A first in-silico trial of quantifying the drug effects of SGLT2i in heart failure.

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Abstract

Chronic heart failure (HF) is one of the most frequent causes of death worldwide, both in the short and long term, with approximately 50% of patients diagnosed with HF dying within 5 years. This suggests only a moderate success for current existing medical therapies despite intensive research into heart failure. Thus, we aim to supplement this by designing an in-silico trial which uses state-of-art personalized heart models and statistical approaches to quantify the benefit of SGLT2i (used in a drug trial) when added to current standard-of-care in attenuating adverse left ventricle (LV) remodelling in patients with heart failure.

The clinical trial provides the essential data for personalised heart models, developed within the SofTMech Centre, which are scaled up to 100 patients (the test group: 50 with SGLT2i, and the placebo group: 50 on placebo), structural and biomechanical trajectories of heart function will be quantified for each patient, and benefits of SGLT2i will be assessed by analysing key biomechanical biomarkers between the two groups from baseline (before treatment) to 24-36 weeks post treatment. Values of using the predictive in-silico model for the design of clinical trials in heart failure patients will be pursued, i.e. reducing the sample size, early termination. We use the completed data to examine any benefits of this new drug in attenuating adverse remodelling in heart failure patients, with preliminary analysis suggesting a benefit in terms of the biomechanical properties, slowing down adverse remodelling with a less stiff myocardium and required contractility to avoid depleting the contractile reserve completely.

We hope that this work helps establish a cornerstone of translating SofTMech-developed personalized heart models into the clinic, leading to the development of in silico trial platform for drug discovery in heart failure.