INTRODUCTION

Myocardial infarction (MI) can be recognized by clinical features, including electrocardiographic (ECG) findings, elevated values of biochemical markers (biomarkers) of myocardial necrosis, and by imaging, or may be defined by pathology.

It is a major cause of death and disability worldwide. MI may be the first manifestation of coronary artery disease (CAD) or it may occur, repeatedly, in patients with established disease[1].

Acute MI results in left ventricular (LV) both systolic and diastolic dysfunction in survivors. During the early phases of MI 38% of patients have impaired relaxation and 24% of patients have restrictive LV filling pattern[2]. Diastolic function can be evaluated with several noninvasive and invasive techniques. Tissue Doppler imaging (TDI) derived indices, including systolic velocity (S), early (Em) and late (Am) diastolic velocities of mitral annulus and early mitral inflow peak velocity (E)/Em ratio are sensitive and widely used parameters to estimate LV filling pressures[2].

The left atrium (LA) plays a major role in LV performance. LA function is a surrogate marker of LV diastolic dysfunction. LA mechanical dysfunction occurs in LV systolic and diastolic dysfunction, coronary artery disease, MI, hypertension, aortic stenosis and cardiomyopathies. In the MI process, the contribution of the LA to LV function may increase if the cardiac myocytes are not affected by direct ischemia. However, myocyte necrosis or ischemia of the LA or significant LV systolic/diastolic dysfunction affects this booster effect. Assessment of LA size and function provides prognostic data for the outcome of patients with MI or ischemia[3].

LA function has been conventionally divided into three phases first, as a reservoir, the LA stores pulmonary venous return during LV contraction and isovolumetric relaxation. Secondly, as a conduit, the LA transfers blood passively into the LV. Thirdly, the LA actively contracts during the final phase of diastole and contributes between 15 and 30% of LV stroke volume. As a continuum of the LV, especially during diastole, its size and function are very much influenced by the compliance of the LV[4].

Left atrial dilatation is well recognized as a strong predictor of adverse outcome, after acut MI and in a range of other cardiac pathologies. The LA is directly exposed to LV cavity pressure during diastole, thus an enlarged LA is a robust marker of increased LV filling pressure in absence of LA volume overload, which provides a causal link between LA dilatation and poor outcome[5].

Traditionally, assessment of LA function has been performed by measuring LA size or volume with two-dimensional (2D) echocardiography. Doppler echocardiographic measurements such as transmitral and pulmonary venous flow can also be used[6,7]. Currently, a method known as strain imaging is used for the quantitative assessment of myocardial deformation[8].

It has been shown that non-Doppler strain imaging is a feasible and reproducible method to assess LA function[9,10]. The LA function is closely related to the ventricular function throughout the cardiac cycle. During ventricular systole, the longitudinal

shortening of the ventricular base increases the filling of the LA from the pulmonary veins. In diastole, the LA contributes to the filling of the LV through both active and passive emptying. Moreover, the LA emptying function might be strongly affected by LV diastolic properties due to the direct interaction of ventricular pressures through the open mitral valve during diastole[(11)].

For this reason, impairment of LV systolic and/or diastolic functions might impair LA function. Impairment of LV systolic and/or diastolic function, with consequent rise in LV end-diastolic pressure (LVEDP), may eventually cause some structural and functional changes in the LA[(12)].

Definition of acute myocardial infarction

The current international consensus definition states that the term 'acute myocardial infarction' (AMI) should be used when there is evidence of myocardial necrosis in a clinical setting consistent with myocardial ischemia[(13)].

Under these conditions, any one of the criteria described in Table (1) meets the diagnosis for spontaneous myocardial infarction.

Table (1) Universal definition of myocardial infarction[(13)]

Detection of rise and/or fall of cardiac biomarker values (preferably troponin) with at least one value above the 99th percentile of the upper reference limit and with at least one of the following: • Symptoms of ischaemia; • New or presumably new significant ST-T changes or new LBBB; • Development of pathological Q waves in the ECG; • Imaging evidence of new loss of viable myocardium, or new regional wall motion abnormality; • Identification of an intracoronary thrombus by angiography or autopsy.
Cardiac death with symptoms suggestive of myocardial ischaemia, and presumably new ECG changes or new LBBB, but death occurring before blood cardiac biomarkers values are released or before cardiac biomarker values would be increased.
Stent thrombosis associated with MI when detected by coronary angiography or autopsy in the setting of myocardial ischaemia and with a rise and/or fall of cardiac biomarker values with at least one value above the 99th percentile URL.

ECG = electrocarciogram; LBBB = left bundle branch block.
[a]Excluding myocardial infarction associated with revascularization procedures or criteria for prior myocardial infarction.

Epidemiology of st-segment elevation MI

Worldwide, coronary artery disease (CAD) is the single most frequent cause of death. Over seven million people every year die from CAD, accounting for 12.8% of all deaths[(14)].

Every sixth man and every seventh woman in Europe will die from myocardial infarction. The incidence of hospital admissions for AMI with ST-segment elevations (STEMI) varies among countries that belong to the European society of cardiology (ESC)[15]. The most comprehensive STEMI registry is probably in Sweden, where the incidence is 66 STEMI/100,000/ year. Similar figures were also reported in the Czech Republic, Belgium[15] and the USA[16].

The incidence rates (per 100,000) of STEMI decreased between 1997 and 2005 from 121 to 77, whereas the incidence rates of non-STEMI increased slightly from 126 to 132. Thus, the incidence of STEMI appears to be declining, while there is a concomitant increase in the incidence of non-STEMI[17].

The mortality of STEMI is influenced by many factors, among them: age, Killip class, time delay to treatment, mode of treatment, history of prior myocardial infarction, diabetes mellitus, renal failure, number of diseased coronary arteries, ejection fraction, and treatment. The in-hospital mortality of unselected STEMI patients in the national registries of the ESC countries varies between 6% and 14%.[18].

Several recent studies have highlighted a fall in acute and long-term mortality following STEMI, in parallel with greater use of reperfusion therapy, primary percutaneous coronary intervention (primary PCI), modern antithrombotic therapy and secondary prevention treatments[16,19,20]. Still, mortality remains substantial with approximately 12% of patients dead within 6 months[20], but with higher mortality rates in higher-risk patients[21], which justifies continuous efforts to improve quality of care, adherence to guidelines and research.

Initial diagnosis

A working diagnosis of myocardial infarction must first be made. This is usually based on:

History of chest pain lasting for 20 minutes or more, not responding to nitroglycerine. Important clues are a history of CAD and radiation of the pain to the neck, lower jaw or left arm. The pain may not be severe. Some patients present with less-typical symptoms, such as nausea/vomiting, shortness of breath, fatigue, palpitations or syncope. These patients tend to present later, are more likely to be women, diabetic or elderly patients, and less frequently receive reperfusion therapy and other evidence-based therapies than patients with a typical chest pain presentation. Registries show that up to 30% of patients with STEMI present with atypical symptoms[22].

Awareness of these atypical presentations and a liberal access to acute angiography for early diagnosis might improve outcomes in this high-risk group. Timely diagnosis of STEMI is key to successful management.

ECG monitoring should be initiated as soon as possible in all patients with suspected STEMI to detect life-threatening arrhythmias and allow prompt defibrillation if indicated. A 12-lead ECG should be obtained and interpreted as soon as possible at the point of first medical contact (FMc) Table (2) [23].

Table (2): Recommendation for initial diagnosis[23].

Recommendations	Class [a]	Level [b]
A 12-lead ECG must be obtained as soon as possible at the point of FMC, with a target delay of ≤10 min.	I	B
ECG monitoring must be initiated as soon as possible in all patients with suspected STEMI.	I	B
Blood sampling for serum markers is recommended routinely in the acute phase but one should not wait for the results before initiating reperfusion treatment.	I	C
The use of additional posterior chest wall leads (V_7–V_9 ≥0.05 mV) in patients with high suspicion of infero-basal myocardial infarction (circumflex occlusion) should be considered.	IIa	C
Echocardiography may assist in making the diagnosis in uncertain cases but should not delay transfer for angiography.	IIb	C

ECG = electrocardiogram; FMC = first medical contact; STEMI = ST-segment elevation myocardial infarction.
[a]Class of recommendation.
[b]Level of evidence.

Even at an early stage, the ECG is seldom normal. Typically, ST-segment elevation in acute myocardial infarction, measured at the J point, should be found in two contiguous leads and be ≥0.25 mV in men below the age of 40 years and ≥0.2 mV in men over the age of 40 years, or ≥0.15 mV in women in leads V2–V3 and/or ≥0.1 mV in other leads (in the absence of left ventricular (LV) hypertrophy or left bundle branch block (LBBB)[13].

In patients with inferior myocardial infarction, it is advisable to record right precordial leads (V3R and V4R) seeking ST elevation, in order to identify concomitant right ventricular infarction[13,24]. Likewise, ST-segment depression in leads V1–V3 suggests myocardial ischemia, especially when the terminal T-wave is positive (ST-elevation equivalent), and may be confirmed by concomitant ST elevation ≥0.1 mV recorded in leads V7–V9[13].

The ECG diagnosis may be more difficult in some cases (Table 3), which nevertheless deserve prompt management. Among these:

1. BBB: in the presence of LBBB, the ECG diagnosis of acute myocardial infarction is difficult, but often possible if marked ST abnormalities are present. Somewhat complex algorithms have been offered to assist the diagnosis[25]. but they do not provide diagnostic certainty[26]. The presence of concordant ST elevation (i.e. in leads with positive QRS deflections) appears to be one of the best indicators of ongoing myocardial infarction with an occluded infarct artery[27].

   Previous data from thrombolysis trials have shown that reperfusion therapy is beneficial overall in patients with LBBB and suspected myocardial infarction. However, most LBBB patients evaluated in the emergency department do not have an acute coronary occlusion, nor do they require primary PCI. A previous ECG may be helpful in determining whether the LBBB is new (and, therefore, the suspicion of ongoing myocardial infarction is high). Importantly, in patients with clinical suspicion of ongoing myocardial ischemia with new or presumed new LBBB, reperfusion therapy should be considered promptly, preferably using emergency coronary angiography with a view to primary PCI or, if unavailable, intravenous (i.v.) thrombolysis. A positive point-of-care troponin test 1–2 h after symptom onset in patients with BBB of uncertain origin may help decide whether to perform emergency angiography with a view to primary PCI. Patients with myocardial infarction and right bundle branch block (RBBB) also have a poor prognosis[28]. Although RBBB usually will not hamper interpretation of ST-segment elevation. Prompt management should be considered when persistent ischemic symptoms occur in the presence of RBBB, regardless of whether or not the latter is previously known.

2. Ventricular pacing may also prevent interpretation of ST-segment changes and may require urgent angiography to confirm diagnosis and initiate therapy. Reprogramming the pacemaker - allowing an evaluation of ECG changes during intrinsic heart rhythm - may be considered in patients known not to be dependent on ventricular pacing, without delaying invasive investigation[13].

3. Patients without diagnostic ECG: some patients with acute coronary occlusion may have an initial ECG without ST-segment elevation, sometimes because they are seen very early after symptom onset (in which case, one should look for hyper-acute T waves, which may precede ST-segment elevation). It is important to repeat the ECG or monitor the ST segment. In addition, there is a concern that some patients with genuine acute occlusion of a coronary artery and ongoing myocardial infarction (such as those with an occluded circumflex coronary Artery[29,30], acute occlusion of a vein graft, or left main disease), may present without ST-segment elevation and be denied reperfusion therapy, resulting in larger infarction and worse outcomes. Extending the standard 12-lead ECG with V7–V9 leads, while useful, does not always identify these patients. In any case, ongoing suspicion of myocardial ischemia—despite medical therapy-is an indication for emergency coronary angiography with a view to revascularization, even in patients without diagnostic ST-segment elevation.[31].

4. Isolated posterior myocardial infarction: Acute myocardial infarction of the infero-basal portion of the heart, often corresponding to the left circumflex territory in which isolated ST-depression ≥0.05 mV in leads V1 through V3 represents the dominant

finding, should be treated as a STEMI. The use of additional posterior chest wall leads [V7–V9 ≥0.05 mV (≥0.1 mV in men < 40 years old)] is recommended to detect ST elevation consistent with infero-basal myocardial infarction[32].

5. Left main coronary obstruction-lead aVR ST elevation and inferolateral ST depression: The presence of ST-depression >0.1 mV in eight or more surface leads, coupled with ST elevation in aVR and/or V1 but an otherwise unremarkable ECG, suggests ischemia due to multivessel or left main coronary artery obstruction, particularly if the patient presents with hemodynamic compromise[33].

In patients with a suspicion of myocardial ischemia and ST-segment elevation or new or presumed new LBBB, reperfusion therapy needs to be initiated as soon as possible. However, the ECG may be equivocal in the early hours and, even in proven infarction, may never show the classical features of ST-segment elevation and new Q waves. If the ECG is equivocal or does not show evidence to support the clinical suspicion of myocardial infarction, ECGs should be repeated and, when possible, the current ECG should be compared with previous tracings. Additional recordings of, for example, lead V7, V8 and V9 may be helpful in making the diagnosis in selected cases[32].

Table (3): Atypical ECG presentations that deserve prompt management in patients with signs and symptoms of ongoing myocardial ischemia

• LBBB
• Ventricular paced rhythm
• Patients without diagnostic ST-segment elevation but with persistent ischaemic symptoms
• Isolated posterior myocardial infarction
• ST-segment elevation in lead aVR

ECG = electrocardiogram; LBBB = left bundle branch block.

Blood sampling for serum markers is routinely carried out in the acute phase but one should not wait for the results before initiating reperfusion treatment. Troponin (T or I) is the biomarker of choice, given its high sensitivity and specificity for myocardial necrosis. In patients who have both a clinically low or intermediate likelihood of ongoing myocardial ischemia and a long prior duration of symptoms, a negative troponin test may help to avoid unnecessary emergency angiography in some patients[32].

Emergency imaging: If in doubt regarding the possibility of acute evolving myocardial infarction, emergency imaging (as opposed to waiting for the biomarkers to become elevated) allows the provision of timely reperfusion therapy to these patients. If locally available, emergency coronary angiography is the modality of choice, as it can be followed immediately by primary PCI if the diagnosis is confirmed. In hospitals or settings in which coronary angiography is not immediately available - provided it does not delay

transfer - rapid confirmation of segmental wall-motion abnormalities by two dimensional echocardiography may assist in making a decision for emergency transfer to a PCI centre, since regional wall-motion abnormalities occur within minutes following coronary occlusion, well before necrosis. However, wall-motion abnormalities are not specific to acute myocardial infarction and may be due to other causes such as ischemia, an old infarction or ventricular conduction defects.

Two-dimensional echocardiography is of particular value for the diagnosis of other causes of chest pain, such as pericardial effusion, massive pulmonary embolism or dissection of the ascending aorta. The absence of wall-motion abnormalities excludes major myocardial infarction. In the emergency setting, the role of computed tomography (CT) scan should be confined to differential diagnosis of acute aortic dissection or pulmonary embolism[32].

Left atrial function: Physiology, assessment, and clinical implications

The thin walled left atrium (LA) is sensitive to changes in left ventricular (LV) filling pressure, related in particular to LV diastolic dysfunction. The LA is a marker not only of the severity of LV diastolic function, but also of its chronicity. Several studies have demonstrated that LA volume is a robust marker of adverse cardiovascular outcomes. Serial measurements of LA volume (and atrial function parameters) may be used to follow disease progression and response to therapy.

The primary role of the LA is to maintain optimal LV filling and cardiac output, despite changes in LV compliance[34]. LA volume has been used as a surrogate measure of LV diastolic dysfunction[35,36], and has been utilised as a marker of the severity and duration of LV diastolic dysfunction[37].

There is extensive literature relating the predictive value of LA size to cardiovascular outcomes in the general population and in various high-risk groups. The Strong Heart study, using a population based cohort, showed that LA diameter independently predicted cardiovascular events, including nonfatal stroke, coronary heart disease, heart failure and cardiovascular mortality (risk ratio 1.04/mm, 95% CI : 1.02-1.07, $p<0.002$)[38].

Similarly LA volume independently predicted mortality in patients with heart failure, above clinical and other echocardiographic variables[39].

LA enlargement has also been associated with atrial fibrillation (AF), hypertension, survival post myocardial infarction and stroke[38]. There are however, still significant gaps in our understanding of atrial function in both health and cardiovascular disease.

Left atrial physiology

The LA has multiple functions in order to maintain optimal LV filling in response to changing hemodynamic[7]. These phasic atrial functions can modify as an adaptive mechanism in a variety of conditions with altered LV diastolic function.

- Conduit function

The LA functions as a conduit that passively transfers blood along a pressure gradient, from the pulmonary veins to the LV, until the pressure equilibrates during

diastasis. The LA conduit phase reflects passive atrial emptying. Conduit function is a complex process determined by ventricular relaxation and influenced by atrial compliance[40]. Altered LV diastolic function results in reduced suction into the LV, and subsequently reduced atrial conduit function[41].

- Contractile function

The atria actively contract during late ventricular diastole, to augment ventricular filling[42]. Active atrial contraction contributes up to 30% of overall cardiac output, and is of particular importance in patients with LV dysfunction. For instance in patients following myocardial infarction, LV ejection fraction correlated inversely with LA contractility[34].

Atrial contractile function is increased in the presence of impaired ventricular relaxation, as a compensatory mechanism to augment volume filling the LV, especially in instances where reduced LV compliance results in decreased early diastolic ventricular filling[43].

- Reservoir function

The LA acts as a reservoir, storing pulmonary venous blood returned during ventricular systole[6,44]. LA reservoir function is also a complex process involving the storage of volume and energy in two stages; early LA relaxation and later LA compliance and ventricular contraction[45,46]. Early LA relaxation may be enhanced in conjunction with augmented active contractility consequent to impaired LV relaxation[47]. This may be followed by reduced atrial compliance in the late reservoir phase via alterations in calcium proteins or endocardial fibrosis[48].

Measurements of left atrial function

Measurement of atrial function is not simple, and there are no established gold standards.

- Doppler measurements

Traditionally, Doppler measurements of flow through the mitral valve and pulmonary veins were used as surrogate markers of atrial function[49,50]. However these techniques are only surrogate measures of blood flow and are dependent on age and instantaneous loading conditions[51], thereby limiting their accuracy. Additionally, these measurements can be affected by respiration, and enable analysis only of atrial contractile function; excluding assessment of conduit or reservoir phases.

Tissue Doppler derived late diastolic mitral annular velocity (A' velocity), associated with atrial contractile function, has also been utilised to predict adverse cardiovascular events, including death and heart failure. It has been demonstrated that an A' velocity of less than 5cm/s was a better predictor than clinical, hemodynamic or other echocardiographic variables in patients with either ischemic or non-ischemic dilated cardiomyopathy[52].

- Volume measurements

Left atrial volume can be used as a surrogate measure of atrial function, is relatively independent of loading conditions, and reflects the severity and duration of increased LA pressure[37]. Additionally, volume assessment of the LA enables quantification of phasic atrial function[6,53]. Numerous reviews on this subject have previously described the utility of maximum and phasic LA volume measurements[4,6,11,54].

Measurement of LA volumes have been included in the recommendations by the American Society of Echocardiography (ASE), to be performed in all clinical echocardiographic studies,[55] and are used in the algorithm to grade LV diastolic function[56]. LA size is emerging as a biomarker of LV diastolic function and of cardiovascular disease[38].

In elderly populations with no previous cardiovascular events, LA enlargement has been shown to be an independent predictor of cardiovascular outcomes, including myocardial infarction, congestive heart failure, need for revascularisation, stroke and death[38,57]. Additionally, LA size is important in conditions affecting the atria, with an incremental risk of developing AF as LA volume increases[58]. Therefore, LA volumes are useful in predicting outcomes. Additionally, changes in LA volume may be used to guide therapy (i.e. good control of blood pressure could result in LA reverse remodeling)[59].

Left atrial enlargement is a surrogate measure of the chronicity and severity of LV diastolic dysfunction[37]. In patients with isolated diastolic dysfunction LA enlargement has been associated with reduced exercise capacity[60].

Left atrial enlargement is common in the general population with an incidence of 16%, in residents over 45 years of age and including subjects with known cardiovascular disease (hypertension, myocardial infarction, congestive heart failure, coronary artery disease and atrial arrhythmias)[61].

Left atrial maximum volume is the currently recommended reference measure of atrial enlargement[55], although LA dimension is often referred to in the literature. M-mode derived LA diameter assessment is less accurate than volume measurements, particularly as there is asymmetric remodelling of the LA with enlargement[62]. Furthermore, LA indexed volume has a stronger association with the presence of cardiovascular disease than LA indexed diameter[61]. Biplane LA volume by echocardiography has been shown to correlate closely with cine computed tomography assessments[63]. However, echocardiographic methods have been shown to underestimate LA volumes compared to magnetic resonance imaging[64].

Three-dimensional (3D) echocardiographic techniques have been developed recently. There is good correlation between 2D biplane LA volumes and 3D LA volumes[65]. There are presently no accepted reference values for 3D LA volumes, or adequate literature on the incremental value of 3D LA volumes as a prognostic marker.

Left atrial phasic volumes can also be calculated using established formulae, based on volume measurements[66], including maximum, minimum and pre 'a' wave volumes. A recent study has shown that LA minimum volume correlated modestly with noninvasive estimates of LV filling pressure[67].

Furthermore, reduced LA reservoir function, as measured by LA total emptying fraction, has been shown to be an independent predictor of the first occurrence of atrial fibrillation[46].

- Strain measurements

Left atrial phasic volumes have been used as markers of atrial function, however these parameters are dependent on geometric assumptions[51,68], thereby limiting their accuracy.

Myocardial strain and strain rate measure intrinsic myocardial deformation, relatively independent of rotation and tethering effects. This technique has also been shown to be less load dependent than traditional parameters of LA function[69], providing a more sensitive and accurate assessment.

Strain and strain rate techniques enable the evaluation of phasic atrial function throughout the cardiac cycle[70]. Peak systolic strain and systolic strain rate serve as measures of LA compliance during the reservoir phase, early diastolic strain rate (Esr) as a measure of passive emptying during the conduit phase and late diastolic strain rate (Asr) as a measure of active atrial contraction.

Phasic atrial strain and strain rate measurements correlated with corresponding atrial volumetric fractions[71] and function[10] for atrial reservoir, conduit and contractile phases.

Atrial strain and strain rate have been utilised to accurately quantitate atrial function and remodelling in hypertension[72], hypertrophic cardiomyopathy[73], atrial septal defects[74], valvular stenosis[75] and AF[76]. In particular, the quantification of atrial reservoir function has emerged as an important predictor of maintenance of sinus rhythm following both cardioversion[77]and ablation for AF[78].

Additionally, atrial reservoir function measured by atrial strain has been shown to add predictive power for cardiovascular events following acute myocardial infarction[79]. Total atrial strain (sum of maximum positive and maximum negative atrial strain) in patients with hypertrophic cardiomyopathy with preserved LV systolic function, has been reported as the strongest predictor of 12-month outcomes, including the development of AF[80]. Furthermore, decreased systolic strain in the atrium has been associated with increased LV end-diastolic pressures[81] and is an important predictor of diastolic heart failure[82].

Strain measures can be performed using tissue Doppler or 2D speckle tracking analysis. Tissue Doppler derived strain measurements utilise high temporal resolution and are not limited by image quality but are angle dependent and require manual frame by-frame tracking, which is time consuming[4]. Conversely 2D strain imaging involves an automated speckle tracking technique[83], which is not angle dependent, but is reliant on high 2D image quality and is associated with lower temporal resolution[4]. Both strain software algorithms were developed primarily for assessment of LV function. Lower variability has been reported with 2D speckle tracking strain compared to tissue Doppler derived strain, although there is no consensus on the appropriate method of measuring atrial strain using the 2D speckle tracking technique[70].

The only study which directly compared these two strain techniques in the atrium was performed in a group of hypertrophic cardiomyopathy patients (n=43), demonstrating that 2D speckle tracking strain was more reproducible and less time consuming than tissue Doppler derived strain[84].

However, tissue Doppler analysis was performed from only two atrial segments, whilst 2D speckle tracking analysis was performed from six segments. Furthermore, only strain measurements were compared and not strain rate. The latter may have provided a more accurate analysis of phasic atrial function and therefore may require the higher temporal resolution associated with tissue Doppler techniques. Further studies are required to compare the validity and sensitivity of performing these two strain techniques in the thin walled LA that is imaged in the far field, particularly with reference to the impact of echocardiographic "drop out" corresponding to the pulmonary vein inlet, interatrial septum and the LA appendage[80].

- **Doppler derived strain and strain rate**

The information gained from color TDE can be used to measure strain and SR. Strain is a measure of tissue deformation and is defined as the change in length (L) of a myocardial segment referenced to its original length (Lo), as given by the following equation: strain = L – Lo/Lo[85].

When both Lo and L at any given time are known, it is referred to as Lagrangian strain. Natural strain is the term applied when L is referenced not to the original length but to the length at a given preceding time interval[86].

Tissue Doppler echocardiography generally measures natural strain, and magnetic resonance imaging measures Lagrangian strain[87]. There are other important differences between the 2 methods of measuring strain, but in practice TDE- and magnetic-resonance imaging– derived strain values appear comparable[88].

The rate at which this change occurs is called strain rate. SR = strain/time (s^{-1})[85]. SR can also be expressed as follows: SR =v1 – v2/d (s^{-1})[89], where (v) is instantaneous tissue velocity measured with TDE at 2 adjacent points of myocardium and (d) is the distance between them (also known as strain length).

Strain is calculated from TDE by measuring SR and integrating it over time[90]. By convention, myocardial lengthening is represented by positive strain and SR values and myocardial shortening by negative values.

Deformation in a 1-dimensional object, such as a thin bar, is limited to lengthening or shortening[85]. Strain is how much the bar is shortened or lengthened relative to its original length (i.e., reduction to half its original length is -50% strain, and an increase to one third longer is +33% strain). Strain rate is the speed at which this change occurs. Strain rate and strain are akin to shortening velocity and shortening fraction, respectively. Thus, to a certain extent, measurements otherwise restricted to experimental models can now be performed clinically[91].

In general, peak systolic strain rate is the parameter that comes closest to measuring local contractile function in clinical cardiology. It is relatively volume independent and is less pressure independent than strain. In contrast, peak systolic strain is volume dependent and does not reflect contractile function as well.

By TDI, strain rate is the difference in velocity between 2 points along the myocardial wall (velocity gradient) normalized to the distance between the 2 points[89]. A similar velocity gradient exists between the endocardium and the epicardium, because the endocardium moves faster. This concept is used to derive myocardial velocity gradient (radial strain rate)[92]. This velocity gradient depicts the rate of change of myocardial wall thickness during systole and diastole. Thus, strain rate measures the rate at which the 2 points of interest move toward or away from each other. Integration of strain rate yields strain, the normalized change in length between these 2 points.

Therefore, tissue velocity is obtained by interrogating a single point in the myocardium, with the reference point being the transducer on the chest wall. For strain rate, 2 points are interrogated in the myocardium. In the longitudinal direction, the points move closer to each other in systole and away from each other in diastole.

The use of strain (deformation) to examine the properties of the heart is not a new concept. Mirsky and Parmley[93], used strain to study the elastic properties of the myocardium.

A torsion or wringing motion also is present between the base and apex. When viewed from the apex, the apex rotates counterclockwise, and the base rotates clockwise in systole (twisting), with the opposite motion (untwisting) in diastole. Strain rate and strain are theoretically less susceptible to translational motion and tethering artifacts and thus may be superior to tissue velocity in depicting regional or global myocardial function.

Images are obtained using a narrow sector because of the thin atrial wall, about 5 mm superior to the atrio-ventricular junction. Images of the lateral and septal walls at high frame rate ~ 200 Hz are obtained from the four- chamber view[54,94]. Anterior and inferior walls from the two-chamber view can also be used[82,95,96].

It is critical to align the atrial wall parallel to the Doppler beam so that signal noise and angle artifacts can be avoided. Using dedicated software and an offline measuring station, the image is tracked frame by frame, ensuring that the sample volume for each frame is moved to its original location in the middle of the segment[54].

The normal longitudinal SR values for LA lateral and anterior and inferior walls were first described in 2006[71], and subsequently, it was also reported 13 segment strain and SRs of healthy persons and confirmed the reproducibility of this method of LA function assessment[97].

Strain curves are monophasic, whereas strain rate curves are triphasic. Negative velocities represent myocardial motion away from the ventricular apex during diastole[95,98]. Peak LA systolic strain and strain rates are used to quantitate global and regional LA contractility[94,99]. A limitation of strain imaging involves signal–noise interference, an issue that can be addressed by increasing the sample distance[88,100].

The use of LA strain imaging has been examined in several clinical scenarios, LA strain during atrial systole is significantly reduced in diastolic HF patients secondary to LA stiffness[82], and improves in HF patients following cardiac resynchronization therapy[101].

Interestingly, LA dysfunction with changes in strain and strain rates has been observed in patients with amyloidosis in the absence of other echocardiographic features of cardiac involvement[94].

- **Speckle tracking technique:**

Deformation or strain measurement using TDI velocity is affected by adjacent structure and tethering of neighboring segments[102]. Two dimensional speckle tracking strain imaging (2D-SI) is a novel technique for the assessment of myocardial deformation. This technique utilizes acoustic speckle tracking as opposed to Doppler myocardial velocities, and perfect ultrasound beam alignment is not necessary. Acoustic speckle is used for reference[103,104], and this has been recently validated against sonomicrometry and tagged MRI[103,105,106]. First described in 2004, there has been increasing evidence suggesting that this imaging modality is highly promising for LA function assessment[107].

Two dimensional speckle tracking imaging uses grey scale sector image and is based on frame-by-frame tracking of small rectangular image blocks with a stable speckle pattern[105].

Conventionally, a line is manually drawn along the LA endocardium when the LA is at its minimum volume. Software will generate the region of interest near the epicardium and mid-myocardial lines (usually about 15 mm width). If necessary, manual adjustments can be made. In one group has utilized five equidistant regions for the apical four and two chambers and three segments from the apical long axis with a total of 13 regions for analyses[107]. The location shift of the markers represents the tissue movements and provides the spatial and temporal data to calculate velocity vectors[108].

Quantitative curves representing all segments are expressed for each 2D-SI variable. The regional LA strain and strain rate curve can be analysed in conjunction with time points of the cardiac cycle, such that the relaxation and contractile functions of each LA segment can be analysed in detail[107].

Left atrial passive and active emptying indices, as assessed by strain, are affected by age, frame rates, loading conditions, and quality of the 2D images[109-111].

Normal aging and atrial strain

Reduced reservoir atrial function, as measured by systolic strain and strain rate have been reported, with increased LA stiffness index, reflective of reduced atrial compliance with normal aging[10,68,112].

This overall decrease in atrial compliance and reservoir function may be attributed to the aging process, similar to that observed in the LV, with an age related increase in interstitial fibrosis within the atrium[113,114].

Studies of atrial strain have demonstrated reduced LA conduit function with age[10,68], corresponding to LV diastolic dysfunction. Previous studies using atrial strain have reported no changes in active atrial contraction with age; however they were performed in a small group (n=50; 41±14 years)[112], and used only a single strain measurement from the LA posterior wall rather than a global function assessment. In

contrast others have reported positive correlations between age and global active atrial function measured by strain and strain rate parameters[10,68].

Atrial fibrillation and atrial strain

Newer strain techniques have also been utilised to evaluate atrial function in patients with AF. Reduced atrial strain in patients with AF has been shown to correlate with the extent of atrial fibrosis, detected by delayed- enhancement magnetic resonance imaging[99]. Patients with persistent AF have lower atrial strain compared to patients with paroxysmal AF[115].

Reduced reservoir function, as measured by atrial strain, was reported in patients with hypertension and paroxysmal AF compared to patients with only hypertension. Furthermore, higher atrial strain values in patients with AF treated by cardioversion or radiofrequency ablation have an increased likelihood of maintaining sinus rhythm[77,96]. Baseline atrial strain and LA volume were demonstrated to be independent predictors of reverse LA remodelling with an increase in atrial strain 13.2±6.7 months following catheter ablation[116].

Hypertension and atrial strain

Hypertension has been associated with reduced atrial strain in numerous studies. Kokubu et al. demonstrated that atrial strain was significantly reduced in hypertensive patients, independent of the presence or extent of LV hypertrophy, compared to normal subjects[117]. Furthermore they demonstrated that the administration of renin-angiotensin system inhibitors normalised atrial reservoir function, as measured by strain, in hypertensive patients without LA dilatation[117].

Additionally, in patients with hypertension, as well as diabetes, a decrease in atrial strain and strain rate has been reported[118]. Furthermore, patients with LV hypertrophy associated with hypertension had significantly reduced atrial systolic strain, (i.e. reservoir phase), compared to both normal controls and athletes with physiological LV hypertrophy[108].

In another report comprising subjects with mild hypertension, maximum LA volume was similar to normal, yet there was a decrease in the early diastolic strain rate, consequent to reduced LV relaxation and diastolic dysfunction[72]. However, reservoir and contractile phases of strain rate were preserved[72].

Cardiomyopathy and atrial strain

Both ventricular and atrial dysfunction have been implicated in the process of cardiomyopathies[70]. The assessment of atrial function in cardiomyopathy has predominantly been performed using atrial strain with a higher sensitivity in the detection of subclinical disease, than other indicators of atrial function.

Patients with hypertrophic cardiomyopathy have reduced atrial strain for all phases of atrial function, whilst atrial contractile function had an additive prognostic value in predicting the type of LV hypertrophy[84]. Additionally, strain derived atrial contractile

function was the only independent predictor of heart failure symptoms (by New York Heart Association class) in patients with hypertrophic cardiomyopathy[73].

Similarly, in cohorts of patients with hypertrophic cardiomyopathy and systemic hypertension, the presence of hypertrophic cardiomyopathy was the only independent predictor of atrial contractile strain rate, after adjusting for LV mass and parameters of diastolic function[119]. Total LA strain was reported as the strongest predictor of death, hospitalisation and occurrence of AF over 12 months, in patients with hypertrophic cardiomyopathy and normal systolic function.

In patients with idiopathic cardiomyopathy compared to ischemic cardiomyopathy, atrial reservoir and contractile function were differentially reduced in the idiopathic cardiomyopathy group, highlighting the more generalized involvement (i.e. LV and LA) in idiopathic cardiomyopathy[120].

Amyloidosis has also been associated with reduced atrial systolic strain and strain rate compared to patients with both diastolic dysfunction and LA enlargement and normal controls[94]. Patients with noncardiac amyloidosis also have reductions in atrial strain rate compared to the control groups, suggesting the early atrial involvement consequent to amyloidosis. Additionally, lower atrial strain rate values were observed in patients with symptoms of congestive heart failure in cardiac amyloidosis[94].