**PROBAST**

Study:

Early Indication of Decompensated Heart Failure in Patients on Home-Telemonitoring

Step 2: Type of prediction study

**Is the study a diagnostic or a prognostic study?**

Diagnostic

**Is the study a development only, development and validation or validation only study?**

Development only

**What is the model of interest?**

MACD algorithm

**What is the outcome of interest?**

Detect heart failure decompensation.

Step 3: Assess risk of bias

**Domain 1: Participants**

**Describe the sources of data and criteria for participant selection**

Six HF clinics in Germany and Spain participated in the collection of the clinical data. Patients were included in the study if they had chronic HF with an elevated N-terminal of the prohormone brain natriuretic peptide (NT-proBNP ≥ 500 pg/ml), were taking at least 40 mg/day of furosemide or an equivalent, and were in the New York Heart Association (NYHA) functional class II, III, or IV. They were excluded if they had the following: severe chronic obstructive pulmonary disease (COPD GOLD Class > 2), primary pulmonary hypertension, renal insufficiency requiring dialysis, a psychiatric or neurological disorder of moderate to severe degree (eg, dementia, schizophrenia, substance disorder, psychotic depression), prior acute myocardial infarction or coronary artery bypass grafting (CABG) in the previous 3 months.

**1.1 Were appropriate data sources used, e.g. cohort, RCT or nested case-control study data?**

**Y**

**1.2 Were all inclusions and exclusions of participants appropriate?**

Y

**Risk of bias introduced by selection of participants:**

Low

**Rationale of bias rating**

Appropriate data source and inclusion criteria

**Domain 2: Predictors**

**List and describe predictors included in the final model, e.g. definition and timing of assessment**

Measurements were carried out in the morning before eating breakfast. Body weight was collected using a weight scale (Philips Medical Systems, Andover,Massachusetts, USA), which automatically logged the measurements.

TTI was measured using a wearable bio-impedance vest.

**2.1 Were predictors defined and assessed in a similar way for all participants?**

Y

**2.2 Were predictor assessments made without knowledge of outcome data?**

Y

**2.3 Are all predictors available at the time the model intended to be used?**

Y

**Risk of bias introduced by predictors or their assessment**

Low

**Rationale of bias rating**

Good to apply. Independent and assessed the same way for everyone.

**Domain 3: Outcome**

**Describe the outcome, how it was defined and determined, and the time interval between predictor assessment and outcome determination:**

Hospitalization from decompensation.

**3.1 Was the outcome determined appropriately?**

Y

**3.2 Was a pre-specified or standard outcome definition used?**

Y

**3.3 Were predictors excluded from the outcome definition?**

Y

**3.4 Was the outcome defined and determined in a similar way for all participants?**

Y

**3.5 Was the outcome determined without knowledge of predictor information?**

N

**3.6 Was the time interval between predictor assessment and outcome determination appropriate?**

Y

**Risk of bias introduced by the outcome or its determination**

High

**Rationale of bias rating**

As mentioned in the limitations, physicians could have intervened based on patient weight development. There is the risk that patients were hospitalized due to changes in weight. So independence of outcome is not guaranteed.

**Domain 4: Analysis**

**Describe number of participants, number of candidate predictors, outcome events and events per candidate predictor**

Among the 91 patients for whom data were included in the analysis, 24 heart failure-related hospitalizations occurred in19 patients. Of the 24 hospitalizations, 9 had less than 3 weekly weight recordings and 12 had less than 3 weekly impedance recordings preceding the hospitalization, and were excluded from the analysis.

**Describe how the model was developed, predictor selection and risk group definition**

Three algorithms introduced, MACD outperformed the other algorithms.

In the MACD algorithm, the long-term average parameter Nl was varied between 10 and 50days in increments of 5 days, and the short-term moving average parameter Ns was varied between 1 and 10 days.

Parameter optimization

**Describe whether and how the model was validated, either internally (cross validation, random split sample) or externally (e.g. temporal validation, geographical validation, different setting, different type of participants)**

LOOCV

**Describe the performance measures of the model, e.g. calibration, discrimination, classification, net benefit, and whether they were adjusted for optimism**

SEN, SPE, PRE, REC

**Describe any participants who were excluded from the analysis**

Of 148 patients recruited from October 2008 to July 2010, 108had the system installed and data recorded; 3 did not fit the criteria, 3 were unavailable at installation, 1 died before installation, and 33 withdrew before system installation. Of the remaining 108 users, 17 used the system on less than 30occasions, leaving 91 patients as the focus of this exploratory analysis.

**Describe missing data on predictors and outcomes as well as methods used for missing data**

Of the 24 hospitalizations, 9 had less than 3 weekly weight recordings and 12 had less than 3 weekly impedance recordings preceding the hospitalization, and were excluded from the analysis.

**4.1 Were there a reasonable number of participants with the outcome?**

N

**4.2 Were continuous and categorical predictors handled appropriately?**

Y

**4.3 Were all enrolled participants included in the analysis?**

N

**4.4 Were participants with missing data handled appropriately?**

PN

**4.5 Was selection of predictors based on univariable analysis avoided?**

Y

**4.6 Were complexities in the data (e.g. censoring, competing risks, sampling of controls)**

**accounted for appropriately?**

Y

**4.7 Were relevant model performance measures evaluated appropriately?**

Y

**4.8 Were model overfitting and optimism in model performance accounted for?**

Y

**4.9 Do predictors and their assigned weights in the final model correspond to the results**

**from multivariable analysis?**

U

**Risk of bias introduced by the analysis**

High

**Rationale of bias rating**

Only very few outcomes. 17 patients removed due to incomplete data, also a lot of outcomes removed due to too little predictor data.

**Overall Risk of bias**

High