Websites:
http://www.lifesciencesite.com
http://www.sciencepub.net

Emails:
editor@sciencepub.net
sciencepub@gmail.com

Life Science Journal

MARSLAND PRESS
Multidisciplinary Academic Journal Publisher

Application of Symmetrical Body Temperature Difference to Improve Early Detection of Covid-19

Zhiqiang Cui[1], Grace Shu[2], Gu He[3], Ying Wang[4], Matthew Lee[5], Kai Shen[6], Qing Ke[7], Danping Li[8], Lili Liu[9], Yun'e Yuan[9], Minjie Gu[10], Shouyi Wang[11]

1. Orient Health Care, New York City, NY 11375, United States;
2. United States Department of Health and Human Services, Washington, D.C., United States;
3. Stego Tech, Prussia, Pennsylvania, United States;
4. American Association of Natural and Integrative Medicine, Bridgewater, NJ, United States;
5. Medical Wisdom Consulting Group, Houston, Texas, United States;
6. Suzhou Aulikang Health Technology, Suzhou, Jiangsu, China;
7. China Academy of Chinese Medical Sciences, Beijing, China;
8. Toplent Pharmaceutical Consulting, LLC, Middlebury, Connecticut;
9. Beijing Modern Digital Infrared Imaging Technology Research Institute, Beijing, China;
10. American Regenerative Medicine Corporation, New York, United States;
11. The University of Texas at Arlington, Arlington, Texas, United States.

Correspondence to:
Zhiqiang Cui, Ph.D.
Orient Health Care, New York City, NY 11375, United States, Email: cuij68@gmail.com

One Sentence Summary: Symmetrical body temperature difference can be a more robust indicator than the single-spot temperature measurement for early detection and screening of asymptomatic patients with infectious diseases, such as COVID-19.

Abstract: At present, body temperature measurement at the forehead, mouth, and ear is commonly used to screen for fever that is one of the major symptoms of COVID-19. However, the single spot temperature measurements are not sensitive enough to screen the risk of COVID-19. There is a considerable rate of missed diagnosis due to the floating nature of body temperature. More than half of COVID-19 infected patients have no obvious symptoms of fever in early stage of COVID-19. The asymptomatic patients are high-risk infection sources when their temperatures are still within normal range. To improve screening efficiency, we propose the use of bilateral symmetrical body temperature difference as an informative indicator to screen asymptomatic people at risk for COVID-19. In this study, we investigated bilateral symmetrical body temperatures for COVID-19 patients and healthy subjects, and identified that the bilateral symmetrical temperature difference is very sensitive to detect health condition imbalance and hidden disease states caused by COVID-19 in early stage. As far as the mechanism is concerned, the difference in body temperature between left and right is not affected by the mutation of the COVID-19 virus. The balance coefficient of left and right body temperature will not change as a result. Therefore, it is still conducive to the monitoring of patients with new mutations such as Omicron. Symmetrical body temperature differences can be detected earlier than confirmative COVID-19 nucleic acid tests. It can be used to screen COVID-19 risk groups with higher accuracy than single-spot body temperature measurement. It can be used as a new and effective risk indicator for self-check of health conditions, large-scale screening of potential COVID-19 patients, helping overcome the tendency of low body temperature in the elderly, help confirm the effectiveness of treatment and guide the rehabilitation process.

[Zhiqiang Cui, Grace Shu, Gu He, Ying Wang, Matthew Lee, Kai Shen，Qing Ke，Danping Li, Lili Liu, Yun'e Yuan, Minjie Gu, Shouyi Wang. **Application of Symmetrical Body Temperature Difference to Improve Early Detection of Covid-19**. *Life Sci J* 2021;18(12):22-33]. ISSN 1097-8135 (print); ISSN 2372-613X (online). http://www.lifesciencesite.com. 4. doi:10.7537/marslsj181221.04.

Keywords: application; symmetrical body; temperature; difference; improve; detection; Covid-19

INTRODUCTION

Measuring body temperature is very important in medicine. Many diseases are characterized by a change in body temperature. The course of a disease can be followed by measuring body temperature, which allows doctors to screen patients' health status and analyze treatment effectiveness. However, single spot temperature measurements are mostly adopted in clinical practice. The temperature may be measured randomly at one side of the ear or armpit, or just at the forehead. The single spot temperature measurements are limited to detect a disease status in the early stage. For example, more than half of COVID-19 infected patients have no obvious symptoms of fever in the early stage. These asymptomatic people with body temperatures within the normal range are high-risk infection sources and the main cause of disease spread in public spaces [1]. In the past ten years, we have used bilateral symmetrical body temperatures as an indicator to evaluate health status and disease development stages for many of our patients [2]. We found that bilateral symmetrical body temperature difference is a sensitive indicator to detect and monitor health status even in the early stage of a disease. In this study, we particularly studied bilateral symmetrical body temperature difference for healthy subjects and COVID-19 patients. The outcome of this study confirmed that bilateral symmetrical body temperature difference can be a promising indicator for early detection and monitoring of COVID-19 patients. In the following, we will introduce the studies on symmetric body temperature and the insight for its potential application for infectious disease prevention. Guide the rehabilitation of the disease.

Studies on Symmetric Body Temperature

It has been observed in clinical practice that axillary measurement of body temperature could vary from one side to the other. More than 40 years ago, the Chinese Medical Association initiated a study to compare the bilateral axillary temperatures of 1,008 healthy people at the People's Hospital of Jilin Province. The study found that the average difference in bilateral axillary temperature of healthy people was 0.126F (0.07℃) with no statistical significance. Thus, the axillary temperature is measured randomly on either left or right sides in clinical practice at Chinese hospitals so far.

In another study of 100 healthy adults, it showed that healthy adults' axillary temperature averaged 36.51±0.41 ℃ on the left side and 36.33±0.44℃ on the right. The statistical difference between the two sides was not significant with a variation range around ±0.2℃ [3]. Sumio Uematsu et. al found that the degree of thermal asymmetry between opposite sides of the body (ΔT) is very small. For example, the value of ΔT for the forehead (mean ± standard deviation) was 0.18°±0.18℃, [4]. In 2016, Turgut Ozal University Hospital conducted a study on 463 healthy subjects (325 women, 138 men) and measured bilateral skin temperatures at three different body regions: the armpit, the thumb, and the external auditory canal. This study showed that the symmetrical temperature differences at the three different regions were within ±0.19℃ [5]. The above data demonstrate that the symmetric body temperatures of a healthy person are basically balanced, with a difference not exceeding 0.2 ℃ which can be considered as a standard reference for the temperature difference in a healthy person. Currently, it is still a common clinical practice to randomly measure body temperature on either the left or right side of a patient. Dr. Georgine Nanos, a family doctor and CEO of Kind Health Group (a telemedicine service provider), said that we tend to treat normal body temperature as a static number, but in fact, a person's body temperature fluctuates throughout the day. A single number cannot represent the "normal" temperature for every person [6]. Recently it was also reported that the average body temperature has decreased from 98.6° F to 97.5° F over the past 100 years [10]. This adds further to the uncertainty of using single spot temperature measurement as an indicator of health status.

Infrared thermography (IRT) is a remote, non-contact and non-invasive temperature monitoring technique. It is fast and makes simultaneous large area screening possible. Interpretations from pseudo color coded thermograms are easier to read. The contralateral (left vs. right) temperature differences in the face, extremities, and trunk areas of healthy human subjects vary within ±0.2°C [7, 8]. Thanks to IRI's contactless features, it is used for fever screening in public areas, particularly in healthcare and transportation hubs such as airports. However, the accuracy and screening rate of COVID-19 are extremely low. With bilateral IRT scanning, the COVID-19 screening rate can be improved by symmetrical temperature difference analysis. It was found that axillary temperature measured by conventional thermometer was highly correlated with the temperature of inner canthi of the eyes measured by IRT. The study further indicated that temperature above 37.5 °C, with ± 0.5 °C tolerance for the measurement system, must be considered as a possible indication of fever instead of 38 °C as reported earlier [9]. Based on current studies, the characteristics of body temperature can be summarized as follows:

1) The body temperature varies in different body regions, at different time during a day, with different thermometers, at different ages, and also gets impacted by antipyretics.
2) The body temperature of some patients with immune deficiency diseases does not rise due to malfunction of the immune system. In this case, the body temperature will not be a reliable indicator for the health status of these patients.
3) The body temperature is incapable of detecting asymptomatic carriers of infectious diseases. If a patient is an asymptomatic carrier or in an early stage of infectious disease, the current body temperature screening method is unable to screen these patients and may result in an uncontrollable source of infection.

Given the limitations above, the regular body temperature measurement is inefficient to monitor health status or early-stage Covid-19 infection. The measurement of the left and right symmetrical temperature difference is a more sensitive way to detect health status changes and has the potential to be utilized for Covid-19 screening.

Physiological Basis for Symmetric Axillary Temperature

According to the Kinetic Molecular Theory, elevation in temperature will increase the average kinetic energy of the molecule [11]. Symmetrical axillary temperature difference reflects the difference in the average kinetic energy in the physiological functions of organs, tissues, and cells in symmetrical structures, and is the basis for the average kinetic energy of human molecules. The kinetic energy of cells is a measure of loss of balance, reflecting the loss of a steady-state between the left and right organ functions. The temperature difference determines the direction of heat transfer between the two systems, so their combined energy is distributed to the greatest extent in their lowest state. We call this distribution "entropy". temperature differences dictate the direction of heat between two systems such that their combined energy is maximally distributed among their lowest possible states [12]. The law and direction of energy consumption and heat conversion are used as individualized observation indicators.

Humans are warm-blooded. The dynamics of bilateral axillary temperature reflects one of the basic physiological attributes in humans. The 242nd National Meeting of the American Chemical Society (ACS) announced that changes in the internal temperature of cells may change the way DNA works or the operating mechanism of protein molecules [13].

The above discussion fully embodies the physiological and biological relationship between body temperature and the functions of human cells and organs. The difference in bilateral axillary temperature determines the direction of heat transfer between the left and right systems. When the clinical data are combined, one can see the dynamics of a person's physique and disease aggravation and remission.

Fever is a sign that something out of the ordinary is going on within the body. The immune system typically will respond. In terms of COVID-19, some patients do not have a fever in the early stage, however, the abnormal health conditions in the body will first be manifested in the symmetrical axillary temperature difference. The increasing or decreasing direction, and the value of the symmetrical axillary temperature differences, are objective criteria for monitoring, diagnosing, and intervening in COVID-19. Therefore, it is important to monitor symmetrical axillary temperature differences as it is an effective indicator for screening risky subjects in public areas.

The standard for detecting fever in the United States has not yet been unified. The normal temperature range for Covid-19 used by the New York Regional Airport is 97.4-99.4°F (36.3-37.4°C). For example, a person with a one-sided temperature of 37.3°C (99.1°F) will be considered within the normal range. However, it may miss the diagnosis of Covid-19 infection at early stage or in asymptomatic carriers. Conversely, the left and right symmetrical temperature difference measurement can be a sensitive signal for diagnosing the patient's disease state.

Based on our study, we set the left and right symmetrical temperature difference measurement not to exceed ±0.3°C (0.54°F) in normal health states. The method is quick and simple to perform and can reduce the missed-diagnosis rate of temperature-based Covid-19 screening.

Insight for Covid-19 Prevention

In the past 18 months, COVID-19 has spread to the world with more than 100 million people in 192 countries and regions having been diagnosed.

Body temperature has been the most extensively used method to screen at-risk populations. Commonly reported symptoms include fever (84%), fatigue (83%), cough (73%) and dyspnea (72%) [14]. The only quick screening indicator with observable symptoms is fever. However, fever can be fleeting, subacute, or if absent, may even provide a false sense of security. It has been reported that 16% of COVID-19 cases in early stages did not have a fever. It is the main reason for missed diagnosis using the current temperature screening tests. In a study of 1,099 hospitalized patients, only 44% of patients had fever on admission, but eventually 89% of patients had fever later during hospitalization [15]. These 16-56% of patients without fever represent the at-risk population using the current screening process. This is an important reason for the missed diagnosis of latent virus carriers using current body temperature measurements [4]. The missed diagnosed “mobile source of infection” of COVID-19 cases imposes a great challenge in stopping the spread of the disease.

There is an urgent need to improve quick screening methods in an effort to reduce the missed diagnosis rate of COVID-19 in public areas worldwide. The detection of symmetrical body temperature imbalance can make up for the above shortcomings to a certain extent. At present, the initial screening for Covid-19 in public places is limited to measuring single-spot body temperature. If body temperature is considered normal, then a passenger will be permitted to access airports, train stations, and many additional public places. In some public areas, infrared detection based methods are used to monitor large groups of travelers. It is a convenient and well-developed technique for remotely detecting body temperature, however, it has issues of fluctuating readings and inconsistent accuracy. Nucleic acid testing is accurate, but it takes time and it is impossible to implement the testing for large groups of people in public places. Currently, there is not an effective Covid-19 screening method, with high sensitivity and precision, to test at-risk groups in public areas. It greatly limits the capability for early detection /early intervention of infectious disease and to prevent its spread worldwide. This study is aimed at helping alleviate this concern.

RESULTS

Bilateral Temperature Characteristics of Healthy Subjects

During the epidemic period from March 29 to April 9, 2020, 17 normal working employees from Taiyuan Xinzhi Naokang Hospital were monitored for bilateral axillary temperatures every day in an effort to prevent further epidemic spread.

Each person's temperature was measured for 16 to 17 days. A total of 284 measurements were collected. According to the statistical analysis using the t-test, the means of axillary temperature differences in all 17 healthy participants stayed within 0.2°C, which is consistent with the normal tolerance threshold reported in the literature. The data are presented in Table 1.

Table 1 Axillary temperature difference summary of people at Taiyuan Xinzhi with 95% confidence interval in monitoring Covid-19 potential (Unit: ℃)

Subject #	Gender	# Days	Mean of ΔT	Mean of |ΔT|	Std	Lwr95	Upr95
1	F	1-17	-0.02	0.02	0.129	-0.088	0.045
2	F	1-17	-0.13	0.13	0.162	-0.21	-0.044
3	F	1-16	0.02	0.02	0.176	-0.072	0.115
4	M	1-17	0.04	0.04	0.196	-0.058	0.143
5	F	1-17	-0.13	0.13	0.24	-0.249	-0.002
6	M	1-16	-0.04	0.04	0.215	-0.152	0.077
7	M	1-17	-0.16	0.16	0.226	-0.278	-0.046
8	F	1-17	0.06	0.06	0.194	-0.044	0.155
9	F	1-16	-0.07	0.07	0.17	-0.156	0.026
10	F	1-17	-0.15	0.15	0.133	-0.217	-0.081
11	F	1-17	-0.1	0.1	0.193	-0.2	-0.002
12	F	1-16	-0.1	0.1	0.258	-0.238	0.036
13	M	1-16	-0.13	0.13	0.139	-0.203	-0.055
14	F	1-17	0.06	0.06	0.15	-0.019	0.135
15	F	1-17	0.11	0.11	0.426	-0.107	0.332
16	F	1-17	-0.04	0.04	0.171	-0.131	0.045
17	F	1-17	0.07	0.07	0.141	-0.006	0.139

Life Science Journal
Websites:
http://www.lifesciencesite.com
http://www.sciencepub.net
Emails:
editor@sciencepub.net
sciencepub@gmail.com
MARSLAND PRESS
Multidisciplinary Academic Journal Publisher

Symmetrical Axillary Temperature Analysis of a COVID-19 Patient Case

In Jan 2021, a 57-year-old patient asked for treatment of Covid-19 symptoms: the person had body aches, dizziness and loss of appetite with no fever on January 20. The details of this patient's bilateral temperatures are presented in Table 2 and summarized as below:

- According to our recommendations, starting at 6 am on Jan 21, the left and right symmetrical temperatures were measured using a mercury clinical thermometer manufactured at Shanghai Clinical Thermometer Factory. The body temperature was below 37℃ at 6 am, but the left and right symmetrical temperature difference was 0.3℃ (L35.0-R35.3℃). There is still no fever at 7:00pm, but the temperature difference rises to 0.4℃ (L36.1-R36.5℃), In other words, the deference of symmetrical temperatures increased. The patient felt uncomfortable, painful, and took anti-fever medicine.
- On Jan 22, the left and right symmetrical temperature difference was 0.2℃ (L35.8-R36.0℃) at 6 am; the patient had a fever in the afternoon and the measured left axillary temperature was 37.5℃ at 16:30. The patient took Tylenol ER (acetaminophen, 650 mg) at 16:30 right after the temperature measurement. The temperature difference was near zero at 19:00 (L36.4-R36.4℃). It can be seen that the immediate effect of antipyretic drugs not only lowered the body temperature but also lowered the body temperature difference. The patient did not understand it at first, so the data collection of temperature measurement was incomplete.
- On Jan 23, the symmetrical temperature difference reached 0.5℃ (L35.2-R35.7℃) at 6 am. The patient took Tylenol ER at 18:00. The temperature difference was 0.2 (L36.3-R36.5℃) at 21:00. The effect of antipyretics on the temperature difference has disappeared after one night, so the temperature difference reached 0.5 ℃, which fully explained the sensitivity of the temperature difference.
- On Jan 24, the symmetrical temperature difference was 0.2℃ (L36.1-R35.9℃) at 7 am. COVID-19 nucleic acid test (nose swab sample) at 3 pm was negative. The patient took Tylenol ER at 18:30 and reported the symmetrical temperature difference of 0.5℃ (L36.2-R36.7℃) at 21:40. Although Tylenol lower the body temperature to the normal range, the abnormal symmetrical temperature difference was detected 4 hours after the fever medication. It suggests that the COVID-19 virus is still in the incubation period. At 23:00, the body temperature rose to 38.7℃ confirming the persistent sickness.
- On Jan 25, 6:00, 35.5-35.8 temperature difference above -0.3℃. From this day onward, the patient continued antipyretic medication three times a day (7:30/12:00/18:00), 10:20 35.6-35.6 with temperature differences reaching 0. Taking antipyretics within 3~4 hours of a fever's return result in body temperature and temperature difference returning to normal. This is the effect of antipyretics. But after 4 hours. 11.20.35.9-36.5 The temperature ·difference is again above -0.6℃;11.44.36.2-36.7 The temperature difference is above -0.5℃; After taking acetaminophen at 12:00 noon, body temperature and temperature difference, measured twice in the afternoon, reached normal again.
- On Jan 26, the left axillary temperature was 37.2℃ at 7:00 and 37.7℃ at 18:08. The patient took Tylenol at 18:08 and 23:00. His symmetrical temperature difference was -0.2℃ (L 36.3- R 36.5) at 23:00.

It can be seen that the patient with the onset of COVID-19 symptoms did not have a fever at the beginning. However, the symmetrical body temperature difference started to exceed 0.3℃ before the fever was detected. With the use of antipyretics, the patient's body temperature dropped and the symmetrical temperature difference also dropped within 4 hours. It indicates that the axillary temperature difference appears earlier than fever in COVID-19 patients. However, it could be interfered by the use of antipyretics. The influence of antipyretics diminished after 4 hours and the bilateral temperature differences exceeding 0.3°C was detected.

The patient woke up at 5 am on January 27, 2021 with a body temperature measured around 37℃. The patient stopped fever medication starting January 27th. The patient got the COVID-19 test at 9:30 am and received a positive test result at 8:05 am on January 28.

In this case, it took eight days for the patient to be diagnosed positive with Covid-19 from the onset of the initial symptoms. It has been suggested that COVID-19 testing tends to be less accurate within the first three days of exposure, and the best time to get tested is five to seven days after exposure

[23]. On Jan 24, the patient's body temperature and symmetrical temperature differences were all normal during the day. COVID-19 Nucleic acid amplification testing were negative. Later that night, the symmetric temperature difference above -0.5℃ and a fever of 38.7℃ was observed. On Jan 25, the symmetric temperatures difference of 0.3℃ was noted in the early morning and 0.5-0.6℃ in the noontime. The patient increased the antipyretic medication to three times a day at 7:30, 12:00, and 18:00. It was observed that the symmetrical temperature differences were minimized within 3-4 hours after antipyretics, for example, the symmetrical temperature difference reached near zero at 10:20 am on Jan 25 but the temperature difference was again above -0.5℃ after 4 hours.

Tale 2. Bilateral axillary temperature test of COVID-19 patients one week before the onset of illness

Date 2021	Time	L℃	R ℃	Difference	Patient Records Before COVID-19 Test Positive
20 Jan					Feeling body aches, dizziness, loss of appetite, discomfort, a little chill, no fever
21 Jan	6:00	35	35.3	**-0.3**	Had headache, dizziness, muscle weakness, can't eat and feel uncomfortable
	19:00	36.1	36.5	**-0.4**	
22 Jan	6:00	35.8	36	-0.2	
	16:30	**37.5**			Took Tylenol ER (acetaminophen, 650 mg)
	19:00	36.4	36.4	0	Took Tylenol before going to bed.
23 Jan	6:00	35.2	35.7	**-0.5**	
	21:00	36.3	36.5	-0.2	Took Tylenol ER 18:00
24 Jan	6:10				Took Tylenol ER
	7:00	36.1	35.9	0.2	
	15:00				**COVID-19 nucleic acid test negative (with fever)**
	18:30	36.2	36.1	0.1	Took Tylenol ER
	21:40	36.2	36.7	**-0.5**	
	23:00	**38.7**			Before go to bed, taking Tylenol ER
25.Jan	6:00	35.5	35.8	-0.3	
	6:10				Took Tylenol ER
	10:20	35.6	35.6	0	
	11:20	35.9	36.5	**-0.6**	
	11:44	36.2	36.7	**-0.5**	
	12:00				Took Tylenol ER
	13:50	36.7	36.8	-0.1	
	15:30	36.9	36.7	0.2	
	18:00				Took Tylenol ER
26 Jan	6:00				Took Tylenol ER
	7:00	37.2			
	18:08	37.7			Took Tylenol ER
	23:00	36.3	36.5	-0.2	Took Tylenol ER
27 Jan	6:00				Took Tylenol ER
	9:30	37.0			**COVID-19 nucleic acid test positive (No fever)**

The patient started to have symptoms on January 20 and recovered quickly in less than weeks. The patient was tested negative for COVID-19 on February 4, 2021 using Coronavirus nucleic acid testing reagents. Between January 20 and February 4, the patient only took anti-fever medicines in the first week when there was a fever. During this period, the patient used symmetrical body temperature difference as a health status indicator to guild his diet and exercise accordingly. Based on the characteristic of symmetrical temperature differences, the patient was detected with a hotter lower body and colder upper body. He was instructed to take a diet to warm up his upper body and cool down his lower body. He was guided to walk for 1 to 1.5 hours a day and to dress warmly for the upper body and keep his lower body cool. The patient gradually reached a symmetrical temperature balance after 14 days. The patient measured basal body temperature on Feb 9, 2021 (L35.95℃-R35.85℃ at 5:42 AM and L35.9℃-R35.9℃ at 7:00 PM) and on Feb 10, 2021 (L35.95℃-R35.85℃ at 5:42 AM, L35.9℃-R35.9℃ at 7:00 PM). His body was managed to achieve symmetric temperature balance using the lifestyle (diet and exercise) adjustments based on symmetrical body temperature monitoring. The patient measured bilateral axillary temperatures continuously for two months, and the overall body temperature remained balanced. His general health status was recovered to the condition prior to Covid-19 infection.

Table 3. Patients feel well after 10 months of treatment with symmetrical balance method

Date 2021	Time	L℃	R ℃	Difference
9 Nov	AM	35.95	35.85	0.1
	PM	35.90	35.90	0
10 Nov	AM	36.30	36.15	0.15
	PM	35.80	36.05	-0.25
11 Nov	AM	36.45	36.15	0.3
12 Nov	AM	36.30	36.20	0.1

After nearly 10 months of balanced and symmetrical lifestyle adjustments, the patient's body temperature feature was slowly changed (Table 3). Initially, the temperature was low on the left side and high on the right. Gradually the temperature of the whole body was brought into balance. This demonstrates that under a balanced and symmetrical lifestyle, the entire body temperature can be brought into balance resulting in an overall recovery from disease. Balanced and symmetrical hyperthermia not only can help in the early diagnosis of Covid-19, but also in a patients' recovery.

Symmetrical Body Temperature Analysis of COVID-19 Patients During Quarantine Period

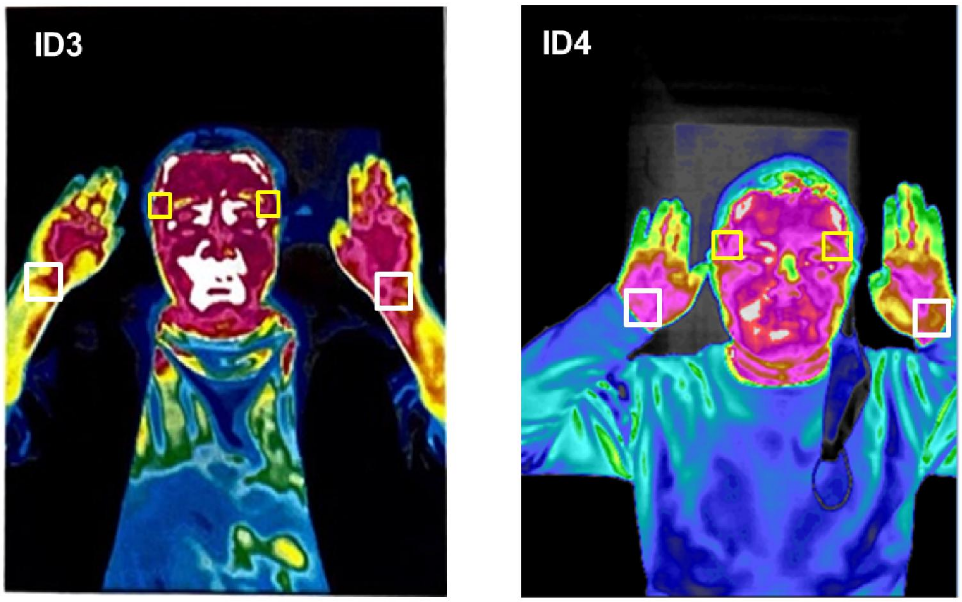
By using infrared imaging technology, we monitored symmetrical axillary temperatures of 10 randomly selected Covid-19 patients who were in post-treatment quarantine after being discharged from Hubei Hospital of Traditional Chinese Medicine in China on March 16, 2020. All these patients tested negative on the COVID-19 nucleic acid test and their body temperatures returned to normal. Each subject received an infrared imaging (IRI) based body temperature measurement using a system manufactured by Jiangshan Traditional Chinese Medicine Visualization Technology Co., Ltd. The youngest patient was 30 years old, the oldest was 83 years old. There were four men and six women, including three elderly people over the age of 60. The temperatures were measured on the glabella and both sides of the temple and wrist. The Infrared thermometers only measure the surface temperature, which is usually 3.5°C lower than the core body temperature. The symmetrical temperature measurements of the 10 post-treatment patients by IRI are summarized in Table 4.

Table 4. Symmetrical Temperature Measurements of 10 Covid-19 Patients after their treatment was completed and released from the China Hubei Hospital of Traditional Chinese Medicine for quarantine observation.

ID	Date Birth	Date	Time	Sex	Left Temple (℃)	Right Temple(℃)	Temple Diff. (℃)	Glabella (℃)	Left Wrist (℃)	Right Wrist (℃)	Wrist Diff. (℃)
1	1990/1/4	2020.03.16	11 AM	M	32.92	31.4	**1.52**	33.22	31.4	32.11	**-0.71**
		2020.03.18	10 AM	M	34.22	34.12	0.1	33.82	33.22	34.22	**-1**
2	1981/5/11	2020.03.16	11 AM	M	33.42	34.41	**-0.99**	33.92	30.89	31.1	-0.21
		2020.03.20	9 AM	M	33.32	33.42	-0.1	33.62	28.83	29.14	**-0.31**
3	1973/7/28	2020.03.17	9 AM	M	31.1	313	-0.2	30.89	31.3	30.79	**0.51**
		2020.03.20	9 AM	M	32.21	32.01	0.2	32.11	31.2	31.3	-0.1
4	1969/11/7	2020.03.16	9 AM	M	31.5	31.81	**-0.31**	32.21	30.99	29.66	**1.33**
		2020.03.18	9 AM	M	33.12	32.82	**0.3**	33.12	31.91	32.01	-0.1
5	1971/9/16	2020.03.15	16 PM	F	32.31	30.79	**1.52**	31.91	29.04	29.14	-0.1
		2020.03.17	10 AM	F	31.61	31.5	0.11	32.52	31.81	32.42	**0.61**
		2020.03.19	10 AM	F	29.86	28.93	**0.93**	29.55	29.45	29.04	**0.41**
6	1969/7/6	2020.03.17	11 AM	F	31.61	33.42	**-1.81**	33.32	32.82	33.12	**-0.3**
7	1965/2/5	2020.03.16	15 PM	F	29.45	29.55	-0.1	29.55	30.69	31.5	**-0.81**
		2020.03.20	10 AM	F	33.92	34.22	**-0.3**	33.32	33.32	33.82	**-0.5**
8	1960/1/29	2020.03.16	10 AM	F	31.91	32.31	**-0.4**	32.92	31.2	29.86	**1.34**
		2020.03.20	10 AM	F	31.1	32.62	**-1.52**	31.1	31.81	31.1	**0.71**
9	1955/6/23	2020.03.17	09 AM	F	30.89	30.38	**0.51**	32.82	30.99	32.01	**-1.02**
		2020.03.20	10 AM	F	34.61	34.22	**0.39**	33.32	34.12	34.12	0
10	1937/2/1	2020.03.15	11 AM	F	34.41	34.02	**0.39**	31.2	27.89	28.31	**-0.42**
		2020.03.18	09 AM	F	27.99	29.97	**-1.98**	30.07	28.2	26.83	**1.37**
		2020.03.21	11 AM	F	29.66	31.1	**-1.44**	30.17	29.55	29.35	0.2

We observed that even though all patients did not have any fever symptoms when discharged from the hospital, their symmetrical temperature differences were still significant, with values ranging between 0.35°C - 1.5°C. The large symmetrical temperature differences indicate that the health status of these patients have not yet fully recovered, and may still be in a contagious state requiring extended quarantine and/or additional treatment. The study results clearly show that the left and right symmetrical temperature difference is a more reliable vital sign measurement indicating physiological and pathological conditions as opposed to the single-spot body temperature measurement method. The symmetrical temperature measurement method is more robust when using different measurement approaches (such as infrared imaging for body surface temperature, mercury thermometer/electronic thermometer for axillary temperature), more robust within different age groups (such as elderly people who generally have lower body temperature than younger groups), more robust for detecting disease infection in early stages before fever appears; and most robust in detecting disease status even after antipyretics are taken to regulate overall body temperatures. The symmetrical temperature difference is a highly informative and robust biomarker when evaluating a person's health status.

Figure 1 shows the infrared body temperature scans for patient 3 and 4. The thermal imaging images can measure multi-point human body's thermal radiation projected to the body surface automatically. Thus, multi-point symmetrical body temperature differences can be conveniently calculated. The symmetrical temperature differences are generally within 0.3℃ for healthy subjects. When the bilateral temperature difference is greater than 0.3℃, it may be a health status alerting signal with clinical significance. In addition, one can also observe the abnormal thermal distribution in different body regions. For example, in Figure 1, the white areas show an abnormally high-thermal state, which may indicate inflammatory conditions; while the blue and dark blue areas show abnormal low-thermal state that may suggests a decreased thermal metabolism activity level of the corresponding body regions.



ID	AGE	Date	Time	Sex	Left temple	Right temple	Temple Diff.	Left Wrist	Right Wrist	Wrist Diff.
3	47	2020031	9 am	M	31.1	31.3	-0.2	31.3	30.79	0.51
4	51	2020031	9 am	M	33.12	32.82	0.3	33.12	31.91	1.21

Figure 1. Symmetric temperature monitoring of two discharged Covid-19 patients using infrared imaging technology. (Note: Above imaging was taken by infrared camera at sensor array size of 320x240, NETD of <40mK at 30ºC and repeatability of ±0.5% of the overall reading. The lenses used in imaging systems are standard lens (IR-lens 24º) for body partial views.)

DISCUSSION

Our view is that temperature can be seen as an evaluation system of the sum of all physiological functions, so the logical reasoning is that a healthy human body should be in a state of equilibrium in terms of function, with the core temperatures of the left and right sides very close to each other when measured. In a disease state, the human body must be in an unbalanced state, and the difference between the core temperatures of the left and right sides must be produced. After excluding interfering factors, when this difference is greater than a threshold value (which we set at 0.3°C), it is reasonable to assume that the measured human body is in a disease state, and this difference is positively correlated with the severity of the disease. In general, we consider a temperature difference between left and right of more than ±0.3°C to indicate an unhealthy state with probably a disease or health disorder. The more severe the disease, the greater the temperature difference is. During recovery or when the disease is resolved, the temperature difference decreases. Our study proposes the use of symmetrical temperature difference measurement as a new disease determination index to address the observation of disease status from a quantitative point of view, in effect going deeper into the quantification of functional aspects. Our study proposes the use of symmetrical temperature difference measurement as a new indicator.

Although current vaccination rates are increasing, the incidence number of Covid-19 remains high. This continues to impede normal life and economic growth worldwide. The bilateral temperature difference is a highly, more sensitive indicator for detecting the early stages of the COVID-19 even if the unilateral body temperature is within the normal range. The temperature difference test can be used at entry screening to reduce the rate of missed COVID-19 diagnoses.

The COVID19 virus is an RNA virus and has the characteristics of being easy to mutate. However, the pathogenic mechanism of virus mutation will not change in any case. The mutation of the virus only changes the binding point of the immune receptor at the microscopic level, but does not change the infection at the macroscopic level. As long as inflammation occurs in the target organs, there will be a temperature difference, which determines that the left and right body temperature difference is still one of the obvious characteristics of COVID-19 after mutation.

The method of symmetrical body temperature is also beneficial in overcoming the effects of low body temperature in the elderly group. Elderly people (65 years and older) usually have low body temperature due to a low metabolic rate. The core body temperature of an elderly person over 65 may be approximately 1℃ lower than that of a younger person. Thus, the missed rate of fever detection for an elderly group is high when using a unified temperature threshold. According to our study, the temperature difference in the elderly always exists. If the difference in the bilateral body temperature of an elderly person exceeds 0.3°C, it can be considered a warning signal and require further evaluation.

The symmetrical body temperature difference can also be used to evaluate COVID-19 treatment effectiveness by monitoring the patients' recovery process. Although imaging and laboratory tests can also accurately evaluate treatment methods, the difference in body temperature between left and right has great advantages in terms of cost, efficiency, and non-invasiveness.

Many new, highly specific detection methods have been created, but they are either expensive or infeasible for quick screening at public areas such as airports. Infrared image detection remains the method of choice, with strict operating protocols and guidelines recommended according to ISO (ISO/TR 13154:2009) and SPRING (TR 15-1: Requirements and Test Methods and TR 15-2: User Implementation Guide) standards for reliable and reproducible fever screening using IRT-based technologies [16, 17, 18, 19, 20], which is currently the common method used in all airports. Despite the availability of standards, its detection rate is still low. The current single-point temperature method is inefficient for screening COVID-19 patients and monitoring post-infection recovery status. As of April 21, 2020, U.S. airports have screened approximately 268,000 passengers, of which only 14 have been found to be infected with COVID-19. The experts in the field of infrared imaging are exploring this issue. Diakides and Bronzino describe recent advances in image processing techniques related to the field of medical infrared imaging [21]. Another aspect of medical image processing is asymmetry analysis, i.e., the analysis of temperature differences between diseased and contralateral healthy body parts [22]. They both tried to solve this problem by applying the statistical theory of joint entropy to observe the reaction and dynamics of the disease from a morphological point of view and by innovating on a technical level through the representation of temperature on infrared morphology.

The modified infrared imaging symmetrical temperature measurement is a simple and effective method for screening patients with COVID-19. It has high sensitivity and accuracy and is particularly suitable for airports and seaports. Although the absolute accuracy of IRI technology is not high due to the drift phenomenon, the symmetrical body parts are in the same environment and the temperature difference can be informative. The resolution of IRI technology can reach 0.01~0.03°C, which is enough to achieve the sensitivity of the measurement. This method does not require any new equipment; it only requires the measurement of temperature on both sides of the body. This method can be used in public places to improve the true positive rates of screening for COVID-19 patients. Many patients do not have a fever during the early stage of infections, however, the symmetrical body temperature difference is sensitive in detecting health condition changes when the deviation exceeds 0.3℃. For patients receiving treatment, the temperature difference can also be used to monitor the recovery process. A patient's health status can be considered recovered when the body temperature difference is reduced to within 0.3℃.

Since other diseases, during active periods, can also cause symmetrical temperature differences to exceed ±0.3°C, this is only a preliminary screening. Further specific testing is also needed. The two-step screening saves time, reduces missed diagnosis rate, and reduces cost. In addition, since symmetrical temperature difference exceeding ±0.3°C is a health problem indicator, it can also be used to screen for other health issues prompting subjects to pursue additional evaluations when indicated. This is useful for human health management. It is noted that symmetrical body temperature difference is not a specific COVID-19 indicator. It is a sensitive indicator to reflect one's healthy state. Further investigation is needed to conduct a large scale study for more precise quantification of symmetrical body temperature difference under healthy and diseased conditions.

In conclusion, the symmetrical axillary temperature difference is more dimensional, more accurate, and more relevant than the body temperature to screen the COVID-19 risk population. Since the COVID-19 will co-exist with humans for a long time, it is of great importance to apply a reliable quick screening method that will help control the disease transmission. We also call for more clinicians to verify the theory of symmetrical body temperature in clinical practice.

MATERIALS AND METHODS

This study investigated the symmetrical vital sign measurement approach, a method used to monitor a person's health status. In our study, the bilateral axillary temperature differences (ΔT) are calculated by subtracting the right side axillary temperature (RT) from the left side axillary temperature (LT), as shown in the equation: $\Delta T = LT - RT$. A tolerance may be chosen by a physician. For instance, when temperature is measured in degrees Celsius, a tolerance of 0.3 is used. In other words, if the absolute value of ΔT (|ΔT|) is less than 0.3°C, then the patient is said to be in a balanced state of health. On the other hand, the higher the bilateral axillary temperature difference |ΔT|, the greater the health imbalance deviates from the healthy state. When |ΔT| is greater than 1.0 °C, the patient is in a serious disease state and may be in danger of death. The value of |ΔT| can be a useful indicator to track a patient's state of health and monitor the effects of treatment [2]. Based on our clinical study, we consider |ΔT| = 0.3℃ as a threshold in screening possible asymptomatic carriers and/or risky subjects in the early stage of Covid-19.

Based on the available temperature measuring instruments, the methods of symmetrical bilateral axillary temperature are summarized as follows:

1) Measuring two sides of the axillary temperature with one single thermometer. Use a mercury thermometer or an electronic thermometer that can read two digits after the decimal point. After measuring the temperature of one side of the armpit, and then quickly measure the temperature of the other side of the armpit.
2) Simultaneously measuring axillary temperatures with a pair of calibrated thermometers. Use two synchronized thermometers to measure the bilateral axillary temperatures of a patient at the same time.
3) Bilateral infrared imaging measurement method. If a person with a high body temperature or a large difference in symmetrical axillary temperature is found, more specific and targeted testing must be carried out, which can effectively increase the detection rate of at-risk subjects. This can become the most efficient screening tool.
4) Specially designed real-time monitoring equipment. We have designed a dual-sided Bluetooth body temperature synchronization detection device that can continuously record bilateral axillary temperature data, blood oxygen saturation, bilateral pulse gap, human acceleration and movement status, and calculate the difference between left and right measured body temperature. The data is transmitted to a central server through Bluetooth and the Internet, with artificial intelligence used to measure symmetrical axillary temperature and identify health states.
5) The environment on each side of the body cannot be significantly different while measuring bilateral temperatures. For example, the measurement will not be accurate if only one side of the body is exposed to the airflow of an air conditioner, heater, or fan.

Acknowledgments:

We are grateful to Dr. Guo Xinzhi (CEO of Taiyuan Xinzhi Brain Health Clinic) for providing generous support on data collection and thoughtful suggestions on this research.

Funding:

This work was supported by Orient Health Care at New York, USA, Aulikang Health Technology at Suzhou, China, and Taiyuan Xinzhi Brain Health Clinic at Taiyuan, China.

Author contributions:

Conceptualization: Zhiqiang Cui, Kai Shen, Qing Ke
Methodology: Zhiqiang Cui
Investigation: Zhiqiang Cui, Valley He, Danping Li, Yun'e Yuan, Lili Liu, Guo Xinzhi
Visualization: Zhiqiang Cui, Shouyi Wang, Valley He, Kai Shen, Lili Liu, Ying Wang
Funding acquisition: Zhiqiang Cui
Project administration: Zhiqiang Cui, Kai Shen
Supervision: Grace Shu, Qing Ke
Writing – original draft: Zhiqiang Cui, Shouyi Wang, Valley He, Matthew Lee
Writing – review & editing: Shouyi Wang, Ying Wang

Competing interests:

Zhiqiang Cui and Matthew Lee are named as inventors on Patent US8684928B2 (2014,4,1): Vitalometries-Based Methods, Devices and Systems for Health/Lifestyle Maintenance and Improvement.

Data and materials availability:

All data associated with this study are in the paper or supplementary materials.

References and Notes

[1]. Vaccines are great, but testing and tracing will stamp out transmission, March.29,2021 https://www.washingtonpost.com/outlook/2

021/03/29/testing-tracing-isolation-coronavirus-endgame/.
[2]. Patent US8684928B2 (2014,4,1): Vitalometries-Based Methods, Devices and Systems for Health/ Lifestyle Maintenance and Improvement.
[3]. Yan Yun (Department of Internal Medicine, Yuquan Hospital, Tsinghua University), Report on Differences in Body Temperatures Under Armpits of Healthy Adults, Journal of Nursing, No. 3, 2005 (In Chinese).
[4]. Sumio Uematsu, M.D., David H. Edwin, Ph.D., William R. Jankel, Ph.D., Joseph Kozikowski, M.S.E.E., and Michael Trattner, R.T. "Quantification of thermal asymmetry" JJ Neurosurg 69:552-555, 1988.
[5]. Demirel, Havva, Arzu Bahar, Nurcan Gokgoz, Muzeyyen Arslan, and Senol Dane. Right-sided lateralization of skin temperature in healthy young persons. Clinical and Investigative Medicine (2016): S121-S124.
[6]. Consumer Reorts: By Rachel Rabkin Peachman, April 02, 2020 What to Know About Fever and COVID-19. https://www.yahoo.com/news/know-fever-covid-19-215933832.html.
[7]. Jones B.F. A reappraisal of the use of infrared thermal image analysis in medicine. IEEE Transactions on Medical Imaging, 1998;17:1019–1027.
[8]. Uematsu S. Symmetry of skin temperature comparing one side of the body to the other. Thermology.1986;1:4–7.
[9]. E.F.J. Ring, A. Jung, J. Zuber, P. Rutowski, B. Kalicki, U. Bajwa, Detecting fever in polish children by infrared thermography, in: 9th International Conference on Quantitative Infrared Thermography, Krakow, Poland, 2008.
[10]. Protsiv, Myroslava, Catherine Ley, Joanna Lankester, Trevor Hastie, and Julie Parsonnet. Decreasing human body temperature in the United States since the industrial revolution. Elife 9 (2020): e49555.
[11]. The Kinetic Molecular Theory, Boundless Chemistry, https://courses.lumenlearning.com/boundless- chemistry/chapter/kinetic-molecular-theory.
[12]. Thermodynamic temperature. https://en.wikipedia.org/wiki/Thermodynamic_temperature.
[13]. Effect of Temperature on the Intrinsic Flexibility of DNA and Its Interaction with Architectural Proteins. https://www. ncbi.nlm.nih.gov/pmc/articles/PMC5451147/.
[14]. Vahey, G.M., Marshall, K.E., McDonald, E., Martin, S.W., Tate, J.E., Midgley, C.M., Killerby, M.E., Kawasaki, B., Herlihy, R.K., Alden, N.B. and Staples, J.E., 2021. Symptom profiles and progression in hospitalized and non-hospitalized patients with coronavirus disease, Colorado, USA, 2020. Emerging infectious diseases, 27(2), p.385.
[15]. Interim Clinical Guidance for Management of Patients with Confirmed Coronavirus Disease (COVID-19). https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-guidance-management-patients.html.
[16]. D. D. Pascoe, E. F. Ring, J. B. Mercer, J. Snell, D. Osborn, and J. Hedley-Whyte "International standards for pandemic screening using infrared thermography", Proc. SPIE 7626, Medical Imaging 2010: Biomedical Applications in Molecular, Structural, and Functional Imaging, 76261Z (9 March 2010); https://doi.org/10.1117/12.843836.
[17]. Ring E. F. J., Mcevoy H., Jung A., Zuber J., Machin G. New standards for devices used for the measurement of human body temperature. Journal of Medical Engineering & Technology.2010;34:249–253.
[18]. Standards Technical reference for Thermal Imagers for Human Temperature Screening Part 2: Users' Implementation Guidelines, SPRING, Singapore, TR 15–2 (2004).
[19]. Standards Technical Reference for Thermal Imagers for Human Temperature Screening Part 1: Requirements and Test Methods, SPRING, Singapore, TR 15–1 (2003).
[20]. ISO/TR 13154:2009. http://www.iso.org/iso/catalogue_detail?csnumber=51236.
[21]. N.A. Diakides, J.D. Bronzino, Medical Infrared Imaging, CRC Press, 2007.
[22]. P.T. Kuruganti, H. Qi, Asymmetry analysis in breast cancer detection using thermal infrared images, in: Proc. of the 2nd Joint EMBS-BMES Conference, 2002, pp. 1129–1130.
[23]. If you've been vaccinated, the best time to get tested is three to five days after an exposure. Henry Winkelhake, September 3, 2021. https://nortonhealthcare-com.translate.goog/news/how-long-after-exposure-to-test-positive-for-covid/?_x_tr_sl=en&_x_tr_tl=zh-CN&_x_tr_hl=zh-N&_x_tr_pto=nui,sc.

12/6/2021