

Received October 4, 2021, accepted November 7, 2021, date of publication November 17, 2021, date of current version December 3, 2021.

Digital Object Identifier 10.1109/ACCESS.2021.3128916

Analysis of the Radial Pulse Wave and Its Clinical Applications: A Survey

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This work was supported in part by the National Natural Science Foundation of China under Grant 61773110 and Grant 61374015, in part by the Natural Science Foundation of Liaoning Province (Key Program) under Grant 20170540312, in part by the Research and Development Plan of Liaoning Province (Key Program) under Grant 2018225024, in part by the Fundamental Research Funds for the Central Universities under Grant N2119008, in part by the Shenyang Science and Technology Plan Fund under Grant 20-201-4-10, and in part by the Member Program of Neusoft Research of Intelligent Healthcare Technology, Company Ltd., under Grant MCMP062002.

ABSTRACT The arterial pulse wave is a physiological signal which can reflect the function of the human cardiovascular system. Owing to the measurement being convenient and safe, radial pulse waves have been often used in noninvasive monitoring of human health, which can further reflect the health status of the cardiovascular system, including information of the aorta and peripheral arteries. Moreover, radial pulse waves can assist clinical diagnosis in the prevention and treatment of cardiovascular disease. This paper systematically reviews the progress in analysis of pulse wave analysis, including pulse wave acquisition, waveform processing, pattern classification, parameter estimation, and clinical applications. In terms of waveform acquisition, this paper reviews a variety of methods to obtain radial pulse waves, including tonometry, photoplethysmography, ultrasound manometry, and flexible tactile pressure sensors. In the aspect of waveform processing, this paper summarizes the methods of radial pulse waves preprocessing and feature extraction. With the rapid development of machine learning and deep learning algorithms, radial pulse waves can be used to identify the status of human cardiovascular systems and to estimate parameters related to cardiovascular function. This paper also discusses the applications of radial pulse waves in clinical practice, including cardiovascular function evaluation and pulse diagnosis in traditional Chinese medicine. Some open-source databases and analysis software are also listed. The current development trend, challenges, and future directions of analysis of radial pulse waves are also offered.

INDEX TERMS Radial artery, pulse wave, waveform processing, feature extraction, pattern classification, parameter estimation.

I. INTRODUCTION

Cardiovascular disease (CVD), including conditions such as hypertension, diabetes, coronary artery disease (CAD), is a leading non-communicable disease, and its mortality accounts for 50% among non-communicable diseases [1]. The number of deaths due to CVD worldwide is increasing year by year. The mortality rate of CVD has brought great pressure to global health care [2]. High systolic blood

pressure is positively correlated with the risk of CVD, which is an index to predict CVD and identify the health status [1]. Noninvasive detection of the arterial pulse wave can effectively evaluate the blood pressure or blood flow, which is useful for diagnosis, treatment, and prevention of CVD.

Noninvasive detection of the arterial pulse wave is a convenient and effective method to detect cardiovascular conditions. Studies have shown that the pulse wave propagation index (the ratio of body height to pulse wave propagation time) is associated with reduced cardiac ejection fraction [3].

The associate editor coordinating the review of this manuscript and approving it for publication was Mohammad Zia Ur Rahman¹.

The pulse wave is a pressure wave or flow wave due to the heart's periodic contraction and ejection of blood into aorta. And this wave spreads along the arterial system from the heart to the periphery. During the propagation along the arterial system, the waveform morphology is affected by the function and structure of the arterial system [4], [5]. Therefore, the arterial pulse wave reflects the information of the heart as well as the vascular system [6]. The general health status of the human body can be assessed by extracting the function of the heart and arteries from pulse waves. For example, the doctors of traditional Chinese medicine (TCM) can learn about human health conditions by examining the pulse at the wrist [4].

The radial pulse wave, an aortic pulse wave generated by the heart, propagates along the arterial network to the peripheral sites. Furthermore, the radial pulse wave is easy to acquire [7]. In terms of obtaining radial pulse waves, there are tonometry methods to detect the radial pressure waveform [7]–[10], photoplethysmography (PPG) measurement related to radial blood volume expansion [11]–[13], and Doppler ultrasound technology to detect velocity of the radial blood flow [14]–[16]. With the development of sensor technologies, flexible sensors have been used to record radial pulse waves [17], [18]. In addition, some researchers have employed multi-sensor fusion methods including multichannel signal fusion [19]–[24], and array signal fusion [20], [25]–[27], to obtain rich information related to the cardiovascular system from radial pulse waves. However, comprehensive analysis of radial parameters, morphological changes, and clinical applications has not been reported.

The processing of the radial pulse wave includes waveform preprocessing and feature extraction. During the acquisition of the pulse wave signal, the recording can be affected by the respiration and motion artefacts. The respiratory signals can lead to baseline drift or distortion of radial pulse waves [10]. It is difficult to accurately extract the waveform features and describe the morphological changes. To obtain a corruption-free and more stable radial signal, the waveform preprocessing can not only reduce the interference components [28]–[33], but should also analyze the morphology of radial pulse waves over a long period [34]–[38]. The purpose of feature extraction is to analyze the information represented by radial pulse waves. The methods include time-domain analysis [5], [6], [31], [39], frequency-domain analysis [11], [40], time-frequency joint analysis [13], [15], [41]–[44], nonlinear dynamics analysis [29], [45]–[48], and feature fusion analysis [22], [49]. The features extracted by these methods can assist in improving methods for diagnosis or treatment of CVD.

With the rapid development of artificial intelligence (AI), machine learning (ML) and deep learning (DL) have been widely used in pattern classification of cardiovascular conditions and estimation of cardiovascular parameters [50]–[59]. The commonly used algorithms include

support vector machine (SVM) [6], [15], [28], [41], [48], [50], artificial neural network (ANN) [28], convolutional neural network (CNN) [52], [53], deep convolutional neural network (DCNN) [12], [35], [54]. Some researchers have used various radial characteristics to distinguish the different physiological and pathological status [53]. Other researchers have employed AI to estimate related cardiovascular parameters such as aortic blood pressure, aortic reflection index, aortic reflection magnitude [58], [59]. Studies show that AI can effectively provide qualitative and quantitative characterization of cardiovascular function through the radial pulse wave. However, there is no comprehensive review on the clinical applications of radial pulse waves using these methods. In clinical cardiovascular examination, the electrocardiogram (ECG) is often used to reflect cardiac functions but limited to the electrical activity of the heart. Radial pulse waves can provide a more comprehensive characterization of cardiovascular function [60]–[63] including changes in properties of blood vessels [64]–[67], respiration, and autonomic nerves [68]–[72].

Presently, there are a variety of measurement methods to obtain radial pulse waves, but it is difficult to obtain high accuracy in waveform analysis and pattern classification. It is noted that many studies have explored pattern classification and parameter estimation of radial pulse waves for clinical applications [50]–[59]. However, there is no comprehensive description on the whole process for analyzing cardiovascular function. This review will present a systematic analysis and description on the analysis of cardiovascular function based on radial pulse waves from four main parts: (i) waveform acquisition, (ii) waveform processing, (iii) pattern classification and parameter estimation, (iv) clinical applications, as shown in Fig. 1. Therefore, the purpose of this article is to provide a comprehensive review about the research effort so far spent in the radial pulse wave, the limitations and challenge that remain to be addressed.

This paper is organized as follows. In Section II, measurement methods and features of radial pulse waves are introduced. Methods of preprocessing and feature extraction of radial pulse waves are described in Section III. Pattern classification and parameter estimation of radial pulse waves are described in Section IV. In Section V, we focus on the clinical applications of radial pulse waves. In Section VI, the current trends for analyzing radial pulse waves are discussed. In Section VII, the limitations, and challenges for analyzing radial pulse waves are described. Finally, the main conclusions of this review are given in Section VIII.

II. WAVEFORM ACQUISITION

To obtain radial pulse waves, there are two types of methods: a single sensor and multi-sensor fusion. There are many kinds of pulse wave sensors such as tonometry, PPG, Doppler ultrasound, and flexible sensors. These types of sensors can be fabricated together to obtain more comprehensive information, a process known as multi-sensor fusion.

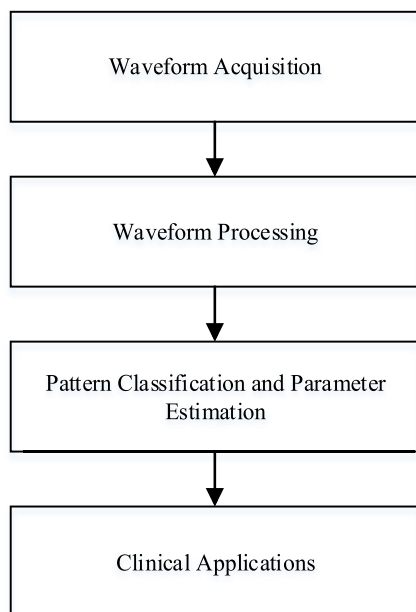


FIGURE 1. Characterization of cardiovascular function based on radial pulse wave analysis.

A. SINGLE-SENSOR MEASUREMENT

1) TONOMETRY

The tonometry measurement of radial pulse pressure is performed by placing a handheld acquisition instrument and applying pressure to radial artery at the wrist [7], [8]. It has been demonstrated that this method can provide a high-fidelity noninvasive and continuous blood pressure waveform and can be calibrated to a blood pressure value. It is convenient and widely used in clinical practice, and harmless to the patients [7]. However, when measuring radial pulse waves, it can be affected by the contact pressure. He *et al.* quantified the contact pressure on radial artery using an adjustable pressure sensor and showed that the radial characteristics gradually weakened with the increase of contact pressure [9].

The tonometry method has also been used to estimate the aortic pressure through mathematical transfer functions, which is an accurate and repeatable non-invasive method for evaluating the aortic pulse pressure [73]. Meidert *et al.* compared the aortic blood pressure measured invasively with the aortic blood pressure estimated from radial pulse waves in ICU patients, and showed that mean and diastolic arterial pressure can be determined accurately using both methods [10].

2) PHOTOPLETHYSMOGRAPHY

Noninvasive assessment method of PPG involves the detection of the blood volume in the radial artery using the infrared radiation. When the infrared radiation is transmitted through the skin, the intensities of the light absorbed by different components of the blood at the radial artery are different. The intensity of the measured reflected or transmitted light further reflects the changes of the radial

pulse waveform [11]–[13]. The PPG measuring radial pulse waves is a reflection measurement, which means that the light source and the detector are located on the same side of the measured artery. There is a certain distance between the light source and the detector [12]. Compared with other peripheral locations such as fingers and earlobes, the more accurate blood volume changes can be measured from radial artery [11]. Besides, the main advantage of PPG is that it does not need external pressure to measure radial pulse waves. Radial pulse waves can be measured or monitored easily, facilitating the applications range of radial PPG, such as monitoring heart rate during exercise as well as use in pulse transit time measurements [13].

3) ULTRASOUND

In contrast to tonometry which senses the pressure pulse and can be affected by the applied pressure, measurement of the flow velocity pulse in the radial artery can be readily performed and unaffected by any contact pressure [14].

Ultrasonic measurement of the blood flow velocity in the radial artery is achieved through Doppler ultrasound scanning. The radial pulse wave can be obtained by extracting the envelope of the Doppler ultrasonic signal [15]. The Doppler ultrasound can also reflect the changes of peripheral blood vessel dimensions at systole and diastole modulated by sympathetic nerve activity. In the evaluation of sympathetic vasoconstrictor functions, fingertip laser Doppler is often used. However, it is difficult to distinguish systolic and diastolic blood flow. Eicke *et al.* found that continuous-wave Doppler ultrasound of the radial artery, which was used to distinguish systolic and diastolic blood flow more clearly, was an effective alternative to fingertip laser Doppler [16].

4) FLEXIBLE SENSORS

The subjects may feel uncomfortable and display unconscious jitter during a long measurement using traditional pressure sensors, affecting the acquisition of radial pulse waves. A problem revealed from traditional pressure sensors is that a sensor with a large working range usually has a poor sensitivity. Hence, a sensor with high sensitivity and a wide working range is needed.

With the continuous progress of electronics, sensor technology also has rapid development. It is high flexibility, light weight, low cost, and easy processing that these types of sensors can be used to measure weak physiological signals [17], [18]. For example, Tao *et al.* measured radial pulse waves using a graphene oxide sheet pressure sensor and demonstrated that this sensor had a large working range and excellent sensitivity [18]. To test the performance of the graphene sensor in measuring radial pulse waves, Xie *et al.* compared the radial frequency components measured by graphene sensor and traditional sensor, demonstrating that the graphene flexible sensor had excellent accuracy [17].

B. MULTI-SENSOR FUSION MEASUREMENT

The pressure sensor and PPG sensor can detect the pressure variation and the change of blood flow volume,

respectively [19], [20]. The ultrasound sensor can also be used to acquire the information of the blood flow velocity [20]. The flexible sensor can improve the sensitivity and working range for measuring radial pulse waves. However, a single sensor can only detect part of the radial information [19]. Therefore, the typical methods of multi-sensor fusion are used to collect radial pulse waves, including multichannel signal and array signal.

1) MULTICHANNEL SIGNAL

The measurement of the multichannel signals is to obtain more comprehensive radial information using multichannel sensors at the same time. The PPG combined with an accelerometer sensor can be used to reduce motion artifact during movement [21], [22]. Obviously, when there is any movement or jitter, the magnitude of acceleration can change significantly. However, it is not enough to use the acceleration signal to reduce motion artifact. Therefore, Bashar *et al.* have used the time-frequency joint analysis method to further identify whether radial PPG were distorted by motion artifact [22]. Besides, Fallot and Vesin proposed an adaptive filtering method to effectively filter the noise in PPG signals when evaluating heart rate during exercise [21].

There are two ways to fuse ultrasound and pressure signals. One method, an ultrasonic probe combined with a pressure sensor to detect the change of blood vessel diameter, can reflect endothelial functions to a certain extent. Arakawa *et al.* analyzed the relationship between radial pressure and changes of arterial diameter, and determined the hysteresis characteristics caused by viscoelasticity of vascular wall [23]. The other method is to optimize the quality of the pressure and flow waveform of arteries through local pulse wave velocity (PWV) using ultrasound imaging. Li *et al.* measured aortic waveform through ultrasound imaging to correct pressure, and demonstrated that the peak of the forward wave of the radial pulse wave was related to the inflection point of aortic pulse wave in the healthy subjects and prehypertension patients, which represented the beginning of pressure increase [24].

2) ARRAY SIGNAL

The measurement of the array signal is obtained by using a variety of sensors integrated in an array. Generally, the sensor for measuring the array signal has the characteristics of small size, high sensitivity and can be attached to the wrist. Huang *et al.* used three highly sensitive pressure sensors to form a linear array to measure radial pulse waves [25]. Roh *et al.* proposed a structure for a multi-array pressure sensor with a hexagonal arrangement to reduce errors caused by measurement position and direction [74]. These array structures can greatly promote the measurement of the radial pressure wave with higher signal quality. However, most pressure sensors can be affected by temperature. Yoo *et al.* used thermistor and simple compensation equations to acquire accurate pressure [75]. To be applied in biomedical signal measurement in vivo, Boutry *et al.* designed a

high-sensitivity pressure array sensor using biodegradable flexible materials [26].

According to the wrist positions of “Cun”, “Guan” and “Chi” described in the classic books on TCM, Wang *et al.* designed a three-channel array system to obtain the information of blood flow and pressure at the radial artery [20]. Radial artery spatial and temporal information simultaneously can be obtained from two different forms using two different sensors. Lee *et al.* used the array sensor combined with electromagnetic sensor and pressure sensor to analyze the three-dimensional pulse image of the wrist, obtaining the temporal and spatial information of the radial pulse wave [27]. Some studies have shown that the accuracy, sensitivity and specificity of the sensors combined together are greater than those of any single sensor in the diagnosis of diabetes [19].

A variety of methods for collecting radial pulse waves are summarized in Table 1. Methods mainly focus on single sensor and multi-sensor fusions. The single sensors include a pressure sensor, a photoelectric sensor, an ultrasonic sensor, a graphene flexible sensor. However, the information obtained by a single type of single-channel signal is always limited. In practice, different sensor types could be used, perhaps in combination according to the measurement position and the nature of the required signal analysis [76]. To obtain a signal with more complete information and wider applications, the multi-sensor fusion is often used. The multi-sensor fusion measurements include multi-channel signal and array signal. In these methods, the acceleration signal is used to reduce motion artifact in pulse wave signals. The ultrasound image information and the pressure signal of the radial pulse wave are used to reflect endothelial functions [23]. The ultrasonic image information is also used to optimize the quality of pulse wave signals. The array signal can be obtained multi-dimensional signals.

III. WAVEFORM PROCESSING

Information from radial pulse waves is extracted by processing and analysis of the waveforms. In this section, the processing of the radial pulse wave is introduced from two aspects: waveform preprocessing and feature extraction.

A. WAVEFORM PREPROCESSING

1) NOISE REMOVAL

During the acquisition of radial pulse waves, there may be a variety of interferences, such as the influence of ambient temperature and light, the high-frequency noise in the measuring instrument, the baseline drift caused by respiration and body movement. Therefore, it is necessary to reduce these interferences and ensure accurate extraction of the features. Paiva *et al.* used a low-pass filter with a cut-off frequency of 30 Hz to filter the noise and enhance the signal [28]. Rangaprakash *et al.* used wavelet to remove the noise [6]. Similarly, Arunkumar and Sirajudeen removed the high-frequency noise and the low-frequency interference

TABLE 1. Summary of acquisition methods of the radial pulse wave.

Form of sensor	Measurement	Physical quantity	Type of sensor	Advantage	Reference	
Single-sensor	Tonometry	Blood pressure	Pressure	Measurement of high-resolution signals	[8-10]	
	PPG	Blood volume	Photoelectricity	Convenient measurement	[11-13]	
	Ultrasound	Blood flow velocity	Ultrasound	Depth information can be obtained	[14-16]	
	Flexible sensor	Blood pressure	Graphene	Flexible, high sensitivity, light weight	[17, 18]	
Multi-sensor		Blood volume	Acceleration, photoelectric	Reduce motion artifact	[21, 22]	
	Multichannel	Blood pressure	Ultrasound, pressure	Reflect vascular functions	[23]	
		Blood pressure	Ultrasound, pressure	Obtain high-fidelity signals	[24]	
	Array		Blood pressure	Pressure	Obtain high-quality signals	[25, 26, 74, 75]
			Blood pressure	Photoelectric, pressure	Obtain flow and pressure signals	[20]
		Blood pressure	Electromagnetic, pressure	Obtain spatiotemporal information	[27]	

to obtain the radial pulse wave with a higher SNR using wavelet analysis [29]. Jiang *et al.* used a band-pass filter of 0.05-35Hz to reduce the noise in radial pulse waves [30]. Wang *et al.* used a Savitzky-Golay smoothing filter to remove the random noise higher than 15 Hz and enhanced the pulse waveform [31]. Combining with the method of empirical mode decomposition, Xu *et al.* proposed an adaptive wavelet threshold denoising method and showed that when the SNR was low, the denoising performance of this method was better than the traditional wavelet threshold denoising method [32]. Wang and Lu proposed a method based on adaptive cascade thresholding to remove the disturbance intervals and showed that an adaptive cascade threshold method could be used to obtain a stable pulse wave [33]. The above studies show that after removing interference, relatively smooth radial pulse waves can be obtained, which is beneficial to analyze the its characteristics.

2) BASELINE WANDER REMOVAL

The baseline drift of the radial pulse wave is mainly due to respiration or body movement. Baseline drift, which can cause errors in feature extraction, can be removed by techniques such as sliding window filtering. Hu *et al.* removed the baseline of the radial pulse wave using a high pass filter [35]. To remove baseline drift and obtain a stable signal under long-term pulse wave signals or other physiological signals, Xu *et al.* attenuated baseline drift of radial pulse waves using an adaptive cascade filter based on wavelet [34]. Research work by Zhang *et al.* showed that the iterative sliding window algorithm could remove the baseline wander [77]. In order to remove respiratory interference, Jiang *et al.* used a cubic curve as the component of respiratory wave and then subtracted it from the original signal to keep on the same horizontal line for the signal [78]. However, pulse waves can reflect a variation synchronous with respiration [36].

Some cardiovascular information may be lost when the respiratory signal is removed. Park *et al.* illustrated that the changes of systolic and diastolic intervals of respiratory signals in the radial pulse wave can reflect the changes of stroke volume and pulse pressure [37]. Wang *et al.* developed an apparatus to detect the heart rate and respiratory rate from the radial PPG, and found that the correlation coefficient could reach 0.97 compared with clinical medical equipment, which is utilized to monitor heart and respiratory rates in routine care [11]. The analysis of respiratory signals extracted from radial pulse waves can be also helpful for further clinical applications.

3) PERIOD SEGMENTATION

The measured radial pulse wave can be a long-term continuous waveform. The period segmentation refers to dividing a long-term waveform signal into several single-period signals according to the cardiac cycle. In the period segmentation, Wang *et al.* accomplished it through detecting the lowest valley value as the segmentation point using the adaptive sliding window [33]. Hu *et al.* utilized Hilbert transform to find the peak point which could be regarded as the marker of periodic segmentation [35].

4) WAVEFORM FITTING

Waveform curve fitting means that the radial pulse wave is decomposed by multiple functions, and then the approximate fitting wave is obtained by superposition. In this method, the error can be obtained after comparing the fitted radial pulse wave with the original waveform to evaluate the fitting performance. Research work by Jo *et al.* showed that an error of less than 6% can be obtained between the pulse pressure waveform derived from the mathematical model and the in vivo data [79]. Jiang *et al.* compared different fitting functions including Raleigh, double exponential, Gaussian, and lognormal functions, and found that the fitting accuracy

of the radial pulse wave with the Gaussian function and lognormal function was higher than other functions [30]. Liu *et al.* studied the influence of different Gaussian fittings on the radial pulse wave and showed that the error was small at 2% using three positive Gaussian functions [38]. Wang *et al.* combined the least squares method and Gaussian function method to fit waves and showed that the number of Gaussian functions could be adaptively determined according to morphologies of the waveform [31]. Jiang *et al.* indicated that the errors of methods based on discrete Fourier series were smaller compared with Gaussian mixture functions [78]. Through this fitting modalities, cardiovascular physiological and pathological information can be obtained by analyzing the radial pulse wave.

5) WAVEFORM NORMALIZATION

The amplitude and period of the pulse wave have individual differences and time-varying differences in the same individual. In analyzing the pulse wave, it is necessary to keep the pulse wave consistent in amplitude and pulse period (length of the cardiac period). Liu *et al.* determined the change in a respiratory period in 10 radial pulse waves and adjusted the signal to 1000 sampling points with the amplitude range from 0 to 1 in the each waveform [38]. Similarly, Jiang *et al.* also used the normalization with one unit amplitude and 1000 sampling points to eliminate the influence of pressure and the various cardiac periods [30]. Waveform normalization can facilitate the comparison of waveform characteristics under the same physiological conditions, which can solve the problem of data heterogeneity in parameter extraction to a certain extent.

B. FEATURE EXTRACTION

1) TIME-DOMAIN CHARACTERISTICS

There are main characteristics in the time-domain. For example, the period of the radial pulse wave in the time domain represents the time of completing a cardiac cycle. The time and amplitude of the first peak value is related to the blood ejection by cardiac systolic pumping. The notch point is associated with aortic valve closure at the end of systole or the beginning of diastole. The time and amplitude of the second peak value represent the artery recovery following closure of the aortic valve [6].

According to wave propagation, a complete radial pulse wave is divided into forward wave and backward wave in one cardiac period [5], [31], as shown in Fig. 2. The forward wave is caused by the ejection of blood into the aorta during cardiac systole, which represents the cardiac function. The backward wave is the reflected wave from the peripheral to the heart due to impedance mismatching such as vascular branching or peripheral vascular beds.

To obtain characteristic parameters in the time-domain, the method of numerical operation based on each characteristic point is used. Rangaprakash and Dutt extracted two types of parameters and analyzed the radial pulse wave in detail [6].

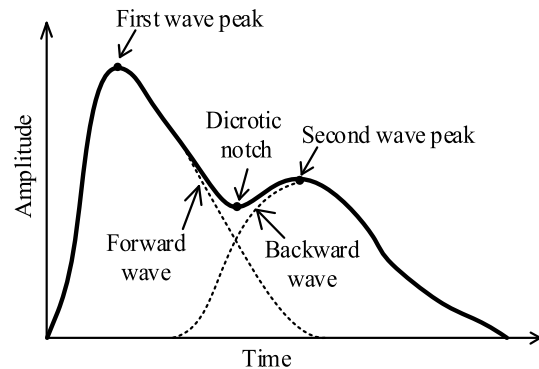


FIGURE 2. Wave components and features of typical radial pulse wave.

Liu *et al.* extracted more time-domain features of the radial pulse wave using the first derivative and the second derivative to estimate cuffless blood pressure [80]. However, with the increase of arteriosclerosis and age, the velocity of the backward wave is faster. As a result, the position of the backward wave is difficult to obtain accurately, resulting in various morphologies. The waveform characteristics of the radial pulse wave (e.g. peak characteristics, notch characteristics) are not obvious. To reflect those characteristics, Tang *et al.* proposed an equal pressure pulse transit time (EP-PTT) method divided into 10 parts according to the amplitude for cardiovascular function assessment [39]. Since it is difficult to find a unified waveform to represent the different morphologies of the radial pulse wave, a typical radial pulse wave can be used to reflect features.

2) FREQUENCY-DOMAIN CHARACTERISTICS

The frequency-domain analysis is to transform the radial pulse wave in the time-domain into the frequency-domain by Fourier transform. The proportion of the first harmonic component in whole frequency spectrum can be calculated. Fast Fourier transform (FFT) is often used to extract features in the frequency analysis. Liao *et al.* extracted the first harmonic component of the radial pulse wave and indicated that the harmonic analysis can improve the recognition of the patients with type II diabetes who need further vascular detection or therapy [40]. Besides, spectral analysis can be used to predict and identify characteristics of CVD. Wang *et al.* extracted frequency components of the radial PPG using FFT and showed that the peak frequency of the radial pulse wave was related to the respiratory rate and heart rate of the subjects [11].

3) TIME-FREQUENCY JOINT CHARACTERISTICS

The time-frequency joint analysis is to analyze the waveform combining the characteristics of time-domain and frequency-domain. It includes the short-time Fourier transform (STFT), wavelet transform, wavelet packet transform decomposition, and Wigner-Ville distribution.

The STFT is that the Fourier transform is used on the local signal through sliding window in a time-domain signal. In this method, the size and structure of the window function are

important parameters. Zong *et al.* analyzed radial PPG during exercise using the STFT with Hamming window and showed that the STFT could track the changes of heart rate during exercise [13].

The wavelet transform is effective to analyze non-stationary and non-periodic physiological signals. Its function is to solve and describe the irregularity, complexity, or unpredictability of pulse wave signals. The wavelet energy and wavelet entropy based on the wavelet coefficients can quantify characteristics of cardiovascular system [41]. Sareen *et al.* extracted the different frequency components of the radial pulse wave through wavelet transform and showed that the feature parameters extracted by wavelet transform were helpful to analyze the variability of the radial pulse wave [42].

The wavelet packet transform can further decompose the high-frequency components of the signal through wavelet decomposition. According to the waveform characteristics, the wavelet packet transform can adaptively adjust the waveform frequency bandwidth. Zhang *et al.* proposed a 4-scale wavelet packet transform according to the characteristics of the radial pulse wave and showed that the wavelet packet transform was useful in analyzing the morphology characteristics [15].

The Wigner-Ville distribution decomposes a signal expressed as a function of time into a signal representing both time and frequency through a series of short windows. The main advantage of the Wigner-Ville distribution is that it can reflect dynamic signals, such as heart rate and blood pressure during exercise [43]. To suppress the cross-interference in the Wigner-Ville distribution, Yan *et al.* analyzed radial PPG using a smooth pseudo Wigner-Ville distribution and showed that the motion artifacts in the radial PPG could be effectively reduced [44].

4) NONLINEAR DYNAMICS CHARACTERISTICS

The nonlinear dynamic analysis is employed because of the complexity of the structure and function of the circulatory system. During the propagation of the pulse wave, the cardiovascular system cannot be simply regarded as linear. Instead, it is necessary according to specific hemodynamic characteristics to identify the complex cardiovascular conditions [45]. Chaos theory is helpful to describe the nonlinear dynamic processes [46]. The commonly used indexes include the Lyapunov exponent, approximate entropy (ApEn), and sample entropy.

The Lyapunov exponent is the rate of local convergence or divergence of the trajectory near the attractor. The positive Lyapunov exponent indicates that the nearby trajectories diverge locally, while the negative Lyapunov exponent indicates that the nearby trajectories approach each other exponentially. Yan *et al.* found that the average Lyapunov index of the healthy group was higher than the CAD group, demonstrating that the cardiovascular system of the healthy group is more chaotic and complex [46]. Li *et al.* calculated

the maximum Lyapunov exponent by least-square fitting to quantify the chaotic degree of the cardiovascular system [47].

The ApEn can quantify the unpredictability of fluctuations in a time series (such as an instantaneous heart rate time series). The small ApEn indicates that the signal contains a relatively stable time series, and the system process can be predicted. On the contrary, the large ApEn indicates that the signal contains complex time series, and the system process is difficult to predict. Arunkumar and Sirajudeen used the ApEn of pulse wave to analyze the nonlinear characteristics of the healthy group and the diabetic group and showed that the ApEn of the healthy group was higher [29].

Generally, the ApEn is suitable for the analysis of small sample datasets. However, there are two problems when ApEn is used to describe the nonlinear system. The first problem is that the ApEn is related to the data length. If the length of the dataset is too short, the estimated ApEn may be too small. The other problem is that the dimension and threshold might change, resulting in lack of consistency in distinguishing signals. Yan *et al.* reduced the problem of data length in the healthy group and CAD group using the sample entropy parameter to solve these problems [48].

The above studies show that the nonlinear dynamic method can analyze the radial pulse wave as an important means of cardiovascular risk prediction. The cardiovascular systems of healthy people have stronger physiological adaptability than the cardiovascular system of the patients.

5) FEATURE FUSION

Sections 3.2.1-3.2.4 introduce four feature extraction methods. Each of them can reflect cardiovascular information. However, the feature parameters extracted by these methods may have heterogeneous data properties due to the difference in the data structure. To solve the problem of heterogeneous data, Liu *et al.* fused the seven features using the multi kernel function and showed that the multi kernel function was effective in enhancing the classification accuracy of pulse waves [49]. Bashar *et al.* fused sample entropy and root mean square of successive difference using the weighted method and showed the new fusion features had good recognition characteristics [22]. Through the analysis of feature fusion, the accuracy of the pattern classification and parameter estimation of the radial pulse wave can be improved, and the potential cardiovascular information represented by radial pulse waves can also be disclosed.

As shown in Table 2, this paper reviews the current analysis methods of radial feature extraction. These methods include four kinds of methods such as time-domain, frequency-domain, time-frequency, and nonlinear feature. In the analysis of waveform characteristics, the greater the characteristic parameters extracted the higher the accuracy of CVD diagnosis. However, too many features can lead to data heterogeneity. To solve the heterogeneous data, this paper introduces two methods of multiple kernel fusion and weighted algorithm. The purpose of feature fusion is to combine more characteristics to

TABLE 2. Summary of extraction methods of radial features.

Feature extraction method	Parameters	Application	Reference
Time domain	Period, time of first peak, amplitude of first peak, time of notch point, and so on	Analysis of the radial pulse wave characteristics	[6]
	First derivative futures, second derivative futures	Estimation of cuffless blood pressure	[80]
	EP-PTT	Assessment of vascular characteristics	[39]
	First harmonic component	Prediction of type II diabetes mellitus	[40]
Frequency domain	Frequency components of pulse wave	Analysis of the respiratory rate and heart rate	[11]
	Wavelet energy, wavelet entropy	Recognition of the radial pulse wave	[41]
Time-frequency joint analysis	Frequency components, normalized interval time	Analysis of the pulse wave peak variability	[42]
	Wavelet packet transform decomposition	Analysis of the whole period signal	[15]
	Short-time Fourier transform	Analysis of dynamic signal characteristics	[13]
	Wigner-Ville distribution	Analysis of dynamic signal features	[43, 44]
Nonlinear analysis	Lyapunov index, Kolmogorov entropy, negative measure entropy	Compare the characteristics of healthy group and CAD group	[46]
	Maximum Lyapunov exponent	Quantitative description of chaotic degree of cardiovascular system	[47]
	Approximate entropy	Compare the nonlinear characteristics of healthy group and diabetic group	[29]
	Sample entropy	Reduce data length of the radial pulse wave in healthy and CAD groups	[48]
Feature fusion	Gaussian kernel functions (time domain kernel function, radial basis function)	Solve the problem of heterogeneous feature data and improve the accuracy of diagnosis	[49]
	Weighted parameter	Improve the accuracy of signal recognition	[22]

reflect more real cardiovascular conditions in the diagnosis of CVD.

C. OPEN-SOURCE RESOURCE

At present, there are some open-source resources to analyze radial pulse wave, which can help researchers to obtain the information of cardiovascular systems and contribute to the development and research of wearable medical devices [81].

The open-source databases, which could help researchers to recognize the morphologies of the pulse wave, are summarized in Table 3. PhysioNet, an online platform, which offers data and algorithms to analyze biomedical signals via the website (<http://www.physionet.org>) [82]. At PhysioNet, the Fantasia database (<https://www.physionet.org/content/fantasia/>), aimed to reflect the age-related alterations in cardiovascular physiological signals, contains twenty 120 min recordings of noninvasive pulse waves and ECG signals collected from two groups of youths and elders [83]. In contrast, the MIMIC-III Waveform database (<https://physionet.org/content/mimic3wdb/>), also from PhysioNet, contains 67830 recordings of approximately 30000 ICU patients, including ECG, pulse waves, respiration, PPG and frequently other signals [84]. There are

many databases containing radial pulse waves in PhysioNet, but there is no extensive database of pulse waves in other parts of the body. To study propagation and cardiovascular characteristics of pulse waves in the body, the Pulse Wave database can be used. The Pulse Wave database (<https://peterhcharlton.github.io/pwdb/>), an open-source database of simulated pulse waves, contains pulse waves from 4374 virtual subjects using one-dimensional computational modeling, including pressure, flow velocity, luminal area, and PPG [85]

Presently, some open-source software can simulate radial pulse waves, and even simulate cardiovascular systems. The details of the software are described in Table 4. Ibrahim *et al.* presented a bio-impedance simulation platform (<http://www.github.com/TAMU-ESP/BioZPulse-Sim-Platform>) to create time-varying radial pressure waveforms [86]. For medical modeling and simulation in the training and clinical decision-making field, Bray *et al.* developed an open-source software called Pulse Physiology Platform (<https://pulse.kitware.com>) [87]. Vahedein and Liberson developed an open-source platform entitled cardiovascular flow analysis (CardioFAN) (<https://github.com/YasharVahedein/CardioFAN>) to analyze pressure and flow wave propagation in cardiovascular

TABLE 3. Summary of open-source databases of radial pulse waves.

Name of data	Research object	Type of signal	Website	Reference
Fantasia	Twenty 120 min recordings from youths and elders	Pressure pulse wave, ECG	https://www.physionet.org/content/fantasia/	[83]
MIMIC-III	67830 recordings of approximately 30000 ICU patients	ECG, pressure pulse wave, respiration, PPG	https://physionet.org/content/mimic3wdb/	[84]
Pulse Wave	4374 virtual subjects	Pressure, flow velocity, luminal area, PPG	https://peterhcharton.github.io/pwdb/	[85]

TABLE 4. Summary of the open-source software for simulation and analysis of the radial pulse wave.

Type of software	Application	Type of signal	Website	Language	Reference
Simulation	Create time-varying radial pressure waveforms	Pressure	http://www.github.com/TAMU-ESP/BioZPulse-Sim-Platform	MATLAB	[86]
	Simulate and model physiological systems	Pressure and flow	https://pulse.kitware.com	C, C++, Java, and python	[87]
	Calibrate patient-specific vascular networks	Pressure and flow	https://github.com/YasharVahedein/CardioFAN	MATLAB	[88]
	Describe patient-specific physiological systems	Pressure and flow	http://archtk.github.com	Python	[89]
Analysis	Detect the onset of radial pulse waves	Pressure	http://www.physionet.org	C	[90]
	Estimate radial PWV	Pressure	https://github.com/WeiweiJin/Estimate-Cardiovascular-Risk-from-Pulse-Wave-Signal	Python	[91]
	Detect heart rate	PPG	https://github.com/marnixnaber/rPPG	MATLAB	[92]
	Analyze ultrasound blood flow	Ultrasound	https://github.com/ccoolbaugh/FloWave.US	MATLAB	[93]

systems, which was used to calibrate arbitrary patient-specific vascular networks to conduct noninvasive diagnostics [88]. Similarly, Manini *et al.* presented an open-source framework entitled python Network Solver to describe patient-specific models of the systemic circulation and upper extremities and released the archToolkit (<http://archtk.github.com>) [89]. The open-source simulation platform can simulate the cardiovascular system, including patient-specific vascular network and systemic circulation, and further help clinicians to study the cardiovascular characteristics in different conditions.

Other open-source software can analyze radial pulse waves, including detecting the onset, evaluating PWV, detecting heart rate and ultrasonic blood flow analysis. As shown in Table 4 [90]–[93]. Zong *et al.* presented an open-source algorithm for detecting the onset of radial pulses and included the algorithm in the open-source waveform database (WFDB) software package, which is freely available from PhysioNet [90]. Jin *et al.* found that

radial pressure waves were used to estimate PWV using ML, instead of carotid-femoral PWV (<https://github.com/WeiweiJin/Estimate-Cardiovascular-Risk-from-Pulse-Wave-Signa>) [91]. Kooij and Naber developed an open-source method termed remote PPG (<https://github.com/marnixnaber/rPPG>) to detect heart rate in a variety of conditions [92]. Coolbaugh *et al.* developed an open-source software entitled FloWave.US (<https://github.com/ccoolbaugh/FloWave.US>), which facilitated the analysis of radial ultrasound signals [93]. These open-source software can help researchers to identify features of the radial pulse wave.

IV. PATTERN CLASSIFICATION AND PARAMETER ESTIMATION

With the development of AI technology, researchers are attracted to pattern classification and parameter estimation of the radial pulse wave. The pattern classification is to classify the radial pulse wave under different physiological and pathological statuses. The parameter estimation uses

various methods to estimate cardiovascular parameters based on the radial pulse wave.

A. PATTERN CLASSIFICATION

1) CLASSIFICATION BASED ON MACHINE LEARNING

In the medical field, there are often high-dimensional and multi-modal biomedical data that need to be analyzed. ML can promote the objectivity of the decision-making process, which is important in computer-aided diagnosis [50]. This paper reviews the ML algorithm for CVD analysis using radial pulse waves. The classification algorithms of ML include SVM, ANN, and fuzzy C-Means (FCM).

SVM is a binary classifier which establishes a hyperplane between the two categories and separates them. In SVM, it is necessary to determine the kernel function. The commonly used kernel functions are linear and Gaussian radial basis. Yan *et al.* distinguished the healthy subjects and the CAD patients based on two types of the SVM with linear and radial basis kernel functions and showed that SVM could be beneficial to the noninvasive detection of CAD with more than 80% accuracy [48]. Jiang *et al.* used SVM with the radial basis function kernel to distinguish health and diabetes with 90.37% the accuracy [78]. Zheng *et al.* used the SVM with the radial basis to classify radial pulse waves of healthy subjects and patients with 95% the accuracy [41]. Similarly, Paiva *et al.* also used the SVM based on the radial basis function to classify the noise signal, the radial pulse wave of the healthy subjects and the patients with an accuracy of 99% [28]. To reduce the required features of the training set, Rangaprakash and Dutt used the SVM based on recursive elimination to classify and recognize radial pulse waves in different statuses after exercise and lunch, with an accuracy of 99% [6]. Zhang *et al.* proposed a soft marginal SVM based on construct original problem's dual problem to distinguish healthy subjects and patients with over 80% accuracy [15].

ANN is used to process data in the working mode of neurons. The main advantage of ANN is suitable for the problem described by a sufficiently representative sample set rather than a strict mathematical model. The network unit of the ANN can be divided into three types including input, processing, and output. The performance of ANN depends on the activation function, the weights connected to each input, and the number of hidden processing units. If the number of hidden processing units is too small, it may lead to poor approximation and generalization ability of decision. Otherwise, it may lead to increase the complexity of the model, resulting in over-fitting. To determine the number of hidden processing units, Paiva *et al.* used the ANN method of forward feedback and back propagation to classify radial pulse waves of the healthy group and the disease group and showed that the accuracy can reach more than 98%, which can reduce the clinical error using radial pulse wave in the diagnosis of CVD [28].

FCM is a common clustering analysis method in statistics. Its purpose is to put all the data into each class so that items in the same class are as similar as possible, while items in

different classes are as different as possible. This algorithm is used to classify two or more different types. Chen *et al.* used the FCM to distinguish between healthy subjects and patients with over 85% accuracy and showed that the FCM improved the accuracy of the diagnosis of disease [14]. Liu *et al.* used the FCM to distinguish radial pulse waves between the patients with myocardial ischemia and healthy subjects, and showed that FCM was effective for the risk assessment of myocardial ischemia [51].

2) CLASSIFICATION BASED ON DEEP LEARNING

DL is a model based on an algorithm set, which has a unique ability to learn features from raw data [50], [52]. In the field of medicine, some researchers use DL technology to analyze one-dimensional physiological signals, such as ECG, electromyogram [52]. The commonly used classification algorithms include CNN, DCNN, fuzzy neural network (FNN).

CNN uses two-dimensional data as input and extracts abstract features through many hidden convolution layers. To input one-dimensional physiological signals into the CNN model, some researchers have transformed one-dimensional signals into two-dimensional image [52]. Li *et al.* used one-dimensional CNN to classify normal pulse wave from the radial pulse in pregnancy and showed that the one-dimensional CNN had a greater averaged accuracy of 97.08% [94]. Li *et al.* optimized the CNN and tested the reliability of the algorithm in the same datasets using two methods which included 6 groups of different pulse waves based on pathological conditions with 95% accuracy and 5 groups based on different physiological parameters, such as blood pressure, brachial-femoral PWV, with 89% accuracy [53]. When a single physiological parameter is used to represent the whole pulse wave, there are some limitations. In other words, the analysis of the radial pulse wave should be considered in all aspects owing to it's the result of a variety of physiological parameters.

DCNN is composed of several convolution layers and a fully connected layer before the output layer. The general convolution process which is to extract features and reduce dimension consists of convolution layer (filtering), nonlinear layer, and pooling layer [12]. Mubashir *et al.* adopted an optimization algorithm with a weight function and a batch normalization and used a 15-layers one-dimensional DCNN to distinguish healthy subjects and lung cancer patients with 99.96% accuracy [54]. Hu *et al.* added a noise module in the training process to improve the generalization ability of the DCNN classifier and classified two kinds of datasets with a dataset included healthy and sub-health subjects with 72.31% accuracy and the other dataset included patients with arteriosclerosis and non-atherosclerosis with 96.33% accuracy [35]. Therefore, DCNN can mine the potential features of the radial pulse wave, which is helpful to distinguish different physiological conditions.

FNN is a network model combining fuzzy algorithm and neural network. The main advantage of the fuzzy algorithm

TABLE 5. Summary table of pattern classification of the radial pulse wave.

Algorithm type	Classification algorithm	Task	Accuracy	Reference
Machine learning	SVM	Distinguish healthy subjects from the patients with CAD	80%	[48]
		Distinguish healthy subjects from the patients with diabetes	90.37%	[78]
		Distinguish between patients and healthy subjects	95%	[41]
	ANN	Distinguish between the subjects before and after lunch, before and after exercise	99%	[6]
		Distinguish the wave of the patients, healthy subjects, and noisy waveforms	99%	[28]
		Distinguish between healthy subjects and patients	80%	[15]
Deep learning	CNN	Distinguish the wave of the patients, healthy subjects, and noisy waveforms	98%	[28]
		Distinguish between patients and healthy subjects	85%	[14]
		Distinguish normal pulse waves from pregnancy pulse waves	97.08%	[94]
	DCNN	Differentiate the radial pulse waves of the patients with five CVD	95%	[53]
		Distinguish radial pulse waves under different physiological parameters	89%	[53]
		Distinguish lung cancer patients from healthy subjects	99.96%	[54]
FNN	FNN	Distinguish the healthy from sub-healthy subjects	72.31%	[35]
		Distinguish between atherosclerotic and non-atherosclerotic statuses	96.33%	[35]
		Classify 16 kinds of radial pulse waves	90.25%	[55]

is that it can adjust the threshold adaptively to adapt to the specific signal characteristics. Xu *et al.* extracted the characteristics of pulse wave, such as period, width, shape, position, and divided 320 groups of pulse wave data into 16 pulse wave patterns using 17 layers of FNN, achieving the accuracy of 90.25% [55].

As listed in Table 5, the AI algorithm can effectively distinguish radial pulse waves in different statuses. In ML, the SVM algorithm is simple and fast. Besides, the SVM has strong generalization ability and is suitable for solving the small sample binary classification problem. Therefore, many researchers often use the SVM to distinguish radial pulse waves in two different conditions.

Some researchers used the ANN to distinguish radial pulse waves of patients and healthy subjects. The FCM can distinguish multiple types of radial pulse waves. Only the binary classifications of the radial pulse wave have been introduced in this paper. Besides, Luo *et al.* summarized five ML methods including random forest, AdaBoost, to identify hypertension using radial pulse waves and showed that the ML methods were helpful to the pattern classification of the radial pulse wave [56].

The main advantage of the DL algorithm is to extract the abstract features from the original data. The hidden

layer of DL is used to analyze and process the features in the pattern classification. As shown in Table 5, CNN can classify radial pulse waves in different physiological conditions and its accuracy is at least 89%. DCNN can also be used to identify cardiovascular conditions and its accuracy is over 72% even reaches 99.96%. The FNN can be used to recognize different waves and its accuracy is over 90%.

Therefore, the AI algorithm is an effective method to analyze radial pulse waves. Through the information from the radial pulse wave, we can further identify the cardiovascular statuses to assist the diagnosis of CVD.

B. PARAMETER ESTIMATION

The pattern classification of the radial pulse wave is to classify the physiological and pathological conditions according to the characteristics of the waveform. Another analysis method is to assess cardiovascular conditions through evaluating cardiovascular parameters, which is called parameter estimation. Parameter estimation methods include traditional transfer functions and AI methods. The traditional transfer functions can analyze aortic pulse pressure, and aortic waveforms. The AI methods evaluate aortic blood pressure, and aortic reflection index.

TABLE 6. Summary of waveform parameter estimation.

Method	Algorithm	Task	Evaluation parameters	Reference
Transfer function	Parameterization	Estimation of aortic systolic pressure	Correlation coefficient 0.846	[45]
	NPMA	Estimation of aortic systolic pressure	Correlation coefficient 0.99	[57]
Artificial intelligence	Regression	Estimation of systolic and diastolic blood pressure	Coefficient of determination >0.79	[25]
	BPNN	Estimation of systolic and diastolic blood pressure	Coefficient of determination >0.78	[95]
	ANN	Estimation of aortic reflection index and reflection magnitude	Correlation coefficient is 0.9	[58]
		Estimation of the effect of age on blood vessels	Significant difference $p < 0.001$	[59]
DCNN	Estimation of the effect of age on CVD	Correlation coefficient is 0.92	[12]	

1) TRANSFER FUNCTION METHODS

The pulse wave is produced by the heart ejection, including aortic pulse waves, carotid pulse waves, brachial pulse waves, radial pulse waves, and finger pulse waves. Although these waveforms have different shapes, they can be related to each other through transfer functions [3]. In clinical applications, aortic pulse pressure and waveform have been shown to provide additional information to the peripheral waveform in evaluating the pathological conditions of patients. Some studies have shown that the brachial pulse pressure maintains a normal level in some hypertensive diseases, but the aortic pulse pressure is different from the normal value [45], [57]. Therefore, an effective evaluation of aortic information is helpful for identifying cardiovascular abnormalities.

At present, many researchers use the transfer function to evaluate aortic information with the radial pulse wave. The processes of transfer function estimation include measurement and building the function. The aortic pulse wave and radial pulse wave are obtained at the same time. And then the transfer function between the aorta and radial artery is obtained by Fourier analysis. The aortic pulse wave can then be obtained using the inverse transfer function and the radial pulse wave. However, this method is not suitable for all cardiovascular systems. There are certain errors in this method. Therefore, it is necessary to modify the assessed aortic waveform to adapt to different cardiovascular conditions. Akalanli *et al.* optimized the generalized transfer function between the radial pulse wave and the aortic pulse wave through parameterization based on the prediction error method and showed that there was good consistency between the reconstructed aortic waveform and the invasive aortic waveform, and the correlation coefficient of systolic blood pressure was 0.846 [45]. Williams *et al.* also evaluated aortic systolic pressure using N-point moving average (NPMA) and showed that the correlation coefficient between the aortic systolic pressure estimated by the NPMA and the invasive aortic systolic pressure reached 0.99 [57].

2) ARTIFICIAL INTELLIGENCE METHODS

The AI algorithm can also estimate the cardiovascular parameters through radial pulse waves. The cardiovascular parameters include blood pressure, and aortic parameters. The commonly used methods include regression, back-propagation neural network (BPNN), ANN, and DCNN.

According to the statistical regression, the estimated parameters are compared with the reference parameters. The quality of the estimated parameters is evaluated by the determination coefficient. Huang *et al.* evaluated systolic and diastolic blood pressures using a variety of regressions and showed that the coefficient of determination between the cuff-based referential blood pressure and the estimated blood pressure using random forest regression was more than 0.79 [25].

BPNN is a multi-layer feed-forward network, which is one of the most widely used neural network models at present. Based on the cardiovascular hemodynamics, Tu and Chao estimated systolic blood pressure and diastolic blood pressure using the BPNN and showed that the coefficient of determination is more than 0.78 [95].

ANN can also estimate some cardiovascular parameters. Xiao *et al.* estimated the aortic reflection index and magnitude using the ANN and obtained over 0.9 correlation after comparison with the reference parameters based on transmission line theory [58]. Similarly, Bratteli *et al.* studied the effect of age on cardiovascular function using ANN [59]. Studies have shown that physiological aging was reflected in pulse pressure rather than mean blood pressure or heart rate [59].

DCNN can also estimate cardiovascular parameters. Chiarelli *et al.* evaluated the correlation between actual age and estimated age, which were used to reflect the degree of cardiovascular aging, using DCNN and showed that when the age difference was 7 years, the performance of DCNN with 0.92 correlation was better than that of multivariate regression and ANN [12].

As listed in Table 6, the noninvasive detection of the radial pulse wave can assess cardiovascular parameters. The transfer function method can evaluate the aortic waveform. It can be concluded from the Table 6 that the correlation between the aortic systolic pressure estimated by the radial pulse wave and the invasive aortic systolic pressure is at least 0.846, and the correlation can reach 0.99 using the NPMA algorithm. Studies have shown that noninvasive detection of aortic pressure is effective and feasible.

The AI method can estimate some cardiovascular parameters. Using the AI method, model parameters need to be adjusted according to the specific situation and avoid the occurrence of over-fitting and non-convergence. It can be found from Table 6 that the correlation coefficient between the parameters estimated by the AI method and the reference parameters is more than 0.78, showing that the AI algorithm is an effective method to estimate cardiovascular parameters.

V. CLINICAL APPLICATIONS

This section summarizes the analysis of the radial pulse wave on cardiac function, vascular function, and quantitative pulse diagnosis method of TCM.

A. ANALYSIS OF CARDIAC FUNCTION

1) ESTIMATION OF CARDIAC OUTPUT

Cardiac output (CO) refers to the volume of blood pumped by the heart per minute [60]. Noninvasive detection of CO is a method to calculate CO after the pulse wave is obtained through the noninvasive detection. Cardiac output power refers to the product of CO and mean arterial pressure [8]. Both CO and cardiac output power are indicators of cardiac functions. Bikia *et al.* proposed an optimization algorithm of CO based on the radial pulse waves of several heartbeats obtained 0.96 correlation between the estimated CO and the vivo CO [61]. It can be found that this study can show that long-term recursive optimization can more accurately estimate CO. This optimized method can also be used to optimize other cardiovascular parameters to identify more accurately cardiovascular function under different conditions.

2) SURROGATE ANALYSIS OF HEART RATE VARIABILITY

Heart rate variability (HRV) refers to the time difference between one heartbeat and another. The R peak in the ECG is often used to calculate the HRV. The pulse rate variability (PRV) refers to the time difference between each pulse wave, which is calculated by the difference between the peak values of pulse waves. Compared with heart rate, the pulse rate is easier to obtain. Constant *et al.* found that PRV could not accurately reflect standing healthy subjects and patients with low HRV [62].

In particular, the systole and diastole of peripheral blood vessels are greatly affected by temperature, which means that lowering body temperature can cause the systole of peripheral blood vessels and reduce the vasomotor functions. Therefore, when analyzing HRV through radial pulse waves, it is also necessary to consider the body temperature of subjects. Huang *et al.* simulated the body temperature change

of subjects using cold and hot tests and showed that the spectral energy within 10-50Hz of the radial pulse wave could more indicate the condition of blood circulation in the hot test [63]. In general, when analyzing HRV with radial pulse waves, it is necessary to consider the changes of measured body position and physiological conditions of subjects.

B. ANALYSIS OF VASCULAR FUNCTION

1) ARTERIOSCLEROSIS

Arteriosclerosis is a key risk factor in evaluating cardiovascular function and predicting CVD. In the early stage of arteriosclerosis, vascular endothelial functions maybe be weak. With the development of arteriosclerosis, endothelial functions can produce lesions [23]. The endothelial cells can adjust some arterial characteristics, including vascular tone, permeability, and angiogenesis to slow down the development of arteriosclerosis [64]. With the information of pressure and diameter at the radial artery, Arakawa *et al.* found that human vascular endothelial functions could be evaluated by the hysteresis characteristics caused by vascular wall viscoelasticity to further analyze the degree of arteriosclerosis [23].

PWV, a marker of arterial stiffness, is one of the indexes to evaluate arteriosclerosis and predict the risk of CVD. As CVD tends to occur earlier, some researchers are increasingly interested in analyzing the increased PWV to evaluate the degree of arteriosclerosis. Zhang *et al.* compared two-point PWV (measuring PWV between the carotid artery and the femoral artery) and single-point PWV (measuring PWV at radial artery) and showed that there was a significant correlation between the single-point PWV and the two-point PWV of healthy subjects under 65 years old in the measurement of arteriosclerosis [65].

With age, the degree of arteriosclerosis increases leading to increase in cardiovascular risk factors. Specifically, with the increase of age, vascular functions can gradually decline while peripheral resistance can gradually increase. To balance weakness of vascular functions and strengthen of cardiac afterload, the heart needs to generate more pressure to deliver blood to the vascular system [8]. Rising pressure can change the heart structure. The change of heart structure can further influence the morphology of the pulse wave. In short, age is an independent factor affecting cardiovascular function [66], [67]. To study the effect of age on vascular functions, Houghton *et al.* compared the blood vessel of young and old subjects and found that the vascular functions could be used as a predictor of cardiac ejection capacity in the elderly [8]. Hickson *et al.* analyzed the influence of age on the degree of arteriosclerosis and vessel diameter using the aortic pulse wave calculated by the radial pulse wave found that the biggest difference in aortic sclerosis was in the abdomen, while the greatest difference in vascular diameter was in the ascending aorta [68]. Bia *et al.* found that with the increase of age, the systolic blood pressure of the aorta and the radial artery both increased, and there would be a sudden increase trend at about age 60 years [72].

TABLE 7. Summary of clinical applications of the radial pulse wave.

Clinical application	Application purpose	Reference
Cardiac function	Estimation of cardiac function based on cardiac output power	[8]
	Estimation of CO	[61]
	Relationship between PRV and HRV	[62]
	Relationship between PRV and HRV under different temperature conditions	[63]
Vascular function	Measurement of endothelial function	[23]
	Prediction of arteriosclerosis	[41]
	Measurement of arteriosclerosis by radial PWV	[65]
	Effect of age on vascular function	[8]
	Relationship between predicted age and vascular function	[68]
	Relationship between predicted age and arterial stiffness	[72]
	Assessment of vascular aging	[39, 72]
	Assessment of atherosclerosis	[69]
	Assessment of CAD	[70]
Relationship between radial pulse waves and peripheral vascular diseases	[71]	
Pulse diagnosis of TCM	Quantitative analysis of TCM pulse diagnosis	[4, 96]
	Analysis of 3D visualization of TCM	[98, 99]
	Digital pulse diagnosis of TCM with artificial intelligence	[100, 101]

2) ATHEROSCLEROSIS

The radial pulse wave can not only identify arteriosclerosis but also analyze the effect of arteriosclerosis. Atherosclerosis is a particular form of arteriosclerosis, which refers to the accumulation (plaque) of fat, cholesterol, and other substances in the intima or wall of arteries. The plaques can change blood flow and sometimes even block blood vessels. Generally, the degree of atherosclerosis is related to the situation of arterial blockage, such as CAD [69, 70], and peripheral artery disease [71]. According to the morphological changes of the radial pulse wave, Xu *et al.* evaluated the atherosclerotic status to distinguish healthy and patients with CAD and found pulse morphology variability of the healthy were higher than those of patients [69]. Kotecha *et al.* indicated that the evaluation of the radial pulse wave was a useful noninvasive clinical trial, which might stratify CAD and help determine whether patients need diagnostic angiography [70]. Zahner *et al.* found that the degree of atherosclerosis was independently related to peripheral arterial disease, and the degree of atherosclerosis in patients with peripheral arterial disease was higher than that in healthy subjects [71].

C. QUANTITATIVE ANALYSIS OF THE TCM PULSE DIAGNOSIS

The TCM relies on the finger to touch the wrist pulse and identifies physiology and pathology through the pulse to treat. However, the TCM lacks objective evaluation in the

diagnosis of human health statuses and relies on subjective diagnosis. Shu and Sun analyzed 13 kinds of radial pulse waves and quantified the differences between waveforms [4]. This quantitative method not only reduces the dependence of TCM pulse conditions, but also can more accurately reflect pathological value in TCM. Xu *et al.* summarized the modern quantitative analysis methods of pulse diagnosis in TCM and showed that modern signal processing methods could facilitate the quantitative or digital analysis of TCM pulse diagnosis [96].

In recent years, some studies have shown that analysis of the three-dimensional radial pulse waves reflects the concept of multi-dimensional pulse condition in TCM [97]–[99]. In order to make the TCM more intuitive and convincing, Chen *et al.* used the array sensor to measure the three-dimensional pulse wave, which is helpful for doctors to make more accurate diagnosis [98]. Peng *et al.* used Fourier series to analyze three types of pulse images, which can quantize the pulse feeling in TCM [99].

In addition, the AI algorithm can also be used for digital processing of TCM pulse diagnosis. Chen *et al.* used BPNN based on Levenberg-Marquardt and a genetic algorithm to classify four common kinds of pulse accurately [100]. Tang *et al.* used a four-layer ANN model to analyze six parameters of radial pressure waves, showing that ANN based on the Levenberg-Marquardt can be improved in eight aspects of pulse diagnosis depth, speed, regularity, width, length, smoothness, stiffness and strength [101]. These studies showed that AI algorithms can effectively generate

pulse conditions to evaluate the cardiovascular system, which is beneficial to quantitative analysis of pulse diagnosis in TCM.

As shown in Table 7, this review summarizes the three clinical areas of investigations of cardiac functions, vascular functions, and TCM pulse diagnosis reflected by the radial pulse wave. In the analysis of cardiac functions, this paper focuses on CO and HRV. Radial pulse waves can be used to evaluate CO as an index of cardiac functions. HRV can reflect the difference between heartbeats. Compared with HRV, PRV is more convenient to measure. However, it is necessary to consider the postural changes and physiological statuses of subjects when analyzing PRV instead of HRV.

In the analysis of vascular functions, this paper mainly focuses on arteriosclerosis and atherosclerosis. Arteriosclerosis includes the characteristics of early arteriosclerosis, the assessment of arteriosclerosis through the radial PWV, and the influence of age on arteriosclerosis. Early arteriosclerosis is closely related to endothelial functions. With age, the vascular wall can gradually become thicker and harder. The degree of arteriosclerosis can be detected by measuring PWV. The radial pulse wave can be used to analyze atherosclerosis conditions, such as coronary artery, peripheral artery.

In addition, the TCM of pulse diagnosis has always relied on experienced doctors to diagnose the patient's condition, which lacks objective indexes. Modern signal processing methods and AI algorithms can quantify and digitize TCM pulse diagnosis, which makes it easier for practitioners to identify TCM pulse diagnosis.

VI. DISCUSSION

Pulse waves are produced by cardiac ejection and spread through the arteries to the periphery. The pulse wave can be measured on the surface of the body. Radial pulse waves contain information on physiological and pathological cardiovascular conditions. Through pulse wave analysis, cardiovascular function can be assessed. In this paper, the radial pulse wave is systematically summarized from four aspects, which are waveform acquisition, waveform processing, pattern classification and parameter estimation, and clinical applications.

In the waveform acquisition, the methods of the single-type sensor include tonometry, PPG, ultrasonic, flexible sensors. Among them, the commonly used method to measure radial pulse wave signals is pressure measurement. This method is greatly disturbed, such as the manipulation of the operator, the wrist position, and physiological conditions of the subject. The PPG is widely used to measure radial pulse waves. Besides, radial PPG can analyze the respiratory signals to further reflect cardiovascular conditions. However, this method is greatly affected by the light intensity of the external environment. The ultrasonic measurement can measure the change of radial blood flow velocity. However, this method is operator dependent. Measurement of radial pulse waves in the long-term can make the subjects feel uncomfortable leading to more motion artifact. To improve this shortcoming, flexible

sensors are used. In addition, they can adapt to changes of the wrist position and have high sensitivity and a wide working range. However, the measured signal using a single sensor is only a certain aspect of the waveform which is the pressure or flow signal. To detect the enhanced radial information simultaneously, multi-sensor fusion methods can be used.

The methods of multi-sensor fusion include multichannel measurement and array signal measurement. Using acceleration and radial PPG can accurately evaluate heart rate during exercise in the multichannel measurement. The method which combines the radial pressure signal and the ultrasonic image reflects cardiovascular function from the perspective of endothelial functions. The array measurement utilizes multiple sensors to integrate measurement. Using array measurement, a high-quality waveform signal can be obtained without the necessity of locating the precise position of the radial artery. The pressure array sensor combined with the photoelectric sensor can accurately reflect the change of blood flow and pressure at the same position. The array combining electromagnetic sensor and pressure sensor can accurately reflect the temporal and spatial information of the radial pulse wave. However, in the measurement of the radial pulse wave, the high-frequency interferences from the measurement environment and the interferences generated by the subjects should be reduced. To reduce the interference signal, Wu *et al.* proposed a pressure sensing system and indicated that the extracted arteriosclerosis indexes were more reliable using this system in comparison with the traditionally measured signal [102].

Preprocessing of the pulse waveform can reduce the influence of interference to obtain high-quality radial pulse waves, which is beneficial to accurately extract the characteristics. The feature extraction methods include time-domain, frequency-domain, time-frequency domain, and nonlinear. When analyzing the waveform in time domain, the waveform is specific and the waveform feature is obvious. However, the waveform characteristics are easily affected by external interference and noise can produce errors in the time domain, for which it is difficult to identify the source. In analyzing the waveform in the frequency domain, the frequency components are comprehensive. However, the waveform features are not obvious. The time-frequency joint analysis means that the frequency domain is used to identify the spectral characteristics of the radial pulse wave and the time-domain waveform reflects the change with time. The time-frequency joint methods include wavelet transform, wavelet packet transform, STFT, and Wigner-Ville distribution. The nonlinear analysis can analyze the complexity of systems and signals. The indexes include the Lyapunov index, approximate entropy, and sample entropy. A variety of nonlinear indexes indicate that the cardiovascular system of healthy subjects is more complex than the cardiovascular system of patients. That means that the healthy physiological adjustment ability is stronger. However, each analysis method has some limitations, and the data structure is different.

Therefore, the method of multiple parameters fusion can improve data heterogeneity of various parameters to enhance the accuracy of assistance in the diagnosis of CVD using radial pulse waves.

In analyzing physiological signals, a variety of signal combination methods can also be used to improve the assessment of cardiovascular function. Liu *et al.* found that the multimodal sensor device was easy to operate and could quickly obtain stable and reliable physiological information [103]. Similarly, Okano *et al.* measured multimodal data to monitor cardiovascular information using a wearable device at the wrist, such as HRV, PWV, and blood flow velocity [104]. The multi-modality analysis can enrich the physiological value of the radial pulse wave. In summary, the analysis of the radial pulse wave tends to be rich in signal and comprehensive features.

In pattern classification, the AI method can distinguish between patients and healthy subjects through analysis of radial pulse waves. In the pattern classification of radial pulse waves, the SVM is suitable for solving the small sample-sized binary classification problem. However, this method also has some limitations, such as the selection of kernel function and features, and the difficulty in processing nonlinear data. Therefore, there are other ML methods to distinguish radial pulse waves, such as ANN, and FCM. The ANN algorithm processes the original data in the manner of the neuron. In the ANN algorithm, the selection of hidden layers has a great influence on the result of the decision classification. Specifically, a small number of hidden layers may lead to weak generalization of the ANN, poor approximation, and inaccurate classification. A large number of hidden layers may lead to overfitting of the ANN algorithm. The FCM algorithm can not only deal with binary-classification problems but also deal with multi-classification problems. And it can improve the accuracy of diagnosis in the diagnosis of a certain type of disease. The DL algorithm can extract features from original waveform, avoiding information loss caused by preprocessing. The commonly used DL classification algorithms include CNN, DCNN, and FNN. DL and ML algorithms can distinguish radial pulse waves under different physiological and pathological conditions, which show that the AI method can effectively identify characteristics of cardiovascular function.

Another way to identify cardiovascular function is to estimate cardiovascular parameters, using analytical method of parameter estimation. Aortic systolic pressure can be obtained from the radial pulse waves through parameterization and NPMA algorithm. However, this method still needs to be individualized. The AI algorithm can also estimate cardiovascular parameters. The typical cardiovascular parameters include blood pressure and vascular function indices such as aortic reflection index. The investigations showed that the method of AI can effectively evaluate cardiovascular parameters with a correlation above 0.78. In the future, AI methods will be used to estimate many more cardiovascular parameters.

In clinical applications, analysis of radial pulse waves can not only be used to assess cardiovascular function but also quantify the pulse diagnosis of TCM. In the study of cardiac functions, CO obtained from the radial pulse wave is analyzed in one cardiac cycle. The characteristics of different radial pulse waves of the same individual can be analyzed in long time-varying signal epochs. In the study of vascular functions, both arteriosclerosis and atherosclerosis can be assessed as cardiovascular risk factors. On one hand, quantitative and three-dimensional TCM pulse diagnosis can further quantify characteristics of pulse diagnosis. On the other hand, it can provide reference indicators for the diagnosis of CVD. In conclusion, in clinical applications of the radial pulse wave, there is a tendency to analyze cardiovascular physiological and pathological information with multiple indexes and all aspects.

In addition, some researchers have explored the relationship between pulse wave and cerebral vessels, which provides a new perspective for the study of radial pulse waves. Pase *et al.* explored the relationship between aortic pulse pressure estimated by the radial pulse wave and cerebral blood flow velocity and showed that there is a positive correlation between them [105]. This study also further supported the view that aging of arteries and atherosclerosis of the aorta can greatly increase the pressure of brain pulsation.

In conclusion, in investigations of the radial pulse wave for analyzing cardiovascular function, the trend towards obtaining high-quality and richer waveform components, more comprehensive analysis methods, and more diverse clinical applications. Especially in clinical applications, pulse waves can be used for providing cardiovascular and cerebrovascular information. Therefore, radial pulse waves can be a reliable means for assessment of human health.

VII. LIMITATIONS AND CHALLENGES

Although the radial pulse wave has a sound physiologic basis and exciting potential in the arena of clinical medicine, published research methods largely ignore its clinical applications. This review is meant to remedy this lack of awareness. Another limitation is that there are few clinicopathological studies related to the radial pulse wave, including tracking the development process of chronic CVD, preventing the occurrence of sudden CVD, detecting the features of cerebral diseases, and analyzing the function of respiration and metabolism. In the future, investigations of clinicopathological characteristics of the radial pulse wave can be enriched by combining medical images and biochemical indexes. The third limitation is that AI has greatly improved the pattern classification and parameter estimation of the radial pulse wave. However, the interpretability of AI is relatively weak. AI combined with hemodynamic characteristics can be used to improve the classification accuracy of radial pulse wave patterns and explain their physiological meaning in the future. Therefore, future studies should not only analyze the

physiological, and pathological characteristics of the radial pulse wave but also pay attention to the combination of research technologies and clinical knowledge to increase its interpretability.

VIII. CONCLUSION

In recent years there has been reemerged in the computer-based pulse wave analysis with development of AI. This review has presented the analysis of the radial pulse wave and described its potential for daily monitoring and clinical applications. The radial pulse wave analysis has made some rapid progress due to AI technology and some technologies on multiple sensor fusion. In the future, the radial pulse wave can be applied to the early monitoring of cardio-cerebrovascular function to reduce the occurrence of cardio-cerebrovascular diseases.

LIST OF ABBREVIATION

AI	Artificial intelligence.
ANN	Artificial neural network.
ApEn	Approximate entropy.
BPNN	Back-propagation neural network.
CAD	Coronary artery disease.
CardioFAN	Cardiovascular flow analysis.
CNN	Convolutional neural network.
CO	Cardiac output.
CVD	Cardiovascular disease.
DCNN	Deep convolutional neural network.
DL	Deep learning.
ECG	Electrocardiogram.
EP-PTT	Equal pressure pulse transit time.
FCM	Fuzzy c-means.
FFT	Fast Fourier transform.
FNN	Fuzzy neural network.
HRV	Heart rate variability.
ML	Machine learning.
NPMA	N-point moving average.
PPG	Photoplethysmography.
PRV	Pulse rate variability.
PWV	Pulse wave velocity.
STFT	Short-time Fourier transform.
SVM	Support vector machine.
TCM	Traditional Chinese medicine.
WFDB	Waveform database.

ACKNOWLEDGMENT

The authors gratefully acknowledge the kind assistance of Yang Yao, Yang Luo, and Shuran Zhou in article structure and writing.

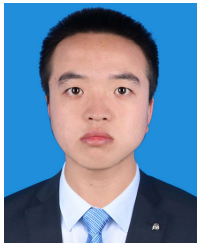
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