Echocardiographic characterization and response to heart failure therapy in patients with early- and late diagnosed anthracycline-induced cardiac dysfunction

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Background

- Anthracycline-induced cardiac dysfunction (AICD) is a notorious side effect of anticancer treatment.
- It has been described as a phenomenon of a continuous progressive decline of cardiac function, that can eventually lead to dilated cardiomyopathy (DCM).
- This progressive nature suggests that patients with a delayed diagnosis have greater compromise of cardiac function and more adverse remodeling, resulting in a poorer response to heart failure treatment.

Objectives

To delineate the impact of a delayed AICD diagnosis on echocardiographic characteristics and response to heart failure treatment.

Methods

- Screening of cardio-oncology outpatient clinic (April 2015 up to February 2019):
  - Inclusion: Patients with cardiac dysfunction caused by anthracyclines (AC)
  - Exclusion: Other cardiotoxic treatment (e.g. trastuzumab); Cardiac dysfunction not caused by AC
- Time to diagnosis: time between 1st anthracycline administration and AICD diagnosis
  - Early (EAICD): <1 year; Late (LAICD): >1year
- Recovery: Patients with a follow-up of at least 6 months
  - Change between LVEF at nadir and last LVEF measurement
  - (Partial) recovery: Improved by ≥ 10 percentage points from nadir
  - No recovery: Less than<10 percentage points improvement from the nadir and remaining >5 percentage points below baseline

Echocardiographic analysis

Analysis of echocardiography at diagnosis:

- 3D Left ventricular ejection fraction (LVEF), global longitudinal strain (GLS), diastolic function
- Enddiastolic volume (EDV), endsystolic volume (ESV) and LV geometry (based on LV mass and relative wall thickness)
- Right ventricular function

		EAICD (n=49)	LAICD (n=43)	p-value
Male sex		38 (78%)	30 (70%)	0.396
Age at diagnosis AICD (years)		52.4 ± 16.1	50.8 ± 16.2	0.646
Anthracycline dose (mg/m²)		329 [IQR 180 - 329]	308 [IQR 200 - 400]	0.114
Time to diagnosis (months)		4.0 [IQR 1.9 – 6.4]	47.7 [IQR 41.7 – 87.3]	
EDV (mL/m²)		63.6 ± 14.8	62.9 ± 16.4	0.840
ESV (mL/m²)		35.9 ± 9.6	36.5 ± 13.0	0.813
LVEF (%)		43.6 ± 4.9	43.0 ± 6.2	0.576
NYHA class	I-II III-IV	47 (96%) 2 (4%)	39 (91%) 4 (9%)	0.312
Recovery	(Partial) recovery No recovery	15 6	5 17	0.001*

Table 1. Characteristics of study participants, echocardiographic- and clinical outcomes of patients with early- and late diagnosed AICD.

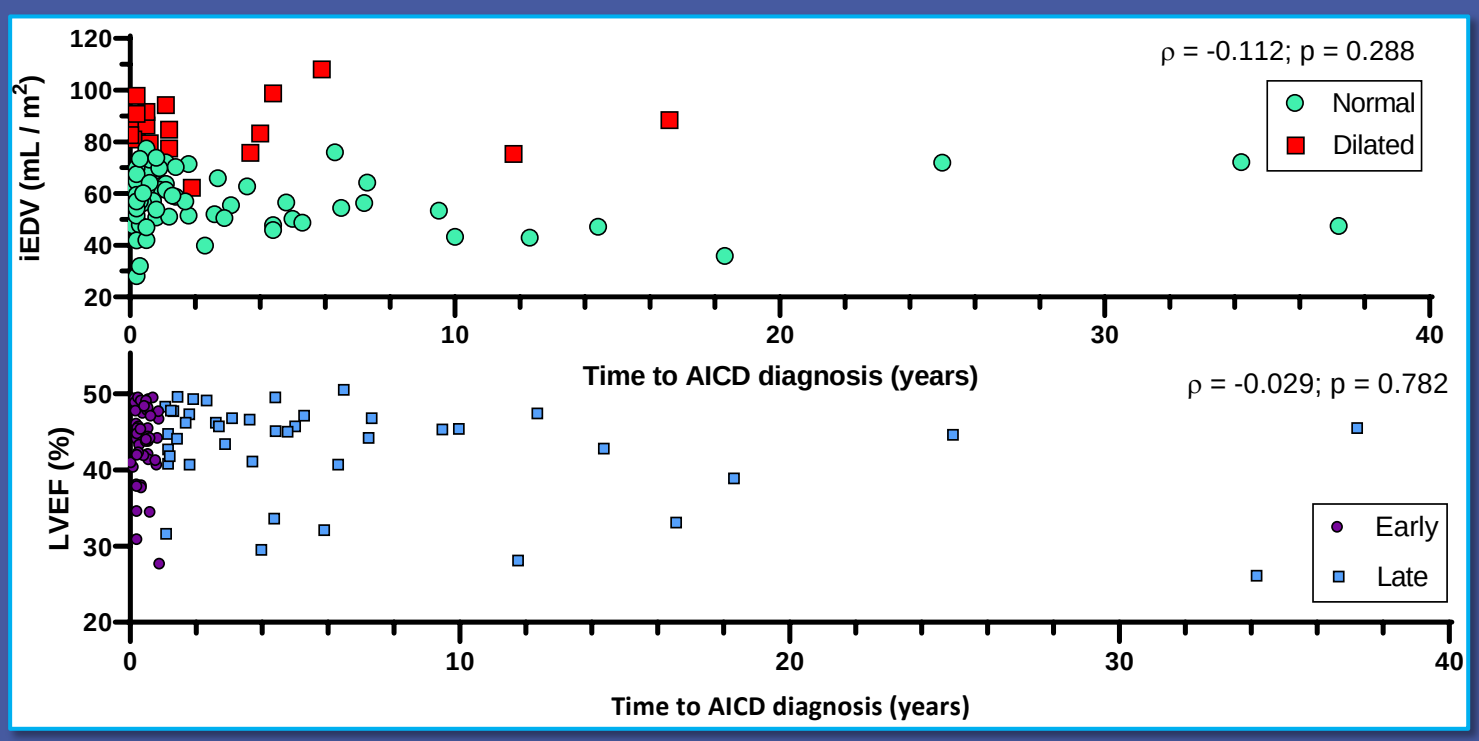

Figure 1. Echocardiographic outcomes at time of diagnosis. Upper: Enddiastolic volume, index for body surface area and classified as 'normal' or 'dilated'. Lower: Left ventricular ejection fraction (%).

Results

- Out of 342 cardio-oncology patients treated with anthracyclines, 49 patients with EAIC and 43 patients with LAIC were identified.
- 83% of patients presented with mild LV dysfunction and in 79% the LV was not dilated.
- No significant differences in left ventricular dimension and –function were found between patients with EAIC and LAIC (Figure 1, 2).
- EAIC patients were more likely to have (partial) recovery of cardiac function upon the initiation of heart failure treatment.

Conclusion

- Patients with AICD presented with a hypokinetic non-dilated cardiomyopathy, rather than typical DCM.
- Timing of AICD diagnosis did not impact disease severity.
- In patients receiving an early diagnosis, cardiac function was more likely to recover.

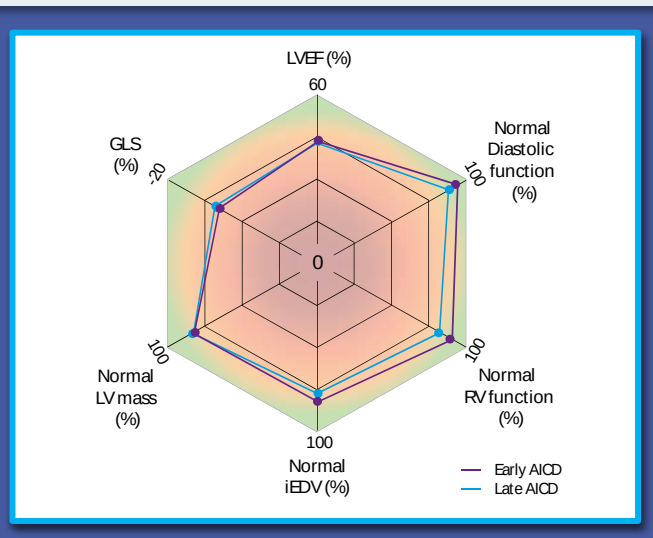

Figure 2. Radar chart with the echocardiographic phenotype of early- and late AICD at diagnosis. LVEF and GLS are expressed as group means, LV mass, iEDV and RV function are expressed as % of patients with normal outcomes and diastolic function is expressed as % of patients with diastolic dysfunction ≤ grade I.

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