The effects of cardio-selective β blockade on diastolic dysfunction in children with sickle cell disease

Parul Rai,[1] Victoria I. Okhomina,[2] Guolian Kang,[2] Nour Akil,[3] Jeffrey A. Towbin,[4,5] Jane S. Hankins[1] and Gary Beasley[4,5]

[1]Department of Hematology, St Jude Children's Research Hospital; [2]Department of Biostatistics, St Jude Children's Research Hospital; [3]Division of Pediatric Pulmonology, Le Bonheur Children's Hospital; [4]Heart Institute, Division of Pediatric Cardiology, Le Bonheur Children's Hospital and [5]Cardio-Oncology/Hematology Services, St Jude Children's Research Hospital, Memphis, TN, USA

Correspondence: P. RAI - parul.rai@stjude.org

Supplemental data

Supplemental Table 1. Adjusted effect of metoprolol usage on echocardiographic parameters

Echocardiographic Measure	Estimate	Standard Error	pFDR
Heart rate (beats/min)	-7.10	4.09	0.16
TRV (m/s)	-0.07	0.08	0.52
LVIDd z-score	-0.55	0.21	0.08
Septal E/e'	-1.00	0.44	0.08
Lateral E/e'	-0.88	0.37	0.08
LAVi (ml/m^2)	-4.09	2.45	0.16
Septal e' (m/s)	-0.003	0.01	0.74
Lateral e' (m/s)	-0.001	0.01	0.88
NOTE: Model estimates are for effect of beta blocker use compared to non-use on echocardiographic parameter after adjusting age, sex (reference: male), HU treatment status (reference: No), and use of chronic transfusions (reference: No). Abbreviations: TRV = tricuspid regurgitant velocity, LVEDd=left ventricular end-diastolic diameter, e'= early annular diastolic velocity, E= early diastolic velocity, LAVi= left atrial volume index, pFDR=p-value adjusted for false discovery rate (FDR)			

Supplemental Table 2. Change in prevalence of abnormal diastolic parameters over study period

	Metoprolol-treatment				Controls			
	Baseline	Post-Initiation	Change in prevalence	p FDR	Baseline	Year 2	Change in prevalence	p FDR
Lateral e' (m/s)	0%	5%	5	>0.99	0%	4.8%	4.8	>0.99
Septal e' (m/s)	14.3%	4.8%	-9.5	>0.99	0%	0%	0	
Lateral E/e'	5%	0%	-5.0	>0.99	5%	23.8%	18.8	0.50
Septal E/e''	20%	9.5%	-10.5	>0.99	20%	33.3%	13.3	0.68
TRV (m/s)	10.5%	0%	-10.5	>0.99	10.5%	4.8%	-5.7	>0.99
LAVi ml/m^2	85.7%	70%	-15.7	>0.99	100%	81%	-19	0.50
LVIDd z-score	23.8%	27.8%	4.0		57.1%	38.1%	-19	0.50
Abbreviations: TRV = tricuspid regurgitant velocity, LVIDd=left ventricular end-diastolic diameter, e'= early annular diastolic velocity, E= early diastolic velocity, LAVi= left atrial volume index pFDR : False Discovery Rate adjusted p-value								

Supplemental Table 3. Safety profile of metoprolol

	Change	pFDR
VOE (ACS + pain events)#	0 [-5,2]	0.77
Spirometry FEV$_1$% predicted	-0.64 (6.39)	0.80
FVC % predicted	1.71 (5.41)	0.77
FEV$_1$/FVC % predicted	-0.02 (0.03)	0.28

PFT=pulmonary function test, FEV$_1$=Forced expiratory volume at 1 second, FVC=forced vital capacity, VOE= vaso-occlusive episodes, ACS= acute chest syndrome, pFDR= false discovery rate (FDR) adjusted p-values

Mean (standard deviation) reported for all except VOE. Change in VOE reported as median [range].

#The change in VOE events between the metoprolol treatment period and the twenty-four-month interval prior to initiation of metoprolol.