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| Abstract | Cancer is a serious disease that causes significant disability and suffering, so naturally Health Related Quality of Life (HRQoL) is a major concern of patients, families and clinicians. This paper intends to relate biometric indices, in terms of HRV metrics, with self-perceived HRQoL from patients with lymphoma. Patients ($N$ = 12) answered FACT questionnaire and used a smartband that collected biometrical data in real-time along the chemotherapy treatment. Our results revealed that Physical Well-Being, Total, Lymphoma subscale and FACT-Lym Trial Outcome domains seem to have a similar pattern that HRV metrics across the treatment cycles. In specific, the FACT domains and the HRV metrics have the lowest average levels on the first cycle and seem to increase along the following cycles (3$^{rd}$ and 6$^{th}$ cycles). This approach of continuous assessment of HRQoL will enable a better accuracy and more supported clinical decision. |



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# An Approach to Assess Quality of Life Through Biometric Monitoring in Cancer Patients

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**Abstract.** Cancer is a serious disease that causes significant disability and suffering, so naturally Health Related Quality of Life (HRQoL) is a major concern of patients, families and clinicians. This paper intends to relate biometric indices, in terms of HRV metrics, with self-perceived HRQoL from patients with lymphoma. Patients ($N$ = 12) answered FACT questionnaire and used a smartband that collected biometrical data in real-time along the chemotherapy treatment. Our results revealed that Physical Well-Being, Total, Lymphoma subscale and FACT-Lym Trial Outcome domains seem to have a similar pattern that HRV metrics across the treatment cycles. In specific, the FACT domains and the HRV metrics have the lowest average levels on the first cycle and seem to increase along the following cycles (3rd and 6th cycles). This approach of continuous assessment of HRQoL will enable a better accuracy and more supported clinical decision.

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**Keywords:** Health-related quality of life · Haemato-oncological diseases · Self-reported measures · Physiological data · Wearable technology · Heart Rate Variability

## 1 Introduction

Cancer is a generic term for a large group of diseases that is characterized by an uncontrolled and abnormal growth of cells [1]. It can affect almost any part of the body and has many anatomic and molecular subtypes each requiring specific management strategies.


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People living with cancer can experience significant disability and suffering, so naturally Quality of Life (QoL) is a major concern of patients, families and clinicians [2]. Moreover, due to factors such as population ageing, it is estimated that by 2030 it will be registered in Portugal 60.000 new cases of cancer per year. In fact, cancer is the second cause of death in this country [3]. Being one of the European countries with the greatest population ageing, according to the United Nations report [4], Portugal has more than one million people over 75 years old. Beyond prolonging life, it is essential also increase patient's QoL. In particular, the treatment of haemato-oncological diseases, such as lymphoma, often implies high-dose chemotherapy, which can be associated with severe symptoms and psychological distress creating difficulties in fulfilling family and social roles (e.g. be able to work or participating in daily social activities) and having a major impact in patient QoL [5]. Despite there is no consensus in the literature, QoL term is seen as a multidimensional (physical, psychological, social, and spiritual), subjective, and dynamic concept [1]. In other words, QoL is a broad concept that encompasses all aspects of human life. For that reason, a distinction regarding focus health-related quality of life (HRQoL) was introduced. This could be defined as self-perceived aspects of well-being that are related to or affected by the presence of a disease or treatment [6]. Therefore, HRQoL provides a more holistic evaluation and positive concept of health, which includes an individual's experiences, beliefs, expectations, and perceptions [7]. Being a subjective concept modulated by cultural and care patterns, the most used way to assess HRQoL is through self-perception questionnaires [2]. However, there is also an objective component of HRQoL [7], related to clinical indicators that evaluate symptoms and individual ability to do daily activities. Because of this multidimensional conceptualization, an appropriate and effective assessment of HRQoL should incorporate both objective functioning and subjective well-being.

Recent technological advances in wearable devices have created new opportunities to collect continuous in real-time, objective patient data in a non-obtrusive manner [8]. Actually, wearable biometric monitoring devices (BMDs) can be an important tool in the continuous monitoring of biometric data, which can be used to assess patient's health status, disease progression and treatment effects [9].

BMDs can be defined as a "biosensor that collects a biological recognition element (such as blood glucose or sodium levels), anatomical structure (such as tumor size, infarct size or hippocampal volume) or integrated physiological parameter (such as heart rate, blood pressure, electroencephalography, mobility, speech and sleep patterns or speed of information processing)" [9]. In particular, Heart Rate Variability (HRV) has been widely used as a diagnostic and prognostic tool [11]. In this paper, we focus on HRV time-domain indices, which quantify the amount of HRV, observed during monitoring periods [10].

Therefore, the purpose of this study was to evaluate HRQoL in lymphoma patients throughout chemotherapy treatment and relate its domains to the most common HRV time-domain metrics assessed in real-time by mobile devices – QLife+ solution.

## 2 State of the Art

### 2.1 Health Related Quality of Life in Cancer Patients

HRQoL is considered as a powerful predictor of mortality and morbidity. Specifically, HRQoL is regarding to both self - reported chronic diseases (e.g. diabetes, arthritis, hypertension, and cancer) and their risk factors (e.g. body mass index, physical inactivity, and smoking status). So, HRQoL assessment can provide insights into the relationships between HRQoL and risk factors as well as determine the burden of preventable disease, injuries and disabilities. Moreover, HRQoL is now considered an important aspect in clinical practice for patients with chronic illnesses [12].

One of the most used questionnaires to evaluate HRQoL in cancer patients is the Functional Assessment of Chronic Illness Therapy (FACT) focusing on the previous 7 days. It includes a combination of inputs from experts and patients ensuring the inclusion of clinically important issues that are also relevant to the patient [13]. It has a general core (FACT-G), which is common for all patients with cancer, it is composed by 27 general items divided into four domains, namely Physical well-being (PWB; 7-items), Social/Family well-being (SWB; 7-items), Emotional well-being (EWB; 6-items), and Functional well-being (FWB; 7-items). Adding to this general core, there are several extensions specific to other chronical illness conditions such as lymphoma (FACT-Lym; 15 items) [13]. In particular, the Trial Outcome Index score have been reported as an efficient summary index of physical/functional outcomes and it is very responsive to change of the patient [13]. "While social and emotional well-being are very important to HRQoL, they are not as likely to change as quickly or dramatically over time or in response to physical health interventions" such as chemotherapy [13]. All items are evaluated in a 5-point Likert scale (from 0 to 4).

It is important to notice that assessing HRQoL throughout questionnaires face some challenges such as: time constraints and frequency overload, the response and recall bias where the patient may not have a complete recollection of their feelings and symptoms and by the desire to enroll in a trial or receive therapy resulting in the over reporting of their health status [8]. Other important challenge associated to questionnaires is "the static nature of the assessment only captured periodically, and the patient's health status is dynamic over the course of the treatment and can change on a daily basis" [8]. Therefore, it is important to complement the questionnaire information with biometric data in an objective and non-invasive manner.

### 2.2 Biometrics Data – Heart Rate Variability

The autonomic nervous system (ANS), composed by the sympathetic and parasympathetic branches, acts as a control system of blood vessels, glands and muscles, including the heart [14]. The continuous non-linear modulation of the ANS, results in complex and non-linear variations in HRV [10, 15]. "HRV is an emergent property of interdependent regulatory systems which operate on different time scales so that the patient has the flexibility to adapt to the environmental and psychological challenges"

[10]. It has been recognized to be a useful non-invasive tool to predict several pathologies such as myocardial infarction, diabetic neuropathy, sudden cardiac death and ischemia, among others [16].

Typically, statistical variables are calculated over 5 min length ECGs segments) [10, 15]. Time-domain indices of HRV quantify the amount of variability in measurements of the interbeat interval, which is the time period between successive heartbeats [10]. There exist a wide variety of time domain parameters, but we will focus on one described on Table 1.

**Table 1.** Time domain parameters description

| Parameters | Unit | Description |
|---|---|---|
| Mean HR | bpm | Mean heart rate |
| Mean RR | ms | Mean RR interval |
| RMSSD | ms | Root mean square of successive differences |
| SDNN | ms | Standard deviation of the RR interval |
| SDANN | ms | Standard deviation of the average RR intervals calculated over short periods |
| pNN50 | % | Proportion of successive RR intervals greater than 50 ms |

The intervals between consecutive heart beats needed to construct the time series are called RR intervals and the instantaneous Heart Rate (HR) is the number of beats per minute.

## 3 Methodology

### 3.1 QLife+ Architecture

The communication architecture implemented in the collection of biometric parameters in the QLife+ project, is based on the Microsoft Band 2 device, connected via Bluetooth protocol, to an Android smartphone, which in turn collects data from the wearable device's sensors. In this architecture, there is a set of proprietary and OpenSource technologies, linked and exchanging data, allow the collection and storage of biometric data. For attending this purpose, we need database tools, web server, mobile application - where these tools have adopted technologies such as PostgreSQL, Microsoft IIS Web Server - and an Android application. In order to provide communication between these technologies, different protocols are used, such as HTTPS in the communication between the mobile application and the web server, and an HTTP in the communication between the web server and the database PostgreSQL, given in a secure internal network.

### 3.2 Data Collection

Participants were recruited from one public Hospital in Portugal. Patient eligibility criteria included: histological diagnosis of lymphoma, being aged 18 years or older, confirmed to receive treatment at that Hospital, and considered by the oncologist and the researchers to be emotionally and physically capable of participating. After oncologist referral, participants were invited to participate and received an informative flyer. All participants provided their written informed consent to participate in this study.

Participants were interviewed at baseline (pretreatment or on the day of their first chemotherapy treatment), at several times during active treatment (first, third, and sixth chemotherapy cycle), and every three months at the follow-up.

At baseline, participants were asked to answer a brief sociodemographic questionnaire. They were given brief training on the BMD, specifically a smartband (Microsoft Band 2), and received written information with general instructions. Participants used the smartband during one or two weeks at pretreatment, and during two consecutive weeks at first, third, and sixth chemotherapy cycle. At the end of each week, they answered FACT-Lym. For this study, data were collected between February until October 2018.

### 3.3 Participants

Forty-seven patients were asked to participate in the study. Of these, 16 patients agreed to take part in the study. However, 4 participants were not included in the analyses due to the reduced biometric data. Six participants (50.0%) were female and 6 (50.0%) were male. Participants averaged 53.17 years old (SD = 16.73, range: 19–71 years). Concerning marital status, five (41.7%) participants were married, three (25.0%) were single, two (16.7%) were widowed, and two (16.7%) were separated. Four participants (33.3%) have the $4^{th}$ grade, two (16.7%) have incomplete or complete $9^{th}$ grade, four (33.3%) have incomplete or complete $12^{th}$ grade, and two (16.7%) have higher education.

### 3.4 Questionnaires and Biometric Data Preprocessing

All domains of the FACT were standardized to 0–100 scale. The physiological sensor in the wearable device is a light source that calculates a RR. The signals were recorded wirelessly and features were extracted after preprocessing the heart rate series, which were created with the standard approach: considering only 5 min length.

Artifacts were removed from the signal using a "adaptive threshold for rejecting value differs from previous and following beats, and from a mobile mean more than a threshold value and removing points that are not within acceptable physiological values" [17].

Measurements described on Table 1 were calculated and it was only selected the ones that matched the dates covered by the questionnaires. All parameters in the selected range were averaged. Moreover, since the measure are calculated based on short-term (5-min) variations it may experience some correlation and so it was selected the HR, RMSSD and the SDNN to analyze.

## 4 Results

Considering the FACT scores, patients experienced lower scores on the Functional Well – Being domain and higher on the Social/Family Domains. Throughout the cycles, patients experienced a decrease of the Lymphoma Subscale, Physical Well-Being and Total in the first cycle regaining the QoL in the third and sixth cycles. FACT-G experienced slight decrease until the third cycle. The Emotional subscale presented an oscillatory trend and Social/Family decreased on the third cycle. The average of the HR did not appear to follow similar trend across the cycles as all the FACT domains scores. It is also important to notice the high variability of the Emotional Well-Being scores in the Third and Sixth cycle and in the Functional domain in the pre-treatment and first cycles. The Physical Well – Being has higher variability in the third cycle.

(Figure 2, Table 2).

**Table 2.** Mean and standard deviation per domain and per cycle of FACT score, HR, SDNN and RMSSD

| Domain | Cycle | FACT Mean ± SD | | HR Mean ± SD | | SDNN Mean ± SD | | RMSSD Mean ± SD | |
|---|---|---|---|---|---|---|---|---|---|
| Emotional well-being | PreTr | 63.7 | ±12.43 | 78.6 | ±5.0 | 79.1 | ±19.5 | 81.1 | ±19.2 |
| | 1st | 74.1 | ±13.28 | 80.1 | ±5.7 | 78.0 | ±14.2 | 78.6 | ±16.1 |
| | 3rd | 69.7 | ±18.86 | 82.5 | ±6.0 | 80.5 | ±16.5 | 82.8 | ±20.3 |
| | 6th | 78.4 | ±17.85 | 82.4 | ±5.8 | 83.4 | ±21.0 | 86.4 | ±24.5 |
| Functional well-being | PreTr | 58.7 | ±19.10 | 78.6 | ±5.0 | 79.1 | ±19.5 | 81.1 | ±19.2 |
| | 1st | 53.6 | ±15.5 | 80.1 | ±5.7 | 78.0 | ±14.2 | 78.6 | ±16.1 |
| | 3rd | 49.9 | ±13.2 | 82.5 | ±6.0 | 80.5 | ±16.5 | 82.8 | ±20.3 |
| | 6th | 59.4 | ±12.1 | 82.4 | ±5.8 | 83.4 | ±21.0 | 86.4 | ±24.5 |
| Lymphoma subscale | PreTr | 74.0 | ±8.4 | 78.6 | ±5.0 | 79.1 | ±19.5 | 81.1 | ±19.2 |
| | 1st | 68.1 | ±11.2 | 80.1 | ±5.7 | 78.0 | ±14.2 | 78.6 | ±16.1 |
| | 3rd | 74.8 | ±16.2 | 82.5 | ±6.0 | 80.5 | ±16.5 | 82.8 | ±20.3 |
| | 6th | 81.2 | ±12.1 | 82.4 | ±5.8 | 83.4 | ±21.0 | 86.4 | ±24.5 |
| Physical well-being | PreTr | 79.1 | ±12.9 | 78.6 | ±5.0 | 79.1 | ±19.5 | 81.1 | ±19.2 |
| | 1st | 57.6 | ±15.0 | 80.1 | ±5.7 | 78.0 | ±14.2 | 78.6 | ±16.1 |
| | 3rd | 72.9 | ±21.1 | 82.5 | ±6.0 | 80.5 | ±16.5 | 82.8 | ±20.3 |
| | 6th | 79.9 | ±17.0 | 82.4 | ±5.8 | 83.4 | ±21.0 | 86.4 | ±24.5 |
| Social/family well-being | PreTr | 79.9 | ±19.1 | 78.6 | ±5.0 | 79.1 | ±19.5 | 81.1 | ±19.2 |
| | 1st | 82.3 | ±15.5 | 80.1 | ±5.7 | 78.0 | ±14.2 | 78.6 | ±16.1 |
| | 3rd | 74.4 | ±15.7 | 82.5 | ±6.0 | 80.5 | ±16.5 | 82.8 | ±20.3 |
| | 6th | 73.1 | ±13.4 | 82.4 | ±5.8 | 83.4 | ±21.0 | 86.4 | ±24.5 |
| FACT-G total score | PreTr | 74.7 | ±9.5 | 78.6 | ±5.0 | 79.1 | ±19.5 | 81.1 | ±19.2 |
| | 1st | 72.3 | ±10.7 | 80.1 | ±5.7 | 78.0 | ±14.2 | 78.6 | ±16.1 |
| | 3rd | 70.7 | ±11.1 | 82.5 | ±6.0 | 80.5 | ±16.5 | 82.8 | ±20.3 |
| | 6th | 78.1 | ±12.5 | 82.4 | ±5.8 | 83.4 | ±21.0 | 86.4 | ±24.5 |

(*continued*)

**Table 2.** (*continued*)

| Domain | Cycle | FACT Mean ± SD | | HR Mean ± SD | | SDNN Mean ± SD | | RMSSD Mean ± SD | |
|---|---|---|---|---|---|---|---|---|---|
| FACT-Lym trial outcome index | PreTr | 71.6 | ±9.9 | 78.6 | ±5.0 | 79.1 | ±19.5 | 81.1 | ±19.2 |
| | 1st | 62.1 | ±7.8 | 80.1 | ±5.7 | 78.0 | ±14.2 | 78.6 | ±16.1 |
| | 3rd | 68.3 | ±14.6 | 82.5 | ±6.0 | 80.5 | ±16.5 | 82.8 | ±20.3 |
| | 6th | 75.6 | ±10.7 | 82.4 | ±5.8 | 83.4 | ±21.0 | 86.4 | ±24.5 |
| Total | PreTr | 71.8 | ±10.0 | 78.6 | ±5.0 | 79.1 | ±19 | 81.1 | ±19.2 |
| | 1st | 67.2 | ±6.2 | 80.1 | ±5.7 | 78.0 | ±14. | 78.6 | ±16.1 |
| | 3rd | 69.5 | ±11.5 | 82.5 | ±6.0 | 80.5 | ±16 | 82.8 | ±20.3 |
| | 6th | 75.6 | ±9.7 | 82.4 | ±5.8 | 83.4 | ±21 | 86.4 | ±24.5 |

In the Physical Well-Being, Total, Lymphoma subscale and FACT-Lym Trial Outcome domains, the SDNN parameters followed the similar pattern exhibited by the domains scores across the cycles (Fig. 3, Table 2). The RMSSD parameter also exhibited similar pattern as the scores across the cycles in the FACT-Lym Trial Outcome Index, Lymphoma subscale, Physical Well-Being and Total (Fig. 4, Table 2). AQ2
Biometric data exhibited high variability in the SDNN index in all chemotherapy cycles (Fig. 1). AQ3

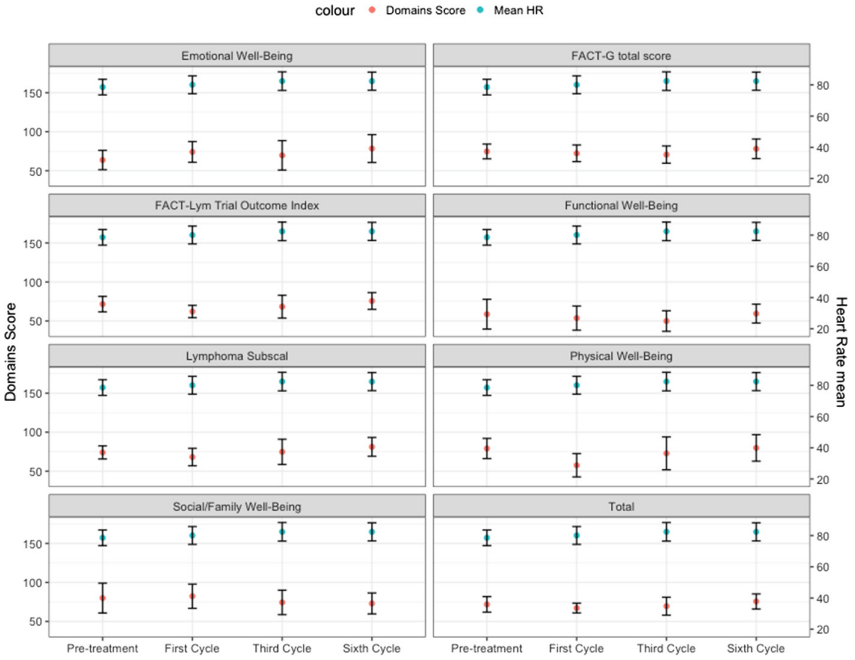


**Fig. 1.** Mean score of FACT (and standard deviation) and mean of HR (and standard deviation) per Domain and per cycle of chemotherapy

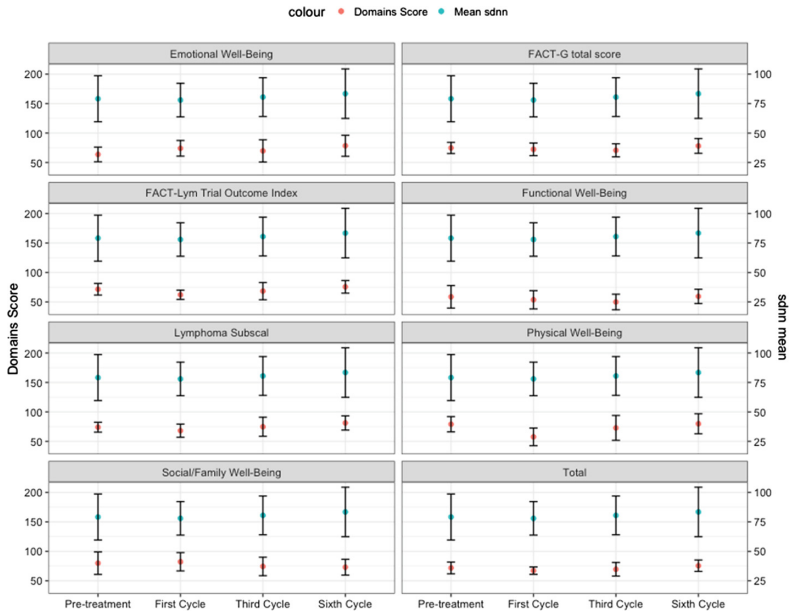


**Fig. 2.** Score of FACT and mean of SDNN per domain and per cycle of chemotherapy

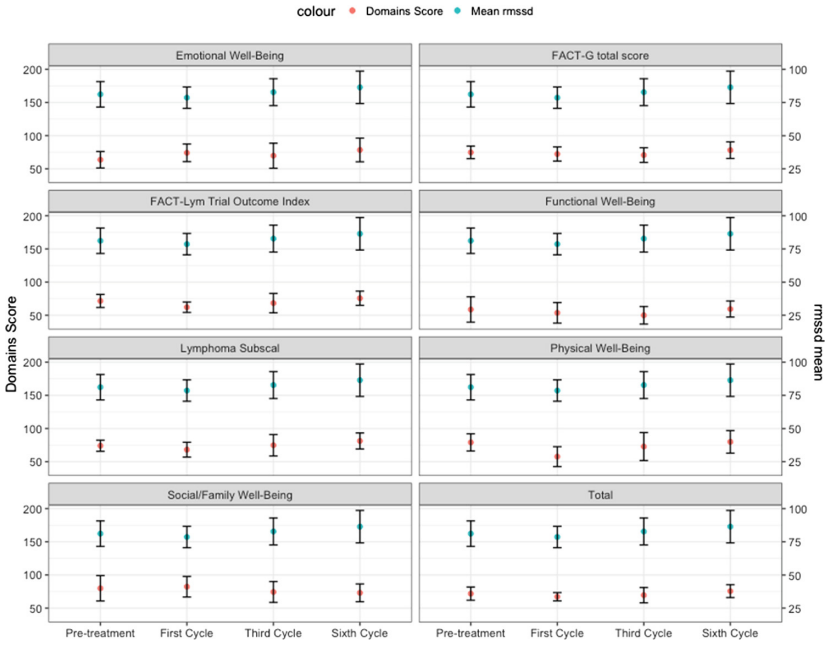


**Fig. 3.** Score of FACT and mean of RMSSD per domain and per cycle of chemotherapy

## 5 Discussion

The QLife+ Solution is an ongoing research, whose main goal is creating a new paradigm for the evaluation of HRQoL in clinical practice. The solution devised is based on an adaptive information system (IS), able to use physical and behavioral data of the patient, allowing continuous assessment of HRQoL that significantly reduce the questionnaires response time without affecting the patient's daily life. Continuous assessment of HRQoL will enable a better accuracy and more supported clinical decision [12].

In this paper, we focused to evaluate the existence of a possible relationship between self-perceived HRQoL domains and physiological data in terms of HRV metrics. Our results revealed that lymphoma patients experienced variations in HRQoL score throughout the cycles, being the Functional Well-being the domain with the lowest scores and the Social/Family with the highest. The first cycle presents as a particularly difficult moment reflected on the FACT-G, FACT-Lym Trial Outcome Index, Physical Well-Being, Lymphoma Subscale and Total.

In general, those results are in accordance with previous researches. In fact, it is common to verify a decline in Functional well-being both in lymphoma patients and survivors [18] that increases with the existence of additional chronic conditions. In comparison, Social/Family well-being has the highest values as found in a previous study [19]. Lymphoma patients commonly report a decrease in Physical Well-Being and overall HRQoL with treatment, as we have found with the lowest levels of well-being in the first cycle of chemotherapy. However, these effects may be reversed with physical activity which is recommended in cancer treatment [18, 20].

HRV seems to provide valuable information in the comprehension of pathological conditions in order to monitor the individuals' well-being [21]. In specific, higher HRV means a good physiological adaptation of the organism whereas lower HRV is a predictor of diseases or adverse events in patients with already diagnosed diseases [22]. Our results revealed that for Physical Well-Being, Total, Lymphoma subscale and FACT-Lym Trial Outcome domains, the SDNN and RMSSD parameters revealed a similar pattern as the domain scores. In specific, the FACT domains and the HRV metrics have the lowest average levels on the first cycle and seem to increase along the following cycles ($3^{rd}$ and $6^{th}$ cycles). These results seem to suggest that individuals are more severely affected in the first cycle exhibiting lower HRV and lower self-perceived HRQoL. According to the literature, it is expected to found lower HRV in individuals during chemotherapy treatment. However, this effects "appeared to be reversible with treatment cessation" [21], which will be evaluated in our future studies, when the participants will have completed the follow-up evaluations. In addition, HRV values depend on the disease stage, being reduced in patients with the more affected disease. Accordingly, our future studies will integrate the patients' clinical data (e.g., clinical stage) to provide a more complete understanding of the HRV and HRQoL according to the disease. This study extends the current knowledge regarding the HRQoL in lymphoma patients by evaluating this construct through self-reported data and biometric information collected in real-time along the chemotherapy treatment.

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