Subjects With Extreme-Duration Type 1 Diabetes Exhibit No Structural or Functional Abnormality on Cardiac MRI

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Medalists represent a unique group of survivors of over 50 years of type 1 diabetes (T1D) (1,2). A subgroup of Medalists, escapers, remains free of micro- and macrovascular complications. To date, there are no published studies on cardiac structure and function in these subjects.

We have undertaken a comprehensive multiparametric cardiac MRI study (3,4) to quantify myocardial structure, function, deformation, perfusion, and fibrosis in a cohort of 13 subjects with extreme-duration T1D and 14 healthy control subjects (Table 1).

The T1D group had a mean duration of diabetes of 47.4 ± 5.1 years (median 48.0 years). Eight participants had a history of retinopathy and 12 were receiving statin and ACE inhibitor therapy. The mean HbA_{1c} over the previous 16 years was 8.3 ± 1.0% (69 ± 11 mmol/mol). The T1D group had higher systolic and lower diastolic blood pressure ($P = 0.05$, $P = 0.01$), lower LDL cholesterol ($P = 0.04$), and higher HDL cholesterol ($P = 0.03$). BMI, total cholesterol, triglycerides, and estimated glomerular filtration rate did not differ between the groups.

We found no evidence of coronary artery disease or previous myocardial infarction on stress imaging and T1 mapping, respectively. Left ventricular mass index was significantly lower in the T1D group ($P = 0.007$), but there was no difference in left ventricular ejection fraction. Myocardial deformation as assessed by radial, circumferential, and longitudinal strain did not differ between the groups. Myocardial blood flow (MBF) at rest and during pharmacological stress

Table 1—Clinical characteristics and cardiac MRI data

	Control subjects	T1D	*P*
Clinical characteristics			
Age (years)	54.6 ± 5.4	61.8 ± 7.6	0.009
Diabetes duration (years)	—	47.4 ± 5.1	—
BMI (kg/m^2)	27.0 ± 3.1	28.1 ± 4.5	0.48
Systolic blood pressure (mmHg)	118 ± 11	128 ± 15	0.051
Diastolic blood pressure (mmHg)	72 ± 10	60 ± 14	0.014
HbA_{1c} (%)	5.7 ± 0.4	8.3 ± 1.0	<0.0001
Total cholesterol (mmol/L)	5.0 ± 0.74	4.6 ± 1.0	0.227
LDL cholesterol (mmol/L)	2.9 ± 0.6	2.1 ± 1.0	0.035
HDL cholesterol (mmol/L)	1.6 ± 0.4	2.1 ± 0.7	0.027
Triglycerides (mmol/L)	1.1 ± 0.5	0.9 ± 0.4	0.265
eGFR (mL/kg/min)	81 ± 9	72 ± 20	0.135
Cardiac MRI			
Volumetrics			
Left ventricular mass index [BSA] (g/m^2)	51.1 ± 10.7	41.0 ± 6.4	0.007
Left ventricular ejection fraction (%)	61.0 ± 6.4	63.1 ± 6.9	0.425
Myocardial strain			
Longitudinal strain	−16.0 ± 10.8	−18.9 ± 5.5	0.394
Longitudinal strain rate	0.9 ± 0.9	1.2 ± 0.4	0.243
Radial strain	−34.3 ± 11.6	−32.1 ± 17.7	0.707
Radial strain rate	1.3 ± 0.7	1.5 ± 0.5	0.412
Circumferential strain	−22.3 ± 2.6	−24.9 ± 5.2	0.109
Circumferential strain rate	2.7 ± 5.7	1.4 ± 0.5	0.29
MBF			
Rest (mL/min/g)	0.75 ± 0.17	0.86 ± 0.24	0.177
Stress (mL/min/g)	2.07 ± 0.42	1.80 ± 0.35	0.094
Stress/rest index	2.81 ± 0.47	2.16 ± 0.66	0.006
ECV			
ECV (%)	0.27 ± 0.05	0.32 ± 0.04	0.01

BSA, body surface area; eGFR, estimated glomerular filtration rate.

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did not differ between the groups; however, the MBF ratio (stress/rest), an index of coronary microvascular perfusion reserve, was significantly lower in the T1D group ($P = 0.006$). We did not find any correlation between myocardial perfusion reserve and markers of cardiac autonomic function. On T1 mapping, extracellular volume (ECV) was significantly higher in the T1D group than in the control group ($P = 0.01$).

This is the first study to describe in detail the cardiac phenotype in a Medalist cohort. Using robust, validated, and reproducible three-dimensional modeling methods for volumetric and structural analyses, we demonstrate normal systolic and diastolic cardiac function in keeping with our recent echocardiographic study (5). There were no differences in MBF, but the stress/rest index was reduced, which is suggestive of coronary microvascular dysfunction. Coronary microvascular dysfunction may partly be mediated through cardiac autonomic dysfunction, but we found no correlation between myocardial perfusion reserve and cardiac autonomic function in our cohort. Quantitative assessment of myocardial ECV, a surrogate of myocardial fibrosis, shows much promise, and we have recently validated this in humans (3). ECV was increased in our Medalist group, which is suggestive of a very early fibrosis as there was no associated left ventricular mechanical dysfunction.

Although our study had limited numbers, we believe the detailed cardiac MRI cardiac phenotyping in this unique cohort of extreme-duration patients with T1D provides considerable insight and confirms that these unique individuals are indeed protected from the long-term complications of diabetes. Clinicians responsible for the care of patients with long-duration diabetes should perform detailed cardiac assessment to aid risk stratification for cardiovascular complications.

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