CORRECTING THE EJECTION FRACTION FOR BETTER HEART FUNCTION REPRESENTATION AND PROGNOSIS IN HEART FAILURE

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Introduction

Ejection fraction (EF), defined as the percentage of blood ejected per heartbeat, is widely used to evaluate heart function during heart failure (HF), but it is known that geometric changes to the heart during disease remodeling can cause it to become an inaccurate assessment of cardiac function [1, 2]. For example, during heart failure preserved ejection fraction (HFpEF), EF did not decrease in cases with failing hearts. Here, we evaluate the dependency of EF on cardiac geometry, and propose here a correction factor to EF to prevent this dependency, and show that the corrected EF (EFc) have improved prognosis capability.

Method

The proposed EFc is theoretically equivalent to obtaining EF from the mid-myocardial wall layer instead of the endocardial layer. It can easily be calculated from routine echo scan results, as:

$$EFc = EF \times 1.9\left(\frac{EDV}{EDV + 0.5 \times LVM/\rho}\right)$$

where EDV was the end-diastolic volume and ρ was the myocardial density. The ability of EF and EFc to indicate cardiac function was first evaluated with a simple cardiac numerical model translating strains to stroke volume and vice versa, and then with a porcine model of HFpEF induced by gradual inflation of the aortic cuff [3]. Finally, the prognosis ability of EF and EFc was evaluated on a retrospective clinical patient cohort admitted to Imperial College Healthcare NHS Trust, UK, composing of patients who were admitted with a troponin test request and echo scan.

Result and Discussion

<u>*Our numerical model*</u> showed that EF elevated with increasing left ventricular (LV) wall thickness and decreased with increasing chamber dilation, even without a change to mid-wall myocardial strains. This demonstrated that EF deviated from trends of cardiac function when geometric remodeling occurred. However, EFc was not affected by geometric changes, and was constant across various cardiac geometries if mid-wall strains were unchanged.

<u>*Our animal model*</u> investigations showed that EFc could distinguish between HFpEF animals from healthy controls, but EF could not (Fig 1).

<u>*Our clinical data*</u> confirmed that patients with HFpEF could be distinguished from those without heart failure with EFc, but not with EF (Fig 2). We used a multivariate Cox proportional hazards regression model to predict hospital readmissions due to heart failure in the cohort. We find that both EF and EFc predicted readmissions equally well in the group with low EF (EF<50%). However, in the group where EF≥50%, predictive models with EFc were significantly more accurate in predicting readmissions within 3 years: the leave one out cross-validation ROC analysis showed 18.6% reduction in errors, while the Net Classification Index (NRI) analysis showed that risk classification of true positive increased by 12.2%, and risk classification of false negative decreased by 16.6%. This demonstrates improved prognosis accuracy.

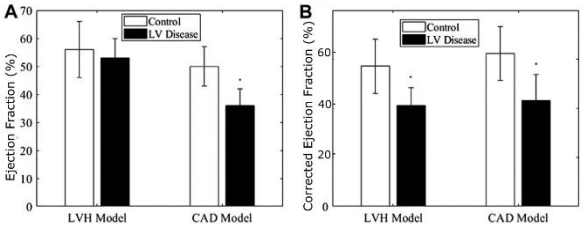

Figure 1: *(A) EF and (B) EFc in a left ventricular hypertrophy (LVH) animal model and a coronary artery disease (CAD) animal model, compared to their appropriate controls. *p < 0.05 compared to control.*

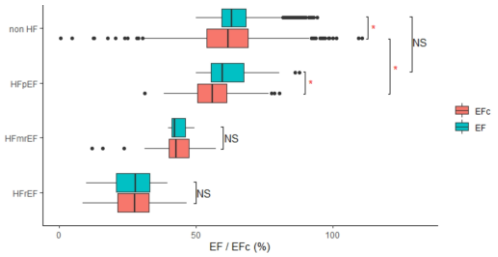

Figure 2: *EF and EFc of all patients, stratified into HFrEF (EF<40), HFmrEF (40≤EF<50) and HFpEF (EF≥50) and non-HF (not diagnosed with HF) based on ICD-10 codes. *p<0.05, NS: not significant, ANOVA.*

Conclusion

We developed a corrected factor to the EF that could mitigate the skewing effects of cardiac geometric remodelling, enable distinguishing between normal and HFpEF hearts, and improve prognosis of hospital readmissions due to heart failure.

References

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