MINOCA

Myocardial infarction with non-obstructive coronary arteries

O. Hlinomaz

ICRC, FN u sv. Anny, Brno

FNUSA ICRC
MINISTRY OF EDUCATION, YOUTH AND SPORTS
EUROPEAN UNION
EUROPEAN REGIONAL DEVELOPMENT FUND
INVESTING IN YOUR FUTURE
2007–13
OP Research and Development for Innovation

MINOCA
Definice a incidence

- Syndrom s různými příčinami
- Klinická evidence MI při normálních nebo téměř normálních koronárních arteriích (stenóza <50%)
- Kolem 10% všech AKS

Agawell S et al.: EHJ (2017) 38, 143-153

One-Year Prognosis of Patients with Myocardial Infarction and Non-Obstructive Coronary Artery Disease (MINOCA)

R. Tavella[1], S. Pasupathy[1], J. Lu[2], M. Arstall[3], D. Chew[4], M. Worthley[1], C. Zeitz[1], JF. Beltrame[1]

(1) The University of Adelaide, Central Adelaide Local Health Network, Adelaide, Australia (2) The University of Adelaide, Adelaide, Australia
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Table 1. Morality Outcomes Between MINOCA and MICAD Patients

	MINOCA % (n)	MICAD % (n)	p value
In-hospital	0.3% (1)	2.1% (58)	<0.05
1 month	0.3% (1)	2.5% (69)	<0.05
12 months	0.9% (3)	3.7% (102)	<0.05

p value from Fisher's exact test

Coronary angiography Database of South Australia (CADOSA) Registry
1.2012-12.2013
3145 pac. koronaro pro AIM
347 (11%) MINOCA

Table 2. Return Hospital Visits for Cardiovascular Cause Between MINOCA and MICAD Patients

	MINOCA % (n)	MICAD % (n)	OR 95% CI	p value
1 month	8.9% (30)	9.4% (257)	0.89 (0.59-1.34)	>0.05
12 months	14% (48)	18% (494)	0.68 (0.49-0.96)	<0.05

MINOCA pac. ↓ celkovou mortalitu
ale stejnou frekvenci návštěv v nem. jako MICAD pac.

AHA 2016

Dg. kritéria

1. AIM kritéria
   - Pozitivní ukazatelé nekrozy myokardu
   - Klinické známky IM
     - Ischemické symptomy
     - Nové změny ST úseků nebo nový BLTR
     - Vznik patol. Q kmitů
     - Nová ztráta viabilního myokardu nebo porucha hybnosti dle zobrazovacích metod
     - Intrakoronární trombus

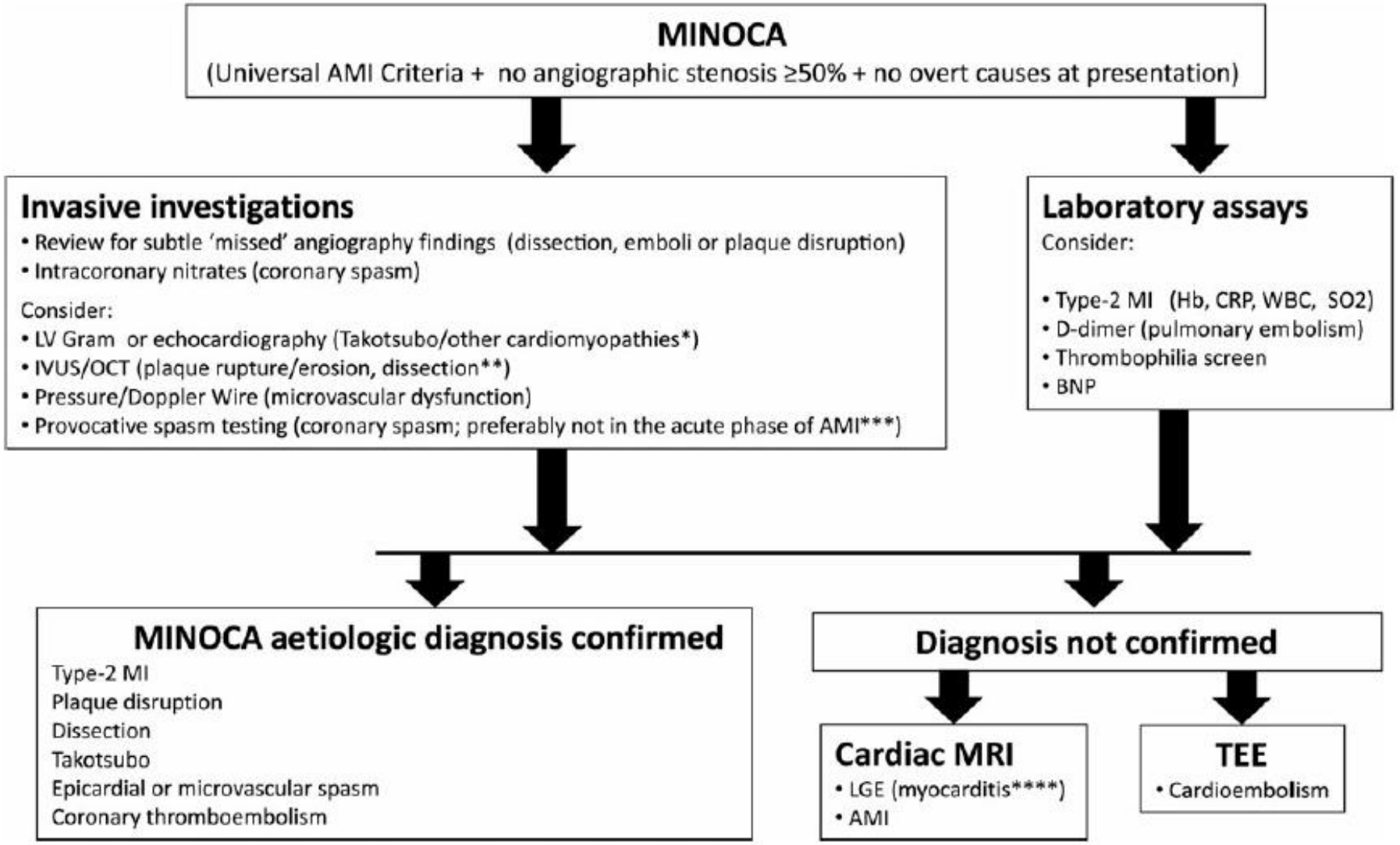
Agawell S et al.: EHJ (2017) 38, 143-153

Dg. kritéria

2. Koronární arterie bez významné stenózy při angiografii (<50%)
   - Normální koronární aa. (≤30%)
   - Mírná koronární ateroskleróza (31-49%)

3. Nejasná příčina akutního stavu v době angiografie
   - Další vyšetření nutností s cílem zjistit příčinu

Agawell S et al.: EHJ (2017) 38, 143-153

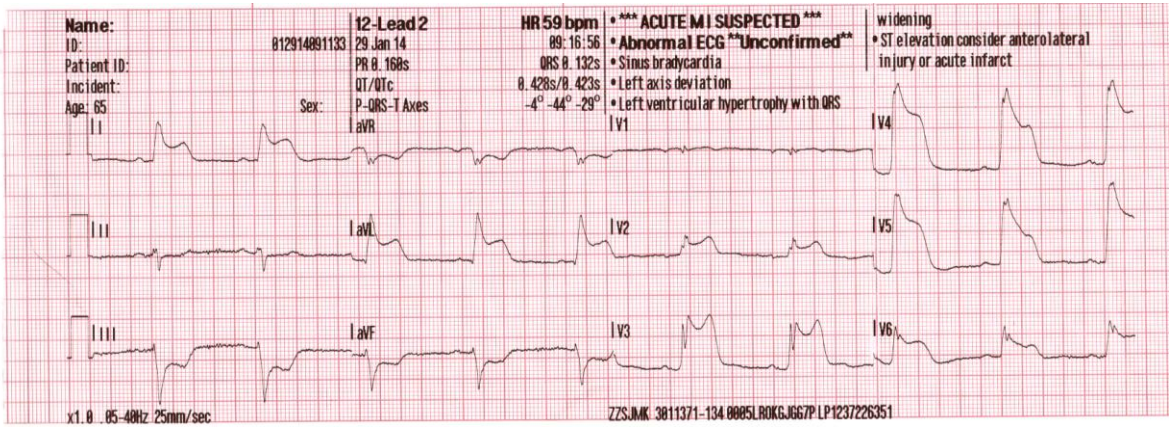


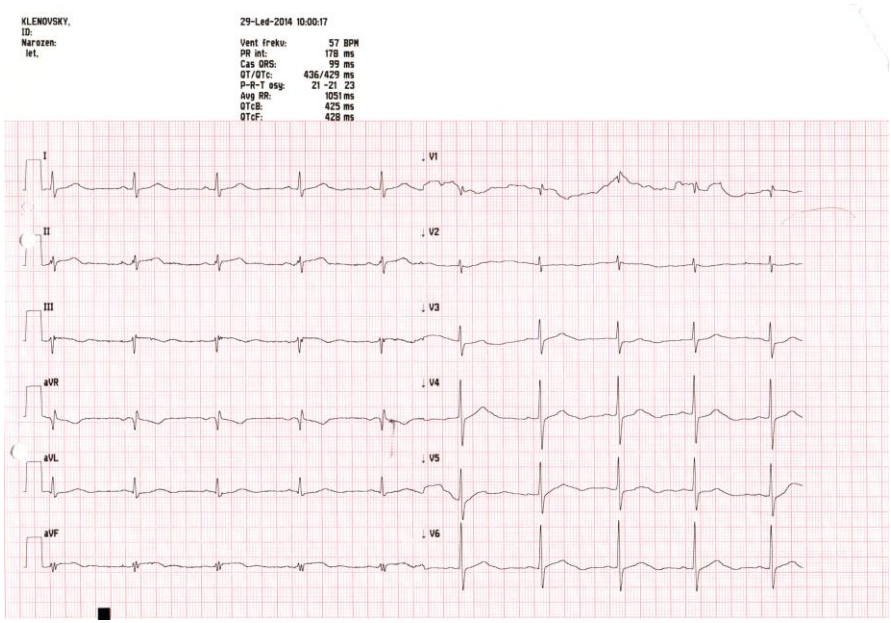
Agawell S et al.: EHJ (2017) 38, 143-153

Příčiny

1. Ruptura atero plátu
2. Spasmus koronární aa.
3. Koronární (tromb)embolismus
4. Koronární disekce
5. Takotsubo kardiomyopatie
6. Myokarditis

1. Ruptura atero plátu





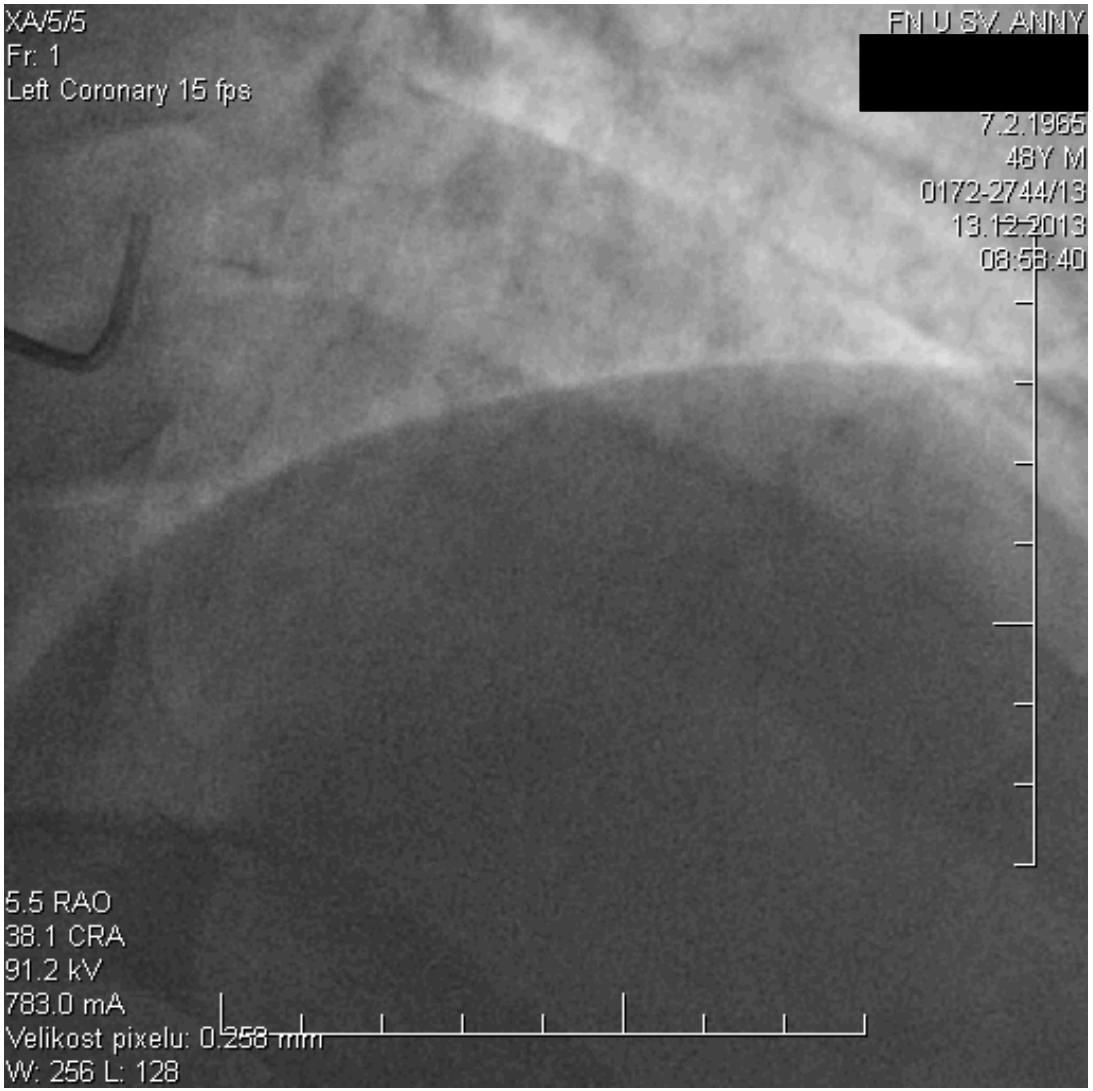
09:16 stenokardie

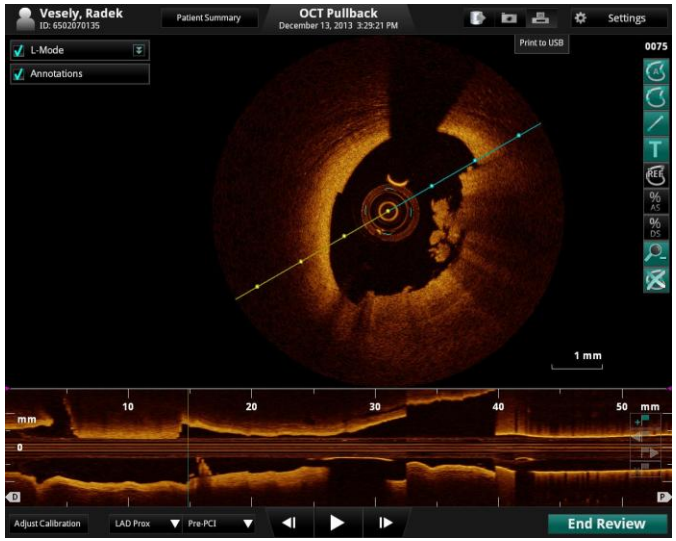
Heparin 5000j i.v.
Kardegic 500mg i.v., Efient 6 tbl.

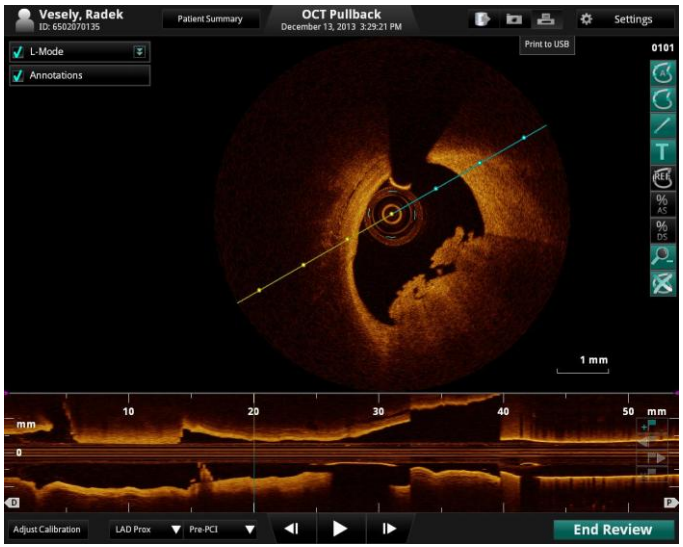
10:00 bez potíží

M, 65 let

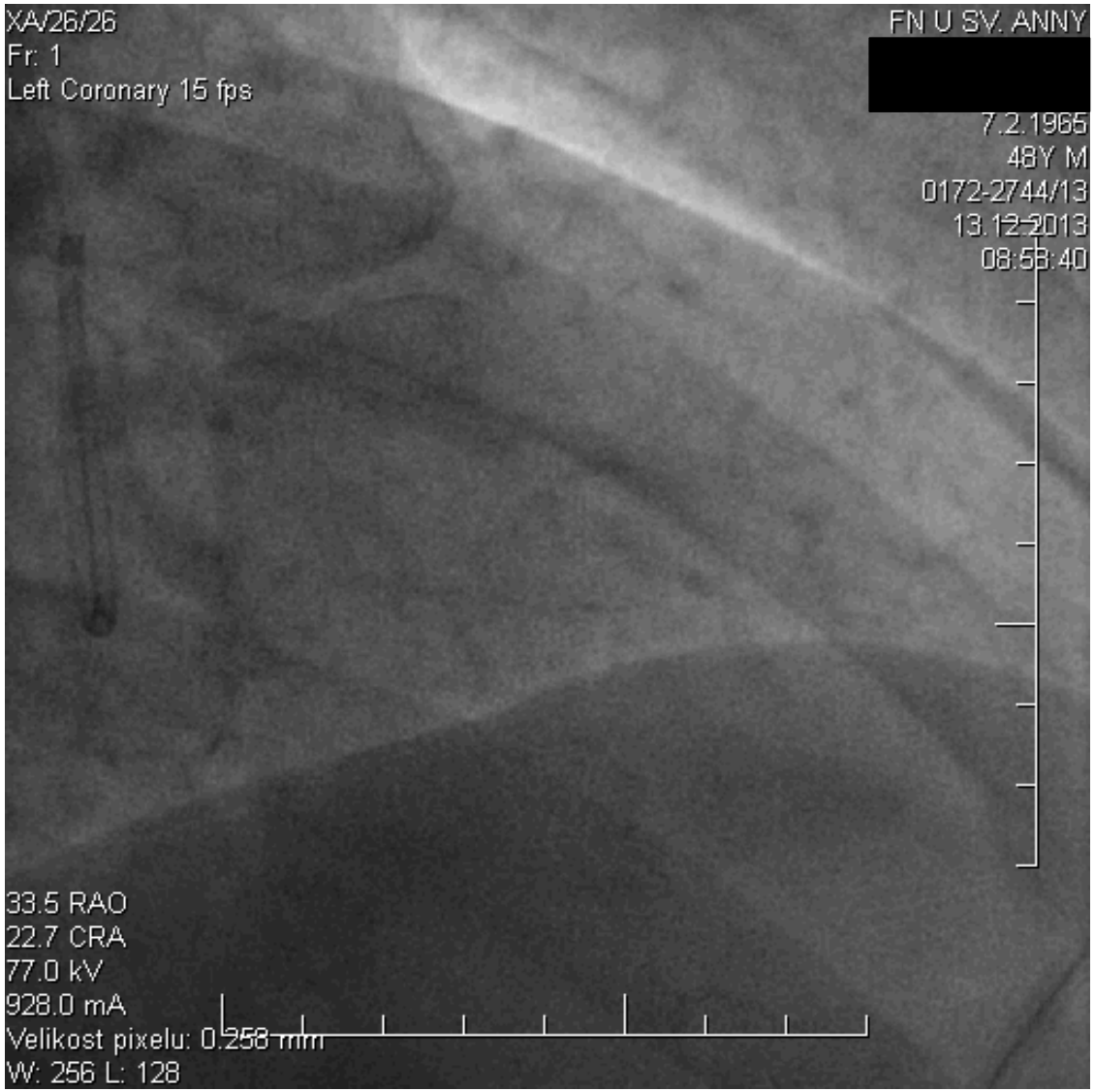
Nejasná culprit léze

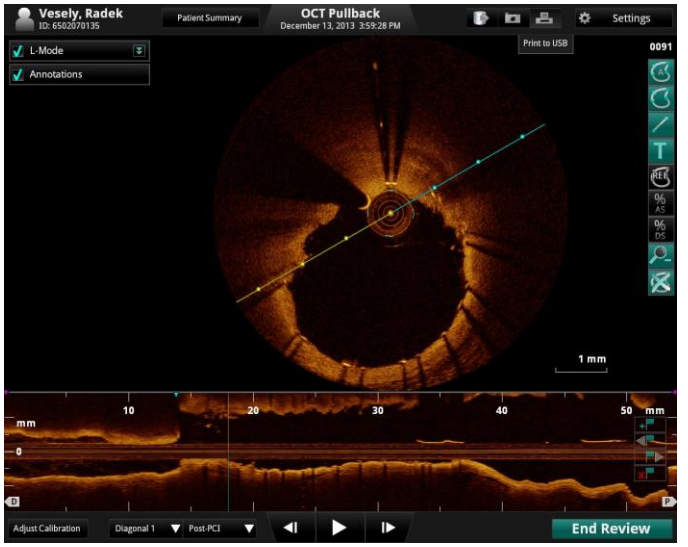


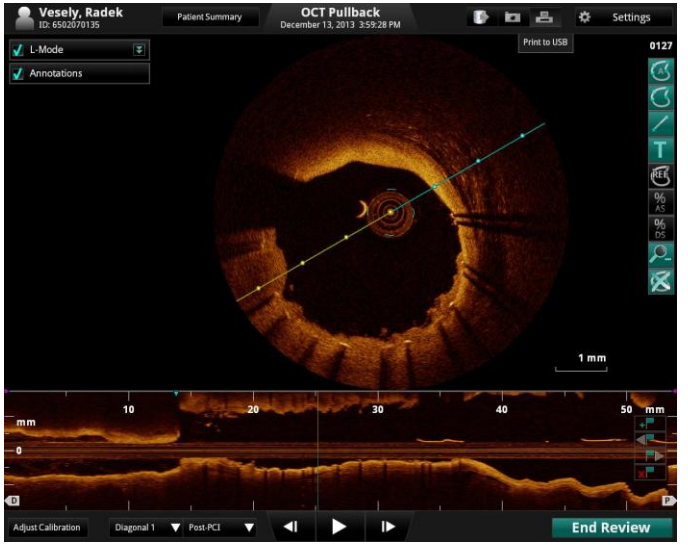


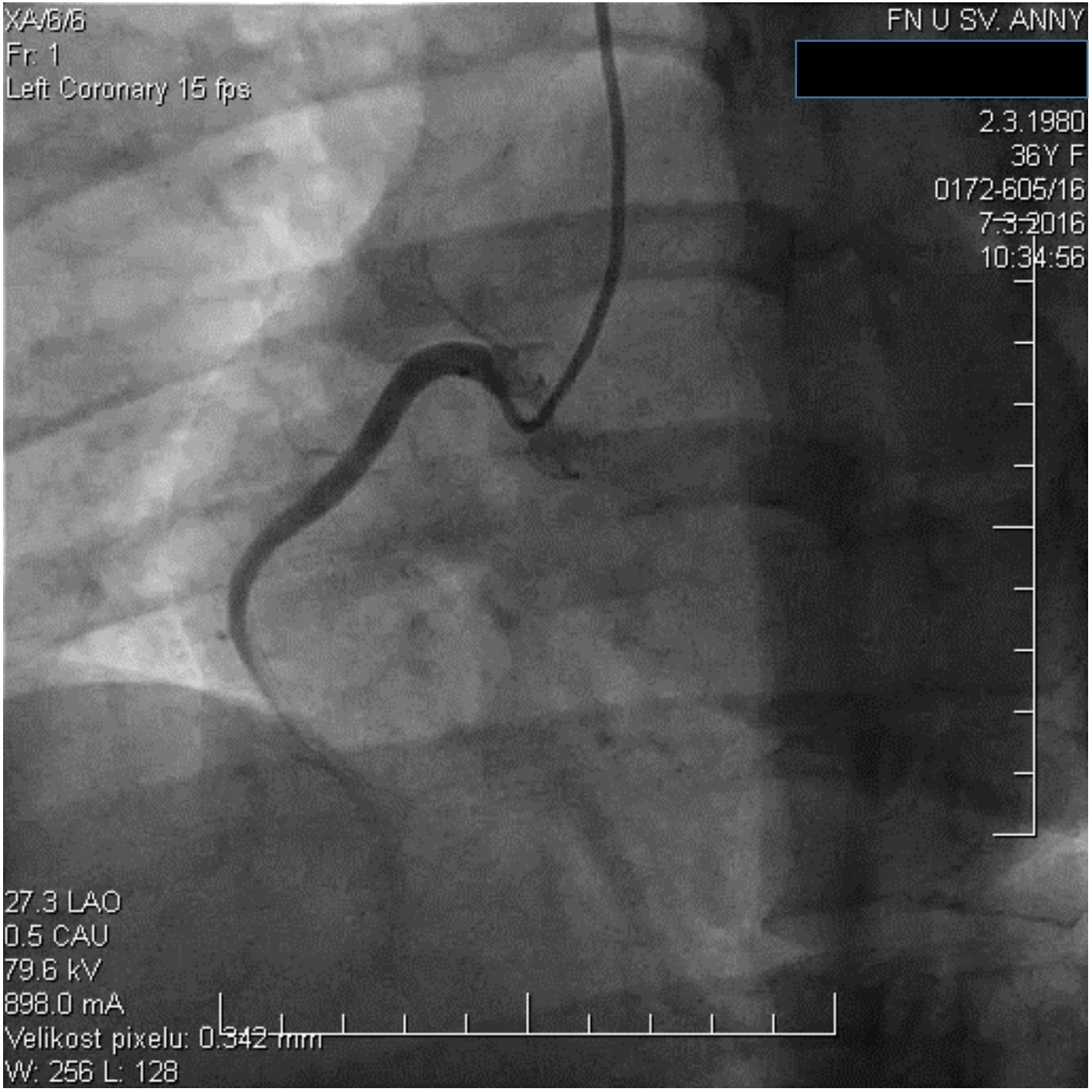


Po implantaci DES

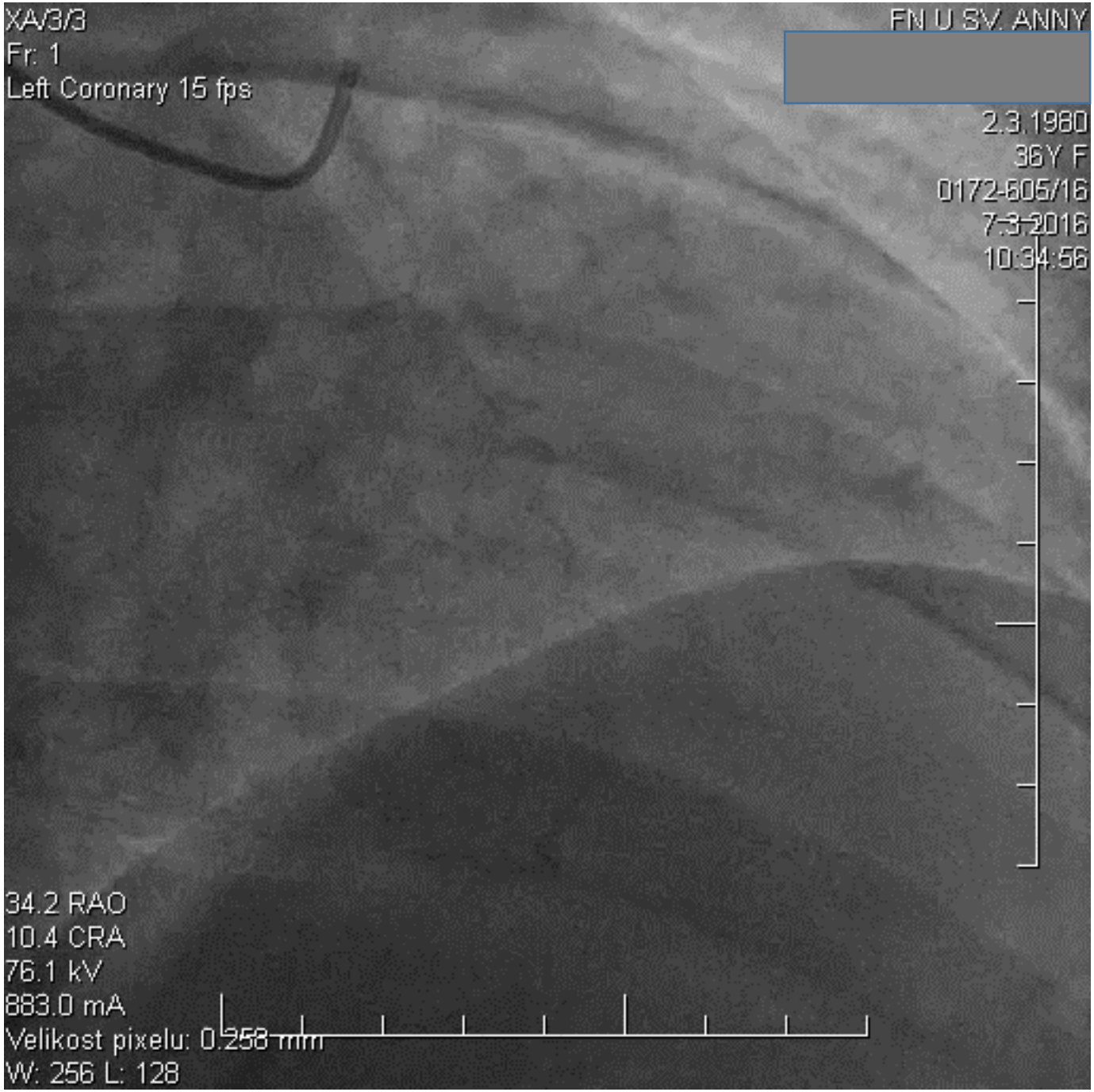


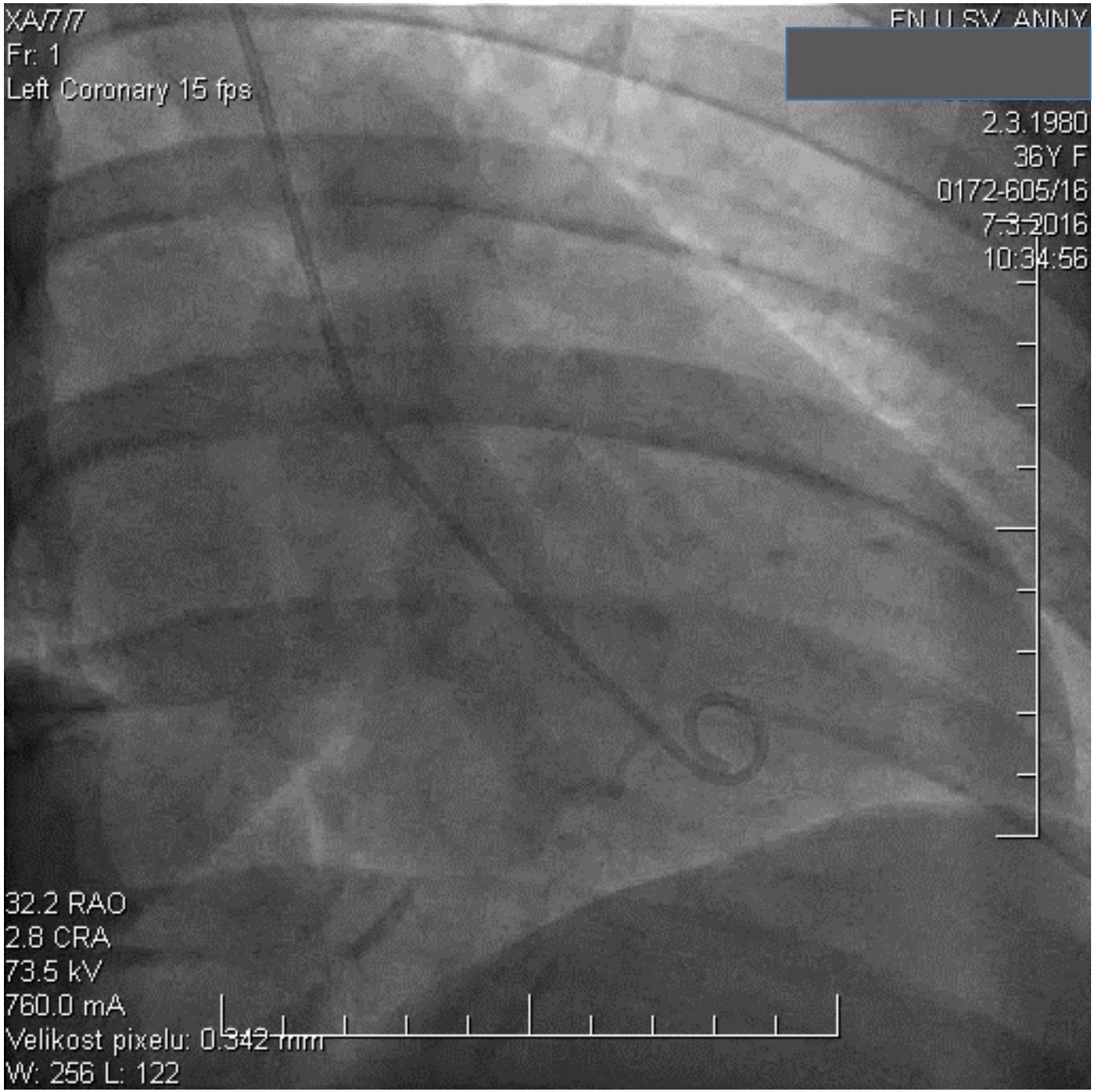




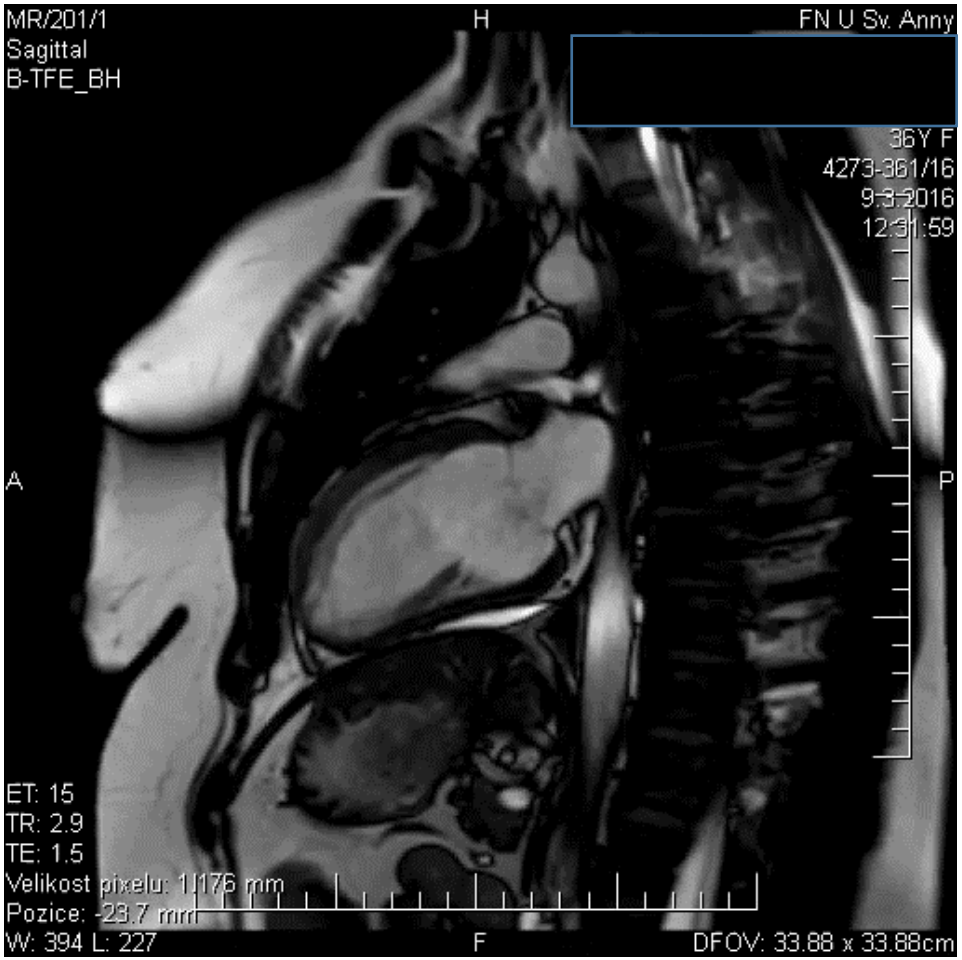

XA/6/6
Fr: 1
Left Coronary 15 fps
FN U SV. ANNY
2.3.1980
36Y F
0172-605/16
7-3-2016
10:34:56
27.3 LAO
0.5 CAU
79.6 kV
898.0 mA
Velikost pixelu: 0.342 mm
W: 256 L: 128

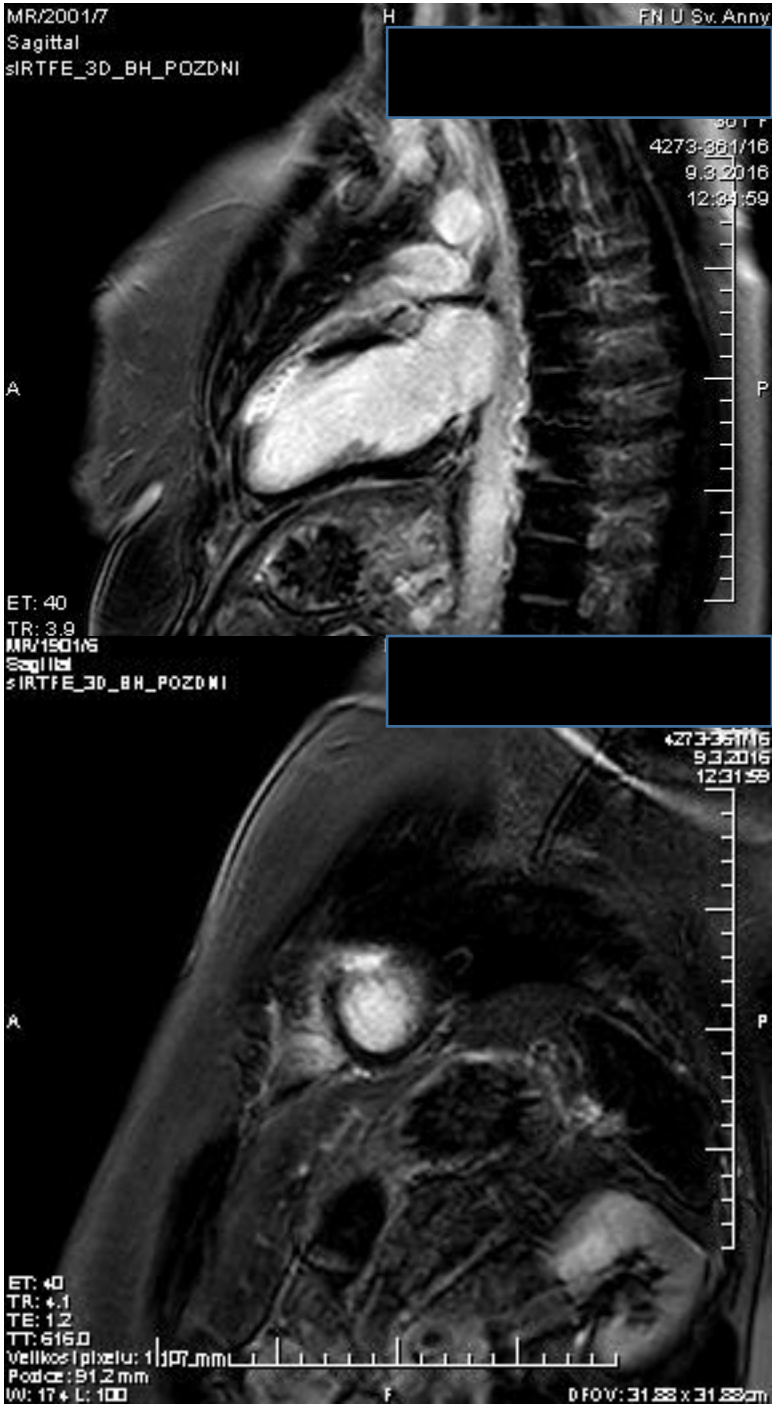
Ž, 36 let


XA/3/3
Fr: 1
Left Coronary 15 fps
FN U SV. ANNY
2.3.1980
36Y F
0172-605/16
7-3-2016
10:34:56
34.2 RAO
10.4 CRA
76.1 kV
883.0 mA
Velikost pixelu: 0.258 mm
W: 256 L: 128

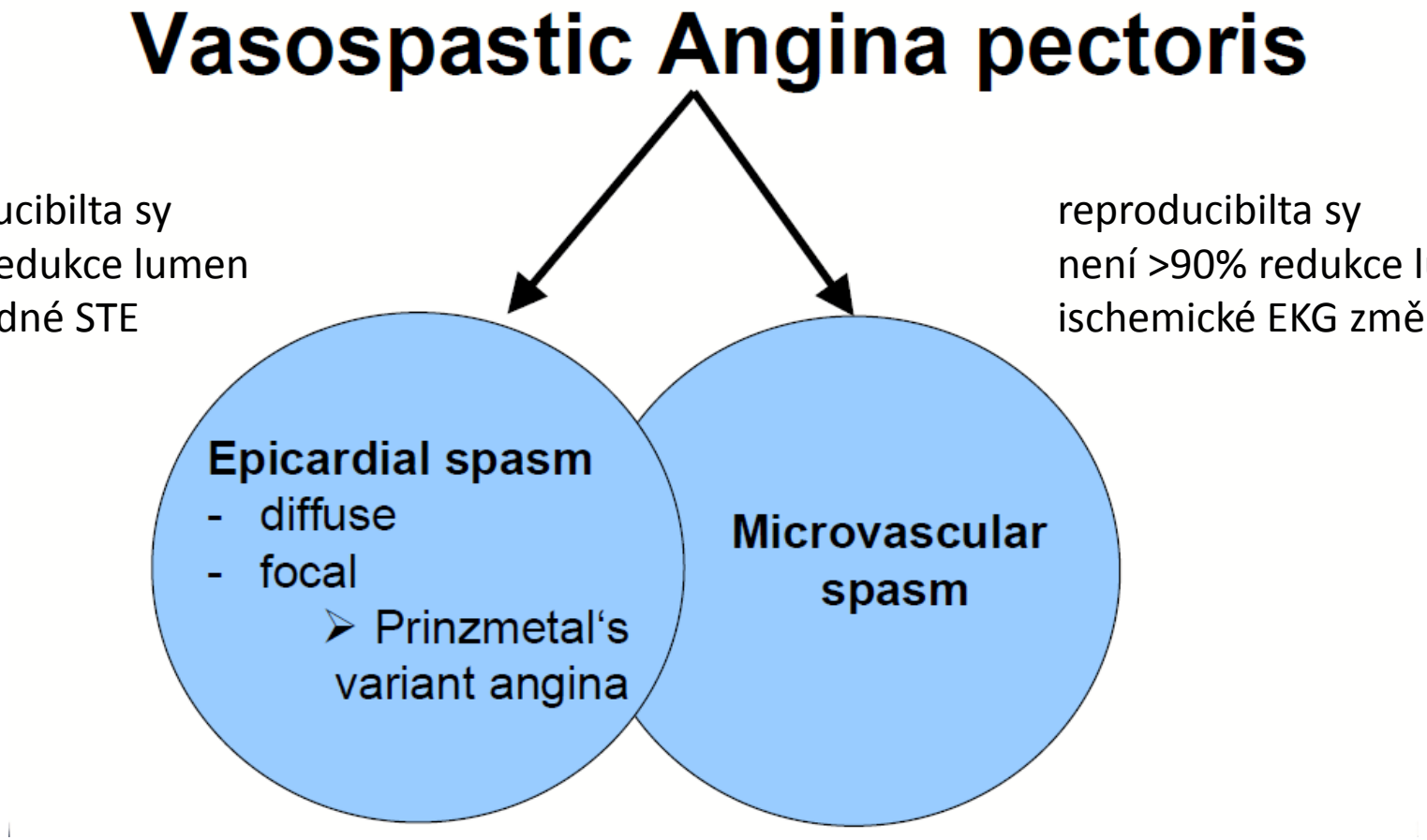

XA/7/7
Fr: 1
Left Coronary 15 fps
2.3.1980
36Y F
0172-605/16
7:3:2016
10:34:56
32.2 RAO
2.8 CRA
73.5 kV
760.0 mA
Velikost pixelu: 0.342 mm
W: 256 L: 122

Transmurální IM PS





2. Koronární spasmus

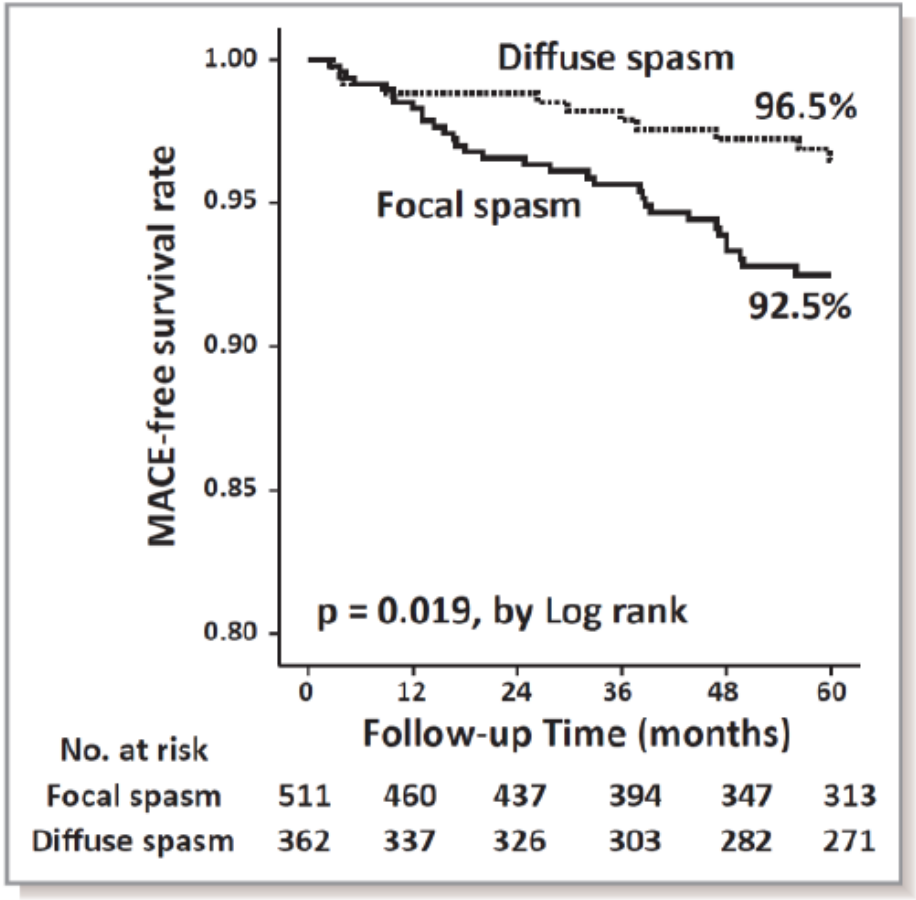


acetylcholin i.v., ergonovine i.v.

Provokační testy na koronární spasmus

Authors	Year	Ergonovine maleate	Acetylycholine	Route
Bertrand et al.	1982	Methergine* 400 mg	N/A	iv
Waters et al.	1983	12.5–400 mg	N/A	iv
Yasue et al.	1986	N/A	20–100 mg (LCA); 20–50 mg (RCA)	ic
Hackett et al.	1987	6–50 mg	N/A	ic
Okumura et al.	1988	200 mg*	20–100 mg (LCA); 20–50 mg (RCA)	iv*(Erg), ic(Ach)
Harding et al.	1992	50–150 mg	N/A	iv
Song et al.	1996	25–50 mg**		iv (Echo)
Akasaka et al.	1997	100 mg (up to 200 mg)	N/A	iv
Sueda et al.	1999	40 mg (RCA); 64 mg (LCA)	20–100 mg (LCA); 20–80 mg (RCA)	ic
Takagi et al.	2003	20–60 mg (LCA); 20–60 mg (RCA)	20–100 mg (LCA); 20–50 mg (RCA)	ic
Japanese Circulation Society	2010	20–60 mg (LCA); 20–60 mg (RCA)	20–100 mg (LCA); 20–50 mg (RCA)	ic
Ong et al.	2014	N/A	Modified from Sueda	ic
Shin, Baek.et al.	2015	Same as JSC	N/A	ic

Fokální spasmus – horší prognóza

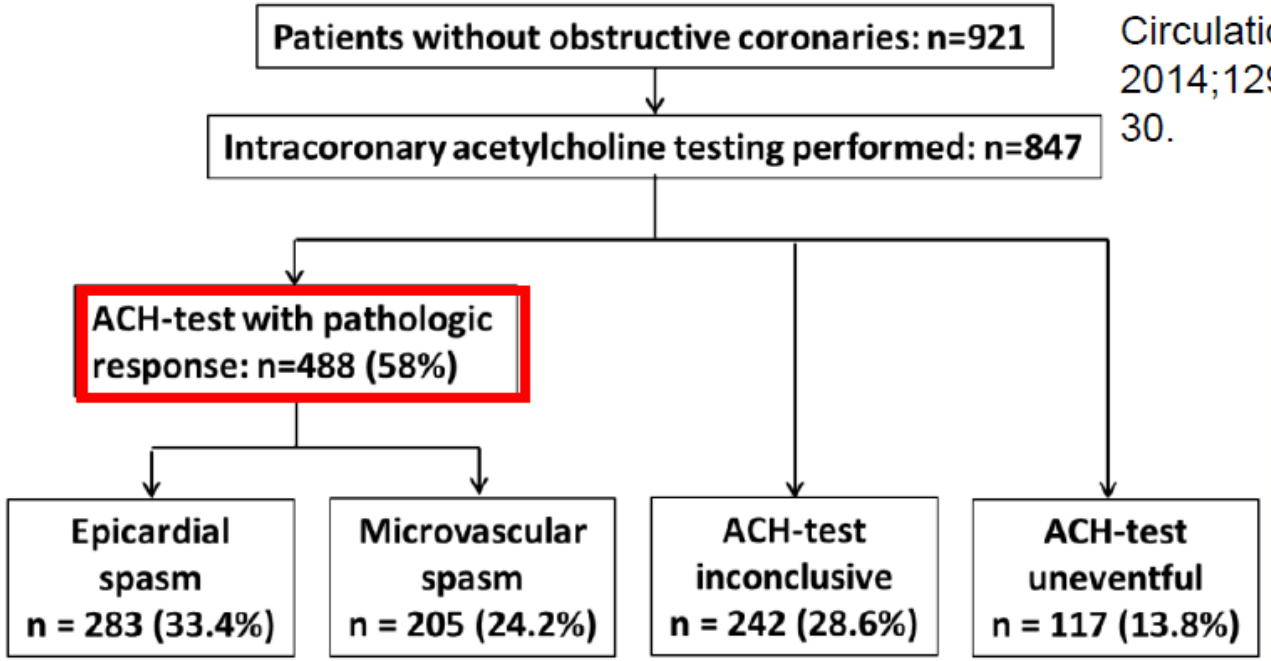


Sato K et al. J Am Heart Assoc. 2013,15;2:e000227

Vasospatická AP je častá ale málo dg.

Clinical Usefulness, Angiographic Characteristics, and Safety Evaluation of Intracoronary Acetylcholine Provocation Testing Among 921 Consecutive White Patients With Unobstructed Coronary Arteries

Peter Ong, MD; Anastasios Athanasiadis, MD; Gabor Borgulya, MD, MSc; Ismail Vokshi, MBBS; Rachel Bastiaenen, MBBS; Sebastian Kubik; Stephan Hill, MD; Tim Schäufele, MD; Heiko Mahrholdt, MD; Juan Carlos Kaski MD, DSc*; Udo Sechtem, MD*



Circulation. 2014;129:1723-30.

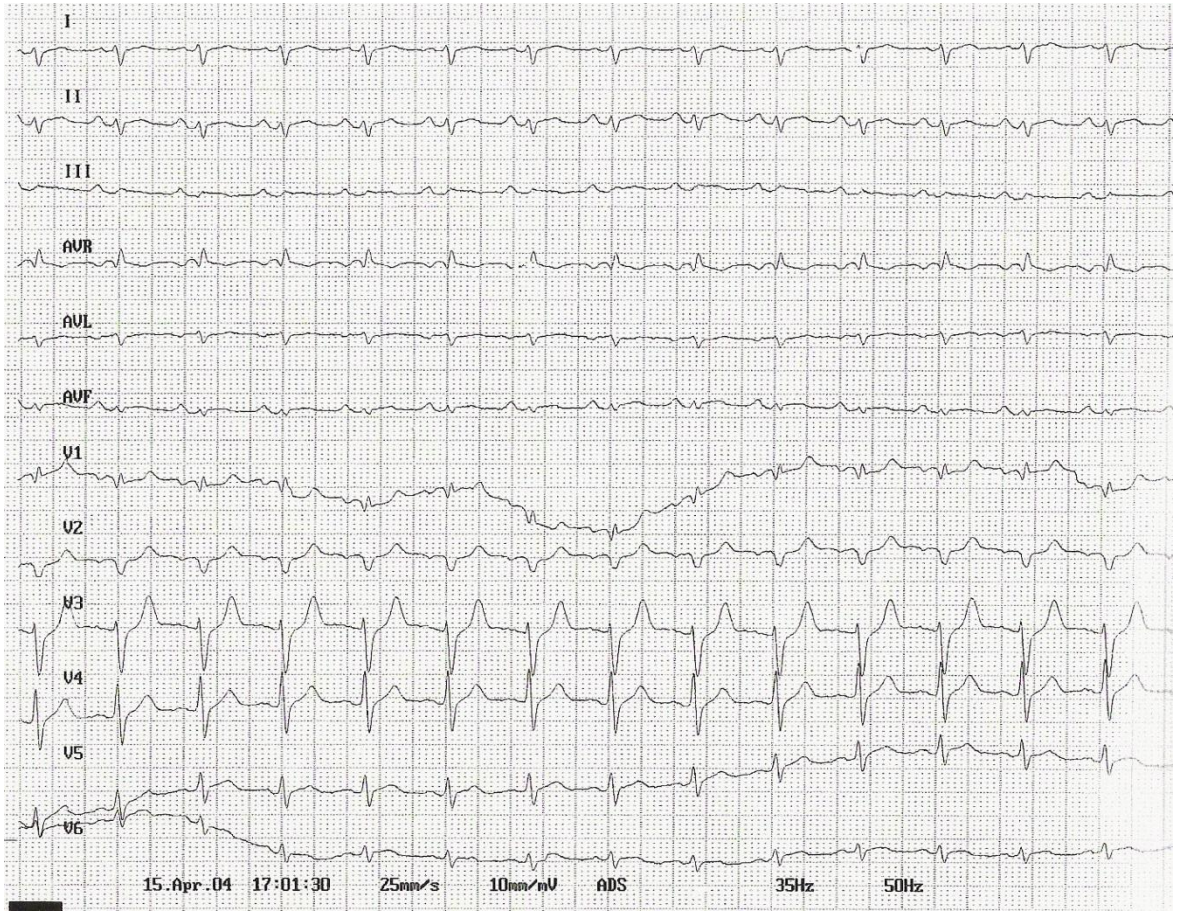
Indikace provokačního testu

- podezření na vasospastickou AP (recid. klid. steno)
- AKS bez prokázané culprit léze
- nevysvětlená srdeční zástava
- nevysvětlená synkopa s předcházejícími stenokardiemi
- opakovaná klidová AP po PCI

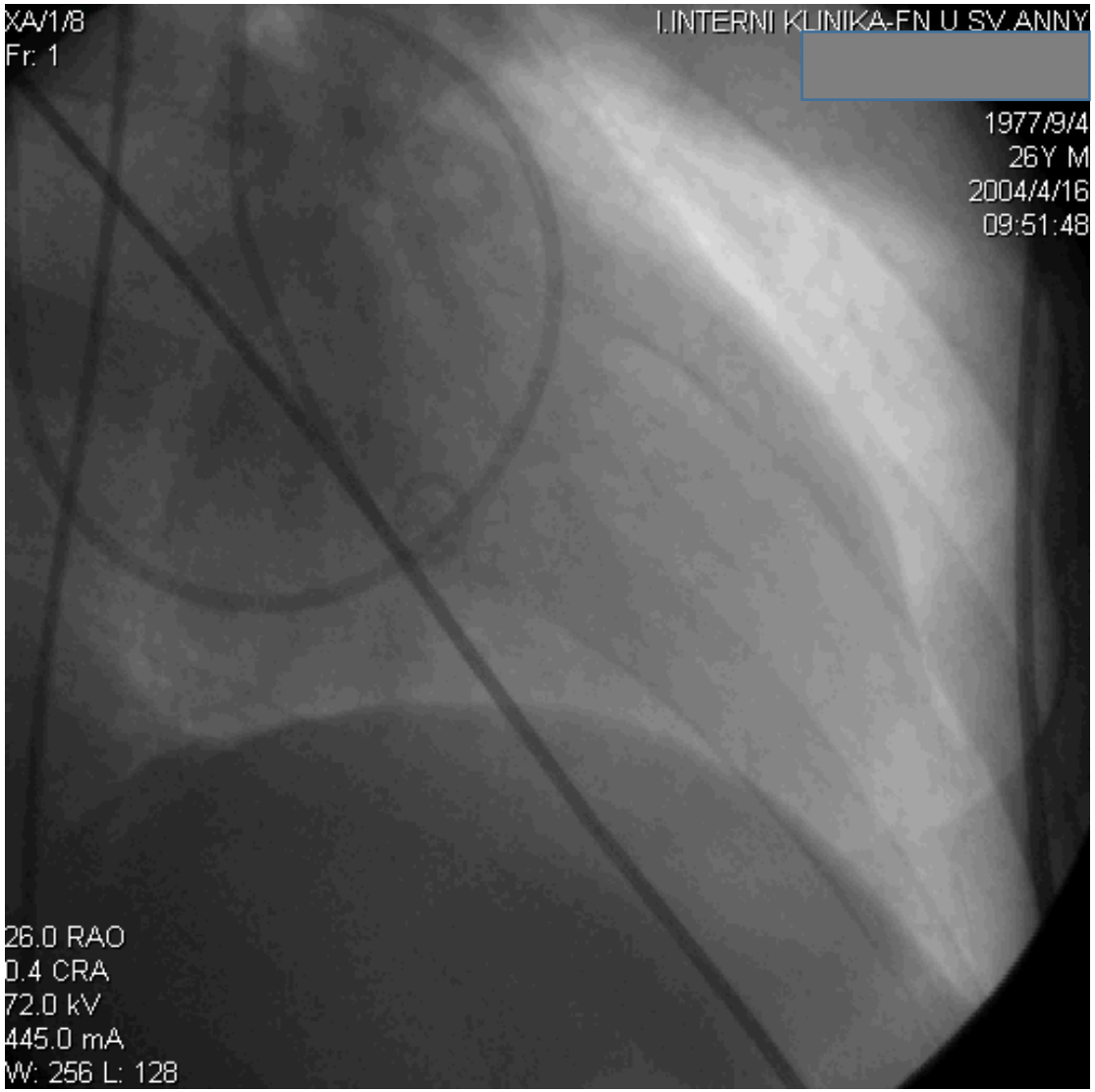
KI: AKS, MVD, těžká deprese funkce LK

3. Koronární embolismus

26-ti letý muž, při potápěčském výcviku po vynoření z 5-ti metrů kolaps, zmatenost, pareza 3 končetin, dušnost, neklid
Hospitalizace ARK 15.4.-18.5.2004 – exitus letalis na multiorgánové srdeční selhání

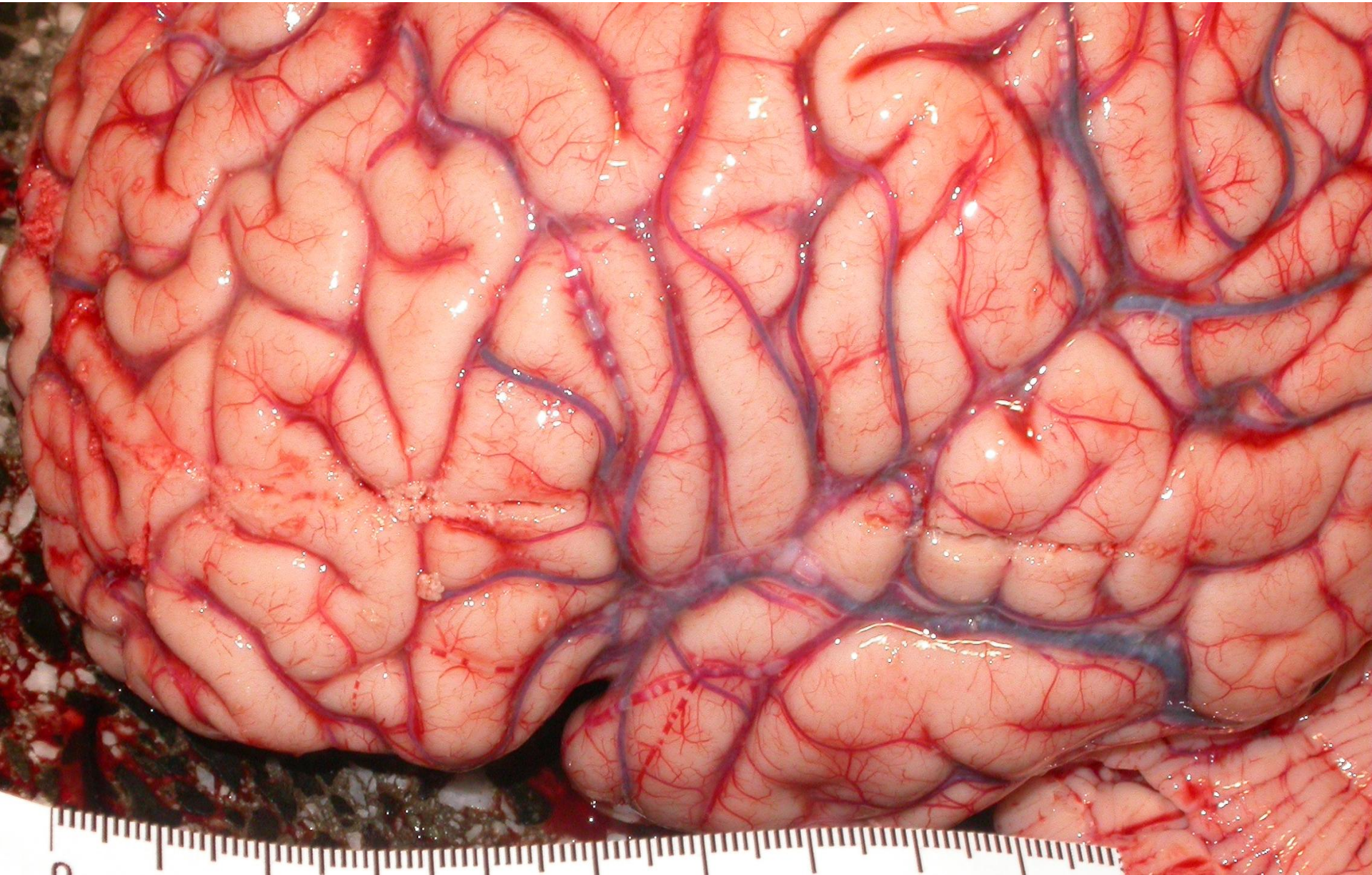


Barotrauma při potápění

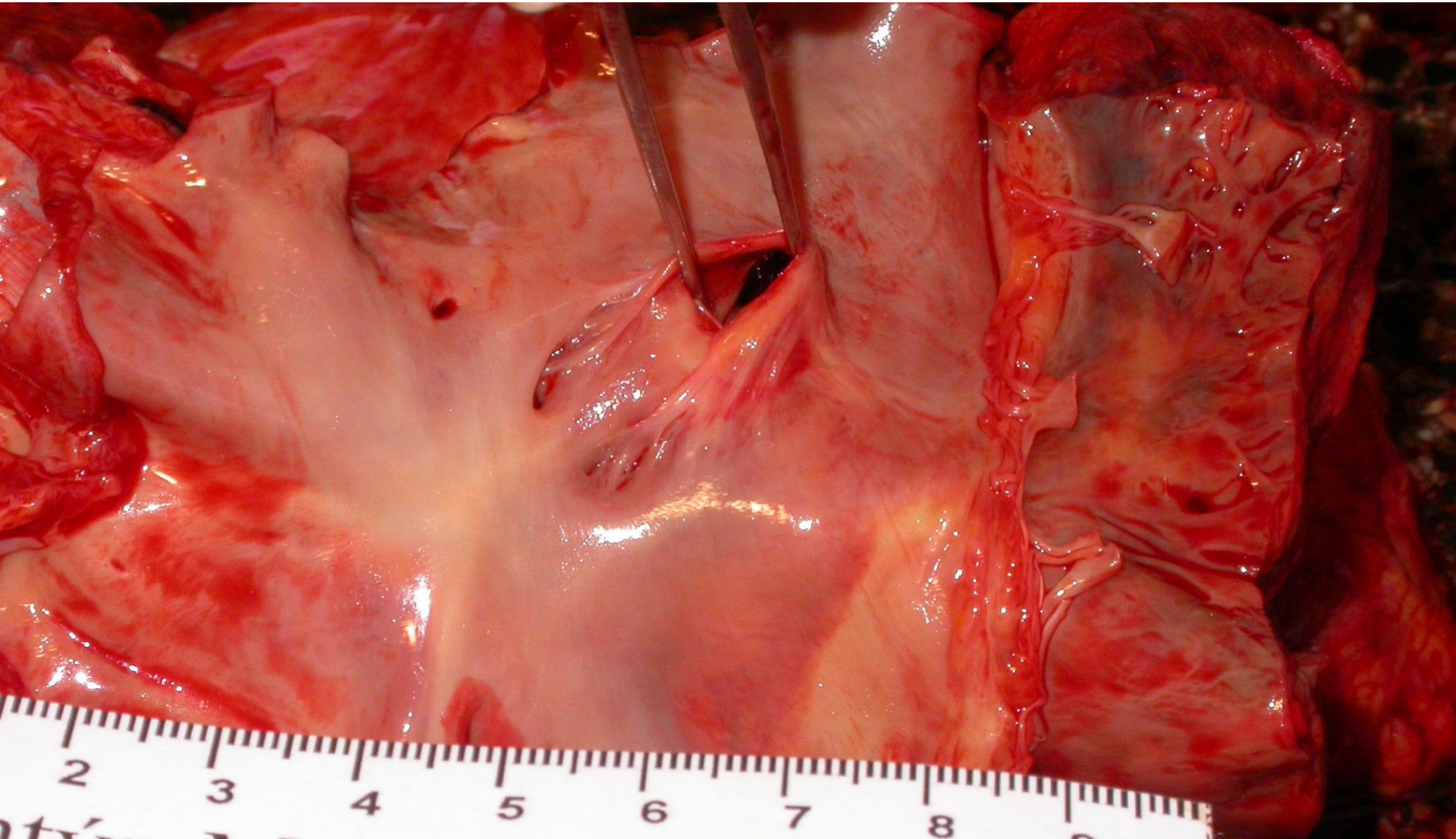


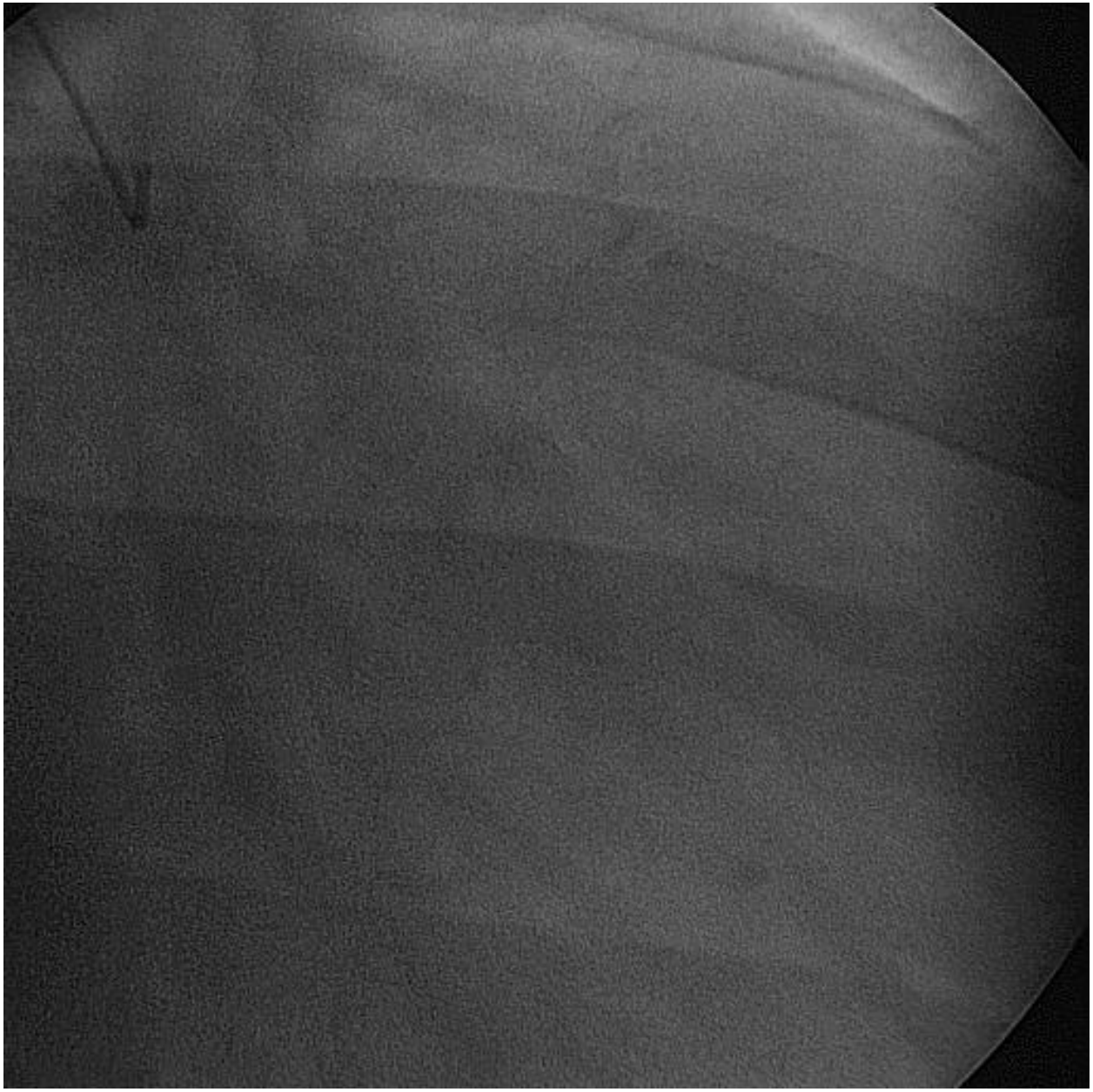
Koronaro 16.4.2004:
hladkostěnné koron. aa.
EF 25%, LVEDP 33mmHg
difuzní porucha kinetiky
Dg.: AIM

Vzduchová embolie

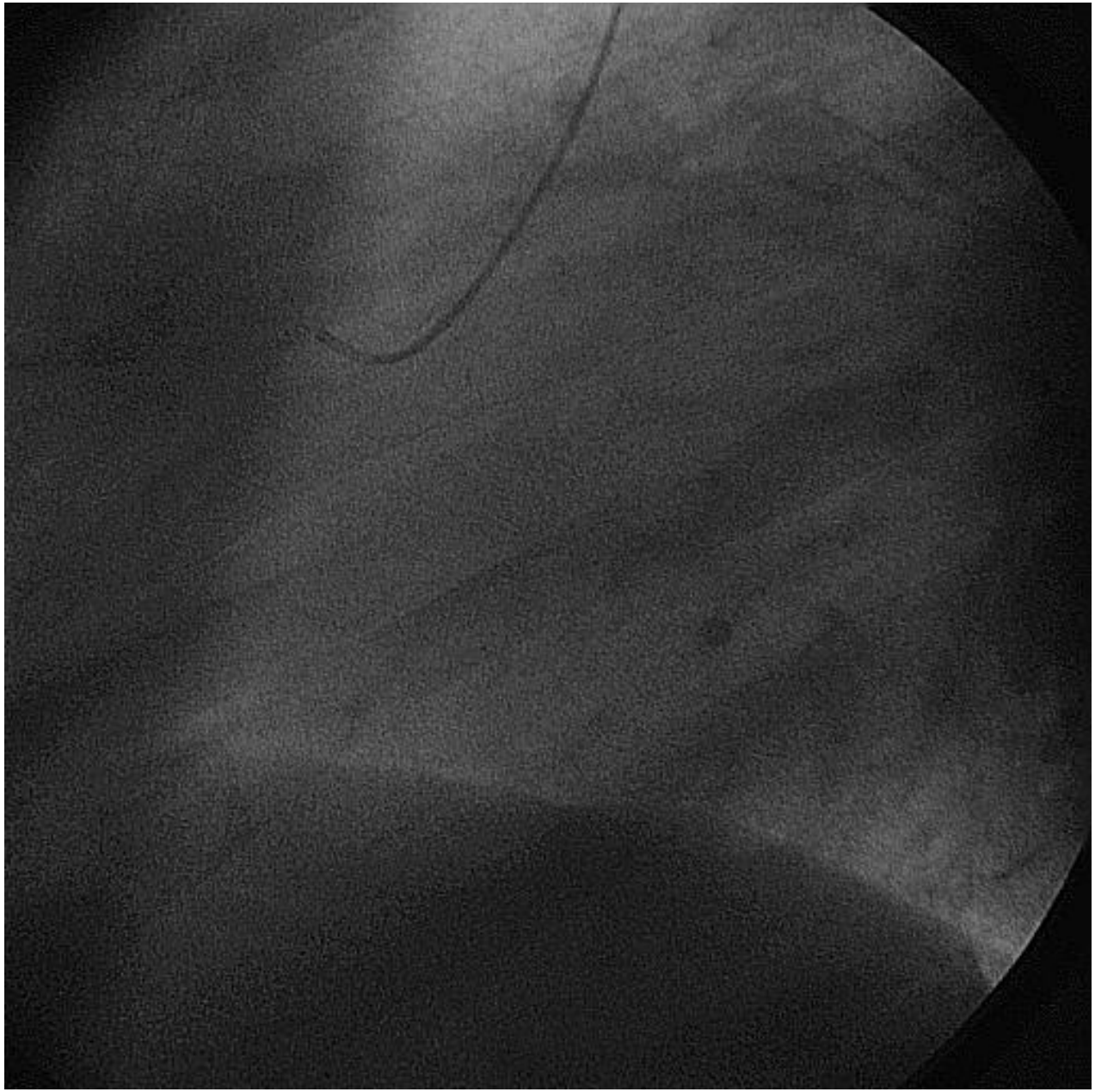


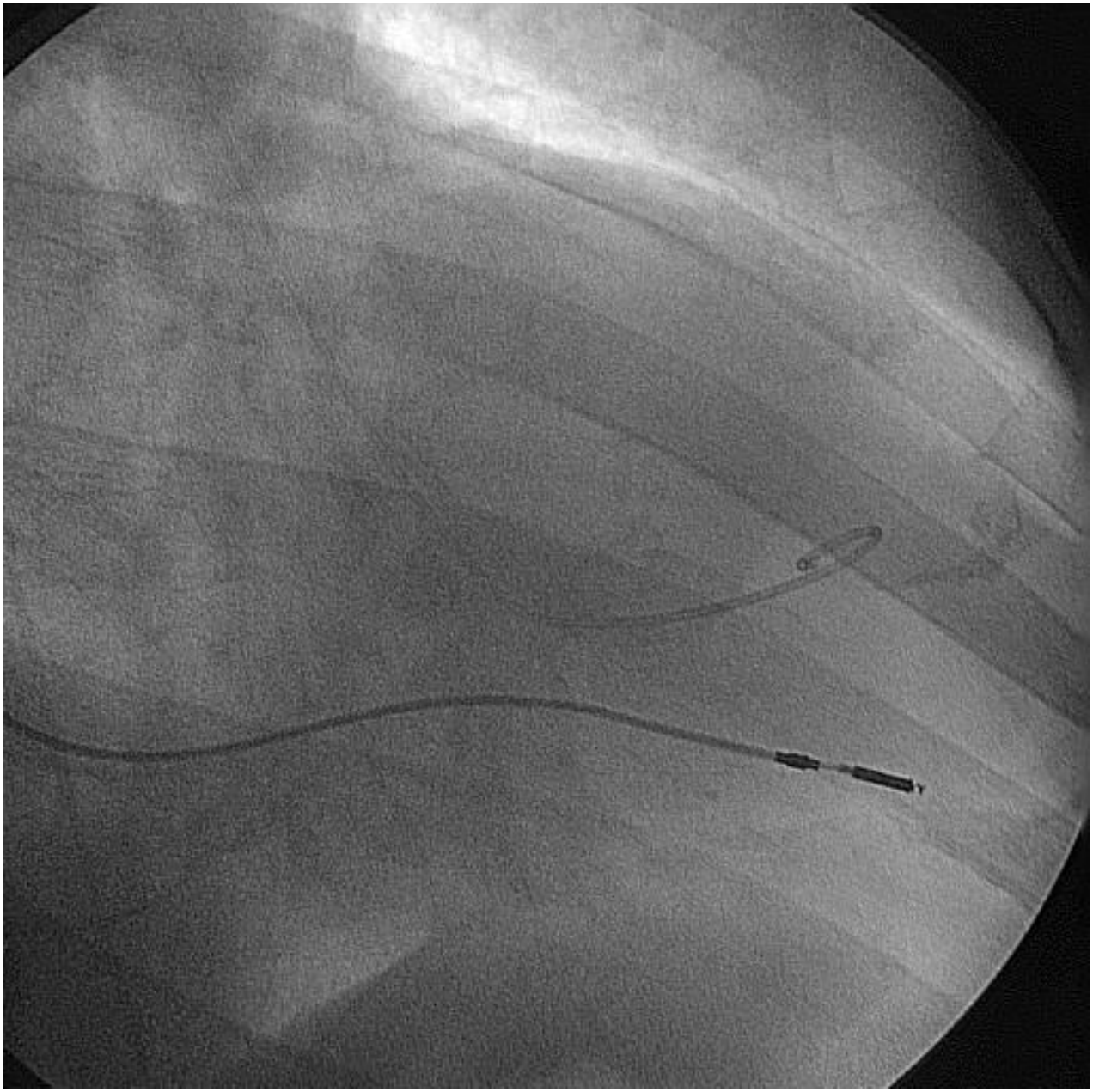
Foramen ovale patens





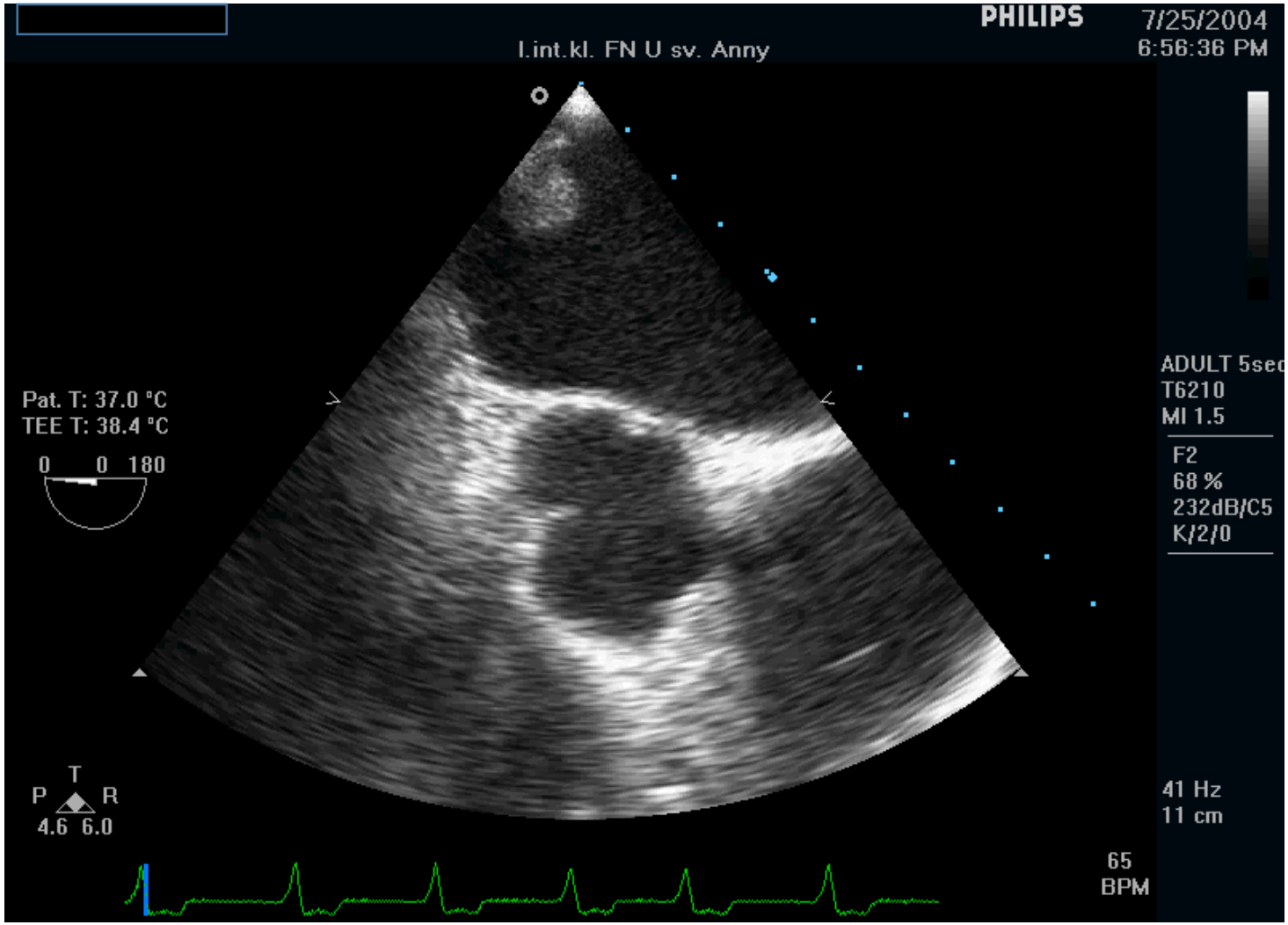
75-ti letý muž,
IM DS subakutní
KBLTR
Killip II





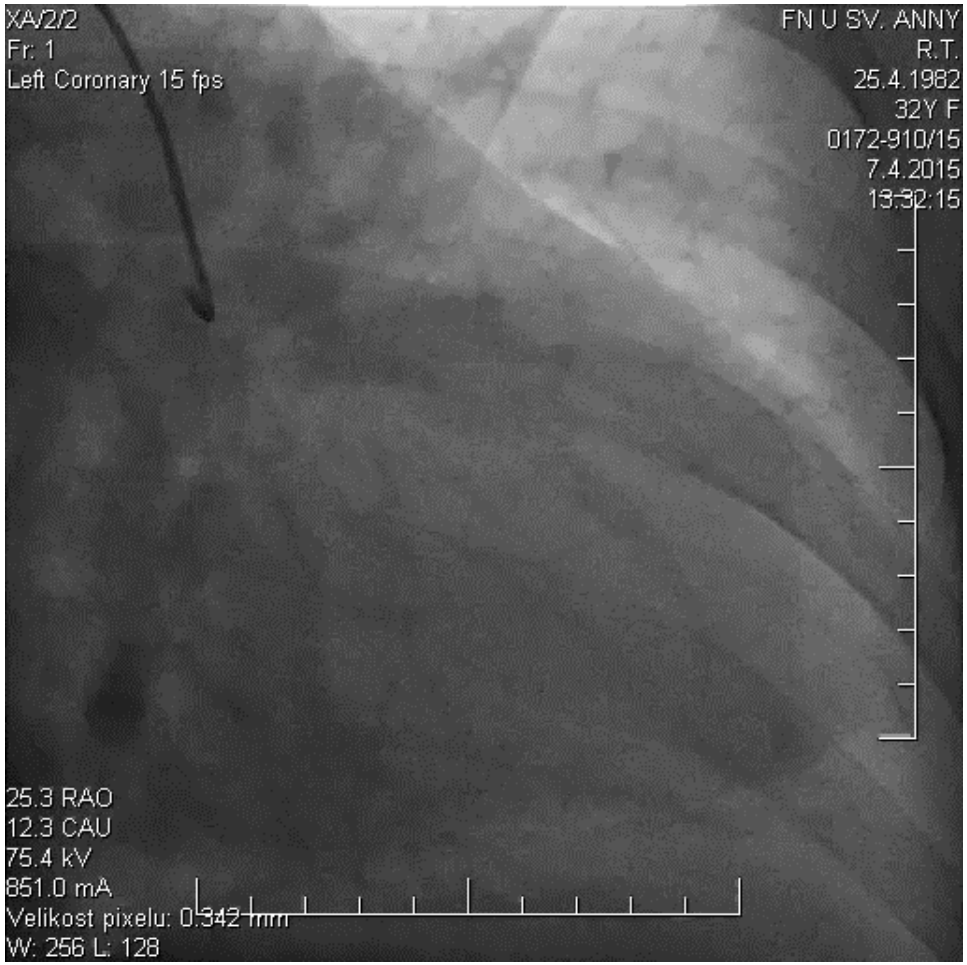
EF 35%
akineza DS

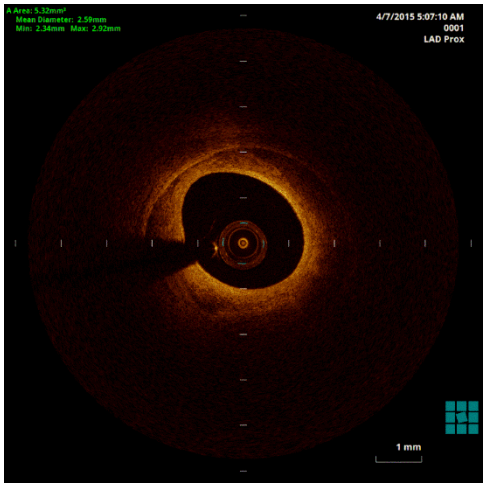
Fibroelastom v levé síni



4. Spontánní koronární disekce

Mladá žena, 32 let, 6 měsíců po porodu , NSTEMI PS



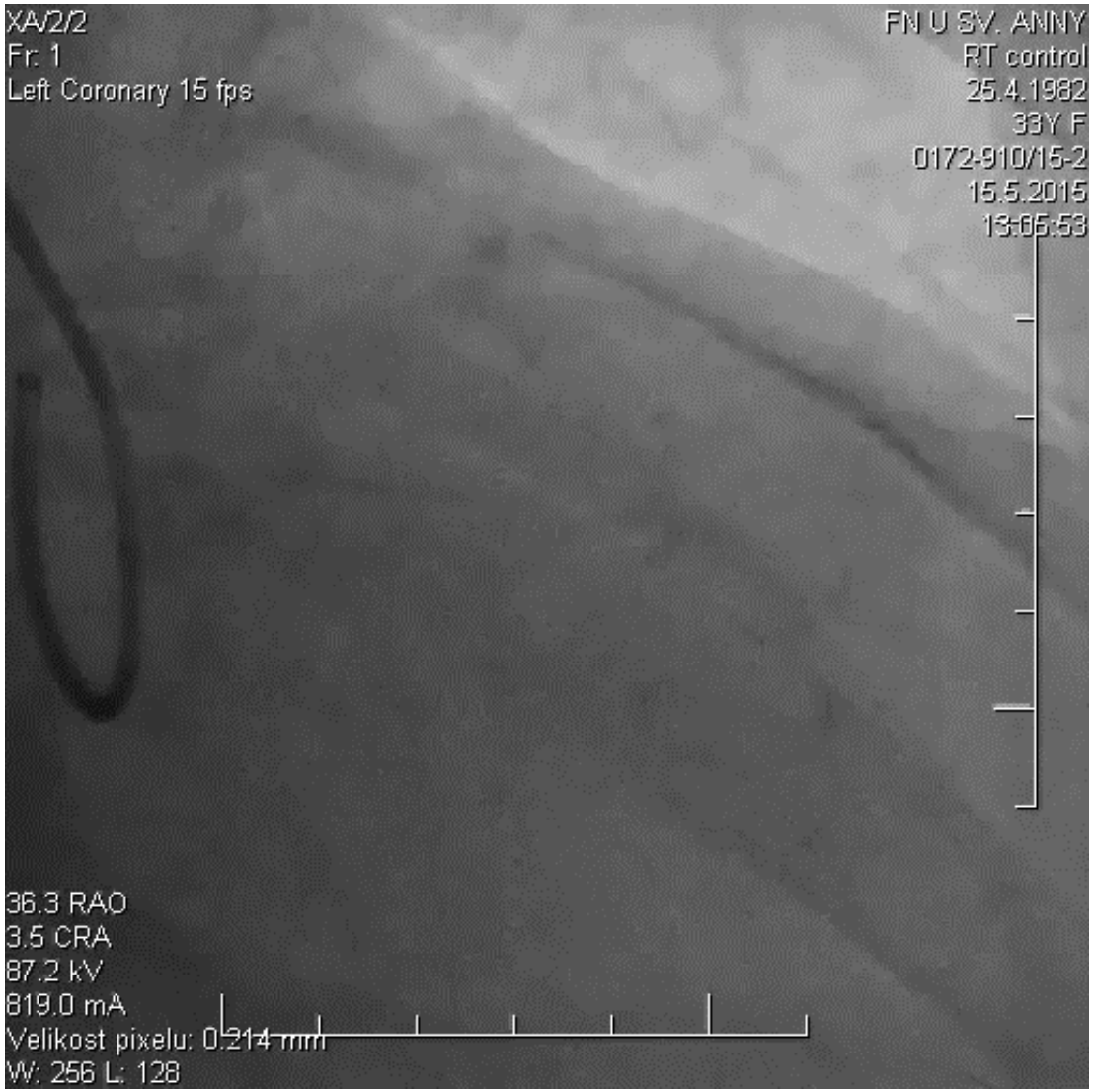


Angiograficky – ohraničená stenóza prox. RIA, na OCT intramurální hematom

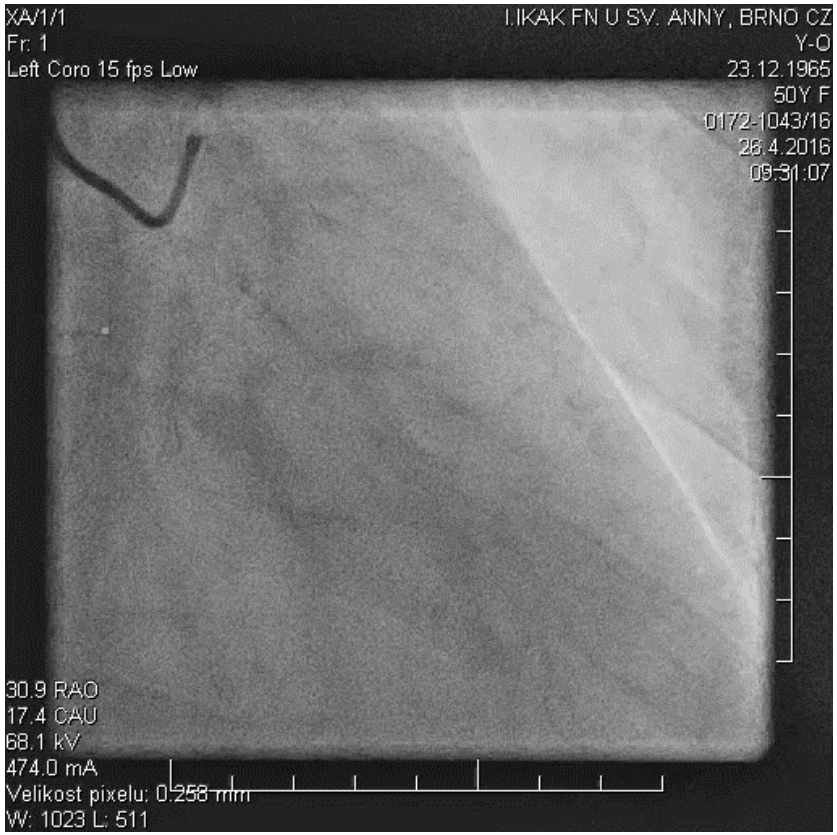
Postup ???

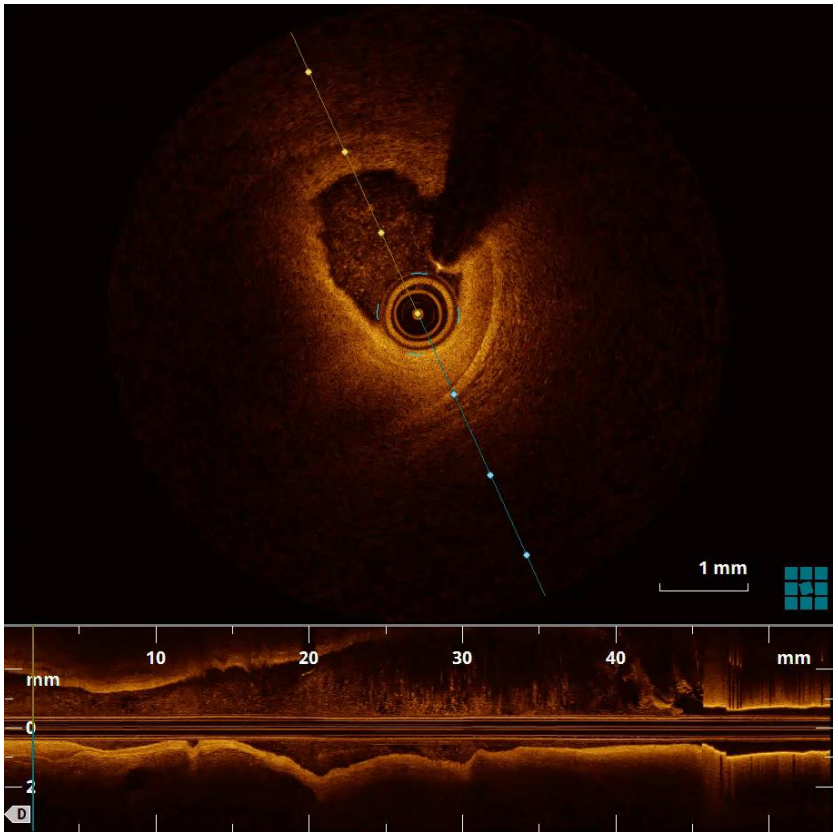
Konzervativně ???? (32 let , mladá žena)
PCI ?????

Konzervativní postup - DAPT, Ca blokátor,
rekoronarografie za 6 týdnů - angio i OCT , plné zhojení



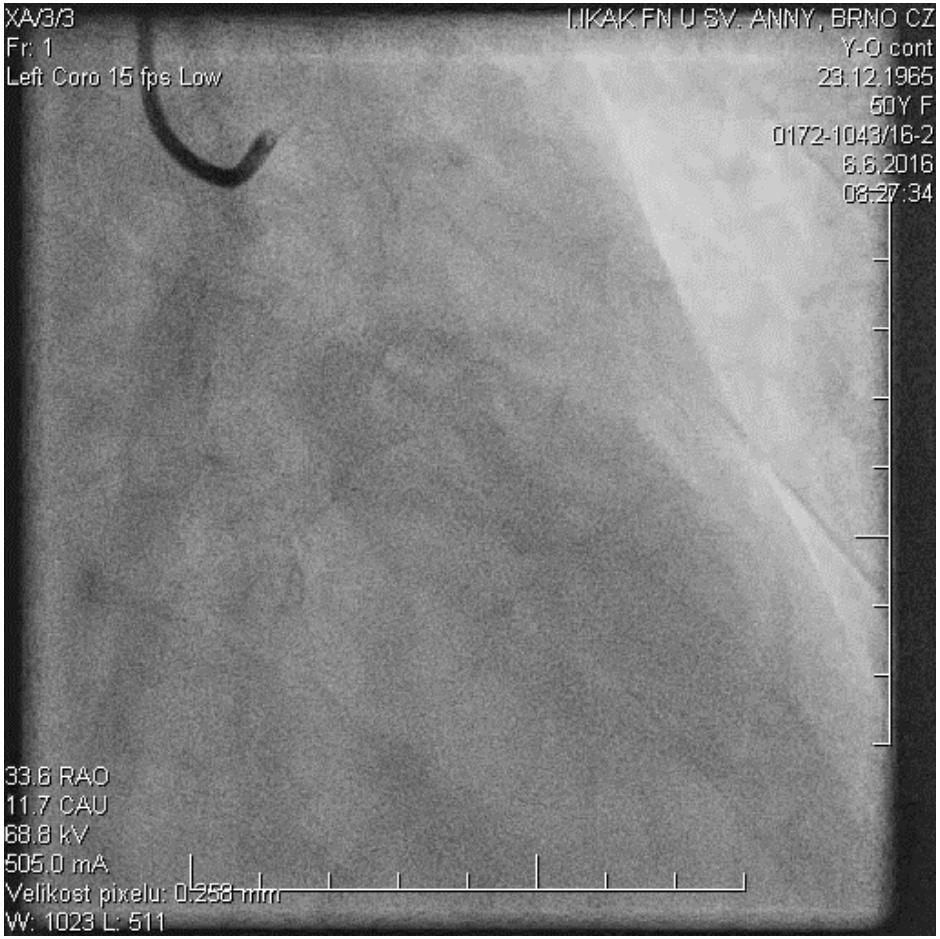
Žena 50 let, bolesti na hrudi, fibrilace komor při po příjezdu do nemocnice, KPR – vyšetřována intubována, ekg - BPRTw

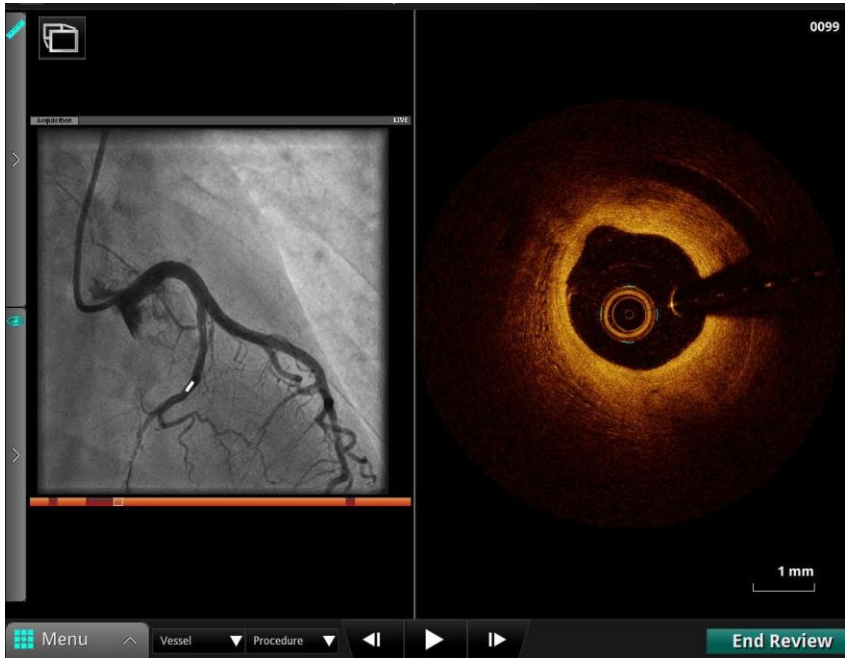




Angiograficky : hraniční stenóza na prox. RC
OCT : intramurální hematom, suspekce ze separace medie a adveticie i na kmeni ACS

Po 6 týdnech – angiograficky normální obraz, OCT- hojící se hematom
rekoronarografie pro opakované potíže po 2 měsících – bez recidivy





5. Takotsubo kardiomyopatie

European Journal of Heart Failure (2016) 18, 8–27
doi:10.1002/ejhf.424

REVIEW

Current state of knowledge on Takotsubo syndrome: a position statement from the task force on Takotsubo syndrome of the Heart Failure Association of the European Society of Cardiology

Alexander R. Lyon[1,2,*], Eduardo Bossone[3], Birke Schneider[4], Udo Sechtem[5], Rodolfo Citro[6], S.Richard Underwood[1,2], Mary N. Sheppard[7], Gemma A. Figtree[8,9], Guido Parodi[10], Yoshihiro J. Akashi[11], Frank Ruschitzka[12], Gerasimos Filippatos[13], Alexandre Mebazaa[14], and Elmir Omerovic[15]

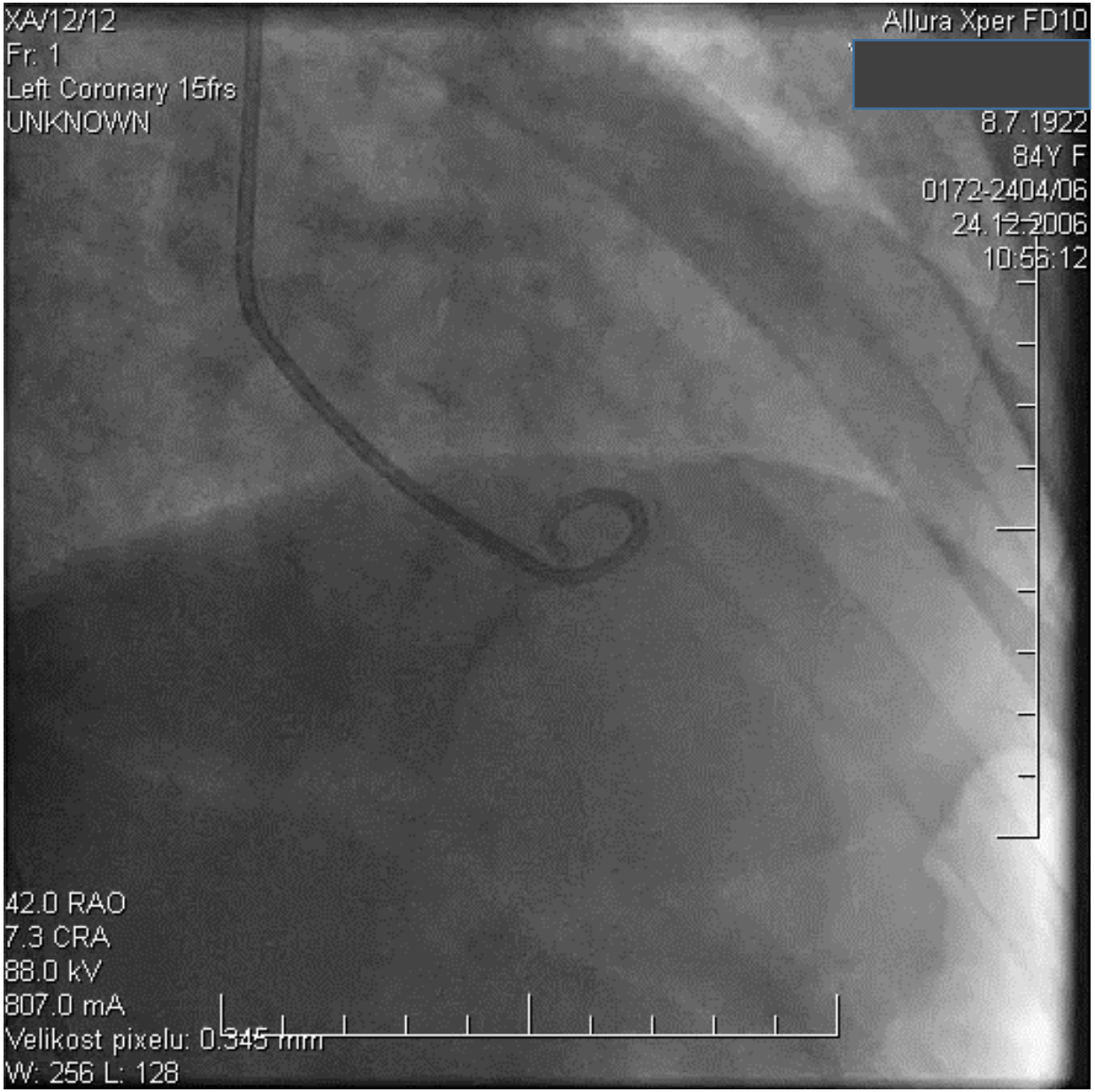
Takotsubo syndrome is increasingly recognized and reported.
It appears to be more common than previously recognized, but the precise incidence is not known.

Many features of TS suggest a different pathophysiological condition from atherosclerotic CAD

Summary of pathophysiological hypotheses

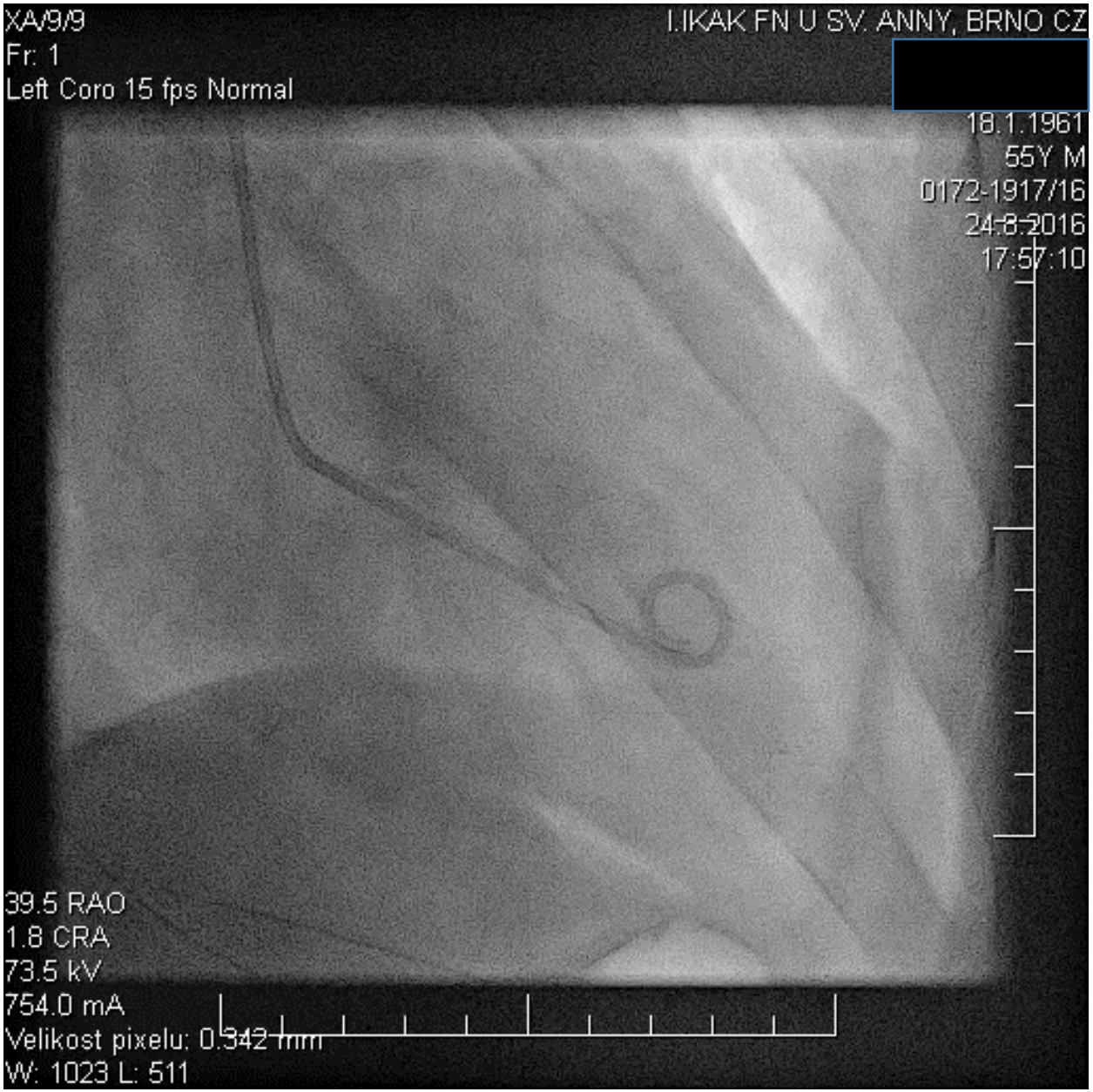
Vascular	Acute multivessel coronary spasm.
	Aborted myocardial infarction with spontaneous recanalization.
	Acute increased ventricular afterload.
Myocardial	Acute left ventricular outflow tract obstruction.
	Direct catecholamine-mediated myocardial stunning.
Vascular and myocardial	Integrated cardiovascular physiology (a cardio-circulatory syndrome).

Apikální typ



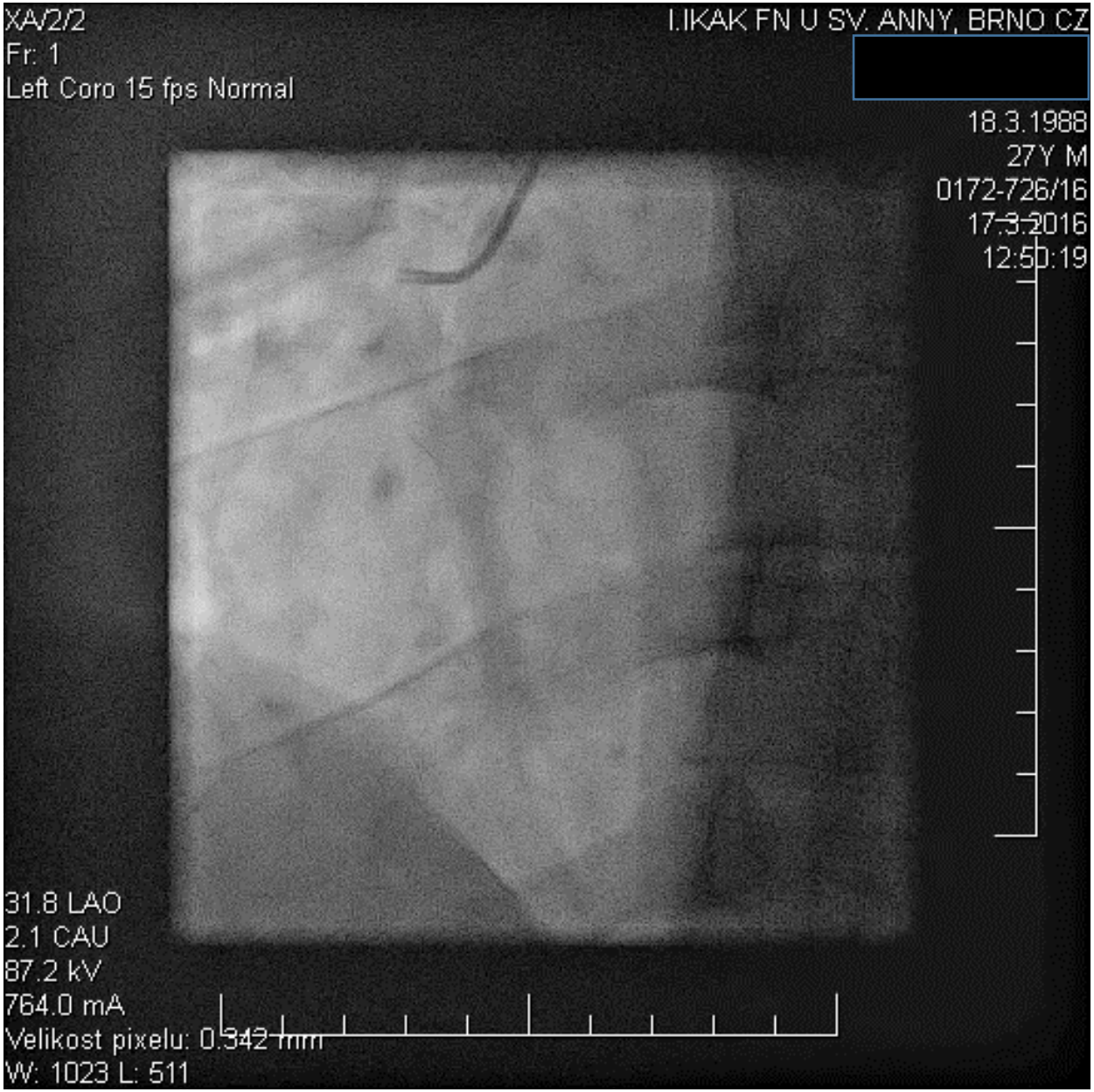
Ž, 84 let
UPV

Midventrikulární typ

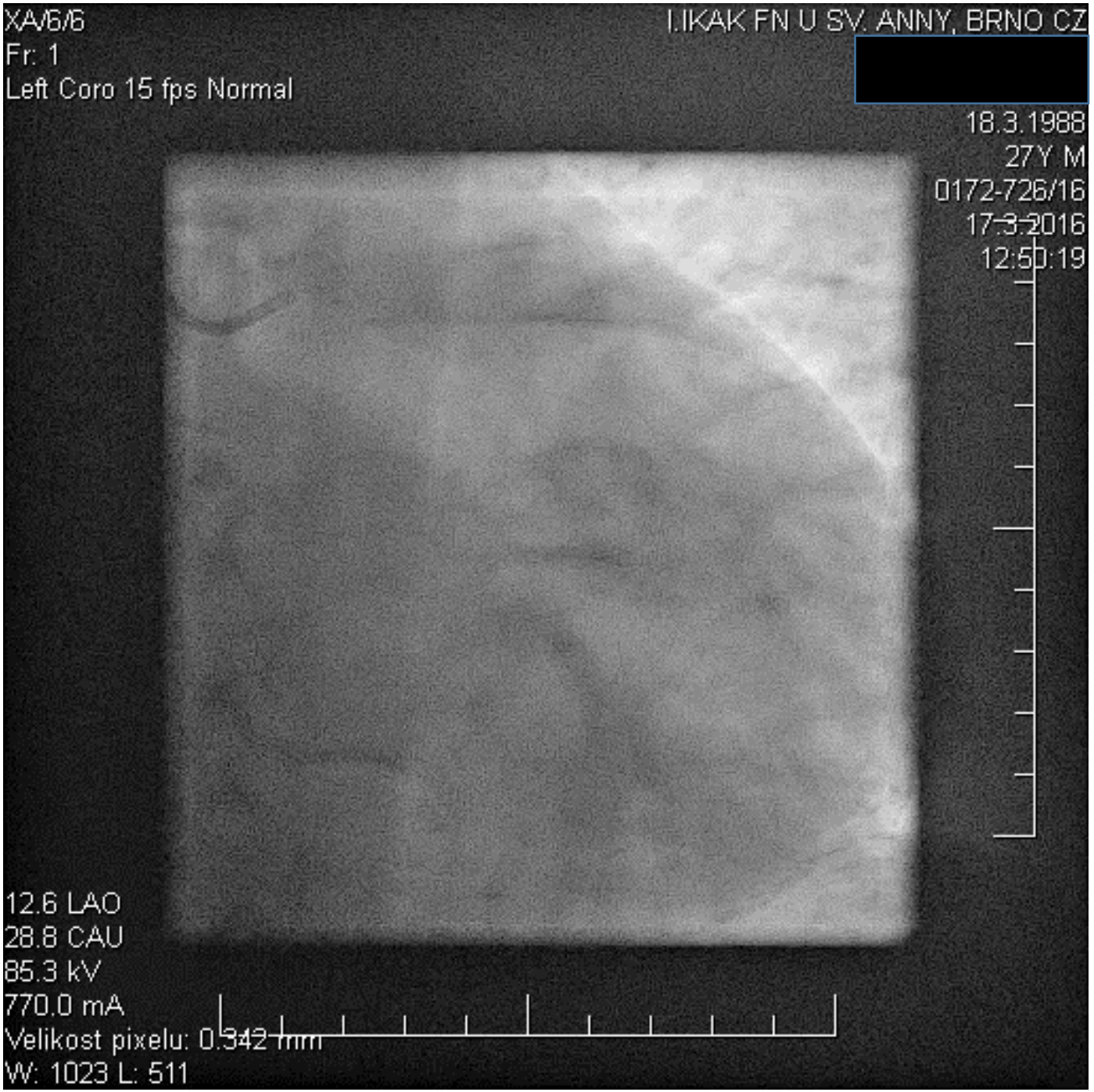


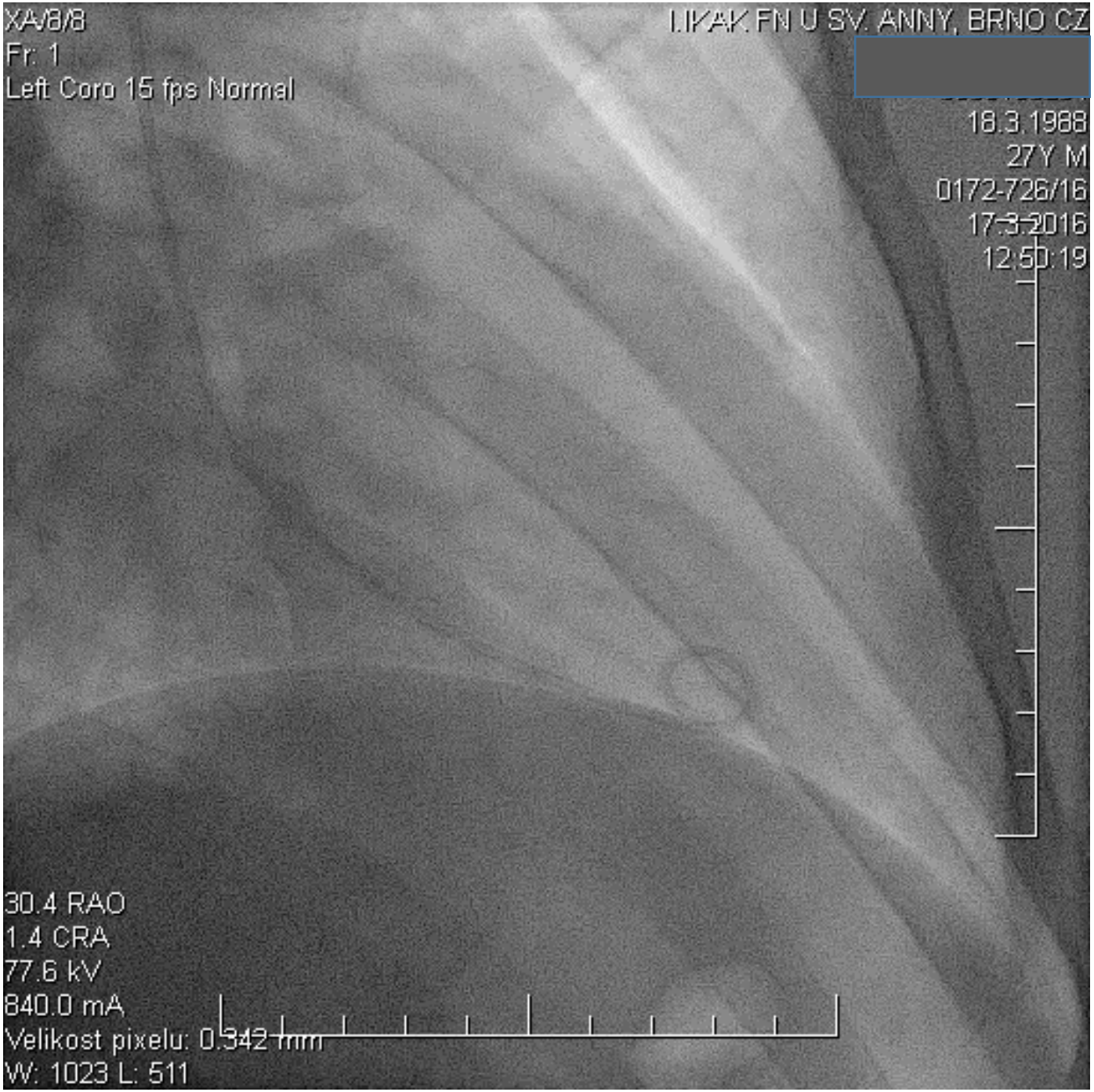
M, 55 let
Ca rekta před OP

6. Myokarditis



M, 28 let


XA/6/6
Fr: 1
Left Coro 15 fps Normal
I.IKAK FN U SV. ANNY, BRNO CZ
[redacted]
18.3.1988
27Y M
0172-726/16
17.3.2016
12:50:19
12.6 LAO
28.8 CAU
85.3 kV
770.0 mA
Velikost pixelu: 0.342 mm
W: 1023 L: 511


XA/8/8
Fr: 1
Left Coro 15 fps Normal
I.KAK. FN U SV. ANNY, BRNO CZ
18.3.1988
27Y M
0172-726/16
17.3.2016
12:50:19
30.4 RAO
1.4 CRA
77.6 kV
840.0 mA
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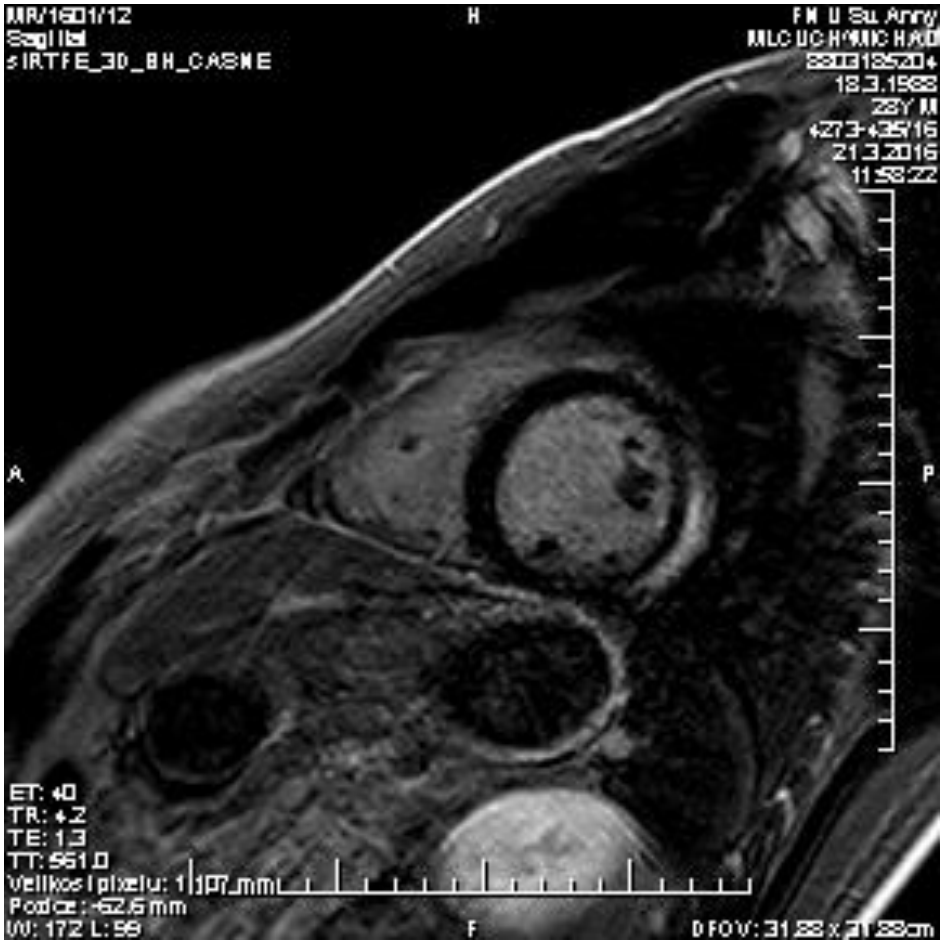
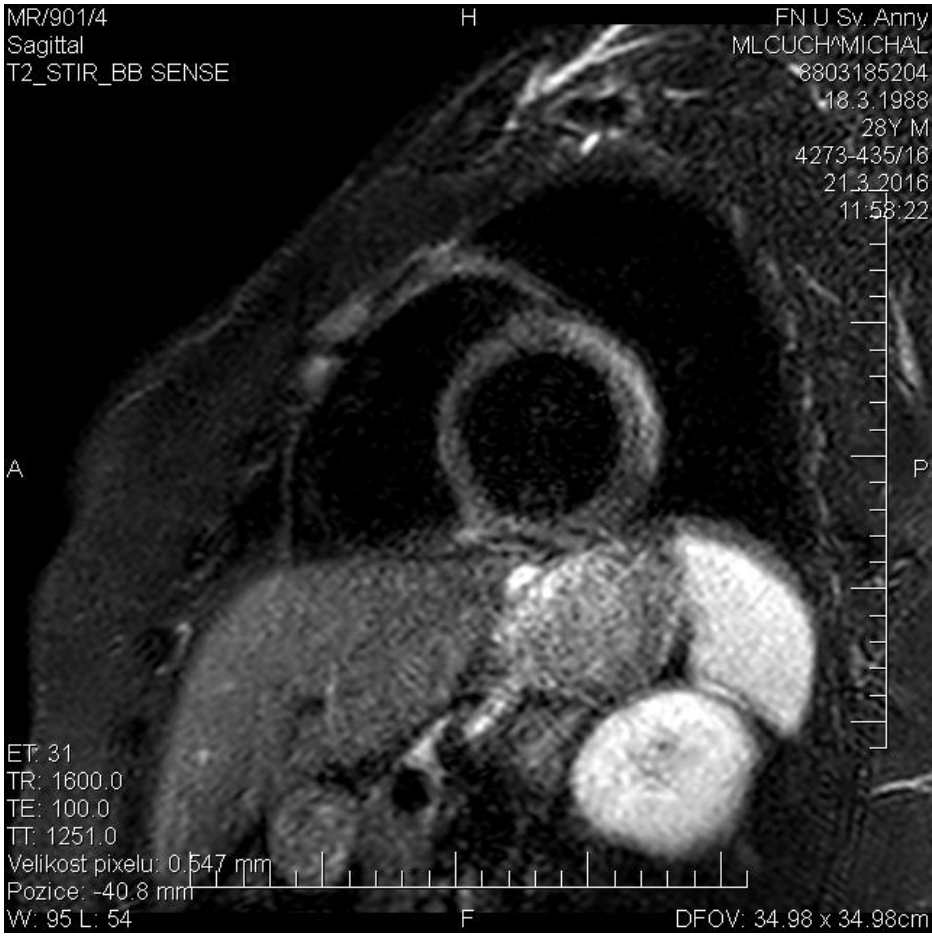
Myokarditis



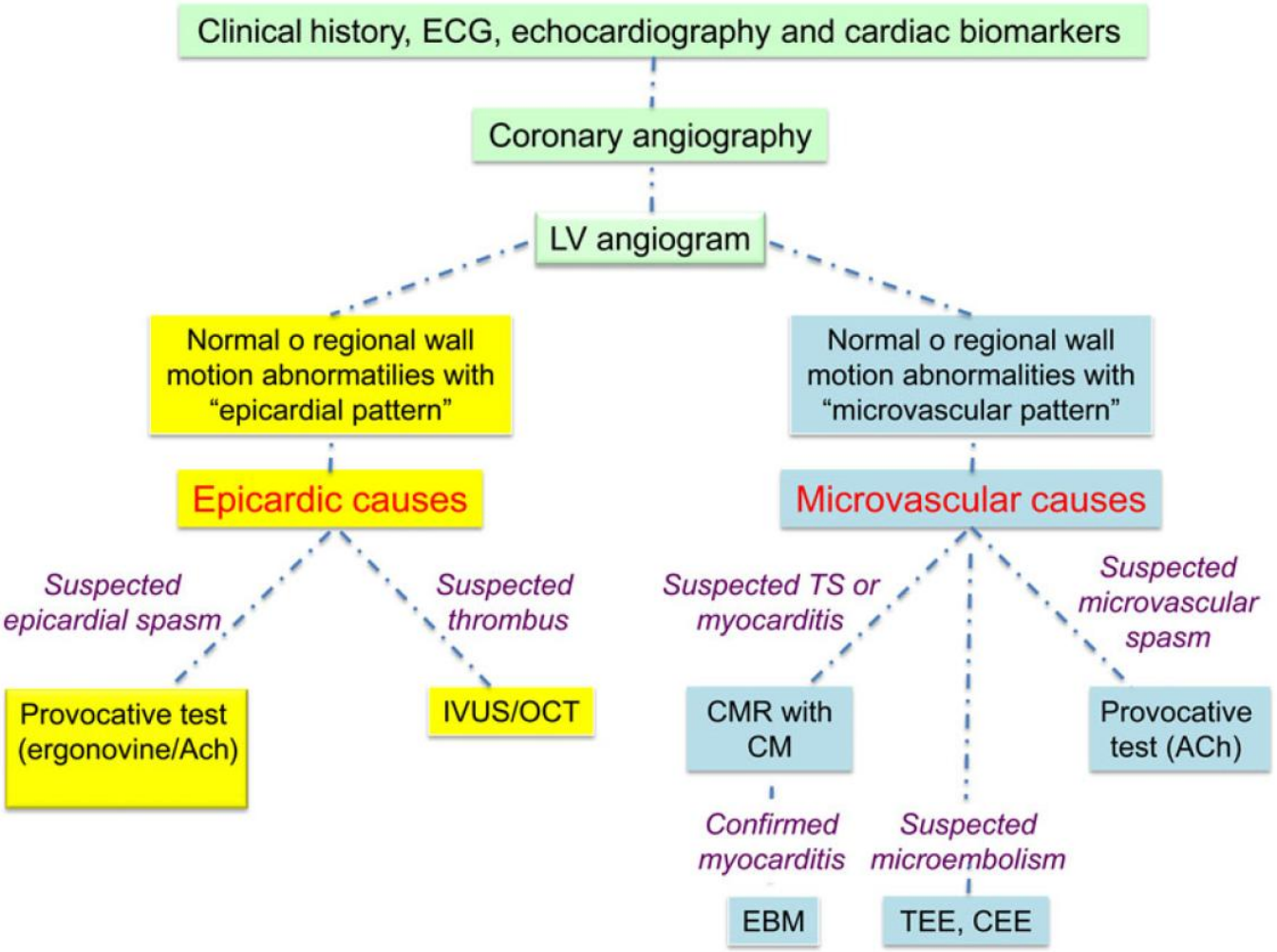


Late gadolinium enhancement subepikardiálně

Závěry

- MINOCA – syndrom
- pátrat po příčině: OCT, NMR, TEE, acetylcholin
- prognóza lepší než u MICAD ale horší než u zdravých
- léčba dle příčiny, často nejednoznačná

Vyšetřovací metody



Niccoli G et al.: EHJ (2015) 36, 475-481

Standard Method of Provocation Test: Intracoronary Ergonovine Administration

1. Control Angiography of Left and Right Coronary Arteries:

- Perform CAG in an appropriate projection that ensures the best separation of the branches of each coronary artery. After injection of ergonovine, perform CAG in the same projection again.

2. Injection of Ergonovine into the Left Coronary Artery:

- Inject 20~60 μg of ergonovine in solution in physiological saline into the LCA over a period of several minutes (about 2~5 minutes).
- Perform CAG 1~2 minutes after completion of the injection.
- In the event of an ischemic change on the ECG or chest symptom, perform CAG at the time of its onset.
- In case of a (-)ve result in the provocation test, proceed to the RCA provocation test 5 minutes later.

3. Injection of Ergonovine into the Right Coronary Artery:

- Inject 20~60 μg of ergonovine in solution in physiological saline into the RAC over a period of several minutes (about 2~5 minutes). The timing of angiography is the same as for the LCA.

4. Left and Right Coronary Angiography after administration of Nitrate:

- Administer a sufficient dose of nitrate into each coronary artery, and perform CAG while the coronary artery is maximally dilated

JCS Joint Working Group.Circ J 2014; **78:** 2779 – 2801

One-Year Prognosis of Patients with Myocardial Infarction and Non-Obstructive Coronary Artery Disease (MINOCA)

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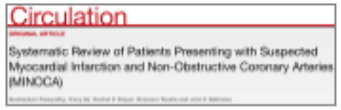
Background

- Myocardial infarction with non-obstructive coronary arteries (MINOCA) is increasingly recognized following acute angiography, with studies reporting a prevalence of approximately 10%.
- A recent meta-analysis highlights the importance of considering MINOCA a 'working diagnosis'



- The European Society of Cardiology position paper indicates large registries are needed to provide reliable estimates of the true prevalence and prognostic relevance of MINOCA.

Aims

- To detail the 12-month prognosis of patients with MINOCA versus patients with myocardial infarction with obstructive coronary artery disease (MICAD) in relation to all-cause mortality and return hospital visits for cardiovascular diagnoses.

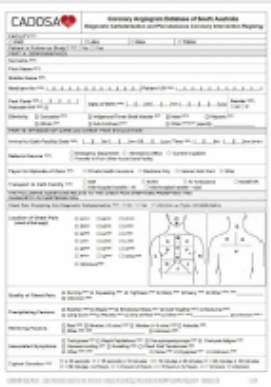
Methods

- All consecutive patients undergoing coronary angiography for acute myocardial infarction (AMI) in South Australian public hospitals from January 2012 to December 2013 were captured utilising the Coronary Angiogram Database of South Australia (CADOSA) Registry.

Methods

CADOSA Registry

CADOSA is a procedural registry of all public cardiac catheterisation procedures in South Australia, Australia (population = 1.6 million).



Definitions

The AMI patients were classified as MICAD or MINOCA on the basis of the presence or absence of a significant angiographic stenosis (≥50%).

Patient Follow-up

Determined from administrative datasets.

Results

- From 3,145 patients undergoing angiography for AMI, 347 (11%) were classified as MINOCA.
- MINOCA patients were younger (59 ± 15 vs. 64 ± 13, p <0.05) and more likely to be female (60% vs. 26%, p<0.05)

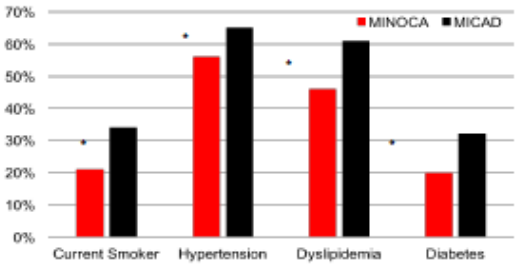


Figure 1: Comparison of clinical characteristics between MINOCA and MICAD. *p<0.01, age adjusted

Results

- Over 12-months, the total prevalence of adverse outcomes (mortality or re-admission) in MINOCA was 19.9% compared to 26.5% in MICAD (OR 0.68, 0.51-0.91, p<0.05, age adjusted).

Table 1. Morality Outcomes Between MINOCA and MICAD Patients

	MINOCA % (n)	MICAD % (n)	p value
In-hospital	0.3% (1)	2.1% (58)	<0.05
1 month	0.3% (1)	2.5% (69)	<0.05
12 months	0.9% (3)	3.7% (102)	<0.05

p value from Fisher's exact test

Table 2. Return Hospital Visits for Cardiovascular Cause Between MINOCA and MICAD Patients

	MINOCA % (n)	MICAD % (n)	OR 95% CI	p value
1 month	8.9% (30)	9.4% (257)	0.89 (0.59-1.34)	>0.05
12 months	14% (48)	18% (494)	0.68 (0.49-0.96)	<0.05

Odds ratio presented for MINOCA patients, obtained from logistic regression and adjusted for age

Conclusion

- Although MINOCA patients have a reduced 12-month all-cause mortality compared to MICAD patients, their re-presentation to hospital is similar and warrants further attention.

Nil Disclosures. Funding acknowledgement: The Coronary Angiogram Database of South Australia is supported by the National Heart Foundation of Australia (South Australian Division) and the Government of South Australia

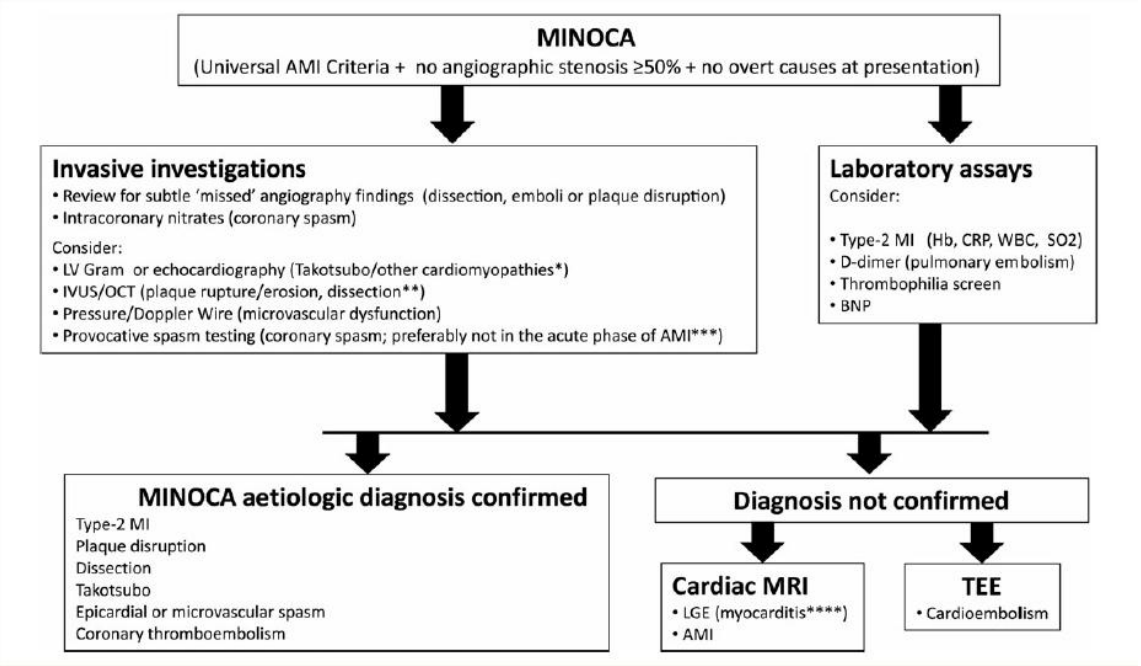
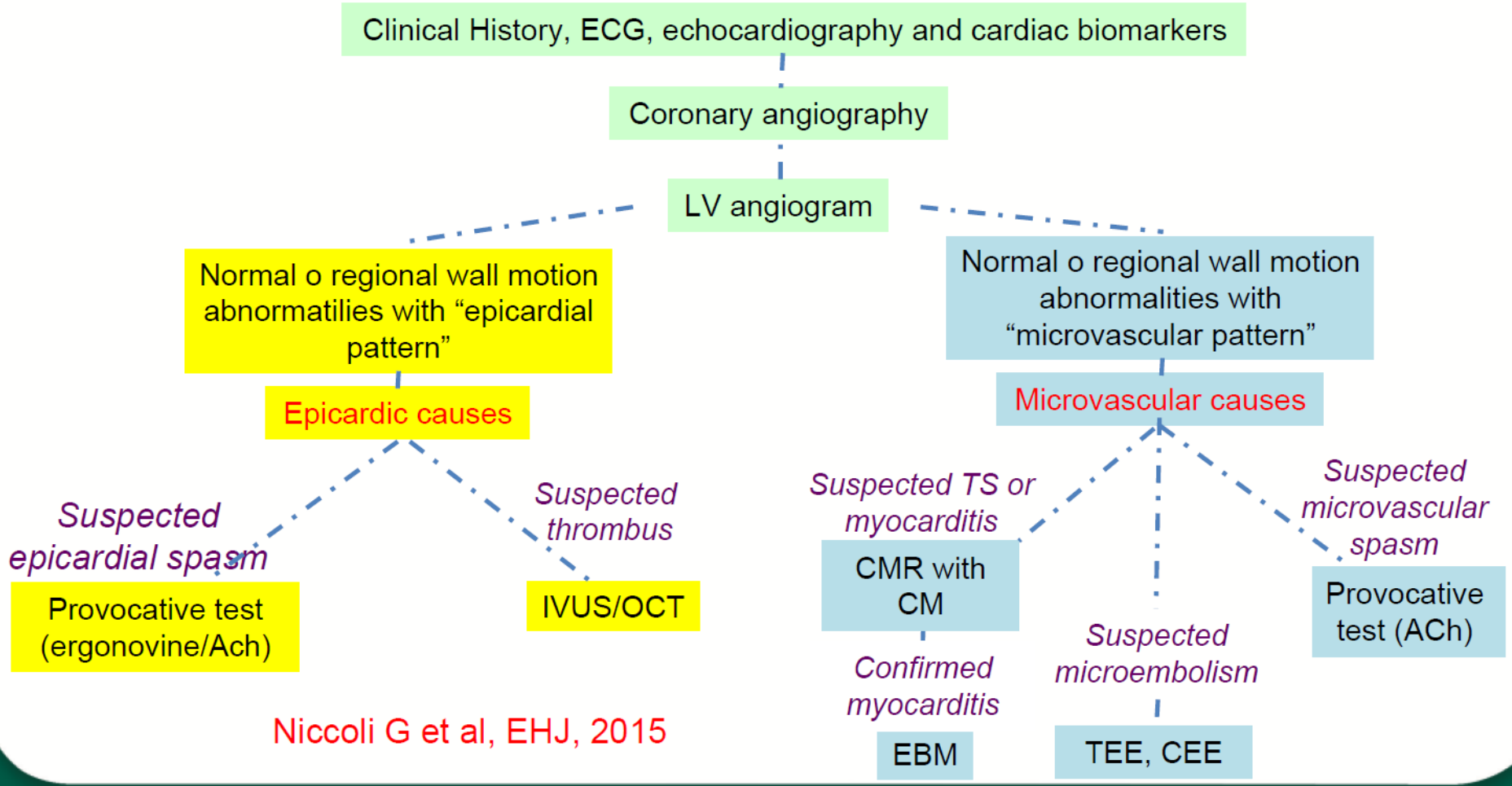
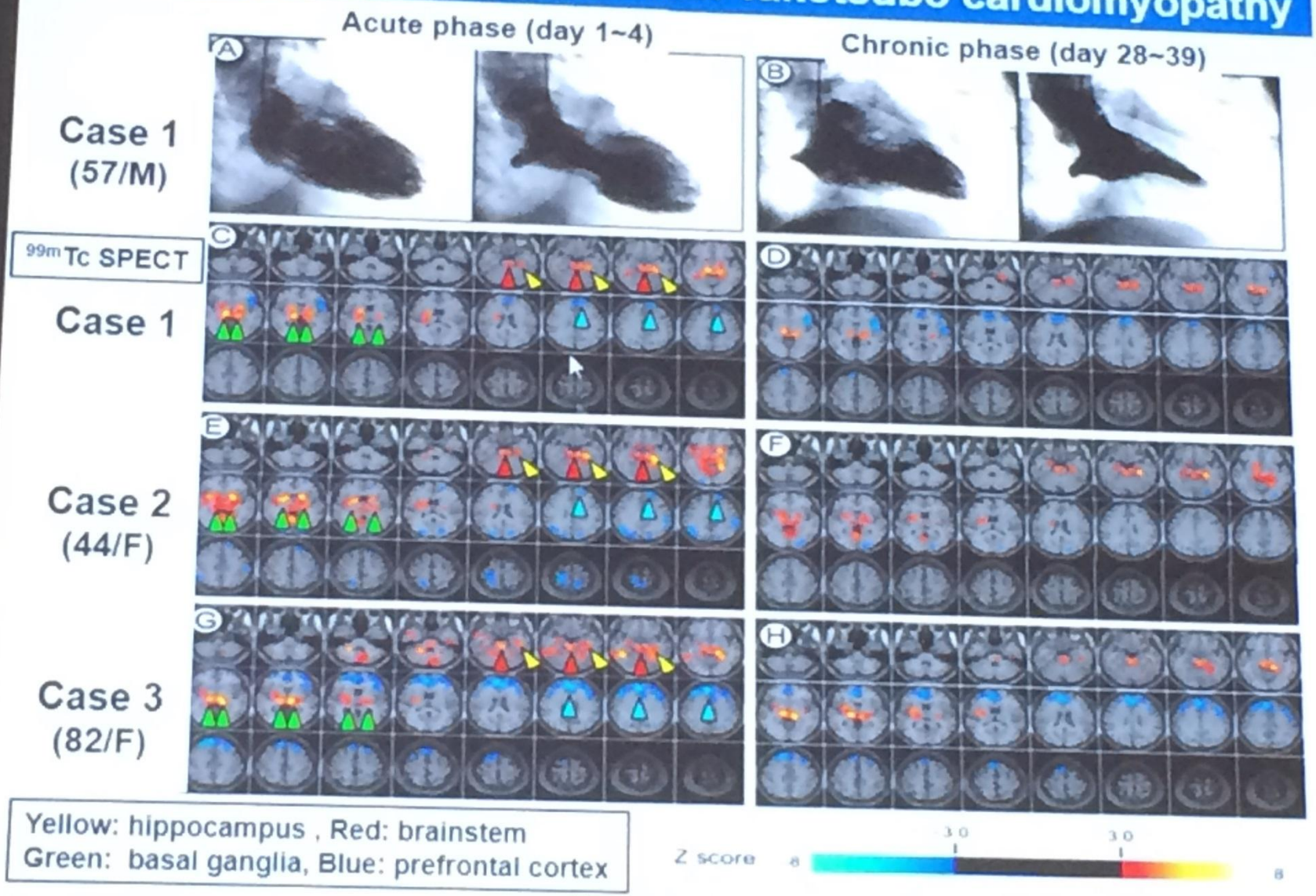


Figure 1 Recommended diagnostic and therapeutic algorithm for myocardial infarction with non-obstructive coronary arteries. * Takotsubo cardiomyopathy cannot be diagnosed with certainty in the acute phase as the definition requires follow-up imaging to document recovery of left ventricular function. In the authors' experience, some patients with apparent takotsubo have unrecognized ischaemic injury or myocarditis. We therefore recommend CMR when takotsubo cardiomyopathy is suspected. ** Plaque disruption (rupture, or erosion) should be suspected and intracoronary imaging considered whenever an alternate aetiology of the clinical presentation such as myocarditis or vasospasm has not been clearly identified, particularly among those patients with evidence of atherosclerosis on the coronary angiogram. Intravascular ultrasound and intracoronary optical coherence tomography frequently show more atherosclerotic plaque than may be appreciated on angiography. They also increase sensitivity for dissection. If intracoronary imaging is to be performed, it is appropriate to carry out this imaging at the time of the acute cardiac catheterization, after diagnostic angiography. Patients should be made aware of the additional information the test can provide and the small increase in risk associated with intracoronary imaging. *** Provocative testing for coronary artery spasm has been safely performed by experienced clinical researchers in selected patients with a recent acute myocardial infarction.[34] However, death cases have been reported (Per Tornvall Tornberg, personal communication) and this should not be a standard procedure among the patients, particularly in the acute phase. **** Clinically suspected myocarditis (no angiographic stenosis $\geq$ 50% plus non-ischaemic pattern on cardiac magnetic resonance imaging) by ESC Task Force criteria.[36] Diagnosis of certainty and aetiological diagnosis of myocarditis requires EMB (histology, immunohistology, infectious agents by PCR). AMI, acute myocardial infarction; BNP, B-type natriuretic peptide; CRP, C-reactive protein; Hb, hemoglobin; IVUS, intravascular ultrasound; LGE, late gadolinium enhancement; LV, left ventricle; MRI, magnetic resonance imaging; OCT, optical coherence tomography; SO2, Oxygen saturation; WBC, white blood cell count.



Niccoli G et al, EHJ, 2015

Brain activation in patients with Takotsubo cardiomyopathy



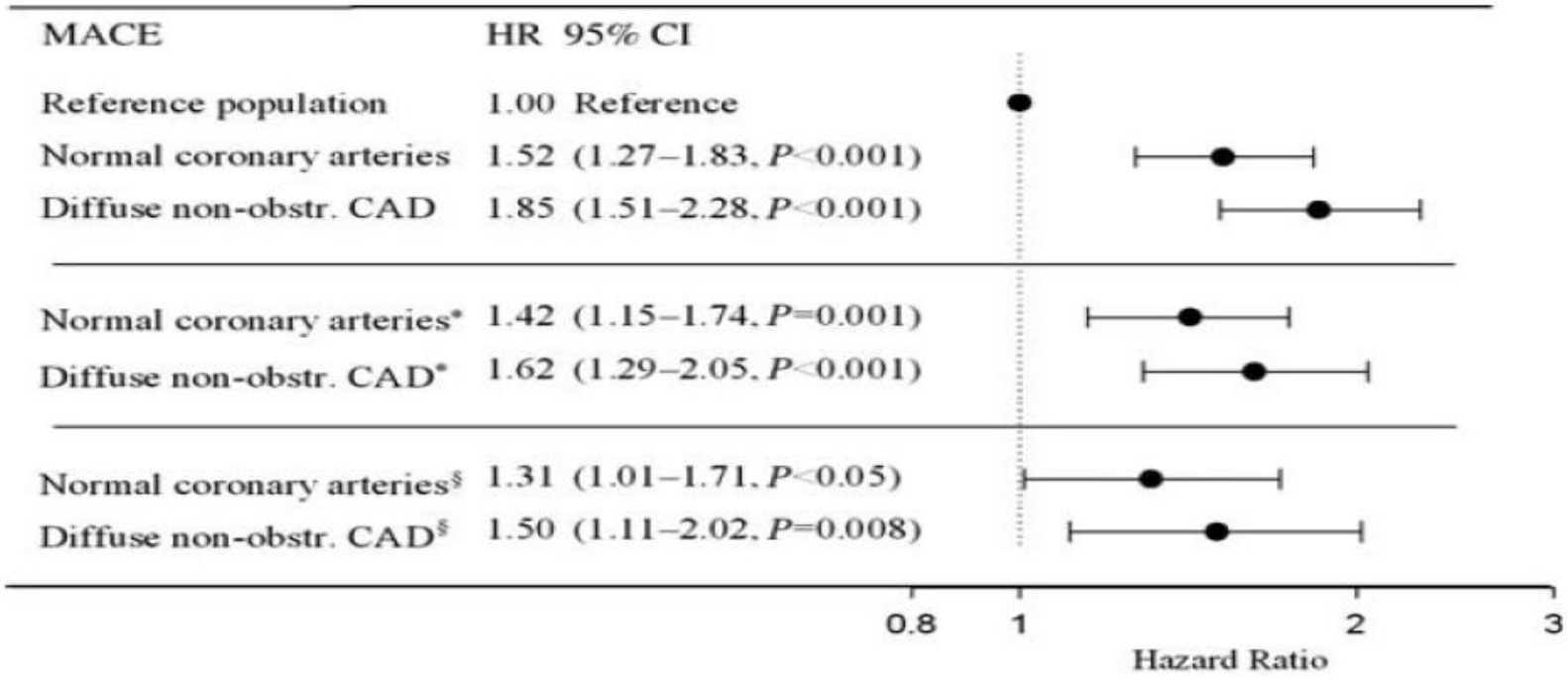
(Suzuki, Shimokawa, et al. *Circ J.* 2014,78:256-258.)

MINOCA

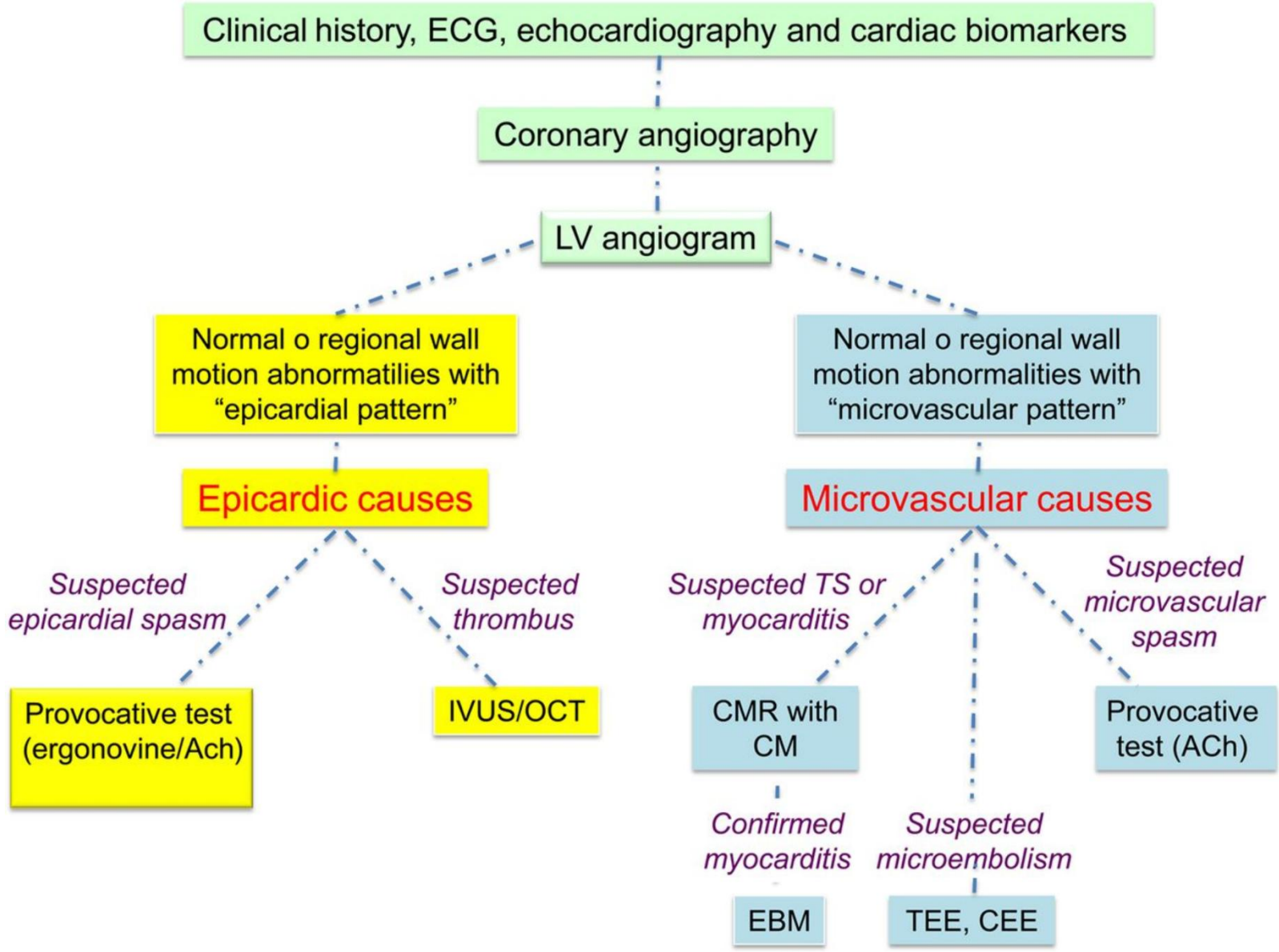
Aetiologies

1. Positive remodeled unstable plaques, plaque rupture, erosion
2. Coronary spasm (epicardial or microvascular)
3. Takotsubo syndrome
4. Myocarditis
5. Thromboembolism
6. Spontaneous dissection (often obstructive disease)
7. Type 2 MI causes (often obstructive disease)

Prognosis of non obstructive CAD



Jespersen L, EHJ, 2012


Clinical history, ECG, echocardiography and cardiac biomarkers
Coronary angiography
LV angiogram
Normal o regional wall motion abnormatilies with "epicardial pattern"
Normal o regional wall motion abnormalities with "microvascular pattern"
Epicardic causes
Microvascular causes
Suspected epicardial spasm
Suspected thrombus
Suspected TS or myocarditis
Suspected microvascular spasm
Provocative test (ergonovine/Ach)
IVUS/OCT
CMR with CM
Provocative test (ACh)
Confirmed myocarditis
Suspected microembolism
EBM
TEE, CEE

Koronární spasmus