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EDITORIAL

Echocardiography: Navigating Complexities to Provide Many Useful Applications in Contemporary Clinical Cardiology

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Echocardiography has been around for more than half a century [1]. Recent decades have seen significant technological advances, with increasing clinical applications of this non-invasive imaging tool, beyond the basic assessment of left ventricular function, with further evolution evident on the horizon. There has also been a burgeoning increase in use: According to the 2017 Australian Medicare Medical Benefits Schedule (MBS) Taskforce, about 900,000 echocardiographic procedures (excluding stress echo) are reimbursed annually, at a cost of over $180 million each year [2]. In addition, the use of echo is growing at a rate of about 8.8% each year [3]. Stress echocardiography accounts for over $56 million in billing annually in Australia and has grown each year at a rate of 12% for the past 5 years [4]. In recognition of this expanding use, this fully commissioned Special Issue of *Heart, Lung and Circulation* presents an overview of contemporary practice in echocardiography.

In a Leading Editorial, Marwick identified the key advances of the last decade as being 3D imaging and myocardial deformation imaging (strain); further, that the processes of miniaturisation and automation have led to three dimensional (3D) transoesophageal echocardiography as well as handheld ultrasound [5].

Stress echocardiography is a long-established imaging modality in evaluation of coronary artery disease, with the advantages of lower cost, greater availability and a lack of radiation exposure when compared with newer imaging modalities like single photon emission computed tomography (SPECT), cardiac magnetic resonance (CMR) and computed tomography (CT) coronary angiography (CTCA). Quah and colleagues report that recent years have seen an evolution of use to include the assessment of non-ischaemic cardiac disease, particularly stenotic and regurgitant valvular disease but also, potentially, in hypertrophic

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cardiomyopathy and pulmonary hypertension [4]. It is the ability of stress echo to assess functional capacity and real time haemodynamic changes with exercise or pharmacological stress that can help to guide therapy and inform prognosis. For example, in patients with ''asymptomatic'' severe aortic stenosis (AS), stress echocardiography can unmask symptoms, and assist in decision-making regarding valve intervention. The utility of supplementary techniques such as contrast-enhanced, 3D and diastolic stress echocardiography is also reviewed [4].

Left ventricular (LV) ejection fraction (LVEF) is the most commonly used echocardiographic parameter to quantify LV systolic function, with significant implications for patient management (e.g., in selecting patients for device insertion and valve surgery) and prognosis. However, LVEF is considered a ''coarse'' measure of global function with several other limitations, including the geometric assumptions made in its calculation [6]. Trivedi and colleagues explain that strain analysis, a measure of myocardial deformation, has recently come to the forefront as a more sensitive measure of myocardial function. Strain analysis can detect early, subclinical LV dysfunction and define regional variation in specific cardiomyopathies; global longitudinal strain (GLS) has been shown to be superior to LVEF in cardiotoxicity prediction [7]. Accordingly, the use of strain analysis in clinical practice—in particular, GLS—is increasing and has recently been addressed in an expert consensus document [8].

Three dimensional imaging allows direct *en face* and anatomical views of cardiac structures, circumventing the geometric assumptions inherent in 2D techniques. Poon and colleagues [9] advocate a focussed 3D echo study after a full 2D study, to allow quantification of LV volumes and ejection fraction. They also advise that 3D echo is superior to 2D echo in the assessment of mitral valve pathologies and atrial septal defects.

Alongside the technological advances, we have seen increasing applications of echocardiography in various clinical settings. In their review, Perry and Selvanayagam demonstrate the usefulness of echocardiography in patients with abnormal thickening of the LV walls due to cardiac involvement in infiltrative diseases such as amyloidosis, sarcoidosis and the potentially reversible Anderson-Fabry disease [10]. Advanced echocardiographic techniques may be especially helpful, both for the diagnosis and differentiation of the various aetiologies. For example, strain and strain rate are sensitive in assessing early LV systolic dysfunction in amyloid heart disease, with a specific strain ''pattern'' demonstrated—a severe impairment of basal longitudinal strain, although with preserved strain in the apical region. Amyloid deposition in the right ventricle (RV) occurs later than in the LV, and is indicative of a worse prognosis. In cardiac sarcoidosis, although Perry and Selvanayagam say more research is required, speckle tracking strain shows promise in detecting the condition, and particularly in patients who do not have access to, or who have a contraindication to CMR or position emission tomography [10]. In Anderson-Fabry disease, tissue Doppler imaging (TDI) may indicate cardiomyopathy progression and assist with the decision for early intervention with enzyme replacement therapy.

The evolution of guidelines in the assessment of diastolic function is described by Prasad and colleagues [11]. They say the development of algorithms was driven by the need for a simple, ''standardised'' approach with improved inter-observer agreement and forecast further development, including assessments involving exercise echocardiography.

A paradigm shift is occurring in the assessment of the RV from a simple, qualitative visual assessment on echocardiography to a more sophisticated routine quantification of parameters of RV structure and function, despite technical difficulties related to its complex, roughly triangular shape that wraps around the left ventricle [12,13]. As one of many examples of clinical utility, dimensions of the right ventricular outflow tract (RVOT) may be used as part of the revised diagnostic criteria for arrhythmogenic right ventricular cardiomyopathy [14]. Right ventricle function is also gaining recognition in the prognosis of various cardiac conditions, including heart failure [15]. Current best practice recommends the use of at least two quantitative assessments during routine transthoracic echocardiography (TTE) [16]. Jones et al. explain the available parameters and recommend the routine measurement of more than two, including structural RV basal and RVOT proximal dimensions, and functional fractional area change (FAC) and tricuspid annular plane systolic excursion (TAPSE). TAPSE measures right ventricular longitudinal shortening and is a surrogate of systolic function [13]. With further technical development in 3D and strain imaging, more assessment may become routine [12,13].

Echocardiographic techniques can also be employed to estimate pulmonary artery pressure and resistance, and right atrial pressure, and to derive indirect information about right heart structure and function, as stated in Cordina and colleagues' review [13]. This allows echocardiography to play an essential role as a screening tool for pulmonary hypertension, although cardiac catheterisation is still required for a formal diagnosis. As well as providing direct and indirect evidence of pulmonary hypertension, potential causes such as congenital heart disease or left ventricular diastolic dysfunction may be identified; echocardiographic parameters also have a developing role in monitoring therapy and as a prognostic marker. Cordina and colleagues discuss the use of additional echocardiographic tools in the setting of pulmonary hypertension including transoesophageal echocardiography (e.g., when a congenital shunt is suspected) and the use of agitated saline administered via a peripheral vein (i.e., a bubble test) to assess the degree of right to left shunting in patients who have hypoxaemia out of proportion to the degree of lung parenchymal or pulmonary vascular disease. They also discuss the currently controversial role for exercise and dobutamine stress echocardiography in the diagnosis of pulmonary hypertension [13].

Echocardiography is essential in the assessment of cardiac heart disease. Chong and colleagues emphasise that contemporary imaging assessment of aortic stenosis (AS) requires a multi-parametric approach that needs critical attention to

detail when performing and analysing fundamental echocardiographic haemodynamic criteria [17]. When there is discordance between the clinical symptoms and imaging results, further measures are needed. In low-flow low-gradient AS, additional functional testing in the form of dobutamine stress echocardiography (DSE) to augment stroke volume and flow can confirm the haemodynamic severity of AS. Low-dose DSE is the recommended investigation to distinguish true anatomically severe AS from apparent pseudo-severe AS; it can also determine the presence of contractile reserve in patients with reduced ejection fraction, relevant to overall clinical prognosis [17].

Vollema and colleagues overview the clinical applications and current role of echocardiographic techniques in patient selection, prosthesis sizing, periprocedural guidance and post-procedural follow-up in transcatheter aortic valve replacement (TAVR) [18]. Transthoracic, transoesophageal and, less commonly, intracardiac echocardiography are important imaging techniques in assisting the TAVR procedure itself. Transoesophageal echocardiology, in particular, can be used to investigate the suspected complication of endocarditis—for the detection of vegetations, abscesses or pseudoaneurysms, and to assess potential involvement of the mitral or tricuspid valve [18].

Although many current guidelines assist in making management decisions in valvular heart disease, Venneri and colleagues explain that such guidelines may not be adequate in managing the varying clinical scenarios of multivalvular heart disease—which is not only highly prevalent but also associated with significant morbidity and mortality [19,20]. The haemodynamic interactions between valves may interfere with several Doppler parameters, previously validated only in patients with a single-valve disease [21]. In these circumstances, they say a multidisciplinary Heart Valve Team is of paramount importance in assessing patients, alongside advanced echocardiography and multimodal imaging. An accurate echocardiographic diagnosis will need to combine different measurements, factoring for co-existent conditions. For example, in degenerative disease, heavy mitral calcification can cast acoustic shadows that prevent visualisation of colour-flow jets (i.e., off-axis views may be needed). Inaccurate conclusions can have significant clinical consequences: for example, in combined AS and mitral stenosis (MS), underestimating the severity of AS can lead to dramatic consequences—isolated relief of MS would suddenly increase preload to a small, hypertrophied, stiff left ventricle, resulting in pulmonary oedema. In the assessment of multiple prostheses, the use of multiple and sometimes off-axis views is critical, to overcome the problem of acoustic shadowing, reverberations and mirror artefacts that are more pronounced for mechanical valves.

Many of the reviews in this Special Issue advise that the role of Echocardiography has expanded from evaluation for diagnostic purposes to a more comprehensive evaluation of the clinical problem—from initial screening to the detection of the disease, to surveillance and management and review of management, to prognosis. The new sub-specialty of cardio-oncology displays this broad spectrum of relevant application. Negishi and colleagues highlight that the emergence of cardio-oncology is a result of the paradigm shift from considering cancer as a ''terminal illness" to a ''chronic condition"—and, one with cardiovascular risks [22]. Cardio-oncology focusses on the risk stratification, prevention, early identification and treatment of cardiovascular complications related to cancer therapy. Three settings of echocardiographic screening for patients with cancer are outlined: baseline (before cardiotoxic chemotherapy), during chemotherapy and after the completion of chemotherapy, and the best use of cardioprotective medications is discussed. With respect to risk stratification, one of the complexities is that the several clinical practice guidelines share similar concepts but also some important areas of difference—such as the cut-off values for cumulative dose of anthracyclines. Negishi and colleagues state the important caveat that, although a dose-dependent association between anthracyclines and cardiotoxicity has been established, no safety threshold exists. Currently underway, the prospective, international, multicentre randomised controlled trial, *Strain sUrveillance during Chemotherapy for improving Cardiovascular Outcomes* (SUCCOUR) *Study*, is testing the hypotheses that information from echocardiographic strain imaging leads to the use of adjunctive cardioprotective therapy that will limit, i) the development of LV dysfunction, ii) interruptions of planned chemotherapy and iii) the development of heart failure during follow-up [23].

Alongside the technological advances and broadening clinical applications in use, questions of workforce and access to echocardiography in resource poor settings have arisen. Brown and colleagues [24] remind us that, in addition to increase in clinical demand, our populations are ageing and survival from cardiovascular (CV) diseases is improving; as a result, the number of older patients with pre-existing CV disease needing echocardiographic evaluation is also growing. Due to these increasing demands, future training and practice models are likely to evolve. Brown and colleagues envision an echocardiography laboratory of the future where much of the measurement and analysis of echocardiograms can be performed off-line, and where new technologies, such as 3D and speckle tracking will be incorporated into clinical guidelines; they say there is no doubt that artificial intelligence, machine learning and robotics will change the way echocardiographers work [24].

Marangou and colleagues remind us that the majority of the global CV disease burden occurs in low- and middle-income countries (LMIC) and indigenous populations [25]. Apart from the major cardiac conditions, like ischaemic heart disease and heart failure, other neglected diseases—like rheumatic heart disease (RHD) in Oceania (including Australia and New Zealand), Sub-Saharan Africa and South Asia; endomyocardial fibrosis in the tropical areas of Saharan Africa, Asia and Latin America, and Chagas cardiomyopathy, especially in Latin America—exact a tremendous toll on human life and its quality.

In rheumatic heart disease, exercise stress echocardiography is useful in the evaluation of mitral valve stenosis when basic echocardiographic data and clinical symptoms are discordant [26]. In Chagas disease, caused by the protozoan *Trypanosoma cruzi*, echocardiography is the most commonly used imaging modality for assessment of patients [27].

Disease screening is challenging, and especially so in resource limited regions. However, Mangalou and colleagues state that echocardiographic screening is our best weapon to detect RHD in those high-risk individuals who develop RHD without a clinical documented episode of rheumatic fever, as early implementation of secondary prophylaxis is known to be the most cost-effective method of halting disease progression and allowing for disease resolution [25].

In the developed world, it is easy to take access to health care for granted; however, for most of the world's population living in resource-limited locations, access to echocardiography and availability of trained sonographers to perform echocardiograms can be restricted. In these settings, handheld echocardiography may be developed, thereby causing a shift in service provision.

As Brown and colleagues say, we are beginning to appreciate that the future is likely to involve multi-modal imaging where echocardiography plays its role alongside other modalities, like CMR and cardiac CT. Further, echocardiography equipment will continue to become more specialised and powerful but simultaneously simpler, as in the case of handheld transducers allowing for clinician-performed ultrasound [24]. Measurements performed are likely to be more automated with the significant increase in artificial intelligence, which will improve test-retest variability and improve reproducibility.

Marwick steers our way forward by reminding us that ultrasound is the least expensive, most accessible and environmentally friendly cardiac imaging modality, and that it will have an ongoing, wide role in clinical cardiology. Among future challenges, Marwick includes the uniform adoption of advances in Australian clinical practice for indications such as heart failure, AS, pulmonary hypertension, mitral regurgitation, and known or suspected coronary disease [5]. Our hope is that the guidance provided in this Special Issue will assist clinicians to fully appreciate the expanding role that advanced echocardiography can play in contemporary clinical practice.

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