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EDITORIAL

What is the Future of Diagnostics in Heart Failure?

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Abstract

Heart failure (HF) is a common and malignant condition. Disease-modifying therapies are available, with early diagnosis being crucial as these therapies modify risk within weeks of commencement. A higher proportion of patients are now being diagnosed with HF during a hospital admission, rather than in the community, with an associated poorer prognosis. There is a need to reduce the time spent to diagnosis and treatment in the community. Advances in the diagnostic tools deployed in HF diagnostics, in particular the use of artificial intelligence, hold promise to deliver this.

Key words: heart failure; diagnosis; artificial intelligence; echocardiography

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Introduction

Heart failure (HF) is a common and, left untreated, malignant condition. 1–2% of the general population has HF (Norhammar et al, 2023). A recent large study of over 55,000 incident HF diagnoses in England over a 20-year period reported a one-year mortality rate of 24% (Taylor et al, 2019). Diagnosis of HF in the community, rather than at the time of hospitalisation, was associated with better one-year survival, at 81% versus 69% one-year survival, respectively. There have also been greater improvements in survival rates by year of diagnosis for patients diagnosed in the community compared to those hospitalised around the time of diagnosis, likely due to advances in disease-modifying pharmacotherapies for HF (McDonagh et al, 2021). National Institute for Health and Clinical Excellence (NICE) guidelines for the diagnosis of HF suggest a triaging assessment based on N-terminal pro B-type natriuretic peptide (NTproBNP) level, with patients with an NTproBNP >2000 ng/L assessed within 2 weeks, 400–2000 ng/L within 6 weeks, and <400 ng/L not requiring assessment (rule out) (National Institute for Health and Care Excellence, 2019). 'Real-world' data describing adherence to these guidelines are limited, although one study described significant geographic variation between two centres in England, with one centre able to assess only 56% of urgent patients within 2 weeks (Zheng et al, 2020). These data are also pre-coronavirus disease (COVID19) pandemic, and it is unlikely that many diagnostic pathways can adhere to the NICE guidance due to backlogs of access to echocardiography. Delays in the time to diagnosis are important, as HF disease-modifying therapies modify the risk of clinical

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events (risk of cardiovascular death, HF hospitalisation, and all-cause death) within weeks of commencement. There appears to be a worrying trend that a higher proportion of patients with HF are being diagnosed during a hospitalisation, rather than in the community (Lawson et al, 2019). This likely represents a missed opportunity to diagnose and initiate treatment before a patient deteriorates to the point of requiring hospitalisation. There is a need to streamline HF diagnostic pathways, to diagnose and treat sooner. Advances in the diagnostic tools deployed in HF diagnostics hold promise to deliver this, both by rationalising and targeting echocardiography and also reducing the time taken to perform echocardiography.

Electrocardiography

One of the oldest and most readily available diagnostic tests for assessing cardiac structure and function is the electrocardiogram (ECG). Despite this, the ECG remains an extremely powerful diagnostic tool. When used in the assessment of HF, a normal ECG can effectively exclude the presence of left ventricular systolic dysfunction (LVSD) (Davie et al, 1996). However, in this study of over 500 patients with suspected HF, assessment of the ECG was performed by cardiologists, which raises the question of how applicable this is in the non-specialist's hands, or whether patients with HF and preserved ejection fraction (HFpEF) would be underdiagnosed by using ECG to screen patients with suspected HF. Advances in machine learning, neural networks, and artificial intelligence (AI) could enable the ECG to be used to triage the timing of, or even decide what patients do not require, an echocardiogram. Derivation and validation studies involving tens of thousands of patients have shown that AI-ECG analyses have excellent diagnostic accuracy at identifying both LVSD and diastolic impairment/LV filling pressures (important in diagnosing HFpEF) (Attia et al, 2019; Lee et al, 2024). AI-ECG analysis has also been shown to accurately identify LVSD based on a single lead ECG from a digital stethoscope recording (Bachtiger et al, 2022). This technology and AI analysis of both audio and ECG data is currently being tested in a multicentre randomised controlled trial of over 200 primary care practices in the UK (NCT05987670). This simple, point-of-care technology could potentially improve the identification of patients who need an echocardiogram, help risk stratify timing of echocardiography, or exclude patients who do not require further investigation.

Biomarkers

Biomarkers, specifically natriuretic peptides, are crucial in any diagnostic pathway and provide an excellent 'rule-out' test. However, some patients may be disenfranchised by this strategy, in particular patients with obesity. Patients with obesity and HF have relatively lower natriuretic peptide levels and could be excluded from access to HF diagnostics using the current NICE guidelines (Vaishnav et al, 2020). Ongoing studies are aimed at investigating if novel biomarkers, or combinations of biomarkers, may be useful in patients with obesity and suspected HF (NCT06101693). Another recent technological advancement that could be deployed in diagnostic pathways is point-of-care natriuretic testing. Conventional

pathways involve a full blood draw in primary care, and a sample analysed in secondary care, with invariable delays of days before a result can be available. Point-of-care NTproBNP testing, performed on a finger prick rather than a venous sample, could reduce this time from days to minutes, which could be a crucial time saving and reduce time to diagnosis, and ultimately time to treatment initiation (Larsson and Eriksson, 2023).

Echocardiography

Despite pathways utilising biomarkers, and potentially AI-ECG in the near-future, to better triage those who require further testing, echocardiography remains the 'cornerstone' diagnostic test for HF. Echocardiography is essential to phenotype patients and guide therapy based on left ventricular ejection fraction (LVEF), into HF with reduced (LVEF $\leq$40%), mid-range (LVEF 41–49%), and preserved ejection fraction (LVEF $\geq$50%). As well as providing LVEF assessment, echocardiography allows detailed assessment of cardiac structure, right ventricular function, valvular function, and markers of diastolic function. Not only is echocardiography the critical diagnostic test, it is often the rate-limiting step in the diagnostic pathway, with long waiting lists and delays. AI-automated analysis of echocardiography is already possible, with automated analyses able to produce not only accurate results but also generate clinical reports (Elias et al, 2024). In addition to producing LVEF measurement, AI-automated analysis can also assist in the diagnosis of HFpEF (Akerman et al, 2023). There are also preliminary data suggesting that AI may assist in the acquisition of echocardiographic images, and even assist non-experts to acquire images (Huang et al, 2024; Tromp et al, 2023). AI-automated analysis could offer significant improvements in workflow efficiency and could increase scanning capacity, by reducing the time taken to report scans. However, despite the exponential increase in number of studies and publications of AI echocardiography, there are minimal clinical trials and studies demonstrating improved patient outcomes when these are deployed into clinical practice. With further improvements and iterations of AI-automated analyses, and better workflow integration, this could potentially translate into benefits for patients.

Predictive Models

Although the use of natriuretic peptides can effectively risk stratify patients, the addition of clinician triage to a diagnostic pathway can also add value and further streamline the diagnostic pathway (Morton et al, 2021). It may be that this process can be further enhanced by using risk modelling instead of expert review, to more accurately identify and triage patients at the highest risk and target these patients for urgent assessment. The Collaboration for the Diagnosis and Evaluation of Heart Failure (CoDE-HF) risk model utilised a machine-learning algorithm to combine NTproBNP with clinical variables to create a risk model which estimates the risk of HF (Lee et al, 2022). Incorporation of accurate risk models into a diagnostic pathway could provide further efficiency and possible cost savings, rather

than relying on NTproBNP or expert clinician triage alone, although this requires testing in clinical trials to demonstrate a clinical benefit.

Conclusion

The future of diagnostics in HF will likely involve the integration of technological advancements, in particular AI, to better triage timing of echocardiography, and echocardiography itself will likely be accelerated. These integrations hold great promise for the early commencement of disease-modifying therapies, and ultimately better patient outcomes.

Key Points

- Heart failure affects 1–2% of the population and is associated with a poor prognosis.
- Early diagnosis and treatment improve patient outcomes.
- Current pathways utilise natriuretic peptides to triage assessment.
- Echocardiography is the key diagnostic test, often associated with lengthy waiting times.
- Future pathways will likely incorporate artificial intelligence to triage assessments, streamline workflows including echocardiography analysis, and potentially reduce time to diagnosis.

Availability of Data and Materials

Not applicable.

Author Contributions

AM and RTC designed the editorial. AM drafted the manuscript. Both authors contributed to important editorial changes of important content in the manuscript. Both authors read and approved the final manuscript. Both authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

Not applicable.

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Conflict of Interest

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