Predicting cardiopulmonary response to incremental exercise test

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***Abstract*—Cardiopulmonary exercise testing is a non-invasive method widely used to monitor various physiological signals, describing the cardiac and respiratory response of the patient to increasing workload. Since this method is physically very demanding, innovative data analysis techniques are needed to predict patient response thus lowering body stress and avoiding cardiopulmonary overload. This paper proposes the Cardiopulmonary Response Prediction (CRP) framework for early predicting the physiological signal values that can be reached during an incremental exercise test. The learning phase creates different models tailored to specific conditions (i.e., *single-test* and *multiple-test* models). Each model can be exploited in the real-time stream prediction phase to periodically predict, during the test execution, signal values achievable by the patient. Experimental results on a real dataset showed that CRP prediction is performed with a limited and acceptable error.**

I. Introduction

Cardiopulmonary exercise testing is an objective method to evaluate the patient cardiac and pulmonary functions during exercise [18]. It has been widely exploited to test normal subjects [19], patients with chronic heart failure [11] and chronic obstructive pulmonary disease [24], and to identify the cause of unexplained exertional dyspnea [23]. Incremental tests are commonly used to progressively increase the mechanical demand that the individual cardiopulmonary system has to match until she/he can no longer maintain the applied workload. Various physiological signals, mainly describing the patient cardiac and respiratory functions, are monitored during the test to analyze the body response to increasing strain. This cardiopulmonary response, when skeletal muscles transform chemical energy into mechanical output, has been shown to be best described by patient's peak aerobic power (VO_{2peak}), i.e., the oxygen consumed by exercising muscles per unit of time at peak incremental effort.

Since cardiopulmonary tests are physically very demanding, long test durations can significantly increase the body stress on the monitored individual and may cause cardiopulmonary overload. It follows that the capability to early predict the patient body response to the exercise during the test execution is a challenging issue. The aim is lowering the body stress, by prematurely interrupting the test and by avoiding its entire execution, without missing the information on the cardiopulmonary adaptation for the monitored individual.

This paper proposes the Cardiopulmonary Response Prediction (CRP) framework for early predicting the physiological signal values that can be reached during an incremental test. During the test execution, CRP analyses various vital signals for the patient executing the test, and automatically predicts the signal values achievable at different subsequent steps of the test (i.e., at the next step, when the test ends or at an intermediate step of the test). Through the periodical prediction of the individual cardiopulmonary response to the test, physicians can decide when to prematurely stop the test execution, thus lowering the body stress.

To obtain an accurate prediction, a suitable model for the currently monitored patient should be exploited. Two different types of prediction models are provided within CRP. The first model (denoted as *single-test* model) is trained using only the measurements collected during the *test currently in execution*. Consequently, it is tightly tailored to the patient response in the ongoing test. The second model (denoted as *multiple-test* model) is trained using a larger reference knowledge base containing a *collection of previous tests*. This model can also be tailored to the patient doing the test, when tests with a similar body response are selected as knowledge base. Both the Support Vector Machines (SVM) and the Artificial Neural Networks (ANN) techniques [22] have been selected to perform the prediction analysis for both models due to their ability to yield good accuracy performance.

In this study we present a first implementation of the CRP framework focusing on the prediction of the heart rate (HR) and oxygen consumption (VO_2) values, that are important indicators of the individual body response to the test. Specifically, in the current implementation CRP allows predicting (i) the HR and VO_2 values reached at the test end (HR_{peak} and VO_{2peak}, respectively) and (ii) the VO_2 value reached at the step following the prediction step (VO_{2next}).

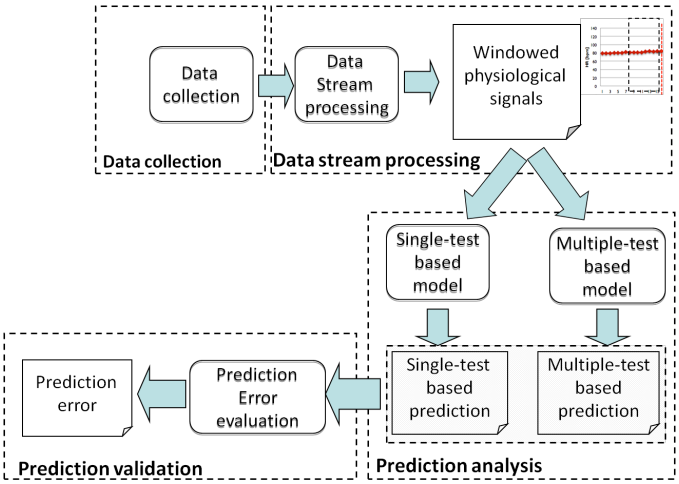

Fig. 1. The CRP framework

The *multiple-test* model is available to predict HR_{peak} and VO_{2peak}, while both *single-test* and *multiple-test* models are provided for VO_{2next} prediction. The experimental evaluation of the proposed approach has been performed on a real dataset containing incremental tests for diverse patients. Tests have been run by using a test protocol (i.e., $5W \times 30sec$) commonly adopted for the functional evaluation of cardiac patients. Experimental results showed that CRP is able to perform the prediction with a limited error, which does not seem to affect the evaluation of the patient's response to exercise. CRP allows reducing the test duration, thus lowering the body stress of patients without loosing key physiological information (as VO_{2peak} and HR_{peak}) on their response to the test.

The paper is organized as follows. Section II presents an overview of the CRP framework. Section III reports and discusses the experimental evaluation of a first implementation of the proposed approach. Section IV discusses previous work on cardiopulmonary analysis. Section V presents future developments.

II. Methodology

The CRP framework analyses the physiological signals collected during the cardiopulmonary exercise test to early predict the values of important signals (as HR_{peak} and VO_{2peak}) that can be reached by the patient in the test. CRP is organised into the following four main phases: (i) data collection, (ii) data stream processing, (iii) prediction analysis, and (iv) prediction validation. The building blocks of the framework are shown in Figure 1 and detailed below.

A. Data collection

The test execution is characterized by the test protocol and the various physiological signals that are continuously monitored during the test. The CRP framework collects data on both the monitored signals and the workload progressively assigned in the text execution.

In the incremental tests considered in this study, the workload is a step signal defined by two parameters: The increment of workload at each step (W_{step}) and the duration of each step (t_{step}) in which the workload is kept constant. These two parameters define the test protocol, denoted $W_{step} \times t_{step}$, meaning that every t_{step} seconds the workload is increased by W_{step} Watt. The protocol is set before the test starts and it is kept constant during the test. The test ends when the individual cannot sustain the current workload. The HR_{peak} and VO_{2peak} values represent the highest values achieved by the individual in the test, for the heat rate and oxygen consumption signals respectively.

Signal name	Abbreviation	Measurement unit
Fraction of inspired oxygen	FIO_2	%
Fraction of expired oxygen	FEO_2	%
Fraction of inspired carbon dioxide	$FICO_2$	%
Fraction of expired carbon dioxide	$FECO_2$	%
Fraction of end-tidal carbon dioxide	$FetCO_2$	%
Fraction of end-tidal oxygen	$FetO_2$	%
Ventilation	VE	l/min
Respiratory rate	RR	$breaths/min$
Inspiratory time	IT	sec
Expiratory time	ET	sec
Heart rate	HR	$beats/min(bpm)$

TABLE I. Monitored physiological signals

During the test execution, various physiological signals are sampled to analyze the patient body response under increasing strain. More specifically, the patient is monitored by means of a set of sensors and a spirometer. Besides the cardiovascular parameters (e.g., the heart rate), the majority of monitored signals describes the patient ventilatory function (e.g., fraction of inspired and expired oxygen). Table I reports the subset of physiological signals collected in CRP to support the prediction analysis. Since collected signals differ both in scale and measurement unit, a *min-max* normalization step [25] has been performed. This technique is typically exploited in time series analysis [14], because it preserves the original data distribution.

According to [17], the patient oxygen consumption VO_2 (expressed in liters per minute, l/min) during the test execution has been calculated based on the oxygen and carbon dioxide inspired and expired by the patient. VO_2 is computed as

$$VO_2 = f_{STPD} \times VE \times [((1-(FEO_2+FECO_2)) \,/\, (1-(FIO_2+FICO_2))) \times FIO_2 - VE \times FEO_2] \quad (1)$$

where f_{STPD} is the factor of Standard Temperature and Pressure Dry air. f_{STPD} allows comparing values regardless of the temperature and pressure conditions at which they are collected. Based on [17], f_{STPD} can be expressed as

$$f_{STPD} = (273^\circ K \,/\, (273^\circ K + T_A)) \times (P_{BAR} - P_{H20}) / (760mmHg) \quad (2)$$

where P_{BAR} is the ambient barometric pressure and P_{H20} is the water vapor pressure at temperature T_A. In this study, T_A was assumed "$36^\circ C$, and consequently $P_{H20} = 44.6mmHg$.

B. Data stream processing

In cardiopulmonary exercise tests, the exact test duration cannot be specified a-priori because it depends on the patient condition and his/her capability to sustain the progressively rise in workload. Consequently, physiological signals monitored during the test execution should be captured as an unbounded stream. For this reason, the CRP framework has been designed to perform the prediction task through the *data stream analysis over a sliding time window*. Specifically, at each step of the test, one single sliding time window over the original data stream is considered for the prediction task. This window contains a snapshot of the physiological signals monitored in the previous instants of the test. It allows describing the recent past response of the patient to the test, and consequently predict his/her response in the next instants of the test (e.g., the achievable HR_{peak} and VO_{2peak} values).

The sliding time window approach required the definition of the three parameters listed below. (i) The sliding time *window size* parameter (w_{length}) determines the temporal context of interest. A too short time window may focus the prediction task on an almost instantaneous evaluation of the patient condition, since only recently collected data are considered while the previous patient behavior is ignored. Instead, a too large time window allows analyzing many data on past patient behavior, but it may introduce noisy information in the prediction analysis. (ii) The *moving step* parameter (s_t, $s_t \leq w_{length}$) defines how often the window moves, and consequently the step when the prediction is performed. (iii) The *prediction horizon* parameter (h_t) defines the distance between the current sample in the time window and the value to be predicted.

C. Prediction analysis

During the test execution, the patient cardiopulmonary response to the exercise in the subsequent steps of the test can be predicted using the CRP framework.

The prediction of the physiological signal values achievable in a new ongoing test Q takes place at each time t_p in which the workload is increased. Two types of prediction models, named *single-test* and *multiple-test* model, can be created in CRP. They differ in the reference knowledge base used for model training.

More specifically, for the *single-test* approach, the prediction model is trained only using the *new test* Q currently in execution. Instead, the *multiple-test* model is trained with a *set of previous tests* run with the same protocol of test Q, and reaching a workload value at least equal to the workload of test Q at the prediction step t_p.

The *single-test* approach provides a *tightly tailored model* to the patient response in the ongoing test. The *multiple-test* approach generates an *enriched model* considering responses collected in more tests. To build a suitable model for the currently monitored patient, previous tests showing response to the exercise similar to the patient response in the ongoing test can be considered. For example, tests reaching workload values within a given range can been selected. In this study, we adopted this criterion.

For both *single-test* and *multiple-test* approaches, the prediction process entails the following two main phases.

(i) *Prediction model creation.* A different prediction model is created for each target physiological signal value (e.g., for HR_{peak} and VO_{2peak} value). The prediction model is trained with the ongoing test Q (*single-test* model) or a set of previous tests (*multiple-test* model). For both (*single-test* and *multiple-test*) approaches, the prediction model is trained by considering the physiological signals listed in Table I. These signals are monitored within a sliding time window preceeding the prediction step t_p.

(ii) *Prediction of the physiological signal values.* The (*single-test* or *multiple-test*) model is used to predict the physiological signal values achievable in one subsequent step of the new ongoing test Q. It is possible to predict the signal values reached by test Q in the step following the current (prediction) step (i.e., the *next* step of the test), when the test ends (i.e., the *final* step of the test), or in an *intermediate* step of the test.

Different data mining algorithm can be chosen for the prediction analysis. Among the available techniques suited for the regression problem (i.e., the prediction of a real value as in this study) we selected Support Vector Machines (SVM) [22] and Artificial Neural Networks (ANN) [25]. Both techniques can be used for both regression and classification problems, and they have been widely exploited in many different applications yielding good accuracy performance. The two techniques are briefly presented below while their configuration in the CRP framework is described in Section III.

Support Vector Machines (SVM) [22] have been first proposed in statistical learning theory. SVM is able to deal with high-dimensional data and it generates a quite comprehensive (geometric) model. An SVM predictor is based on a kernel function K that defines a particular type of similarity measure between data objects. Examples of kernel functions are linear, RBF (Radial Basis Function), polynomial, or sigmoid kernel. The SVM learning problem can be formulated as a convex optimization problem, in which different algorithms can be exploited to find the global minimum of the objective function.

Artificial Neural Networks (ANN) [25] simulate biological neural systems. The network consists of an input layer, n hidden layers, and an output layer. Each layer is made up of nodes. Each node in a layer takes as input a weighted sum of the outputs of all the nodes in the previous layer, and it applies a nonlinear activation function to the weighted input. The network is trained with backpropagation and learns by iteratively processing the set of training data objects. For each training data object, the network predicts the target value. Then, weights in the network nodes are modified to minimize the mean squared prediction error. These modifications are made in the backwards direction, that is, from the output layer through each hidden layer down to the first hidden layer.

D. Prediction validation

This block measures the ability of the CRP framework to correctly predict, for a new ongoing test, the physiological signal values achievable in a subsequent step of the test (e.g., when the test ends). To this aim the *absolute prediction error* is computed. It is the absolute difference between the predicted

and the actual value of the signal in the test. During the test execution, the signal value is periodically predicted each time an increment of workload occurs, and the corresponding prediction error is evaluated.

In this study, the leave-one-out cross-validation method [25] is used for prediction error evaluation. At each workload increment (i.e., at each prediction step t_p), the subset of tests still running is selected from the dataset. In turn, a different test is picked out of this subset, while the remaining tests are used as knowledge base to predict the considered values. To perform the prediction, the chosen test for the prediction and the reference knowledge base used for the prediction model creation are described by their values within the sliding time window (with size w_{length}). The *Mean Absolute Error* (MAE) [25] at prediction step t_p is the average of the absolute prediction errors computed for all tests in the subset.

III. Experimental results

This section presents the experimental results for our first implementation of the CRP framework. In the current implementation, CRP allows predicting (i) the HR and VO_2 values reached at the test end (HR_{peak} and VO_{2peak}) and (ii) the VO_2 value reached at the step following the prediction step (VO_{2next}). The *multiple-test* model is provided to predict HR_{peak} and VO_{2peak} values, while both *single-test* and *multiple-test* models are available for VO_{2next} prediction. Both *multiple-test* and *single-test* models have been created using both SVM and ANN algorithms. The ability of the CRP framework in correctly predicting the values above is evaluated by analysing the prediction error (MAE) and its distribution. To measure the efficiency of CRP in performing the prediction analysis, the training and prediction time are also discussed.

The experimental evaluation has been performed on a real dataset including several incremental tests for diverse anonymized patients collected at "Exercise pathophysiology laboratory - Cardiac rehabilitation division - Fondazione Salvatore Maugeri IRCCS", Veruno, Italy [16]. Tests have been run using the $5W \times 30sec$ test protocol commonly adopted for the functional evaluation of cardiac patients. The dataset includes 125 tests done by cardiac patients who have reached a maximum workload in the range $[85W \div 115W]$ in the tests. Table II reports the main data distribution of the monitored physiological signals (introduced in Table I), the computed VO_2 (as described in Section II-A), and the peak values for VO_2 and HR (i.e., VO_{2peak} and HR_{peak}).

In the current CRP implementation, the data stream processing has been implemented by using the Windowing operator available in the RapidMiner toolkit [20]. Both SVM and ANN predictors have been implemented using the corresponding operators available in RapidMiner. The prediction validation block of CRP has been implemented in Python programming language using the X-Validation operator of RapidMiner.

For the results reported in this study, the CRP framework has been configured as follows. For the sliding time window approach, the time window size (w_{length}) has been set to 3, the moving step (s_t) to 1, and the prediction horizon (h_t) to 1 (for VO_{2next} prediction) or to the test duration (for HR_{peak} and VO_{2peak} prediction). For the SVM operator, the RBF (Radial Basis Function) kernel has been selected, and $Gamma$, C and $Epsilon$ parameters have been set to 0, 500, and 0.001, respectively. To configure the ANN operator, we set activation function as sigmoid function, training cycles 100, learning rate 0.3, momentum 0.2, $errorepsilon$ 1.0E-5, and hidden layer 2. The effect of varying the CRP configuration parameters is discussed in [12]. Experiments have been run on a 2 GHz Intel Centrino Dual-Core PC, with 1 GB of RAM and running Linux kernel 2.6.27.

Signal Name (unit)	Mean ± SD	MIN	MAX
FIO_2 (%)	0.205 ± 0.0021	0.2	0.21
FEO_2 (%)	0.17± 0.0064	0.15	0.19
$FICO_2$ (%)	0.00096± 0.00025	0.00035	0.0027
$FECO_2$ (%)	0.035± 0.0053	0.017	0.052
$FetCO_2$ (%)	0.05± 0.0058	0.032	0.066
$FetO_2$ (%)	0.152± 0.0092	0.121	0.184
VE (l/min)	28± 12	7	76
RR ($breaths/min$)	23.07± 5.71	6.05	46.75
IT (sec)	1.24± 0.35	0.60	3.48
ET (sec)	1.594± 0.52	0.69	6.58
HR (bpm)	99.61± 20.04	58.17	163.17
VO_2 (l/min)	0.796± 0.28	0.175	1.76
HR_{peak} (bpm)	128.93 ± 15.24	79.33	163.17
VO_{2peak} (l/min)	1.22± 0.18	0.72	1.76

TABLE II. Characteristics of the dataset. For all signals, mean and standard deviation (SD), minimum, and maximum values are reported.

A. Analysis of the prediction accuracy

This section analyses the accuracy of the CRP framdwork in predicting physiological signal values during the test execution. In all reported charts, step=1 corresponds to the *first step* in the test, when workload 5 W is assigned. The last prediction time corresponds to the achievement of a steady-state heart rate. According to the test protocol in the collected tests, every 30 seconds the prediction is performed.

Prediction of HR_{peak} and VO_{2peak}. Figures 2 and 3 plot the mean absolute error (MAE) (see Section II-D) for the prediction of the HR_{peak} and VO_{2peak} values reached at the test end. The results are promising, as the MAE value is always below 12 bpm for HR_{peak} and below 0.18 l/min for VO_{2peak}, for both SVM-based and ANN-based predictors. For both signals and both predictors, the MAE value decreases when postponing the prediction time and progressively tends to zero.

Experimental results show that the CRP framework would allow to prematurely end a cardiopulmonary exercise test even in the early steps of an incremental protocol, with a limited prediction error on both HR_{peak} and VO_{2peak} values. This would reduce the test duration, thus lowering the body stress of patients without loosing key physiological information (as VO_{2peak} and HR_{peak}) on their response to the test. Importantly, the prediction error of our method does not seem to affect the evaluation of the patient's response to exercise. For example, Figure 3 shows that estimating VO_{2peak} at step 10 of a cardiopulmonary exercise test, i.e., at 50 W workload, would yield a MAE for VO_{2peak} prediction equal to 100 ml/min. In a 75-kg man, this would correspond to 1.3 ml/kg/min, indeed quite an acceptable error for the VO_{2peak} estimate in the clinical setting.

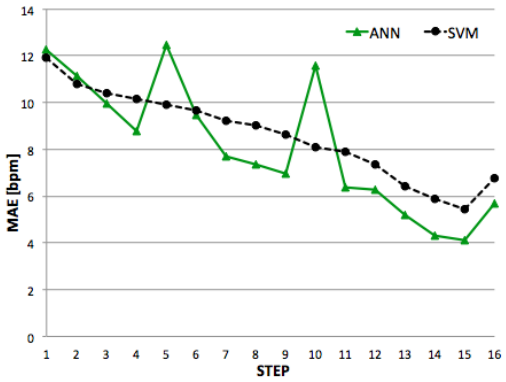

Fig. 2. *multiple-test* model for HR_{peak} prediction: MAE by varying the prediction time

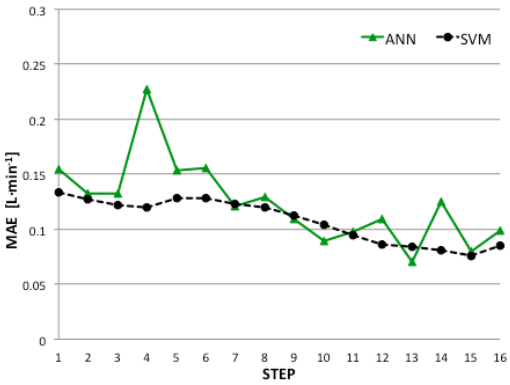

Fig. 3. *multiple-test* model for VO_{2peak} prediction: MAE by varying the prediction time

Figures 2 and 3 show a decreasing trend on the MAE value on HR_{peak} and VO_{2peak} prediction. This trend is mainly due to the following reasons. (i) The error is higher in the early steps because the reference knowledge base used for prediction contains the majority of the considered dataset. Consequently, tests with different durations (i.e., tests with workload in the range $[85W - 115W]$) contribute to the prediction task. Later, the prediction becomes more accurate because the reference knowledge base tends to progressively include a subset of tests with similar durations. (ii) When postponing the prediction time, the prediction horizon (i.e., the time interval between the prediction step and the test end) reduces and tends to zero. Thus, the body response at the prediction step tends to get closer to the response at the test end. Because of these two conditions, the prediction of both HR_{peak} and VO_{2peak} is initially affected by a larger, but limited, error. We can also observe that in both Figures 2 and 3 MAE curves are more irregulars and not strictly decreasing for the ANN predictor. It follows that, the ANN prediction model is more sensitive than the SVM one in considering a reference knowledge base including tests with different durations.

Prediction of VO_{2next}. As a reference example of the next step prediction task, the VO_{2next} prediction is reported in this study. Both *single-test* and *multiple-test* models are considered. Results, for SVM and ANN prediction algorithms, are reported in Figures 4 and 5 respectively. For both models, the MAE

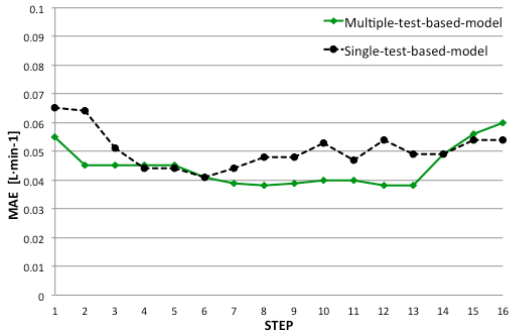

Fig. 4. VO_{2next} prediction using SVM: MAE by varying the prediction time

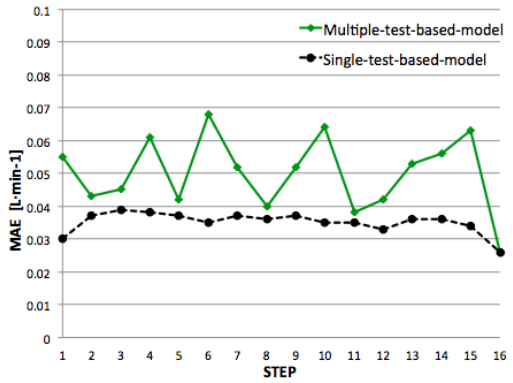

Fig. 5. VO_{2next} prediction using ANN: MAE by varying the prediction time

value is very low (in the range $0.035 \div 0.06$ l/min), being the horizon prediction always equal to 1 step.

For the SVM predictor (Figure 4) the *multiple-test* approach slightly improves the *single-test* one except for few prediction times, showing that a larger reference knowledge base can increase the accuracy of the model. Instead, the ANN predictor shows an opposite trend (Figure 5), since the *single-test* approach is slightly better than the *multiple-test* one. However, in both cases the prediction error is very limited for all prediction times.

Performance evaluation. For the considered dataset, the ANN predictor requires a long training time (i.e., more than 12 hours) to build the prediction model, while SVM requires about 3 hours. Once the model is defined, prediction is very efficient (i.e., few seconds) for both predictors.

IV. Related work

Data mining techniques have been widely used both in the healthcare and sports domain to analyze physiological signals and support clinicians and exercise physiologists. Common techniques as support vector regression, artificial neural network and other classifiers have been used for blood glucose level prediction [8], emotion recognition [9], and other kinds of disease-related predictions through physiological signal analysis [6]. The early prediction of maximum workload value reached by the individual in the incremental test was first studied in [3], [4] for endurance sports testing. Different from

these works, CRP addresses the early prediction of different physiological signal values relevant in the clinical domain (e.g., the heart rate and the oxygen consumption). It is also a more general approach because it supports the body response prediction both at the final and next step of the test.

In the field of cardiopulmonary signal analysis, many research efforts have been devoted to analysing the patient cardiopulmonary response through: (i) the analysis of signal patterns collected during exercise tests [1], [2], [7], [13], [15], [21], such as CRP or the (ii) electrical simulation models [5], [10], [26]. Cardiopulmonary exercise testing can be used by analyzing accessible physiological signal patterns collected during exercise, such as ventilation, VO_2, HR, blood pressure and body temperature [19]. VO_{2peak} has been estimated in both normal subjects and several patient populations from submaximal signals, such as rating of perceived exertion, workload, and heart rate [1], [2], [7], [13], [15], [21]. Most of the above work is based on statistical analysis of periodic snapshots of physiological parameters on a weekly or monthly basis. Instead, the CRP framework using data mining techniques allows to early predict the signal values achievable at different subsequent steps of the test *during the test execution*. Signals prediction during the test execution allows to indirectly assess the key physiological information on the patient's response to the test (e.g., VO_{2peak}), thus and reducing the test duration and lowering the body stress of patients.

V. Conclusions and Future Works

This paper presented the CRP framework to analyse the patient's cardiopulmonary response through the analysis of physiological signals monitored during the test. Experimental results, obtained on a real dataset, showed that CRP is able to predict both HR and VO_2 at the next and final steps of the test with a limited and acceptable error.

As future developments of this work, the following issues can be addressed. (i) *Exploitation of different data mining algorithms* to perform the prediction, (ii) *development of visualization tools* to graphically show the prediction with the corresponding error during the test, (iii) *applying the* CRP *framework in a larger cohort of maximal cardiopulmonary exercise tests*.

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