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

**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): >1 year
- 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

**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.

**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

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

<table>
<thead>
<tr>
<th></th>
<th>EAICD (n=49)</th>
<th>LAICD (n=43)</th>
<th>p-value</th>
</tr>
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<tbody>
<tr>
<td>Male sex</td>
<td>38 (78%)</td>
<td>30 (70%)</td>
<td>0.396</td>
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<tr>
<td>Age at diagnosis AICD (years)</td>
<td>52.4 ± 16.1</td>
<td>50.8 ± 16.2</td>
<td>0.646</td>
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<tr>
<td>Anthracycline dose (mg/m²)</td>
<td>329 [IQR 180 - 329]</td>
<td>308 [IQR 200 - 400]</td>
<td>0.114</td>
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<td>Time to diagnosis (months)</td>
<td>4.0 [IQR 1.9 – 6.4]</td>
<td>47.7 [IQR 41.7 – 87.3]</td>
<td></td>
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<tr>
<td>EDV (mL/m²)</td>
<td>63.6 ± 14.8</td>
<td>62.9 ± 16.4</td>
<td>0.840</td>
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<tr>
<td>ESV (mL/m²)</td>
<td>35.9 ± 9.6</td>
<td>36.5 ± 13.0</td>
<td>0.813</td>
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<td>LVEF (%)</td>
<td>43.6 ± 4.9</td>
<td>43.0 ± 6.2</td>
<td>0.576</td>
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<tr>
<td>NYHA class</td>
<td>I-II 47 (96%)</td>
<td>II-IV 39 (91%)</td>
<td>0.312</td>
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<tr>
<td>Recovery</td>
<td>15 (31%)</td>
<td>6 (14%)</td>
<td>0.001*</td>
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**Figure 1.** Echocardiographic outcomes at time of diagnosis. Upper: Eddiastolic volume, index for body surface area and classified as ‘normal’ or ‘dilated’. Lower: Left ventricular ejection fraction (%).

**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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