Sex-specific difference in cardiac function in patients with systemic sclerosis: association with cardiovascular outcomes

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Funding Acknowledgement: Type of funding sources: None.

Background: Cardiac involvement is an important cause of hospitalization and mortality in patients with systemic sclerosis (SSc) and advanced echocardiographic measures such as left ventricular (LV) global longitudinal strain (GLS) have already demonstrated to improve risk-stratification. However, possible sex differences in echocardiographic parameters including LV GLS have not been explored so far.

Purpose: To compare standard and advanced echocardiographic parameters between men and women with SSc and evaluate their association with cardiovascular outcomes.

Methods: A total of 746 SSc patients from four different centers were included of which 628 (84%, 54±13 years) women and 118 (16%, 55±15 years) men. Baseline transthoracic echocardiographic (TTE) data with standard and advanced (LV GLS) measurements as well as clinical characteristics were analysed. The study endpoint was the composite of all-cause mortality and cardiovascular hospitalisations.

Results: Men and women showed several differences in terms of disease characteristics: greater modified Rodnan skin score, higher prevalence of diffuse cutaneous SSc, lung fibrosis and myositis, more impaired pulmonary function (DLCO) and higher creatine phosphokinase were observed in men, while women were characterized by longer disease duration, higher NT-proBNP and lower glomerular filtration rate. By TTE, men showed larger LV indexed volumes, lower LV ejection fraction and more impaired LV GLS [–19% (IQR –20% to –17%) vs. –21% (IQR: –22% to –19%, $p<0.001$)]. Considering the significant differences in clinical characteristics between men and women, a propensity matching score was applied to explore whether sex-differences in TTE parameters were maintained. The matching was performed according to age, disease duration, presence of diffuse SSc, lung fibrosis, DLCO and NT-proBNP (n=140); after matching, LV GLS still showed significant difference between men and women [–19% (IQR –20% to –18%) vs. –20% (IQR –22% to –18%, p=0.03)] while LV volumes and ejection fraction did not. After a median follow-up of 48 months (IQR: 26–80), the combined endpoint occurred in 182 patients and Kaplan-Meier survival analysis (Figure) showed that men experienced higher cumulative event rates as compared to women (Chi-square 8.648; Log rank 0.003) even after matching for clinical characteristics (Chi-square 7.211; Log rank 0.007); however, sex difference in outcomes was neutralized after matching groups according to LV GLS. Furthermore, LV GLS showed a significant association with prognosis in the overall group (HR: 1.173; 95% CI: 1.106–1.244, $p<0.001$) without significant interaction with sex (p=0.373), indicating a consistent prognostic value of LVGLS for both men and women.

Conclusions: Among patients with SSc, LV GLS is more impaired in men as compared to women even after matching for clinical characteristics, and its impairment is associated with higher prevalence of death and cardiovascular hospitalization.

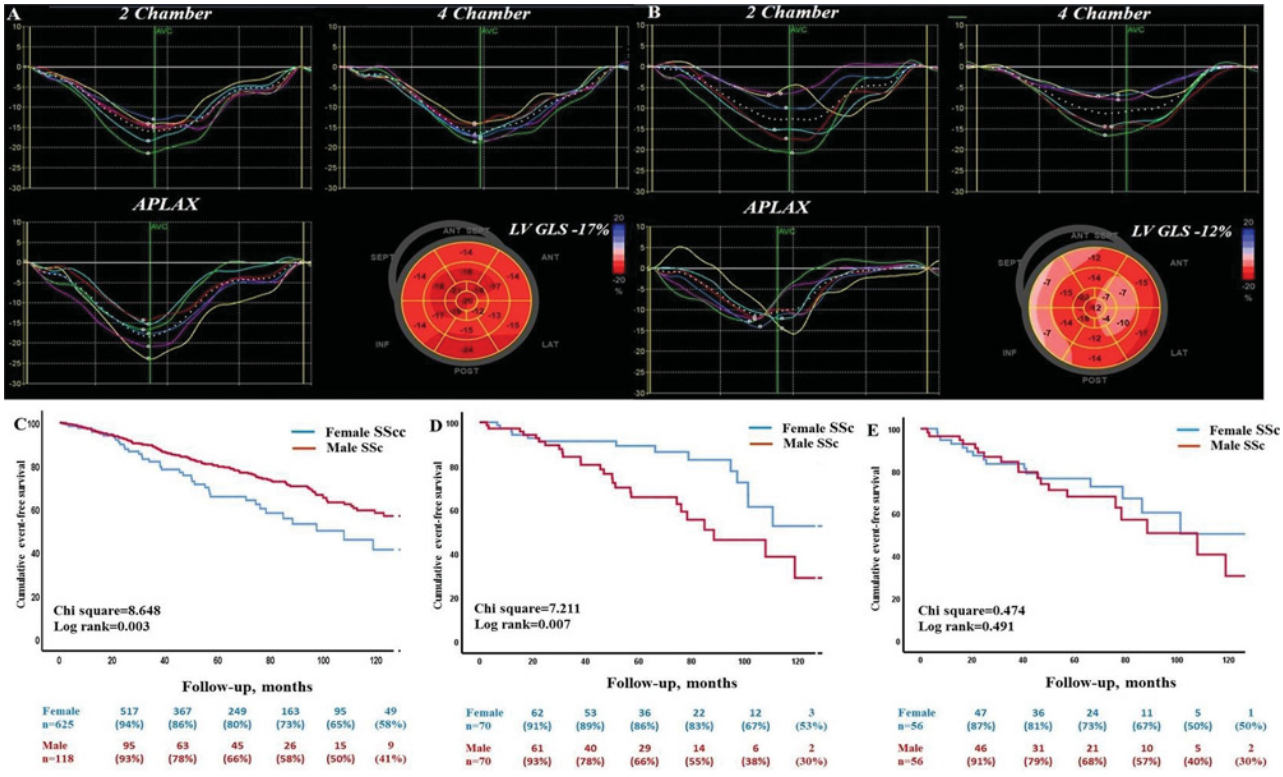

Figure: *LV GLS in woman (A) and man (B) SSc patients, Kaplan Meier survival curve for women and men SSc (C) patients, also adjusted for clinical variables: Age, diffuse SSc, DLCO-SB, lung fibrosis, disease duration, NT-pro BNP (D) and clinical variables +LV GLS (E).*