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TEST OF PHYSIOLOGICAL PERFORMANCE: RATIONALE AND FEASIBILITY

IVAN CORAZZA*, MARIA FRANCESCA MORRONE, MICHELA OLIVIERI, MARGHERITA ZECCHI and ROMANO ZANNOLI

Medical Physics Coordination Centre
Department of Experimental Diagnostic
and Specialty Medicine (DIMES)
Alma Mater Studiorum University of Bologna
Bologna, Italy
**ivan.corazza@unibo.it*

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Rigorous clinical evaluation of the physiological performance is currently performed with complex and long procedures which need expensive technology and skilled operators. In a wide range of situations (frail patients, daily clinical practice, etc.), these approaches are difficult to be applied and simpler tests, with a lack of scientific background, are mandatory. To avoid these problems, we propose a test (test of physiological performance (TOPP)) to evaluate the physiological behavior of a subject, in a really easy and safe clinical setting, measuring only the heart rate. The subject is submitted to an active standing-up test and then two submaximal exercises (with a low power load) on a cycle-ergometer. The heart rate modifications due to each submaximal step are analyzed by exponential interpolation to calculate the ascending and descending time constants and evaluate the way each subject adapts his heart rate to work. The standard deviation of the RR for each stationary phase (warm-up, load, recovery) was calculated as an index of short-term variability. Then a standard Fourier analysis of the stationary periods of the standing-up procedures allows to quickly and easily evaluate the autonomic nervous activation. We tested the protocol on five healthy subjects to verify the feasibility and the acceptance of the procedure. The five subjects demonstrated a good tolerance of the entire procedure. The standing-up showed a behavior of the autonomic system consistent with the physiology (with an increase in sympathetic activation in the passage to standing position). The analysis of the two submaximal steps highlights how younger and trained subjects present lower heart rates (both in the ascending phase and in the recovery) with a quicker adaptation ability (smaller time constants) consistent with what is expected. The short-term variability of heart rate is greater in young and trained subjects, thus confirming how the sympatho-vagal balance, in these

*Corresponding author.

subjects, is more dynamic. The proposed test is well tolerated by the subjects and the results, albeit in a small cohort of healthy volunteers, are consistent with what is expected from physiology and is already present in the literature. Our work aims to be a proposal with a feasibility check of a method for evaluating performance. The work to be done for the clinical validation of the TOPP is still long, but we are aware that it can give important results and that the TOPP can become an effective tool for the assessment of the physiological performance even of fragile subjects.

Keywords: Physiological performance; low-intensity exercise; HRV; exponential interpolation; time constant; HR short-term variability.

1. Introduction

Clinical activity uses many instrumental procedures to evaluate the functional status of a subject, but the procedural complexity and the results are not always adequate to the specific need. An example of this situation is the case of elderly and frail subjects, where a correct valuation of functional capacity is necessary to optimize the therapeutic strategy but most of the standard methods show to be inadequate, for loading conditions or technical and instrumental complexity. To overcome these difficulties, the clinicians are forced to use simplified methods, with lower scientific value but higher practical feasibility.

One example of this compromise is the "6-min walking test"[1] which offers a simple execution with a quantitative result and permits to make comparisons and analyses: simply, longer the walked distance, better the performance. It is an obvious, trivial evidence, but with low scientific value, since the test depends on many uncontrolled parameters (age, distance tracks, environment of execution, control by technical personnel and subjective behavior of the patient).[2–5] Nevertheless, the application of these methods deserves growing attention as they are also used in the field of telemedicine, leaving the methods of execution to individuals, without direct technical supervision.[6–14] For this reason, the scientific community is currently trying to find more repeatable and controlled approach to evaluate the performance.[13,15–17] A rigorous, scientifically powerful alternative exists: the cardiopulmonary stress test,[18–20] but impossible to apply in many situations for extreme loading conditions and instrumental complexity.[20–23]

Between the extremes of "6-min walking test" and "cardiopulmonary stress test", we are trying to outline a functional test which could join an easy feasibility, also on very impaired subjects, with a scientific rich content, suitable for information extraction, evaluation and comparison. In this technical note, we describe the basics of our "test of physiological performance (TOPP)" and we show his application on five different aged healthy volunteers. We also discuss the rationale of the choices and the possible empowerments. The objective of this presentation is to show the feasibility of the test and to highlight the differences between the subjects' records. The clinical validation of the test will follow, with adequate methods and numbers and the rules of clinical data management. The TOPP protocol we are presenting needs only a very basic set of instrumentations (cycle-ergometer and electrocardiographic device) and a personal computer for data acquisition and analysis.

2. Methods

Two major elements do not permit to use the cardiopulmonary stress test[20–23] on impaired subjects: (a) a face mask to monitor respiration and collect the expired air; (b) a progressively increasing physical load up to the subject's anaerobic threshold. In many cases, with elderly or impaired subjects, these limitations make the procedure not correctly feasible and the result are not valid. Moreover, the test requires a very complex instrumental apparatus and technical resources, which increase the cost behind an acceptable threshold for large-scale studies. Our proposal overcomes these limitations by sampling only the electrocardiogram (ECG) and asking the subject to perform simple physical actions with a very limited load. This under the assumption that the heart rate (HR) adaptation to a limited increase of physical load and recovery to baseline condition, is strictly related with the subject's functional capacity.[24] In fact, HR is the first physiological parameter which adapts the cardiac output to a physical load change[25] and the time course of this adaptation probably changes following an exponential model[26–28] with the subject's training and neurological driving[29] both for maximal and submaximal loads.[30–33]

With a step increase or decrease of the load, we can observe a subject-related HR change, roughly exponential with different time constant, an excessive change with overshoot followed by HR oscillations or different combinations related to subject's physical and neurological performance, both for onset and recovery phase.[34,35] We believe the study of HR adaptation to a small step increase or decrease of load, permits to evaluate the physiological performance of a subject.[24] Moreover, knowing the close connection between physical performance and neural driving, we can use the same ECG signal to calculate the patient's HR variability (HRV)[36] in the different conditions[37] and to observe this side of the problem. From a simple test, we can obtain a lot of information; it is our duty to extract and to analyze them. The test has been outlined mostly for elderly or impaired subjects during training programs or therapeutic procedures; the total duration is less than 30 min; it does not require particular technical or medical experience and is almost risk free. This small cohort of five subjects was used to outline and to describe the test procedure, to evaluate the feasibility and to verify if the load adaptation and recovery HR curves change with the subject. Due to the complete noninvasive approach and extremely low load, for these five volunteers, no ethical committee approval was necessary.

At the moment of recruitment, four electrodes (R, L, F and N) are applied on the chest of the subject and the ECG recording (I, II and III) starts. A ClickECG device (Cardioline SPA, Trento, Italy) interfaced to the Anscovery System (SparkBio S.R.L. Bologna, Italy)[38] was used. For 5 min, with the patient sitting while the assistant collects the anamnesis and fills the administrative forms, an ECG signal is sampled and verified for amplitude and noise. Then the subject is asked to lie, without speaking, on the ambulatory bed, the arterial pressure is measured (through a standard sphygmomanometer) and the basal ECG recording is maintained for at least 5 min.

The patient is then put in stand-up position for 5 min (active standing test[39]), ECG is recorded, the arterial pressure is measured again and the patient is asked to move to a cycle-ergometer (Mod. RHC 400, Air Machine, Cesena, Italy) and to pedal at a constant speed of 50 repetitions per minute (rpm) with no load for 3 min. When the cardiac frequency is stabilized, without informing the subject, the load is suddenly increased to 50 W and stays for 5 min or up to cardiac frequency stabilization. During this "active" phase, the patient is asked to be quiet and to maintain the same pedaling speed of 50 rpm. The load is then removed, pedaling is stopped and the monitoring continues, to record the full HR recovery curve (passive recovery phase). Then the patient starts pedaling again with no workload and the baseline recording continues for more 5 min and the load is eventually repeated, increased, or removed depending on the particular goal of the test. The pressure is measured and the test is finished.

In summary, the proposed TOPP provides ECG recording for the following:

(1) 5 min of clinostatic position;
(2) 5 min of standing;
(3) 3 min of pedaling (50 rpm) on a cycle-ergometer with no load;
(4) At least 5 min of exercise (50 rpm), after a sudden increase of the workload to 50 W;
(5) 5 min of passive recovery phase with the patient stopping pedaling;
(6) Repetition of the procedure from step 3. The workload at step 4 can be equal or greater of the first one. For the preliminary phase, the second load was fixed to 70 W.

A typical record is shown in Fig. 1. Then the job moves to the ECG signal analysis, which is performed at the end of the test and focused on two aspects:

(a) The way of HR adaptation to the increased load, the stabilization and the recovery phase following the load removal;
(b) HRV in the frequency domain in the subsequent physiological stationary phases during initial clinostatic and subsequent standing-up position.

Being the ECG, the only signal used for the evaluations, a preliminary intervention on it is performed with Anscovery software, on subsequent steps:

(1) Removal of transitory "patient-movement"-related artifacts on the ECG recording;
(2) RR intervals series (tachogram) extraction;
(3) Tachogram resampling (4 Hz, cubic spline);
(4) Low-pass filtering of resampled tachogram with a moving-average algorithm with a cutoff frequency of 0.5 Hz.

The subsequent action is focused to the analysis on the transition phases (during load changes), both positive and negative aimed to a quantitative description of the load

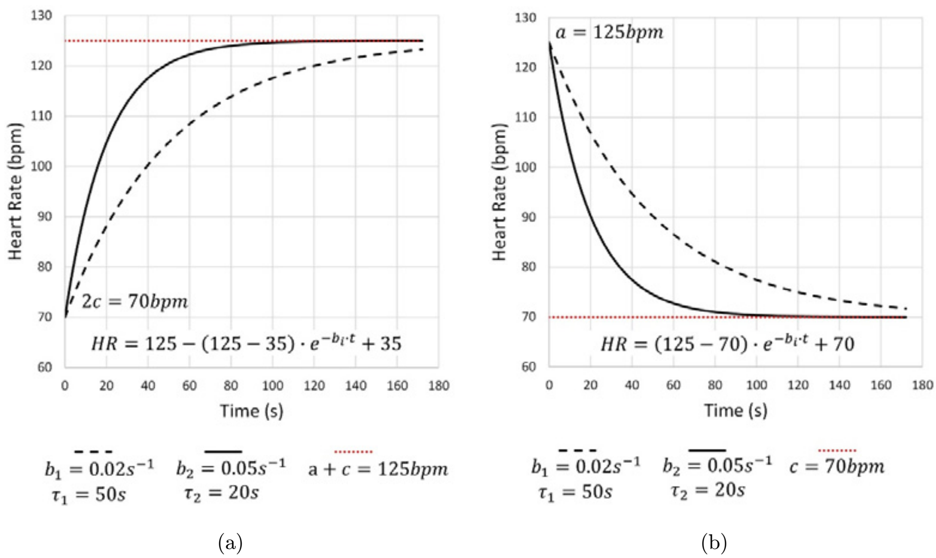

Fig. 1. Examples of interpolations for ascending (a) and descending (b) phases. Straight and dotted lines represent two different conditions of time constant (τ). If τ is higher, HR reaches the final asymptotic value more slowly, meaning a longer time for the subject to adapt his HR.

adaptation and recovery curve. Since in most cases, these curves have an exponential shape, their description is obtained by exponential[24,26,27,31] interpolation and coefficients extraction. Interpolation was obtained by a trust-region algorithm[40] performed with MATLAB software (Mathworks, Natick, Massachusetts, USA).

For the rising phases, the following interpolation curve was used:

$$\mathrm{HR} = a - (a - c) \cdot e^{-bt} + c,$$

where **2c** represents the starting lowest HR (when $t = 0$) and (**a**+**c**) the value to which the curve tends asymptotically ($t = \infty$).

For the descending phases, we have

$$\mathrm{HR} = (a - c) \cdot e^{-bt} + c,$$

where **a** is the starting highest frequency (when $t = 0$) and **c** is the asymptotic value (for $t = \infty$).

To have an index more easily suitable for comparisons for different subjects or for the same subject in different training phases, the time constant τ (tau) of the ascending and descending exponential phases was then calculated (in seconds) as the reciprocal of $\mathbf{b}(b^{-1})$. Figure 1 shows an example of our approach.

Moreover, to have a simply evaluation of the oscillatory behavior of the HR, the HR standard deviation (SD) over each stationary period (before, during and after each step) was calculated.[36] Finally, the HRV analysis in frequency domain was performed on the RR intervals during supine and standing periods. For the HRV, a

Table 1. Subjects' data.

Subj.	Age	Sex (male/female)	Weight	Height	Smoker	Sporting activity
1	70	M	75 kg	1.73 m	No	1
2	25	F	58 kg	1.81 m	No	4
3	24	F	49 kg	1.57 m	Yes	1
4	39	M	62 kg	1.63 m	Yes	4
5	29	F	65 kg	1.67 m	Yes	2

standard FFT approach was used.[36] LF (0.04–0.4 Hz) and HF (0.14–0.4 Hz) band powers were extracted from the PSD plot and expressed both in absolute (ms^2) and normalized units (in percentage without considering the VLS power band). All the

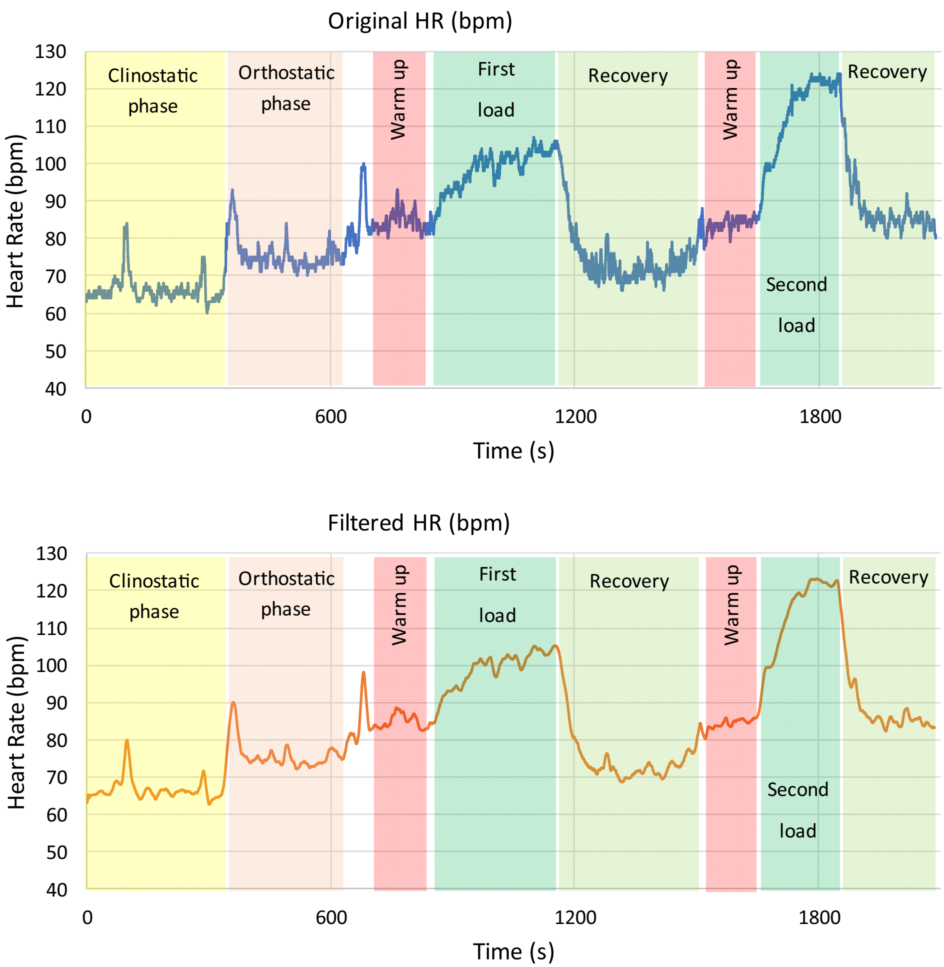

Fig. 2. Example of resampled tachogram (subject 1), before and after low-pass filtration. Initial peaks due to changes in posture were not considered in the subsequent analysis procedures.

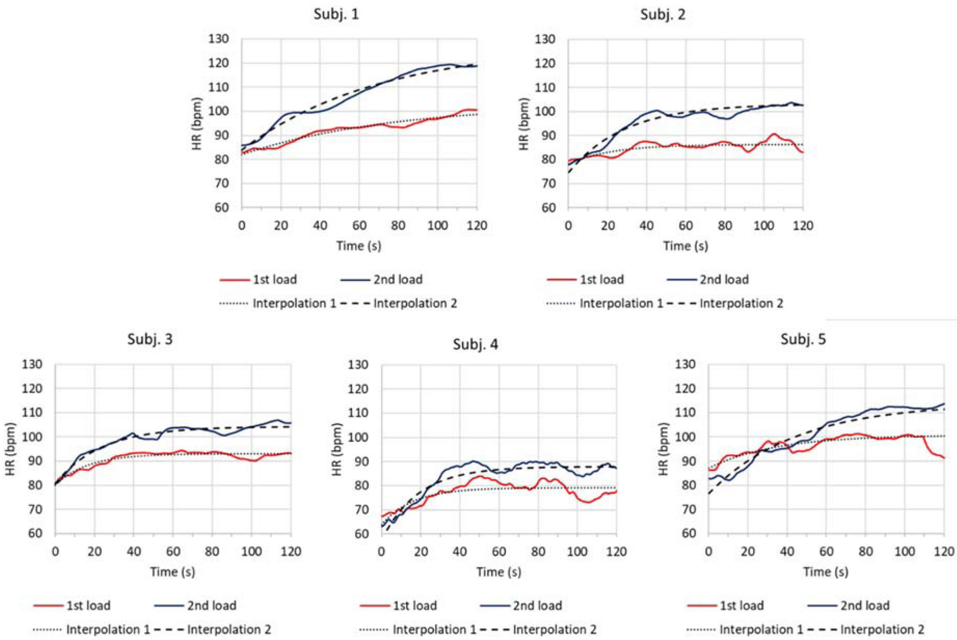

Fig. 3. Exponential interpolation of HR rising phases for each subject with two different loads (Y-scale for subject 3 is different from the other ones since the HR values are very different).

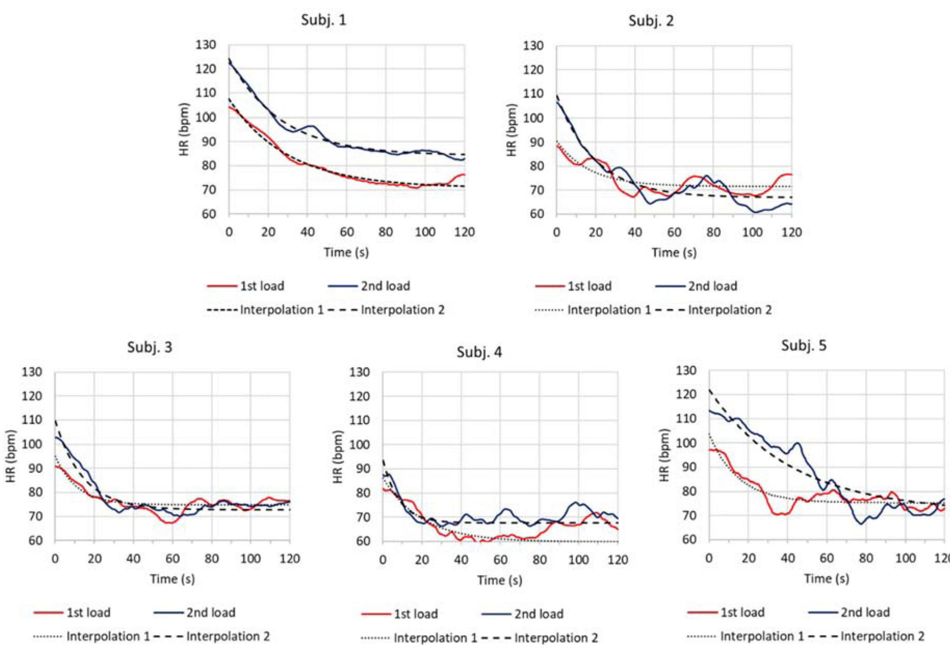

Fig. 4. Exponential interpolation of the HR recovery phases for each subject and both loads (Y-scale for subject 3 is different from the other ones since the HR values are very different).

Table 2. Results of exponential interpolation.

Subj.	Starting HR (bpm)	Ending HR (bpm)	Tau (CI 95%) (s)	Starting HR (bpm)	Ending HR (bpm)	Tau (CI 95%) (s)
	First load, rising phase			First load, descending phase		
1	82	103	76.3 (72.6–80.5)	108	71	30.4 (29.7–31.2)
2	78	86	22.2 (18.7–27.1)	90	71	16.8 (14.7–19.7)
3	80	93	16.6 (15.5–18.0)	95	75	11.2 (9.9–12.8)
4	64	79	16.1 (14.0–19.1)	86	60	19.7 (18.3–21.4)
5	88	100	33.7 (30.1–38.2)	104	75	14.8 (13.7–16.2)
	Second load, rising phase			Second load, descending phase		
1	84	127	69.9 (67.5–72.5)	124	84	26.8 (26.1–27.4)
2	74	103	28.6 (25.9–32.0)	109	67	19.8 (18.7–21.1)
3	80	104	22.9 (21.8–24.1)	110	73	14.2 (13.4–15.1)
4	58	88	17.5 (16.5–18.7)	94	68	8.2 (7.5–9.0)
5	76	113	44.1 (42.1–46.3)	122	71	42.4 (39.5–45.7)

calculations were performed with Kubios HRV (Kubios Oy, Kuopio, Finland). LF/HF ratio was then calculated as an expression of the balance between sympathetic and vagal activations. Statistical comparisons were performed with a T-student analysis. Statistically significant difference was considered for $p < 0.05$.

3. Results

Table 1 shows the data of the five subjects involved in the preliminary testing of our proposal. For each subject, the level of sport activity was evaluated by a simple score ranging from 1 to 5: 1 — sedentary (no activity), 2 — occasional (less than 3 times/month), 3 — one time a week, 4 — more than one time a week, 5 — agonism.

A complete test HR record (raw and filtered) is shown in Fig. 2 and HR changes, original and exponentially interpolated are shown in Figs. 3 and 4.

The numerical values of the exponential curves shown in Figs. 3 and 4 are shown in Table 2.

Figure 5 shows the time constants for each subject and each phase.

To evaluate the HRV during exercise, the SD was calculated during the stationary phases for each step. Results are reported in Table 3.

For what it concerns the SD, with the only exception of subject 2, the short-term variability decreases between warm-up and peak and then decreases during rest. It is interesting to highlight how the variability during recovery is higher than the starting one during warm-up. Then the HRV was evaluated during active standing. Table 4 shows the Mean HR (± SD), LF/HF ratio for each phase and for each patient.

Mean HRs during clino and ortho phases are statistically different ($p < 0.05$) and the LR/HR ratio behaves accordingly what we expect (an increase of the

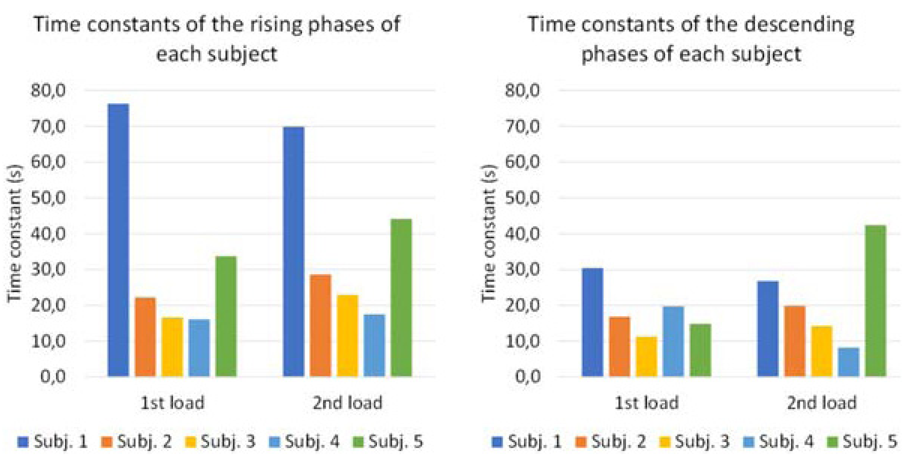

Fig. 5. Representation of the time constants tau for each subject and each phase.

Table 3. SDs calculated over the stationary periods of the different loads.

	First load			Second load		
	Warm-up	Peak	Recovery	Warm-up	Peak	Recovery
Subj.	SD HR (bpm)	SD HR (bpm)	SD HR (bpm)	SD HR (bpm)	SD HR (bpm)	SD HR (bpm)
1	1.7	1.1	2.5	1.2	0.9	1.5
2	3.1	4.1	3.6	2.4	3.7	4.3
3	4.1	2.0	3.2	2.8	2.1	3.6
4	5.2	4.6	4.8	5.2	3.6	5.5
5	3.5	3.0	6.0	3.6	1.8	5.4

Table 4. Results of HRV analysis during the clinostatic and orthostatic phases of the active standing test.

	Clino		Ortho	
Subj.	Mean HR $\pm$ SD (bpm)	LF/HF	Mean HR $\pm$ SD (bpm)	LF/HF
1	66 ± 1	2.91	75 ± 1	8.70
2	63 ± 1	2.63	78 ± 2	25.24
3	65 ± 1	0.15	83 ± 1	3.52
4	55 ± 1	0.82	71 ± 1	1.56
5	68 ± 1	1.33	81 ± 2	13.83

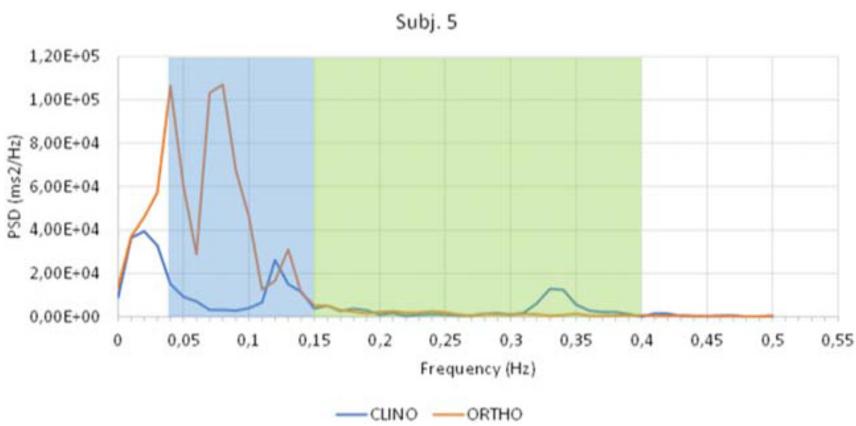

Fig. 6. An example of PSD (subject 5) subject during clinostatic and orthostatic phases.

sympathetic activity during standing). An example of the power spectral density plot is shown in Fig. 6.

4. Discussion

This first paper is focused on the feasibility of the test and to show the curves obtained on a small group of subjects with different age and lifestyle. A future step will be to demonstrate, in a larger population, if and how the changes of the adaptive and recovery HR behavior can describe the changes of performance consequent to training or therapeutic approach. In this phase, we assume this possibility on the basis of previous experience with cardiopulmonary test, but we have to verify if the changes obtained with a limited load are suitable for quantification and description. We are confident because also in this small population, differences between subjects exist, easily demonstrated by a simple comparison between the curves and related quantitative values.

Another aspect must be discussed: why to introduce the HRV, which is mostly related to autonomic nervous system (ANS) regulation, in a test aimed to evaluate the physical performance of a subject? Because our previous experience[35,41–43] demonstrates a very important involvement of the ANS in the process of physical training of athletes, and we believe this is possible (or also enhanced) on impaired subject with sedentary habit. In the rehabilitation or maintenance of fragile subjects, the HRV analysis may offer an interesting possibility to have a look on this side. We know that the HRV curve modifies following the training programs on athletes and normal subjects and for this reason, the proposed name of the test is TOPP, because it takes a look also on nonpurely physical side.

The TOPP puts together different evaluations that are commonly done separately: already published paper propose method to analyze the ANS during cardiovascular tests[37]; other papers present the analysis of the recovery phase after a maximal or submaximal load[26,27,31,32]; other authors tried to analyze the adaptation phase of the HR to a load.[30] Our approach put everything together, providing a simple test which can be easily performed without any technical difficulty, as demonstrated by our experience.

Another possible application of this test could be important: the functional stratification of subjects. In many large-scale training programs aimed to preserve or improve wellness, it is very difficult to organize the different activities to satisfy the desires of all the subjects: some of them are physically trained and want to execute heavy loads, others are physically impaired, and for them only a very low load is possible. It is necessary to stratify the whole group in subgroups the basis of physical performance: this test can be appropriate for this and may follow each subject within the protocol, adapting the loads to the performance changes.

Our experience on this small cohort demonstrates that the test can be easily performed and accepted by all the subjects and requires a minimal technological and technical support. Also, the time required is absolutely acceptable and lower than for alternative tests. Moreover, the simple ECG signal alone demonstrates a very powerful information content and is able to deeply characterize the different subjects and give a huge data frame to be scientifically explored.

About the signals, the exponential interpolation of the adaptation curves seems adequate, both in HR onset and recovery phase. The ascent time constants (to reach each step) are always greater than the corresponding descent constant ($p < 0.05$ except for subject 4, first load and subject 5, second load), regardless of the departure and arrival frequencies. The most trained subjects (2 and 4) are those who start from lower basal frequencies (before each step) (first load: 78 bpm and 64 bpm; second load: 74 bpm and 58 bpm) and reach lower frequencies (first load: 86 bpm and 79 bpm; second load: 103 bpm and 88 bpm) with quite low time constants (first load: 22.2 s and 16.1 s; second load: 28.6 s and 17.5 s). This happens without apparent dependence on age. Subjects 1 and 5 are the ones with the higher time constants, both for the first and second steps, probably related to a less trained physical condition (subject 5) and higher age (subject 1). These results, despite not presenting any statistical meanings, are coherent with the age and the physical condition of each subject and compatible with the evidences can be found in the literature.[26,32,44]

Figures 2 and 3 show different behaviors between subjects, not only related to the different initial and final HR: both rising and descending phases of subject 1 are quite smooth, without fluctuations. All the other cases show, in the final part of both rising and descending phases, more or less evident oscillations overlapped to the exponential trend. These fluctuations were not quantified in this paper but are interesting, since probably due to a change in adaptation modality to the final load. The first-older subject adapts its HR "quickly" without any fluctuation due to an adequate intervention and balance of the sympathetic and vagal systems. The other subjects seem to have a more difficult adaptation to the final load and the ANS tries to adapt the HR to the load with successive interventions. Apparently, this behavior can appear as "dysfunctional" but at a deeper reading, it is probably related to the younger age of the subjects and their intrinsic HRV.[45] Our interpretation is only a suggestion that may be obviously deepened and verified by a dedicated protocol.

As highlighted by the other authors,[34,43] short-term variability (calculated as the standard deviation of the beats during each period) decreases between baseline and load but increases reaching values greater than baseline at the end of recovery (see SDs in Table 3). The only one subject that presents a different trend on the first load is subject 5. The HRV analysis of the standing shows for all subjects an increase in the LF/HF ratio respect the supine phase, corresponding to a sympathetic activation (as expected).

At this moment, we cannot outline the role of HRV to describe the whole physiological performance of the subjects, but we can affirm that differences are evident, and that each subject shows his clear pattern and the results obtained in term of exponential interpolation, standing-up test and short-time variability are coherent between each other. On this basis, we can move on and observe how the subjective pattern changes with training, pathology and therapy. Every day we affirm our technological power to extract clear information from big data repositories: here we have the information which changes with individual changes, let us try to analyze and extract! Maybe we will obtain no more than with other simple tests, but anyway here the result is based on a rigorous scientific and instrumental approach and not on a simple comparison of quantitative crude data.

5. Conclusions

We started to think this test, as a mean to evaluate the physical performance of a subject, under the assumption that the adaptation of a complex biological system to a load change is more rapid and efficient if the system is trained and able to support the load; subsequently, by considering the signal used for the evaluation (ECG), his complexity, the HRV measurement to characterize also the neurovegetative driving, we decided to indicate the test more as a physiological test than a physical test, and this is the actual proposed name: TOPP. We know that we have a lot to do and many obstacles to jump, but we are opening a new research field, with a clear clinical and social need, with a deep connection with our research methods. What more we need to move on?

Authors' Contributions

Conceptualization: IC, RZ; Methodology: IC, MFM, MZ; Formal analysis and investigation: MFM, MO, MZ; Writing — Original draft preparation: IC, RZ; Writing — Review and editing: IC, MZ.

Ethical Compliance

The study was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments, no ethical approval accordingly with the guidelines and regulations of University of Bologna for submaximal noninvasive tests performed only on healthy anonymous volunteers. Each subject was informed about the procedure, gave his written consent and could always decide to stop the test at any time.

Conflict of Interests

Nothing to declare.

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