature only

Study ID	Method	Patient characteristics	Intervention(s)	Results	Critical appraisal of review quality
Singer 2016	• SR • Funding/CoI: supported by grant R01 NR013372 from the National Institute of Nursing Research, a Cambia Health Foundation Sojourns Award, and the California HealthCare Foundation ; no CoI • Search date: Jan 2015 • Databases: Medline, Embase, PsycInfo, CDSR, Web of	• Eligibility criteria: ○ Adults at least 18 years old with advanced illness, and/or their caregivers ○ Health service interventions addressing patient and/or caregiver quality-of-life-related elements in intervention design and/or as outcomes ○ Cancer, heart failure and other cardiac conditions, chronic pulmonary disease, dementia and other neurological conditions, end-stage liver disease, or end-stage renal	Palliative care interventions	No RCT on ACP in heart failure patients	• High-quality review

Study ID	Method	Patient characteristics	Intervention(s)	Results	Critical appraisal of review quality
	Science, CareSearch Palliative Care Knowledge Network Review Collection • Study designs: RCTs • N included studies: N=124	disease, or any advanced illness populations receiving palliative care, hospice, or end-of-life care ○ Randomized controlled trials ○ Published between January 1, 2001, and January 8, 2015			

Primaire studies

Study ID	Method	Patient characteristics	Interventions	Results	Critical appraisal of study quality
Denvir 2016	• Design: RCT • Funding/CoI: funded by Marie Curie Research (Project Grant A15867); no CoI • Setting: • Sample size:	• Eligibility criteria: patients during an unscheduled hospital admission with heart failure and/or acute coronary syndrome based on European Society of Cardiology	Future care planning (N=25): 3 main components, i.e. (1) initial one hour semi-structured meeting with the trial	Quality of life: CRITICAL OUTCOME • EQ-5D: no significant adjusted mean difference at the 12 (-0.01; 95%CI -0.16 to 0.13) or 24 week time points (-0.07; 95%CI -0.25 to 0.11) Quality of death: CRITICAL OUTCOME	Level of evidence: high risk of bias • Risk of selection bias: out of 137 eligible patients, 87 were not randomised, of which 54 for

Study ID	Method	Patient characteristics	Interventions	Results	Critical appraisal of study quality
	N=50 • Duration: enrolment Oct 2013 – Sept 2014; 24w follow-up	guidelines; predicted 12-month mortality risk of 20% or greater estimated using the Global Registry of Acute Coronary Syndrome (GRACE) score for ACS and the Enhanced Feedback for Effective Cardiac Treatment (EFFECT) score for heart failure and patients with aortic stenosis who presented with heart failure; no dementia, prognosis < 30d or on palliative care register • *A priori* patient characteristics: intervention vs. control ○ Mean age: 81.9 vs. 80.2y ○ Male : 68% vs.	cardiologist (MD) and the trial nurse specialists involving the patient and their carer; followed by two 1 hour meetings with the trial nurse in the patient's home at 6 and 12 weeks; (2) Discussion and documentation of an agreed personal Future Care Plan which was sent to each patient and uploaded by the general practitioner using the electronic KIS; (3)	• Deaths: 4 vs. 3 • Place of death: home 1 vs. 0 <u>Satisfaction of patient</u>: CRITICAL OUTCOME • Patients appreciated the ongoing contact and communication <u>Satisfaction of family</u>: CRITICAL OUTCOME • No difference in mean QoL score, anxiety/distress score and caregiver burden between the intervention groups <u>Readmission</u>: CRITICAL OUTCOME • No difference in the number of unscheduled readmissions to hospital: 12 weeks RR 1.25 (95%CI 0.54-2.89), 6 months RR 1.23 (95%CI 0.64-2.34) • No difference in the number of unscheduled cardiovascular readmissions: 12 weeks RR 1.22 (95%CI 0.41-3.62), 6 months RR 0.83 (0.33-2.11)	unclear reasons • Very probably unblended • No intention-to-treat analysis for some outcomes

Study ID	Method	Patient characteristics	Interventions	Results	Critical appraisal of study quality
		52% ○ Heart failure: 56% vs. 80%	Ongoing telephone support (available Monday to Friday, 9am–5pm) from the trial nurse for the 12 weeks offering advice, support and information about their healthcare and social needs <u>Usual care</u> (N=25)	<u>% CPR in end stage</u>: CRITICAL OUTCOME • Not reported	
Dev 2012	• Design: comparative observational study • Funding/CoI: National Heart, Lung, and Blood Institute (N01-HV-98177); Duke Clinical	• Eligibility criteria: patients hospitalised with advanced heart failure • *A priori* patient characteristics: intervention vs. control ○ Median age: 64 vs. 56y ○ Male : 65% vs.	<u>DNR order</u> (N=26): do not resuscitate <u>Full code order</u> (N=349): 'attempt CPR' or 'attempt CPR but do not intubate'	<u>Quality of life</u>: CRITICAL OUTCOME • Time-trade-off utility: median willingness to trade 12 versus 1of 24 months of theoretical survival time • Seven of 13 (54%) DNR patients expressed a desire for 'half time-trade-off' (willingness to trade ≥12 months of 24 month survival) compared with 60	Level of evidence: high risk of bias • Patients were included in the ESCAPE randomised trial • Lost-to-follow-up for time-trade-off: 13 vs. 70

Study ID	Method	Patient characteristics	Interventions	Results	Critical appraisal of study quality
	Research Institute, Durham, NC, USA; no CoI • Setting: multicentre, US • Sample size: N=375 • Duration: inclusion Jan 2000 – Nov 2003; 1 month follow-up	74%		of 279 (22%) Full Code patients (p=0.007, X^2) <u>Quality of death</u>: CRITICAL OUTCOME • Not reported <u>Satisfaction of patient</u>: CRITICAL OUTCOME • Not reported <u>Satisfaction of family</u>: CRITICAL OUTCOME • Not reported <u>Readmission</u>: CRITICAL OUTCOME • DNR patients did not differ in 6-month rehospitalization rate (p=0.79, log-rank test) <u>% CPR in end stage</u>: CRITICAL OUTCOME • Not reported	
Dunlay 2012	• Design: comparative observational study • Funding/CoI: supported by grants from the National	• Eligibility criteria: patients presenting with heart failure • *A priori* patient characteristics: intervention vs. control	<u>Advance directive</u> (N=249) <u>No advance directive</u> (N=359)	<u>Quality of life</u>: CRITICAL OUTCOME • Not reported <u>Quality of death</u>: CRITICAL OUTCOME • Patients with AD specifying limits were less likely to	Level of evidence: high risk of bias • No blinding

Study ID	Method	Patient characteristics	Interventions	Results	Critical appraisal of study quality
	Institutes of Health (HL72435) and the Rochester Epidemiology Project from the National Institute of Aging (R01 AG034676); some authors have links with Boston Scientific • Setting: population-based study, US • Sample size: N=608 • Duration: inclusion Oct 2007 – Oct 2011; mean follow-up 1.8y	○ Mean age: 79.8 vs 70y ○ Male : 49% vs. 59% ○ NYHA 3 or 4: 63% vs. 67%		receive mechanical ventilation compared with others who died without an AD or with an AD without limits (adjusted OR 0.26; 95%CI 0.06–0.88; p=0.03) • No difference in risk of ICU care (adjusted OR 0.45; 95%CI 0.16 –1.29; p=0.14) <u>Satisfaction of patient</u>: CRITICAL OUTCOME • Not reported <u>Satisfaction of family</u>: CRITICAL OUTCOME • Not reported <u>Readmission</u>: CRITICAL OUTCOME • No difference in the risk of hospitalization in the last month of life in those with an AD with limits compared with those without (adjusted OR 1.26; 95%CI 0.64 –2.48; p=0.51) <u>% CPR in end stage</u>: CRITICAL OUTCOME • Not reported	

Abbreviations: 95%CI: 95% confidence interval; ACP: advanced care plan; CoI: conflicts of interest; CPR: cardiopulmonary resuscitation; MA: meta-analysis; MD: mean difference; NS: not significant; OR: odds ratio; QOL: quality of life; RCT: randomized controlled trial; RR: relative risk; SR: systematic review.

Referenties

Denvir MA, Cudmore S, Highet G, et al. Phase 2 Randomised Controlled Trial and Feasibility Study of Future Care Planning in Patients with Advanced Heart Disease. Sci Rep. 2016;6:24619 LID - 10.1038/srep [doi].

Dev S, Clare RM, Felker GM, et al. Link between decisions regarding resuscitation and preferences for quality over length of life with heart failure. Eur J Heart Fail. 2012;14(1):45-53.

Dunlay SM, Swetz KM, Mueller PS, et al. Advance directives in community patients with heart failure. Circ Cardiovasc Qual Outcomes. 2012;Cardiovascular Quality & Outcomes. 5(3):283-9.

Kirolos I, Tamariz L, Schultz EA, et al. Interventions to improve hospice and palliative care referral: a systematic review. J Palliat Med. 2014;17(8):957-64.

Singer AE, Goebel JR, Kim YS, et al. Populations and Interventions for Palliative and End-of-Life Care: A Systematic Review. J. Palliative Med. 2016;19(9):995-1008