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Prediction of white blood cell count during exercise: a comparison between standalone and hybrid intelligent algorithms

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Decades of research in exercise immunology have demonstrated the profound impact of exercise on the immune response, influencing an individual's disease susceptibility. Accurate prediction of white blood cells (WBCs) count during exercise can help to design effective training programs to maintain optimal the immune system function and prevent its suppression. In this regard, this study aimed to develop an easy-to-use and efficient modelling tool for predicting WBCs count during exercise. To achieve this goal, the predictive power of a range of machine-learning algorithms, including six standalone models (M5 prime (M5P), random forest (RF), alternating model trees (AMT), reduced error pruning tree (REPT), locally weighted learning (LWL), and support vector regression (SVR)) were assessed along with six types of hybrid models trained with a bagging (BA) algorithm (BA-M5P, BA-RF, BA-AMT, BA-REPT, BA-LWL, and BA- SVR). A comprehensive database was constructed from 200 eligible people. The models employed post-exercise training WBCs counts as the output parameter and seven WBCs-influencing factors, including intensity and duration of exercise, pre-exercise training WBCs counts, age, body fat percentage, maximal aerobic capacity, and muscle mass as input parameters. Comparing the prediction results of the models to the observed WBCs using standard statistics indicated that the BA-M5P model had the greatest potential to produce a robust prediction of the number of lymphocytes, neutrophils, monocytes, and WBC compared to other models. Moreover, pre-exercise training WBCs counts, intensity and duration of exercise and body fat percentage were the most important features in predicting WBCs counts. These findings hold significant implications for the advancement of exercise immunology and the promotion of public health.

Keywords Immune system, Exercise, Leukocyte, Machine-learning, Hybrid model

The immune system is a complex organization of organs, cells and proteins with specialized roles to defend the host against possible microorganism invasions[1]. One of the body's immune system lines of defence against invasion is white blood cells (WBCs) which do not operate in isolation and are profoundly influenced by exercise as physical stress[2] and individual characteristics, including gender, age, body fat percentage (BFP), maximal aerobic capacity (VO_2 max), body mass index (BMI), and muscle mass (MM)[2,3]. Among these factors, exercise, as a direct factor that can be easily controlled, is important in maintaining people's health because exercise with unsuitable intensity and duration can result in immune dysfunction and increases the risk of contracting various diseases (e.g., viral infections, cancer, and inflammatory diseases)[4]. Despite the multiple studies that have been conducted to understand the interactions between exercise and the immune system function, the study of the optimal pattern of exercise based on immunological responses in the blood is limited. Because these interactions are very complicated and influenced by diverse factors[5]. To the best of our knowledge, only a random forest (RF) model has been used to predict WBCs during exercise[6]. Considering that applying other intelligent models[7] and other characteristics[6] may enhance the predicting accuracy of WBCs, hence, more studies are needed.

In several past decades, the use of machine-learning (ML) algorithms as an innovative and powerful technology for information processing, data mining, and modelling has substantially increased[7–10]. Having a nonlinear structure, the ability to predict complex phenomena, handling big datasets with different scales, and insensitivity

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to missing data are advantages of these algorithms[11]. Recently hybrid algorithms as one of the advanced ML tools have been applied to solve regression and classification issues in the field of medicine and exercise around the world, including the diagnosis and prediction of cardiovascular diseases[12], cancers[13], Type-2 Diabetes[14], adherence to physical activity[15], athletes' competitive ability[16], and human activity[17]. Most of these studies have compared different ML models with hybrid models and confirmed the superiority of hybrid models compared with other methods for similar conditions.

Although advances have been achieved related to the impacts of exercise on the immune system and the predictive power of hybrid algorithms has been proven in a wide spectrum of applications in different fields, the performance of these algorithms to predict the number of WBCs and their comparison with diverse standalone algorithms has not been studied. Therefore, the main objectives of this study are: (1) producing predictions of lymphocytes (LYMPH), neutrophils (NEU), monocytes (MON), and WBC counts during exercise using standalone algorithms, namely M5 Prime (M5P), random forest (RF), alternating model trees (AMT), reduced error pruning tree (REPT), locally weighted learning (LWL), and support vector regression (SVR) along with six types of hybrid algorithms trained with a bagging (BA) algorithm namely BA-M5P, BA-RF, BA-AMT, BA-REPT, BA-LWL, and BA- SVR; (2) comparing the predictive power of these algorithms; and (3) performing a sensitivity analysis of WBCs-influencing factors. Moreover, to the best of the authors' knowledge, no studies have assessed factors of age, BFP, and MM as WBCs estimators in modelling using intelligent algorithms. Therefore, this study is the first attempt for assess of these factors and the proposed models in predicting LYMPH, NEU, MON, and WBC counts during exercise.

Methods

Subjects

To test the objectives of this study, data from 200 eligible healthy subjects (100 men, 50.0%) in the age range of 18–60 years were collected (Table 1). Before the start of the study, three steps were performed; (1) screening the subjects with the questionnaire to investigate their health condition based on the absence of infectious, cardiovascular, inflammatory or immune diseases; (2) explaining the research process to all of the subjects and asking them to provide written consent; and (3) asking to subjects to refrain from exercise training or vigorous physical activity, and not to take anti-inflammatory agents, steroids and vitamin supplements for two weeks before the exercise sessions. This study was approved by the Research Ethics Committee, and all processes were conducted in accordance with the relevant regulations.

Variable	Min–Max	Mean ± SD
Age (years)	18–60	36.54 ± 10.86
Weight (kg)	49–130	76.09 ± 12.83
Height (cm)	154–191	169 ± 9
BMI (kg m^{-2})	18.44–40.12	26.65 ± 4.38
BFP (%)	21.9–58.70	30.29 ± 7.14
MM (kg)	22.69–60.38	41.84 ± 4.94
VO_2 max (ml kg^{-1} Min^{-1})	21.1–55.74	37.03 ± 7.63
$HR_{target1}$ (bpm)	116–175	141.93 ± 14.19
$HR_{target2}$ (bpm)	131–189	155.57 ± 15.88
Duration (min)	1–138	46.19 ± 38.23
WBC_1 ($10^3/mm^3$)	4.25–10.32	7.14 ± 1.52
$LYMPH_1$ ($10^3/mm^3$)	1.01–4.71	2.42 ± 0.70
NEU_1 ($10^3/mm^3$)	1.65–6.48	3.76 ± 1.15
MON_1($10^3/mm^3$)	0.28–1.00	0.56 ± 0.15
WBC_2 ($10^3/mm^3$)	5.36–14.23	8.90 ± 1.96
$LYMPH_2$ ($10^3/mm^3$)	0.86–6.86	3.32 ± 1.22
NEU_2 ($10^3/mm^3$)	1.85–8.73	4.63 ± 1.39
MON_2 ($10^3/mm^3$)	0.22–1.30	0.74 ± 0.21

Table 1. Statistical parameters of studied variables for the total data [1]. BMI = body mass index. BFP = body fat percentage. MM = muscle mass. VO_2 max = maximal aerobic capacity. $HR_{target1}$ = the minimum of target heart rate of subjects in determined intensity. $HR_{target2}$ = the maximum target heart rate of subjects in determined intensity. Duration = exercise training duration. WBC_1 = pre-exercise training white blood cell counts. $LYMPH_1$ = pre-exercise training lymphocyte counts. NEU_1 = pre-exercise training neutrophil counts. MON_1 = pre-exercise training monocyte counts. WBC_2 = post-exercise training white blood cell counts. $LYMPH_2$ = post-exercise training lymphocyte counts. NEU_2 = post-exercise training neutrophil counts. MON_2 = post-exercise training monocyte counts.

Development and application of machine-learning algorithms

Preparation of modelling dataset

Characteristics of participants (weight, height and BMI) and input and output datasets were measured using standard techniques. According to the manufacturer's instructions, BFP and MM data were estimated using a multi-frequency bioelectrical impedance analysis (BIA) device (Tanita BIA MC-180MA. VO_2 max was measured using a Bruce test[18] for each subject in the cardiology clinic. Based on the previous studies, three intensities, namely low intensity (50–63% of HR_{max}), moderate intensity (64–76% of HR_{max}), and high intensity (77–93% of HR_{max}) were considered for exercise protocol[6,19]. For this, the maximum heart rate (HR_{max}) using Tanaka formula[20] for each subject was calculated. Then, the minimum and maximum target heart rate (HR_{target}) using Karvonen method[21] and in accordance with the determined intensity for each subject was achieved. The subjects implemented the exercise protocol based on the characterised HR_{target} on a treadmill (Rodby, RL1602E, Sweden). Their heart rate during protocol execution was monitored continuously with a Polar watch and chest strap (Polar Electro Oy, Kempele, Finland) to ensure that the heart rate of samples is between their minimum and maximum HR_{target}. It should be noted that subjects were tested in an individual training condition in a public fitness centre. Although for each person, the exercise training intensity was randomized and each subject performed one specified intensity (only one of the intensities mentioned above), the duration of exercise training was according to the capacity of the subjects and wasn't pre-determined. The individual's capacity depends on various parameters such as age, gender, BMI, and intensity of the exercise[22]. For measurement of leukocyte levels, blood samples (3 millilitres of peripheral venous blood) of subjects were taken at baseline and immediately after the completion of the exercise training.

Finally, the collected data from 200 people were used for WBC modelling. In this study, to avoid over-fitting, the K-fold cross-validation method was applied to train and test machine-learning models[6]. In this method, data was randomly partitioned into equal-sized subsamples (5 subsamples) in which four samples (160 subjects) for training and one remaining sample (40 subjects) for validating were applied, and the process repeated 5 times.

Features importance

The analysis of feature's importance in ML models is critical because it helps to remove factors that reduce the prediction capability of the models or have no contribution to modelling results[23]. In this study, the method of mean decrease in impurity (MDI) in the RF algorithm was applied to determine feature's importance and selection of input vectors. We assessed the importance of effective factors on post-exercise training WBCs counts, including pre-exercise training WBCs counts, age, BFP, VO_2 max, MM, and the intensity (the minimum and maximum HR_{target}) and duration of exercise for determination of the optimum structure of models for predicting LYMPH, NEU, MON, and WBC.

Descriptions of the models

This study investigates some tree-based, lazy-based learner, function-based, and ensemble-based algorithms for predicting WBCs counts during exercise for healthy people, specifically:

<u>M5 prime (M5P).</u> The M5P algorithm as a DT-based algorithm is the expanded version of the M5 algorithm that was originally proposed by Quinlan[24]. This algorithm is known for its robustness when dealing with missing data, flexibility, and ability to handle a large number of data sets with many attributes[25]. This algorithm performs in 4 steps, in the first step, the input space is split into several sub-spaces to construct a tree, in the process of building of the tree using the standard deviation reduction (SDR), error reduction is maximized. In the next step, a linear regression model is generated in each sub-spaces. Then, a pruning technique is applied to eliminate undesired sub-trees and overcome the over-training problem. In the final step, the smoothing process compensates for the sharp discontinuities between adjacent linear models[26].

<u>Support vector regression (SVR).</u> SVR is a support vector machine (SVM) version that performs regression instead of classification. In this approach, which was introduced by Vapnik[27] the separator hyperplane in SVM becomes the fitting function of data. In this method, the use of the structural risk minimization (SRM) principle results in an overall optimal response and elevates the model's power[28]. In the SVR method, various types of kernel functions (e.g., linear, nonlinear, polynomial, radial basis function (RBF), and sigmoid) are used, among which the RBF kernel is the most widely used function[29].

<u>Reduced error pruning trees (REPT).</u> The REPT model as a tree-based model integrates the reduced error pruning model with decision tree algorithms introduced by Quinlan[30] and is employed for classification and regression. This algorithm performs in 4 steps, in the first step, multiple trees in various iterations are generated [31]. In the next step among them, the best tree is selected. Then, the reduced error pruning approach integrated with decision tree algorithms to reduce the size of tree branches and prevent over-fitting[32]. Finally, missing values are managed, and values of numerical attributes are sorted.

<u>Random forest (RF).</u> The RF algorithm introduced by Breiman[33] is a popular general-purpose algorithm in modern times[34]. This algorithm, as a tree-based algorithm, needs few parameters to tune and can deal with small sample sizes[35]. In this algorithm, a forest of decision trees is produced from the combination of randomized decision trees in which every tree forecasts a class and the final decision is produced by averaging all predicted classes[7]. Generally, RF training involves drawing a bootstrap sample from the training data, growing

a decision tree for each bootstrap sample, and finally repeating these steps until a large enough number of trees are generated[36].

Alternating model trees (AMT). The AMT algorithm introduced by Freund and Mason[37] shows the prediction capability of decision tree algorithms just in a single tree-based structure, which includes separator and prediction nodes. This algorithm includes three steps. In the first step, the separator variable is selected considering all input variables. The next step applies two basic linear regressions to the data. In the final step, the prediction at each prediction node is multiplied by the shrinkage parameter and then summed together to obtain the target prediction.

Locally weighted learning (LWL). LWL as a lazy-based learner is a nonparametric regression model that can manage various data distribution types and prevent boundary and cluster effects[38]. This method depends on the distance function, smoothing parameter, and weighting function. The distance function is used to recover the nearest neighbours of a given query example[39], and the weighting function computes the weight of the sample neighbour query. The bandwidth parameter is used for the smoothing parameter, which determines the range of generalisation.

Bagging (BA). BA is one of the robust ensemble techniques proposed by Breiman to solve classification and regression problems[40]. The method can enhance the overall accuracy of the ensemble by weakening the defects of poorly performing ensemble members[40]. The training process in the BA algorithm includes three steps, the first step is selecting randomly and independently the samples from the primary training datasets and building a specified number of sub-datasets. The next step is to characterize the base learning algorithm to train the sub-datasets. In the final step, predictions are created from each model, and afterwards, the final prediction is generated using averaging[41].

Statistical evaluation metrics
To validate and compare the performance of the models, the six most commonly used quantitative metrics, including coefficient of determination (R^2), root mean squared error (RMSE), mean absolute error (MAE), relative absolute error (RAE), root relative square error (RRSE), and Nash–Sutcliffe efficiency coefficient (NSE), were applied in the testing dataset. The equations for the metrics mentioned above are expressed in Table 2. Higher NSE and R^2 values and lower RMSE, MAE, RAE and RRSE values indicate better efficiency of models; RMSE, MAE, RAE and RRSE range from 0 to $+\infty$, NSE ranges from $-\infty$ to 1, and R^2 ranges from 0 to 1[6,42].

Results and discussion
Feature importance analysis
Feature importance scores for each factor were determined using MDI method (Fig. 1). Feature selection results based on this method showed that: (1) for predicting WBC_2, WBC_1 is the most important factor, followed by $HR_{target1}$, $HR_{target2}$, BFP, duration, VO_2 max, MM and age, respectively; (2) for predicting NEU_2, NEU_1 is the most important factor, followed by $HR_{target2}$, $HR_{target1}$, BFP, duration, VO_2 max, MM and age, respectively; (3) for predicting $LYMPH_2$, $LYMPH_1$ is the most important factor, followed by $HR_{target2}$, $HR_{target1}$, BFP, duration, MM, VO_2 max, and age, respectively; and (4) for predicting MON_2, MON_1 is the most important factor, followed by duration, $HR_{target1}$, $HR_{target2}$, VO_2 max, BFP, MM and age, respectively. Table 3 is visualized in Fig. 1 for a better understanding of feature ranking and importance according to the used technique.

Based on the obtained results, the most effective parameters for predicting post-exercise training WBCs counts were pre-exercise training WBCs counts, followed by intensity and BFP for predicting WBC_2, $LYMPH_2$, and NEU_2, and intensity and duration of exercise for predicting MON_2. The high importance of intensity and duration of exercise are consistent with the results of the previous studies[3,6]. Moreover, multiple studies have confirmed function changes of MON, NEU, NK, T and B cells and other biomarkers of immune that after exercise training[43–45]. Exercise influences the immune system through circulatory (hemodynamic) changes and endocrine hormones[46–48]. The importance of body fat can be justified in this way, in the regulation of immune and inflammatory processes, adipose tissue plays a critical role not only as an energy store but also as an important endocrine organ[49]. The previous studies also have identified the various products of adipose tissue, including adipokines and cytokines and several pathways linking adipose tissue metabolism with the immune system[49,50].

No	Equation	No	Equation
(1)	$RMSE = \sqrt{\frac{1}{n}\sum_{i=1}^{n}(O_i - P_i)^2}$	(4)	$MAE = \frac{\sum_{i=1}^{n}\lvert O_i - P_i\rvert}{n}$
(2)	$NSE = 1 - \frac{\sum_{i=1}^{n}(O_i - P_i)^2}{\sum_{i=1}^{n}(O_i - \bar{O})^2}$	(5)	$R^2 = \left[\frac{\sum_{i=1}^{n}(O_i - \bar{O})(P_i - \bar{P})}{\sqrt{\sum_{i=1}^{n}(O_i - \bar{O})^2}\sqrt{\sum_{i=1}^{n}(P_i - \bar{P})^2}}\right]^2$
(3)	$RAE = \frac{\sum_{i=1}^{n}\lvert O_i - P_i\rvert}{\sum_{i=1}^{n}\lvert O_i - \bar{O}\rvert}$	(6)	$RRSE = \sqrt{\frac{\sum_{i=1}^{n}(O_i - P_i)^2}{\sum_{i=1}^{n}(O_i - \bar{O})^2}}$

Table 2. Model evaluation metrics. n is the number of data, $O_{i:}$ is the ith observed WBCs, P_i is the ith predicted WBCs, $\underline{O}$ is the average of observed WBCs, $\underline{P}$ is the average of predicted WBCs.

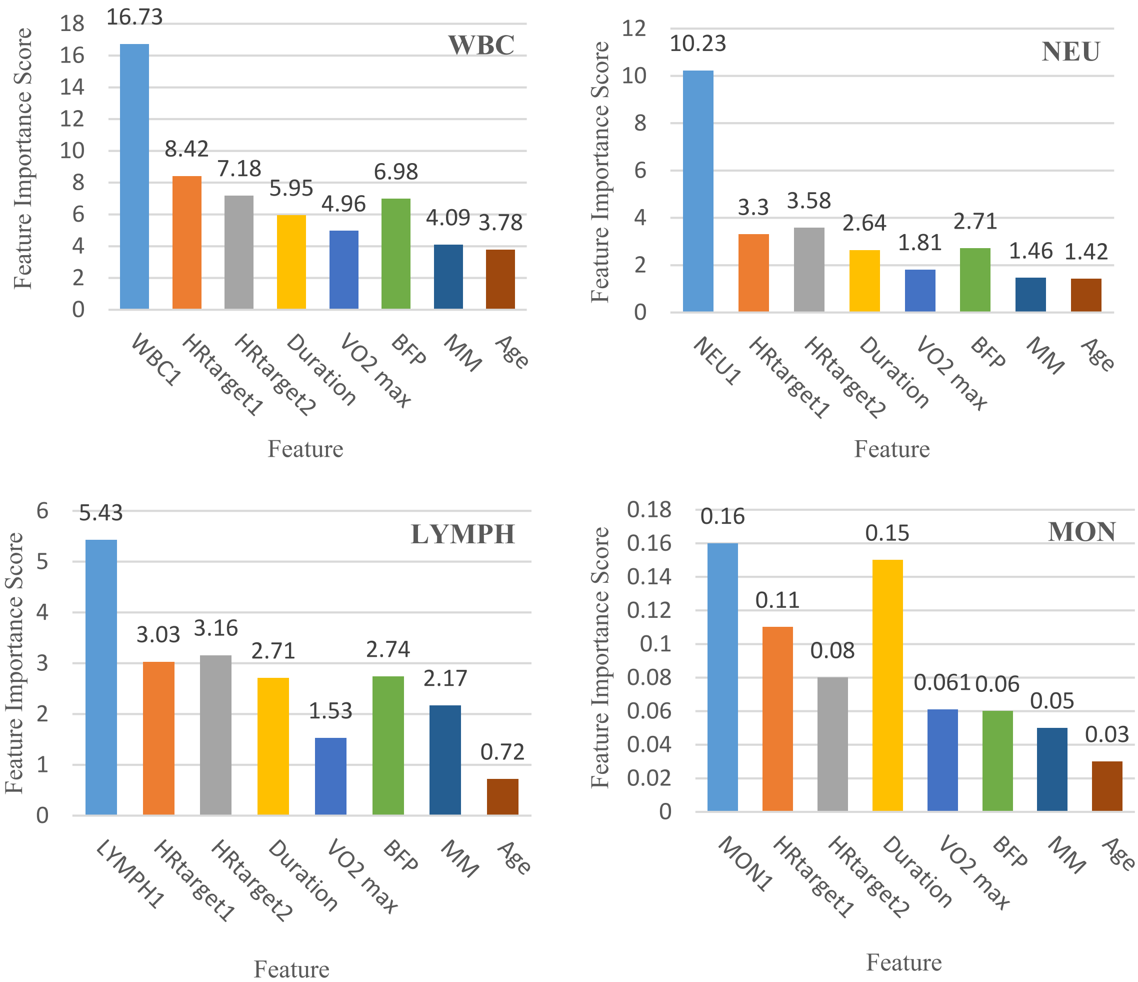

Fig. 1. Graphical representation of features importance in predicting WBCs.

Excessive body fat provokes the reduction of plasma anti-inflammatory mediators, leading to the development of a chronic low-grade systemic inflammatory state[51]. The next important factor is cardiorespiratory fitness and physical activity levels which are negatively associated with total WBC counts in adults[52,53]. Higher levels of cardiorespiratory fitness are related to lower pro-inflammatory cytokines levels (e.g., IL-6 and tumour necrosis factor-α (TNF-α))[54], which may stimulate neutrophils through cortisol and the hypothalamic–pituitary axis[55]. Moreover, we considered MM as a required input since the communication between the skeletal muscle and the immune system happens in many different ways and involves different aspects[56]. The previous findings have demonstrated a significant association between higher levels of circulating inflammatory markers and lower skeletal muscle strength and muscle mass; this relationship's strength differ depending on population and gender[57]. Our results showed that although age had the lowest impact on predicting WBCs, it is an influencing factor on the immune system. In this way with aging (especially with the beginning of the sixth decade of life), the human immune system undergoes changes that include reduced production of B and T cells in the bone marrow and thymus and diminished function of mature lymphocytes in secondary lymphoid tissues[58,59].

Model evaluation

After determining the importance of input variables, all models were validated using performance indices (RMSE, MAE, RAE, RRSE, NSE, and R^2) during the testing phase. The results for predicting LYMPH, NEU, MON, and WBCs are shown in Tables 3, 4, 5 and 6, respectively.

Analysis of the results based on standard statistical parameters showed that: (1) for predicting WBC, the BA-M5P model had the highest prediction power, followed by the BA-SVR, M5P, SVR, BA-RF, BA-AMT, RF, BA-REPT, BA-LWL, AMT, REPT, and LWL models, respectively; (2) for predicting NEU, the BA-M5P model had the highest prediction power, followed by the BA-SVR, M5P, SVR, BA-AMT, BA-RF, RF, BA-REPT, BA-LWL, REPT, AMT and LWL models, respectively; (3) for predicting LYMPH, the BA-M5P model had the highest prediction power, followed by the BA-SVR, M5P, SVR, BA-RF, RF, BA-AMT, BA-REPT, AMT, REPT, BA-LWL, and LWL models, respectively; and (4) for predicting MON, the BA-M5P model had the highest prediction power followed by the BA-SVR, M5P, SVR, BA-RF, RF, BA-REPT, BA-AMT, AMT, BA-LWL, REPT, and LWL models, respectively. Therefore, an assessment of the predictive capability of the twelve developed models showed that for predicting WBCs, the three best models were BA-M5P, followed by BA-SVR, and M5P, respectively, and the worst model was LWL.

The classification of performance based on both NSE and R^2 metrics showed that: (1) for predicting WBC, the M5P, SVR and RF standalone models and all hybrid models except for BA-LWL had very good performance; (2) for predicting NEU, the M5P and SVR standalone models and the BA-M5P, BA-SVR, and BA-AMT hybrid models had very good performance; (3) for predicting LYMPH, none of the models had very good performance but M5P, SVR, BA-M5P, and BA-SVR had good performance; and (4) for predicting MON only BA-M5P and BA-SVR had good performance.

Model	RMSE (10^3/mm^3)	MAE (10^3/mm^3)	RAE (%)	RRSE (%)	NSE	R^2
AMT	1.37	1.00	65.2	64.75	0.57	0.63
REPT	1.44	1.11	71.73	68.12	0.52	0.52
M5P	0.92	0.69	46.63	44.68	0.83	0.83
RF	1.01	0.75	49.99	48.51	0.78	0.79
LWL	1.50	1.16	74.31	70.72	0.48	0.52
SVR	0.92	0.69	47.01	44.77	0.82	0.82
Bag-AMT	1.01	0.73	49.07	48.21	0.78	0.79
Bag-REPT	1.01	0.76	50.88	48.83	0.77	0.77
Bag-M5P	0.89	0.66	44.78	43.38	0.85	0.85
Bag-RF	0.99	0.73	49.25	47.87	0.78	0.81
Bag-LWL	1.31	1.03	66.53	66.53	0.61	0.65
Bag-SVR	0.91	0.67	45.42	44.08	0.83	0.83

Table 3. Performance of 12 models for prediction of WBC.

Model	RMSE (10^3/mm^3)	MAE (10^3/mm^3)	RAE (%)	RRSE (%)	NSE	R^2
AMT	0.98	0.67	67.84	72.96	0.47	0.57
REPT	0.87	0.6	62.43	66.29	0.57	0.60
M5P	0.55	0.34	40.98	45.22	0.83	0.83
RF	0.71	0.49	52.81	55.80	0.70	0.73
LWL	0.98	0.71	70.98	72.96	0.47	0.48
SVR	0.55	0.35	39.81	45.19	0.82	0.83
Bag-AMT	0.62	0.38	43.86	49.86	0.78	0.81
Bag-REPT	0.72	0.49	53.01	56.52	0.70	0.72
Bag- M5P	0.52	0.33	41.33	43.34	0.84	0.84
Bag-RF	0.71	0.46	50.40	55.72	0.71	0.73
Bag-LWL	0.82	0.58	60.36	62.92	0.62	0.65
Bag-SVR	0.54	0.36	42.16	43.67	0.83	0.84

Table 4. Performance of 12 models for prediction of NEU.

Model	RMSE (10^3/mm^3)	MAE (10^3/mm^3)	RAE (%)	RRSE (%)	NSE	R^2
AMT	0.94	0.73	69.63	69.12	0.47	0.57
REPT	1.03	0.77	74.12	77.35	0.35	0.40
M5P	0.70	0.55	51.26	50.15	0.74	0.74
RF	0.82	0.63	60.22	59.69	0.61	0.63
LWL	1.14	0.89	86.72	85.09	0.20	0.28
SVR	0.74	0.57	53.48	53.35	0.73	0.74
Bag-AMT	0.83	0.61	57.62	60.52	0.60	0.65
Bag-REPT	0.86	0.66	62.85	62.7	0.57	0.59
Bag-M5P	0.68	0.53	49.40	48.64	0.75	0.76
Bag-RF	0.81	0.62	58.49	58.97	0.62	0.65
Bag-LWL	1.04	0.82	78.88	76.74	0.34	0.36
Bag-SVR	0.69	0.54	50.18	49.64	0.75	0.75

Table 5. Performance of 12 models for prediction of LYMPH.

Model	RMSE ($10^3/mm^3$)	MAE ($10^3/mm^3$)	RAE (%)	RRSE (%)	NSE	R^2
AMT	0.15	0.10	66.26	69.81	0.46	0.53
REPT	0.16	0.12	73.23	75.92	0.36	0.44
M5P	0.12	0.08	54.57	57.31	0.64	0.65
RF	0.12	0.08	54.19	58.45	0.63	0.63
LWL	0.17	0.13	79.40	79.50	0.29	0.31
SVR	0.12	0.08	53.81	58.22	0.63	0.64
Bag-AMT	0.13	0.08	53.64	63.58	0.55	0.61
Bag-REPT	0.12	0.08	54.84	60.71	0.59	0.61
Bag- M5P	0.10	0.07	50.33	54.43	0.69	0.70
Bag-RF	0.12	0.08	54.74	58.29	0.63	0.64
Bag-LWL	0.15	0.11	69.05	70.55	0.45	0.45
Bag-SVR	0.11	0.08	51.64	56.16	0.66	0.67

Table 6. Performance of 12 models for prediction of MONO.

Also, an assessment of the base models compared with their ensemble counterparts showed that ensemble models improve prediction accuracies of various base regression models[60]. For example, this improvement is indicated by an increase of 2.41% in the NSE and R^2, and a decrease of 3.26%, 4.35%, 3.97%, and 2.91% in the RMSE, MAE, RAE, and RRSE, respectively, in the Bag-M5P model as the best model compared to the M5P model for predicting WBC. Moreover, it can be said that in most cases, the performance of the hybrid models depends on the base model used. For example, in this study, although the incorporation of the bagging algorithm improved the prediction power of all standalone models, the BA- M5P model had the highest prediction power since the M5P base model had a higher performance compared to other base models.

Generally, although hybridization increases the model's complexity and consumption of time, hybrid models can more easily identify the non-linearity of variables relationship compared to standalone models and eliminate the inherent shortcomings of base models[11]. The improvement in the results of the bagging algorithm is because it enables several weak learners to work together to enhance their predictive capability. Also, it reduces the variance in performance measures while the bias almost is the same[61]. Moreover, since sampling is carried out by bootstrapping, the training data becomes more diverse, leading to this method becoming more effective[62].

For a visual analysis and assessment of the applied models, scatter plots of testing dataset are presented for the best models in predicting LYMPH, NEU, MON, and WBC (Fig. 2).

The comparison of plots for the best model (Bag-M5P) indicated that there was the closest agreement between observed WBC and predicted WBC compared with LYMPH, NEU, and MON.

The assessment of the modelling results also showed that some predicted WBCs were not accurate, which it often occurs in modelling. The reason may be that we didn't consider the other WBCs-influencing factors, including psychological stress, diet, temperature, and relative humidity[3], in developed models. Additionally, various factors, such as the menstrual cycle in females, can affect WBCs[63], which were not controlled in this study. Therefore, these samples are not reflective of the general women population. On the other hand, the use of the other intelligent models[7], high-quality data[64], more data[65], and meta-heuristic optimization algorithms for adjustment of model parameters[66] may improve results. It should be noted that the use of other methods for more accurate assessment of body composition, such as Dual-energy X-ray absorptiometry (DEXA)[67], can lead to more precise results, which should be considered in future studies. Generally, the results obtained from this study indicated that the hybrid algorithms presented more accurate predictions of WBCs compared to the standalone algorithms. In particular, M5P trained with the bagging data mining algorithm had very good performance in predicting WBC (NSE = 0.85 and $R^2 = 0.85$) and NEU (NSE = 0.84 and $R^2 = 0.84$) and had good performance in predicting LYMPH (NSE = 0.75 and $R^2 = 0.76$) and MON (NSE = 0.69 and $R^2 = 0.70$) during exercise. These results show the usability of the proposed model. On the other hand, not having samples in age groups under 18 and over 60, as well as samples with medical conditions, are the main limitations of the present study which this problem should be investigated in future studies because results may not be applicable to children, old people, and individuals with medical conditions. Thus, although the results of this study provide a simple modelling tool for convenient use by athletes, non-athletes, and the personnel involved in health care, more detailed studies should investigate the potential of this approach with various WBCs-influencing factors and with more data in the future.

Conclusion

The development of approaches that are both reliable and available for the accurate prediction of WBCs count during exercise can help to determine the proper intensity and duration of exercise based on the immune system response and as a result maintain people's health. Considering the non-linear and complex behaviour of the immune system in interaction with exercise, intelligent algorithms can have the potential for accurate prediction of WBCs count during exercise. This study tested this potential by examining the prediction power of standalone algorithms (M5P, RF, AMT, REPT, LWL, and SVR) and hybrid algorithms (BA-M5P, BA-RF, BA-AMT, BA-REPT, BA-LWL, and BA- SVR). Our findings revealed that combining BA with the standalone models could improve the performance of these models. Also, the BA-M5P model produced superior results in predicting LYMPH, NEU,

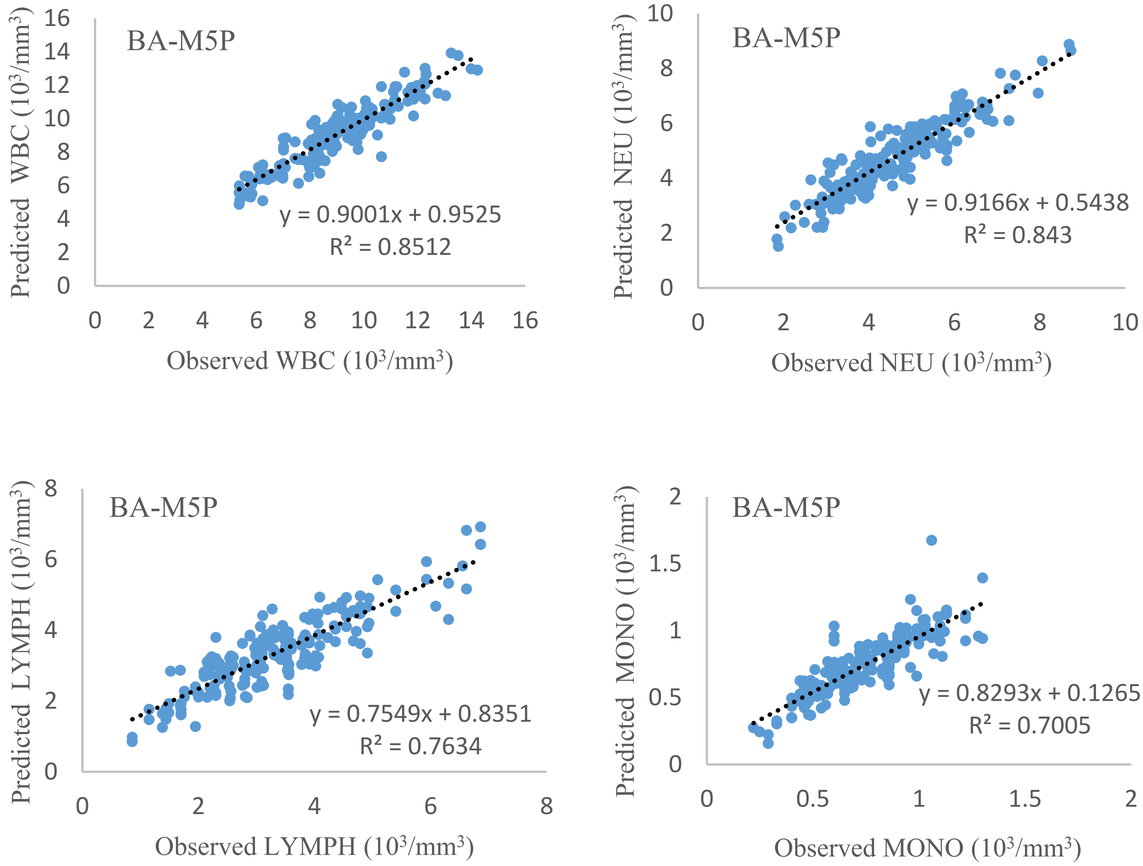

Fig. 2. Scatter plots of the observed values and predicted values for the best models in predicting LYMPH, NEU, MON, and WBC.

MON, and WBC compared to other models, as well as was the most successful in assessing WBC. Moreover, the results of feature importance indicated that after initial WBCs counts, the three most significant features were intensity and duration of exercise and BFP. Generally, the results of this study provide a relatively cheap and applicable method for fast predictions of WBCs during exercise that has important potential implications for public health and for clinicians caring for athletes and athletic teams.

Data availability
Data are available by contacting the corresponding author upon reasonable request.

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Author contributions

S.A. conceptualized the study. S.A., B.T. and M.A.M. were involved in the study methodology. S.A. was involved in providing study materials, data curation, and data visualization. S.A. did the formal data analysis and validated the data. B.T. supervised the study. S.A. wrote the first draft of the manuscript. B.T., M.A.M., and R.E. wrote, reviewed, and edited the manuscript. All authors read and approved the final manuscript.

Competing interests

The authors declare no competing interests.

Ethical approval

This study involved human participants and was approved by the Research Ethics Committee of Allameh Tabataba'i University (reference number IR.ATU.REC.1401.052). Participants gave informed consent to participate in the study before taking part.

Additional information

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