Metabolic phenotyping of heart failure cohort

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Background and Study Aim

Heart Failure (HF) is a heterogeneous clinical syndrome that is characterized by the inability to pump enough blood (1). The current classification of heart failure is based on the left ventricular ejection faction (LVEF). Patients are subdivided into three categories: HF with preserved ejection fraction (HFpEF) with LVEF ≥ 50%, the mid-range group (HFmrEF) with LVEF 40–49% and reduced ejection fraction (HFrEF) with LVEF < 40% (1). Although the clinical definitions of heart failure phenotypes and stages are well established, there is considerable heterogeneity within these phenotypes in terms of patients' clinical characteristics and worsening of heart failure prognoses. This heterogeneity results in groups of patients responding differently to treatments and achieving different outcomes.

Numerous and complex molecular perturbations involving energy metabolism, inflammation and autophagy, among other processes, characterize and precede myocardial dysfunction in heart failure (Figure 1). Therefore, the inclusion of molecularly defined endotypes could lead to the improvement of existing prevention strategies, including early preventive measures, and contribute significantly to more effective therapies through personalized treatment plans. With this in mind, investigating molecular states may be a promising strategy for identifying molecular biomarkers associated with the onset and progression of heart failure.

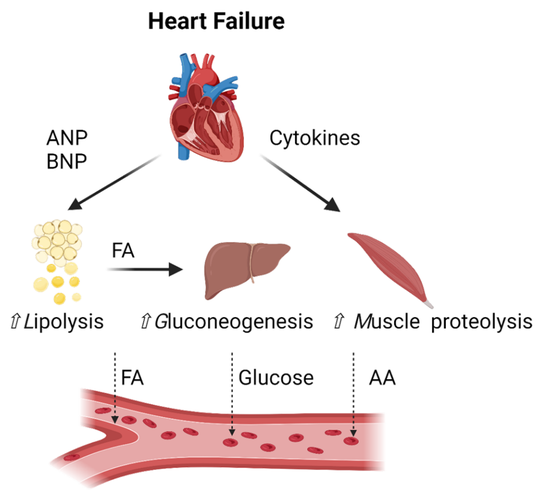
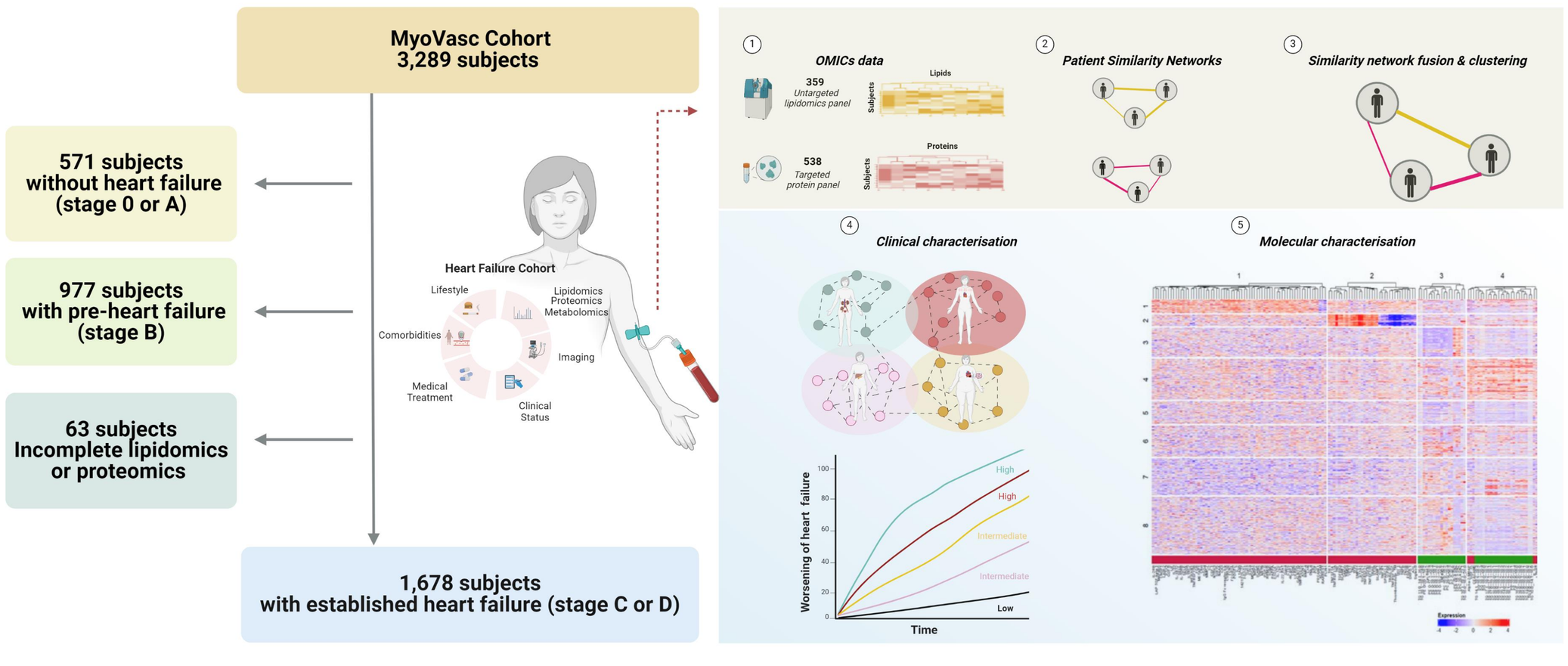


Figure 1. Numerous and complex molecular perturbations involving energy metabolism, inflammation and autophagy, among other processes, characterize and precede myocardial dysfunction in heart failure.

Previous studies have already attempted to cluster heart failure patients, based on various clinical and biochemical parameters. The current study will overcome some of the limitations of previous clustering attempts by investigating patients in heart failure stages C/D from the MyoVasc cohort (2). MyoVasc is an investigator-initiated, prospective, single-center cohort study based in the city of Mainz, in central-western Germany, featuring sequential deep clinical phenotyping, biobanking, and multi-omics data measurements. It involves all heart failure phenotypes (2), and we apply to it the clinically unbiased approach Similarity Network Fusion (3), which takes advantage of the complementary nature of the OMICs platform to define potentially clinically relevant patient clusters. To confirm the clinical relevance of the computational data-driven analysis, the anamnesis of the subjects, medication intake and risk factors are compared among obtained patient clusters.

Methods



Conclusion

This study leverages the large number of variables from a deeply clinically and molecularly characterized heart failure cohort, the MyoVasc study, together with the power of molecular data integration by Similarity Network Fusion (SNF) to identify novel heart failure patient subtypes and discriminating protein and lipid biomarkers that can be used in the clinic to tailor treatments and predict outcomes. We have demonstrated that Similarity Network Fusion (SNF) enables more accurate patient stratification by integrating multiple types of OMICs data, and further analyses integrating additional molecular datasets will enhance the identification of distinct molecular subgroups of heart failure patients for personalized treatment approaches.

References

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