Supplementary Methods

CMR was performed on 1.5T scanners. Vectorcardiographic gated sequences were performed in the ventricular long and short axis planes for chamber sizes, ejection fraction, and ventricular mass. Late gadolinium enhancement (LGE) imaging was performed with a standard phase sensitive inversion recovery sequence protocol 10 minutes after injection with gadolinium-DTPA. ECV was measured from T1 maps acquired with a modified Look-Locker inversion recovery (MOLLI) sequence in the short and long axis planes before and 10 minutes after contrast injection. ECV was calculated by the formula: $ECV = (1 - hematocrit) \times (\Delta R1_{myocardium} / \Delta R1_{blood})$, where R is relaxation time.

Cardiac chambers and function were assessed by transthoracic echocardiography. Peak mitral inflow velocities at early (E) and late filling (A) were measured by pulsed-wave Doppler. Mitral valve annular velocities in early (e') and late diastole (a') at both the septal and lateral annulus were measured by tissue Doppler imaging. Peak tricuspid regurgitant jet velocity (TRV) was quantified by continuous-wave Doppler sampling., modified for sickle cell patients as we previously reported (Supplementary table).

Supplemental Table 1.

Subject ID	Age at time of echocardiography	LA volume (mL/m²)	TRV (m/sec)	Lateral e' (cm/sec)	Lateral E/e'	E/A ratio	Diastolic Classification
CCH01	11	16.9	2.63	17.8	5.7	1.7	Normal
CCH02	17	10.8	2.36	13.5	6.8	1.4	Normal
CCH03	8	26.8	2.91	14.7	9.7	2.5	Inconclusive
CCH04	7	27.1	2.29	24.6	4.8	2.2	Normal
CCH05	7	26	2.06	21.3	5.8	1.9	Normal
CHL01	20	23.9	2.6	22.9	6.1	2.2	Normal
CHL02	21	33.7	2.3	13.4	9	1.4	Normal
CHL03	21	32.4	2.65	17	8	2.2	Normal
CHL04	14	27.4	1.78	20.7	7.5	2.1	Normal
CHL05	17	27.4	1.78	20.7	7.5	2.4	Normal
CHL06	11	35.2	2.2	15.7	7.8	2.8	Inconclusive
CHL07	16	32	2.4	16.3	6.7	2.1	Normal

LA: left atrium; TRV: tricuspid regurgitant jet velocity

Values in red denote abnormal value for age.

Patients were considered to have diastolic dysfunction if they had LA enlargement (LA volume index ≥ 34 mL/m² for adults or >2SD above mean for age) in addition to abnormal e' (<2 SD below the mean for age, gender, and body size) and E/e' ratio (>2 SD above the mean for age, gender, and body size).

Supplementary Table 2.

CMR measure or laboratory result	No early therapy (N=25)	Early therapy (N=12)
Age (years)	23 ± 13	16.9 ± 7.2
Sex (F, M)	(14, 11)	(8, 4)
LV end-diastolic volume index (ml/m^2)	111.2 ± 23.2	92.2 ± 15.8
LV mass index (g/m^2)	65.9 ±18.3	57.5 ± 11.5
LV cardiac index (L/min/m2)	5 ± 1.2	3.7 ± 1.4[$]
Ejection fraction (%)	59.2 ± 2.4	63 ± 4.5
Hemoglobin (g/dL)	9.7 ± 1.5	9.8 ± 1.1
Reticulocyte count (%)	8.3 ± 5.2	9.3 ± 6.4
Hematocrit (%)	0.28 ± 0.04	0.29 ± 0.03
Total bilirubin (mg/dL)	2.4 ± 1.5	2.7 ± 1.4
Lactate dehydrogenase (U/L)	556 ± 267	691 ± 504[&]
NT-proBNP (pg/mL)	127.1 ± 182.8	69.5 ± 56[$]

[$] data is missing on one participant
[&] data in missing on 3 participants
None of the differences were statistically significant