FAKULTNÍ NEMOCNICE OLOMOUC

Lékařská fakulta
Univerzita Palackého v Olomouci

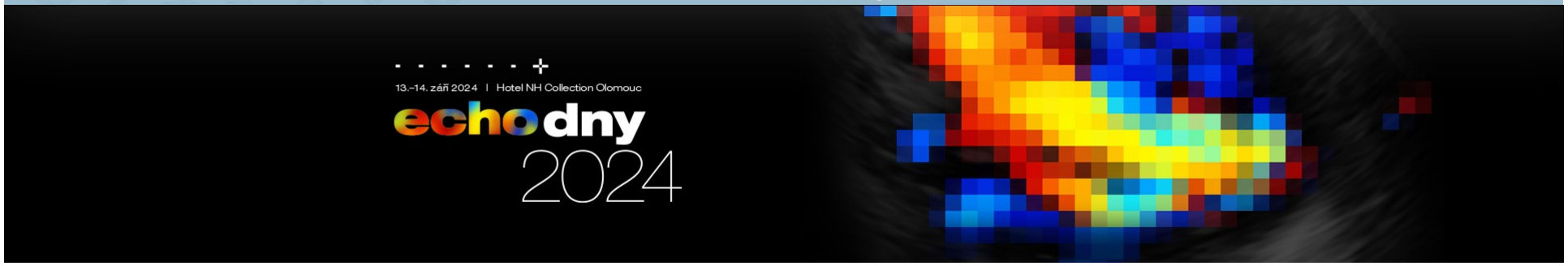
KOMPLEXNÍ KARDIOVASKULÁRNÍ CENTRUM
FAKULTNÍ NEMOCNICE OLOMOUC

ZDROJE KARDIOEMBOLIZMU

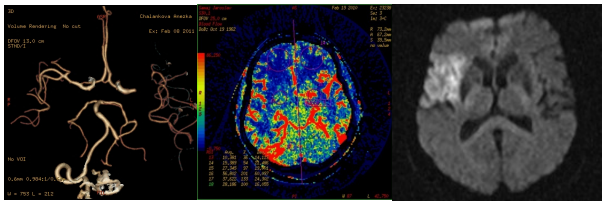
Nejen patentní foramen ovale, ale i jiné zkratové vady…

Martin Hutyra

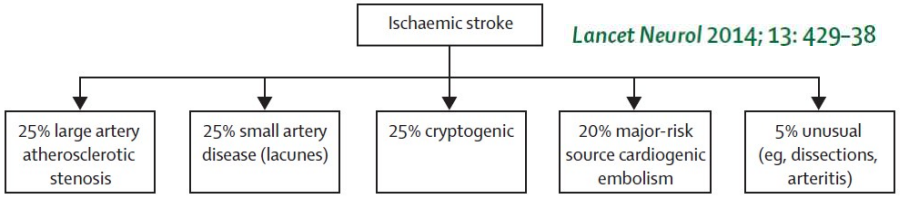
1. interní klinika - kardiologická, Lékařská fakulta a Fakultní nemocnice Olomouc



Introduction



Ischaemic stroke is a major cause of disability and mortality worldwide.
Cardioaortic embolism to the brain accounts for approximately 15–30% of ischaemic strokes and is often referred to as 'cardioembolic stroke'.
Cardioembolic stroke is generally severe and prone to early and long-term recurrences. Identifying potential cardiac sources of embolism is a key objective, because treatment may vary according to the cardiac condition diagnosed.
Unfortunately, and often despite comprehensive evaluation of the underlying cause, up to 30% of ischaemic strokes remain **'cryptogenic'** (i.e. without an established cause).
Consequently, a new entity has recently been defined: **embolic strokes of undetermined source (ESUS)**.



Lancet Neurol 2014; 13: 429–38

Embolic strokes of undetermined source: the case for a new clinical construct

Robert G Hart, Hans-Christoph Diener, Shelagh B Coutts, J Donald Easton, Christopher B Granger, Martin J O'Donnell, Ralph L Sacco, Stuart J Connolly, for the Cryptogenic Stroke/ESUS International Working Group

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Definitions

Cerebral infarction

Cerebral infarction is defined as brain, spinal cord, or retinal cell death attributable to ischaemia, based on neuroimaging, neuropathological evidence, and/or clinical evidence of permanent injury.

Transient ischaemic attack

TIA is a transient episode of neurological dysfunction caused by focal brain, spinal cord, or retinal ischaemia, without acute infarction.

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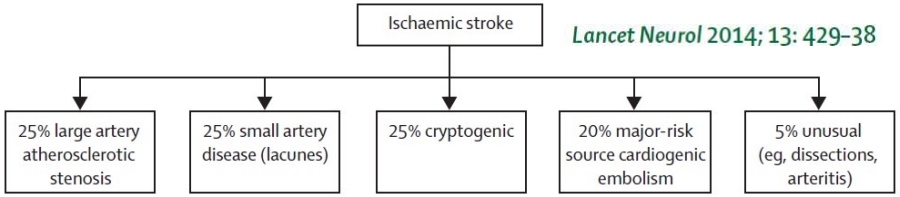
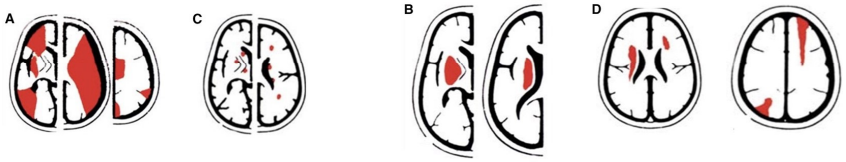
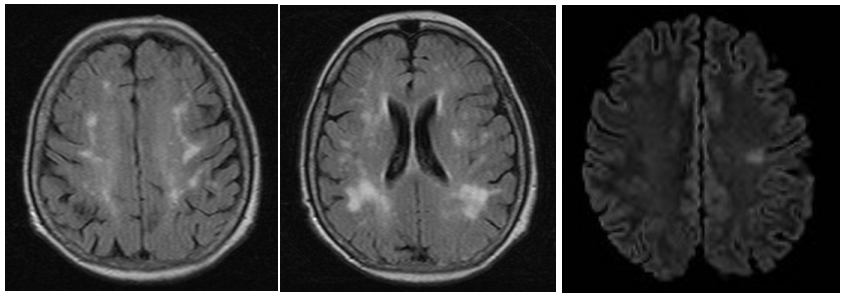


Lancet Neurol 2014; 13: 429–38

Schematic drawings of patterns of brain infarctions signalling different stroke mechanisms:

(A) Cardioembolic stroke is probable in cortical infarcts with territorial distribution;
(B) the same holds true for large striatocapsular infarcts;
(C) but not for lacunar infarctions, by definition located subcortically;
(D) low-flow infarct can be located subcortical or cortical (right panel), but their distribution is interterritorial not territorial.





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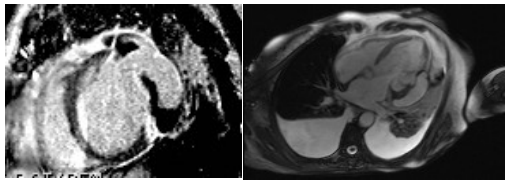
The diagnosis of cardioembolic stroke is often difficult because the presence of a potential cardiac source of embolism alone does not establish the stroke mechanism. The clinical significance of minor or uncertain sources of cardiac risk remains. Approximately **25% of patients have more than one cardiac source of embolism** and **15% have significant cerebrovascular atherosclerosis**.

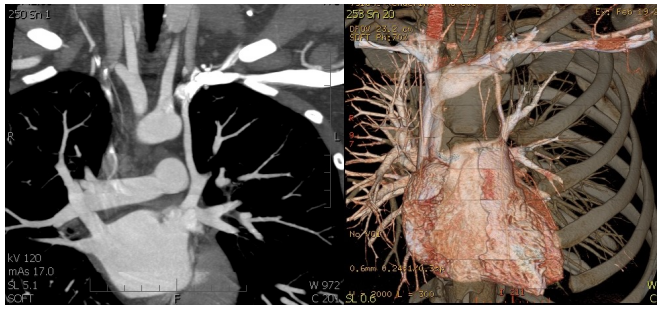
Combined, these clinical factors emphasize the role of cardiac imaging—transthoracic echocardiography (TTE) and transoesophageal echocardiography (TOE) as the first-line, and cardiac computed tomography (CT) and magnetic resonance imaging (MRI) in addition—in the evaluation of patients with stroke, in the diagnosis of potential cardiac sources of embolism, and for therapeutic guidance.

Cardiovascular imaging tools

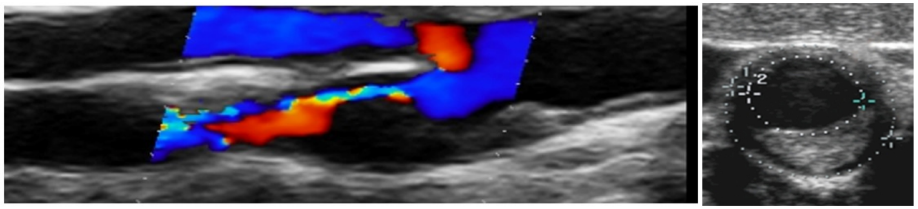
1. Transthoracic and transoesophageal echocardiography

2. Computed tomography and magnetic resonance imaging





3. Vascular imaging



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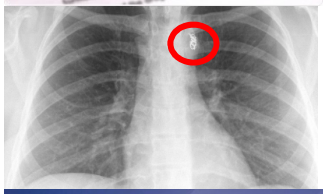
Transthoracic and transoesophageal echocardiography

- More than 30 cross-sectional studies have evaluated **the yield of TTE or TEE, in detecting cardiac sources of embolus** in patients with stroke. In consecutive patients, the yield of echocardiography for the detection of intracardiac masses ranged from 0% to 21%. Pooled data from these studies suggest an overall yield of 4% for TTE and 11% for TEE.
- In a retrospective study that included 1458 patients hospitalized for stroke with a suspected cardioembolic cause, **TEE changed the management** in approximately 16% of patients, leading to the introduction of anticoagulation and antibiotics, closure and surgical closure of patent foramen ovale (PFO), and coil embolization.
- In a meta-analysis of 12 studies, the **pooled rate of reported anticoagulation therapy attributed to abnormal TEE findings** among 3562 patients with ischaemic stroke was 8.7%.



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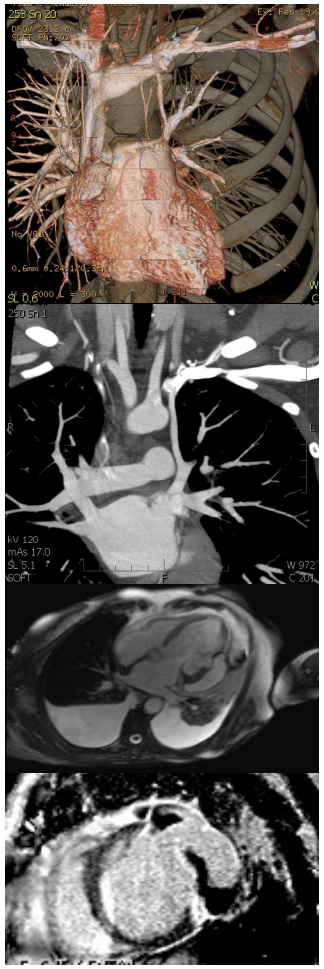
Computed tomography and magnetic resonance imaging

- Both CT and MRI are highly accurate for detecting **LAA thrombosis** in patients with AF, with 100% sensitivity and specificity relative to TOE.
- CT also allows the identification of **valvular prosthesis thrombosis, aortic atheroma, PFO, atrial septal defect, and intracardiac tumours**.
- CMR is more sensitive and accurate than TTE for the detection of **intraventricular thrombi** after acute or chronic MI, and allows the detection of LV thrombi in patients with ESUS and a history of MI that may have been missed on TTE.

Table S2 CT and MRI in the diagnosis of cardiac source of embolism

Reference	Patients	Techniques	Input of CT or MRI for the detection of for detection of cardiac sources of embolism
Boussel 2011[1]	46 patients with ischaemic stroke	CT vs. TOE	Sensitivity of CT was 72% and specificity was 95% for detection of CSE CT facilitated correct aetiologic classification for 83% of patients
Hur 2009[2]	137 patients with ischaemic stroke	CT vs. TOE	Sensitivity of CT was 89% and specificity was 100% for detection of cardiac source of embolism
Sipola 2013[3]	101 patients with ischaemic stroke	CT vs. TTE/TOE	CT + TTE/TOE vs. TTE/TOE for detection of cardiac source of embolism: sensitivity 91% vs. 41%, respectively, $P < 0.001$; specificity 98% vs. 99%
Haeusler 2017[4]	103 patients with acute ischaemic stroke of undetermined origin	MRI vs. TOE	Cardiac MRI identified stroke aetiology in an additional 6.1% of patients
Liberman 2017[5]	93 patients with ischaemic stroke, including 64 with cryptogenic stroke	MRI vs. TOE	Cardiac MRI reduced the percentage of patients with cryptogenic stroke by slightly more than 1%
Zahuranec 2012[6]	20 patients with ischaemic stroke	MRI vs. TOE	TEE identified more potential cardioembolic sources than CMR imaging
Baher 2014[7]	85 patients with ischaemic stroke and 21 with transient ischaemic attack	MRI vs. TOE	Cardiac MRI and delayed enhancement cardiac MRI resulted in a 26.1% reduction and a 39.1% reduction, respectively, of cryptogenic strokes

CSE, cardiac source of embolism; CMR, cardiac magnetic resonance; CT, computed tomography; ESUS, embolic strokes of undetermined source; MRI, magnetic resonance imaging; TOE, transoesophageal echocardiography; TTE, transthoracic echocardiography.



ESC European Society of Cardiology European Heart Journal - Cardiovascular Imaging (2021) 22, e24–e57 doi:10.1093/ehjci/jeab008

EACVI DOCUMENT

EACVI recommendations on cardiovascular imaging for the detection of embolic sources: endorsed by the Canadian Society of Echocardiography

(Chair) Ariel Cohen[1,2*], (Co-Chair) Erwan Donal[3], Victoria Delgado[4], Mauro Pepi[5], Teresa Tsang[6], Bernhard Gerber[7], Laurie Soulat-Dufour[1,2], Gilbert Habib[8], Patrizio Lancellotti[9,10], Arturo Evangelista[11], Bibiana Cujec[12], Nowell Fine[13], Maria Joao Andrade[14], Muriel Sprynger[15], Marc Dweck[16], Thor Edvardsen[17], and Bogdan A. Popescu[18]

Recommendations for cardiovascular imaging tools[45]

TTE, TOE, CMR

TTE should be performed systematically before TOE for evaluation of the cardiovascular source of embolus.

Contrast TTE, using intravenous injection of agitated saline, should be performed systematically at baseline and after provocative manoeuvres (Valsalva manoeuvre, coughing, both).

General indications in search of cardiac or aortic sources of embolism

Contrast TTE is the initial imaging modality of choice for evaluation of the cardiac and aortic sources of embolus.

Contrast TOE should be done in selected patients for evaluation of the cardiovascular sources of embolus if no identified source is found on TTE.

Contrast TOE should be performed according to the clinical context, but emergent indications are limited (e.g. fever, prosthesis).

Contrast TOE should be performed rapidly (ideally within 48 h) in case of ischaemic stroke, peripheral embolism, or previous heart valve replacement (percutaneous or surgical).

Contrast TOE is not indicated in ischaemic stroke patients with a previously identified source.

A comprehensive stroke CT protocol, including the intracranial and cervical arteries, aortic arch, cardiac chambers and walls, and coronary arteries, can be proposed in trained centres as an alternative initial imaging modality for evaluation of the cardiac and aortic sources of embolus.

CMR could be proposed in unselected patients with cryptogenic stroke who have a non-diagnostic cardiac evaluation including contrast TOE.

Vascular imaging

Doppler ultrasound (first-line), CTA, and/or MR angiography are recommended for evaluating carotid stenoses.

When carotid stenting is being considered, it is recommended that any Doppler ultrasound study be followed by either MR or CTA to evaluate the aortic arch, as well as the extra- and intracranial circulation.

When CEA is considered, it is recommended that Doppler ultrasound be corroborated by MR or CTA or repeat Doppler ultrasound performed by an expert.

Cardiac sources of cerebral embolism

ESC European Society of Cardiology
European Heart Journal - Cardiovascular Imaging (2021) 22, e24–e57
doi:10.1093/ehjci/jeab008
EACVI DOCUMENT

EACVI recommendations on cardiovascular imaging for the detection of embolic sources: endorsed by the Canadian Society of Echocardiography

Major sources of stroke risk	Minor or unclear sources of stroke risk
Atrial fibrillation	Mitral valve prolapse
Recent myocardial infarction	Mitral annulus calcification
Previous myocardial infarction (LV aneurysm)	Spontaneous echo contrast
All cardiomyopathies including non-compaction and takotsubo cardiomyopathies	Calcified aortic stenosis
Cardiac masses (except calcifications)	Valvular strands
Intracardiac thrombus	Atrial septal aneurysm without PFO
Intracardiac tumours	
Fibroelastoma	
Marantic vegetations	PFO
Rheumatic valve disease (mitral stenosis)	
Aortic arch atheromatous plaques	Atrial septal pouch
Endocarditis	Giant Lambl's excrescences
Prosthetic valve (mechanical especially)	

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Panel 1: Causes of embolic strokes of undetermined source

Minor-risk potential cardioembolic sources*

Mitral valve
- Myxomatous valvulopathy with prolapse
- Mitral annular calcification

Aortic valve
- Aortic valve stenosis
- Calcific aortic valve

Non-atrial fibrillation atrial dysrhythmias and stasis
- Atrial asystole and sick-sinus syndrome
- Atrial high-rate episodes
- Atrial appendage stasis with reduced flow velocities or spontaneous echodensities

Atrial structural abnormalities
- Atrial septal aneurysm
- Chiari network

Left ventricle
- Moderate systolic or diastolic dysfunction (global or regional)
- Ventricular non-compaction
- Endomyocardial fibrosis

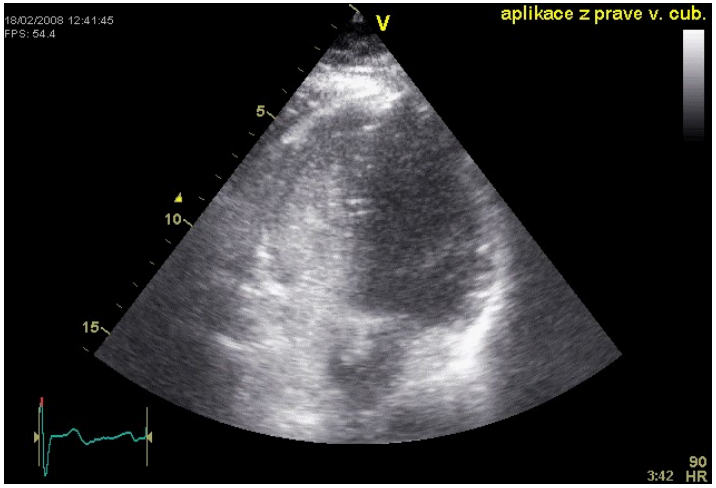
Covert paroxysmal atrial fibrillation

Cancer-associated
- Covert non-bacterial thrombotic endocarditis
- Tumour emboli from occult cancer

Arteriogenic emboli
- Aortic arch atherosclerotic plaques
- Cerebral artery non-stenotic plaques with ulceration

Paradoxical embolism
- Patent foramen ovale
- Atrial septal defect
- Pulmonary arteriovenous fistula

Hart RG, Diener HC, Coutts SB, et al. Embolic strokes of undetermined source: the case for a new clinical construct. Lancet Neurol 2014;13:429-38.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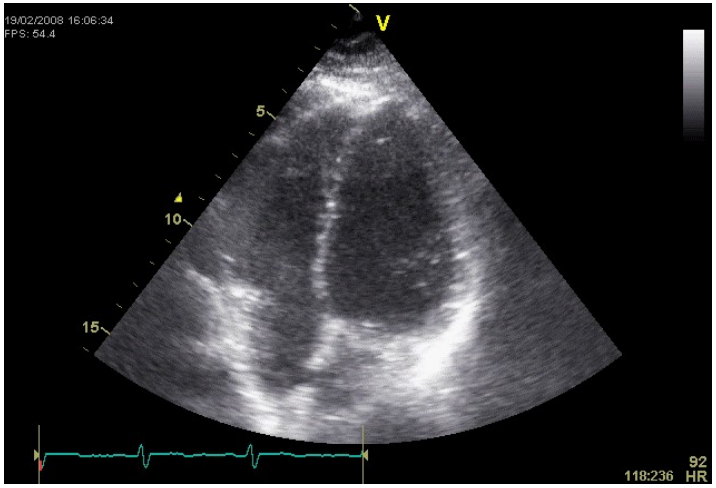
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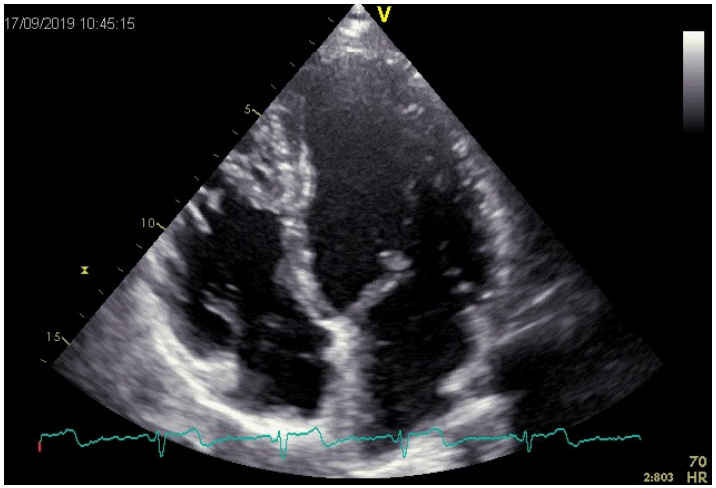
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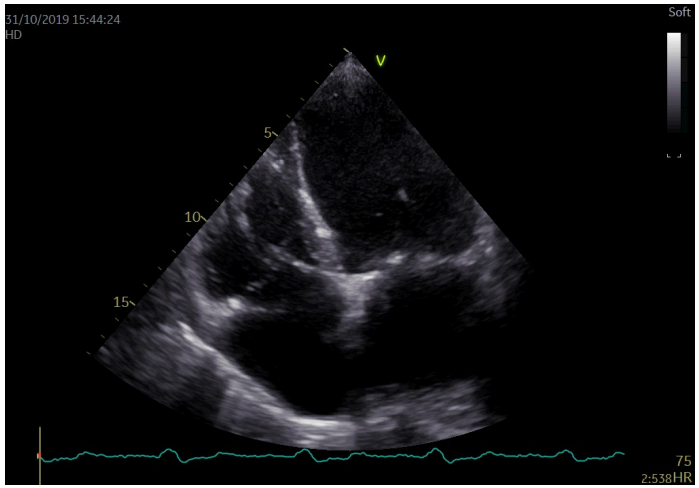
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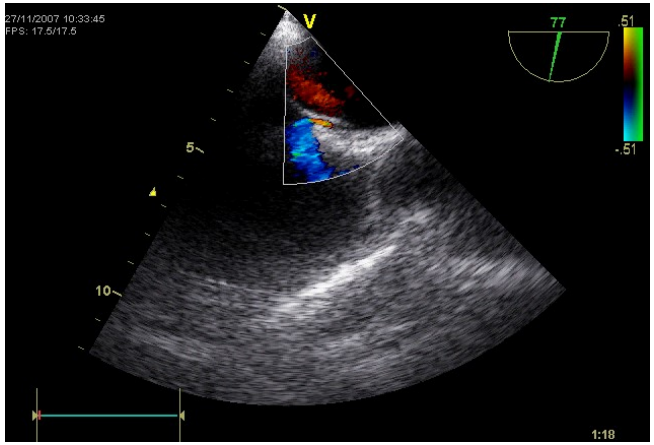
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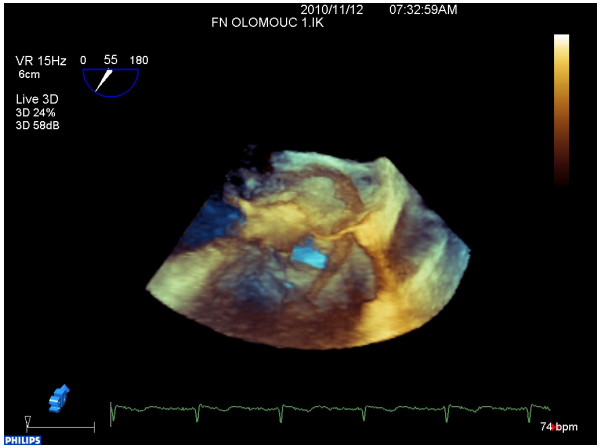
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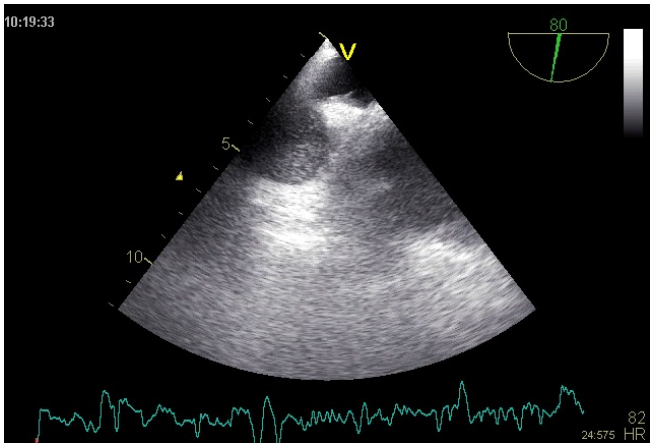
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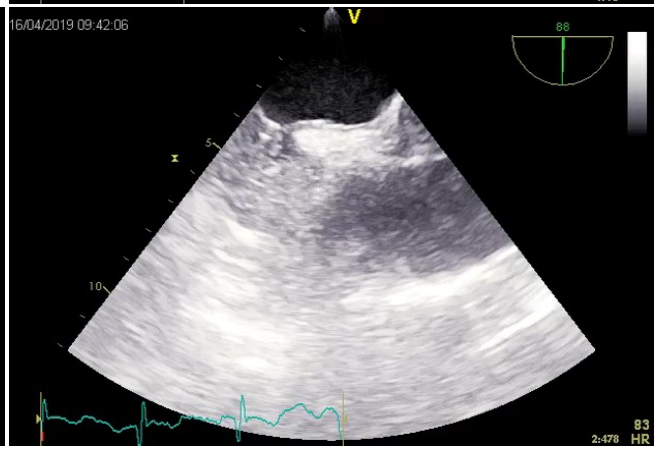
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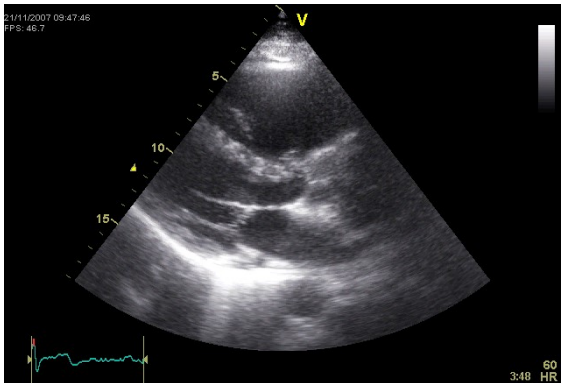
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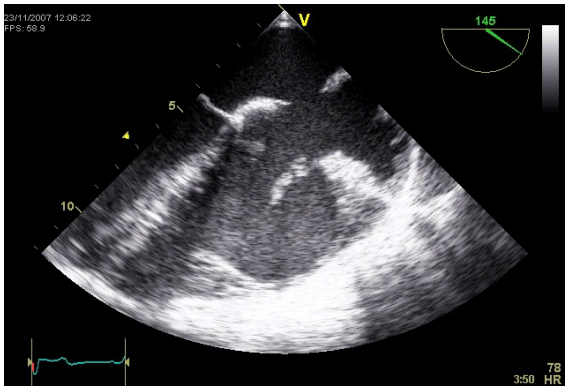
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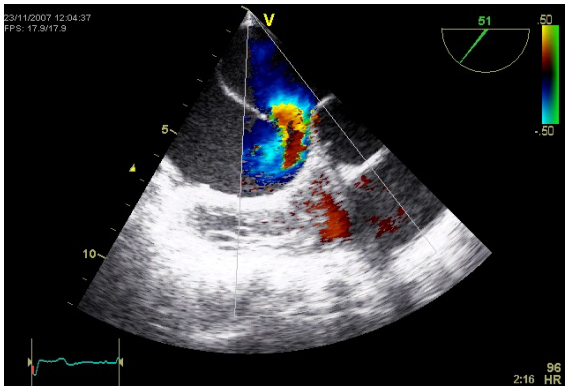
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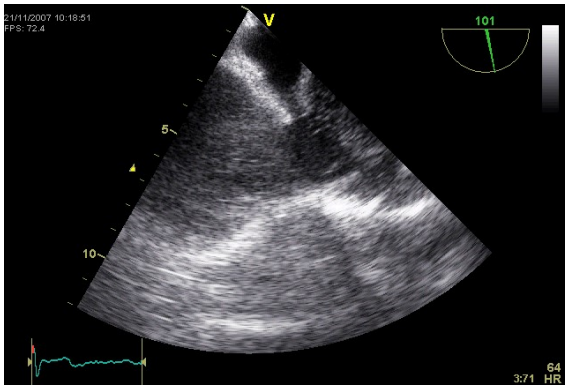
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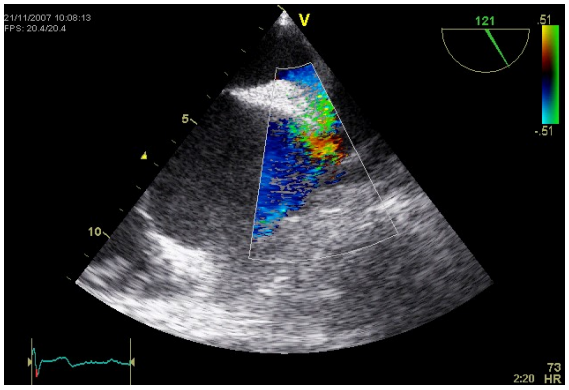
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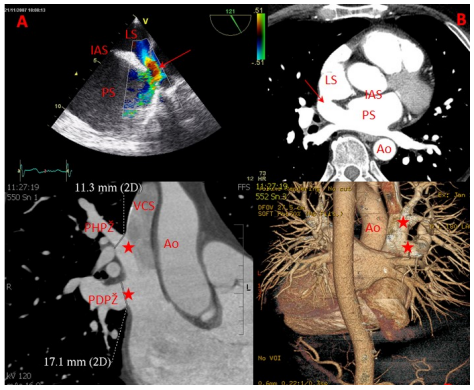
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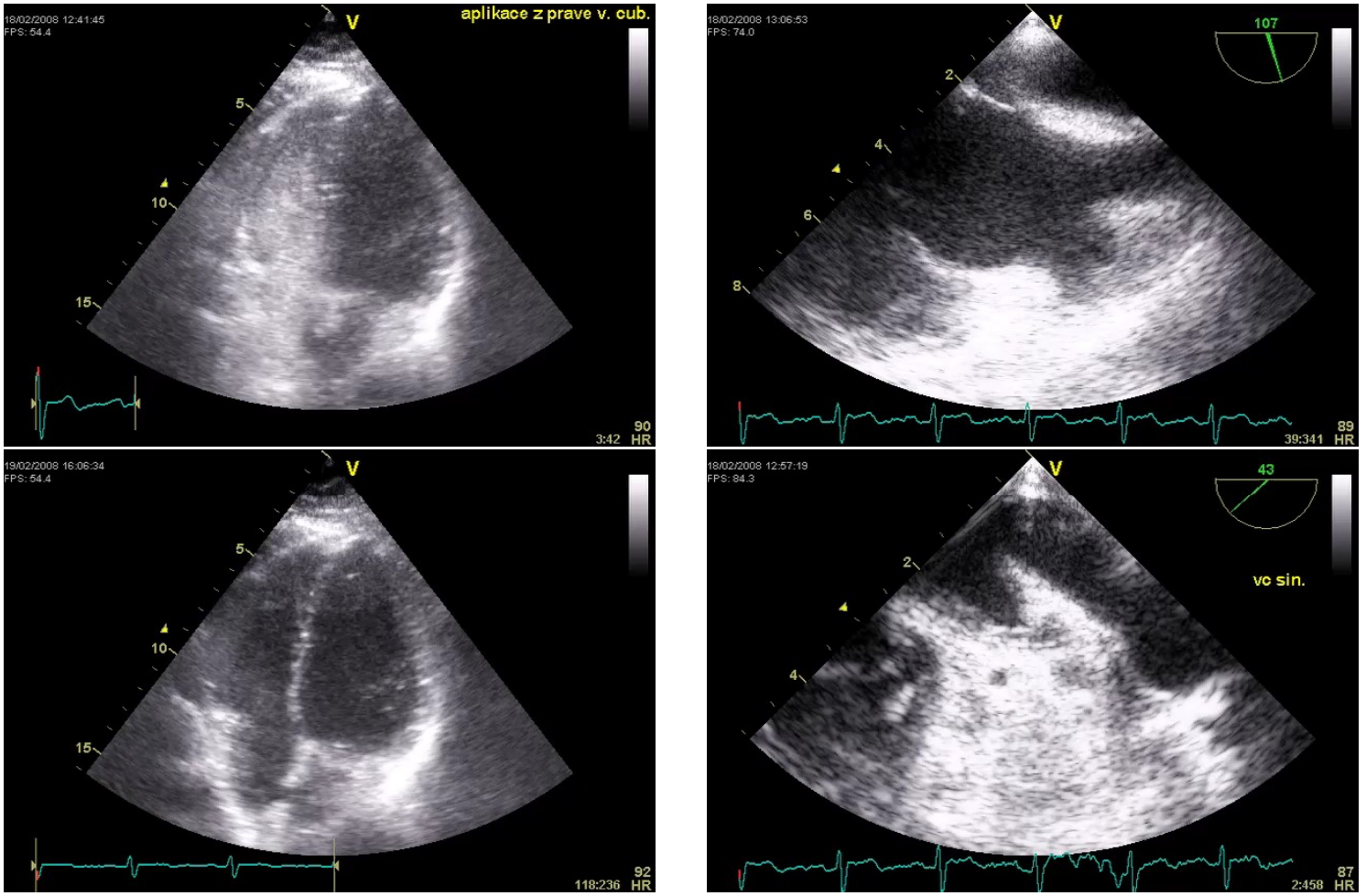
Persistent left superior vena cava - screening

(A) After injecting agitated saline into the right antecubital vein, there was a normal sequence of opacification of the right heart chambers with no penetration of microbubbles into the left heart chambers.
(B, C) In A4C and midoesophageal bicaval TEE views of the patient lying on the left side, synchronous saturation of the left and right heart chambers was noticeable after applying a contrast agent into the left antecubital vein. There was no evidence of echocontrast agent flow from the region of the non-dilated coronary sinus into the left or right atrium. (D) TEE focused on the pulmonary vein revealed a clear inflow of the contrast agent into the left atrium through the left superior pulmonary vein (white arrow).

Eur J Echocardiogr, Volume 11, Issue 9, October 2010, Page E35, https://doi.org/10.1093/ejechocard/jeq079



Eur J Echocardiogr, Volume 11, Issue 9, October 2010, Page E35, https://doi.org/10.1093/ejechocard/jeq079

Persistent left superior vena cava - detection

Computed tomography of the chest.

Reconstructed images using volume rendering (A) and a two-dimensional image (B) demonstrates that the persistent left superior vena cava originates from the left brachiocephalic vein (white arrow) and drains (yellow arrow) into the left upper pulmonary vein, which leads directly into the left atrium.
Ao, aorta; PA, pulmonary artery

Eur J Echocardiogr, Volume 11, Issue 9, October 2010, Page E35, https://doi.org/10.1093/ejechocard/jeq079

Persistent left superior vena cava – confirmation and occlusion

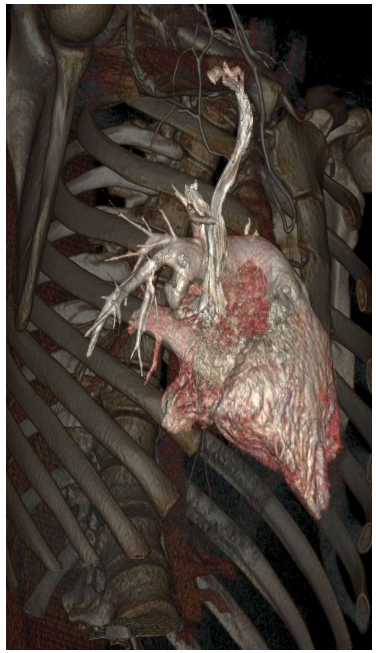
Venography (A) and chest X-ray after catheter closure of PLSVC (B)

(A) After application of a contrast agent, the persistent left superior vena cava can be seen, originating from the left brachiocephalic vein (white arrow) draining into the left upper pulmonary vein at the conflux with the pulmonary vein (yellow arrow), from where the flow is seen as a negative contrast (darker endovascular content) is apparent. Furthermore, there is an evident of normal venous inflow into the right atrium through the superior vena cava. **(B)** The position of the coil under the left clavicle is visible after the catheter closure procedure (red arrow).

Eur J Echocardiogr, Volume 11, Issue 9, October 2010, Page E35, https://doi.org/10.1093/ejechocard/jeq079

Pulmonary artery to left atrial fistula

- Communication between right pulmonary artery and left atrium is a rare anomaly. It was first described in 1950 by Friedlich et al., it is usually a congenital anomaly, however it can also occur in a post-traumatic setting. True prevalence of this anomaly is unknown, in current literature approximately a hundred cases exist, almost all of them from right pulmonary artery (PA) to left atrium (LA), only three cases of left PA-to-LA fistula have been reported.
- In 70 % cases it is diagnosed before age of twenty, in 30 % before the age of ten. Prevalence is higher in men than women (3:1)
- Typical symptoms are shortness of breath, cyanosis, clubbing of the fingers, polycythemia, hypoxia. Larger shunts usually present earlier with heart failure and subsequent death. First symptoms in moderate shunts can be paradoxical embolism resulting in infarcts or abscesses throughout the body.



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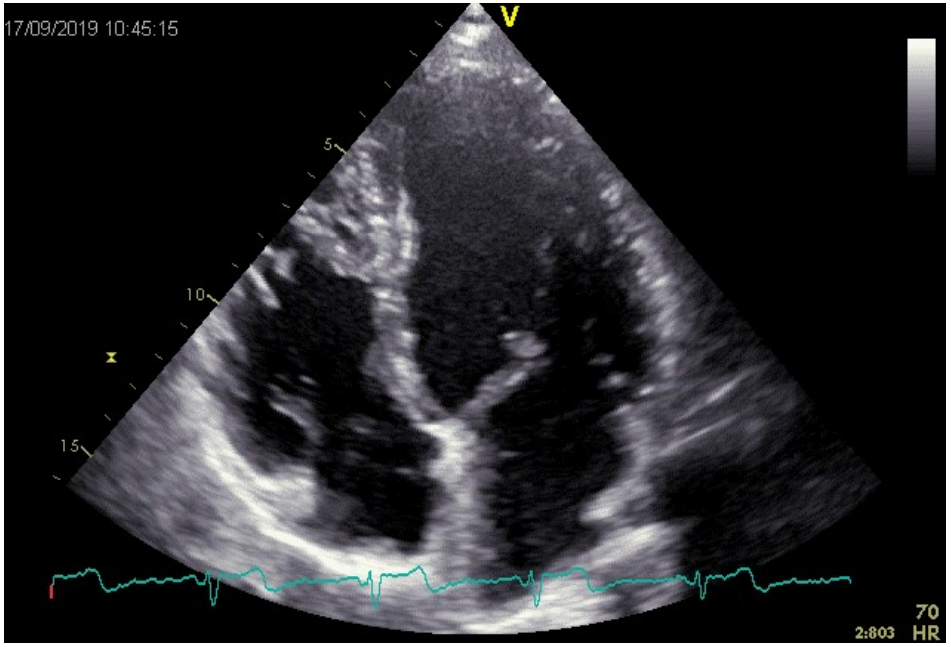
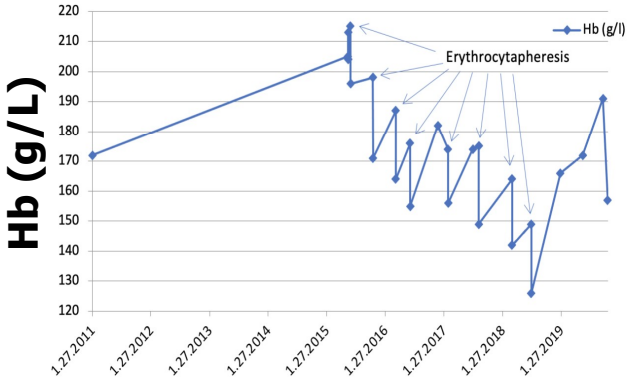
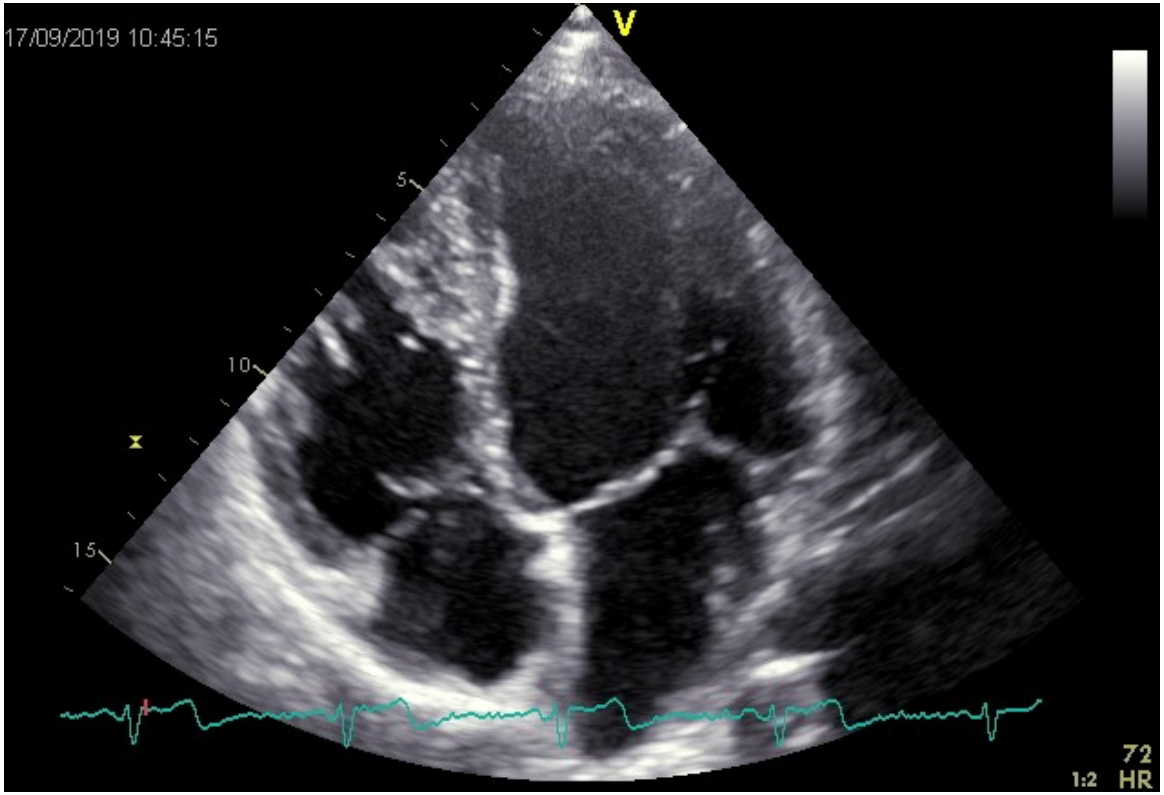
De Souza. Communication bertween right pulmonary artery and left atrium. Am J Cardiol 1974,34:857-863.

Pulmonary artery to left atrial fistula – screening

Contrast echocardiography. After injection of agitated saline into the left cubital vein there was abnormal opacification and early filling (into 3 cycles) of left heart, in movie clip is certainly known that filling of left atrium with microbubbles is through the pulmonary vein.



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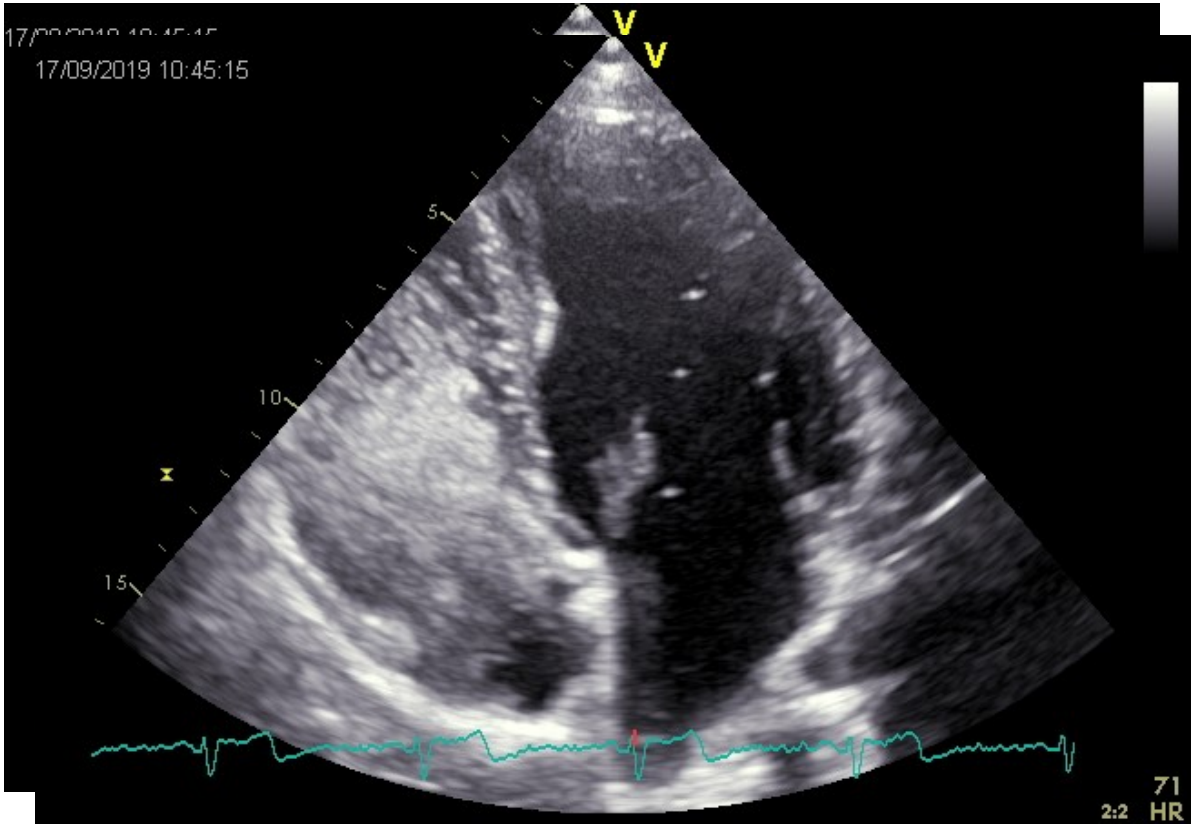
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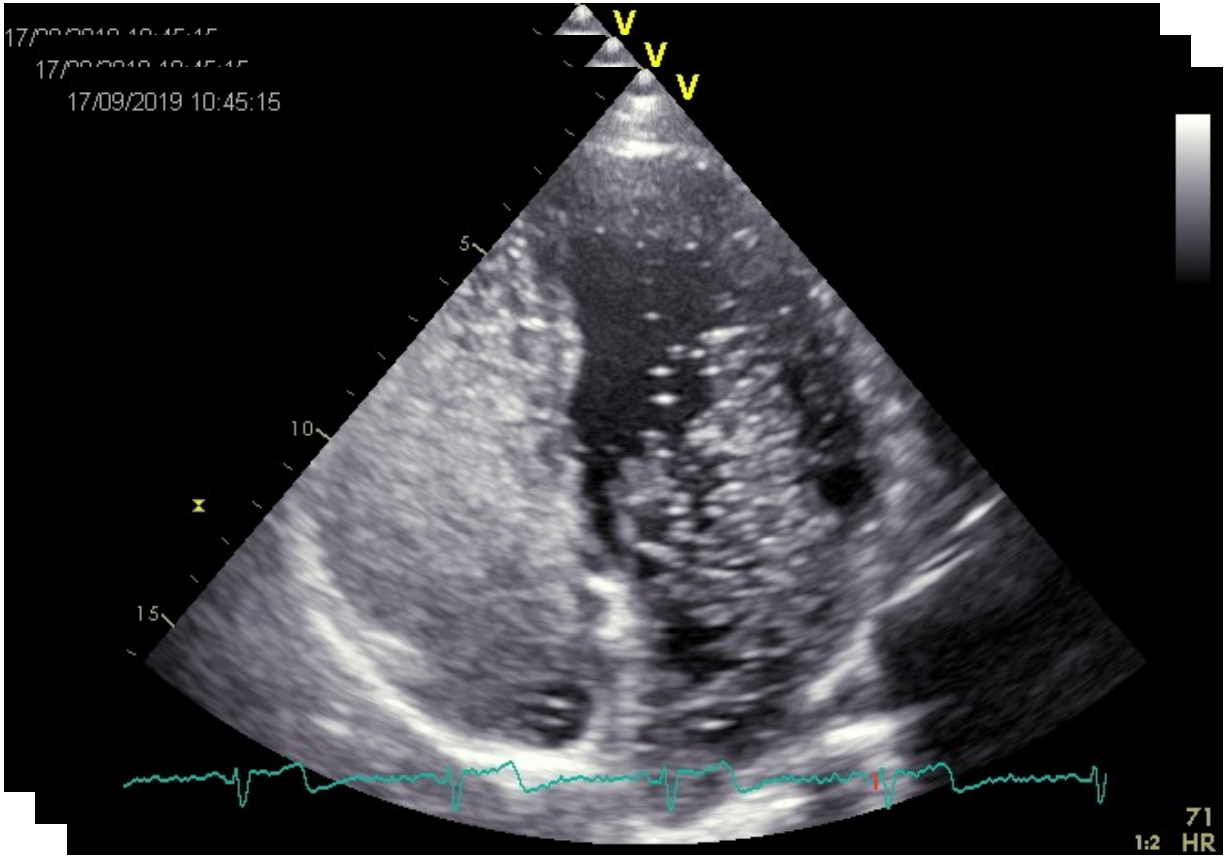
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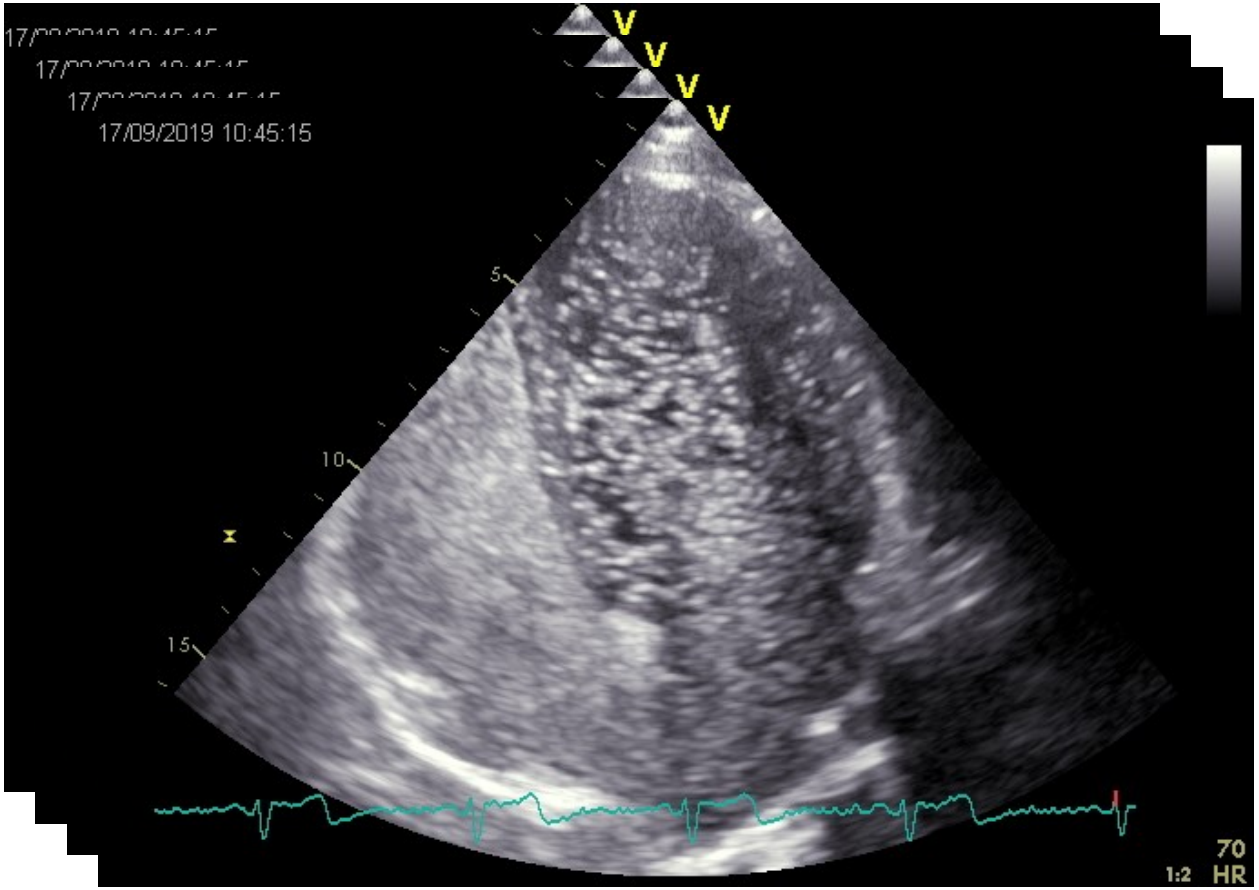
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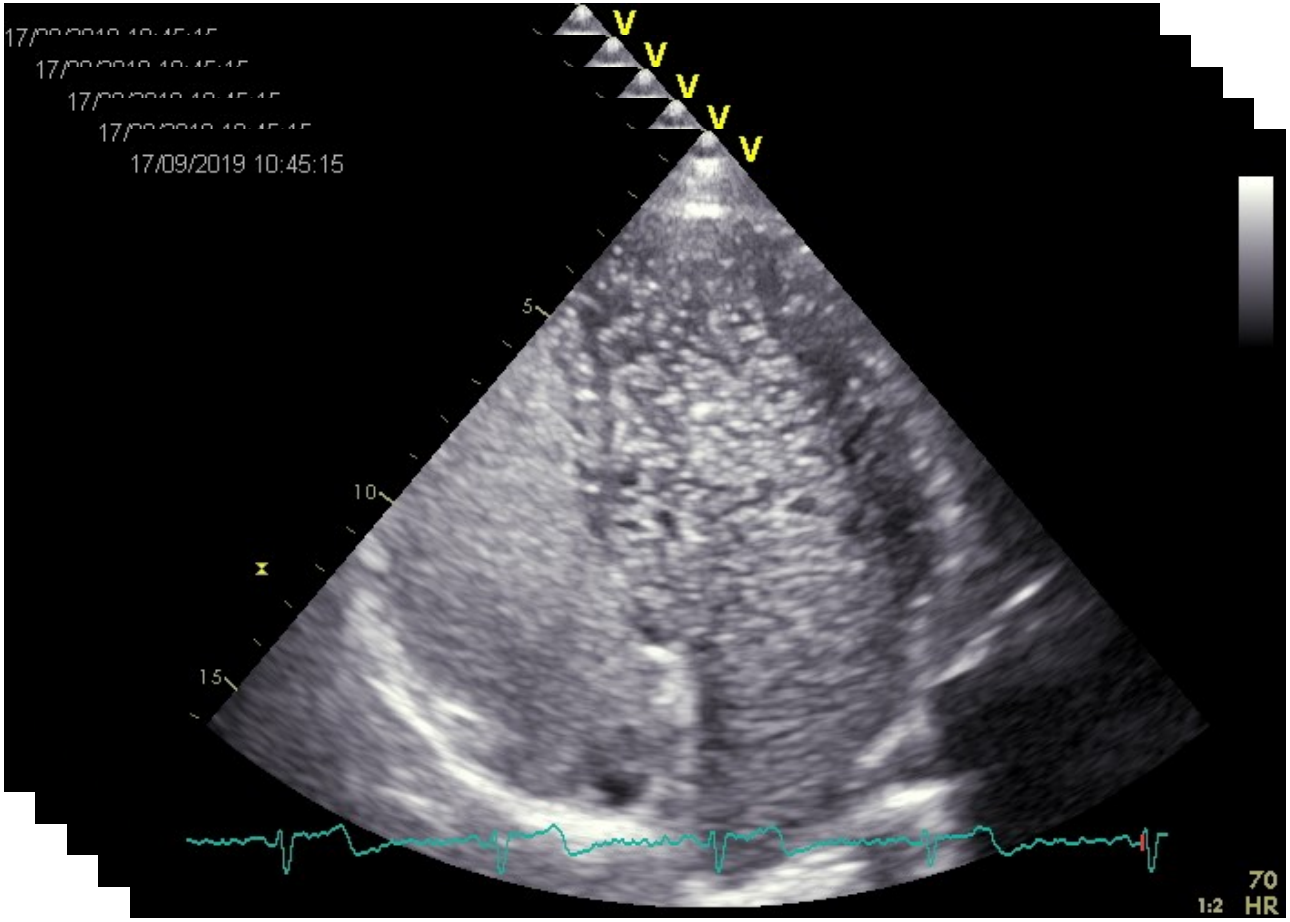
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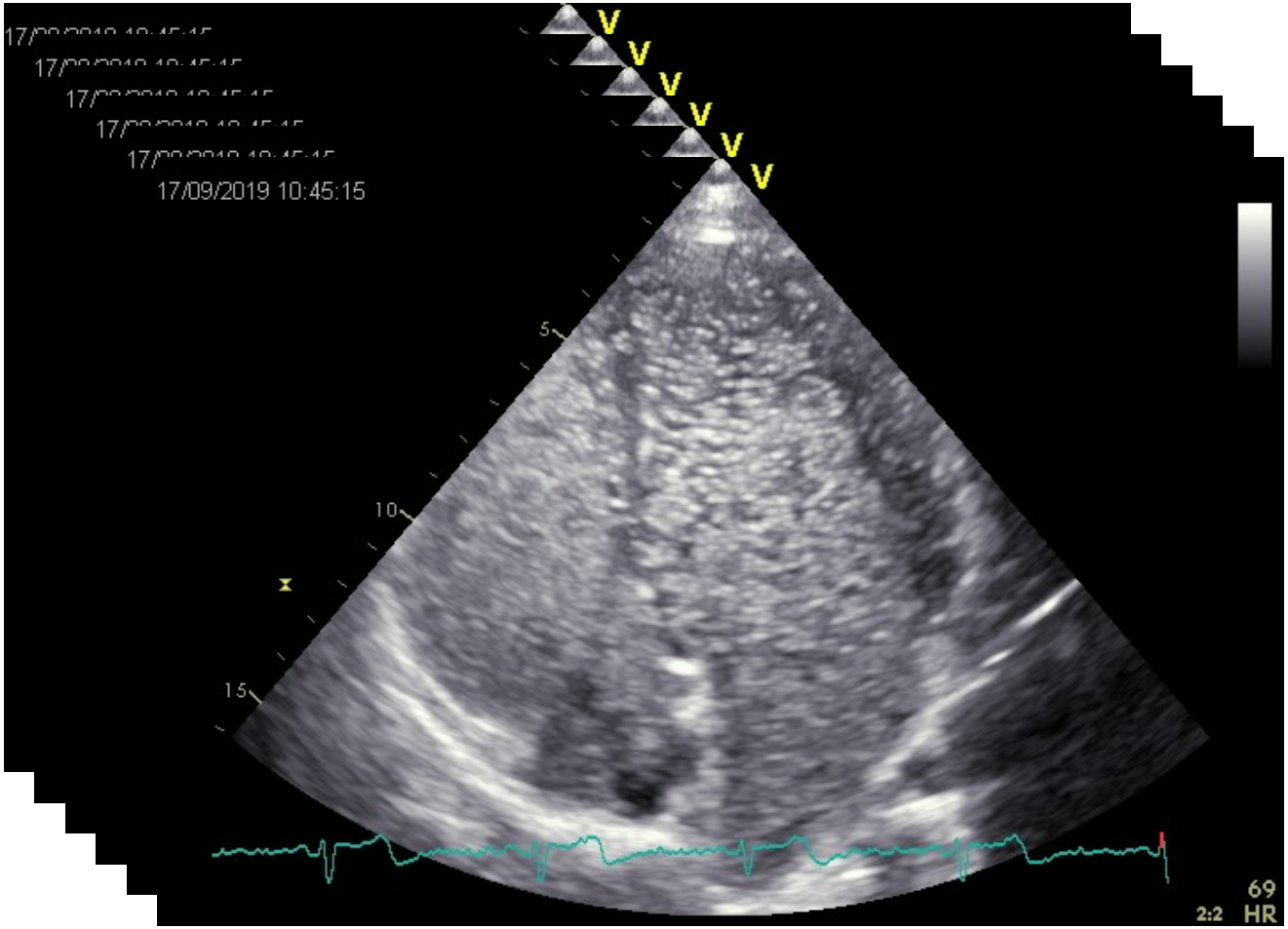
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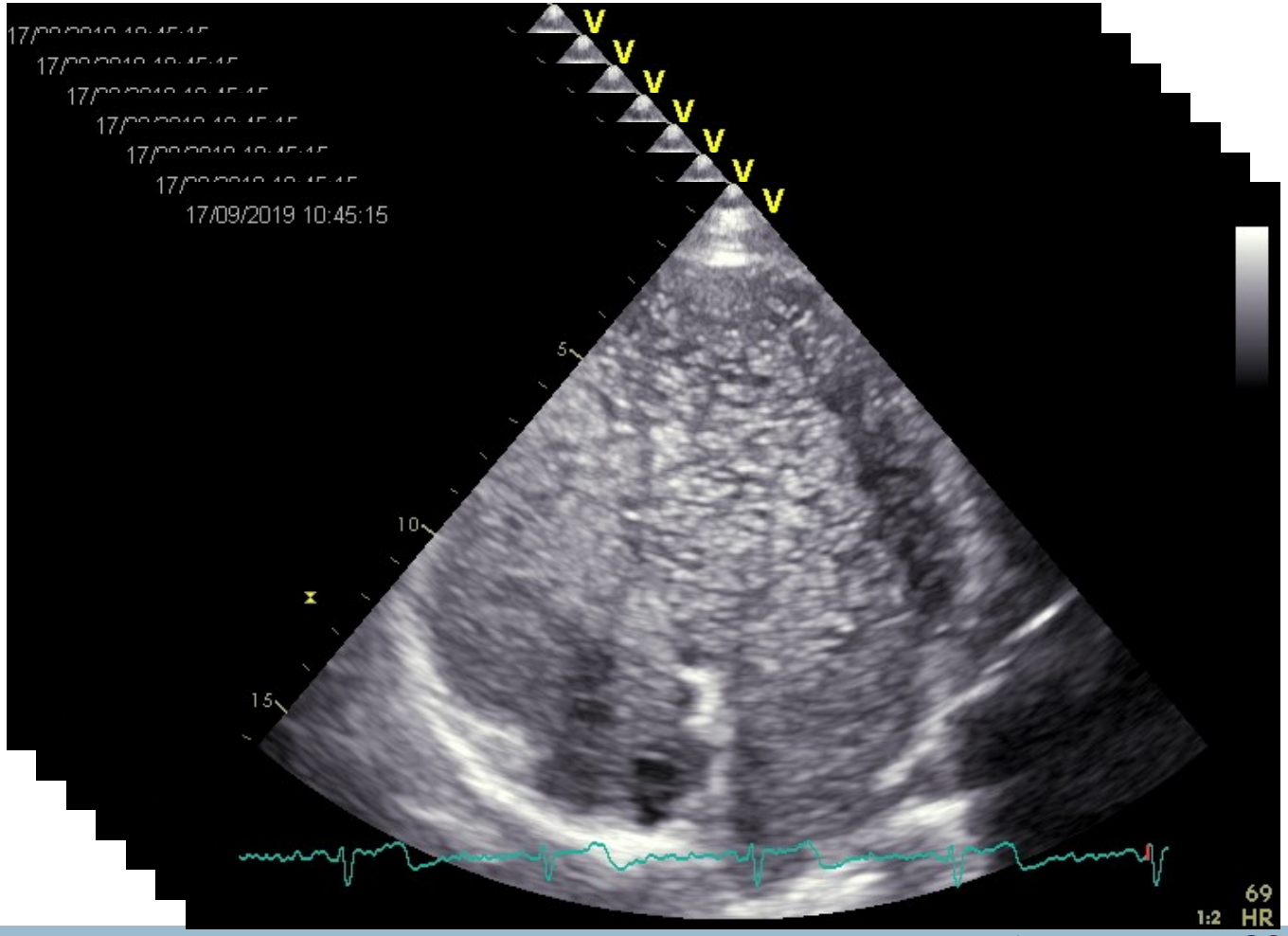
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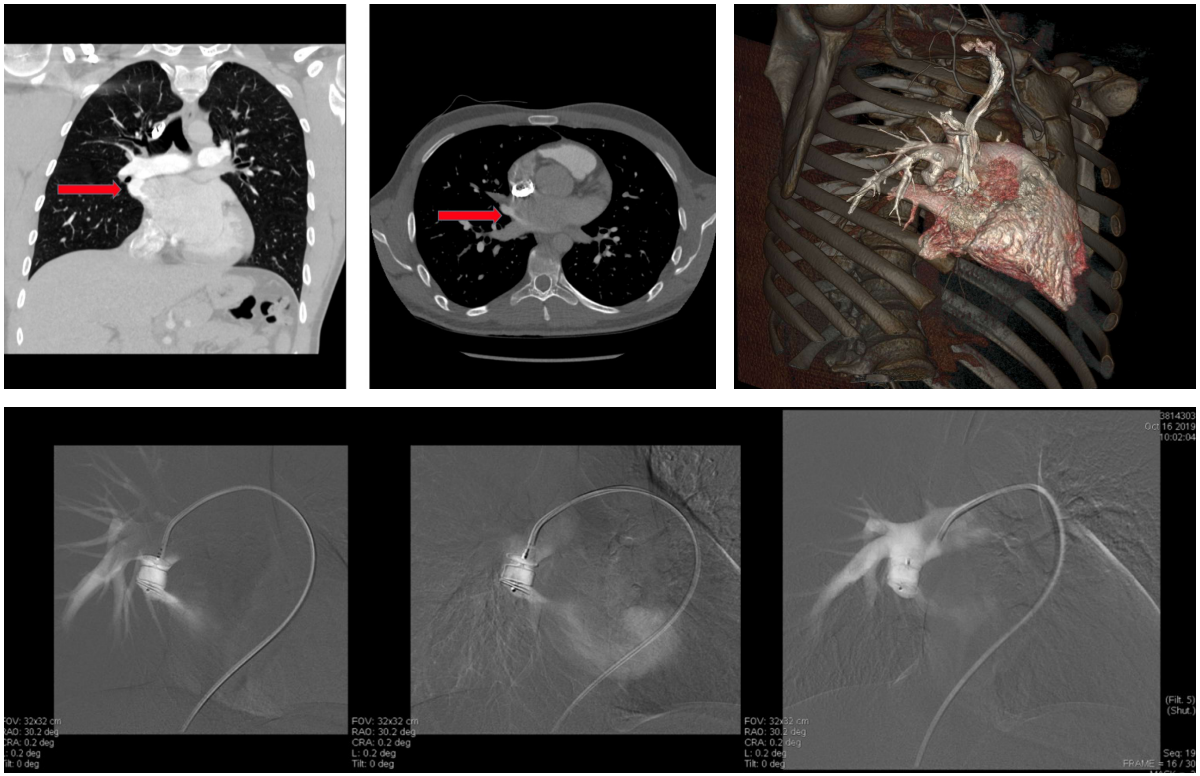
Pulmonary artery to left atrial fistula – detection and occlusion

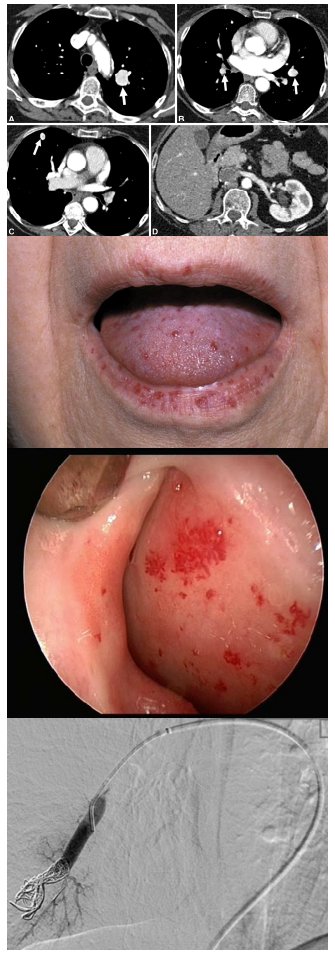


CT angiography of the chest. Reconstruction (2D and 3D) demonstrates the communication between right pulmonary artery and left atrium.

Digital subtraction angiography and interventional treatment with implantation of occluder.

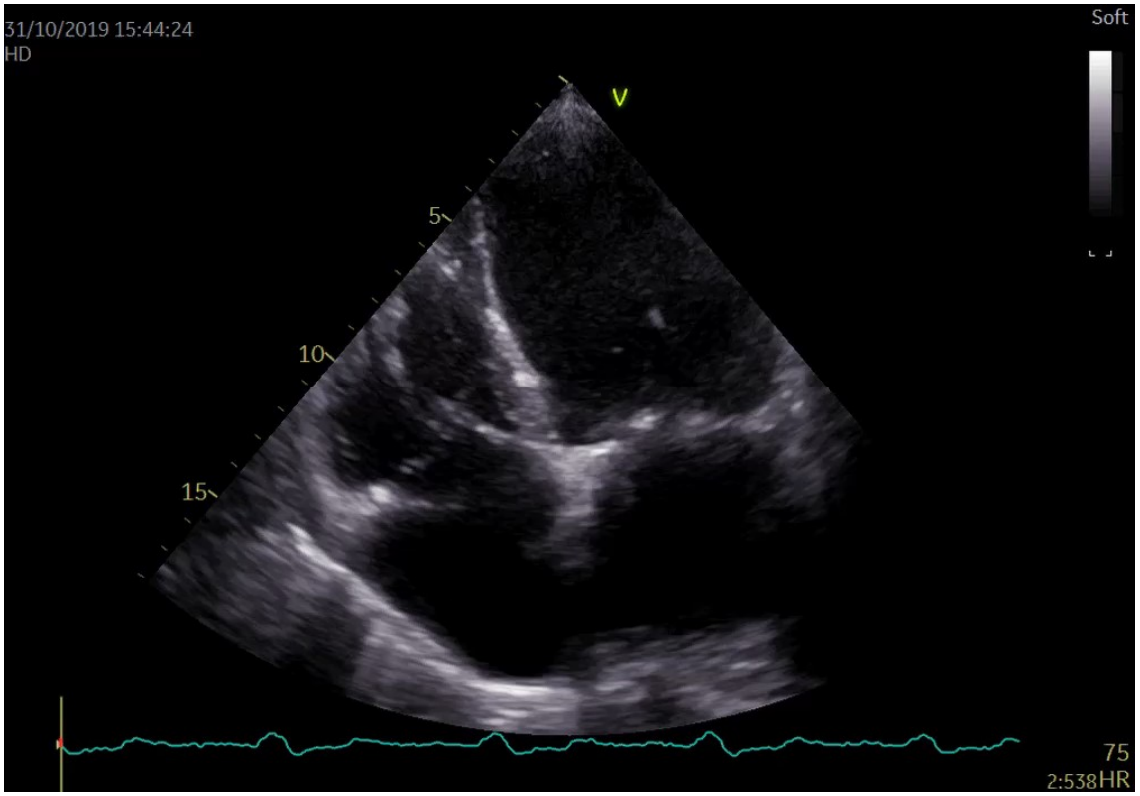
Pulmonary AV malformation

- Pulmonary arteriovenous malformations (PAVMs) are characterised by the presence of a direct pulmonary artery–vein shunt
- Most PAVMs are congenital and are closely associated with hereditary haemorrhagic telangiectasia.
- PAVMs have a low incidence worldwide and usually produce no obvious clinical manifestations. However, serious complications such as stroke, brain abscesses, haemoptysis, haemothorax, and hypoxaemia sometimes occur because of the absence of a capillary bed.
- Endovascular embolisation is recommended as the first-line treatment for PAVMs with a feeding artery of ≥ 3 mm in diameter.

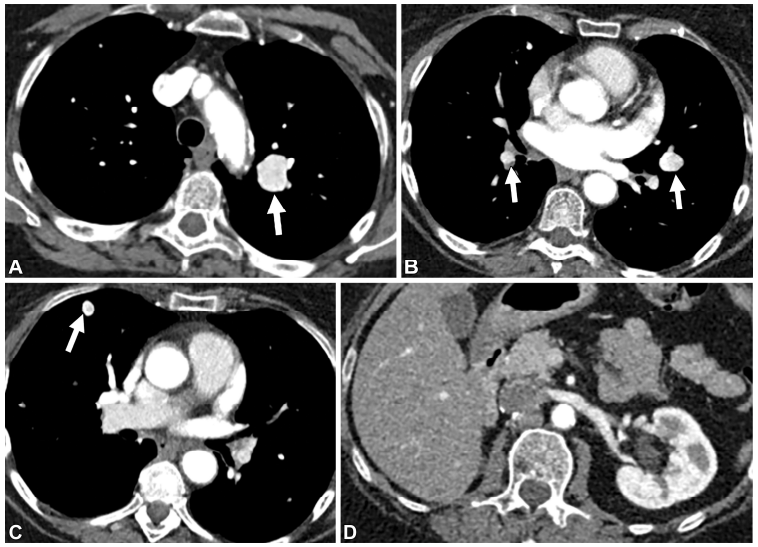


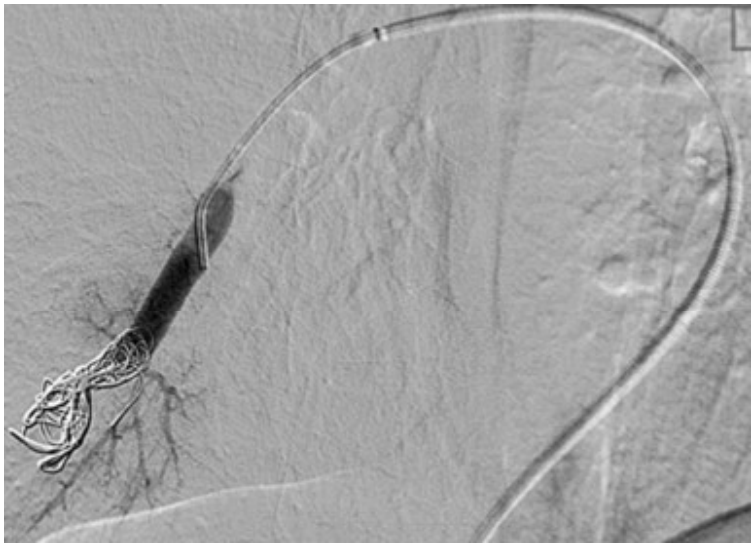
Ma, X., Li, LL., Yu, D. *et al.* Management of pulmonary arteriovenous malformations involves additional factors aside from the diameter of feeding arteries: a 3-year case-case retrospective analysis. *Respir Res* **23**, 107 (2022). https://doi.org/10.1186/s12931-022-02030-9

Pulmonary AV malformation - screening



Pulmonary AV malformation – detection and closure





Diagnostic algorithm: proposal for a diagnostic approach based on the current evidence

In the case of normal contrast TTE, cardiac rhythm (atrial tachyarrhythmia vs. sinus rhythm) should be taken into account.

In patients with AF, contrast TTE can detect the presence of thromboembolic risk markers (LA size, LA strain alteration, and LVEF <40%). The indication for contrast TOE cannot be part of a routine indication, except to answer a specific question or for inclusion in a research protocol. Without TTE-derived thromboembolic risk markers, contrast TOE indication is mandatory.
In the case of sinus rhythm (i.e. cryptogenic stroke), contrast TOE and a Holter electrocardiogram are mandatory.

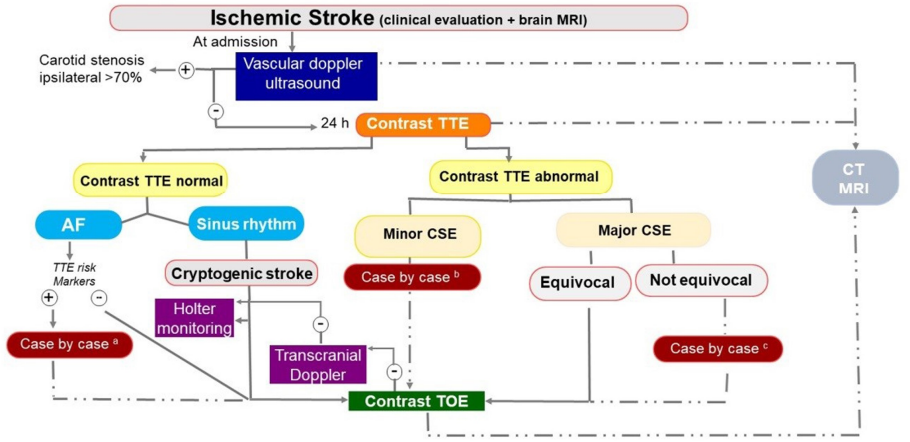
In the case of abnormal contrast TTE, a minor cardiac source of embolism has to be distinguished from a major cardiac source of embolism.

If a minor cardiac source of embolism is detected, contrast TOE might be indicated: (i) if another potential cardiac source of embolism (>20% of cases) is suspected; (ii) before percutaneous interatrial septum closure; and (iii) in the event of unequivocal results on contrast TTE.In the case of negative contrast TOE, a transcranial Doppler is indicated. In case of a negative transcranial Doppler, a Holter monitoring should be considered.
If a major cardiac source of embolism is detected and is an unequivocal potential source of embolism, the indication of contrast TOE may be debatable. However, its input is indisputable for the detection of potential cardiac sources of small size (below the resolution of contrast TTE), such as atrial or LV thrombosis, atrial or LV tumour, or valvular vegetation.
When contrast TTE is equivocal, contrast TOE indication is mandatory.

ESC European Society of Cardiology
European Heart Journal - Cardiovascular Imaging (2021) 22, e24–e57
doi:10.1093/ehjci/jeab008
EACVI DOCUMENT

EACVI recommendations on cardiovascular imaging for the detection of embolic sources: endorsed by the Canadian Society of Echocardiography

(Chair) Ariel Cohen[1,2]*, (Co-Chair) Erwan Donal[3], Victoria Delgado[4], Mauro Pepi[5], Teresa Tsang[6], Bernhard Gerber[7], Laurie Soulat-Dufour[1,2], Gilbert Habib[8], Patrizio Lancellotti[9,10], Arturo Evangelista[11], Bibiana Cujec[12], Nowell Fine[13], Maria Joao Andrade[14], Muriel Sprynger[15], Marc Dweck[16], Thor Edvardsen[17], and Bogdan A. Popescu[18]



[a]Contrast TOE could be useful to identify the presence of a LA/LAA thrombogenic status (LA/LAA thrombus, dense LA/LAA SEC or dysfunction). Biomarkers could be useful (e.g. D-dimers, B-type natriuretic peptide, troponin, von Willebrand factor, C-reactive protein, interleukin 6) to identify a subgroup of patients at higher thromboembolic risk.
[b]Contrast TOE is mandatory in the search of other cardiac source of embolism, before percutaneous closure and in case of questionable contrast TOE.
[c]Contrast TOE could be useful to identify small size or questionable abnormalities beyond the resolution of TTE, such as LA/LV thrombus, LA/LV tumours, left-sided vegetations.

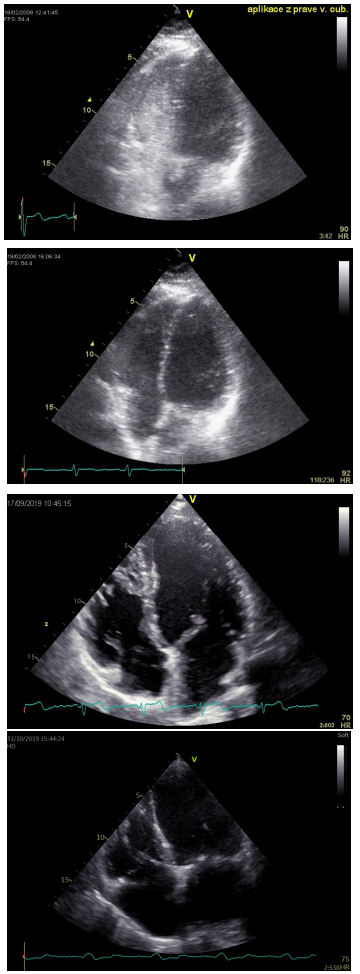
Take home message

1. Echocardiography constitutes the primary choice for cardiac imaging after acute ischaemic stroke, with **TTE and TEE** providing complementary information.
2. Cardiac **CT and MRI** are valuable alternatives in specific situations.
3. AF remains the **main cardiac source of embolism**, although the role and imaging characteristics of LA/LAA dysfunction remain debatable (LAA geometry, LAA dysfunction, LA strain, LA/LAA SEC).
4. Improved imaging of **aortic atheromas** (TEE > CT), **ventricular thrombus** (MRI > TTE), **atrial thrombus** (TEE or CT > MRI), **valvular masses** (3D TOE > MRI or CT) may lead to better aetiological work-up in patients with ischaemic stroke.
5. Atrial **septal anomalies** deserve careful examination to describe at-risk PFO and to discuss the indications of PFO closure in patients with cryptogenic stroke, after in-depth discussion and the ruling out of other possible causes, including occult AF (Holter or prolonged rhythm monitoring, insertable cardiac monitors).

Eur Heart J Cardiovasc Imaging, Volume 22, Issue 6, June 2021, Pages e24–e57, https://doi.org/10.1093/ehjci/jeab008

In contrast echocardiography, it is important…

1. administer contrast medium into the **left upper extremity vein**
2. observe the **sequence of filling of the heart** with the contrast agent
3. to record the site of contrast agent **entry** into the heart (there may be more than one at the same time)
4. observe the presence of contrast agent **in the left atrium, left ventricle and aorta** and determine **the (semi)quantity** of contrast agent in the left atrium spontaneously and during provocation manoeuvres
5. describe the **delay** in contrast agent penetration into the left-sided cardiac compartments compared with the right atrium



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DĚKUJEME ZA POZORNOST

FAKULTNÍ NEMOCNICE OLOMOUC

KOMPLEXNÍ
KARDIOVASKULÁRNÍ CENTRUM
FAKULTNÍ NEMOCNICE OLOMOUC