



Metformin Improves Left Ventricular Size and Function in Adolescents with Type 1 Diabetes



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Introduction

- People with type 1 diabetes (T1D) have higher rates of cardiovascular disease (CVD) despite modern advances in glucose control.
- We previously demonstrated vascular and cardiac dysfunction in adolescents with T1D.
- In the EMERALD study, we showed that metformin improves BMI, body composition, insulin sensitivity, arterial stiffness, and carotid intimal media thickness in T1D adolescents.
- We hypothesized that metformin, with insulin-sparing effects, also improves cardiac function.

Methods

- 43 T1D youth ages 12-21 years in the EMERALD study underwent a comprehensive evaluation of cardiovascular health, insulin sensitivity, and body composition.
- After baseline assessments, participants were randomized 1:1 to 3 months of either 2000 mg of metformin daily or placebo with repeat evaluations performed after treatment.
- Standard echocardiographic exams using the EchoPac program (GE Healthcare) were completed to evaluate aortic and cardiac function.
- 2D speckle-tracking was used for cardiac strain and synchrony analysis.

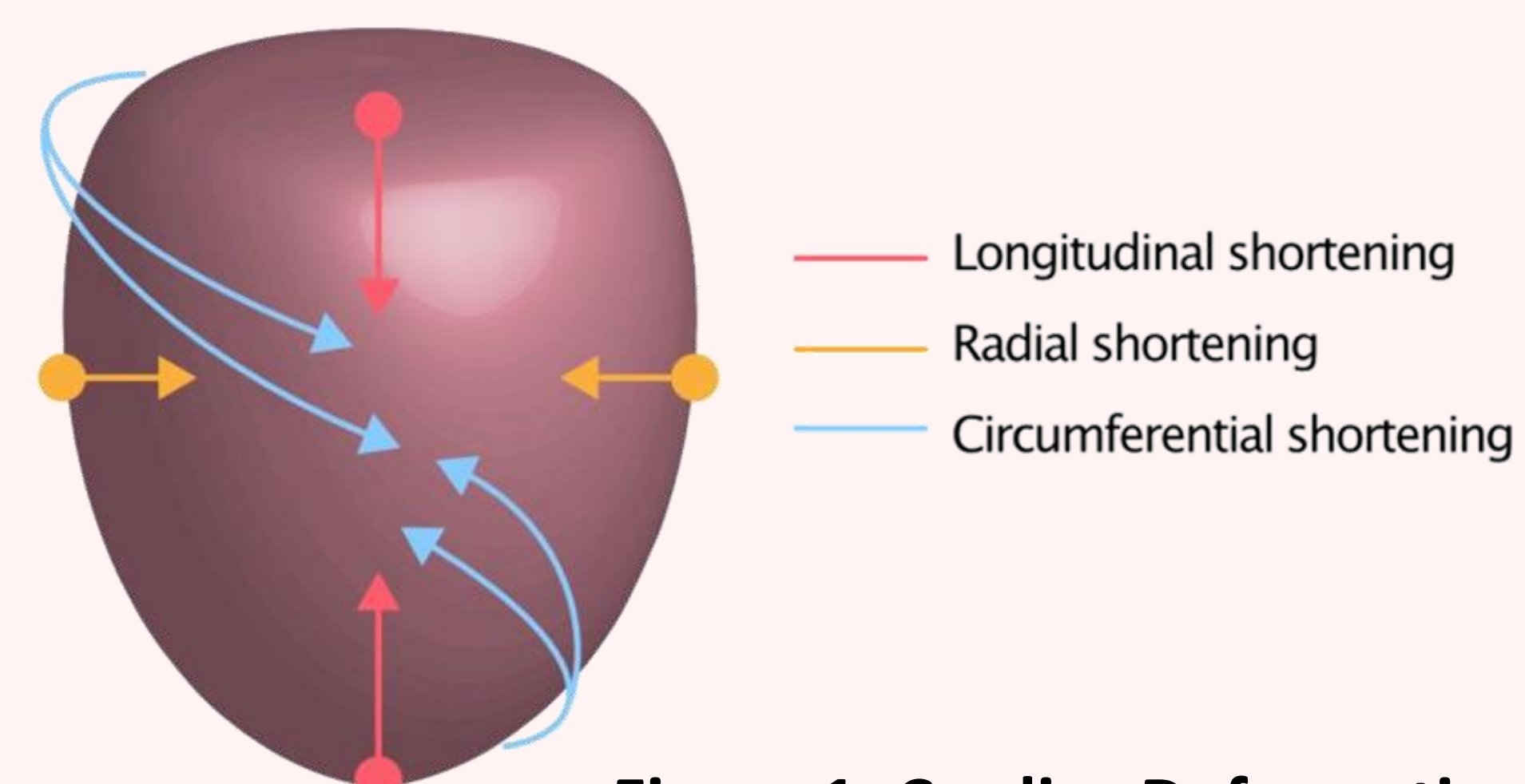


Figure 1. Cardiac Deformation

Methods

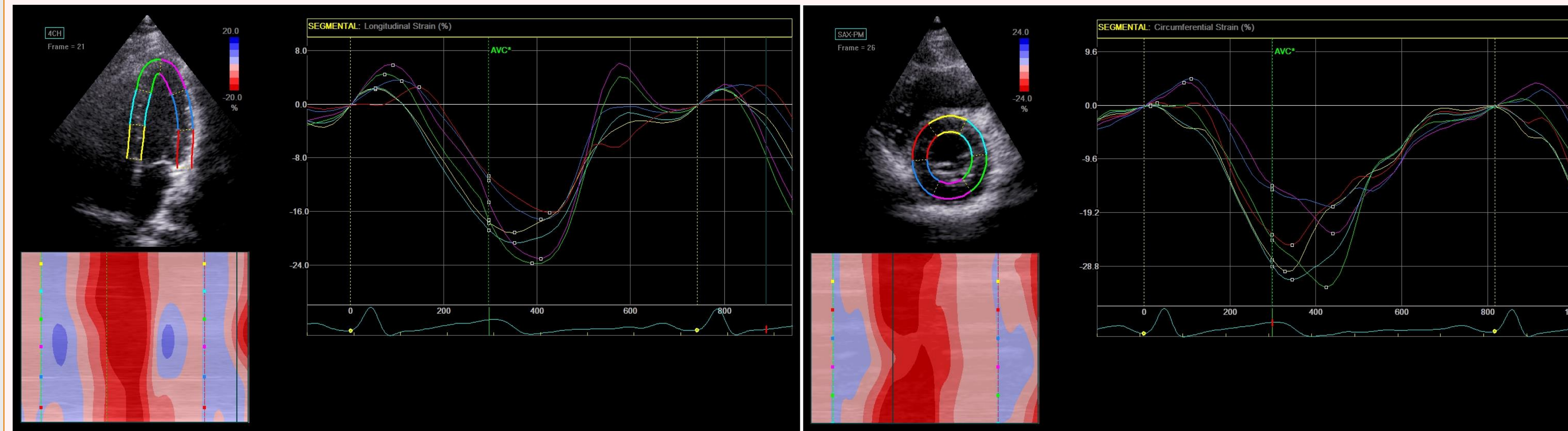


Figure 2. Cardiac Strain Analysis by 2D speckle-tracking assessment for longitudinal and circumferential strain

Results

Baseline Participant characteristics (n=43)

- Age 16.8 ± 2.5 years
- HbA1c $8.6 \pm 1.5\%$
- BMI 25.1 ± 4.3 kg/m²
- Diabetes duration 7.7 ± 4.2 years

	Metformin (n=23)			Placebo (n=20)		
	Month 0	Month 3	p-value	Month 0	Month 3	p-value
Ao Diam (cm)	2.57 ± 0.32	2.51 ± 0.39 [†]	0.482	2.61 ± 0.30	2.73 ± 0.28 [†]	0.244
IVSd (cm)	0.72 ± 0.11	0.76 ± 0.10	0.165	0.72 ± 0.13	0.72 ± 0.18	0.853
LVPWd (cm)	0.73 ± 0.09	0.76 ± 0.09	0.245	0.73 ± 0.103	0.73 ± 0.13	1.000
LVIDd (cm)	4.45 ± 0.47 *	4.26 ± 0.50 *	0.019	4.36 ± 0.33	4.38 ± 0.37	0.776
LVIDs (cm)	2.89 ± 0.39 *	2.69 ± 0.36 *	0.022	2.84 ± 0.29	2.83 ± 0.34	0.867
EF (%)	68.2 ± 4.1	68.0 ± 6.4	0.911	67.2 ± 5.0	67.6 ± 6.1	0.833
FS (%)	35.0 ± 6.3	36.8 ± 8.0	0.389	35.5 ± 6.2	36.0 ± 6.0	0.773
MV A wave (m/s)	0.56 ± 0.09	0.59 ± 0.16	0.483	0.54 ± 0.14	0.56 ± 0.15	0.285
MV E wave (m/s)	0.92 ± 0.17	0.87 ± 0.19	0.265	0.96 ± 0.19	0.93 ± 0.20	0.574
MV E/A Ratio	1.67 ± 0.44	1.55 ± 0.42	0.178	1.88 ± 0.49	1.72 ± 0.34	0.067
LV Dyssynchrony (ms)	98.0 ± 36.9 *	81.7 ± 27.5 *	0.014	96.2 ± 26.8	92.3 ± 35.6	0.723
GLS (%)	-17.4 ± 3.1	-17.3 ± 3.4	0.894	-18.0 ± 3.1	-17.2 ± 4.1	0.350
GCS (%)	-20.8 ± 4.6	-21.9 ± 4.6	0.371	-22.0 ± 3.0	-21.5 ± 3.8	0.602

Table 1. Echocardiography data by treatment arm

* p<0.05 for pre- vs. post- treatment

[†] p<0.05 for placebo vs. metformin

Results

- LV diameter (4.45 ± 0.47 vs. 4.26 ± 0.50 cm, p = 0.019) at end-diastole and end-systole (2.89 ± 0.39 vs. 2.69 ± 0.36 cm, p = 0.022) significantly improved within the metformin group.
- LV dyssynchrony (98.0 ± 36.9 vs. 81.7 ± 27.5 milliseconds, p = 0.014) significantly improved within the metformin group.
- Aortic root diameter (2.51 ± 0.39 vs. 2.73 ± 0.28 cm, p = 0.042) was significantly lower in the metformin vs. placebo group.

Conclusions

- Metformin improves multiple markers of cardiac and vascular function in T1D youth.
- Analysis of sex differences, and the impact of changes in blood pressure, BMI, % fat, insulin sensitivity, glycemic control, and other lab markers will be assessed in relation to the improved echocardiogram findings.
- The benefits of improving insulin action in T1D should be investigated longer-term.
- Echocardiography and/or other noninvasive biomarkers may prove helpful in screening T1D youth to identify those youth early-on in need of more intensive cardiovascular risk management.

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Acknowledgments

All authors declare there are no conflicts of interest to disclose.

Thank you to the co-authors, especially my mentors Dr. Kristen Nadeau and Dr. Uyen Truong, for making this project possible.