

INPLASY PROTOCOL

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Higher BNP/NT-pro BNP levels stratify prognosis equally well in patients with and without heart failure – a meta-analysis with more than 89,000 patients

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Review question / Objective: We performed a meta-analysis to investigate, whether the value of BNP/NT-proBNP as predictors of long-term prognosis differentiates in cohorts with and without heart failure.

Condition being studied: The standardised cut-off levels for BNP and NT-proBNP that are currently used in clinical practice are based on the stratification of patients with heart failure. In patients without heart failure, however, relatively lower values are observed. This leads to the assumption that the prognosis for patients with BNP/NT-proBNP levels at the upper limit of the normal range might be worse than the prognosis for patients with BNP/NT-proBNP levels lower in the range, even if both are determined to be within the normal boundaries. However, a specific cut-off level of BNP/NT-proBNP for the prediction of prognosis in patients without heart failure has not yet been determined. Therefore, we performed a meta-analysis of existing studies investigating the value of BNP/NT-proBNP as a predictor of long-term prognosis in patients with heart failure and the general population.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 30 April 2022 and was last updated on 30 April 2022 (registration number INPLASY202240175).

INTRODUCTION

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METHODS

Search strategy: We performed a systematic review and meta-analysis of existing studies to evaluate the predictive ability of BNP/NT-proBNP for the long-term prognosis in patients with and without heart failure. The systematic review and meta-analysis of studies were performed following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and in accordance with the 'Meta-analysis Of Observational Studies in Epidemiology (MOOSE)' recommendations and the Cochrane Handbook for Systematic Reviews of Interventions. The database searches were performed by two authors in PubMed, the Cochrane Library, SCOPUS, and Web of Science. We used the following key search terms: "BNP" or "NT-proBNP" and "prognosis". Manuscripts with prospective data assessments published prior to 24 April 2020 were included in our search. We made our search specific and sensitive using Medical Subject Heading terms and free text. The search was restricted to full-text articles with human subjects that were published in English. All duplicates were identified and removed manually.

Participant or population: We included studies analyzing clinical as well as population based cohorts.

Intervention: We did not specifically search for any interventions.

Comparator: To ensure comparability, we analysed studies by dividing and analysing them based on the increments and BNP/NT-proBNP thresholds.

Study designs to be included: Studies evaluating the occurrence of events other than MACEs or all-cause mortality (e.g., atrial fibrillation) were excluded. Records were screened and studies were excluded with undesired topic, if no or only the abstract was available, if the full text article was not available in English language. Secondly, only full text articles were assessed for eligibility. Retrospective, meta-analysis, systematic reviews and undesired study designs were excluded. We excluded, studies not subdividing heart failure and non-heart failure individuals. However, analysing increase or decrease of BNP/NT-pro.

Eligibility criteria: The primary endpoint was defined as all-cause mortality or major cardiac events (MACE). MACE was defined differently in the included studies, however only studies including at least one of the following definitions were added: cardiovascular or all-cause mortality, myocardial infarction, stroke, or heart failure hospitalization.

Information sources: PubMed, the Cochrane Library, SCOPUS, and Web of Science.

Main outcome(s): BNP/NT-proBNP levels are predictors for adverse long-term outcome in patients with and without known heart failure.

Data management: All analyses were performed using Review Manager 5.4 (The Cochrane Collaboration).

Quality assessment / Risk of bias analysis: In order to preclude publication bias we performed publication bias analysis in form of funnel plots.

Strategy of data synthesis: All analyses were performed using Review Manager 5.4 (The Cochrane Collaboration).

Subgroup analysis: To ensure comparability, we analysed studies by dividing those that separated the BNP/NT-proBNP levels into quartiles using pre-defined cut-off levels and those that calculated hazard ratios via log-transformed BNP/NT-proBNP levels or per 1 SD increase and analysing them.

Sensitivity analysis: No sensitivity analysis was performed.

Language: English.

Country(ies) involved: Germany.

Keywords: BNP, NT-proBNP, prognosis, general population cohorts.

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