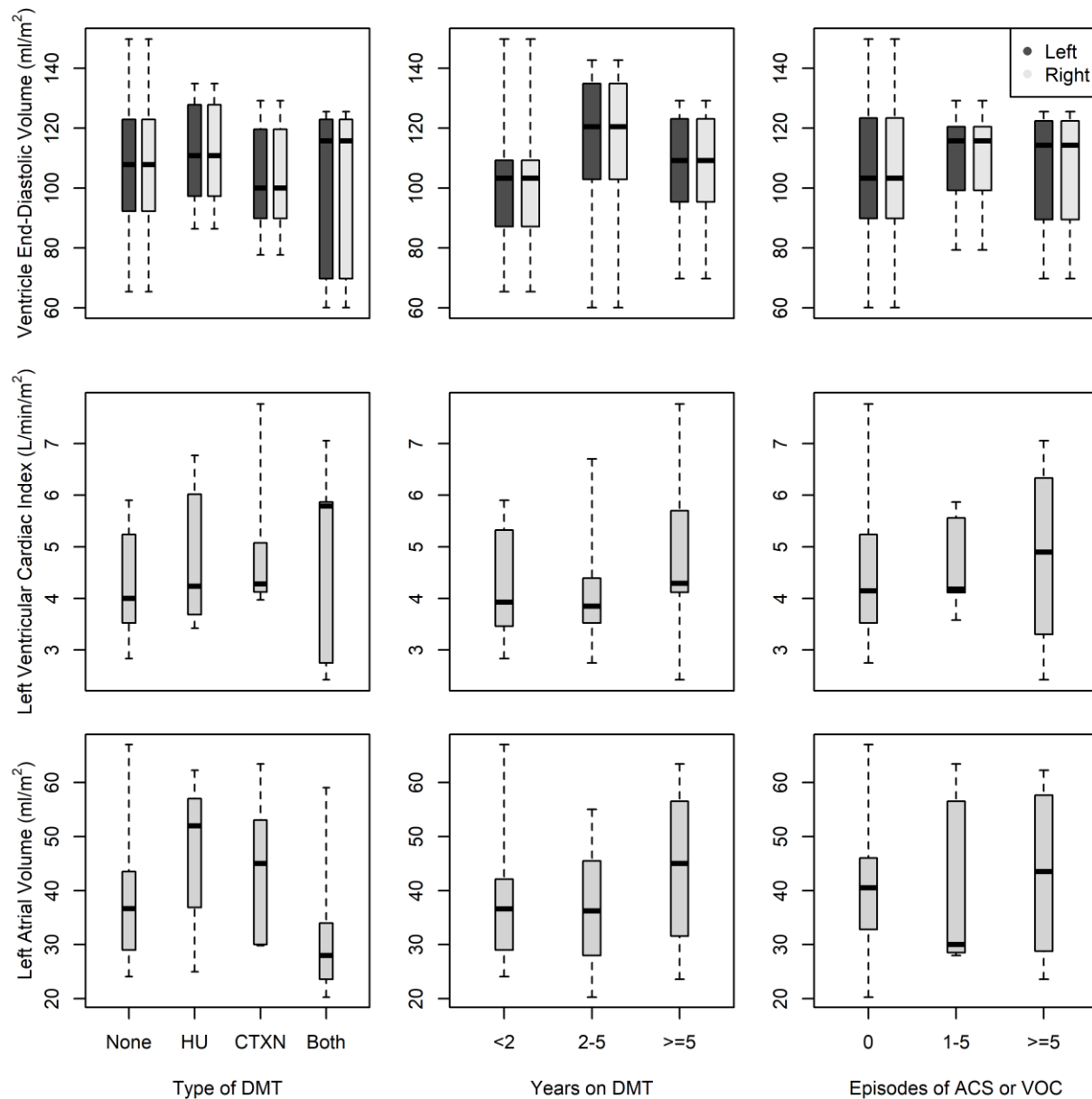
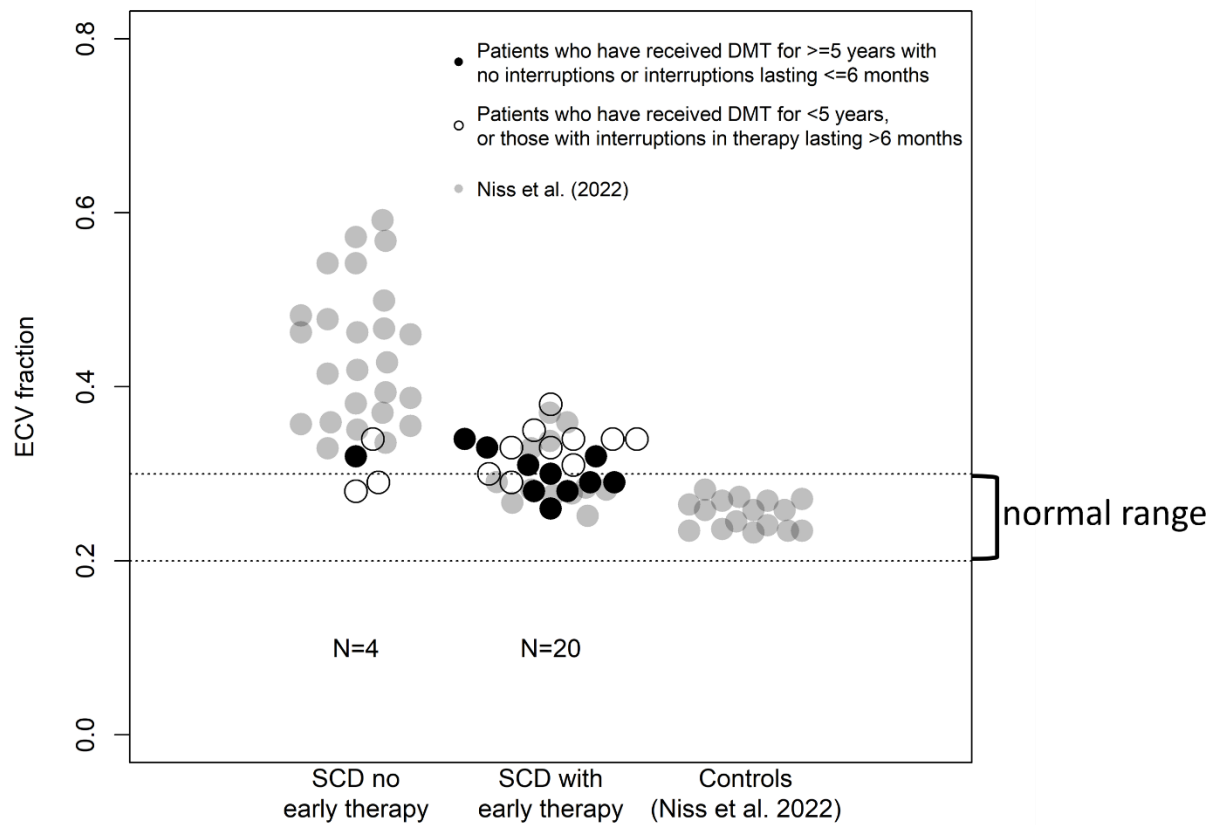


**Supplementary Figure 1.** Mid short-axis extracellular volume (ECV) map of a patient with hemoglobin SS. A region of interest (ROI) is drawn in the mid inferoseptal wall (black line).



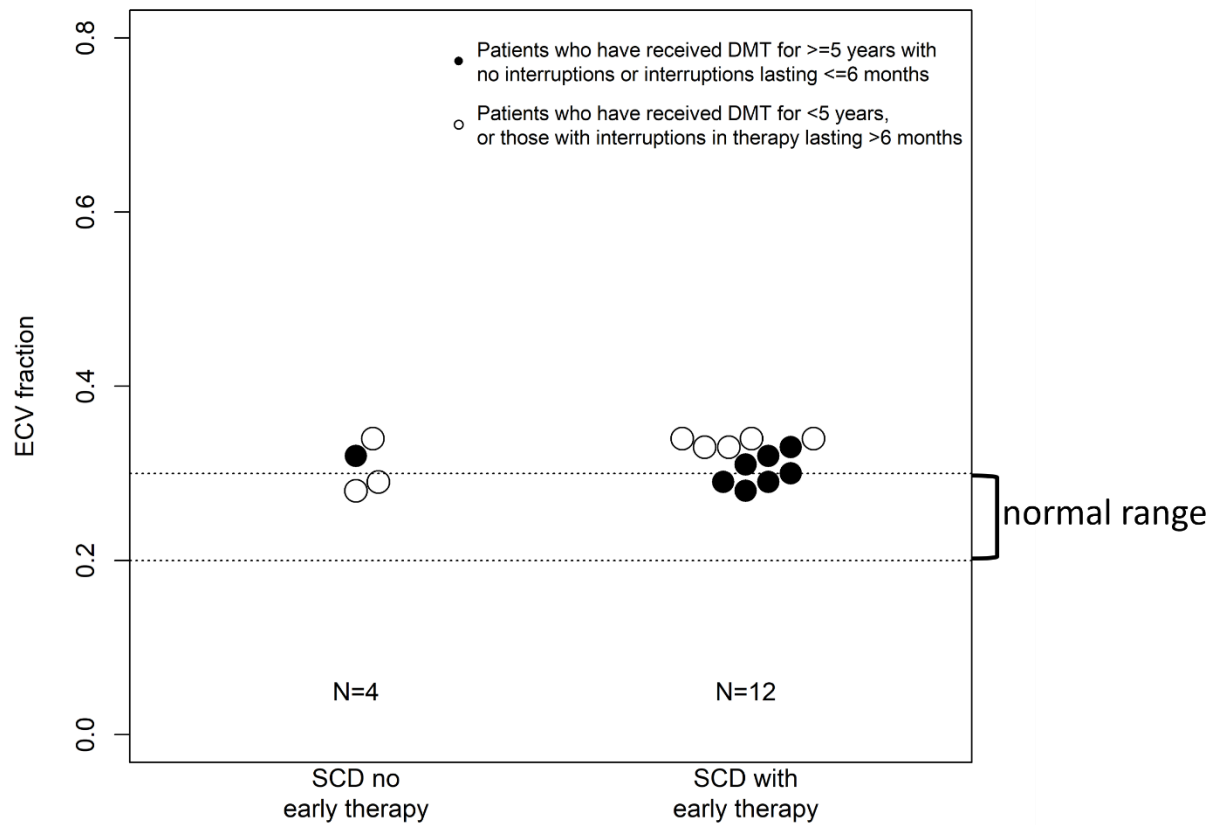
**Supplementary Figure 2.** Cardiac chamber dilation (left ventricle [LV], right ventricle [RV], and left atrium [LA]) is a common feature in children with SCA and does not change appreciably with the type of disease-modifying therapy (DMT), years on DMT, or the number of episodes of acute chest syndrome (ACS) or veno-occlusive crises (VOC). Elevated cardiac index (CI) is common in children with SCA despite receiving hydroxyurea (HU) and chronic transfusion therapy (CTXN).

### Disease modifying therapy begun at <6 years or >=6 years



**Supplementary Figure 3.** ECV was not different among children who started disease-modifying therapies at less than six years of age (SCA with early therapy) or after (SCA no early therapy) even when patients who had ever received chronic transfusion therapy were excluded from the SCA no early therapy group (Similar to the exclusion in the Niss *et al.* study). Datapoints from our cohort are overlayed in solid black circles or open circles. Solid grey circles represent data points from Niss *et al.* (2022) for comparison.

### Disease modifying therapy begun at <3 years or >=3 years



**Supplementary Figure 4.** Starting disease-modifying therapy at an even earlier age (at less than three years of age) has no further protective effect and the ECV of the two cohorts (SCA with early therapy vs. SCA no early therapy) excluding patients who had ever received chronic transfusion therapy from the SCA no early therapy group. Datapoints from our cohort are overlaid in solid black circles or open circles. Solid grey circles represent data points from Niss *et al.* (2022) for comparison.

**Supplementary Table 1.** Echocardiographic characteristics of the entire cohort.

	Median (IQR)
Days before CMR	93 (11 – 182)
Weight (kg)	56.0 (43.1 – 68.5)
BSA (m <sup>2</sup> )	1.59 (1.38 – 1.82)
3D LVEDVi (ml/m <sup>2</sup> ) <sup>1</sup>	72.9 (60.0 – 81.0)
3D LVESVi (ml/m <sup>2</sup> ) <sup>1</sup>	27.2 (21.7 – 32.3)
3D LVEF (%) <sup>1</sup>	60.0 (59.0 – 63.5)
LA Volume (ml/m <sup>2</sup> )	37.2 (27.8 – 46.9)
Global Longitudinal Strain (%)	-20.3 (-22.1 – -19.4)
Septal E / E'	7.0 (6.3 – 8.3)
Tricuspid Annular Plane Systolic Excursion (cm)	2.5 (2.3 – 2.8)
Tricuspid Regurgitation Velocity Maximum (m/sec) <sup>1</sup>	2.3 (2.1 – 2.5)
Tricuspid Regurgitation Peak Gradient (mmHg) <sup>1</sup>	21.3 (17.8 – 25.9)

<sup>1</sup> 4 patients missing 3D data, tricuspid regurgitation velocity maximum and peak gradient