**EuPreCHO – Study Synopsis**

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| **Project Title:** | EuPreCHO: European study on perioperative management and outcome following Preoperative Transthoracic Echocardiography in noncardiac surgery patients. |
| **Short Title :** | EuPreCHO |
| **CTGOV ID** | NCT06409234 |
| **Protocol Version and Date:** | Version 1.0, dated 25June2024 |
| **Project design:** | International, prospective case control study |
| **Background and Rationale:** | In August 2022 the European Society of Cardiology (ESC) published updated guidelines (previous version 2014) including recommendations on preoperative transthoracic echocardiography (TTE). The update resulted in broadened criteria for preoperative TTE. The impact of preoperative TTE on outcome is controversial and the evidence was mostly derived from administrative databases. There is also a knowledge gap in terms of what changes in perioperative management are derived from TTE information in current daily practice and what their impact on outcome may be. Further, a secondary analysis in a large international cohort suggests that the criteria endorsed by the ESC guidelines to define the class of recommendation of TTE may not be efficient. Suggest: In August 2022, the European Society of Cardiology (ESC) published updated guidelines (previous version: 2014), which include new recommendations on preoperative transthoracic echocardiography (TTE). These updates have broadened the criteria for preoperative TTE. However, the impact of preoperative TTE on patient outcomes remains controversial, with most evidence derived from administrative databases. There is a knowledge gap regarding how TTE information influences perioperative management in current practice and its subsequent impact on outcomes. Additionally, a secondary analysis of a large international cohort suggests that the ESC criteria for TTE recommendations may not be efficient. |

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| **Objective(s):** | **Main objective:**<br>EuPreCHO aims at answering the following 3 research questions (RQ) with regard to patients undergoing intermediate and high-risk noncardiac surgery procedures:<br>1. does the perioperative management of patients evaluated with vs those not evaluated with preoperative TTE differ in current clinical practice?<br>2. does the outcome of patients evaluated with vs those not evaluated with preoperative TTE differ in current clinical practice?<br>3. what factors (model) enhance the prediction of major pathologies in preoperative TTE?<br><br>**Secondary objectives:**<br>To answer the question: does preoperative NTproBNP compared to preoperative troponin contribute to the prediction of major cardiac pathologies in patients that undergo preoperative TTE.<br><br>**Tertiary objective**<br>To explore how information on TTE detected major pathologies compared to preoperative troponin and to preoperative NTProBNP information, respectively, contributes to the prediction of 1) disability-free survival and 2) major adverse cardiac events (should the number of events be sufficient). |

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| **Outcomes(s):** | **RQ1**: Primary endpoint will be intensified perioperative management defined as one or more of the following:<br>• discussion in preoperative multidisciplinary board and derived decisions (e.g. technique modifications, cancellations, postponing of scheduled procedure)<br>• optimization of cardiovascular medication<br>• cardiac workup<br>• invasive or advanced intraoperative haemodynamic monitoring<br>• goal-directed haemodynamic management<br>• anaesthesia technique<br>• planned ICU/IMC admission or planned extended PACU stay.<br><br>**RQ2**: Primary endpoint will be disability- free survival at 30 days (12-item WHODAS questionnaire). Secondary endpoints will be: 30-day all-cause mortality, 30-day composite of all-cause death and myocardial infarction, 30-day major adverse cardiac events (cardiac death, myocardial infarction, cardiac arrest, coronary revascularization, acute heart failure/ decompensation of chronic heart failure), days-alive-and-out-of-hospital (DAOH) at 30 days, and in-hospital complications (Clavien-Dindo Class ≥3). Tertiary endpoints are ICU/IMC (re)-admission and length of ICU/IMC stay.<br><br>**RQ3:** The endpoint will be a composite of major pathologies in TTE consisting in<br>• Moderate-severe left ventricular systolic dysfunction<br>• Significant (Grade II or more) LV diastolic dysfunction with evidence of increased LV filling pressures<br>• Significant right ventricular dysfunction<br>• Severe left-sided valvulopathies |
| **Inclusion / Exclusion criteria:** | *Included* are inpatients planned for elective, inhospital, intermediate or high-risk noncardiac surgery procedures AND either aged ≥65 years or presenting ≥2 cardiovascular risk factors or with known cardiovascular disease. 'Exposed' will be patients in whom TTE was performed up to 6 months before surgery. 'Non-exposed' will be patients in whom TTE was NOT performed.<br>*Exclusion criteria* are age <18 years, day surgery, urgent/emergency procedures, ICU patient at time of enrollment, cardiac surgery up to 30 days prior to the index noncardiac procedure, unwilling or unable to provide informed consent, unable to complete the WHODAS questionnaire (literacy or language barrier), previous enrollment in EuPreCHO (in case of repeated surgery) |

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| **Project assessments:** | Baseline: 12-item WHODAS questionnaire and troponin measurement (where applicable + NTproBNP); extraction of relevant clinical data (history of illness, planned operation, etc.) from medical charts; extraction of TTE findings from clinically indicated TTE.<br>At discharge: extraction of relevant clinical data (ICU admission, in-hospital complications, length of stay, etc.) from medical charts.<br>At day 30 after surgery: follow-up by mail or by phone for outcome assessment (12-item WHODAS questionnaire and the collection of information on postoperative events). |
| **Number of Participants:** | 5393 exposed (TTE within 6 months before surgery) and 2696 non-exposed.<br>*Of note, the 2:1 exposed-to-non-exposed ratio was chosen to reduce the burden for centres both in terms of data collection and in terms of preoperative biomarkers to be measured, while maintaining the power for the modelling to improve prediction of major pathologies in TTE.* |
| **Project Duration, schedule:** | Follow-up duration is 30 days. |
| **Statistical Considerations:** | RQ1: multilevel logistic regression with predefined variables. As alternative statistical approach (sensitivity analyses), we will calculate the propensity score for receiving TTE using logistic regression and insert it as a covariate in a logistic regression model, both bivariately and multivariately (double robust).<br>RQ2: multilevel logistic regression with predefined variables. In sensitivity analyses, clinical factors will be substituted by clinical risk scores (RCRI, NSQIP MICA, AUB-HAS2 Cardiovascular Risk Index). As alternative statistical approach (sensitivity analyses), we will calculate the propensity score for receiving TTE using logistic regression and insert it as a covariate in a logistic regression model, both bivariately and multivariately (double robust). For DAOH, due to the expected non-normal distribution, a quantile regression will be conducted.<br>RQ3: multivariable logistic regression with predefined covariates |
| **Risk-Benefit statement:** | The study is observational, i.e., it will collect pseudonymized data from preoperative TTE that are requested upon clinical decision of the attending clinicians (i.e., TTE is **NOT** study-mandated) and record information on the resulting perioperative management. Therefore, routine clinical management will not be affected. Study assessments consist of answering the WHODAS questionnaire and one preoperative blood sample (5 mL). Data handling will comply with the General Data Protection Regulation (GDPR) (EU) 2016/679. As such the risk associated with the study appears minimal. The benefit for future noncardiac surgery patients appears relevant as the data collected may contribute to more targeted, preoperative TTE therefore reducing potentially unnecessary testing and reducing procrastination of surgical procedures potentially resulting from "clogged" echo labs. On the other hand, the study will potentially identify risk groups where more targeted TTE will reduce the chance of missing relevant findings. |