INTRODUCTION

Aneurysmal disease is a process involving the degeneration of the arterial wall. This degeneration is a result of increased elastolysis, which leads to dilatation, and collagen failure, which precedes dissection. This often increases the stiffness, or rigidity, of the arterial wall. Aortic aneurysms are dilations of the aorta to more than 1.5 times their normal diameters. They are classified based on their location in either the thoracic or abdominal aorta. Abdominal aortic aneurysms (AAAs) are most common and are typically associated with aging and atherosclerosis. Thoracic aortic aneurysms (TAAs) are often degenerative, but may also be the result of genetic diseases, and thus can occur in people of all ages and do not necessarily show association with cardiovascular risk factors. Aortic dissection occurs when tears or ulcerations allow blood from the aortic lumen to flow into the media, resulting in separation of the aortic wall layers. This is followed by either aortic rupture if the adventitia is disrupted, or blood flowing back into the aortic lumen through a second intimal tear. Preventative treatments include medical therapy, open surgery, or endovascular stent graft. Aortic aneurysms are often asymptomatic until the point of dissection or rupture, which then leads to hemorrhage, tamponade, or death. This emphasizes the importance of proper screening, monitoring, and prophylactic aortic replacement surgeries. Currently, aortic disease is assessed via computed tomographic imaging, magnetic resonance imaging, or echocardiographic examination to measure absolute aortic diameter and growth rate. However, the need for frequent monitoring, in addition to the variability of measurements associated with these
imaging techniques, makes the diagnosis and management of aortic aneurysms challenging. There is a call for models that are superior to aortic diameter to predict rupture and determine the optimal time for surgical or endovascular intervention. Recent advances in cardiovascular imaging technology allow us to better understand the aortic biomechanics of these patients, which may in turn facilitate their management. In this review, we summarize the utility of noninvasive imaging modalities for assessment of aortic biomechanics and prediction of rupture risk (Table 1).

2 | BIOMECHANICS OF AORTIC ANEURYSMS

It is widely recognized that aneurysmal disease is a process involving the degeneration of the arterial wall. Previously, it was thought that biomechanical changes associated with aneurysmal disease strictly included elastolysis, which led to aneurysmal dilatation, and collagen failure, which preceded dissection. However, while the degradation of elastin is now known to play a definitive role in aneurysm formation, the association between collagen content and aneurysm formation is less well understood. Elastolysis in combination with collagen’s rapid turnover time has been shown to cause a relative increase in collagen concentration that shifts arterial mechanical properties to the stiffer range of collagen fibers (Figure 1). However, this stiffness that has historically been associated with aneurysm formation is not universally accepted. In fact, recently Niestrawska et al showed that the wall distensibility of AAAs may increase compared to a healthy control if the nonlinear elastic properties are considered. Moreover, Wilson et al showed that an increase in wall distensibility precedes AAA rupture. Taken together, these findings highlight the uncertainty regarding the biomechanical properties of aortic aneurysms and call for further research using noninvasive modalities to gain insight on the topic.

3 | ULTRASOUND ASSESSMENT OF AORTIC BIOMECHANICS

Currently, the only clinically used value for the prediction of aortic aneurysm rupture risk is diameter. However, aneurysmal growth is nonlinear and rupture can occur even in aneurysms with small diameter. Therefore, researchers have turned to other biomechanical parameters to predict risk of rupture or dissection.

3.1 | Pulse wave velocity measurements using Doppler echocardiography

Carotid-femoral pulse wave velocity (PWV) is the current “gold-standard” measurement of arterial stiffness. Current noninvasive tools estimate PWV by acquiring pulse waves generated by systolic ejection at two distinct locations such as the carotid and femoral artery, and then taking into consideration the time delay due to pulse wave propagation along the arterial tree (Figure 2). Blood flow is impeded by the tensile nature of the aorta, which creates a relatively low-velocity pressure wave. As blood flows throughout the body, the diameter and properties of the aortic wall influence the pulse wave velocity, the propagation velocity of a pressure wave down a blood vessel. The velocity is calculated by dividing the difference in distance between two sensors and the left ventricle by the difference in time it takes for the blood to flow to each sensor. PWV is a measure of aortic stiffening, which is a result of structural and functional changes in the aortic wall. Specifically, increased stiffness compromises the reservoir function of the aorta and increases PWV. Many disease states including hypertension, atherosclerosis, and aortic aneurysms have been related to stiffening of the central arteries. One of the major limitations of present noninvasive measurements of PWV is the determination of the travel distance of the pressure wave. The reasons for this include body surface measurements not accurately representing the true length of arterial segments, the inclusion of arteries with different elastic properties than the aorta, and inclusion of bidirectional pulse wave travel—up the carotid artery and down the thoracic aorta simultaneously. These limitations suggest the need to develop and validate noninvasive methods that can directly measure the deformation of the arterial wall.
aortic wall, to better estimate aortic stiffness. Moreover, the devices used for PWV measurements usually use either a tonometer or a mechanotransducer to detect the pulse wave and these are not always readily available to clinicians who care for patients with aortic aneurysms. Tonometry requires specialized training, and therefore, its use is typically limited to the research setting and some clinical settings which have highly trained operators.

Doppler echocardiographic PWV is typically more accessible than tonometer-based PWV measurements. Using continuous Doppler probes, two flow pulses can be simultaneously recorded in order to obtain the delay in flow wave between the points. In addition, PWV can be estimated sequentially with one probe, by employing ECG gating. This technique has been validated in patients who underwent simultaneous intra-arterial pressure recording during cardiac catheterizations. This study demonstrated a minimal difference of 0.13 ± 0.79 m/sec between the two techniques for measuring PWV, confirming the use of Doppler echocardiography as a reliable method of aortic PWV measurement. Since studies using classical PWV measurement have shown higher PWV values in patients with abdominal aortic aneurysms compared to controls, Doppler echocardiographic PWV measurements may also show promise as a parameter for monitoring the aortic aneurysms and risk of rupture. To this aim, researchers have used this technique to show that endovascular aneurysm repair patients have a significantly higher postoperative PWV measurement than those undergoing open abdominal aortic aneurysm repair, potentially highlighting their future cardiovascular risk.

3.2 | Tissue Doppler imaging

Tissue Doppler imaging (TDI) is a technique by which displacement of tissue can be measured. This technique functions by detecting the frequency shifts of ultrasound signals that are reflected from the pulsatile wall motion of an arterial segment. Filters are applied to differentiate between signals from moving tissue and blood flow. Low-pass wall filters select for signals originating from moving tissues, allowing for information to be extracted regarding aortic wall movement, without the interference of high-velocity signals from blood flow (Figure 3).
Researchers have used TDI to better understand the biomechanics of the aorta in the context of cardiovascular disease. Generally, echocardiographic images are taken in either short-axis or parasternal long-axis views, 3 cm above the aortic valve, and demonstrate the tissue velocities during expansion and contraction of the aorta. With transesophageal echocardiography, the ascending and descending thoracic aorta can be assessed. Peak velocity during systole (SAo), early contraction peak velocities during diastole (EAo), and late contraction peak velocities during diastole (AAo) are obtained. Tissue Doppler imaging can also be used to assess strain rate, the rate of tissue deformation velocity (measured in s$^{-1}$). Peak systolic strain rate denotes maximal tissue deformation velocity in systole. Strain can then be calculated by integrating strain over time. Strain is a measure of deformation of a tissue segment and is reported as a percentage of the original dimension. Vitarelli et al. used TDI to assess aortic function in healthy and hypertensive adults. Hypertension is the leading risk factor for degenerative thoracic aortic aneurysm formation and expansion. They found that hypertensive patients had increased aortic stiffness and reduced wall strain. Anterior wall aortic expansion velocity (SAo) and early diastolic retraction velocity (EAo) were both reduced in hypertensive patients compared to controls. In another study, Vitarelli et al. used transesophageal echocardiogram to assess the thoracic aorta in patients with repaired coarctation. Patients with a history of coarctation are at higher risk of aneurysm formation and dissection despite repair, particularly at the site of repair. Vitarelli et al. found that patients repaired coarctation continue to have increased proximal aortic wall stiffness, reduced systolic aortic wall velocities, and reduced strain. Although there is limited assessment of the thoracic aorta, TDI has also been used to assess abdominal aortic aneurysms. Long et al. used tissue Doppler velocity measurements to calculate the displacement of the anterior and posterior abdominal aortic wall with each cardiac cycle. They measured the maximal mean segmental dilatation (MMSD), which is an average of the maximal systolic dilatation of the abdominal aorta during a cardiac cycle, and segmental compliance, and is calculated as follows: $\frac{2 \cdot \text{MMSD}}{\text{Pulse pressure (µm/Pa)}}$. MMSD and segmental compliance were found to be higher in patients with larger abdominal aneurysms (≥45 mm) than smaller aneurysms (<45 mm). Therefore, the larger the AAA, the greater the radial extension of the aorta, which may represent the loss of elastin as the abdominal aorta dilates. The reported increase in compliance in this study contrasts the previously mentioned TDI studies, where an increase in stiffness was reported in aneurysmal aortas. This emphasizes the uncertainty in the field and the need for further research regarding aortic biomechanics in the context of aneurysmal dilation. Vizzardi et al. used tissue Doppler imaging to assess the aortas of a group of patients with α1-antitrypsin deficiency (AATD). α1-antitrypsin is a glycoprotein that inhibits proteinases. Some proteinases can promote connective tissue degeneration. Abdominal aortic aneurysms and thoracic dissections have been documented in AATD patients, and their findings confirmed that AATD patients have abnormal aortic biomechanics. Patients with AATD had increased stiffness and abnormal aortic strain which may be secondary to changes in the connective tissues of the aorta secondary to α1-antitrypsin deficiency. Vitarelli et al. used transesophageal echocardiography to assess the ascending aorta in 31 patients with Marfan syndrome. They found that systolic maximal wall expansion velocity (SAo) and peak systolic strain were better predictors of dissection than aortic diameter with odds ratios of 3.31 and 4.46, respectively. These findings reinforce that TDI may have an important role in identifying patients at risk for aortopathies.

Taken together, these data outline the role of TDI as a noninvasive tool for assessing aortic biomechanics of aneurysmal aortas and aortas at risk for aneurysm formation. Further outcome data studying the relationship between these properties and risk of aortic complications are needed to establish normal values and cut off threshold values in the management of thoracic aneurysms.

### TABLE 1

<table>
<thead>
<tr>
<th>Modality</th>
<th>Parameter Assessed</th>
<th>Advantages</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doppler echocardiographic pulse wave velocity</td>
<td>Aortic stiffness</td>
<td>• Noninvasive • Accessible • Cost-effective • Highly validated</td>
<td>• Body surface measurements may not represent true length of arteries • Inclusion of arteries with different elastic properties than aorta • Inclusion of bidirectional pulse wave travel</td>
</tr>
<tr>
<td>Tissue Doppler imaging</td>
<td>Aortic wall movement</td>
<td>• Noninvasive • Accessible • Cost-effective • Allows for visualization of wall movement</td>
<td>• Limited assessment of thoracic aorta • Highly angle-dependent • Inaccurate if vessel tortuosity present • One-dimensional</td>
</tr>
<tr>
<td>Speckle-tracking echocardiography</td>
<td>Strain (longitudinal, circumferential, and radial)</td>
<td>• Two-dimensional • Angle-independent</td>
<td>• Relies on good acoustic windows • Artifacts • Limited assessment of thoracic aorta</td>
</tr>
</tbody>
</table>
3.3 | Speckle-tracking echocardiography

Speckle-tracking echocardiography (STE) is a semi-automated technology that follows echo dense speckles to calculate deformation.\textsuperscript{19} The benefit of speckle-tracking echocardiography is that measurements of deformation are \textit{angle-independent}, which was a limitation of tissue Doppler-derived strain measurements.\textsuperscript{39} Originally used to measure deformation of the myocardium and ventricular function, the technique has been adapted for use in the aorta to measure aortic strain and strain rate. It allows for the measurement and calculation of strain in a longitudinal, circumferential, and radial direction\textsuperscript{40} (Figure 4). The ascending aorta is typically assessed from a transthoracic parasternal long-axis view, 3 cm above aortic valve when transthoracic imaging is used.\textsuperscript{39,41} In patients with good imaging windows, the aortic arch can also be assessed from the suprasternal notch view.\textsuperscript{39} The cross-sectional view of the aorta is divided into six segments where each segment has a strain value (Figure 1). It is also possible to average all the strain measurements over the entire aorta and obtain a global strain measure in each dimension (longitudinal, radial, and circumferential). Only two directions of strain can be measured in 2D STE. For example, one can only measure longitudinal and radial strain from a long-axis view. Alternatively, only circumferential and radial strain can be obtained from a short-axis view. With 3D STE, strain in all three directions is available from the same 3D image acquisition but with lower temporal and spatial resolution.\textsuperscript{43}

Recently, the value of STE for assessing mechanical properties of the aorta in patients with aortic aneurysms has been established. Bieseviciene et al\textsuperscript{44} used STE to determine whether there was a difference in aortic stiffness in patients with dilative pathology of the ascending aorta (DPAA) compared to normal aortas. The group found that the ascending aortas of DPAA group with wider aortas (>45 mm) had reduced strain, reduced distensibility, and increased stiffness compared to controls. Batagini et al\textsuperscript{45} used STE to assess maximum circumferential strain, global rotation of the aorta in patients with normal aortas, and abdominal aortic aneurysms. They found that maximum circumferential strain was lower in the aneurysm group compared to controls. Furthermore, maximum global rotation was the highest in the control group and lowest in AAAs ≥5.5 cm.\textsuperscript{45} A study by Taniguchi et al\textsuperscript{46} showed that aortic strain rate was lower, but also had greater heterogeneity in patients with abdominal aortic aneurysm than in those with normal aortas. Furthermore, some groups have used speckle tracking to assess groups at risk for aortic aneurysms. Some patients with tetralogy of Fallot (TOF) are prone to aortic dilatation and consequently are at risk for dissection and rupture. Cruz et al\textsuperscript{47} (2018) studied 82 patients with repaired TOF and compared them to age-matched controls. TOF patients had stiffer aortas as demonstrated by lower circumferential strain values when assessed by STE. Circumferential strain values also negatively correlated to ascending aortic Z scores.

Taken together, these studies have demonstrated the widespread study of STE for examining biomechanical properties of the aorta and correlation to disease states. These novel approaches are driven by a need for better noninvasive methods of predicting risk in the diseased aorta earlier. Overall, this work indicates that compliance is reduced in aneurysmal aortas compared to normal controls. Detection of reduced compliance could be applied to patients at risk for the development of aortic aneurysms due to genetic conditions, such as those with Marfan, Ehlers–Danlos, and Loeys–Dietz syndromes, in order to better stratify patients based on their risk for aneurysm development and rupture. However, certain limitations remain; namely, normal threshold values and outcome-related study are lacking. Additionally, speckle-tracking echocardiography relies on good acoustic windows in order to adequately analyze all segments of the aorta, which is often not possible by the standard echo protocol. The presence of atherosclerotic plaque in the aorta can cause artifact which can interfere with the speckle-tracking algorithm. Finally, assessment of the ascending aorta in the region visualized by echo may not be representative of the entire thoracic aorta.

\textbf{FIGURE 4} Speckle-tracking echocardiographic (STE) assessment of aortic strain from the parasternal view. Transesophageal echocardiography was used to obtain a parasternal view of the descending aorta. The aorta was divided into six segments. Segments with “X” depict those that were not in frame, and thus, no strain value was obtained for these segments. The plot shows strain measurements for each in frame segment.
Recently, studies have used three-dimensional STE to determine whether this technique could more accurately depict the mechanical properties of the aorta. Derwich et al. used 3D STE to assess the biomechanical properties of the aorta in the context of age and presence of aneurysm. They found that the mean circumferential strain, which is the average relative length change in the aortic circumference, was higher in the young than in the old or aneurysmal aorta. Karatolios et al. utilized 3D STE to determine whether the increased resolution would allow for more accurate measurements of local peak strain values throughout the aorta. In their small cohort, they found that aneurysm of the aorta was correlated with reduced mean strain values, increased heterogeneity in strain distribution, and more marked dyssynchrony in aortic wall motion than healthy controls.

Bihari et al. aimed to determine whether real-time 3D STE could be used to determine local wall displacement and strain of abdominal aortic aneurysms. After validating the 3D STE technique in vitro, it was found that in their small cohort of five patients, there were local variations in displacement and wall strain within the AAAs. This is of particular interest because it positions 3D STE as a noninvasive tool for assessing rupture risk of AAAs. Disseldorp et al. have utilized time-resolved 3D ultrasound, known as 4D ultrasound, to perform a patient-specific AAA wall stress analysis, and they have shown that this modality can be used for AAA measurements over a large diameter range albeit limited by a low frame rate.

### 4 | SIGNIFICANCE & CONCLUSIONS

The measurement of aortic stiffness using TDI and STE shows promise as a tool in the assessment of the aorta in order to risk-stratify patients, and potentially prevent conditions such as aortic dissections. Studies to date compare parameters of abnormal aortic biomechanics to aortic size, the current parameter used to decide timing of aortic intervention. However, some patients have larger aneurysmal aortas and do not have complications, and other patients have dissections or ruptures despite a smaller aneurysm size. Further evaluation of how TDI and STE parameters relate to complications of aortic dissection or rupture is required to determine parameters and cutoffs which can be used to help predict clinical outcomes. A translational collaboration between physicians and bioengineers could aid in further developing these novel imaging modalities to capture structural changes in the wall of the aorta and potentially guide timing of intervention. Before these novel noninvasive techniques may be considered to guide clinical management, further work is required to develop normal threshold values, correlation of abnormal values to important clinical outcomes, and the standardization of the measurement technique by dedicated software.

### ACKNOWLEDGMENTS

This work was supported by a Canada Foundation for Innovation and Ontario Research Fund (CFI#29051), a Ministry of Research, Innovation, and Science Early Research Award (#ER15-11-029), Southeastern Ontario Academic Medical Organization, and the Heart and Stroke Foundation of Canada (Phase I Career Award to AMJ), Kingston, Canada.

### DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

### ORCID

Laura E. Mantella  [https://orcid.org/0000-0002-6527-426X](https://orcid.org/0000-0002-6527-426X)

Syed M. Ali Hassan  [https://orcid.org/0000-0002-2845-3023](https://orcid.org/0000-0002-2845-3023)

### REFERENCES
