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Ultrasonography Techniques for Atherosclerosis Assessment: A Narrative Review

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Abstract

Ultrasound is very important for the diagnosis and treatment of vascular emergency patients. In recent years, the number of deaths caused by atherosclerosis, represented by ischemic heart disease, has increased rapidly and become a very important part of emergency medicine. This article aimed to review the application and research progress of various vascular ultrasound techniques in emergency medicine to provide a reference for the diagnosis and treatment of panvascular diseases in early first-aid emergencies.

Keywords: Atherosclerosis, Emergency, Doppler ultrasonography, Vascular

1. Background

In 2002, Peter Lanzer and Eric Topol first proposed the concept of "panvascular diseases" based on their unified understanding of vascular diseases (1-2). Panvascular refers to the vascular system of the human body. It is a complex network composed of arteries, veins, and lymphatic vessels. It is the "irrigation canal" of important organs of the body and the "lifeline" of human health. Panvascular medicine starts from the holistic view of the unity of human structure and function and uses the method of systems biology to explore the occurrence and development of vascular diseases in a multidimensional way (3-5).

Scholars in China and other countries have gradually realized the limitations of the study and treatment of panvascular diseases according to a single site; therefore, they propose to understand and study such diseases from a systematic and holistic perspective. A panvascular disease is a group of systemic vascular diseases with vascular diseases as the common pathological characteristic (95% of which are atherosclerosis), which mainly harm the heart, brain, kidney, limbs, arteries, and other important organs.

In recent years, the number of deaths caused by atherosclerosis (AS), represented by ischemic heart disease, has increased rapidly and become a very important part of emergency medicine (6-10). The common risk factors for AS include hypertension, hyperlipidemia, hyperglycemia, smoking, and obesity. The main pathological changes are the formation of lipid striae, fibrous plaque, or atheromatous plaque in the intima of large and middle arteries and secondary plaque hemorrhage, rupture, thrombosis, and stenosis. The concept of prevention and control of avascular diseases embodies the unity of commonness and individuality. The treatment plan includes improvement of lifestyle, control of risk factors, and the usage of anti-AS and anti-thrombotic medications.

The diagnosis of panvascular disease is inseparable from the development of vascular imaging technology. Digital subtraction angiography (DSA) has radioactive hazards and is unable to identify the formation of new blood vessels. Magnetic resonance imaging can identify the neovascularization of plaque, but it is expensive and time-consuming. Ultrasound has the advantages of being non-invasive, convenient, economical, real-time, and intuitive with good repeatability. In particular, vascular ultrasound can grade the stenosis degree of carotid atherosclerotic plaques structurally and also assess the stability of plaque risk. Moreover, it can also pass vascular function-related tests, such as hardness, compliance, and pulse wave velocity (PWV).

Challenging emergency vascular systems that are difficult to evaluate using traditional Doppler modes or ambiguous Doppler cases require more advanced applications with the highest sensitivity to blood flow to provide clearer and more accurate diagnoses in emergency treatment. The newly developed innovative ultrasound technology emphasizes the role of ultrasound in the accurate diagnosis of various vascular pathology and conditions, including the visualization of atherosclerotic plaque and plaque ulcer, detection of significant internal leakage in patients after intravascular aneurysm repair, identification of arterial patency in organ transplantation, and accurate diagnosis of near occlusion and its difference from central or peripheral arterial total occlusion.

In many pathological situations mentioned above, a reliable ultrasound (US) tool is essential for improving the diagnostic ability of the US and the reliability of imaging results. In addition, a safe and highly diagnostic technique is needed to screen for vascular pathology in emergency settings and provide a sensitive and robust tool for lifelong follow-up of major vascular conditions. The application of new technologies, such as endothelial cell function can realize the early prediction of AS, especially in emergency departments. This article aimed to review the latest innovations in ultrasonography of panvascular diseases based on atherosclerotic lesions in emergency departments with examples of their applications as well as a discussion of their strengths and weaknesses to answer the questions summarized in Table 1.

Table 1. Clinical questions regarding ultrasonography of panvascular diseases based on atherosclerotic lesions in the emergency department

Clinical questions
1. Where is the possible vascular disease?
2. How do we check the vascular condition?
3. What are the steps for checking blood vessels?
4. How do we determine the best vascular ultrasound examination?
5. What are the main methods available for vascular ultrasound examination?
6. What traps or artifacts should we pay attention to when using vascular ultrasound?

1.1. Ultrasonography of vascular structure

1.1.1. Ultrasonography of routine vascular structures

Conventional two-dimensional US images of vascular US can clearly show the structure of the vascular wall, the echo in the lumen, the thickness of the medial membrane of the vascular wall, and the inner diameter of the lumen (Figure 1A, B, C, and D). When the AS plaque is formed, the size, echo, calcification degree of the plaque in the vascular lumen, and the degree and scope of the stenosis of the lumen can be observed (11-15). Color Doppler flow imaging was mainly used to observe the filling of color blood flow in the lumen; pulse and continuous Doppler technology can realize the analysis of intravascular fluid dynamics.

1.2. Ultrasonography of fine vascular structures

1.2.1. Contrast-enhanced ultrasound

Contrast-enhanced ultrasound (CEUS) combines the dual characteristics of high spatial and temporal resolution of standard vascular US and the excellent imaging ability of intravascular contrast agent microbubbles (16-20). Moreover, it is more accurate in assessing the formation and stenosis rate of arterial lumen AS plaques (Figure 2A). The CEUS can also be used for visual inspection of the formation of new blood vessels in plaques. It is used to assess the stability of plaques according to the formation of microvessels, stratify plaque risk, predict the risk of stroke, and assess the progression of AS.

The increase in microvessel density is associated with the rupture of plaques. The density of blood vessels in vulnerable plaques is twice as much as that in stable plaques, and the density of blood vessels in ulcer plaques is four times more than that in stable plaques (21-24). The evaluation of carotid plaque by CEUS was divided into 4 grades, namely grade 0: no enhancement after angiography, grade I: enhancement at 1-2 places after angiography, grade II: enhancement at 3~4 places after angiography, and grade III, more than 4 points of enhancement or more than 2 linear enhancements after angiography. Grades 0~I are stable plaques, and grades II~III are vulnerable plaques. Vulnerable plaques are mainly seen in hypoechoic plaques and mixed echo plaques related to recent or previous stroke history (25-28).

1.2.2. Superb microvascular imaging

Neovascularization in plaques is the key feature of plaque instability in panvascular disease (29-30). Superb microvascular imaging (SMI) is a new imaging technology derived from color Doppler US (Figure 2B). It automatically identifies and eliminates the influence of blood flow motion artifacts through special algorithms, improves the sensitivity to low-speed blood flow recognition, and has high resolution and accuracy. Therefore, the visualization of new blood vessels in plaques can be realized (31-33). The SMI assessment of unstable plaque is accurate, fast, and economical; however, it requires high operator skills and is subject to many interference factors. Comprehensive analysis is needed in clinical applications to balance advantages and disadvantages.

The application of various vascular US technologies in emergency vascular diseases is very important. For example, emergency stroke patients undergo emergency carotid artery US. The use of effective examination methods to achieve an accurate and rapid diagnosis of cervical artery stenosis is of great significance for the diagnosis and treatment of cerebral ischemic vascular diseases. The DSA has always been the gold standard for the evaluation of the degree of narrowing or occlusion of neck blood vessels; however, it has several disadvantages, such as trauma, complicated operation, high price, and many complications.

The SMI or PWV examination in carotid vascular US does not have the shortcomings of the two above-mentioned examinations, which can clearly show whether the endovascular membrane and the medial membrane are thickened, whether there is plaque formation, the location, size, nature, and extent of plaque formation, and detect blood flow parameters and other data. Previous studies have shown that emergency US vascular examination has a good

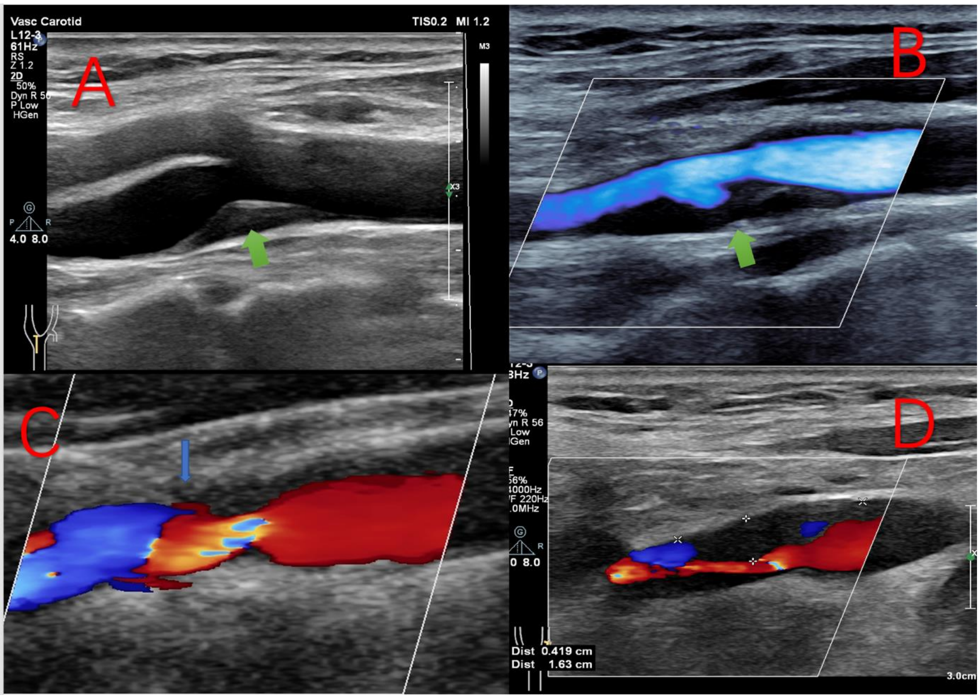

Figure 1. A: longitudinal section of carotid artery grayscale ultrasound (B-mode) plaque
B: fragile intraplaque ulcers with blood flowing into the ulcer
C and D: hypoechoic plaques of the internal carotid arteries and luminal stenosis

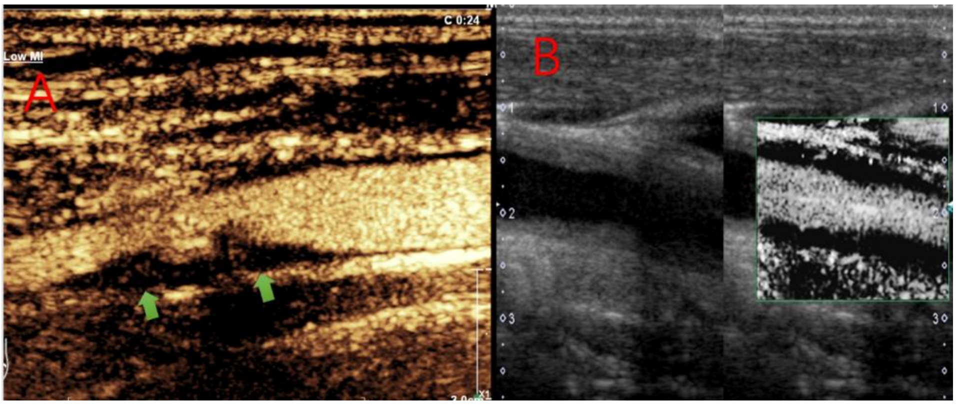

Figure 2. A: Ultrasonography showed neovascularization in the plaque, suggesting fragile plaque
B: Superb microvascular imaging technique was used to check for neovascularization within the plaque

consistency with DSA in the evaluation of extracranial artery stenosis. The above-mentioned US is used slightly less than spiral computed tomography angiography in the emergency department for the diagnosis of mild and moderate stenosis of the cervical artery. It should be mentioned that the diagnostic results for severe stenosis or occlusion and carotid artery stenosis are consistent.

1.2.3. Three-dimensional and four-dimensional color Doppler blood flow imaging

The 3D technology is used to synthesize the three-dimensional image of AS plaque, measure the plaque volume, and reflect the plaque size and progress more accurately and comprehensively than grayscale US measurement of plaque area (34-37). Real-time 3D/4D color Doppler blood flow imaging (35) displays the 3D structure and spatial relationship of blood vessels from multiple directions. Besides, it can also be employed for quantitative analysis of blood flow and research on the stability of carotid plaques using quantitative blood flow data (Figure 3A, B).

1.2.4. Intravascular ultrasound

Based on 3D vascular reconstruction, intravascular ultrasound (IVUS) has expanded from the role of simple auxiliary diagnosis to the application of intraoperative navigation (Figure 3C). It helps clinicians to select treatment plans and guide the interventional treatment process by accurately judging the extent and scope of lesions (38-39); however, IVUS is an invasive examination. In

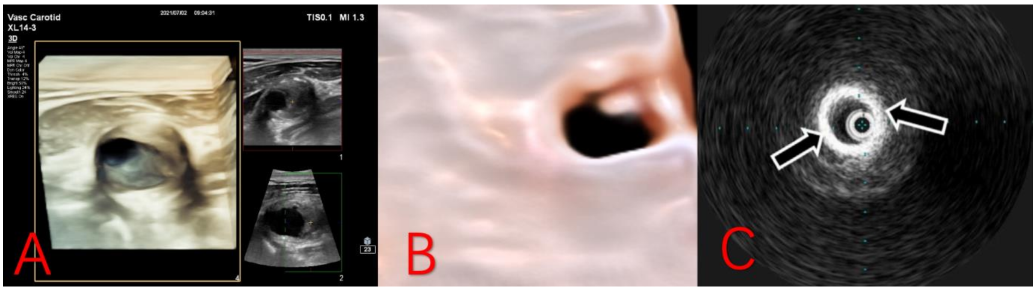

Figure 3. A and B: 3D ultrasound showed regular and irregular plaque morphology and smooth and unsmooth surfaces
C: Intravascular ultrasound showed narrowed arteries

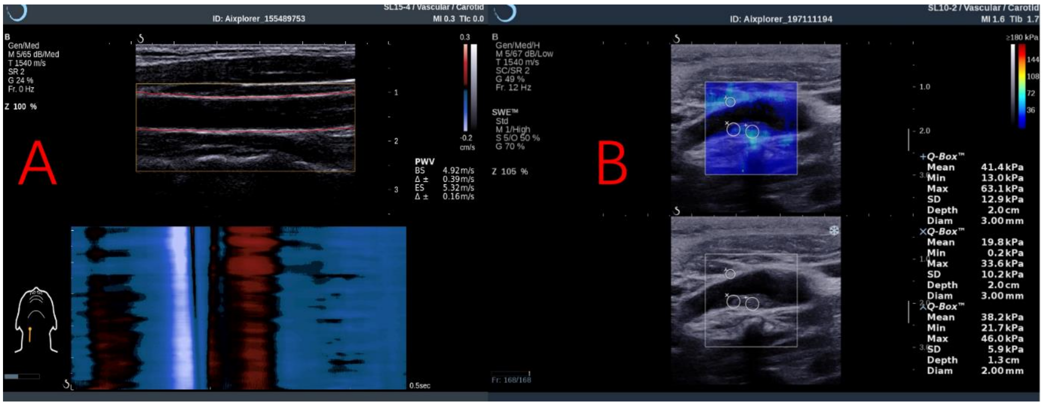

Figure 4. A: Pulse wave velocity evaluated arterial elasticity. B: Echo-tracking technology tracks the activity of the anterior and posterior walls of blood vessels in real-time

addition, surgical operation and post-operative monitoring involve further improvement of smart catheters; therefore, they have not been widely used in clinical practice.

In the future, with the continuous development and improvement of new technologies, it is believed that the application of the US examination of fine vascular structures in panvascular diseases will gradually increase. Acute lower extremity arterial thrombosis or emergency deep vein thrombosis are often evaluated and treated with IVUS for lumen evaluation and emergency treatment.

The IVUS is currently utilized for the guidance of various interventional procedures and assessment of vascular lumen and walls. It aids in selected cases of balloon angioplasty and stent placement with complex vascular anatomy and unclear findings at angiography. It facilitates accurate measurements of the vessel dimensions and reveals the extent of the intravascular disease. Furthermore, it allows accurate measurement of the vessel lumen and assessment of the atherosclerotic plaque for the selection of proper angioplasty balloon size as well as confirmation of full expansion and attachment of the stent or stent graft to the arterial wall. Additionally, IVUS provides guidance for percutaneous fenestration of a dissection flap, facilitates placement of a vena cava filter, and aids in peripheral endovascular interventions.

1.3. Ultrasonic evaluation of vascular function

1.3.1. Shear wave elastography

Compared to 2D US, shear wave elastography (SWE) can provide elastic imaging information inside organs and tissues. In AS plaque diagnosis, SWE can be used for the early assessment of the hardness of the artery wall with impaired endothelial function through Young's modulus value, showing advantages in the quantitative diagnosis of vulnerable plaques (40-42). For instance, SWE can quickly and accurately screen vulnerable plaques according to the hardness of the plaques. In addition, the average Young's modulus value for vulnerable plaques dominated by lipids was lower than that of stable plaques. Therefore, the difference in plaque hardness can indirectly reflect the difference in the pathological components of plaques, providing strong evidence for the assessment of vulnerable plaques. Its limitation is that when the detection target is too small (<5 mm), SWE cannot accurately reflect the hardness and nature of the plaque and also requires high operator manipulation.

1.3.2. Pulse wave velocity

Pulse wave velocity refers to the propagation velocity of the pressure wave along the great artery wall generated by the ejection of each heartbeat (Figure 4A). Larger PWV measurement values lead to worse vascular elasticity and a higher risk of cardiovascular disease. There are two main manifestations of arterial lesions, namely, structural lesions and functional lesions. Arterial degenerative diseases and AS often have functional changes at first and subsequently, develop into structural diseases. The functional changes are mainly endothelial function changes related to nitric oxide and endothelin.

Carotid femoral artery PWV and carotid brachial or radial artery PWV are classic indexes for the evaluation of arterial stiffness. Ultrafast pulse wave velocity (43-45) not only reflects early AS but also provides a research basis for the non-invasive evaluation of microvascular injury in patients with slow coronary flow. The PWV can lead to the early quantitative detection of arterial stiffness and predict future cardiovascular risk events. Its limitation is that it cannot directly assess the local vascular status.

1.3.3. Vascular echo tracing

The diameter of the artery changes with the contraction and relaxation of the heart. This change process includes phase information in addition to the periodic changes and amplitude of the wall activity (Figure 4B). The vascular echo tracking (ET) technology system device can track the activities of the anterior and posterior walls of the blood vessels in real-time, collect and process the original information containing these phase changes, that is, radio frequency signals, convert these phase changes into distance information through the zero crossing method, and display the activities of the anterior and posterior walls and the changes in the inner diameter in the form of curves.

It is a non-invasive technology that is not limited by subjective factors and vascular conditions. It can sensitively and quantitatively detect and evaluate arterial elasticity and endothelial cell function before morphological changes in the arterial wall to accurately and objectively evaluate the stiffness and compliance of blood vessels. The five parameters for the automatic calculation of vascular stiffness are elastic modulus, stiffness, compliance, swelling index, and PWV. The decrease in arterial elasticity reflects the early pathological changes in blood vessels. Echo tracking can evaluate the early changes in AS before the thickening of arterial walls and plaque formation and also assess the effect of drug treatment, smoking cessation (46-48), and other behaviors controlling risk factors. Moreover, it can provide an accurate and fast detection method for the screening of vascular diseases and the evaluation of clinical medication.

1.3.4. Shear wave dispersion imaging

Viscosity is a physical property of the organization, which is expressed by viscosity and reflects the resistance of the medium to deformation. Shear wave dispersion is an imaging method based on acoustic radiation force that can well reflect tissue viscosity (49-50). In pure elastic tissue, the propagation velocity of the shear wave is independent of the frequency, and its velocity changes in a straight line. For viscoelastic tissues, the propagation speed of the shear wave is related to the frequency. Under the same elasticity, the viscosity and dispersion value increase, which is shown by the increase in the slope of the velocity change curve.

Arterial remodeling is a potentially important pathophysiological change in the development of AS. The arterial wall has certain viscoelastic biomechanical properties (51-52), and the viscoelastic response reflects the adaptability of the vascular wall to mechanical and hemodynamic stimulation. The tissue characteristics of vascular smooth muscle cells, extracellular matrix collagen, and elastin of arteries play a crucial role in the evaluation of viscoelasticity. The changes in arterial wall viscosity reflect the age characteristics and the degree of disease progression. At present, there are few studies on the application of SWD for blood vessels, and there is still a lack of multi-center and large-sample research data in clinical practice.

1.3.5. Combined elastography

Combined elastography, which is strain imaging and shear wave imaging, has rarely been reported. A report on liver fibrosis showed that the operation of shear wave imaging is simple, but it is difficult to correctly diagnose liver fibrosis in cases of inflammation and jaundice. Instead, strain imaging can diagnose liver fibrosis and is not affected by inflammation. The combined strain imaging and shear wave imaging are superior to other conventional diagnostic methods in the diagnosis and evaluation of liver fibrosis and inflammation index (53-57). The formation of AS plaques is also an inflammatory reaction of the vascular wall, and the increase in arterial wall hardness in the early stage of AS is closely related to fibrosis of the arterial wall. Therefore, in the future, combined elastic imaging technology may be applied to panvascular disease screening. The preventive effect of panvascular disease is greater than that of treatment. Therefore, new ultrasonic techniques are urgently needed for the early detection of damages and changes in the arterial wall to provide a reliable objective basis for active clinical prevention and early intervention.

2. Conclusion

Conventional US and new technology US have their own characteristics and advantages in the application of panvascular diseases based on AS. Grayscale US, color Doppler US, and spectrum Doppler US can be used for routine examination of arterial structural lesions. The application of 3D, 4D, CEUS, SMI, and other new US technologies can lead to the fine evaluation of vascular lesions and observation of the subtle structural lesions of blood vessels.

The application of SWE, PWV, ET, and SWD, combined with new elastic imaging technology, can evaluate early lesions of vascular wall function (Figure. 5). The latest technological advancements and development of clearer US imaging software for the assessment of vascular flow have brought hope for changing the current view that the US is only a screening tool and a non-invasive method for evaluation of carotid circulation.

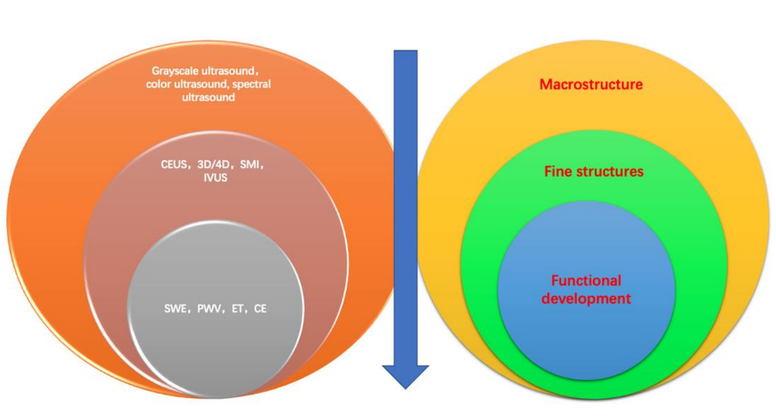

Figure 5. SWE: shear wave elastography; PWV: pulse wave conduction velocity; SWD: shear wave dispersion imaging; ET: vascular echo tracking; CEUS: ultrasonography; 3D: three-dimensional; 4D: four-dimensional; SMI: ultrafine flow imaging; IVUS: endovascular ultrasound

With this new technology, the US is able to not only compete with computed tomography angiography and magnetic resonance angiography, but actually surpass their capabilities as it can better characterize the 3D characteristics of carotid artery plaques (wall irregularity, composition, 3D size, and the presence or absence of ulcers), measure the degree of lumen stenosis more accurately, and most importantly, evaluate the flow dynamics of the proximal and distal plaques. These factors may have a significant impact on emergency surgical decisions for intervention.

The ability to accurately determine the flow rate of normal blood vessel segments and significant stenosis will completely change the thinking about the necessity of emergency surgery or medical management of carotid artery plaques. Panvascular medicine is a new discipline based on the concept of multidisciplinary cooperation and interdisciplinary integration.

With the aggravation of the health conditions of the aging population, it is urgent to explore the pathogenesis of panvascular disease and effective prevention and control strategies from the basic to clinical levels. The application of vascular US, including conventional vascular US, and combined new technologies can obtain accurate quantitative US parameters and precisely evaluate the macro and fine structures and functions of blood vessels. Therefore, it is possible to provide valuable information and prepare a basis for the prevention, diagnosis, and treatment of AS-based vascular diseases in emergency medicine.

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Footnotes

Conflicts of Interest: ??
Author Contribution: ??
Funding: ??
Ethical statements: ???

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