New auscultation: can we detect heart failure by auscultation ?

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Abstract: Heart failure (HF) is the terminal stage of many cardiovascular diseases. The echocardiography, B-type natriuretic peptide, and N-terminal pro-B-type natriuretic peptide are still the main auxiliary examinations in HF diagnosis. Auscultation is non-invasive, cost-effective, and requires minimal equipment. However, its use is limited by the low diagnostic sensitivity and accuracy. The acoustic cardiography synchronizes phonocardiogram signals with electrocardiogram signals. Previous research has demonstrated that the indicators of acoustic cardiography could be used to evaluate left ventricular function, predict adverse events, and improve the accuracy of the HF diagnosis. The computer-aided detection technique realizes the automatic comprehensive analysis of heart sounds. The purpose of this review is to summarize the current research of heart sounds used in HF and propose new auscultation in the future.

Keywords: heart failure; heart sounds; acoustic cardiography; computer-aided detection techniques

1. Introduction

Heart failure (HF) is the terminal stage of many cardiovascular diseases, such as cardiomyopathy, coronary heart disease, and heart valve ailments. HF patients suffer from low quality of life, high medical costs, and high mortality **[1]**. Therefore, the diagnosis and treatment of heart failure have attracted widespread attention. In current clinical practice, echocardiography, B-type natriuretic peptide (BNP), and N-terminal pro-B-type natriuretic peptide (N-terminal pro-BNP) are still the most widely used methods to detect cardiac function. Left ventricle ejection fraction (LVEF) plays an important role in prognosis, diagnosis, and therapy **[2]**, but measurement of LVEF by echocardiography has significant inter-observer and intra-observer variability, and it is highly dependent on image quality and modality **[3]**. The plasma B-type natriuretic peptide and N-terminal pro BNP are also elevated in other diseases, such as atrial fibrillation, myocardial fibrosis, pulmonary arterial hypertension, hypertension **[4]**. It can also raise in renal insufficiency and infectious diseases.

Auscultation is non-invasive, cost-effective, and requires minimal equipment, making it very suitable for cardiac examination, especially in small primary health care clinics **[5]**. It is still widely used in clinical work. However, the low diagnostic sensitivity and accuracy are caused by human ear limitation, clinical disagreement, and skill discrepancy among examiners **[6]**. At present, many researchers have committed to improving the accuracy of auscultation through various attempts. Phonocardiogram (PCG) is the visualized heart sound signal, but it only carries the signal of mechanical activity of the heartbeat. Acoustic cardiography synchronizes PCG signals with electrocardiogram (ECG) signals. It provides a comprehensive assessment of both mechanical and electronic functions **[6]**. In the past decades, computer-aided detection techniques which aim to realize automated auscultation attract wide attention. Previous studies have demonstrated that heart sounds could be used to evaluate left ventricular function, predict adverse events, and improve the diagnostic ability of HF.

The purpose of this review is to summarize the current research of heart sounds used in HF and propose new auscultation in the future.

2. Indicators of acoustic cardiography related to heart failure

2.1. S1

The first heart sound (S1) is caused by the closure of the atrioventricular valves, its amplitude is affected by the pressure gradient across the atrioventricular valve **[7]**. The previous studies showed that its amplitude was correlated with myocardial contractility **[8,9]**.

2.2. S3

The third heart sound (S3) is caused by the rapid deceleration of the blood against a stiff ventricle during early diastolic filling **[10-12]**. S3 can be "normal" in young people before the age of 40 and abnormalin people after that **[13,14]**.

2.3 S4

The fourth heart sound (S4) is produced in late diastole due to the atrial contraction causing vibrations of the left ventricle (LV) muscle, mitral valve apparatus, and LV blood mass **[15]**. S4 was significantly more prevalent and more pronounced during sleep in those aged > 40 years **[14]**. Its presence is associated with increased LV end-diastolic stiffness **[16]** and impaired relaxation **[17]**.

2.4. EMAT and % EMAT

Electromechanical activation time (EMAT) is defined as the time period from the start of the ECG Q peak to the heart sound wave S1 first peak **[1]**. % EMAT is defined as EMAT divided by RR interval**[1].**

2.5. EMAT/LVST

The LV systolic time (LVST) means the interval between the peak components of the S1 and the second heart sound (S2) during the same cardiac cycles; EMAT/LVST is that EMAT divided by LVST **[18]**.

2.6. S3 score

S3 score used to evaluate the probability of S3 existence based on its intensity, frequency, and persistence of S3, scaled between 0 and 10 **[19,20]**. S3 score > 5 generally indicates the presence of the third heart sound **[19]** and S3 score > 4 indicates patients with restrictive filling patterns **[20]**.

2.7. Systolic dysfunction index

Systolic dysfunction index (SDI) is calculated by a formula which is [(S3 score÷10) ×QRS duration × QR interval × % EMAT], scaled between 0 and 10 **[21]**. SDI > 5 indicates LVEF < 50 % and SDI >7.5 indicates LVEF < 35 % **[21]**.

3 Acoustic cardiography and heart failure

3.1. Evaluation of left ventricular function

3.1.1 Detecting left ventricle ejection fraction

HF can be divided into three types according to LVEF, including HF with preserved EF (HFpEF, LVEF ≥ 50 %), HF with mid-range EF (HFmrEF, 40 % ≤ LVEF < 50 %), and HF with reduced LVEF(HFrEF, LVEF < 40 %), and different types have different treatment **[2]**. PCG and ECG signals can be used to evaluate the LVEF.

S1 amplitude has been proved to be correlated with myocardial contractility **[8,9]**. In a study conducted by Calò et.al, they found that S1 with best cutoff of 1.5 mG (area under curve (AUC) = 0.59) could detect LVEF < 35 % with 28 % (95 % CI 19 % –40 %) sensitivity and 88 % (95 % CI 80 % –93 %) specificity **[22]**. In a study of 199 patients, Li et.al demonstrated that an EMAT ≥ 104 ms for the diagnosis of EF < 50 % was with a sensitivity of 92.1 % and a specificity of 92 % **[1]**. A previous study with a total of 25 HFpatients had shown that % EMAT diagnosed LVEF < 40 % with 54 % sensitivity, 92 % specificity, and accuracy 72 % **[23]**. In another study conducted by Moyers et.al, they confirmed that EMAT and EMAT/LVST were associated with left ventricular dysfunction which is defined as the presence of both left ventricular end-diastolic pressure (LVEDP) > 15 mmHg and LVEF < 50 % with low sensitivity and high specificity **[24]**. They also demonstrated that EMAT/LVST performed better than EMAT. In addition, EMAT could improve the diagnostic accuracy of intermediate N-terminal pro BNP identifying dLVEF **[1,24]**. Wang et.al conducted a study to determine whether acoustic cardiography can accurately identify HF and its phenotypes **[25]**. Boubaker et.al found that EMAT, LVST, and EMAT/LVST combined with Valsalva maneuver could be helpful to detect or rule out left ventricular dysfunction which was defined as LVEF ≤ 50 % in patients admitted to the emergency for COPD exacerbation **[31]**.

Some comprehensive indicators such as SDI are also confirmed to be related to the LVEF. A previous study showed that SDI > 5 indicated LVEF < 50 %, and SDI > 7.5 indicated LVEF < 35 % **[21]**. Wang et.al found that SDI > 5 could discriminate patients with EF ≤ 35 % from those with 35 % < EF < 50 % with 87 % sensitivity, 60 % specificity, 2.16 positive likelihood ratio (PLR), and 0.22 negative likelihood ratio (NLR) **[20]**. Some research combines multiple parameters to detect LVEF. A multiplicative combination of acoustic parameters, calculated by (QRS Duration) ∗ (QR interval) ∗ (S3 Strength) ∗ (% EMAT), detected LVEF < 50 % with 90 % specificity and 77 % sensitivity **[26]**. In a study of 81 adults which defined LV dysfunction as both an LVEDP > 15 mmHg and LVEF < 50 %, S3 and EMAT/LVST individually demonstrated high specificity and low sensitivity for the detection of LV dysfunction, but the integration of S3 and EMAT/LVST increased the sensitivity and accuracy of the testwithout compromising specificity **[18]**.

The single indicator used to evaluate the LVEF, such as S1, EMAT, EMAT/LVST, had an obvious limitation. Its sensitivity is rather low in most research. Compared with a single indicator, combining with multiple metrics solved the problem of the low sensitivity of a single indicator without reducing specificity. Some comprehensive indicators may have a better performance in LVEF detection.

3.1.2 Detecting left ventricular systolic dysfunction

Left ventricular systolic dysfunction (LVSD) is defined as maximum LV dP/dt <1600 mmHg/s. Maximum LV dP/dt is a well-established and accurate marker of LV systolic dysfunction **[27]**.

The decreased force of LV contraction revealed by a low maximum LV dP/dt was associated with a prolonged EMAT **[28]**. In a study that compared the abilities of acoustic cardiography, LVEF, and QRS duration to detect LVSD, EMAT performed better than LVEF or QRS duration **[29]**. An EMAT could also be a robust measurement in atrial fibrillation even with other concurrent disease conditions **[27]**. Its possible reason was that EMAT was only affected by preload while maximum LV dP/dt was influenced by preload and afterload.

EMAT is the main indicator used to detect LVSD. The EMAT can also be applied in atrial fibrillation. It exhibits a more stable capability in LVSD detection.

3.1.3 Detecting restrictive filling pattern

Restrictive filling pattern (RFP) is defined as E/A ratio≥ 2 or the combination of E/A ratio between 1 and 2 and deceleration time ≤ 140 ms **[22]**. RFP reflects the decreased ventricular diastolic function which is always evaluated by echocardiogram. It has become increasingly clear that abnormalities of diastolic function have a major role in producing signs and symptoms in patients presenting HF **[22,32]**. Calò et.al found that S3 with best cutoff of 0.9 mG (AUC = 0.91) could detect RFP with 85 % sensitivity and 82 % specificity **[22]**. Wang et.al found that an S3 score > 4 identified patients with RFP with 0.76 AUC (95 % CI, 0.67–0.84), 81 % sensitivity and 55 % specificity **[20]**. Previous research had found that RFP, particularly its persistence after therapy, was associated with a more severe clinical status and increased mortality in HF **[22, 33-35]**. S3 may serve as a potential indicator of the evaluation of the therapeutic effects of HF.

3.2. Improve the accuracy of heart failure diagnosis

The diagnosis of acute heart failure (AHF) is often based on history, physical examination, and auxiliary tests such as an echocardiogram, BNP, and N-terminal pro BNP. How to differentiate the AHF patients from the patients with dyspnea in the emergency department (ED) quickly is still a challenge, especially in the patients with intermediate BNP or N-terminal pro BNP levels.

Patients with acute decomposition compared to chronic heart failure (CHF) elicit a higher incidence of the S3 **[36]**. The combination of the S3 and intermediate BNP levels can improve the diagnostic accuracy of AHF **[12,13]**. In a study of 343 patients admitted to ED, Collins et.al confirmed that the addition of the S3 to intermediate BNP levels improved the PLR from 1.3 to 2.9 and the positive predictive value (PPV) from 53 % to 80 % in determining decompensated heart failure **[12]**. However, in another study conducted by Collins et.al, they found that S3 was specific for AHF but did not improve diagnostic accuracy **[37]**. The reason was its low sensitivity **[37]**. In a study of 855 patients admitted to ED with acute dyspnea, Trabelsi et.al found that EMAT/LVST and LVEFare highly correlated **[38]**. It increased the PLR of the intermediate BNP levels diagnosing HF from 1.8 to 3.6. Moreover, the EMAT and LVST in patients with preserved LVEF were not statistically different from patients without HF in this study. The previous study showed that BNP used for LV dysfunction diagnosis was with a sensitivity of 55 %, specificity of 75 %, and PLR of 2.3 **[30]**. Combination S3, % EMAT and BNP increased sensitivity and specificity to 69 % and 100 % with a PLR of 69.

BNP and N-terminal pro BNP are important in heart failure diagnosis. However, they are very susceptible to other diseases. This has a big impact on the early recognition of AHF. The S3 exists in HF with low sensitivity. It greatly limited its application. The other indicators such as EMAT and EMAT/LVST are relatively stable. They may play a larger role in assisting in the early recognition of AHF.

3.3. Prediction of adverse events at admission, before and after discharge

The high risk of HF readmission persists well beyond the first 30 days after hospital discharge and its rate was 6 %–11 % within 30 days and 7 %–18 % within 90 days **[39,40]**. Preventing hospitalization by detecting early evidence of HF decompensation in an outpatient setting can improve patients' quality of life and reduce medical costs **[39]**.

In the Multi SENSE study, Cao et.al demonstrated that S3 measured by CRTD had stronger prognostic power to predict episodes of future heart failure events in HF patients **[41]**. In another multicenter research conducted by Gardner et.al, they found that the S1 amplitude, S3 amplitude, the ratio of S3 to S1 amplitude, respiratory rate, rapid shallow breathing index, and heart rate changed dynamically from pre-event to the recovery period **[7]**. These parameters began to change approximately 30 days or more in advance of an HF event. Another research showed that an algorithm that uses multiple parameters including S1 and S3 could detect HF decompensation with a median alert window of 34 days before the HFevent with a sensitivity of 70 % **[42]**. Drazner et.al confirmed that S3 was associated with an increased risk of HF in patients with asymptomatic or minimally symptomatic left ventricular dysfunction **[43]**. Moreover, S3 was also associated with an increase in in-hospital all-cause death in patients with AHF **[44]**. The reasons may be that an audible S3 was caused by the marked diastolic dysfunction, elevated filling pressure, and volume overload **[44]**.

Chang et.al found that night-time EMAT, but not daytime EMAT, significantly predicted post-discharge events during a mean follow-up of 389 ± 281 days **[45]**. The possible reason was the worsening of central pulsatile hemodynamics due to increased venous return from the legs. But the S3 did not exhibit night-time and daytime changes. In this study, they also found that % EMAT was not significantly different between patients with and without events. However, in a previous study conducted by Chao et.al, they found that % EMAT quickly measured at admission, pre-discharge, and post-discharge could predict the post-discharge cardiovascular events. **[46]**. The predictions remained significant after adjustment for other parameters. Moreover, Chang et.al proved that nighttime EMAT %, but not daytime EMAT %, was associated with the high risk of HF readmission and mortality after discharge **[47]**. In a study conducted by Zhang et.al, they demonstrated that an elevated % EMAT was an independent risk factor for in-hospital cardiac adverse events in CHF patients with LVEF < 50 % **[48]**. The % EMAT >13.8 % achieved a sensitivity of 81.8 % and a specificity of 65.9 %.

The S3, EMAT, and % EMAT are the main indicators for the prediction of cardiac adverse events, HF readmission, and mortality. The identification of the HF decompensation before it happens can prevent disease progression. It can reduce the risk of death and medical burden effectively. Acoustic cardiography may also be usedin guidance for the post-discharge management of HF, but the related research is rare.

4. Computer-aided detection techniques and heart failure

The computer-aided detection techniques used to analyze HS include traditional machine learning and deep learning methods. The steps of traditional machine learning used to process HS include denoising, segmentation, feature extraction, and classification **[5, 49-51]**. Hand-crafted feature extraction is a crucial step in traditional HS analysis which is to find out a small number of representative features to replace the high-dimensional raw signals **[50,52]**. Barma et.al proposed a precise method based on the nonlinear single decomposition and the time-frequency localization to detect the S3 correctly with the accuracy rate of S3 detection is as high as 93.9 % **[53]**. Zheng et.al proposed an intelligent system for the diagnosis of CHF by analyzing the indexes such as D/S, S1/S2 and heart sound characteristics such as adaptive sub_EF synchronously. The result achieved diagnostic accuracy, sensitivity, and specificity of the proposed system were 95.39 %, 96.59 %, and 93.75 % respectively **[51]**. In another study also conducted by Zheng et.al, they extracted and analyzed the linear and nonlinear features of HS signals from the healthy subjects and patients with congestive heart failure. They found that the chaotic property and complexity of HS signals from theCHF patients were lower than those from the healthy people which could be as supplementary indexes or efficient clues for the diagnosis of CHF **[54]**. Liu et.al proposed an automatic approach using an ELM classifier for HFpEF identification based on HS characteristics. They extracted 11 features of the HS based on multifractal detrended fluctuation analysis achieved an accuracy of 96.32 %, a sensitivity of 95.48 %, and a specificity of 97.10 % **[55]**. Three main limitations exist in traditional machine learning. Firstly, feature extraction relies on a lot of professional knowledge in the fields of medicine and signal processing; Secondly, the extraction of hand-crafted features may miss valuable deep features which contain the latest information of HS; Thirdly, some hand-crafted features are ineffective when thesample quality varies greatly **[52,56]**.

Deep learning methods can learn the features from the input automatically without hand-crafted feature extraction. Gao et.al proposed a novel HF screening framework based on a gated recurrent unit (GRU) model to identify subjects of normal, HFpEF, and HFrEF with an average accuracy of 98.82 % **[52]**. The results show that the GRU model gives a better performance than the long short-term memory (LSTM) model, fully convolution network (FCN) model, and the traditional SVM model. HF patients always have many comorbid conditions. Comorbid hypertension, diabetes mellitus, atrial fibrillation, and vascular disease all increased in HF patients over time **[57]**. The normal HS of this study was obtained from the Physio Net/ Computing in Cardiology Challenge 2016. It may overestimate its accuracy. The deep learning method is a powerful tool and can learn the feature from the input automatically. It has a better generalization ability but requires a very large amount of data. The lack of relevant databases hinders its further research. It’s urgently needed to establish some feasible databases in the future.

5. Limitation and future direction

The limitations are shown as follows. Firstly, a single indicator predicts the occurrence of HF with high specificity and low sensitivity. The combination of multiple parameters can improve specificity and sensitivity. Combining more parameters may be a promising method to analyze HS. Secondly, computer-aided detection techniques, especially deep learning methods, are powerful tools used to analyze HS. Traditional machine learning and deep learning have their own disadvantages. Traditional machine learning and deep learning fusion model may solve the problems. Thirdly, the indicators of acoustic cardiography are non-invasive and easily available. It can serve as a daily monitoring method after discharge and even the guidance for the post-discharge management of HF. But there is still a lot of work that needs to do.

6. Conclusion

Auscultation is non-invasive, cost-effective and heart sounds are real-time changing. That makes it suitable to apply in the primary health care clinics for remote heart failure patient monitoring and early recognition of HF. Previous research has demonstrated that indicators of heart sounds could be used to evaluate left ventricular function, predict adverse events, and improve the HF diagnosis. The development of computer-aided detection techniques realizes the automatic comprehensive analysis of heart sounds. In the future, new auscultation may combine acoustic cardiography and computer-aided detection techniques. It may serve as a daily monitoring method and even the guidance for the post-discharge management of HFor other cardiac diseases. However, there is still a lot of work that needs to do.

7. Conflicts of Interest: The authors declare no conflict of interest.

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