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Advances in the Application of Non-invasive Myocardial Work Assessment in Evaluating the Risk and Prognosis of Stroke-Heart Syndrome in Patients with Acute Ischemic Stroke

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Abstract: Timely assessment of the risk of stroke-heart syndrome (SHS) in patients with acute ischemic stroke (AIS), accurate prediction of clinical prognosis and optimization of clinical treatment strategies are crucial for improving the overall clinical outcomes of such patients. Traditional assessment methods including conventional echocardiography and single serological tests have inherent limitations, such as insufficient sensitivity and low specificity for detecting early myocardial dysfunction, which make it difficult to fully reflect the pathophysiological changes of SHS. The non-invasive myocardial work (MW) technique integrates speckle-tracking echocardiography with left ventricular pressure-strain loop analysis to dynamically quantify the mechanical properties and energy metabolism efficiency of the myocardium, thus providing a novel non-invasive approach for the evaluation of SHS in AIS patients. By reviewing the recent relevant literature, this article elaborates on the fundamental principles of the MW technique and its clinical applications in SHS risk screening, prognostic assessment and guidance of clinical treatment decisions in AIS patients. It also discusses the current limitations and future development directions of this technique, aiming to clarify the clinical value of the MW technique in the diagnosis and management of AIS patients complicated with SHS.

Keywords: Non-invasive Myocardial Work; Acute Ischemic Stroke; Stroke-heart Syndrome.

1. Introduction

There is a close pathophysiological association between the nervous system and the cardiovascular system. Acute ischemic stroke (AIS), as one of the leading fatal and disabling diseases worldwide, has become a major challenge for clinical neurology and cardiology departments[1]. Although the popularization of acute interventional therapies such as thrombolysis and mechanical thrombectomy has significantly reduced the short-term mortality of AIS patients, SHS—a common post-stroke complication characterized by myocardial injury, arrhythmia and left ventricular dysfunction—still poses a severe threat to the long-term prognosis of AIS patients, and can lead to major adverse cardiovascular events (MACE) including recurrent stroke, acute myocardial infarction and heart failure[2]. Therefore, how to identify AIS patients at high risk of SHS at an early stage, dynamically monitor the changes in their myocardial function and optimize clinical treatment strategies accordingly has become an urgent clinical problem to be solved.

At present, the commonly used methods for assessing SHS include conventional echocardiography, serum myocardial marker detection and cardiac magnetic resonance (CMR)[3, 4]. Yet all these methods have obvious limitations: conventional echocardiography is mainly based on left ventricular ejection fraction (LVEF) for assessment, which has insufficient sensitivity to early myocardial dysfunction and segmental myocardial injury; single serum markers such as cardiac troponin are susceptible to interference from brain tissue injury, systemic inflammation and other factors, resulting in low specificity for diagnosing SHS in AIS patients; although CMR is regarded as the gold standard for detecting myocardial pathological changes such as edema and fibrosis, and can accurately evaluate the myocardial pathological alterations in SHS, its clinical application is restricted by high examination cost, long scanning time, and inapplicability to AIS patients with incompatible metal implants or severe renal insufficiency.

In recent years, the MW technique, as a novel echocardiographic functional assessment method, has been increasingly applied in the field of cardiovascular disease evaluation, showing unique clinical advantages. By combining speckle tracking echocardiography (STE) with left ventricular pressure-strain loop analysis, this technique can dynamically quantify myocardial mechanical properties and energy metabolism efficiency, overcoming the shortcomings of traditional assessment methods that are easily affected by myocardial load and lacking sensitivity[5]. Studies have shown that the MW technique, as a cutting-edge non-invasive method for evaluating left ventricular function, has the characteristics of high sensitivity, real-time monitoring, and cost-effectiveness. It can identify subclinical myocardial dysfunction at an early stage, and its core parameters are closely correlated with the left ventricular function and the long-term risk of MACE in patients[6]. The MW technique enables early identification of AIS patients at high risk of SHS and aids clinicians in developing individualized intervention strategies, which is critical for improving long-term outcomes in AIS patients. This article summarizes the research progress of the MW technique in the assessment of risk and prognosis of AIS patients complicated with SHS.

2. Pathophysiological Mechanisms of Stroke-Heart Syndrome in Acute Ischemic Stroke Patients

In AIS patients, cerebral vascular occlusion leads to cerebral ischemia and hypoxia, which rapidly triggers dysregulation of the central neurohumoral system. This pathological process first activates the sympathetic-adrenomedullary system, leading to an excessive release of catecholamines into the blood circulation. Excessive catecholamines induce a sharp increase in myocardial oxygen demand, coronary artery spasm, and cardiomyocyte calcium overload, which directly result in myocardial injury[7]. Meanwhile, ischemic necrosis of brain tissue induces a systemic inflammatory response, resulting in a significant increase in the levels of pro-inflammatory factors such as tumor necrosis factor-α and interleukin-6, which further aggravate impaired myocardial microcirculation and cardiomyocyte apoptosis. In addition, the activation of the hypothalamic-pituitary-adrenal axis leads to abnormal cortisol secretion, which disrupts myocardial metabolism and cardiac electrical stability[8]. The combined effects of the aforementioned pathophysiological mechanisms ultimately lead to SHS development, which is characterized by myocardial injury, arrhythmia and left ventricular dysfunction. SHS not only exacerbates the cardiocerebral cross-talk injury, but also is closely associated with the long-term occurrence of MACE. Therefore, prompt interventions including myocardial protection and sympathetic blockade are required to improve the prognosis of AIS patients complicated with SHS[3, 9].

3. Principles of Non-invasive Myocardial Work Echocardiography

Myocardial work echocardiography is a novel myocardial function evaluation technique based on two-dimensional speckle tracking imaging (2D-STI), which establishes a non-invasive assessment system for myocardial work by quantifying the area of regional left ventricular pressure-strain loops[10]. The core of this technique is to innovatively integrate myocardial strain data with left ventricular pressure data to construct a standardized pressure-strain loop, so as to achieve accurate quantitative evaluation of myocardial work. This method can effectively correct the interference caused by fluctuations in left ventricular afterload, and more truly reflect the intrinsic contractile function efficiency of the myocardium compared with traditional echocardiographic techniques.

The implementation of the MW technique consists of three core steps:

First, acquisition of myocardial strain data based on 2D-STI. Dynamic echocardiographic images of the standard apical four-chamber, three-chamber and two-chamber views are collected with a frame rate of at least 40 frames·s^{-1}, and at least three consecutive cardiac cycles are recorded for each view to ensure the reliability of the data[5]. After the images are processed by the post-processing workstation, the system automatically tracks the acoustic speckles in the myocardial tissue and calculates their spatial displacement trajectories during the cardiac cycle, so as to obtain the myocardial strain values. Among them, global longitudinal strain (GLS) is the fundamental parameter for evaluating the overall myocardial contractile function[11]. Conventional strain parameters are easily affected by afterload, and the MW technique can effectively overcome this limitation by integrating left ventricular pressure data in the subsequent steps.

Second, construction of a non-invasive left ventricular pressure curve, which is a key advantage of the MW technique over traditional 2D-STI. In clinical practice, the brachial artery systolic and diastolic blood pressures measured by the cuff method are usually used as reference values, and combined with a standardized left ventricular pressure waveform template to fit a dynamic left ventricular pressure curve synchronized with the cardiac cycle[12]. The left ventricular pressure curve constructed by this non-invasive method can provide a key quantitative basis for the calculation of myocardial work.

Finally, generation of the pressure-strain loop and calculation of core MW parameters. The corresponding relationship between the synchronously acquired left ventricular pressure (vertical coordinate) and myocardial strain (horizontal coordinate) during the cardiac cycle is plotted to form a closed loop, and the area inside the loop represents the amount of work done by the myocardium. Based on the pressure-strain loop, four core quantitative parameters of the MW technique are derived[10, 13]: global work index (GWI), which reflects the total work level of the left ventricle; global constructive work (GCW), which represents the positive work generated by effective myocardial contraction for blood ejection; global wasted work (GWW), which refers to the energy consumed by myocardial contraction that does not contribute to ventricular ejection; and global work efficiency (GWE), which is the ratio of GCW to the total myocardial work (GWI) and is the key index for evaluating the efficiency of myocardial contraction. These parameters together constitute a comprehensive load-corrected quantitative assessment system for myocardial function.

4. Clinical Application of Non-invasive Myocardial Work Technique in the Assessment of AIS Patients Complicated with SHS

4.1. Application in Early Risk Screening of SHS

Compared with conventional echocardiographic parameters, MW parameters based on the left ventricular pressure-strain loop (LVPSL) have superior sensitivity and specificity in assessing early myocardial abnormalities and screening SHS in AIS patients[14]. LVEF, the main assessment index of conventional echocardiography, only reflects the overall contractile function of the left ventricle and is not sensitive to subclinical segmental myocardial injury. Serum troponin is susceptible to interference from brain tissue injury and systemic inflammation, with a specificity of less than 50% for diagnosing SHS in AIS patients[3]. A prospective study including 176 AIS patients explored the association between myocardial work parameters and stroke severity as well as neurological deficits. The results showed that GWE and GCW on admission were not only correlated with the degree of neurological deficits in AIS patients, but also served as independent risk factors for predicting SHS. When the cut-off value of GWE was set at 0.62, the area under the curve (AUC) was 0.81, with a sensitivity of 78% and a specificity of 75%; when the cut-off value of GCW was set at 850 mmHg·%, the AUC was 0.78, with a sensitivity of 72% and a specificity of 70%[15]. This confirms that MW parameters can effectively make up for the deficiencies of traditional assessment methods in early SHS screening. Another study focusing on the effects of infarction in different cerebral artery supply areas on left ventricular function found that in AIS patients with infarction in the basilar artery supply area, the degree of abnormality of local myocardial work efficiency (MWE) and GCW in the corresponding myocardial segments was significantly negatively correlated with the severity of SHS, and the reduction of local MWE in these patients was more than 20%, which was significantly higher than that in patients with infarction in the middle cerebral artery supply area[16]. This suggests that the MW technique can analyze the site-specific characteristics of cardiocerebral cross-talk injury through segmental myocardial work parameters. However, most of the existing studies are single-center and small-sample designs, which do not include AIS patients with underlying diseases such as hypertension and atrial fibrillation, and lack controlled validation with the CMR gold standard, thus limiting the generalizability of the study findings.

4.2. Value in Prognostic Assessment of AIS Patients

Zheng et al[16] found that MW parameters of AIS patients complicated with SHS showed characteristic abnormal changes that were closely related to the clinical prognosis: GWW, which reflects myocardial injury, was significantly increased, while GWI, GWE and GCW, which evaluate myocardial contractile function, were significantly decreased, with statistically significant differences ($P < 0.05$). Moreover, the more severe the abnormal changes of these parameters, the higher the risk of long-term MACE in patients. In addition, a study focusing on the association between ischemic stroke location, etiological subtype, neurological outcome and cardiac autonomic function[17] further confirmed that AIS patients with brainstem infarction (vertebrobasilar artery infarction) had significantly more severe abnormal changes in global and segmental MW parameters than those with cortical infarction, and the reduction of local MWE in the former was more than 20% ($P < 0.05$), which could directly reflect the impairment of cardiac autonomic function. This is consistent with the core conclusion that stroke lesion location is closely related to cardiac autonomic function and neurological outcome: the brainstem is the key regulatory region of the autonomic nervous system, and the more significant the abnormal changes of MW parameters caused by brainstem infarction, the more severe the damage to cardiac autonomic function, and the worse the neurological outcome and long-term prognosis of AIS patients. This fully verifies the core value of the MW technique in the prognostic assessment of AIS patients.

Further studies have shown that the myocardial work efficiency difference (ΔWE) between the infarcted and non-infarcted myocardial segments can effectively predict the risk of long-term left ventricular remodeling and MACE in AIS patients, with a predictive sensitivity of 69%, a specificity of 74% and an AUC of 0.770; the incidence of MACE is significantly increased in patients with elevated ΔWE[18]. At the microcirculation level, Zhang et al[15] found that segmental MWE was significantly correlated with myocardial microcirculatory perfusion, and regional MW parameters could be used as a novel marker for prognostic risk stratification of AIS patients, which provides a new entry point for the accurate clinical assessment of the prognosis of AIS patients complicated with SHS. However, most of the existing studies are single-center and small-sample designs, which fail to fully include AIS patients with underlying diseases such as hypertension and atrial fibrillation, and lack sufficient controlled validation with CMR. In addition, the standardized analysis method of regional myocardial work needs to be further improved. These factors to a certain extent affect the accuracy and clinical application scope of the MW technique in the prognostic assessment of AIS patients.

In view of these limitations, it is recommended that multicenter cohort studies be conducted in the future, including AIS patients with different clinical characteristics. The degree of myocardial injury should be defined by combining with CMR technology, and a unified standard for regional myocardial work analysis should be established. This will provide more reliable data support for the inherent association between MW parameters and the prognosis of AIS patients, and further enhance the clinical utility of the MW technique. In conclusion, the MW technique shows good potential in the prognostic assessment of AIS patients, which can effectively reflect the degree of myocardial injury and predict the risk of long-term adverse clinical outcomes, but the relevant conclusions need to be further verified by multicenter and large-sample prospective studies.

4.3. Guidance for Clinical Treatment Decision-Making and Risk Stratification

In summary, the non-invasive MW technique can not only accurately assess the degree of myocardial injury in AIS patients complicated with SHS and predict the risk of long-term MACE, but also provide a reliable quantitative basis for the formulation of clinical treatment plans, thus realizing individualized risk stratification management of AIS patients. Effective risk stratification is crucial for optimizing the treatment strategies of AIS patients, reducing SHS-related complications and improving the overall clinical prognosis.

Studies have shown that MW parameters can be used as key predictors in the risk stratification model of AIS patients complicated with SHS, among which GWE and GCW have the highest clinical application value[15]. Taking GWE = 0.62 and GCW = 850 mmHg·% as the optimal cut-off values has significant clinical value in identifying AIS patients at high risk of SHS, and AIS patients can be divided into high-risk and low-risk subgroups accordingly: high-risk patients with GWE < 0.62 and GCW < 850 mmHg·% suggest severe involvement of the autonomic nerve center and low efficiency of myocardial energy metabolism, and early initiation of β-adrenergic receptor blockers and intensive myocardial protection therapy are recommended; for low-risk patients with normal MW parameters, unnecessary cardiovascular medications can be reduced to avoid overtreatment. The advantages of this risk stratification strategy have been supported by targeted clinical studies. A controlled study by Trimarchi et al[19] including 240 AIS patients showed that the sensitivity of MW parameters centered on GWE in identifying SHS-related subclinical myocardial injury was 81%, which was significantly higher than that of the traditional LVEF index (52%). This effectively makes up for the deficiency of LVEF in the early identification of occult myocardial dysfunction due to insufficient sensitivity.

In addition, the MW technique can also guide the timing of non-cardiac operative procedures and rehabilitation treatment in AIS patients. A study on the mechanism and risk stratification of perioperative stroke management[20] further pointed out that myocardial dysfunction in patients with perioperative stroke was significantly positively correlated with the risk of stroke recurrence and long-term MACE. The MW technique can accurately identify the high-risk group of perioperative stroke patients complicated with subclinical myocardial injury by quantifying myocardial work parameters, which provides a core basis for the formulation of individualized perioperative management strategies. Meanwhile, in the management of critically ill AIS patients, the MW technique, with the advantages of bedside, non-invasive and real-time monitoring, can dynamically track the changes of GWW, MWE and other parameters, timely detect the signs of aggravated myocardial injury, and provide precise guidance for the adjustment of circulatory support therapy in the intensive care unit (ICU).

However, there are still some limitations in the application of the MW technique in the risk stratification of AIS patients. First, there are obstacles to the popularization and application of the technique: some echocardiographic equipment in primary medical institutions lacks MW analysis function, and the operators have insufficient ability to interpret segmental MW parameters and ΔWE, making it difficult to carry out standardized risk stratification assessment. Second, the performance of the current risk stratification model remains suboptimal: most of the current stratification strategies only incorporate MW parameters at a single time point, without integrating clinical information such as underlying diseases (atrial fibrillation, hypertension, etc.) and neurological deficit scores. For elderly AIS patients with multiple complications, the accuracy of risk stratification is insufficient.

In view of the above shortcomings, it is proposed that a joint prediction model integrating MW parameters and multidimensional clinical data be constructed in the future based on the application experience of machine learning in the cardiovascular field. Studies have confirmed that the Transformer-based time series model can integrate MW parameters (GWI, GCW, etc.) at different time points, stroke location and inflammatory indicators through the self-attention mechanism, which can significantly improve the accuracy of SHS risk prediction[21]. In addition, an interpretable machine learning model based on the XGBoost algorithm combined with the SHapley Additive exPlanations (SHAP) technique can improve the prediction efficiency to AUC $\geq$ 0.9, and clarify the contribution of each MW parameter to risk stratification, thus providing an intuitive basis for clinical decision-making[21]. Subsequent studies can rely on machine learning technology to establish an individualized SHS risk prediction model for AIS patients, which can help primary medical institutions rapidly identify high-risk patients, formulate precise intervention plans for patients with different risk levels, further optimize the allocation of medical and health resources, and reduce the incidence of SHS and the long-term risk of MACE in AIS patients.

4.4. Multimodal Integration and Technological Expansion

The MW technique mainly dynamically assesses the myocardial contractile function of AIS patients from a mechanical perspective, but it faces some challenges in clinical application: (1) it has low sensitivity to SHS-related myocardial microcirculation injuries (including microvascular spasm and edema), making it difficult to accurately distinguish the pathological types of myocardial injury; (2) it cannot microscopically locate the correlation between myocardial dysfunction areas and stroke lesion locations, and is also difficult to quantify key pathological parameters such as the degree of myocardial fibrosis. At present, CMR remains the gold standard for the accurate assessment of myocardial histological changes[22], and its late gadolinium enhancement (LGE-CMR) can clearly display the areas of myocardial edema, fibrosis and infarction, providing an important basis for verifying the biological rationality of MW parameters.

A study focusing on the multimodal imaging assessment of myocardial hypertrophy[6] combined LGE-CMR with the MW technique, and found that local GWI, GCW and MWE in LGE-positive fibrotic myocardial regions were significantly lower than those in remote non-fibrotic myocardial segments ($P < 0.05$), and these parameters were significantly negatively correlated with the degree of myocardial fibrosis[23]. This result suggests that MW parameters can effectively quantify the degree of stroke-related local myocardial injury, and reveal the functional heterogeneity of cardiocerebral cross-talk injury through the mechanical properties of the myocardium, providing a biomechanical basis for MW parameters to be used as prognostic markers of SHS. The multimodal integration of LGE-CMR and the MW technique can realize the dual assessment of myocardial structure and function, and provide a new method for the accurate diagnosis of SHS in AIS patients.

In recent years, deep learning technology has provided a new development direction for the multimodal integration of the MW technique. A review focusing on the application of deep learning in electrocardiography (ECG)[24] systematically summarized the technical path of deep learning algorithms in the detection and localization of myocardial injury, and confirmed that the multimodal data fusion system formed by the combination of deep learning models and ECG feature extraction can be effectively applied to the MW technique, thus constructing a high-accuracy assessment system for myocardial microcirculation injury. Through multi-source modal data alignment technology, this system integrates the time-frequency domain features of the MW dynamic strain curve and the electrophysiological features of ECG, which can accurately identify and locate the myocardial dysfunction areas related to SHS. In the stage of injury analysis, relying on the feature mining advantage of deep learning models, the system focuses on the abnormal coupling regions of "mechanical parameters - electrophysiological signals" to optimize the spatial accuracy of injury localization, and ultimately realize the accurate mapping of SHS-related myocardial microcirculation injury. In the future, it is expected to construct a multimodal assessment model coupling radionuclide perfusion parameters, CMR fibrosis parameters and MW mechanical parameters, and establish a three-dimensional cardiac function atlas based on these data, so as to realize the multidimensional integration of myocardial tissue structure, function and metabolism, and further advance the time window for predicting the risk of SHS in AIS patients.

5. Current Challenges and Future Directions

Although the MW technique has demonstrated unique advantages of non-invasiveness and high sensitivity in the assessment of AIS patients complicated with SHS, its clinical translation and widespread application still face many challenges. Future research should focus on multi-dimensional exploration to solve the existing problems. At the technical level, the sensitivity and specificity of MW parameters vary significantly in different studies, which is closely related to the heterogeneity of included patients (different stroke subtypes), the type of echocardiographic equipment and the standardization of operating procedures[25]. Meanwhile, the selection of the region of interest (ROI) in the MW technique relies on manual judgment, which has strong subjectivity and seriously affects the reproducibility of the test results. Therefore, it is imperative to establish a unified national or international standard for MW data acquisition and analysis, define ROI classification criteria for different stroke subtypes, carry out multicenter validation of the consistency of different echocardiographic equipment, and enhance the universality and clinical acceptance of MW parameters.

At the clinical translation level, most of the existing studies are single-center and small-sample exploratory analyses, lacking large-sample prospective cohort studies. In addition, head-to-head comparison studies with the CMR gold standard are insufficient, and the optimal decision cut-off values of MW parameters have not been established for special clinical scenarios such as severe AIS and stroke recovery period. In the future, multicenter prospective cohort studies covering different age groups, comorbidities and stroke subtypes should be conducted to clarify the causal association between MW parameters and SHS development, and develop a clinical risk score based on MW parameters to improve the clinical practicability of the technique.

In the direction of emerging research, artificial neural network-assisted automatic analysis algorithms are expected to overcome the limitations of manual analysis: for example, deep learning-based strain-loop segmentation algorithms have been proven to improve the efficiency and accuracy of data analysis in the field of cardiovascular diseases, but their generalization ability in AIS patients complicated with SHS still needs to be further verified. At the same time, dynamic monitoring of the changes of MW parameters from the acute phase to the rehabilitation phase of AIS can provide a key basis for the formulation of individualized cardiac rehabilitation programs for patients. More importantly, the application value of the MW technique in special AIS populations such as the elderly, patients with combined cognitive impairment and pediatric patients have not yet been clarified, and targeted clinical studies should be carried out for these special populations in the future to expand the application boundary of the MW technique.

6. Conclusion

In summary, non-invasive myocardial work echocardiography plays a key role in the risk screening, prognostic assessment, clinical decision-making and risk stratification of AIS patients complicated with SHS by virtue of its advantages of non-invasiveness, real-time monitoring and high sensitivity. By quantifying myocardial work, the MW technique can identify subclinical myocardial injury that is difficult to be detected by conventional echocardiography, and accurately predict the risk of long-term adverse cardiovascular events in AIS patients, thus providing a new research perspective for the study of the mechanism of cardiocerebral cross-talk injury.

Although the MW technique still faces challenges such as the lack of standardized operation norms, insufficient clinical validation and scarce research data in special populations, with the advancement of multicenter large-sample studies, the deep integration of multimodal imaging technology and the wide application of machine learning algorithms, its clinical value in the diagnosis and management of AIS patients complicated with SHS is expected to be further enhanced. It is anticipated that the MW technique will become a routine examination tool for the assessment of myocardial function in AIS patients in the future, providing a robust technical basis for improving long-term outcomes in AIS patients.

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