Elevated resting heart rate is a marker of subclinical left ventricular dysfunction in Hodgkin lymphoma survivors

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Elevated resting heart rate is a marker of subclinical left ventricular dysfunction in hodgkin lymphoma survivors

Julius C. Heemelaar a, Augustinus D.G. Krol b, Marloes Louwerens c, Saskia L.M.A. Beeres d, Eduard R. Holman e, Martin J. Schalij f, M.L. Antoni g,h

a Department of Cardiology, Heart Lung Center, Leiden University Medical Centre, Leiden, the Netherlands
b Department of Radiotherapy, Leiden University Medical Centre, Leiden, the Netherlands
c Department of Internal Medicine, Leiden University Medical Centre, Leiden, the Netherlands
d Department of Cardiology, Heart Lung Center, Leiden University Medical Centre, Leiden, the Netherlands
e Department of Cardiology, Heart Lung Center, Leiden University Medical Centre, Leiden, the Netherlands
f Department of Cardiology, Heart Lung Center, Leiden University Medical Centre, Leiden, the Netherlands
g Department of Cardiology, Heart Lung Center, Leiden University Medical Centre, Leiden, the Netherlands
h Corresponding author at: Department of Cardiology, Heart Lung Centre, Leiden University Medical Centre, Albinusdreef 2, 2333ZA Leiden, The Netherlands.
E-mail address: m.l.antoni@lumc.nl (M.L. Antoni).

ABSTRACT

Background: Thoracic irradiation is one of the cornerstones of Hodgkin lymphoma (HL) treatment, which contributes to high rates of long-term survivorship, but begets a life-long increased risk of heart disease including heart failure. At the cardio-oncology (CO) clinic, persistent sinus tachycardia or elevated resting heart rate (RHR) is frequently observed in these patients. The aim of this study was to evaluate the relation between RHR and left ventricular (LV) dysfunction.

Methods: In 75 HL survivors visiting our CO-clinic echocardiographic evaluation of LV systolic and diastolic function including global longitudinal strain (GLS) was performed to assess subclinical LV dysfunction.

Results: Median age of HL diagnosis was 24 [25th-75th percentile: 19, 29] years with a 17 [12, 25] year interval to CO-clinic visit and 31 patients (41%) were male. Average RHR was 78 ± 14 bpm and 40% of patients (N = 30) had an elevated RHR defined as ≥80 bpm. While there was no difference in LV ejection fraction (55.6 ± 4.3 vs. 54.8 ± 6.6; p = 0.543), patients with elevated RHR had abnormal GLS (-15.9% vs. -18.3%, p = 0.045) and higher prevalence of diastolic dysfunction (73.3% vs. 46.7%; p = 0.022). GLS, E/e’ ratio and presence of diastolic dysfunction were independently associated with RHR when correcting for age, sex and mantle field irradiation. A significant improvement was observed of the RHR-association model with solely extracardiac confounders when LV-function parameters were added to the model (F-statistic = 6.36, p = 0.003).

Conclusions: This study indicates RHR as a possible marker for subclinical LV-dysfunction in HL survivors. © 2021 The Authors. Published by Elsevier B.V. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).

1. Introduction

The successful implementation of thoracic irradiation and anthracycline-containing chemotherapy regimens in Hodgkin lymphoma (HL) - one the most prevalent malignancies in adolescents and young adults - led to a long term survival of above 80% [1]. The reverse of the medal is that these treatment modalities beget a life-long increased risk of a multitude of cardiovascular disease in HL survivors compared to the general population [2–4].

To mitigate this risk – as recommended by international guidelines - specialised cardio-oncology (CO) clinics for the detection of late cardiovascular side effects of cancer treatment have been established [5–7].

Frequently HL survivors who received thoracic irradiation show persistent sinus tachycardia or an elevated resting heart rate (RHR) [8,9]. RHR over the years is a thoroughly studied research topic and is identified as an important prognostic factor in the general population [10,11] and in cardiovascular disease patients [12–14]. Custodis and colleagues accurately depict RHR as a central factor that influences all stages of cardiovascular disease: from risk factor, to the occurrence of adverse cardiac events and heart failure. An
elevated RHR in cancer patients predicts increased mortality rates [9,15].

Most research regarding elevated RHR in cancer survivors focuses on autonomic dysfunction caused by thoracic irradiation [16,17]. Groarke and colleagues also displayed prognostic implications of the presence of autonomic dysfunction in these patients. However, there is limited knowledge about the relation between left ventricular (LV) dysfunction and elevated RHR in patients after cancer treatment.

Several studies have already demonstrated that cancer survivors whom underwent thoracic irradiation or anthracycline treatment often show echocardiographic evidence of LV dysfunction [18–21]. Also, in the early stages of heart failure increased adrenergic activity is a well-known phenomenon [22].

Therefore, we hypothesised that there may be a relation between the presence of an elevated resting RHR and LV dysfunction in HL survivors whom underwent thoracic irradiation and evaluated echocardiographic parameters of systolic and diastolic function in these patients presenting at the CO-clinic.

2. Methods

A retrospective cohort study among HL survivors treated with mediastinal irradiation referred to the cardio-oncology outpatient clinic at the Leiden University Medical Centre was performed. Patients are referred to the CO-clinic through the national HL survivorship care pathway, where all HL survivors between 15 and 60 years of age are eligible for routine cardiovascular screening. Between 2012 and 2019 88 unique HL survivors were identified (Fig. 1). All patients underwent transthoracic echocardiographic examination according to clinical protocol. Patients were eligible for inclusion in the study if they (i) were diagnosed with a histologically confirmed HL, and (ii) received thoracic radiotherapy at least ten years prior to referral to the CO-clinic. For the purpose of this study patients with a history of myocardial infarction or cardiac surgery prior to echocardiographic examination were excluded. Furthermore, patients were excluded in case of incomplete HL diagnosis- and treatment history or incomplete echocardiographic examination. Also patients with persistent atrial fibrillation and evaluated echocardiographic parameters of systolic and diastolic function in these patients presenting at the CO-clinic.

![Diagram showing selection process of the study population. MI = myocardial infarction, CABG = coronary artery bypass grafting.]
Differences in baseline characteristics and echocardiographic parameters between patients with- and without elevated RHR were evaluated using unpaired Student’s t-test, Mann-Whitney U test, Chi-square or Fisher’s exact test, where appropriate.

Both simple- and explanatory multilinear regression modeling was performed to evaluate the association of echocardiographic parameters to RHR as a continuous variable. Possible confounders were identified by literature review added to the multilinear model: age, sex, mantle field irradiation.

Furthermore, an F-test for nested regression model comparison was used to compare a model restricted to extracardiac confounders (age + sex + mantle field irradiation) - and an unrestricted model with both extracardiac confounders and markers of cardiac function in relation to RHR.

Missing data was accounted for using complete-case analysis. Imputation methods for missing echocardiographic measurements were not contemplated, because they were assumed to be Missing Not At Random.

All statistical analyses were performed in R version 3.6.3 (R Foundation for Statistical Computing, Vienna, Austria).

3. Results

A total of 75 patients were enrolled in the study. The selection process is shown in Fig. 1. Baseline characteristics of the study population are shown in Table 1. The median age of HL diagnosis was 24 [19.0–29.5] years with an interval of 17.6 [12.4–25.8] years to index CO-clinic visit. The median cumulative mediastinal radiation dose was 36 [25th - 75th percentile: 35-40] Gy, and the majority of patients received concomitant anthracycline-containing chemotherapy regimen(s) (N = 54, 72%). Only few patients used medication at index CO clinic visit with 6 patients (8%) using betablockers. Sixty patients (80%) did not use any medication. All patients had sinus rhythm at index CO-clinic visit.

The average RHR in the study population was 77 ± 14 bpm with 30 patients (40%) having an elevated RHR (91 ± 10 vs. 69 ± bpm, p<0.001). There were no significant differences in baseline characteristics between patients with and without elevated RHR. Furthermore, patients with concomitant anthracycline-containing chemotherapy did not have a significantly increased RHR compared to patients whom received only thoracic irradiation (80 ± 11 vs. 77 ± 15; p = 0.453).

A summary of echocardiographic parameters of systolic and diastolic function is presented in Table 2. While LVEF was similar in patients with and without elevated RHR, GLS was significantly lower in patients with an elevated RHR (−15.9% vs. −18.3%, p = 0.045).

Furthermore, presence of diastolic dysfunction was more prevalent among patients with elevated RHR as compared to patients without an elevated RHR: 73.3% vs. 46.7% (p = 0.022). This is emphasized by a significantly decreased e’ wave velocity (Asymp. p = 0.038), and increased E/e’ ratio - which has been well correlated with LV filling pressure (Asymp. p = 0.034) in patients with elevated RHR [27]. Moreover the presence of diastolic dysfunction was asso-

Table 1

<table>
<thead>
<tr>
<th>Variable</th>
<th>Overall (N = 75)</th>
<th>Heart rate &lt; 80 bpm (N = 45)</th>
<th>Heart rate ≥ 80 bpm (N = 30)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resting heart rate, bpm</td>
<td>77 ± 14</td>
<td>69 ± 8</td>
<td>91 ± 10</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age, yrs</td>
<td>46.0 ± 11.5</td>
<td>45.3 ± 12.6</td>
<td>47.0 ± 9.8</td>
<td>0.505</td>
</tr>
<tr>
<td>Male</td>
<td>31 (41.3)</td>
<td>19 (42.2)</td>
<td>12 (40.0)</td>
<td>0.840</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>24.5 [22.6, 27.1]</td>
<td>24.4 [22.8, 27.6]</td>
<td>24.7 [22.0, 26.6]</td>
<td>0.368</td>
</tr>
<tr>
<td>Cardiovascular risk factors</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>10 (13.3)</td>
<td>6 (13.3)</td>
<td>4 (13.3)</td>
<td>0.885</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>3 (4.0)</td>
<td>1 (2.2)</td>
<td>2 (6.7)</td>
<td>0.560</td>
</tr>
<tr>
<td>Hypercholesterolaemia</td>
<td>10 (13.3)</td>
<td>6 (13.3)</td>
<td>4 (13.3)</td>
<td>1.000</td>
</tr>
<tr>
<td>Family history of heart disease</td>
<td>13 (17.3)</td>
<td>5 (11.1)</td>
<td>8 (26.7)</td>
<td>0.152</td>
</tr>
<tr>
<td>Smoking</td>
<td>3 (4.0)</td>
<td>3 (6.7)</td>
<td>0 (0.0)</td>
<td>0.270</td>
</tr>
<tr>
<td>Chronic renal insufficiency</td>
<td>3 (4.0)</td>
<td>2 (4.4)</td>
<td>1 (3.3)</td>
<td>0.810</td>
</tr>
<tr>
<td>Cardiovascular medications</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Beta-blocker</td>
<td>6 (8.0)</td>
<td>5 (11.1)</td>
<td>1 (3.3)</td>
<td>0.392</td>
</tr>
<tr>
<td>Non-dihydropyridine CCB</td>
<td>3 (4.0)</td>
<td>2 (4.4)</td>
<td>1 (3.3)</td>
<td>0.810</td>
</tr>
<tr>
<td>ACE inhibitor</td>
<td>4 (5.3)</td>
<td>2 (4.4)</td>
<td>2 (6.7)</td>
<td>0.675</td>
</tr>
<tr>
<td>Diuretic</td>
<td>5 (6.7)</td>
<td>4 (8.9)</td>
<td>1 (3.3)</td>
<td>0.642</td>
</tr>
<tr>
<td>Statin</td>
<td>6 (8.0)</td>
<td>3 (6.7)</td>
<td>3 (10.0)</td>
<td>0.678</td>
</tr>
<tr>
<td>Age at time of HL diagnosis, yrs</td>
<td>24.0 [19.0, 29.5]</td>
<td>25.0 [19.0, 32.0]</td>
<td>23.5 [21.0, 26.8]</td>
<td>0.721</td>
</tr>
<tr>
<td>Interval from HL therapy, yrs</td>
<td>17.6 [12.4, 25.8]</td>
<td>15.5 [12.1, 23.7]</td>
<td>23.6 [12.8, 26.9]</td>
<td>0.119</td>
</tr>
<tr>
<td>Ann Arbor stage III-IV</td>
<td>21 (28.0)</td>
<td>15 (33.3)</td>
<td>6 (20.0)</td>
<td>0.319</td>
</tr>
<tr>
<td>Radiotherapy type</td>
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<td></td>
<td></td>
<td>0.061</td>
</tr>
<tr>
<td>Mantle field &amp; subtotal nodalirradiation*</td>
<td>33 (44.0)</td>
<td>16 (35.6)</td>
<td>17 (56.7)</td>
<td></td>
</tr>
<tr>
<td>IFRT including mediastinal irradiation</td>
<td>39 (52.0)</td>
<td>28 (62.2)</td>
<td>11 (36.7)</td>
<td></td>
</tr>
<tr>
<td>IFRT without mediastinal irradiation</td>
<td>3 (4.0)</td>
<td>1 (2.2)</td>
<td>2 (6.7)</td>
<td></td>
</tr>
<tr>
<td>Cumulative mediastinal radiation dose, Gy</td>
<td>36 [35,40]</td>
<td>36 [30,40]</td>
<td>36 [30,36]</td>
<td>0.659</td>
</tr>
</tbody>
</table>

Variable                                | Overall (N = 75) | Heart rate < 80 bpm (N = 45) | Heart rate ≥ 80 bpm (N = 30) | p-value |
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Chemotherapy regimen</td>
<td></td>
<td></td>
<td></td>
<td>0.668</td>
</tr>
<tr>
<td>ABVD*</td>
<td>21 (35.0)</td>
<td>12 (33.3)</td>
<td>9 (37.5)</td>
<td></td>
</tr>
<tr>
<td>MOPP/ABV*</td>
<td>17 (28.3)</td>
<td>11 (30.6)</td>
<td>6 (25.0)</td>
<td></td>
</tr>
<tr>
<td>EBVP*</td>
<td>7 (11.7)</td>
<td>3 (8.3)</td>
<td>4 (16.7)</td>
<td></td>
</tr>
<tr>
<td>BEACOPP*</td>
<td>3 (5.0)</td>
<td>1 (2.8)</td>
<td>2 (8.3)</td>
<td></td>
</tr>
<tr>
<td>MOPP*</td>
<td>6 (10.0)</td>
<td>5 (13.9)</td>
<td>1 (4.2)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>6 (10.0)</td>
<td>4 (11.1)</td>
<td>2 (8.3)</td>
<td></td>
</tr>
<tr>
<td>Cumulative anthracycline dose, mg/m²</td>
<td>210 [150, 300]</td>
<td>205 [150, 285]</td>
<td>210 [150, 300]</td>
<td>0.583</td>
</tr>
</tbody>
</table>

Mean ± standard deviation, median [25th, 75th percentile], count (%); ACE = angiotensin-converting enzyme; CCB = calcium channel blocker; IFRT = involved field radiotherapy; HL = Hodgkin lymphoma; *other radiotherapy types did not include mediastinum.* both techniques always include mediastinal irradiation.

*chemotherapy regimen contains anthracycline.
ciated with higher RHR: 82 ± 14 bpm vs. 71 ± 12 in absence of dias-
tolic dysfunction; see Fig. 2. Also, abnormal GLS was associated
with higher RHR (83 ± 14 vs. 71 ± 12, \( p < 0.001 \)).

Noteworthy, left atrial volume in the total population was low:
19.5 ± 5.2 mL/m². Due to this lack of atrial dilation, it was not fea-
sible to further classify diastolic dysfunction from grade I to grade
III, as atrial dilation is required by the aforementioned guidelines
[24].

In multilinear regression analysis GLS (per %), E/e’ ratio (per
point) and presence of diastolic dysfunction were independently
associated with RHR when controlling for age, sex and mantle field
irradiation: see Table 3. Per % reduction in GLS, RHR increased with
1.30 bpm (95% CI: 0.12 – 2.48; \( p = 0.031 \)) and in case of diastolic
dysfunction RHR increased with 8.38 bpm (95% CI: 1.50–15.26,
\( p = 0.018 \)).

When we compared an extracardiac confounder model (age +
sex + mantle field irradiation) with an unrestricted model that
included the before-mentioned confounders (GLS and diastolic
dysfunction, we observed a significant improvement in association
with RHR [F-statistic = 6.36, \( p = 0.003 \)]. This further supports our
hypothesis that LV function is associated with RHR.

4. Discussion

The present study reports the result of comprehensive echocar-
diographic examinations in HL survivors treated with thoracic irra-

![Table 2](image-url)
variety of solid tumours [36–38]. Several studies showed a minor
been conducted to assess the favourable effect of beta-blockers in a
known to promote tumour growth and metastasis, and conse-
mortality aside of patients heart failure with reduced ejection frac-
serves as a therapeutic target to reduce cardiovascular events and
should be further investigated.

vedilol has been studied in small clinical trials for the prevention of
Multilinear association model of echocardiographic parameters of left ventricular function with resting heart rate.

<table>
<thead>
<tr>
<th>Determinant</th>
<th>B</th>
<th>95% for B</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>GLS, per %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unadjusted</td>
<td>2.23</td>
<td>1.16 – 3.31</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Adjusted*</td>
<td>1.81</td>
<td>0.69 – 2.92</td>
<td>0.002</td>
</tr>
<tr>
<td>E/e', per point</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unadjusted</td>
<td>1.94</td>
<td>0.81 – 3.07</td>
<td>0.001</td>
</tr>
<tr>
<td>Adjusted*</td>
<td>1.29</td>
<td>0.03 – 2.54</td>
<td>0.045</td>
</tr>
<tr>
<td>Abnormal diastolic function</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unadjusted</td>
<td>11.05</td>
<td>4.95–17.15</td>
<td>0.001</td>
</tr>
<tr>
<td>Adjusted*</td>
<td>8.38</td>
<td>1.50 – 15.26</td>
<td>0.018*</td>
</tr>
</tbody>
</table>

mean ± standard deviation, median [25th, 75th percentile], count (%); GLS = global longitudinal strain

diation to assess the association of LV function and the presence of
an elevated RHR.

Key findings of the study are (i) systolic- and diastolic dysfunction are more prevalent among patients with an elevated RHR, and (ii) both GLS and diastolic dysfunction are independently associated with RHR. To our knowledge this is the first study to demon-
strate an association between RHR and subclinical LV dysfunction in cancer survivors. The results confirm earlier studies showing high prevalence of both systolic and diastolic dysfunction in patients treated with thoracic irradiation and/or anthracyclines [18–21,28–31].

RHR is the product of a balance between vagal and sympathetic stimulation of the sino-atrial node. Increased adrenergic drive with positive chronotropic effects is one of the key mechanism in early stages of heart failure [22]. While at first increased RHR acts as a compensatory mechanisms to restore cardiac output, it later becomes detrimental to LV function as heart failure progresses. For this reason an elevated RHR in cancer survivors treated with radiation- and/or chemotherapy might reflect subclinical LV dysfunction and indicate worse long-term prognosis [9,15,32,33].

Moreover, while LVESVi remained similar between both strata of RHR, there was a trend towards smaller LVEDVi in patients with an elevated RHR. As previously described, this reduction in stroke volume could be the consequence of myocardial fibrosis and LVEDVi shrinkage associated with cardiotoxic cancer treatment. Izzo et al. demonstrated the inverse correlation with stroke volume changes and plasma norepinephrine (NE) concentrations in 68 mild hypertensive patients [34]. Possibly, elevated RHR in long term HL survivors could be the result of these increased plasma levels of NE. Grassi et al. displayed that elevated RHR can be consid-
ered a marker of sympathetic hyperactivity in both the general population and patients with cardiovascular disease. However, its value for this purpose is limited and the relation was most evident in heart failure and obese patients. In contrast, patients with essential hypertension did not show a correlation between elevated RHR and indices of sympathetic hyperactivity. While the HL survivors in this study do not have clinical heart failure, their background is also different from that of the general population or patients with cardiovascular disease because they have chemotherapy- and/or radiation induced myocardial fibrosis and impaired diastolic func-
tion [35]. The value of resting heart rate in this specific population should be further investigated.

Accordingly, several studies focused on whether RHR could serve as a therapeutic target to reduce cardiovascular events and mortality aside of patients heart failure with reduced ejection frac-
tion, where heart rate reduction is a cornerstone of therapy. In cancer biology, sympathetic nervous system activation has been known to promote tumour growth and metastasis, and conse-
quently a multitude of observational epidemiological studies have been conducted to assess the favourable effect of beta-blockers in a variety of solid tumours [36–38]. Several studies showed a minor benefit in overall survival, but this has not been supported by clinical trials and meta-analyses reported conflicting results [39]. Car-
vediol has been studied in small clinical trials for the prevention of anthracycline-induced cardiotoxicity in breast cancer patients and did show preservation of LV function compared to placebo, but well-powered randomised controlled trials with clinical endpoints have yet to be performed [40,41]. Physical exercise in cancer sur-
vivors is known to lower RHR and in several studies lower RHR has been associated with lower all-cause mortality and therefore serves as an interesting target for supportive care during and after cancer treatment [42–44].

Both systolic and diastolic dysfunction were more prevalent among patients with an elevated RHR and importantly abnormal GLS, increased E/e'-ratio and any grade of diastolic dysfunction were independently associated with RHR. The relation between RHR and LV function was underlined by a significant improvement of the association model between RHR and extracardiac determinants – age, sex and use of mantle field irradiation – when echocar-
diographic parameters of LV function were included (e.g. GLS and presence of diastolic dysfunction). These findings suggest that an elevated RHR in these patients might not be a harmless sign, but a potential marker for underlying LV dysfunction as a result of anti-cancer treatment. It must be noted, while GLS and E/e' were significantly more abnormal in patients with an elevated RHR, the observed systolic and diastolic dysfunction was subtle and the clinical implication of this subtle dysfunction needs to be fur-
ther investigated. However, these findings were observed during the first echocardiographic examination ten years after mediasti-
 nal irradiation in an overall young population. It is likely that sys-
tolic and diastolic dysfunction will become increasingly more important during longer follow-up as several publications have shown that compared to the general population, HL patients have a significantly increased risk of cardiovascular disease [45,46]. Fur-
ther studies are needed to evaluate serial changes in left ventricu-
lar function during longer follow-up and the relation with adverse outcome.

Another notable finding is that in patients with diastolic dys-
function left atrial volume was low. Increase in left atrial size is usually one of the first signs of increased LV filling pressure and is therefore incorporated in classification algorithms of diastolic function [24]. Because there was no substantial atrial dilation in our cohort, diastolic dysfunction was identified through tissue doppler imaging and further grading of diastolic function was not possible. A possible explanation could be that mediastinal irradiation also leads to fibrosis and scarring of the atria [29,47,48]. Dia-
tolic dysfunction induced by mediastinal irradiation therefore has a different pathogenesis and left atrial size in this population may remain normal due to the fibrosis that leads to atrial stiffening and less atrial dilatation. The average E/A was 1.0 in the study pop-
ulation, which suggest another possible explanation for the absence of left atrial enlargement: a possible large proportion of patients having early (grade I) diastolic dysfunction, where left atrial enlargement is less frequent.

Thoracic irradiation leads to a broad range of cardiac complica-
tions - including coronary artery disease, radiation valvulopathy, pericarditis and heart failure - through damaging both cancer-
and healthy cells by creating reactive oxygen species that induce
local inflammation and tissue fibrosis [3]. Anthracyclines are frequently combined with irradiation therapy and have the potential to induce dose-dependent cardiomyopathy by causing irreversible oxidative damage to cardiac mitochondria resulting in apoptosis [49,50]. The increased risk of adverse cardiac events extends beyond forty years after treatment in HL survivors [2]. While there are clear childhood cancer survivorship guidelines, post-treatment surveillance for cardiac adverse effects in (young) adult cancer survivors has been troublesome [6,51] and additional indicators of occult late-cardiotoxicity are needed. Our findings suggest that an elevated RHR is a potential marker for early myocardial dysfunction and could be helpful to define patients at risk for adverse cardiac events. More research is needed to elaborate on the clinical implications of elevated RHR and subclinical LV dysfunction in cancer survivors to further improve risk stratification and guide long term follow up.

In our study a cut-off value of 80 bpm was used to define elevated RHR. Over the years both higher and lower thresholds have been utilized. While dichotomization of RHR - as being elevated or not - is helpful for conceptualization purposes, a “true” RHR is substantially influenced by testing circumstances, measuring method and medication. For instance, some patients used betablockers or non-dihydropyridine calcium channel blockers which have negative chronotropic properties and could lower RHR. While in regression analysis betablocker use and RHR were not independently associated, our study population was too small to study the effect of these medications on RHR. Furthermore, while RHR was determined when a stable heart rate had established, it is possible that some misclassification in RHR strata can occur as a result of physical discomfort by the ultrasound probe.

To objectively assess LV function, patients with acute coronary syndrome or cardiac surgery have been excluded from our study populations, therefore the implication of these results cannot be extrapolated to all HL survivors. Furthermore, there is little spread in cumulative mediastinal irradiation dose in the study population and for this reason it is not possible to draw conclusions on dose-dependent occurrence of subclinical LV dysfunction or presence of an elevated RHR, but earlier studies have already supported this principle [52].

5. Conclusion

The results of our study indicate that elevated RHR is a common finding in HL survivors treated with thoracic irradiation. Importantly, elevated RHR was associated with LV diastolic dysfunction and subclinical systolic dysfunction as assessed by GLS.

Funding

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References


