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An infectious disease/fever screening radar system which stratifies higher-risk patients within ten seconds using a neural network and the fuzzy grouping method

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Summary *Objectives:* To classify higher-risk influenza patients within 10 s, we developed an infectious disease and fever screening radar system.
Methods: The system screens infected patients based on vital signs, i.e., respiration rate measured by a radar, heart rate by a finger-tip photo-reflector, and facial temperature by a thermography. The system segregates subjects into higher-risk influenza (HR-I) group, lower-risk influenza (LR-I) group, and non-influenza (Non-I) group using a neural network and fuzzy clustering method (FCM). We conducted influenza screening for 35 seasonal influenza patients and 48 normal control subjects at the Japan Self-Defense Force Central Hospital. Pulse oximetry oxygen saturation (SpO_2) was measured as a reference.
Results: The system classified 17 subjects into HR-I group, 26 into LR-I group, and 40 into Non-I group. Ten out of the 17 HR-I subjects indicated SpO_2 <96%, whereas only two out of the 26 LR-I subjects showed SpO_2 <96%. The *chi-squared* test revealed a significant difference in the ratio of subjects showed SpO_2 <96% between HR-I and LR-I group ($p < 0.001$). There were zero and nine normal control subjects in HR-I and LR-I groups, respectively, and there was one influenza patient in Non-I group.

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Conclusions: The combination of neural network and FCM achieved efficient detection of higher-risk influenza patients who indicated SpO_2 96% within 10 s.

Introduction

The highly pathogenic avian influenza virus subtype H5N1 causes severe respiratory disease in humans, inducing threats of pandemic to increase.[1] Such a severe influenza infection elevates the risks of developing influenza-related complications, which is one of the leading causes of death during the epidemic season.[2,3] When a pandemic occurs, the rapid screening of infected patients with a severe infection can help clinicians make better medical decisions and provide improved patient care.[4] To conduct mass screenings of people with higher-risk influenza, we developed a radar system based on a neural network and the fuzzy clustering method for screening of influenza.

Infrared thermography has been applied as a means of fever screening at airports for almost 10 years, having been implemented after the severe acute respiratory syndrome outbreak of 2003.[5–8] However, the taking of an antifebrile drug results in the rapid modification of the body temperature and directly affects the efficacy of the thermography. Some recent studies have indicated that fever screening using thermography does not provide a satisfactory method of detecting febrile passengers.[9] Considering the defective fever screening method, we previously developed a non-contact screening system for performing medical examinations within 10 s using measured vital signs (i.e. heart rate, respiration rate, and facial temperature).[10] As a result of being infected, not only body temperature but also heart and respiration rates will invariably increase. Therefore by adding heart and respiration rates as new screening parameters, the system provided a higher screening sensitivity than using thermography alone.

Infection screening using multiple vital signs presents a multi-dimensional data classification problem, given that it is complex and exhibits non-linear boundaries. Since a neural network provides an efficient method of classifying multi-dimensional data, we have proposed a method that uses a neural network to distinguish influenza patients from normal control subjects. This method was developed in our previous study, which uses Kohonen's self-organizing map[11] (SOM) and the k-means clustering algorithm[12] (a non-linear clustering algorithm).[13] The advantage of using SOM together with the non-linear clustering algorithm is that it allows the specification of any number of classification groups, not just two. Therefore, it is rational to increase the number of groups to three to investigate whether the higher-risk patients can be gathered together into a newly created group.

In present study, we enhanced the SOM by incorporating a fuzzy clustering method (FCM) to cluster the subjects into three groups, i.e. a higher-risk influenza (HR-I) group, a lower-risk influenza (LR-I) group, and a non-influenza (Non-I) group. FCM is a non-linear clustering method that is used in a wide range of fields, including biometric recognition, pattern recognition, and medical data mining.[14–16] Unlike the k-means clustering method, FCM supports the use of classified data, which may belong to more than one group but with different degrees of membership. The membership represents the probability that the data belongs to a specific group based on fuzzy logic. Therefore, FCM is suitable for classifying multi-dimensional data without clearly defined boundaries, such as our multiple vital-signs data. The aim of this study was to evaluate the efficacy of the radar screening system for detecting higher-risk influenza patients in clinical settings. We tested the system at the Japan Self-Defense Forces Central Hospital during the 2012—2013 influenza season.

Patients and methods

The neural-network-based infectious disease screening radar system

We redesigned our previously developed system[10,17] to improve its portability and stability. The main advantage of this portable system is that it can be used in confined spaces such as inside an aircraft.[18] The system consists of three biosensors, namely, a thermograph to monitor facial temperature (NEC/AVIO Infrared Technologies Co., Ltd., C-200, Japan), a 10-GHz microwave radar for the non-contact determination of the respiration rate[19] (new-JRC, NJR-4175, Japan), and a finger-tip photo-reflector to measure the heart rate (Rohm, RPR-220, Japan). All of the

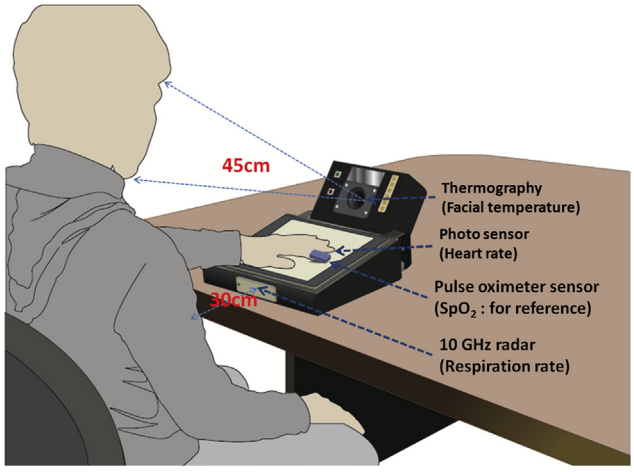


Figure 1 A pulse oximeter module was used to measure the SpO_2 levels. The respiration rate was measured using the 10-GHz respiration radar by monitoring the respiratory motion of the chest, the heart rate was measured by a finger-tip photo-reflector, and the facial temperature was measured by means of thermography. The thermograph was placed 45 cm from the subject's face, and the respiration radar was placed 30 cm from the subject's chest.

biosensors were integrated into a single instrument body measuring 27 cm long, 28 cm wide, and 10 cm thick. The system is illustrated in Fig. 1. The signals from the biosensors are sent to a laptop computer, where they are analyzed and displayed in real time. The software environment was developed in LabVIEW (National Instruments, Austin, Texas, USA) for recording the signals and in MATLAB (Mathworks, Natick, MA, USA) for calculating the neural network based discriminant function. Within 10 s, the pulse waves, respiratory curves, and facial thermal image are displayed on the laptop screen. The screening results (i.e. '0 = Non-influenza', '1 = Lower-risk influenza', or '2 = Higher-risk influenza') are obtained by the neural network and fuzzy clustering algorithm, based on the derived multiple vital signs (Fig. 2).

Screening of influenza patients in a hospital

The present study was carried out at the Japan Self-Defense Force Central Hospital from January to February 2013. A total of 35 patients, admitted with influenza-like illnesses were diagnosed as having seasonal influenza. The patients were all male and were Self-Defense Forces members in Japan with an average age of 22 years (18—35 years). All of patients were treated with an anti-viral medication (Oseltamivir or Zanamivir). Their axillary temperatures averaged 37.2 ± 0.8 °C (35.7 °C ≤ body temperature ≤ 39.1 °C). All of the 48 normal control subjects were male students at Tokyo Metropolitan University with no symptoms of fever, headache, or sore throat. The average age of the normal control subjects was 21 years (18—30 years). Their axillary temperatures averaged 36.6 ± 0.4 °C (34.9 °C ≤ body temperature ≤ 37.1 °C).

Measurements using the screening system were performed between 10:00 a.m. and 12:00 noon, with all of the above-mentioned influenza patients and normal control subjects being examined. The heart rate, respiration rate, facial temperature, and SpO_2 of each subject were determined using the system. The axillary temperatures of both the influenza patients and normal control subjects were measured using a clinical thermometer (TERUMO, C220, Japan). The study was approved by the Ethics Committee of the Japan Self-Defense Force Central Hospital and the Committee on Human Research of the Faculty of System Design, Tokyo Metropolitan University. All subjects gave their informed written consent.

Classification of patients with higher-risk of influenza by using a neural network and the fuzzy clustering method

To assess the possibility of identifying higher-risk influenza patients, we enhanced our previous version[13] of the neural network by using FCM to increase the number of classification groups. The neural network and FCM were created in MATLAB by using Neural Network Toolbox 7.0.1 and Fuzzy Logic Toolbox 2.2.18. A two-layer neural network, with an input layer and an output layer, was constructed. The input layer has three inputs which are derived parameters: heart rate, respiration rate, and facial temperature. The proposed clustering algorithm consists of two steps, as follows (Fig. 3).

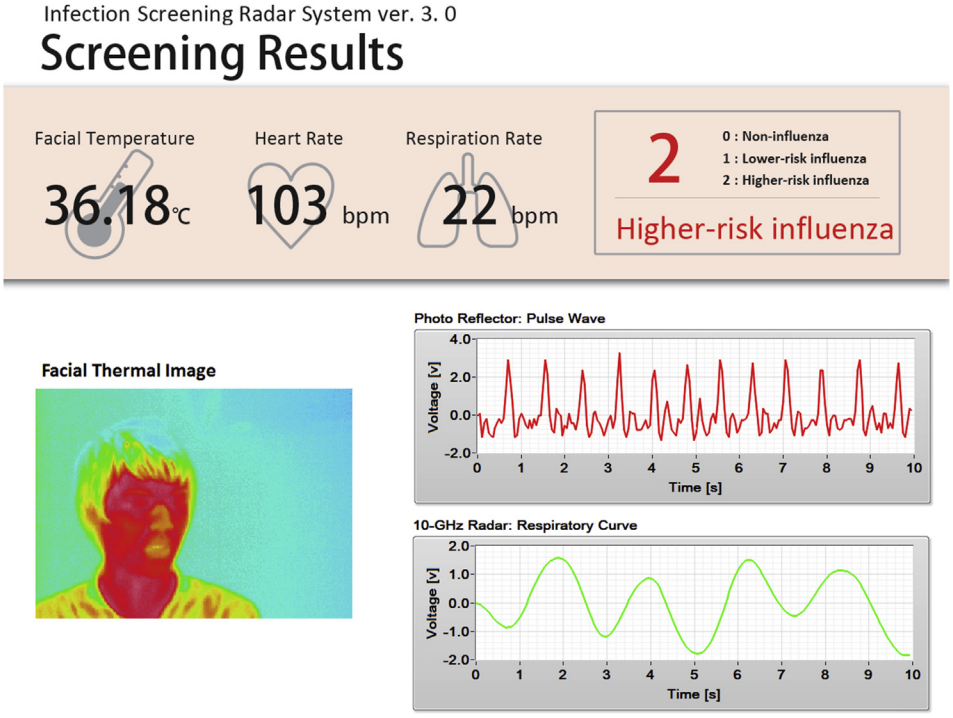


Figure 2 The pulse wave, respiratory curves, and facial thermal image are displayed on the laptop screen, followed by the screening result ('0 = Non-influenza', '1 = Lower-risk influenza', or '2 = Higher-risk influenza') obtained by the SOM and fuzzy clustering algorithm.

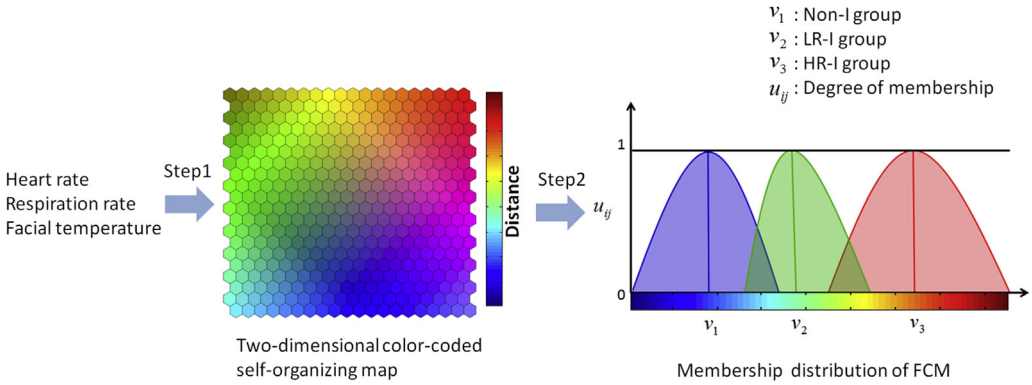


Figure 3 Schematic representation of the SOM combined with fuzzy clustering algorithm to create a non-linear discriminant function for distinguishing the HR-I and LR-I groups from the Non-I group.

Firstly the vital-sign data for all of the 83 subjects, that are, the 35 influenza patients and 48 normal control subjects, were used to create SOM clusters. The SOM clustering results were visualized on a color-coded, two-dimensional map based on a unified distance matrix. However, it proved the difficulty of detecting a specified number of clusters simply by visually inspecting the two-dimensional SOM map. As a second step, to reduce the number of SOM clusters to three, FCM was applied to identify the three specified clusters. FCM is based on the minimization of an objective function J, which is defined as follow.[20]

$$J = \sum_{j=1}^{N} \sum_{i=1}^{c} u_{ij}^{m} \left\| x_j - v_i \right\|^2 \quad (1)$$

where u_{ij} is the degree of membership of each item of data between the cluster center, and the membership represents the probability of the data belonging to a specific group based on Fuzzy logic. The $\| \bullet \|$ is the distance between the data x_j and cluster center v_i, c is the number of clusters, N is the number of items of data, and m is the degree of fuzziness. FCM iteratively updates the membership function u_{ij} and cluster center v_i until the maximum difference between cluster center is reached. Finally, the screening results ('Non-I', 'LR-I', or 'HR-I') can be obtained from the output layer.

Statistical analysis

We evaluated the performance of the screening by using SOM and FCM to detect influenza patients by calculating the clinical sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). Moreover, the classified vital-sign values among the Non-I group, the LR-I group, and the HR-I group were compared using the non-parametric Kruskal—Wallis one-way analysis. A *p-value* of less than 0.05 was considered to indicate statistical significance.

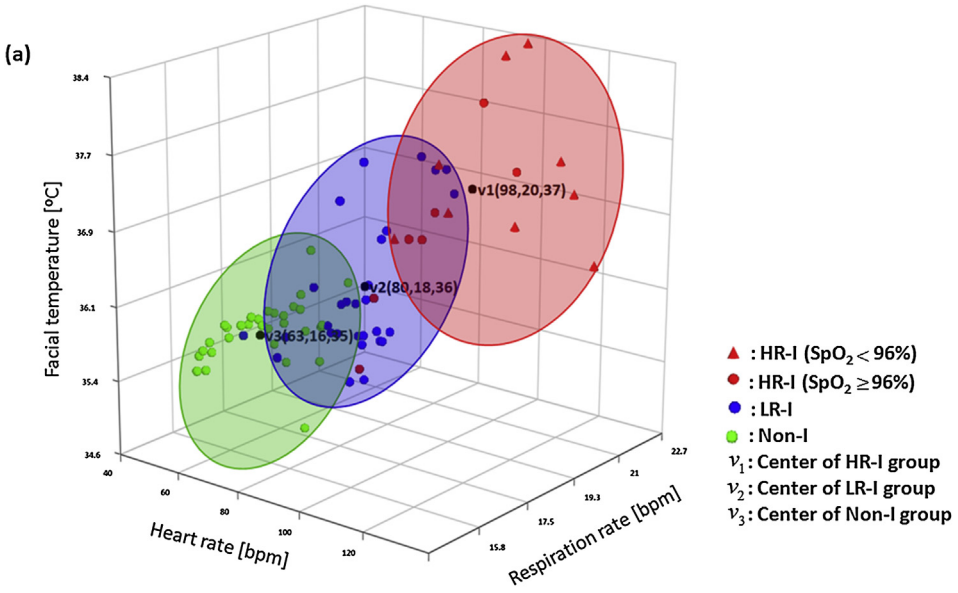
SpO_2 level (<96%) was used as a reference to evaluate whether a patient can be placed in the HR-I group, since one of the most significant features of higher-risk influenza patients is their lower SpO_2 level.[21] A comparison of the SpO_2 levels of the patients in the HR-I and the LR-I groups was conducted by using the *chi-squared* test. Statistical analysis was performed using StatMate III (ATMS, Tokyo).

Results

The screening results of SOM and FCM are shown as a three-dimensional scatter plot in Fig. 4(a). The 83 subjects were divided into three groups: 17 were placed in the HR-I group, indicated by red spheres and cone dots bounded by red ellipses; 26 were placed in the LR-I group indicated by the blue sphere dots bounded by blue ellipses; and 40 were included in the Non-I group indicate by the green sphere dots bounded by green ellipses. The screening results are summarized in Fig. 4(b). The 43/83 subjects were classified into the influenza group including 34 influenza patients (HR-I and LR-I) and 9 misclassified normal control subjects; 40/83 subjects were classified into the Non-I group including 39 normal control subjects and one misclassified influenza patient. The corresponding sensitivity, specificity, PPV, and NPV were 97.1%, 81.3%, 79.1%, and 97.5%, respectively.

The SpO_2 value was used as a reference to determine the stage of influenza infection. With an SpO_2 cut-off value of 96%, the HR-I group and the LR-I group were compared. The details are summarized in Table 1. Ten out of the 17 HR-I group cases exhibited an SpO_2 of less than 96%, whereas only two out of the 26 LR-I group cases exhibited an SpO_2 of less than 96%. The *chi-squared* test revealed significant differences between the HR-I group and the LR-I group ($\chi^2 = 13.36$; degree of freedom $= 1$; $p < 0.001$). In the Non-I group, there were no subjects with an SpO_2 of less than 96%, which indicates that no higher-risk influenza patients were misclassified as normal. To investigate the clustering tendency, the vital-signs data and reference data are shown in part in Table 2. The 17 influenza patients classified into the HR-I group all have an SpO_2 level of less than 96%, or have notably increased vital signs.

Moreover, the vital-sign values and SpO_2 were compared for the Non-I, the LR-I, and the HR-I groups. Fig. 5a shows that the average heart rate differed significantly among the three groups (Non-I = 68 bpm, LR-I = 84 bpm, HR-I = 98 bpm; $p < 0.05$). Fig. 5b shows that a significant difference was identified between the Non-I and the LR-I groups ($p < 0.05$), but there is no significant difference between the LR-I and the HR-I groups in terms of respiration



(b)

		Influenza patients (n = 35)	Normal control subjects (n = 48)	
Screening Results	Influenza group (HR-I and LR-I)	HR-I = 17	HR-I = 0	PPV=79.1%
		LR-I = 17	LR-I = 9 (False Positive)	
	Non-I group	1 (False Negative)	39	NPV=97.5%
		Sensitivity=97.1%	Specificity=81.3%	

Figure 4 Results of SOM screening with fuzzy clustering algorithm, shown as a three-dimensional scatter plot. The 83 subjects were divided into three groups: the Non-I group ($n = 40$), LR-I group ($n = 26$), and HR-I group ($n = 17$). The 43/83 subjects were classified into an influenza group (red and blue clusters) including 34 influenza patients and 9 misclassified normal control subjects; 40/83 subjects were classified into a non-influenza group (green cluster) including 39 normal control subjects and one misclassified influenza patient. The corresponding sensitivity, specificity, PPV, and NPV were 97.1%, 81.3%, 79.1%, and 97.5%, respectively.

rate (Non-I = 16 bpm, LR-I = 19 bpm, HR-I = 20 bpm). Fig. 5c shows that a significant difference was found between the Non-I and the LR-I groups ($p < 0.05$), but there is no significant difference between the LR-I and the HR-I groups in terms of facial temperature (Non-I = 35.7 °C, LR-I = 36.3 °C, HR-I = 37.0 °C). For the reference SpO_2 data (Fig. 5d), there was a significant difference among the three groups (Non-I = 97%, LR-I = 96%, HR-I = 95%; $p < 0.05$).

Discussion

In March 2013, the first human infection by the novel influenza A (H7N9) virus was reported in mainland China.[22] An influenza virus such as H7N9 can trigger severe pneumonia or acute respiratory distress syndrome, which results in significant morbidity and mortality.[23,24] When a novel influenza virus emerges, enhanced public health surveillance is essential during the epidemic season. To attain this, we set out to develop this screening system for the mass screening of infected individuals, based on multiple vital signs.

Table 1 Number of higher-risk influenza (HR-I) patients and lower-risk influenza (LR-I) patients by SpO_2 level with a cut-off value of 96%.

	SpO_2 <96%	SpO_2 ≥96%	Total
HR-I group	10	7	17
LR-I group	2	24	26

$\chi^2 = 13.36$; degree of freedom = 1; $p < 0.001$

The infection screening radar system quickly measured the vital signs and comprehensively analyzed the derived data by using a neural network in real time. The most significant advantage of this system is that it can be used to detect influenza patients who have taken medication with normal body temperature. In the present study, although the 35 influenza patients were treated with anti-viral medication and more than half of the patients had normal body temperature, our system attained higher detection sensitivity than that reported in some recent studies using only thermography.[9,25] This higher sensitivity can be attributed to the fact that, those patients even with normal body temperature under antifebrile medication, exhibited relatively high rates of heart and respiration in comparison with the normal control subjects. The idea of using vital signs stems from the fact that infectious diseases are associated with inflammation when patients become symptomatic. Body temperature, heart, and respiration rates

Table 2 The vital signs and reference data (SpO_2 and axillary temperatures) of higher-risk influenza (HR-I) group, a lower-risk influenza (LR-I) group, and a non-influenza (Non-I) group are shown in part in this Table.

Screening parameters			References	
Heart rate [bpm]	Respiration rate [bpm]	Facial temperature [°C]	Axillary temperature [°C]	SpO_2 [%]
HR-I group (red cluster)				
98	23	38.5	39.1	94
106	23	37.7	38.0	94
92	18	37.1	37.6	95
99	20	36.8	37.3	95
111	23	36.6	37.7	95
125	22	36.2	36.6	94
LR-I group (blue cluster)				
75	19	34.8	36.5	99
76	19	36.1	38.5	98
85	19	35.7	37.1	96
87	18	35.8	38.0	98
Non-I group (green cluster)				
82	19	35.5	36.5	98
77	16	35.9	36.1	98
78	18	36.0	36.7	99
65	17	35.3	36.8	99

are also included in the diagnostic criteria for the systemic inflammatory response syndrome (SIRS). In addition, the abnormal white blood cell (WBC) count ($>12{,}000/mm^3$, $<4000/mm^3$, or $>10\%$ bands) are also included in the SIRS diagnostic criteria. However, testing for WBC count requires a blood sample, and this would not be compatible with a fast-screening process. Therefore, we did not adopt WBC count as a screening parameter in this study. Furthermore, it is important to know the extent to which the screening parameters affect the results while performing a multiple-parameter-based screening for infection. Therefore, the classified parameters were compared statistically (Fig. 5); the most informative parameter was heart rate, while facial temperature and respiration rate were the second most informative parameters.

In this study, our enhanced neural network (i.e., Kohonen's self-organizing map) combined with the fuzzy clustering method showed a sensitivity of 97.1% and a NPV of 97.5%. These results are comparable to our previous work, in which we used a k-means clustering algorithm.[13] More importantly, the proposed optimal neural network and fuzzy clustering method were used to classify the multiple-dimensional vital-sign data to detect higher-risk influenza patients. The high level of accuracy of the

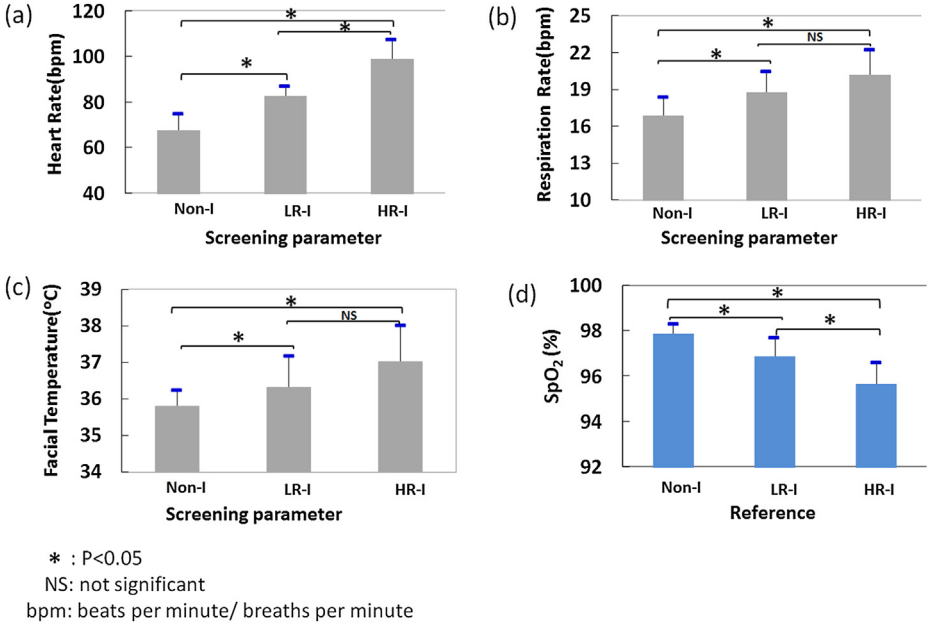


Figure 5 Heart rate, respiration rate, facial temperature, and SpO_2 compared within the HR-I group, LR-I group, and Non-I group.

automatic infection screening system has a number of clinical implications. The system can be used as a first step for screening infectious patients at an emergency outpatient unit or at an airport quarantine station. The proposed system also appears to offer a promising means of identifying and selecting higher-risk groups for further assessment. These features enable the system to be used for preventing secondary exposure of physicians during outbreaks of highly pathogenic infectious diseases such as the Ebola virus disease. However, the main limitation of our study was that it was conducted in a specialized hospital. The subjects were inpatients and were from a limited age group (18-years) and were all of the same gender. The system should be further tested with a large and completely random sample of influenza patients.

In summary, the neural network and FCM could efficiently detect higher-risk influenza patients within 10 s using multiple vital signs. Our system has the potential to serve as a helpful tool for rapid screening of infectious diseases in clinical settings at places of mass gathering.

Authors' contributions

Study concept and design: GS and TM.
Acquisition of data: GS, TM, and YH.
Analysis and interpretation of data: GS, TM, YH, and SA.
Drafting of the manuscript: GS and TM.
All authors final approval of the version to be submitted.

Conflicts of interest

The authors declare no conflicts of interest.

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