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REVIEW ARTICLE

Prospect of clinical application of ECG imaging technology

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ABSTRACT

Routine 12 lead ECG is a basic method for clinical evaluation and diagnosis of various cardiovascular diseases. However, due to its low accuracy of ECG mapping, it is seriously limited in the study of potential electrophysiological mechanism of arrhythmia and mapping of origin matrix. The emerging non-invasive ECG imaging technology (ECGI) can reverse reconstruct the spatio-temporal dynamic information of electrophysiological activities at various locations of the heart, explore the occurrence and development mechanism of various arrhythmias, and accurately locate their origin, effectively make up for the lack of traditional mapping technology, and play a very important role in guiding clinical diagnosis and treatment. In recent years, studies at home and abroad have shown that ECGI plays an important role in the diagnosis and treatment of various cardiovascular diseases, such as arrhythmias and cardiac resynchronization therapy. As a non-invasive method, three-dimensional ECGI is a significant progress in conventional ECG mapping, and its great potential to guide clinical diagnosis and treatment needs to be tapped. This article reviews the progress of clinical application of ECGI.

Keywords*:* ECG imaging technology; noninvasive electrophysiological mapping; arrhythmia

1. Introduction

The prevalence of cardiovascular disease is on the rise, and the mortality rate of cardiovascular disease is still the highest. Two out of every five patients die of cardiovascular disease [1]. Since the British scientist Walker recorded the first ECG in 1887, ECG has been used for non-invasive analysis and evaluation of various cardiovascular diseases for more than a century. At present, it has become one of the most important and widely used technologies in clinical diagnosis and treatment[2]. However, ECG has many inherent defects, such as the accuracy of spatial resolution of cardiac information provided by ECG is not high[3], especially for atrioventricular bypass, ventricular premature contraction / ventricular tachycardia (hereinafter referred to as ventricular tachycardia), etc. The evaluation of electrocardiographic response and electrocardiographic synchronization after cardiac resynchronization therapy (CRT) is also severely limited. Therefore, for the definite diagnosis, evaluation and treatment of arrhythmias, invasive intracavitary electrical mapping methods are often required. While these methods increase the risk, there are still many limitations in clarifying the electrophysiological mechanism of complex arrhythmias such as atrial fibrillation (hereinafter referred to as atrial fibrillation) [4]. The emerging

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electrocardiographic imaging (ECGI) technology effectively makes up for the shortcomings of traditional ECG mapping and invasive mapping. Especially for some complex types of arrhythmias, ECGI can inversely reconstruct a three-dimensional visual cardiac electrical activity model by combining the ECG information of the multi-channel conjoined surface and the simulated anatomical model of the heart trunk, so as to provide accurate analysis of the characteristics of arrhythmia mechanism, Provide guidance for the diagnosis and treatment of such diseases[5-6]. This article reviews the progress of clinical application of ECGI.

2. ECGI overview

ECGI, also known as electrocardiographic mapping technology, is to inversely reconstruct unipolar electrograms at more than 1000 sites of the heart by combining multi lead (up to 252 electrodes) body surface electrocardiographic information and heart trunk anatomical information through mathematical calculation, build spatio-temporal dynamic information of electrophysiological activities at each location on the three-dimensional cardiac simulation model, and non invasively record and build ECG activation patterns, activation sequence isochrons and repolarization ECG patterns, It can effectively make up for the limitations of routine ECG in complex arrhythmia mapping. ECGI has the characteristics of noninvasive, high-resolution and continuous mapping. It can even reconstruct the excitation information of the whole heart in one heart beat cycle, providing a more advantageous mapping method for clinical evaluation, diagnosis and treatment of arrhythmias and the study of electrophysiological mechanism of complex arrhythmias [5–6].

3. Clinical application of ECGI

Since the concept of ECGI technology was born in 1977, after more than 40 years of technological innovation, its ECG imaging algorithm and reconstruction technology have become mature. Many previous studies have applied this technique to different types of experimental animals, explored their electrophysiological characteristics under different physiological and pathological conditions, accumulated more evidence, and promoted the continuous development of its theory and technology. At present, there are more than 40 clinical studies at home and abroad, which have fully evaluated the role of ECGI as a diagnostic tool in the diagnosis and treatment of different types of arrhythmias, such as atrial arrhythmia, ventricular arrhythmia and so on, and its practical clinical value [7].

3.1. Ventricular arrhythmia

Ventricular premature contraction and non sustained ventricular tachycardia are common types of arrhythmias in clinic. Their clinical manifestations vary greatly, and they can be asymptomatic, cause hemodynamic disorders and even cause sudden cardiac death. At the same time, frequent ventricular arrhythmias can lead to left ventricular dysfunction and dilated cardiomyopathy [8]. It is very important to determine the origin and specific pathogenesis of potential structural heart disease and ventricular arrhythmia for the formulation of effective treatment. As mentioned above, ECG mapping is severely limited in mapping the mechanism of ventricular arrhythmia and locating the origin of arrhythmia due to its inherent defects of low accuracy of ECG mapping [9]. ECGI has shown high accuracy and effectiveness in the mapping of ventricular arrhythmias, especially in the basic research and clinical validation of ventricular premature contraction, ventricular tachycardia and other diseases. Many clinical studies at home and abroad have focused on ECGI in the study of ventricular arrhythmia matrix, localization of origin and guidance of arrhythmia radiofrequency catheter ablation (hereinafter referred to as ablation), and have done a lot of exploratory work [4].

At present, the evidence of drug treatment for ventricular premature contraction / ventricular tachycardia is relatively insufficient, and the effect of drug treatment varies from person to person. Some ventricular premature contraction / ventricular tachycardia is very stubborn, accompanied by obvious clinical symptoms. In recent years, the rapid development of ablation therapy for symptomatic ventricular premature contraction / ventricular tachycardia has fully demonstrated its effectiveness, safety and reliability. However, this invasive examination and intracavitary mapping scheme also has limitations, such as low spatial resolution of intraoperative pacing mapping, dependence on continuous spontaneous premature contraction or short array ventricular tachycardia for localization of the origin, etc., resulting in a long time for invasive electrophysiological examination and operation. Through noninvasive mapping, ECGI can provide the operator with a more accurate location of arrhythmia origin before operation, which is of great significance for the formulation of operation plan and preoperative risk assessment[9]. For example, Jamil Copley et al.[10] used ECGI technology to locate the origin of ventricular extrasystole. The results showed that the success rate was 96%, while the accuracy of ECG group was only 37%~58%. Erkapic et al. [11] further compared the mapping accuracy of ECGI and invasive mapping system by using a randomized controlled study. The results showed that the accuracy of ECGI in identifying the cardiac cavity and specific location of ventricular arrhythmia origin reached 95.2%, while the accuracy of ECG diagnosis was only 76.2%. At the same time, using ECGI to guide ablation helped to reduce the operation time and discharge times. Similarly, in previous studies, our team compared the accuracy of ECGI and ECG location of origin based on 27 patients with ventricular premature contraction / ventricular tachycardia. The results showed that the accuracy of ECGI location was significantly higher than that of ECG protocol (95.5% vs 59.15%) [12].

In terms of ventricular tachycardia mapping, more than 90% of persistent monomorphic ventricular tachycardia is mostly caused by the reentry of surviving tissues in the ventricular scar area after myocardial infarction [13]. Ablation is also an important method to change scar matrix and treat ventricular tachycardia, such as ablation to block ventricular tachycardia electrical conduction circuit in scar tissue. However, for most patients with ventricular tachycardia, even if the hemodynamics is stable, there are still many difficulties in scar mapping [13]. With the help of ECGI tools, it can provide guidance for patients to clarify the mechanism of ventricular tachycardia and make plans. For example, cuculich et al. [14] found that ventricular tachycardia related scars can be characterized by low voltage, fragmentation potential and potential delay on ECGI, which can accurately mark the abnormal ECG "Scar" area on the anatomical model, with a sensitivity of 89% and a specificity of 85%. Meanwhile, Wang et al. found that ECGI can accurately locate ventricular tachycardia related scars by identifying myocardial scars and abnormal areas of ECG signals.

Similarly, some scholars have explored the feasibility of using ECGI technology to study abnormal matrix mapping of ventricular fibrillation based on the study of "tremor center" or ventricular fibrillation trigger point during ventricular fibrillation (hereinafter referred to as ventricular fibrillation). For example, haissaguerre et al. [15] studied 24 surviving patients with idiopathic ventricular fibrillation and found that nearly 2/3 of patients with idiopathic ventricular fibrillation had subclinical changes in local electrophysiological matrix structure. Frontera et al. [16] also proposed the verification of abnormal matrix of ventricular fibrillation and explored the feasibility of ablation of these key parts. The emergence of ECGI provides a new non-invasive method for matrix mapping of ventricular tachycardia and ventricular fibrillation. For patients with ventricular premature contractions, ECGI can locate the origin position with high accuracy and noninvasive before operation, which is of great benefit to improve the effectiveness and safety of radiofrequency ablation.

3.2. Atrial arrhythmia

Many studies have shown that ECGI also has high accuracy in mapping the focal origin of atrial arrhythmia or the reentry mechanism of atrial tachycardia (hereinafter referred to as atrial tachycardia), and has a good correlation with the results of intracavitary electrical mapping [17]. For example, Shah et al. accurately located the origin of local atrial tachycardia based on the large turn back loop mechanism when mapping atrial tachycardia based on ECGI; Wang et al. [18] located the earliest origin of atrial tachycardia after pulmonary vein isolation; And cakulev et al. [6] defined the different characteristics and key isthmus positions of isthmus dependent and non isthmus dependent atrial flutter based on ECGI. The above evidence shows the role of real-time mapping ECGI in matrix research and origin localization of atrial tachycardia, especially for some unsustainable, difficult to induce and less frequent atrial premature contractions and atrial tachycardia, ECGI can even complete mapping within one cardiac cycle.

Atrial fibrillation is one of the most common arrhythmias in clinic. The ablation strategy based on pulmonary vein electrical isolation is the cornerstone of atrial fibrillation ablation, but its long-term success rate is still not ideal. The reason is that the underlying electrophysiological mechanism of atrial fibrillation is not clear, and empirical ablation also has a strong arrhythmogenic effect. At present, there is no ideal ECG mapping method [19]. The emergence of ECGI technology has brought hope to the global mapping of atrial fibrillation. Its non-invasive, sustainable, high-density and synchronous global mapping of left and right atrium has solved the shortcomings of traditional mapping methods, and is a powerful weapon for the study of its electrophysiological mechanism. Cuculich et al. [20] explored the mechanism of atrial fibrillation in 26 patients and showed the complexity of atrial fibrillation. There are focal and reentrant wavelet activities in the drivers of atrial fibrillation. At the same time, it is found that the complexity of atrial fibrillation is related to the duration of atrial fibrillation and the type of atrial fibrillation. Haissaguerre et al. [21] studied the characteristics of ECG activity in 103 patients with persistent atrial fibrillation, indicating that focal electrical activity and reentry activity are the main mechanisms of atrial fibrillation. At the same time, some studies have also shown that the complexity of AF increases with the increase of its duration. As paroxysmal AF turns into persistent AF, the drivers can be diffusely distributed to both atria; Reentry drivers are mostly located at the pulmonary vein orifice and its surrounding structures [22]. Cochet et al. [5] described the characteristics of the rotor movement on the epicardium and accurately detected the core position of its trajectory. The above research results have also been confirmed in the recent relevant research of our team. The emergence of ECGI not only provides a more optimized non-invasive tool for mapping the mechanism of atrial fibrillation, but also enables the clinic to have a more in-depth understanding of the occurrence, development and maintenance mechanism of atrial fibrillation. More importantly, identifying the characteristics and complexity of electrophysiological mechanisms in patients with atrial fibrillation through ECGI is helpful for risk stratification of patients with atrial fibrillation, screening patients for appropriate ablation treatment, guiding individualized radiofrequency ablation strategies based on electrophysiological mechanisms, and further improving their success rate.

3.3. CRT

As an integral part of non drug treatment of heart failure, CRT is an effective intervention for heart failure with reduced ejection fraction, which can improve its heart failure symptoms, quality of life and survival rate [23]. However, a number of studies have shown that about 30% of patients in clinic still show no response to CTR [24]. Fuzzy recognition and judgment of the degree of asynchrony of cardiac electrical activities may be the main reason for the low success rate of CRT [25].

The degree of ventricular activation synchronization can be assessed by the duration of QRS complex. However, the narrow QRS complex can also have significant ventricular asynchrony contraction, and even some patients have better response to CRT than those with wide QRS complex. However, ECG can not distinguish the above patients, and it is also impossible to assess the activation relationship within the local region of the heart or between different regions. ECGI can evaluate the degree of ventricular synchronization by evaluating the spatial dispersion of local and global activation time. For example, Silva et al. [26] studied the asynchronization parameters of patients' ECG activities with the help of ECGI, and found that the parameter values of patients with CRT response were significantly lower than those without response. Based on the data, it can effectively evaluate which patients will benefit from CRT. Revishvili et al. [27] and ploux et al. [28] further introduced the concept of ventricular electrical uncoupling (VEU), and found that the evaluation of CRT implantation indications through VEU has high sensitivity and specificity, which can more effectively screen patients suitable for CRT implantation.

Another great advantage of ECGI is that it can define the local electrophysiological matrix information, determine the location of the latest activation area and its matrix characteristics, and provide more detailed information through non-invasive mapping, so as to guide the placement of ventricular leads [29], so that each patient can obtain the most suitable lead placement location and the most effective device programming, fully realize the formulation of patient personalized programs, and help to improve the CRT response rate [30].

3.4. Other arrhythmias

In addition to atrial and ventricular arrhythmias, many researchers at home and abroad have also used ECGI to analyze and evaluate the electrophysiological mechanism of other and special types of arrhythmias. For example, Vijayakumar et al. [31] used ECGI to map the characteristics of electrophysiological matrix in patients with long QT syndrome (LQTS) and found that one of the characteristics of electrophysiological matrix in LQTS is the increase of ventricular epicardial repolarization dispersion and the prolongation of local action potential duration. The results further support the reentry theory as the main mechanism of LQTS, suggesting that ECGI can be used for risk assessment and risk stratification in such patients. At the same time, for Brugada syndrome (BRS), research shows that patients with BRS can show characteristic electrophysiological abnormalities in ECGI, such as abnormal conduction and coexistence of repolarization [32]. Zhang et al. [33] found that ECGI can also distinguish BRS patients with similar body surface ECG and non BRS right bundle branch block patients based on the above electrophysiological matrix abnormalities, which is of great value for the diagnosis, treatment and prognosis of patients.

Clinically, researchers used ECGI to locate the bypass of preexcitation syndrome. For example, cakulev et al. [34] and Berger et al. [35] used ECGI to accurately predict the location of ventricular preexcitation bypass, which was verified by intracavitary electrical mapping. For patients with early repolarization syndrome (ers), nademanee et al. [36–37] realized the accurate localization of the origin of early repolarization pattern in these patients with the help of ECGI high-density biventricular endocardial and epicardial mapping, and gave ablation treatment. After a median follow-up of 37 months, it was found that ablation prevented 81% of ers patients from recurrence [22], it shows the clinical value of ECGI in some patients with special types of arrhythmias that cannot be determined by traditional mapping.

4. Defects and technical progress of ECGI

Since the ECGI technology was first proposed in 1977, the pace of ECGI technology update and research progress has never stopped from basic algorithm research to large animal model research, as well as the current extensive clinical research [22]. However, there are still many difficulties in the promotion and application of ECGI technology. Among them, the most important is the construction of the reverse reconstruction algorithm for the reverse projection of the body surface ECG to the heart in ECGI reconstruction. At present, most inverse reconstruction algorithms regard the heart trunk as a homogeneous volume conductor, which assumes that the human body is homogeneous and isotropic, and the thoracic surface potential only depends on the geometry of the thoracic and epicardial surfaces and the geometric relationship between them [38]. However, the real human heart trunk model is affected by complex factors such as viscera, fat and muscle, which also directly leads to the pathological characteristics of ECGI ECG reverse reconstruction algorithm [39].

Of course, with the continuous R & D iteration of ECGI, this error is gradually narrowing. For example, bacoyannis combined artificial intelligence with ECGI to develop β- CVAE system further improves the imaging accuracy. The reverse reconstruction algorithm proposed by the research team in previous studies also shows high reconstruction accuracy [39]. On the other hand, at present, ECGI mostly focuses on the inversion and reconstruction of epicardial potential. Due to the influence of myocardial thickness and scar, there are often differences between epicardial and endocardial excitation, which also leads to inaccurate mapping of some special types of arrhythmias and depends on intracavitary ECG mapping. More importantly, the process of ECGI acquisition, reconstruction and analysis is complex and requires team cooperation and participation. However, there are differences in acquisition equipment, number of body surface electrodes, model reconstruction algorithm and ECG inversion algorithm used by different countries and teams. Although the ECG imaging alliance established in 2014 put forward the international unified standard and framework for ECGI research, the results of different studies are still difficult to compare and verify, which limits the clinical application of the results to a certain extent [41]. More than 40 ECGI clinical studies have been conducted or are in progress at home and abroad, most of which are small sample clinical human trials. The research results still need to be confirmed and popularized by more large-scale multi center clinical randomized controlled studies.

According to the development trend in recent years, with the maturity of ECGI ECG imaging algorithm and reconstruction technology, the homogeneity and quality of clinical trials are also continuously improved. Therefore, there is still much room for improvement in the basic research and clinical application of ECGI technology in the field of cardiovascular disease diagnosis and treatment, For example, risk assessment and stratification for different types of arrhythmias, evaluation of left atrial function in atrial fibrillation, construction of scoring system for atrial fibrillation recurrence and prognosis based on the characteristics of ECGI atrial matrix, etc., and it is expected to use ECGI to develop catheter ablation strategies with individual specificity and based on the characteristics of arrhythmia matrix, so as to assist or guide the clinical treatment of complex arrhythmias. The publication of the above research results is also expected to break through a series of technical bottlenecks in the diagnosis and treatment of complex arrhythmias such as atrial fibrillation, and provide new technologies and schemes for their clinical intervention and research.

5. Summary and outlook

As a non-invasive ECG mapping technology, ECGI has the characteristics of noninvasive, high-resolution and continuous mapping, and effectively makes up for the lack of 12 lead ECG and invasive ECG physiological examination. Although there are some defects in the current ECGI system and algorithm, with the development of the times and the deepening of various studies, these defects will eventually be gradually improved. More and more clinical evidence at home and abroad shows that ECGI plays a great role in exploring the mechanism of various arrhythmias, including atrial and ventricular arrhythmias, and guiding clinical treatment. It helps to realize patients' personalized treatment schemes based on the characteristics of electrophysiological mechanism, so as to improve the diagnosis and treatment effect. It has a great application prospect in the future clinical and scientific research process.

Conflict of interest

The authors declare no conflict of interest.

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