

Non-invasive thoracic electrical bioimpedance technique-derived hemodynamic reference ranges in Chinese Han adults

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To the Editor: Continuous monitoring of hemodynamic status can be used to detect early abnormal circulation and is very helpful for the management of the critically ill. Today, different minimally invasive and non-invasive monitoring systems can measure functional hemodynamic parameters to guide treatment planning and improve patient care. Among them, the thoracic electrical bioimpedance (TEB) technique is widely available and is accurate for most patients, especially after open-heart surgery. However, there are ethnicity-related differences among hemodynamic characteristics and the hemodynamic response to the same cardiovascular disease differs among racial groups. Currently, no nationwide hemodynamic parameter reference ranges can be used for healthy Chinese Han adults. A large-scale, forward-looking research investigation of the hemodynamic state markers in China has not been wholly reported. Therefore, it is necessary to establish ethnicity-specific hemodynamic reference ranges for the Chinese Han population and evaluate the relationship between these parameters and age/sex, in order to promote efficient and accurate judgment in clinical practice. From July 2012 to September 2017, a prospective, nationwide study led by the Ministry of Science and Technology of the People's Republic of China was designed, organized, and performed to establish normal reference ranges of hemodynamic parameters for the Chinese Han population and to confirm the impacts of age and sex on these parameters.

The study protocol was approved by the local Center of Disease Control and Prevention, and written informed consent was obtained from all participants in this study. This cross-sectional cohort study was organized in six provinces and autonomous regions of China, including Heilongjiang, Hebei, Sichuan, Guizhou, and Hainan provinces and the Xinjiang Uygur autonomous region. With a multistage, stratified cluster design, a group of 1535

Chinese Han adults aged 20 to 79 years was initially registered for the study. The inclusion criteria required that all subjects had normal blood pressure, normal physical examination, and no symptoms or history of heart diseases. The exclusion criteria included patients with hypertension, stroke, heart failure, coronary artery disease, structural heart disease, abnormal liver or renal function. In addition, pregnant women, professional athletes, and subjects addicted to alcohol were excluded. Then, the whole study population was divided into six groups according to age: 20 to 29, 30 to 39, 40 to 49, 50 to 59, 60 to 69, and 70 to 79 years (approximately 50% men in each group).

The research group utilized the same BioZ digital non-invasive hemodynamic monitor (CardioDynamics Company, San Diego, CA, USA) in six provinces. All TEB measurements were conducted by two operators who had completed regular training in the use of the TEB technique. Subjects needed to rest for 30 min before testing and were placed in the supine position. First, the neck/chest/abdomen skin was cleaned with alcohol and wiped dry. Two pairs of TEB electrodes were placed on the upper abdomen/neck parallel to the spine. The remaining two pairs of electrodes were placed at the level of the diaphragm and the root of the neck. Following electrocardiography signals and the digital processing of the TEB, the processor extracted data describing the systemic hemodynamics of the subject, including values for blood flow (cardiac output [CO], cardiac index [CI], stroke volume [SV], and stroke index [SI]), contractility and left ventricle performance (left cardiac work [LCW], pre-ejection period [PEP], and left ventricular ejection time [LVET]) and afterload (systemic vascular resistance [SVR],

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mean arterial pressure [MAP], and thoracic fluid conductivity [TFC]). At the same time, demographic features of the entire population were collected, including height, weight, systolic blood pressure, diastolic blood pressure, and heart rate. The body surface area (BSA) was calculated by the Stevenson formula.

Continuous variables were normally distributed and were expressed as the mean ± standard deviation. The mean values between women and men and between subjects aged 20 to 29 years and the remaining subjects were compared with independent-samples *t*-tests. Comparisons between the multiple age groups were performed using analysis of variance. Analyses were performed using SPSS version 24.0 (IBM Corp., Armonk, NJ, USA). Two-tailed *P* < 0.05 were considered statistically significant.

A total of 1478 subjects who satisfied the selection criteria were investigated in the final cohort. There were 769 women, aged 45.3 ± 12.9 years, and 709 men, aged 44.6 ± 13.2 years. We also collected ten important and frequently used hemodynamic parameters by the TEB technique from the 1478 subjects. The average values of the weight, height, body mass index, BSA, systolic blood pressure (SBP), and diastolic blood pressure (DBP) were all higher in men than those in women. There was no age difference in heart rate for either gender. The highest values of SBP were obtained in subjects aged 70 to 79 years for both sexes. The highest values of DBP were obtained in female subjects aged 50 to 59 years and in male subjects aged 40 to 49 years. Hemodynamic parameters reference ranges in the study population stratified by sex were shown in Table 1. For the whole population, the blood flow

values, including CO, CI, SV, and SI, were all significantly higher in men than those in women. CO, SV, and SI decreased significantly with increasing age groups in both sexes. CI first decreased then increased with age in women and the lowest value was obtained among aged 60 to 69 years. At the same time, LCW was higher in men than that in women for the whole population, whereas the PEP and LVET were significantly shorter in men than those in women. On the other hand, there were no significant differences in LCW, PEP, and LVET among the six age groups in both sexes. In the last, MAP and TFC were significantly higher in men than that in women for the study population, although SVR was considerably lower in men than that in women. Meanwhile, MAP and SVR gradually increased with age for both men and women, while no significant difference was observed in the TFC among the six male age groups. The lowest value of TFC was in female subjects aged 50 to 59 years.

The TEB technique is based on measurements of bioimpedance via the transmission of small electrical currents throughout the chest area. In our body, electrical current passes through conduits of low and high conductance, and different body tissues have different levels of electrical conductivity. Changes in impedance recorded by the TEB device can collect hemodynamic data and reflect the hemodynamic status. Pulmonary artery thermodilution is an invasive method of hemodynamic monitoring that has been used for more than four decades and it remains the gold standard. Prior studies demonstrated that there is an obvious correlation between the values for hemodynamic data obtained by the TEB technique and by pulmonary artery thermodilution

Table 1: Hemodynamic parameters reference range of population in 6 provinces stratified by sex (n = 1478).

Sex	Parameter	Mean ± SD	95% CI	Percentile					
				5th	10th	50th	90th	95th	
Men (n = 709)	CO (L/min)	5.91 ± 2.91	5.69–6.12	3.63	3.99	5.18	8.23	12.58	
	CI (L·min ⁻¹ ·m ⁻²)	3.41 ± 1.51	3.30–3.52	2.28	2.47	3.01	4.64	6.74	
	SV (mL)	81.40 ± 36.73	78.69–84.10	45.95	53.20	73.00	109.80	144.95	
	SI (mL/m ²)	46.89 ± 18.88	45.49–48.28	29.55	32.30	42.40	61.10	84.10	
	LCW (kg·m)	6.46 ± 3.19	6.22–6.71	3.60	4.10	5.70	9.24	12.94	
	PEP (ms)	106 ± 17	105–107	80.00	90.00	110.00	130.00	130.00	
	LVET (ms)	338 ± 75	333–344	250.00	260.00	330.00	430.00	480.00	
	SVR (d·s ⁻¹ ·cm ⁻⁵)	1230 ± 412	1200–1261	508.00	780.00	1223.00	1662.00	1793.00	
	MAP (mmHg)	85.92 ± 9.82	85.19–86.64	71.00	75.00	85.00	97.00	103.00	
	TFC (L/kΩ)	25.40 ± 4.33	26.08–26.72	20.40	21.60	26.00	32.80	33.30	
	Women (n = 769)	CO (L/min)	4.81 ± 2.00*	4.66–4.95	3.03	3.36	4.40	5.93	8.61
		CI (L·min ⁻¹ ·m ⁻²)	3.13 ± 1.20*	3.04–3.21	2.09	2.30	2.88	3.79	5.51
		SV (mL)	63.57 ± 24.51*	61.83–65.30	39.55	43.70	59.40	81.00	107.10
SI (mL/m ²)		41.36 ± 14.76*	40.31–42.40	26.30	29.60	39.00	51.20	67.50	
LCW (kg/m)		4.97 ± 2.15*	4.82–5.12	3.01	3.40	4.50	6.60	8.73	
PEP (ms)		109 ± 16*	108–110	80.00	90.00	110.00	130.00	130.00	
LVET (ms)		350 ± 79*	344–356	250.00	270.00	340.00	450.00	490.00	
SVR (d·s ⁻¹ ·cm ⁻⁵)		1397 ± 431*	1366–1428	667.00	928.00	1355.00	1934.00	2240.00	
MAP (mmHg)		82.15 ± 9.79*	81.46–82.85	67.00	70.00	82.00	95.00	100.00	
TFC (L/kΩ)		23.15 ± 4.48*	22.83–23.46	17.80	18.70	22.40	27.70	30.20	

* *P* < 0.05 (women vs. men). CI: Cardiac index; CI: Confidence intervals; CO: Cardiac output; LCW: Left cardiac work; LVET: Left ventricular ejection time; MAP: Mean arterial pressure; PEP: Pre-ejection period; SI: Stroke index; SV: Stroke volume; SVR: Systemic vascular resistance; TFC: Thoracic fluid content.

($r = 0.818$) and pointed out that the former method was intended to act as an alternative method for hemodynamic monitoring.^[1] Meanwhile, the TEB technique does not require a proficient operator, and operator variability is less likely. The rate of variation in the TEB technique is lower than that of the above-mentioned method. Since the 1990s, the TEB technique has been increasingly used for the monitoring of hemodynamic status, which has promoted the application of the TEB technique to a stage where its theory is used to guide daily clinical practice. The TEB monitor can acquire specific parameters reflecting left ventricular contractility, which cannot be obtained by pulmonary artery thermodilution and provide crucial information for determining the worsening of left ventricular systolic function, especially for major adverse cardiovascular events and mortality. The present study found that men had better left ventricle contractility performance than women. Furthermore, there were no significant differences in LCW, PEP, or LVET among the age groups for either sex. However, some scholars reached different conclusions. Mahindrakar *et al*^[2] pointed out that the PEP and LVET showed a significant positive correlation with advancing age. Such differences may be partially due to the differences in the sample sizes ($n = 1478$ vs. $n = 50$) and the ages of the subjects (44.9 ± 13.1 vs. 38.9 ± 15.2 years). Additionally, the elasticity and hardness of blood vessels are more affected by advancing age, while the contractility of the heart itself may not change with age. However, further research is still needed to understand the causes of the formation and development of these phenomena. In addition, the TEB technique also has essential value in the hemodynamic monitoring of critically ill patients. By using hemodynamic monitoring, we aim to guide clinical management to treat or prevent organ failure and improve patient outcomes. Especially in the context of the high prevalence of respiratory viruses, hemodynamic monitoring based on the TEB technique can reduce occupational exposure of medical staff and help physicians be alert for any physical changes.

Another important parameter obtained by the TEB technique is TFC, which represents the whole fluid component in the thorax and is related to body weight, blood circulation state, and myocardial contractility. Some researchers have noted that TFC obtained by the TEB monitoring may be a potential determinant of ventilatory efficiency in patients with heart failure and even pointed out that it may be a promising substitute to ultrasound for

the assessment of extravascular lung water. However, we noted that TFC did not show an apparent trend with age for either men or women in the current study, which is drastically different from other parameters. Krzesiński *et al*^[3] also found a similar “U-shaped” pattern of age-related change for TFC, especially in men. These authors interpreted the decrease with age to be the compensatory fluid loss caused by vasoconstriction. The inversion of the trend may indicate the transmission of high left ventricular diastolic pressure to the left atrium and pulmonary circulation.

This is a rare prospective and most extensive study that defines normal reference ranges of these hemodynamic parameters for Chinese Han adults with a wide range of age. The age- and sex-related impacts on all hemodynamic parameters were also summarized and presented. But there are several limitations. First, medical histories of the participants were reviewed at their corresponding institutions. Therefore, the presence of unrecognized cardiovascular disease, such as sub-clinical coronary artery disease, cannot be ruled out. Second, the cross-sectional study was only organized in six provinces of China and the samples may lack of relative national representation. At the same time, data from different geographical characteristic are lacking. To achieve these, further in-depth and more large-scale studies are required.

Conflicts of interest

None.

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