Stress With Bubbles: Echocardiographic Visualization of a Typical Pathway Between the Spine and the Heart

Robin Kluthke, MD, Christian Perings, MD, Matthias König, MD, and Andreas Helfen, MD, *Lünen, Germany*

INTRODUCTION

Stress echocardiography is one of the established noninvasive methods to diagnose coronary artery disease.[1] Basically, a distinction can be made between exercise stress echocardiography (e.g., bicycle stress) and pharmacological stress echocardiography (e.g., using dobutamine). Exercise stress is the preferred method for patients that can attain an adequate level of exercise. Exercise capacity is frequently limited by degenerative diseases of the joints or spondylosis deformans.

In the presented case, physical exercise led to an unusual phenomenon during stress echocardiography in the right heart and demonstrated the typical pathway between the spine, especially the intervertebral spaces and intervertebral disks, and the heart.

CASE PRESENTATION

Due to recurrent symptoms of weakness and complaints of thoracic tightness on exertion, an 85-year-old woman presented to a primary care physician. The patient was in good health, had a normal nutritional status (height, 164 cm; weight, 58 kg; body mass index, 21.6 kg/m^2), and was regularly physically active and rode a bicycle several kilometers daily.

Arterial hypertension was the only known cardiovascular risk factor for coronary artery disease. The patient's heart rate was regular at 72 bpm, and blood pressure was in the normotensive range under medical therapy with irbesartan 150 mg, lercandipine 20 mg, and amlodipine 5 mg (demand medication). Occasionally the patient suffered from chronic back pain due to lumbar spine syndrome. Previous surgery or trauma was denied.

Physical examination revealed euvolemic status without peripheral edema, normal auscultation of the lungs, and no heart murmur. The mobility in the lower thoracic/lumbar spine was remarkably restricted.

The electrocardiogram showed a normal sinus rhythm at 82 beats per minute (bpm), no prolongation of AV or QRS interval, and no evidence of ischemia. The previous day, the primary care physician had already performed a blood draw and an echocardiogram at rest. Echocardiography showed mild aortic valve sclerosis without stenosis. Regional wall motion abnormalities were not reported. Blood chemistry was unremarkable, and in particular there was no evidence of infection. The patient was referred to our clinic for stress echocardiography. Because of the daily bicycle training, exercise stress echo was preferred.

Stress echocardiography was performed on an ergometer in the left lateral position tilted by 20°. Apical 3-, 2-, and 4-chamber views were recorded at each stress level. Exercise was started with 25 watts and increased by 15 watts every 2 minutes. Peak stress was attained at 55 watts after 6 minutes.

Heart rate increased from 74 bpm at rest to 130 bpm at peak stress (Figure 1, Video 1). The test was stopped according to protocol after maximum heart rate was achieved (130 bpm, 96% of maximum heart rate, calculated as 220 minus age). No symptoms of angina occurred. The electrocardiogram revealed no signs of ischemia, and no wall motion abnormalities could be detected. Surprisingly, gas bubbles appeared in the right atrium and ventricle at the second stress level (Video 2). The number increased at the peak stress level (Video 3), and the bubbles mostly disappeared during recovery (Video 4). Stress echocardiography was performed without inserting a venous line and without injection of fluids.

Continuous-wave Doppler recording was technically difficult but suggestive for normal pulmonary artery pressure at peak stress (Figure 2). While searching for the origin of the gas bubbles, a computed tomography (CT) scan of the spine showed inclusion of gas within the intervertebral disk space L3/L4 and L4/L5 (Figure 3). A CT scan was ordered for further differential diagnosis due to back pain.

DISCUSSION

Gas as a partial replacement for intervertebral disks was first described in 1910 and has been called the vacuum phenomenon (VP) since 1937.[2] Accumulation of gas is a rare incidental finding in conventional x-ray or CT/magnetic resonance imaging examinations. It can also occur intra-articularly and intraosseously. Causes include degenerative joint disease, chondropathy, osteoporosis with or without fractures, metastases, abscesses, osteomyelitis, multiple myeloma, surgical introduction of air, joint effusions, Schmorl's nodes, or ligament tears.[3] When detecting VP it is indispensable to consider a spondylodiscitis gas-forming infection.

The phenomenon occurs as a result of an increase and subsequent fast decrease in local pressure in a closed joint space without a synovia. As the volume expands, a negative pressure occurs. This pressure affects the plasma in the trabeculae of the bone marrow, and gas fills the space, consisting of about 90% nitrogen in combination with oxygen, carbon dioxide, and other trace gases.[4]

Low nitrogen solubility and minimal nitrogen metabolism in the body are the main reasons for the formation of the VP and its transfer

From the Department for Cardiology, Electrophysiology, Pneumology, Intensive Care Medicine (R.K., C.P., A.H.), and Department for Diagnostic and Interventional Radiology and Neuroradiology (M.K.), Marienhospital Lünen, Lünen, Germany.

Keywords: Stress, Endocarditis, Vacuum phenomenon, Spondylodiscitis

Correspondence: Robin Kluthke, MD, St-Marien-Hospital Lunen, Department for Cardiology, Germany. (E-mail: *Kluthke.Robin@klinikum-luenen.de*).

2468-6441

https://doi.org/10.1016/j.case.2022.09.005

VIDEO HIGHLIGHTS

Video 1: Stress echocardiography, apical 4-chamber view, rest stage, normal left ventricular function without evidence of regional wall motion abnormalities. No pathologic findings were seen.

Video 2: Stress echocardiography, apical 4-chamber view, 40 watts, submaximal heart rate, normal left ventricular function without evidence of regional wall motion abnormalities. First bubbles appear in the right atrium and ventricle.

Video 3: Stress echocardiography, apical 4-chamber view, 50 watts, maximum heart rate, right heart centered. In the right atrium and even in the right ventricle, more bubbles appear.

Video 4: Stress echocardiography, apical 4-chamber view, poststress stage, right heart centered. A few bubbles can still be seen in the right atrium.

View the video content online at www.cvcasejournal.com.

back into the blood. It is well-known that even small amounts of gas bubbles can be detected by ultrasound. In the presented case, nitrogen bubbles became visible in a way comparable to the use of agitated saline administration in echocardiography. In contrast to commercial contrast agents, the nitrogen bubbles consist solely of gas without a monolayer shell. Therefore, the half-life time is very short (<30 seconds).

It is reasonable to assume that the nitrogen bubbles have a diameter larger than 9 μm because they were not seen in the left heart. Incidentally detected intervertebral VP without any evidence of infection usually presents with chronic back pain. Symptoms occur especially in the morning hours, when getting up, or in case of a change of barometric pressure.[5]

Spontaneous echo contrast is a well-described phenomenon in patients with implanted mechanical prosthetic valves. The development of these microbubbles typically occurs on the left side and during closure of the prosthetic valve, due to the Venturi effect. This seems to be enhanced at an increased heart beat frequency.[6]

Spontaneously appearing gas bubbles detected by echocardiography are described in the context of decompression phenomena in divers. Eftedal *et al.*[7] reported nitrogen gas bubbles even in asymptomatic divers with and without decompression. In addition, when imaging from the subcostal window using fundamental or tissue harmonics, Kerut *et al.*[8] observed occasional particle matter in the inferior vena cava in patients without known cardiac pathology. In this case, the bubbles differ somewhat from the morphology of spontaneous echo contrast. However, particle matter in the inferior vena

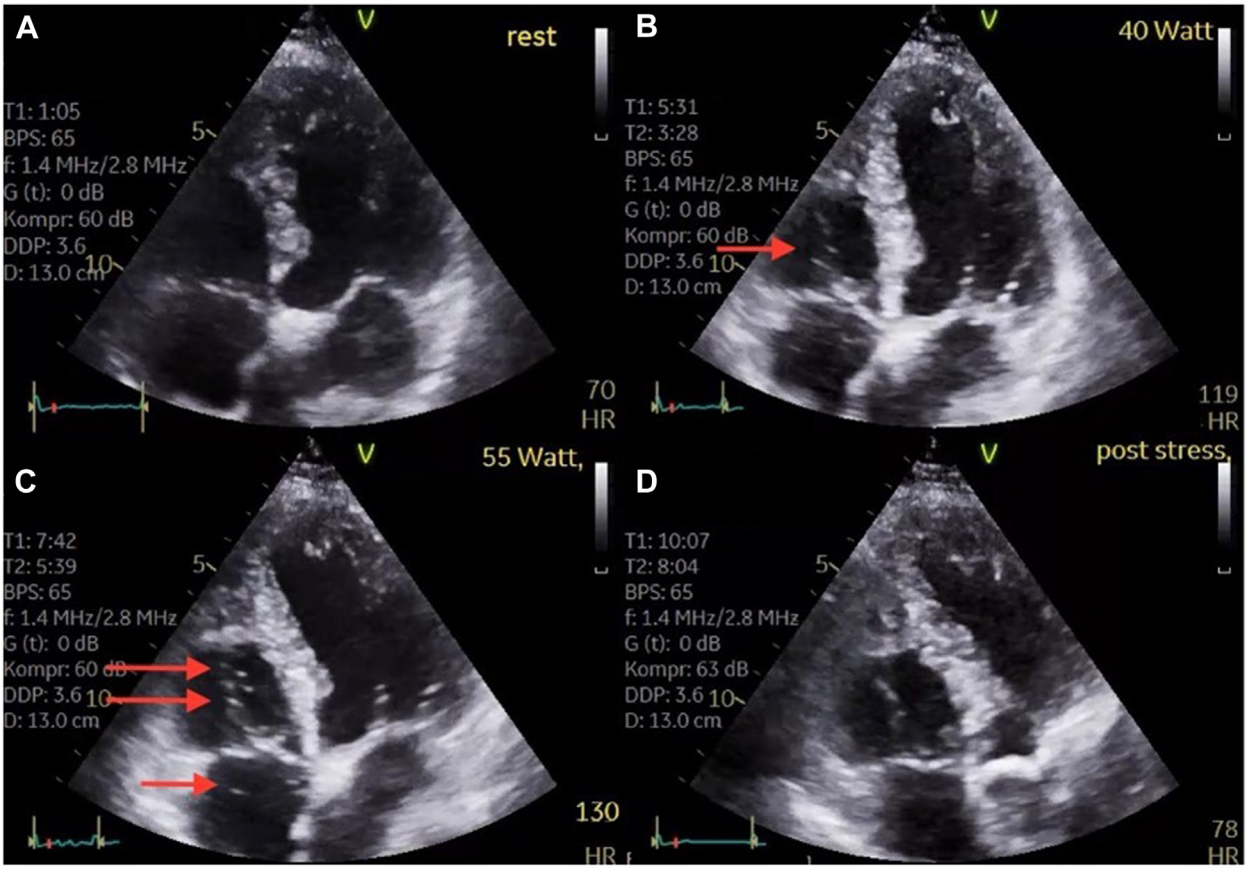

Figure 1 Comparison of apical 4-chamber views (right heart centered) during different stress levels. At stress levels 40 watts **(B)** and 55 watts **(C)**, echogenic bubbles appear only in the right atrium and right ventricle *(red arrows)*. Bubbles are not recorded at rest **(A)** or in the late recovery period **(D)**.

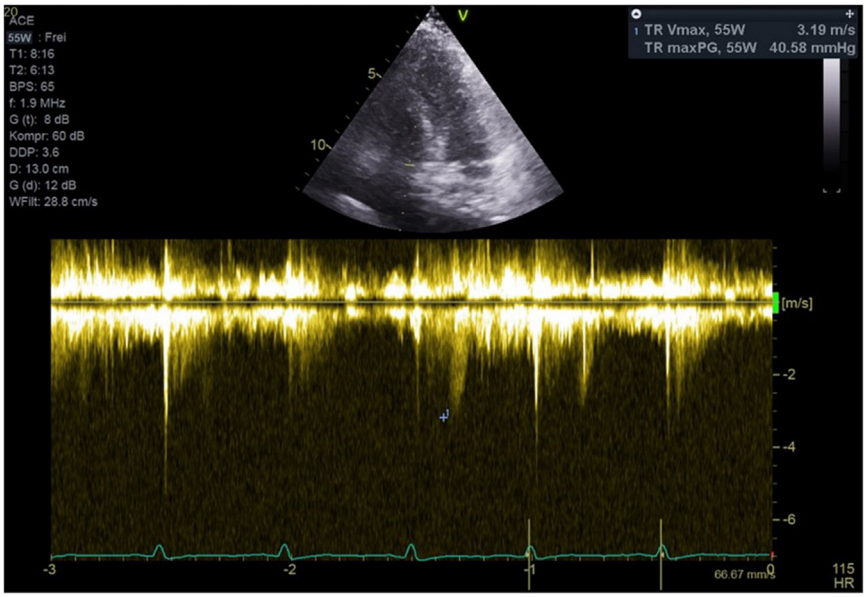

Figure 2 Apical 4-chamber view (right heart centered) during stress echocardiography at 55 watts, continuous-wave Doppler of the tricuspid valve, weak and incomplete Doppler signal slightly above the upper limit (3.2 m/sec) at peak stress. The signal quality is not sufficient to ultimately exclude a slight increase in pulmonary pressure.

cava is characterized by occurrence under bradycardia, left ventricular dysfunction, and low cardiac output.[8]

Reports of spontaneous and solely right-sided microbubbles are rare. The cases described are limited to individual case reports and one small case series. For instance, spontaneous right-sided microcavitation has been observed in patients with diseases of the intestine. There, gas may be absorbed from ulcerative gastrointestinal tumors,[9] an early sign of bowel necrosis after resuscitation,[10] or necrotizing enterocolitis in neonates,[11] which reaches the heart through portal and systemic vein shunts.

Patel *et al.*[12] presented a case report with an incidental finding of microcavitations in a 75-year-old female patient with a structurally normal heart. Echocardiography was performed because of isolated peripheral edema in a routine examination. The etiology of the bubbles observed there remains unclear. The authors hypothesize that it may be caused by an undetected portocaval shunt. Spontaneous—non–surgically created—shunts are extremely rare but have been described in association with gastric cancer.[13] Alternatively, it is possible that normocytic anemia in this patient should be discussed as an independent predictor of spontaneous vesicle formation.

In a case series, Iliceto *et al.*[14] described the appearance of right-sided bubbles in patients with significant tricuspid regurgitation. They identified the pathomechanism as a lateral pressure drop due to tricuspid regurgitation. In the present case report, this cause could be excluded and is therefore ruled out as a differential diagnosis.

In all of the aforementioned case descriptions, a CT of the spine was not performed, so that a VP was not ruled out. Conversely, no further imaging of the intestinal tract was performed in our patient. Thus, intestinal malignancy as well as protocaval shunt cannot be ultimately ruled out. However, these seem unlikely in the absence of clinical symptoms of malignancy.

We hypothesize the association with exercise, heart rate, and perhaps cardiac output can be highlighted as a reason for these bubbles appearing only during exercise. Due to the increased cardiac output, the usually poorly circulated intervertebral space experiences improved blood flow, allowing the bubbles to enter the systemic circulation.

The demonstrated pathway of the bubbles from the intervertebral disk to the heart is particularly interesting with respect to the relationship between endocarditis and spondylodiscitis. In approximately 8% of infective endocarditis cases a spondylodiscitis is diagnosed. In this context, the disk compartments L2/3 or L4/5 are frequently affected, and neurologic symptoms are found in approximately 60% of cases. Accordingly, spondylodiscitis is reported as a frequent complication of infective endocarditis. Vice versa, endocarditis occurs in approximately 33% of patients with spondylodiscitis and is associated with a significantly increased mortality.[15]

We assume that the gas was released by compression and decompression of the intervertebral space during physical exercise. This demonstrates the short and unobstructed pathway for bacteria from the intervertebral disk to the heart and may help to explain why spondylodiscitis is associated with a high rate of endocarditis. The phenomenon has not been described in the literature so far, possibly due to the fact that physical stress is rarely performed in the corresponding patient collective, where it is often not feasible due to a lack of mobility and as a result pharmacological stress is favored.

In the present case, there was no evidence of spondylodiscitis, systemic infection, malignancy, anemia, or dysfunction of any valve. The back pain was caused by degeneration, which also adequately explained the motion-dependent thoracic pain. A plausible diagnosis of generalized weakness could not be elicited and was attributed to old age. The case report is limited by the lack of additional information on pulmonary vessels and any intrapulmonary shunts recruited only during exercise and a lack of imaging of the gastrointestinal tract regarding potential malignancies. Further lung and abdominal imaging as well as a complex assessment of respiratory function was rejected

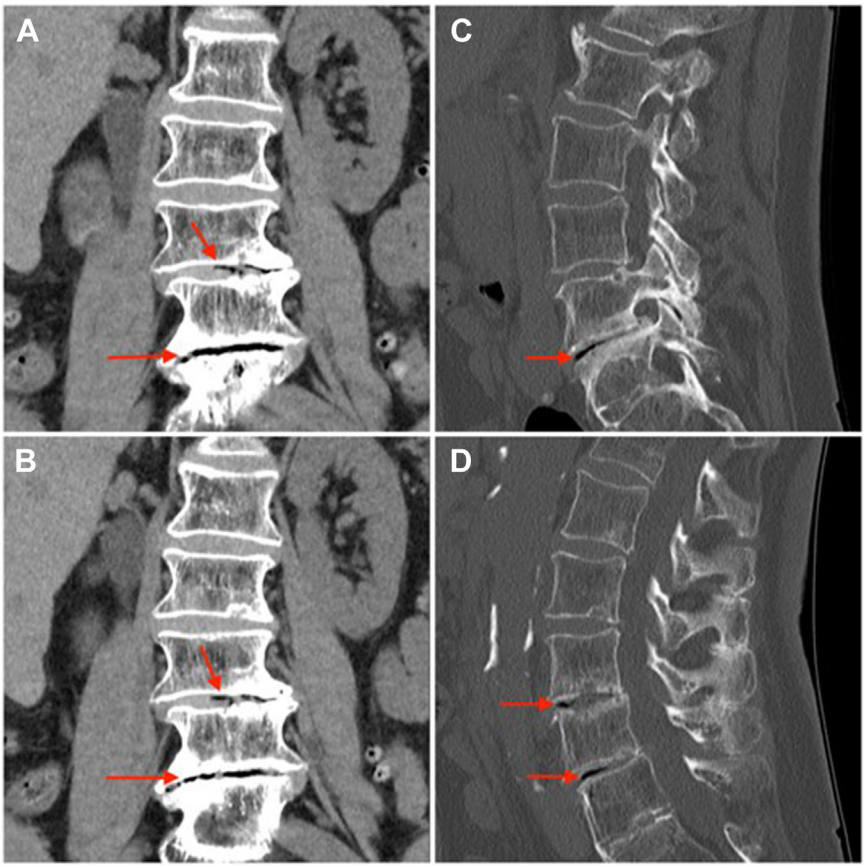

Figure 3 Four images from a CT scan of the lumbar spine. **(A, B)** Two consecutive coronal images (soft tissue window, slice thickness 3 mm, 173 mA, 120 kv). **(C, D)** Two consecutive sagittal images (bone window, slice thickness 3 mm, 173 mA, 120 kv). The *red arrows* show the hypodense structures (gas accumulations) in the intervertebral spaces L3/L4 and L4/L5.

by the patient during follow-up due to good exercise tolerance and subjective well-being.

CONCLUSION

Gas from the intervertebral space can enter the circulation. Thus, the intervertebral space may be a potential site of origin for bubbles detected by stress echocardiography. The same pathway is imaginable for bacteria in the case of spondylodiscitis.

ETHICS STATEMENT

The authors declare that the work described has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans.

CONSENT STATEMENT

Complete written informed consent was obtained from the patient (or appropriate parent, guardian, or power of attorney) for the publication of this study and accompanying images.

FUNDING STATEMENT

The authors declare that this report did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

DISCLOSURE STATEMENT

The authors report no conflict of interest.

SUPPLEMENTARY DATA

Supplementary data to this article can be found online at https://doi.org/10.1016/j.case.2022.09.005.

REFERENCES

1. Pellikka PA, Arruda-Olson A, Chaudhry FA, Chen MH, Marshall JE, Porter TR, et al. Guidelines for performance, interpretation, and application of stress echocardiography in ischemic heart disease: from the American Society of Echocardiography. J Am Soc Echocardiogr 2020;33:1-418.

2. Hood CR Jr, Jackson WA, Floros RC, Bernstein DA. The vacuum phenomenon in the ankle joint: air bubbles on CT. Foot Ankle Online J 2018;11. https://doi.org/10.3827/faoj.2018.1102.0002.
3. Gohil I, Vilensky JA, Weber EC. Vacuum phenomenon: clinical relevance. Clin Anat 2014;27:455-62.
4. Ford LT, Gilula LA, Murphy WA, Gado M. Analysis of gas in vacuum lumbar disc. AJR Am J Roentgenol 1977;128:1056-7.
5. Kasai Y, Takegami K, Uchida A. Change of barometric pressure influences low back pain in patients with vacuum phenomenon within lumbar intervertebral disc. Clin Spine Surg 2002;15:290-3.
6. Vriz O, Arshi F, Ahmed M, Alhumaid M, Galzerano D, Emmanual S, et al. Cavitation phenomenon in mechanical prosthetic valves: not only microbubbles. Echocardiography 2020;37:876-82.
7. Eftedal OS, Lydersen S, Brubakk AO. The relationship between venous gas bubbles and adverse effects of decompression after air dives. Undersea Hyperb Med 2007;34:99-105.
8. Kerut EK, Dearstine M, Dottery P, Nanda NC. Particulate matter within the inferior vena cava. Echocardiography 2008;25:803-4.
9. Barak M, Katz Y. Microbubbles: pathophysiology and clinical implications. Chest 2005;128:2918-32.
10. Labbé V, Hafiani el M. Echocardiographic air bubbles. Early sign of intestinal pneumatosis. Am J Respir Crit Care Med 2015;192:e44.
11. Abraham BP, Sachdeva R, Vyas PG, Thomas Collins R. An unusual presentation of necrotizing enterocolitis on an echocardiogram. Pediatr Cardiol 2012;33:1427-9.
12. Patel H, Boateng S, Singh G, Feinstein S. Spontaneous right-sided microcavitations in a healthy adult. Echo Res Pract 2015;2:K33-6.
13. Takeda J, Hashimoto K, Tanaka T, Koufuji K, Kakegawa T, Arishima T. Spontaneous portacaval shunts in patients with gastric cancer and hepatic cirrhosis. Kurume Med J 1991;38:33-7.
14. Iliceto S, Papa A, Ciociola G, Sorino M, Girardi F, Biasco G. [Spontaneous microcavitations in the right cardiac chambers. Microcavitations in the right sections]. G Ital Cardiol 1984;14:577-82.
15. Behmanesh B, Gessler F, Schnoes K, Dubinski D, Won SY, Konczalla J, et al. Infective endocarditis in patients with pyogenic spondylodiscitis: implications for diagnosis and therapy. Neurosurg Focus 2019;46:E2.