

# Early Detection of Anthracycline Induced Cardiomyopathy in Survivors of Childhood Cancer

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## Background

Childhood cancer survival has tripled since the 1960's. Anthracyclines are utilised in 50-60% of cases and are fundamental to this survival rate. Anthracycline induced cardiotoxicity is however associated with high morbidity and mortality rates. Paediatric patients are at particularly high cardiomyopathy risk and can experience late effects decades after treatment.

Research in breast cancer survivors has shown that an absolute Global Longitudinal Strain (GLS) <-19% is associated with marked risk of reduced ejection fraction (EF).<sup>1</sup>

## Methods

This Northern Ireland wide study reviewed all adult survivors of childhood cancer who received anthracycline based chemotherapy referred by paediatric oncology.

We examined the demography and characteristics of this population, the therapies used, cardiovascular risk factors, symptoms, biomarkers, ECG, and echocardiography findings including GLS.

## Demographics

We studied 75 adult (39 female and 36 male) survivors of childhood cancer (age 16-38, mean age 22 years). Age at treatment completion was 1-17 years (mean age 8 years).

60 patients received Doxorubicin, 4 received Daunorubicin, 4 received combination therapy and 7 patients had no documentation in their adult notes of therapy received.

25 patients completed treatment below the age of 5 years of age, 40 patients had anthracycline doses >250mg/m<sup>2</sup> and 11 had concomitant chest radiotherapy resulting in higher cardiomyopathy risk. 3 patients received the cardioprotective agent Dexrazoxane.

Patient Characteristics	Patients
Current Smoker	7 (3 ex)
Raised Clinic Blood Pressure	3
Diabetic	2
Abnormal Cholesterol	5
CKD	0
Concurrent Cardiac Condition	1
History of Device Implantation	0
Pregnancy	5
Family History of Cardiomyopathy	0
Family History of Ischaemic Heart Disease	7
Family History of Sudden Cardiac Death	0

Figure 1. Patient Characteristics

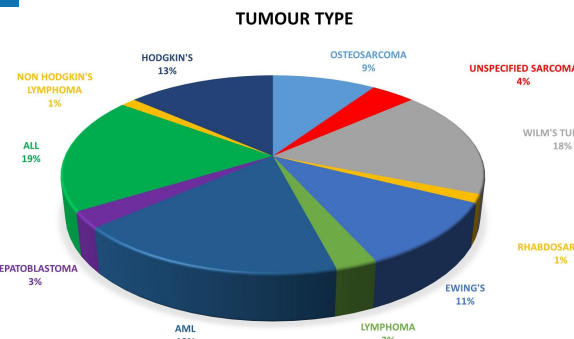


Figure 2. Frequency of tumour type

## Results

### Symptoms

70 patients attended for review. 1 patient was classed as NYHA III, 4 had palpitations, 2 chest pain, 1 presyncope and 1 syncope.

### ECG Findings

58 patients had a documented ECG. 44 patients were in normal sinus rhythm, 12 had sinus bradycardia, 2 sinus tachycardia. There was no documented pathological QTc prolongation (>450ms males, >470ms females).

### Ejection Fraction

72 patients attended for echocardiography assessment. Overall the estimated ejection fraction (EF) was impaired (<55%) in 8 (11.1%) patients.

5 patients had mild (EF 45-54%), 2 moderate (EF 36-44%) and 1 severe (EF ≤ 35%). Ejection fraction was associated with a negative trend with time from treatment (p=0.059, R=-0.223). 7 patients had a borderline ejection fraction of 55%.

### Strain

The assessment of relative change in Global Longitudinal Strain (GLS) as recommended in European and American guidelines was not possible as most patients had only one documented echocardiogram. Furthermore with different normal values proposed by vendors and by age ranges a consensus opinion for an absolute value in cut off has yet to be reached

GLS was measured in 55 patients (54 on a GE Vivid E9, 1 patient on a Philips IE33).

Utilising the cut off proposed by Sawaya et al. when assessing adult breast cancer survivors GLS was abnormal (>-19%) in 45 patients (81.8%) and normal (<-19%) in 10 patients (18.2%).

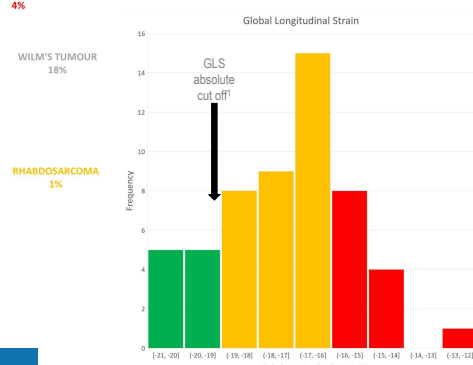


Figure 3. Frequency of Global Longitudinal Strain values (%)

### Biomarkers

Natriuretic peptide was measured in 57 patients and abnormal (≥125pg/ml) in 11 (14.7%). NTproBNP significantly correlated with time from treatment (p=0.001, R=0.442).

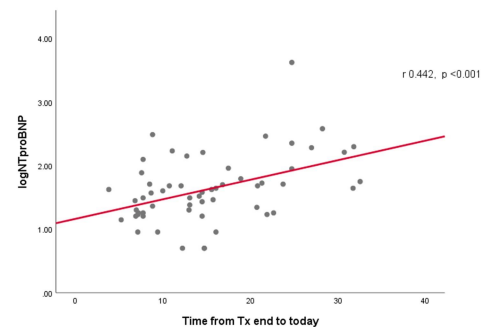


Figure 4. NTproBNP vs time from treatment completion

## Conclusion

A significant proportion of this young cancer survivor population have already crossed the threshold into systolic impairment.

Extrapolating absolute GLS values from breast cancer patients to childhood cancer survivors has shown a large number with cardiomyopathy risk.

Further research and review can facilitate early detection and treatment of this lethal iatrogenic condition and to establish standardised guidance.

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## Declaration of Interest

The authors have nothing to declare.



## References

1. Sawaya H, Sebag IA, Plana JC, et al. Assessment of echocardiography and biomarkers for the extended prediction of cardiotoxicity in patients treated with anthracyclines, taxanes, and trastuzumab. Circ Cardiovasc Imaging 2012;5: 596-603.