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Longitudinal analysis of myocardial function using strain in patients receiving cardiotoxic chemotherapy

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Longitudinal myocardial function assessment for chemotherapy-related cardiotoxicity and possible association with genetic polymorphism in pediatric population

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INTRODUCTION

- Chemotherapy-related cardiotoxicity (CTRC) can result in significant morbidity and mortality in long term cancer survivors.
- Our goal was to assess longitudinal myocardial function using left ventricular ejection fraction (LV-EF) and left ventricular global longitudinal strain (LV-GLS).
- Our secondary objective was to identify cardiovascular genetic polymorphism that may influence CRTC.

METHODS

- 50 Subjects ≥ 10 years of age who survived >2 years after completion of cancer treatment.
- 29 Subjects consented for genetic analysis and longitudinal evaluation with echocardiography.
- LV-EF: Measures using area-length method.
- LV-GLS: Measured by using speckle tracing with 2D STE offline analysis software developed by TomTec Imaging Systems.
- Whole exome sequencing for genetic polymorphism was performed.
- GLS $\leq -18\%$ was considered normal.
- Data was analyzed with chi-square and paired T-test for categorical and continuous variables, respectively.

RESULTS

- 59% had longitudinal echocardiographic data for serial LV-EF and LV-GLS measurements.
- Baseline EF: $60.1\% \pm 5.4\%$; Baseline GLS: $-21.71\% \pm 2.36\%$
- Mean follow-up duration was 4.1 years [range 2.2-6.5 years].
- All were clinically asymptomatic, NYHA Class I.
- Follow-up evaluation:
 - Mean reduction of LV GLS: $1.4\% \pm 2.1\%$ [$p=0.015$]
 - Mean Reduction of EF: $1\% \pm 5.6\%$ [$p=0.45$]
- Longitudinal data:
 - Decrease in GLS by $>2\%$ in 47% of patients
 - Decrease in EF by $\geq 5\%$ in 11.7% of patients

Table 1. Baseline characteristics at cumulative anthracycline dose <200 and ≥ 200 mg m^{-2}

	All Patients	Cumulative anthracycline dose (mg m^{-2})	
		< 200	≥ 200
N (%)	29	16	13
Age (years)	17 ± 4	16.7 ± 3.7	17.4 ± 4.8
Female (%)	14 (48.3)	7 (43.8)	7 (53.8)
Type of Cancer (%)			
Solid	18 (62.1)	9 (56.2)	9 (69.2)
Leukemia	11 (37.9)	7 (43.8)	4 (30.8)
Radiation Exposure (Gy)	9.5 ± 15.9	12.5 ± 19.6	8.7 ± 13.2
Bone marrow transplant	5 (17)	1 (6.2)	4 (30.8)
Follow up duration (years)	4.1 ± 1.5	3.4 ± 1	5.1 ± 1.6

RESULTS

Fig 1. Association between cumulative anthracycline dose < 200 and ≥ 200 mg m^{-2} and LV-EF and LV-GLS. There is a consistent trend toward decrease in LV-GLS in subjects who received ≥ 200 mg m^{-2} of anthracyclines. There is no identifiable trend in LV-EF and for subjects who received < 200 mg m^{-2} of anthracyclines.

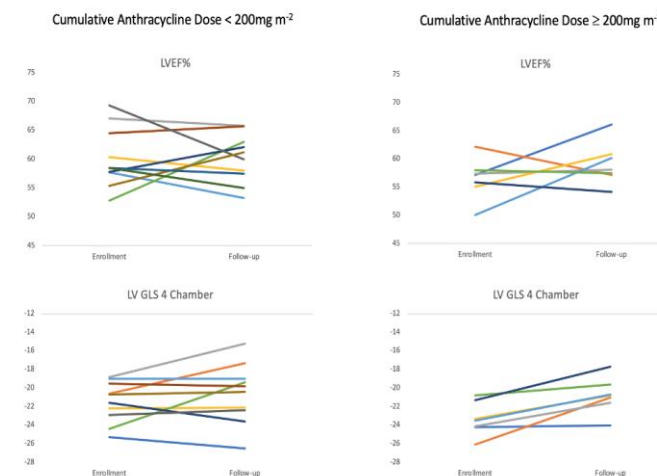


Table 2. Genetic polymorphism associated with changes in LV-GLS

Category	Cardiac Genes
$> 2\%$ reduction in LV-GLS	CACNA1C, CASR, CAT, CDH2, DTNA, FTO, MYH14, NCOR2, PRDM 2
$\leq 2\%$ reduction in LV-GLS	ASPH, CHRM2, TENM4, TNNT3K, VCL, XYLT1

CONCLUSION

- LV-GLS is a more sensitive marker for longitudinal analysis of cardiac function than LV-EF.
- Certain polymorphisms may influence CRTC and can be a valuable tool in risk-stratification of these patients.