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How late is too late to recanalize carotid and intracranial thrombosis after stroke? Late Stroke interventions. Cardiologist's point of view

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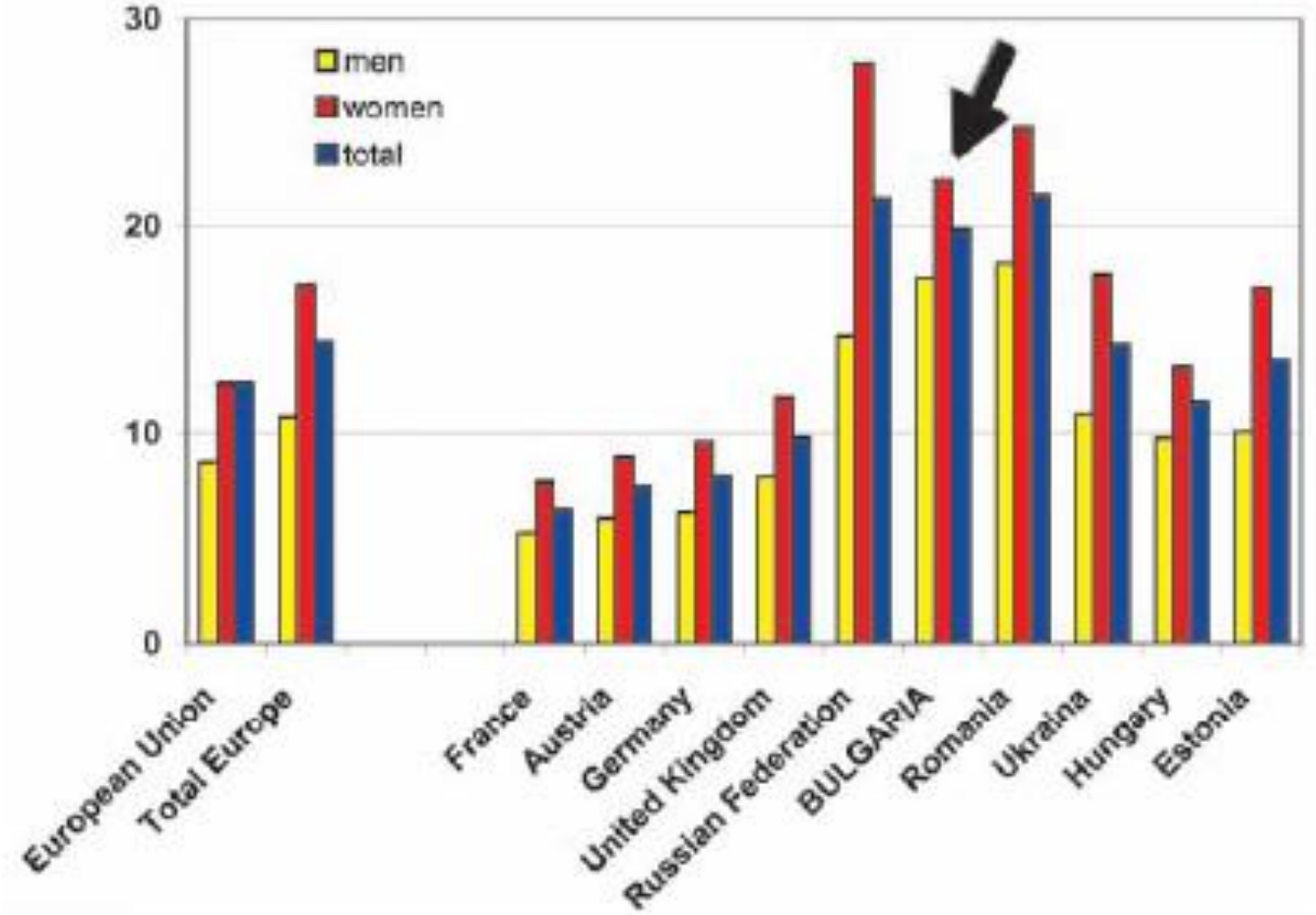
DISCLOSURE STATEMENT OF FINANCIAL INTEREST

I, Ivo Petrov, DO NOT have a financial interest/arrangement or affiliation with one or more organizations that could be perceived as
a real or apparent conflict of interest in the context of the subject of this presentation.

Endovascular experience after 6 years of work:

- 13800 endovascular cases (“Head to toe”):
  - CTO and Left main Coronary interventions
  - EVAR/TEVAR
  - TAVR
  - Intracranial thrombus retrieval in stroke
  - CAS and intracranial EVI (>900)
  - Radial approach for complex peripheral cases
  - Complex venous interventions (including May-Thurner, CCSVI)
  - Renal denervation

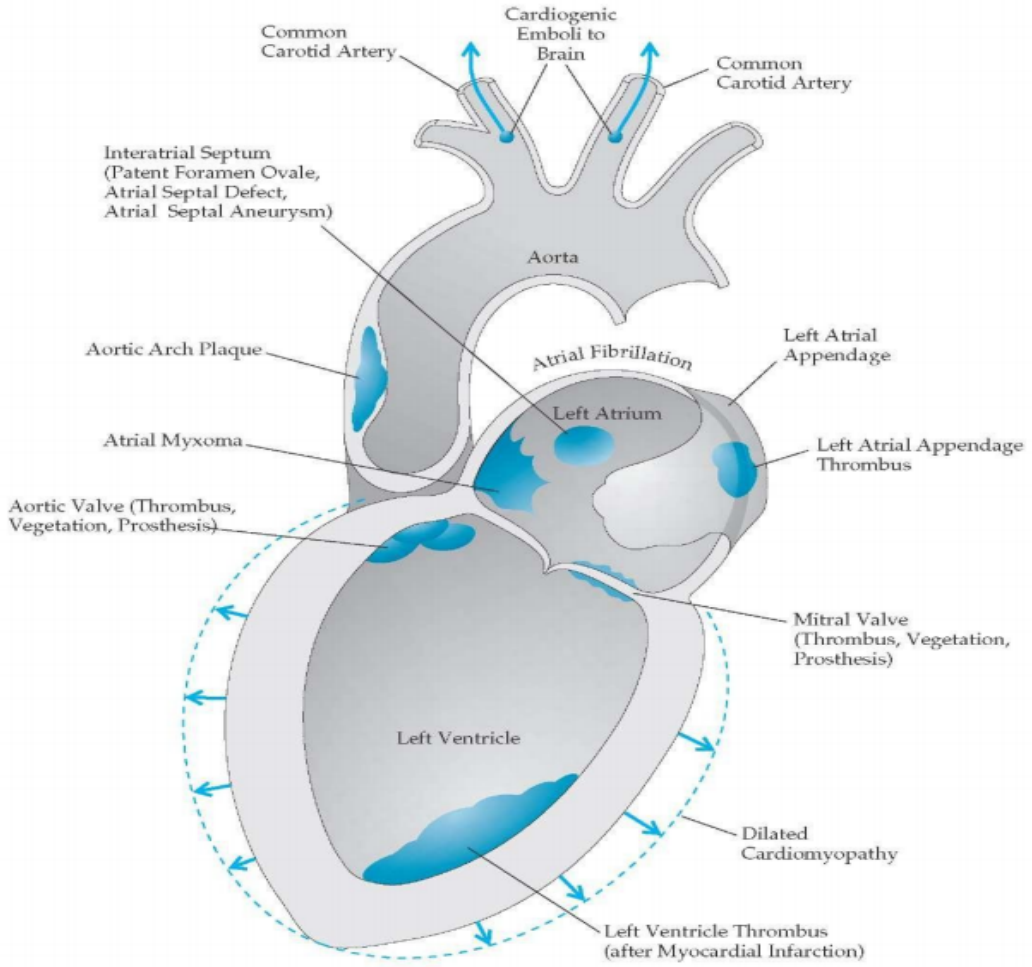
Proportion: Stroke mortality to general mortality in Bulgaria 2013



Фиг. 1. Смъртност от инсулти като процент от общата смъртност в Европа, Европейския съюз и някои от европейските страни.

Cardiovascular embolus formation

- Rheology
- Hypercoagulability
- Endothelial injury



- **Atrial fibrillation (AF)**
- Reduced LV contractility = CHF
- Recent MI (<4 weeks)
- Regional LV akinesis
- Aneurysm of the LV
- Cardiomyopathy
- Infective Endocarditis
- Rheumatic valve disease
- Heart valve replacement
- overt foramen ovale (permissive)
- Atrial Myxoma

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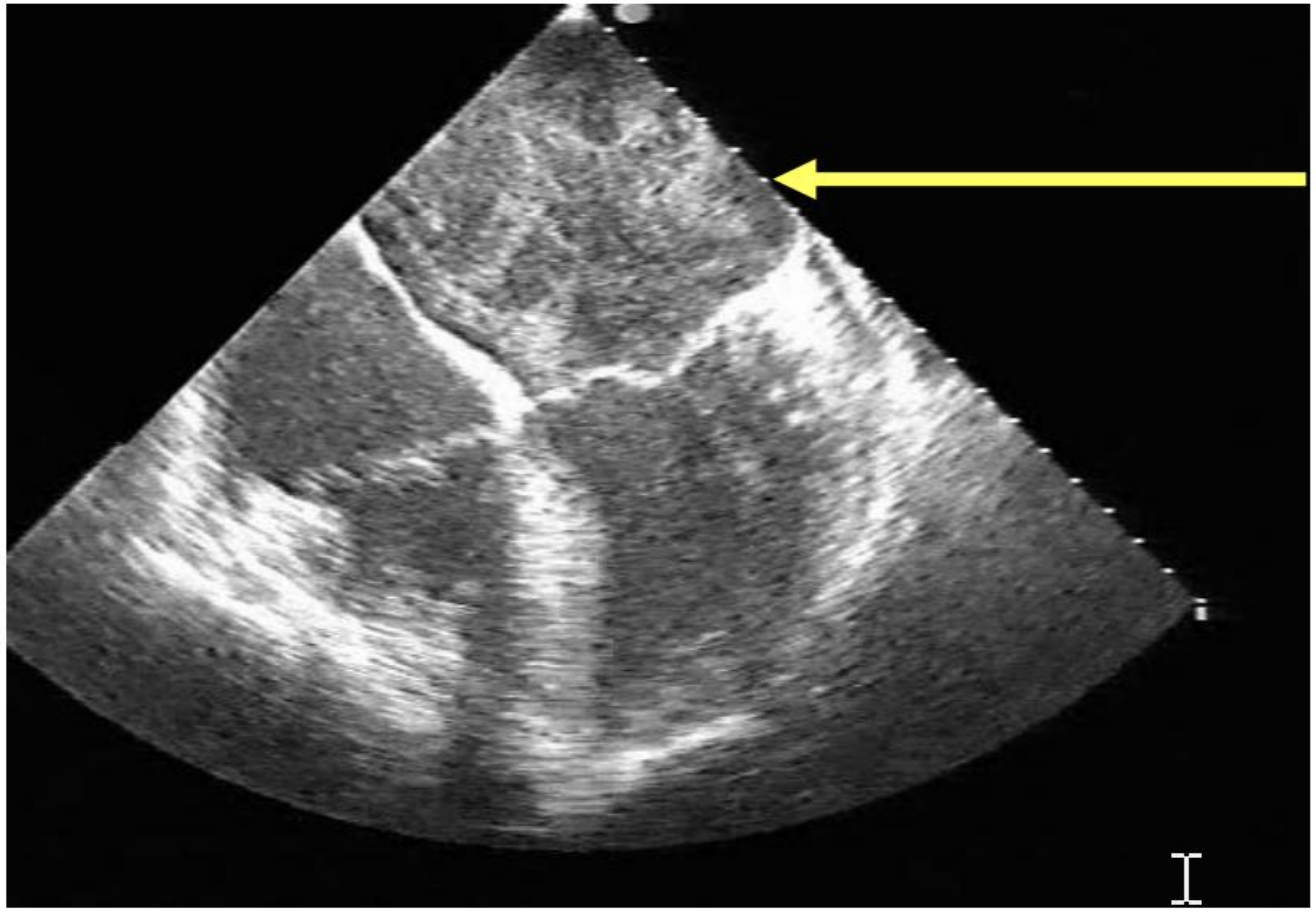
CHF: High risk of cardiac thrombembolism

even in maintained sinus rhythm

CHF = Increase ventricle size + Reduced contractility



Spontaneous echocardio-graphic contrast

- **low blood flow**
- **Hypercoagulability**
- **Endothelial injury**

= Pro-thrombotic state

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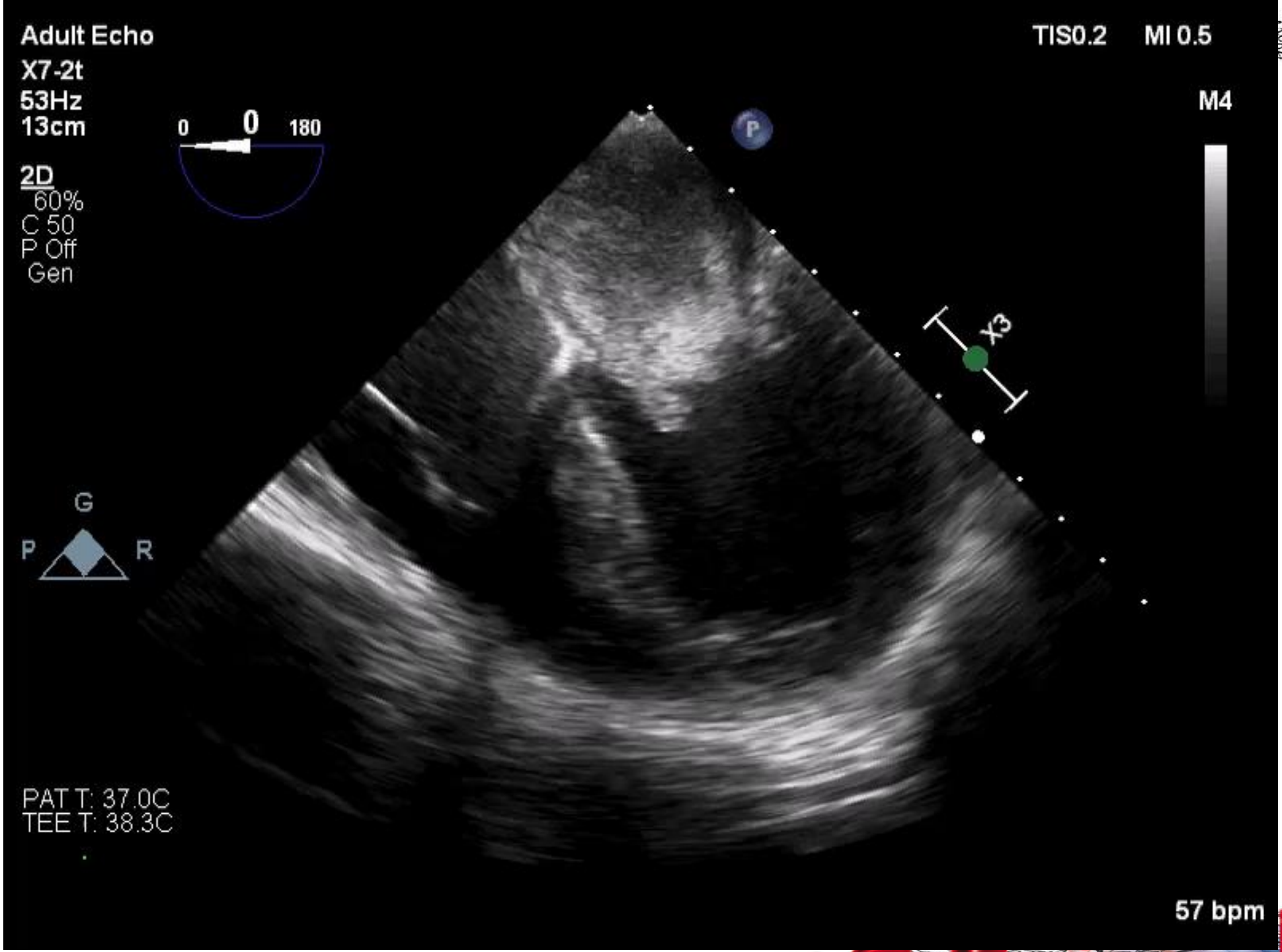
Huge LA mixoma in a patient with AIS



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Mobile LV thrombus in a patient with severe dilative cardiomyopathy and AIS

Time Is Brain—Quantified

Jeffrey L. Saver, MD

Stroke.2006;37:263-266.

Average infart growth:
5.4 mL / h

BRAIN

Estimated Pace of Neural Circuitry Loss in Typical Large Vessel, Supratentorial Acute Ischemic Stroke

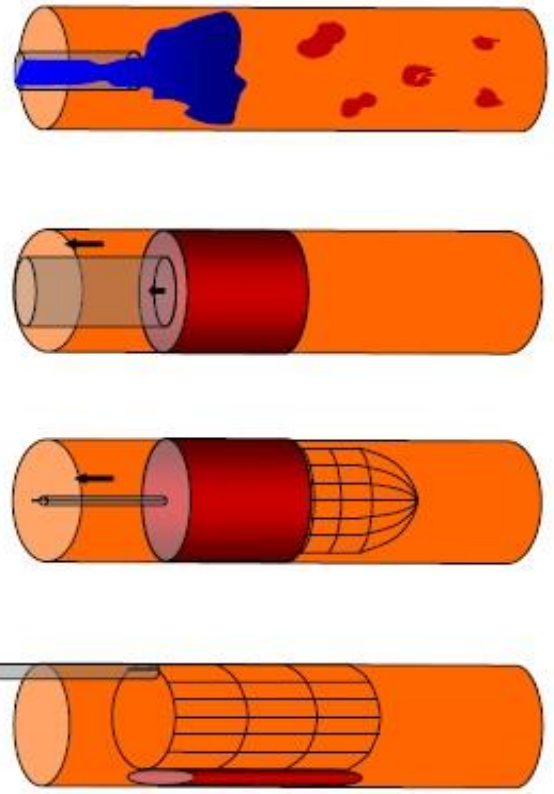
	Neurons Lost	Synapses Lost	Myelinated Fibers Lost	Accelerated Aging
Per Stroke	1.2 billion	8.3 trillion	7140 km/4470 miles	36 y
Per Hour	120 million	830 billion	714 km/447 miles	3.6 y
Per Minute	1.9 million	14 billion	12 km/7.5 miles	3.1 wk
Per Second	32 000	230 million	200 meters/218 yards	8.7 h

VOLUME INFARCT

TIME ONSET

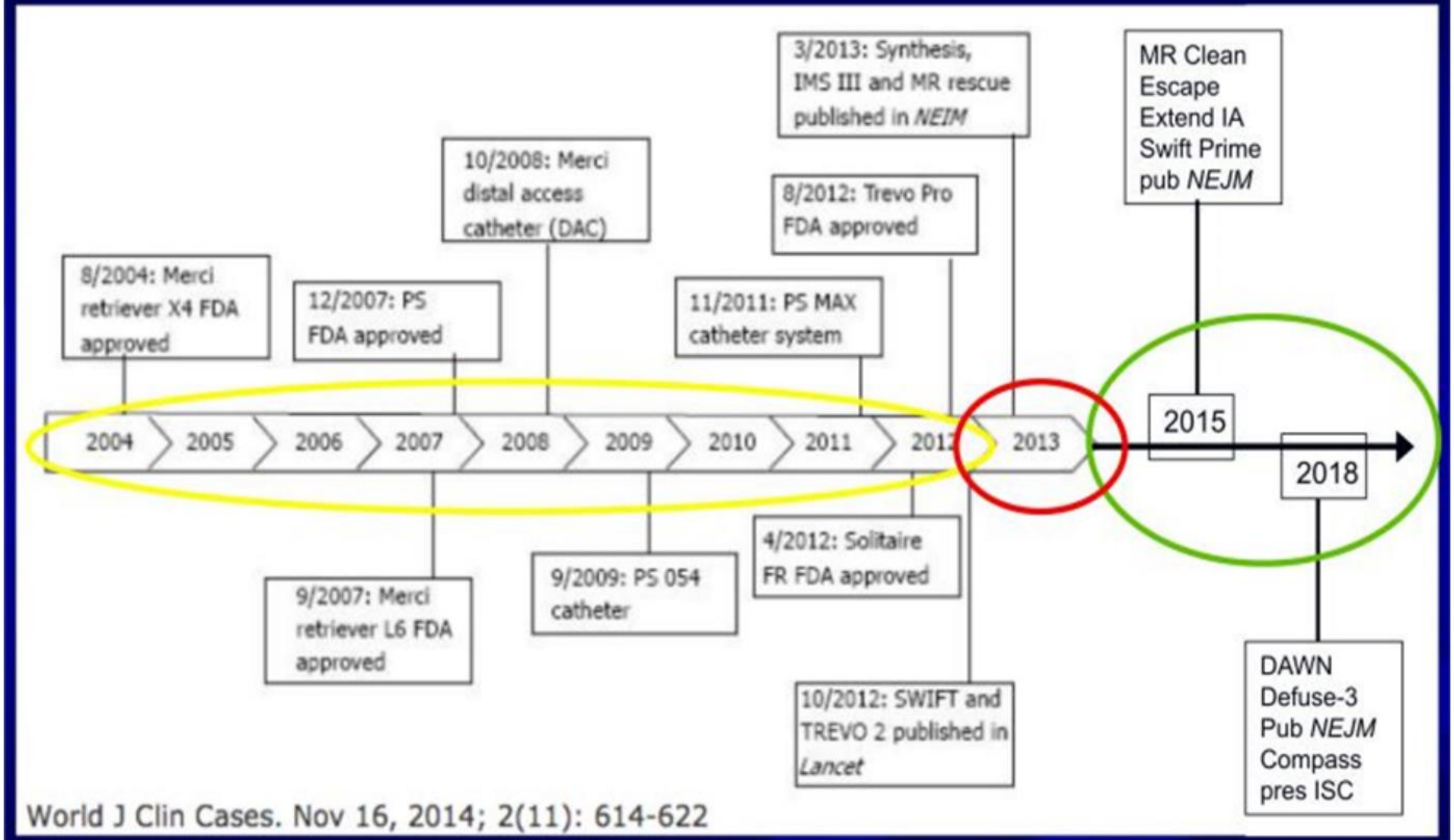
Mechanical thrombectomy

- Intraarterial thrombolysis
- Proximal thrombectomy
- Distal thrombectomy
- Mechanical recanalisation



- Different modalities in catheter based stroke tharapy

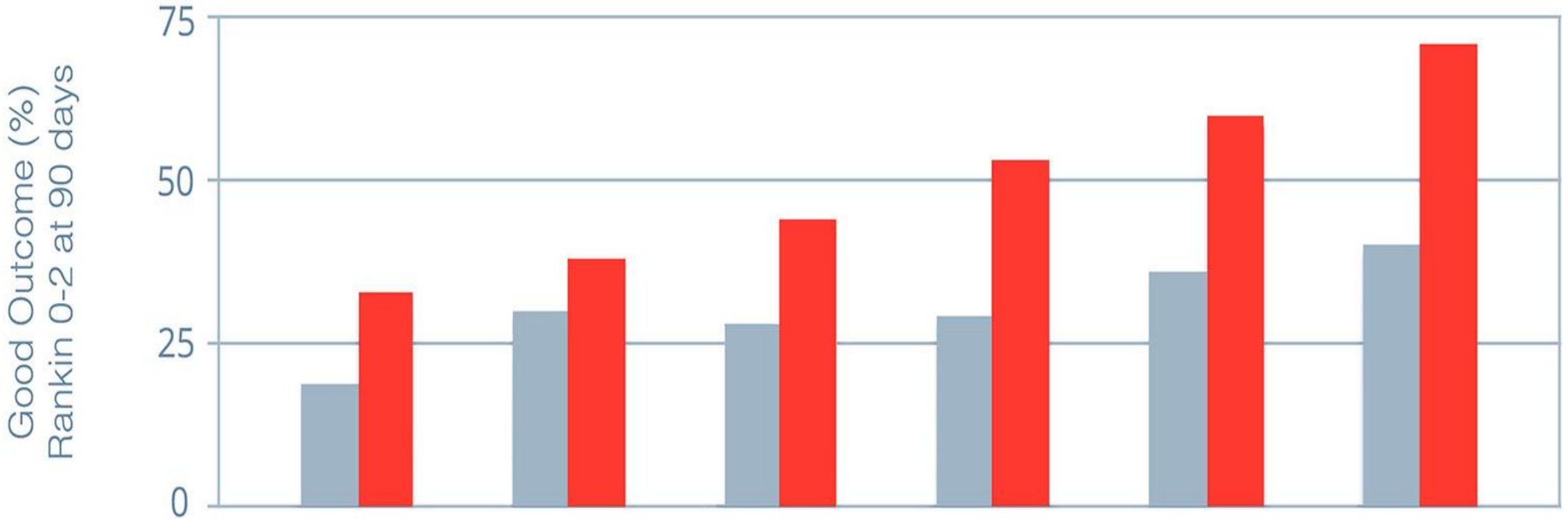
Stroke EVT Timeline



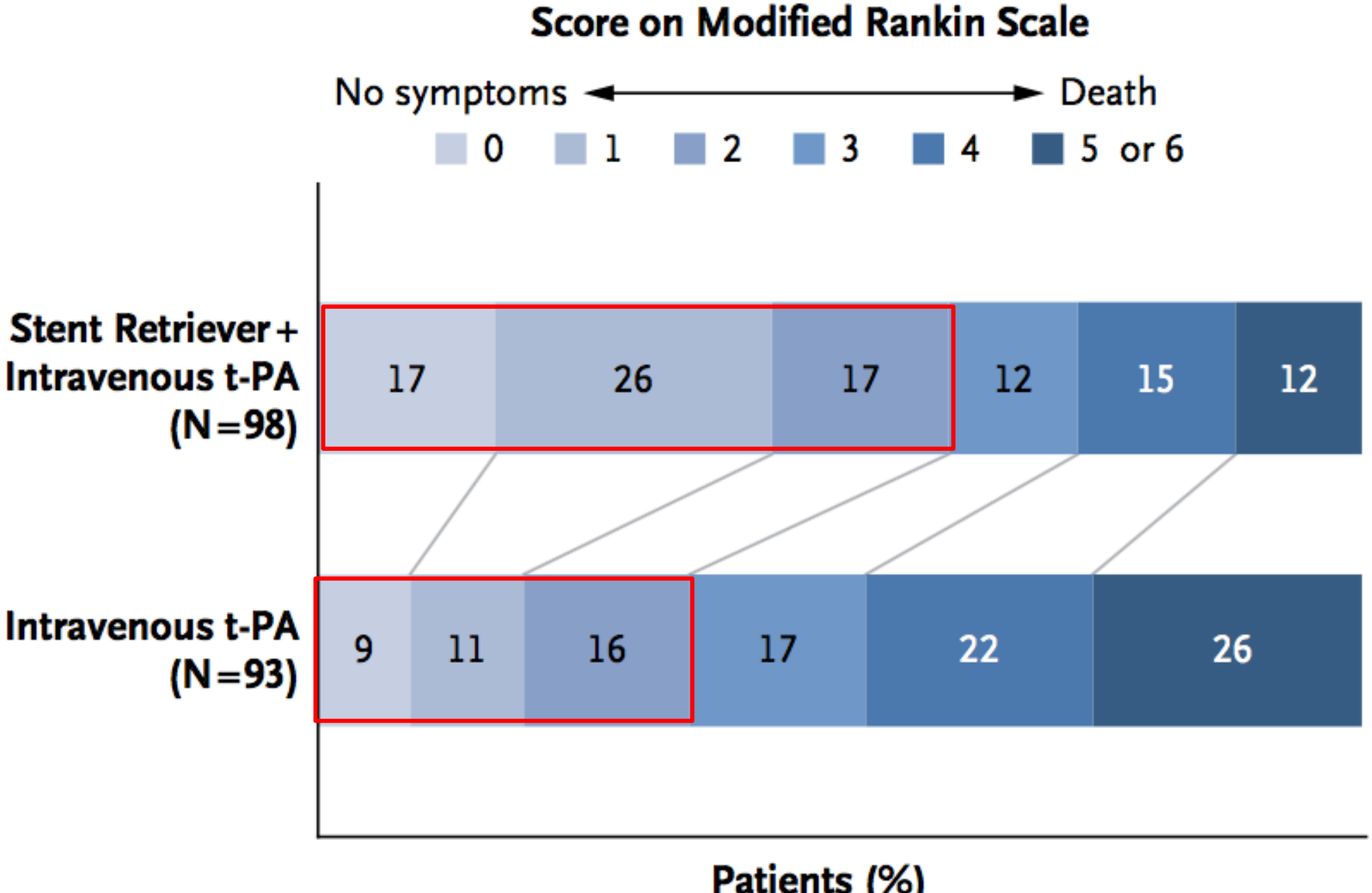
World J Clin Cases. Nov 16, 2014; 2(11): 614-622

RANDOMIZED ENDOVASCULAR TRIAL RESULTS

Within 6 hrs of symptoms onset



	MR CLEAN	THERAPY	REVASCAT	ESCAPE	SWIFT PRIME	EXTEND-IA
	Non-contrast CT	CTA Clot ≥ 8 mm	ASPECTS ≥ 6	ASPECTS ≥ 6 CTA collaterals	CT/MR Perfusion **RAPID (80%)**	CT Perfusion **RAPID (100%)**
Endovascular	33%	38%	44%	53%	60%	71%
Control	19%	30%	28%	29%	36%	40%


Score on Modified Rankin Scale
No symptoms
Death
0
1
2
3
4
5 or 6
Stent Retriever + Intravenous t-PA (N=98)
17
26
17
12
15
12
Intravenous t-PA (N=93)
9
11
16
17
22
26
Patients (%)

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EVT of AIS beyond 6 hours

Table 1. Characteristics of the included trials

Characteristic	ESCAPE[7]	REVASCAT*[8]	DEFUSE-3[4]	DAWN[5]
Number of patients	59	206	182	206
Median age, years	66	66	70	70
Females, %	31 (52)	109 (32)	92 (50)	113 (55)
Median NIHSS score at admission	15	17	16	17
Functional independence at 90 days, %	23 (39)	69 (33.5)	56 (30.7)	65 (31.5)
TICI grade 2b or 3	31	67†	69†	90†
Neuroimaging selection criteria				
ASPECTS score at baseline	✓	✓	✓	✓
Infarct volume assessment			✓	✓
Mismatch assessment			✓	
Collaterals assessment	✓			

S. Vidale et al. Mechanical…J Clin Neurol 2018;14(3):407-412

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Stroke EVT beyond 6 hours

Study or subgroup	Mechanical thrombectomy Events	Total	Medical therapy Events	Total	Weight (%)	Odds ratio M-H, Random (95% CI)
DAWN 2018	52	107	13	99	29.7	6.25 (3.12–12.54)
DEFUSE 3 2018	41	92	15	90	29.9	4.02 (2.02–8.02)
ESCAPE 2018	16	33	7	24	18.5	2.29 (0.75–6.96)
REVASCAT 2015	15	35	12	36	21.9	1.50 (0.57–3.93)
Total (95% CI)		267		249	100.0	3.33 (1.81–6.12)
Total events	124		47			

Heterogeneity: $Tau^2=0.20$, $Chi^2=6.33$, df=3 ($p=0.10$), $I^2=53\%$

Test for overall effect: Z=3.86 ($p=0.0001$)

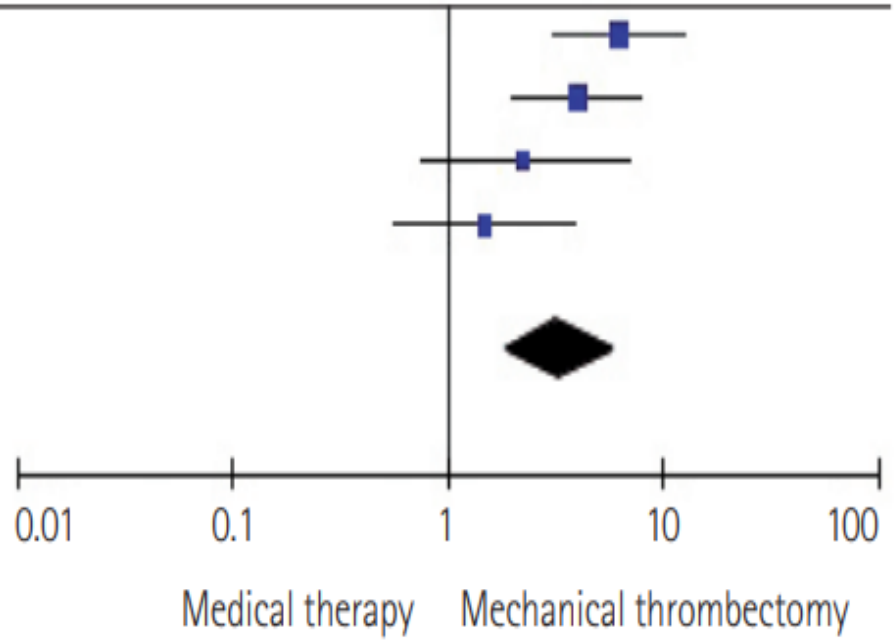

Fig. 2. Forest plot of the primary endpoint.

Functional independence at 90 days from stroke onset, mRss= 0,1,2

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AHA/ASA Guideline

2018 Guidelines for the Early Management of Patients With Acute Ischemic Stroke

A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association

(*Stroke.* 2018;49:e46–e99. DOI: 10.1161/STR.0000000000000158.)

Endovascular treatment of stroke

3.7. Mechanical Thrombectomy (Continued)	COR	LOE
3. Patients should receive mechanical thrombectomy with a stent retriever if they meet all the following criteria: (1) prestroke mRS score of 0 to 1; (2) causative occlusion of the internal carotid artery or MCA segment 1 (M1); (3) age ≥18 years; (4) NIHSS score of ≥6; (5) ASPECTS of ≥6; and (6) treatment can be initiated (groin puncture) within 6 hours of symptom onset	I	A

3.7. Mechanical Thrombectomy (Continued)	COR	LOE
7. In selected patients with AIS within 6 to 16 hours of last known normal who have LVO in the anterior circulation and meet other DAWN or DEFUSE 3 eligibility criteria, mechanical thrombectomy is recommended.	I	A
8. In selected patients with AIS within 16 to 24 hours of last known normal who have LVO in the anterior circulation and meet other DAWN eligibility criteria, mechanical thrombectomy is reasonable.	IIa	B-R

Stroke. 2018;49:e46–e99. DOI: 10.1161/STR.0000000000000158.

EUROPEAN STROKE JOURNAL

European Stroke Organisation (ESO) – European Society for Minimally Invasive Neurological Therapy (ESMINT) Guidelines on Mechanical Thrombe Stroke

Endorsed by

Guillaume Tur
Pooja Khatri[7],
Peter D. Schel
Philip White[15]

European Stroke Journal
2019, Vol. 4(1) 6–12

DOI: 10.1177/2396987319832140
journals.sagepub.com/home/eso
SAGE

Abstract

Background: Mechanical thrombectomy (MT) has become the cornerstone of acute ischaemic stroke management in patients with large vessel occlusion (LVO). The aim of this guideline document is to assist physicians in their clinical decisions with regard to MT.

Methods: These Guidelines were developed based on the standard operating procedure of the European Stroke Organisation and followed the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) approach. An interdisciplinary working group identified 15 relevant questions, performed systematic reviews and meta-analyses of the literature, assessed the quality of the available evidence, and wrote evidence based recommendations. Expert opinion was provided if not enough evidence was available to provide recommendations based on the GRADE approach.

Results: We found high quality evidence to recommend MT plus best medical management (BMM, including intravenous thrombolysis whenever indicated) to improve functional outcome in patients with LVO-related acute ischaemic stroke within 6 hours after symptom onset. We found moderate quality of evidence to recommend MT plus BMM in the 6-24h time window in patients meeting the eligibility criteria of published randomized trials. These guidelines further detail

PICO Question	Recommendations	Expert opinion
PICO 1: For adults with LVO-related acute ischaemic stroke within 6 hours of symptom onset, does MT plus BMM compared with BMM alone improve functional outcome ?	In adults with anterior circulation LVO-related acute ischaemic stroke presenting within 6 hours after symptom onset, we recommend MT plus BMM, including IVT whenever indicated, over BMM alone to improve functional outcome. Quality of evidence: High ⊕⊕⊕⊕ Strength of recommendation: Strong ↑↑	There is a consensus among the guideline group (11/11 votes) that patients with M2 occlusion fulfilled the inclusion criteria in most randomized trials and therefore mechanical thrombectomy is reasonable in this situation. There is a consensus among the panel (11/11 votes) that in analogy to anterior circulation LVO and with regard to the grim natural course of basilar artery occlusions, the therapeutic approach with IVT plus MT should strongly be considered.
PICO 2: For adults with LVO-related acute ischaemic stroke 6 to 24 hours from time last known well, does MT plus BMM compared with BMM alone improve functional outcome ?	In adults with anterior circulation LVO-related acute ischaemic stroke presenting between 6 and 24 hours from time last known well and fulfilling the selection criteria of DEFUSE-3* or DAWN**, we recommend MT plus BMM over BMM alone to improve functional outcome. Quality of evidence: Moderate ⊕⊕⊕ Strength of recommendation: Strong ↑↑	Patients should be treated with MT plus BMM up to approximately 7 hours 18 min after stroke onset, without the need of perfusion imaging-based selection. 10/11 experts agree that patients can be treated in the 6-12 hour time window if they fulfill the ESCAPE criteria, notably ASPECTS ≥6 and moderate-to-good collateral circulation. However, such patients

Imaging based decision for EVT of stroke

DAWN used a stratification by age and National Institutes of Health Stroke Scale score leading to differing maximum infarct core cutoff volumes measured by a specific imaging software in an automated fashion (>80 years core up to 20 mL, 1.8 (ratio) and 15 mL (penumbra volume), again measured by a specific imaging software in an automated fashion. The median infarct core volume was 8 and 10 mL in DAWN and DEFUSE 3, respectively. More than half of all the trial subjects presented with wake up strokes in both trials.

Multiple strategies have been adopted, including clinical-core mismatch, perfusion-imaging mismatch or NCCT ASPECTS to estimate infarct core, and mCTA to assess collateral status. This range of potential selection tools highlights current uncertainty about the best inclusion criteria.

Motyer R, et al. J NeuroIntervent Surg 2018;0:1–4. doi:10.1136/neurintsurg-2017-013575

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Table 1 Outcomes for endovascular thrombectomy >12 hours from symptom onset

Outcome variable	Outcome (n=25)
Gender, n (%)	Male: 13 (52) Female: 12 (48)
Median age (IQR)	69 (55–80)
Median NIHSS score (IQR)	14 (11–18.5)
Median ASPECTS (IQR)	8 (8–9)
Moderate-good collateral status, n (%)	24 (96)
Median time to groin puncture (IQR)	14 hours 40 min (12 hours 36 min– 16 hours 18 min)
Successful recanalization: mTICI 2b–3, n (%)	22 (88)
Symptomatic ICH, n (%)	0 (0)
Functional independence: 90-day mRS 0–2, n (%)	13 (52)
90-Day mortality, n (%)	3 (12)

ASPECTS, Alberta Stroke Program Early CT Score; ICH, intracranial haemorrhage; mRS, modified Rankin Scale; mTICI, modified Thrombolysis in Cerebral Infarction; NIHSS, National Institute of Health Stroke Scale.

Motyer R, et al. J NeuroIntervent Surg 2018;0:1–4. doi:10.1136/neurintsurg-2017-013575

Acute Ischemic Stroke Care Today . Time is BRAIN

Symptoms

Call

EMS

Primary Stroke Center

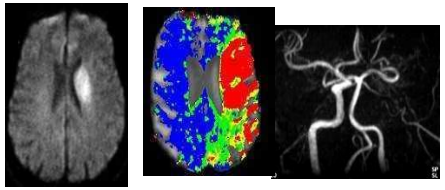
Imaging

Telemedicine

IV Lytic

EMS

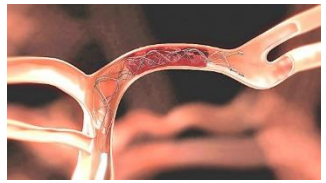
Stroke Center



Advanced Imaging

INR Cath Lab

Angiogram



Clot retrieval

Stroke Unit

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Acute Ischemic Stroke Care Today . Time is BRAIN

Symptoms

Call

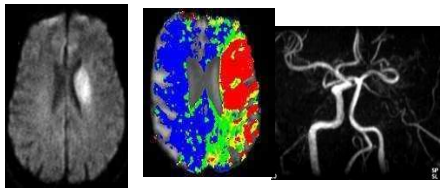
Direct transfer from EMS to CathLab

Imaging

Telemedicine

IV Lytic

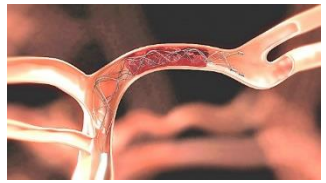
EMS



Advanced Imaging

INR Cath Lab

Angiogram



Clot retrieval

Stroke Unit

doi:10.1093/eurheartj/ehy442

Thrombectomy for stroke by cardiologists

Cardiologists are willing to cooperate with neurologists / strokologists to help patients with acute ischemic stroke

Report from the joint session of the European Society of Cardiology (ESC) Council on Stroke and the European Association for Percutaneous Cardiovascular Interventions (EAPCI) during the EuroPCR Congress in Paris, 25 May 2018

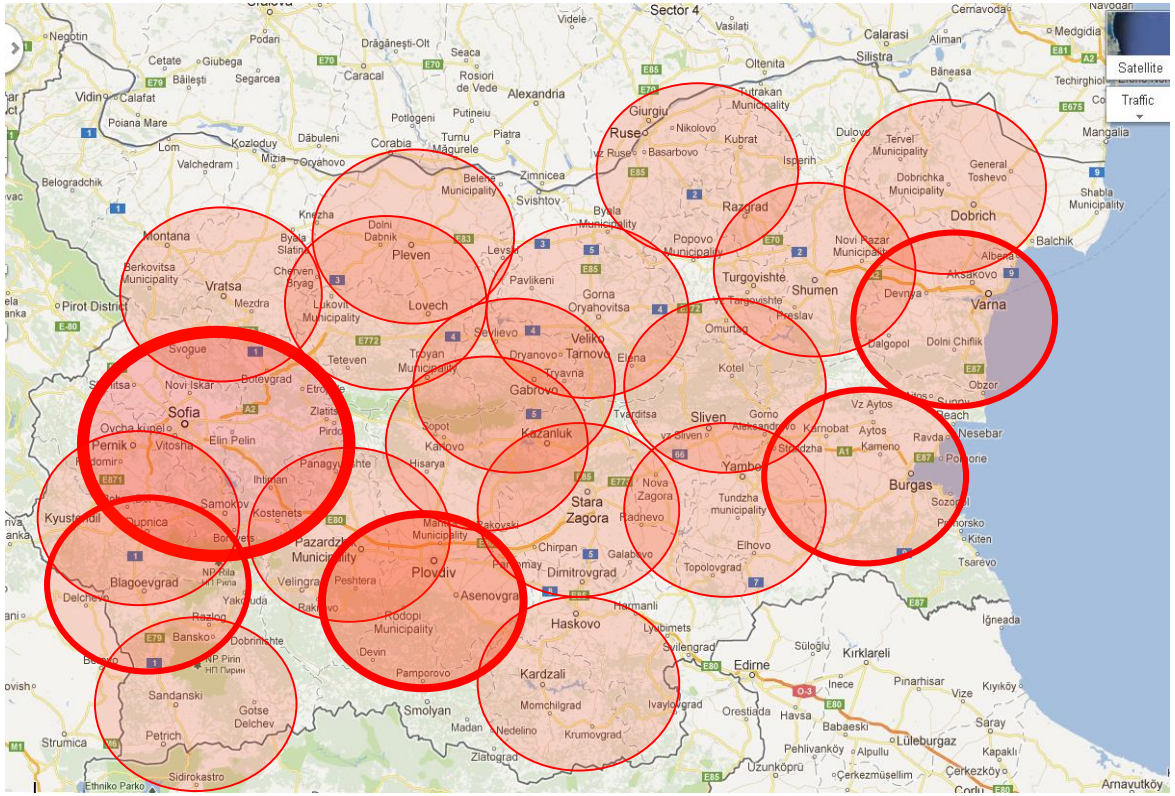
Acute ischaemic stroke is a devastating disease with high mortality and even higher long-term (frequently permanent) severe disability. The most effective treatment of acute ischaemic stroke (when it is caused by a large artery occlusion) is known: immediate recanalization of the blocked artery by percutaneous endovascular mechanical thrombectomy (ideally immediately following of so-called 'bridging' i.v. thrombolysis, which can be given immediately after the diagnosis is established by brain imaging).

thrombectomy to a much broader population of stroke patients worldwide—in those areas, where neuroradiology services are either missing or are not able to cover 24/7/365 service availability. The aim was to present the proposal for shorter training requirements for those interventionalists, having previous experience with elective carotid interventions.

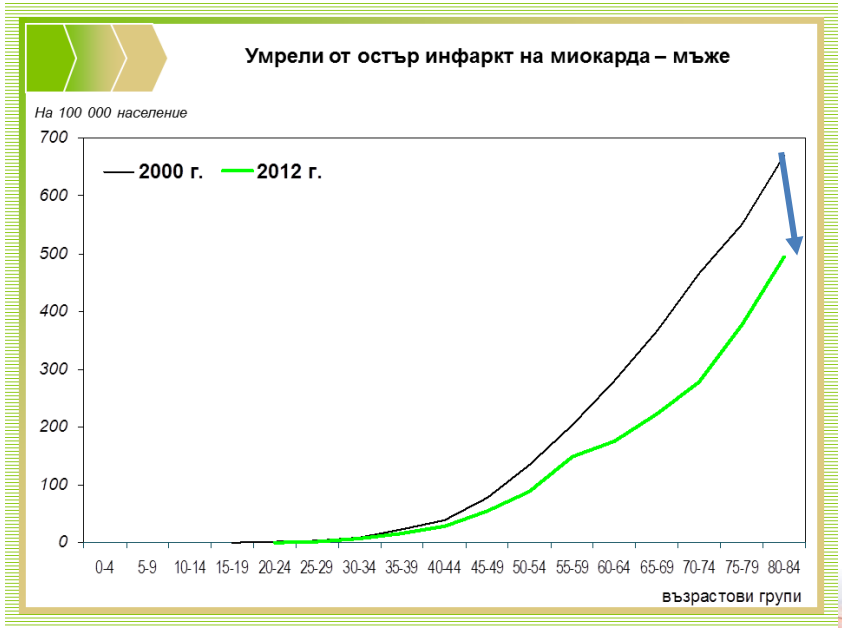
L.N. Hopkins (neurosurgeon from Buffalo, US) presented the current training requirements for endovascular interventions in stroke as

Bulgaria. pPCI coverage
After ESC "Stent for life" initiative implementation

2017



Stent for life experience
STEMI mortality reduction:



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NATIONAL CONSENSUS
for Mechanical Thrombectomy in Acute Ischemic Stroke

НАЦИОНАЛЕН КОНСЕНСУС
за механична тромбектомия при остър исхемичен мозъчен инсулт

At the initiative of
The Bulgarian Society of Endovascular Therapy

По инициатива на
Българското дружество по ендоваскуларна терапия

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Проф. А. Постаджиян, д.м.
Председател на Дружеството

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Interventional recanalization of intracranial arteries. City Clinic experience 2016-2018 (n=18)

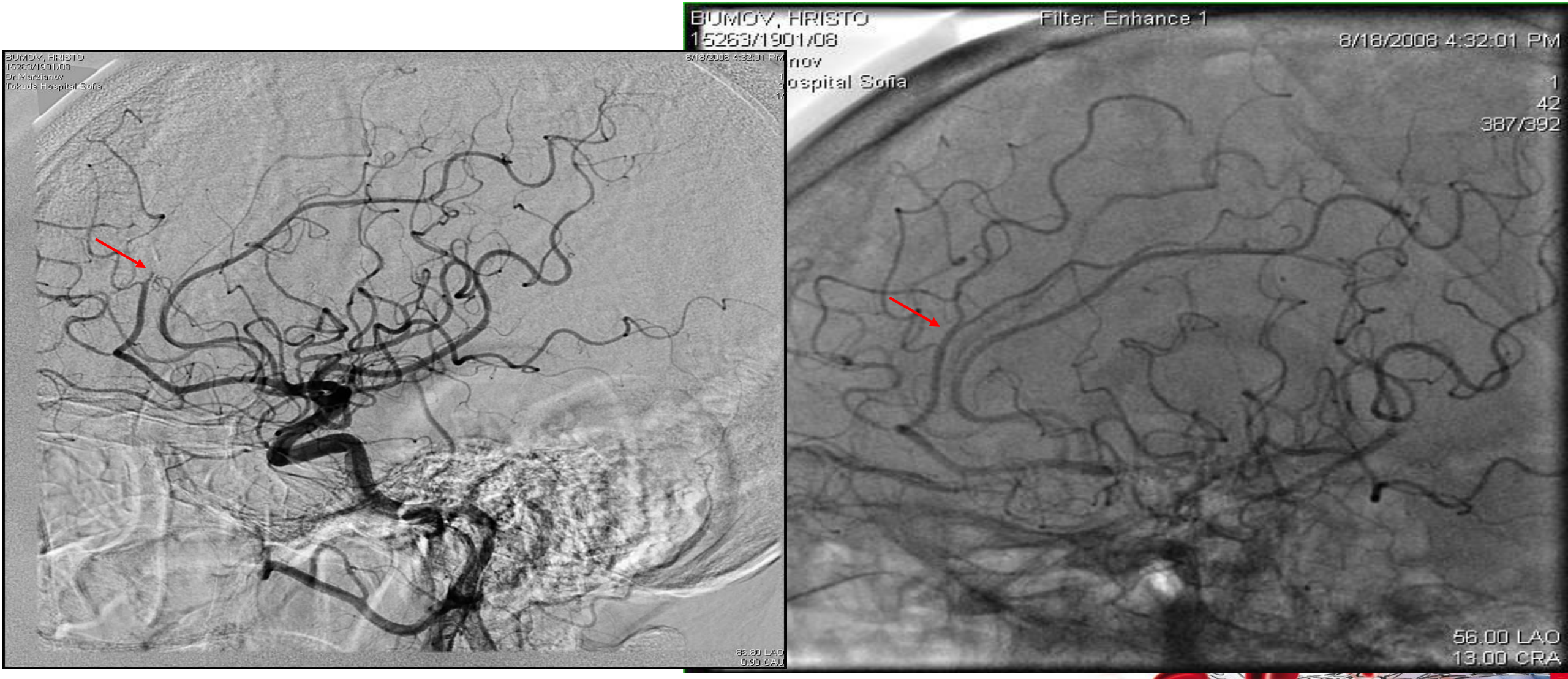
Parameter	Distribution
CT imaging at baseline	15 (83.3%)
MRI imaging at baseline	9 (50%)
Occlusion site	
MCA	10 (55.6%)
ICA (2 high-grade stenosis and 1 T-occlusion)	3 (16.7%)
Basilar artery	2 (11.1%)
Vertebral artery	1 (5.6%)
Anterior cerebral artery	1 (5.6%)
Pericallosal artery	1 (5.6%)
Onset-to-needle time (min) – mean ± SD	187 ± 112
Groin puncture-to-recanalization time (min) - mean ± SD	68,6 ± 14.3
Onset-to-TICI 2b/3 recanalization time (min) - mean ± SD	255 + 113
Intravenous thrombolysis	7 (38.9%)
Penumbra system (PS) mechanical thromboaspiration (A-method)	4 (22.2%)
PS, balloon PTA and low-dose supraselective intra-arterial thrombolysis (B-method)	4 (22.2%)
Wire manipulation, balloon PTA and low-dose supraselective intra-arterial thrombolysis (C-method)	5 (27.8%)
Supraselective intra-arterial thrombolysis (D-method)	5 (27.8%)
ICA stenting	2 (11.1%)
TICI 2b-3 flow	4+9 (72.3%)

Med - Clin Res & Rev, 2018

EVT Stroke team
4 neurolgists
2 neuroimaging specialists
3 interventional cardioangiologists
12 anaestesiologists
2 cathlabs/24 hrs

Reocclusions after EVT and Device related complications	0 (0%)
Symptomatic ICH	2 (11.1%)
Asymptomatic ICH	1 (5.6%)
Minor systemic bleeding	3 (16.7%)
NIHSS final - mean ± SD	8.7 ± 7.2
mRS 0-2 at 90 days	9 (50%)
Mortality at 3 months	1 (5.6%)

First ever mechanical recanalization of stroke related artery 2001 in Bulgaria. Performed by a cardiologist.



Clinical case 1. Wake-up stroke

Variables/ Parameters	Pt No 1, V
Age (years) / Gender	54 y/o, man
NIHSS Pretreatment	15
Initial mRS	5
Initial CT / MRI imaging	CT, CT-A
Acute occlusion site	Left extracranial ICA
Stroke etiology	Cardioembolic
	Wake-up Stroke 2nd Postooperative day
Patient Diseases	IHD, Triple Vessel Cardiac Disease, STEMI, AH 3, DM 2 TYPE, ACB x 4
Average time from onset to groin puncture (h)	Unknown (<6 h)
Average time to TICI 2b/3 recanalization (min)	
Final TICI result	TICI 3
NIHSS at discharge (* dif)	5 (12 DAY)
mRS on discharge	3
mRS, 90 day	1
Device related complications	No
Device tips and tricks	
Symptomatic ICH	No
Mortality	No

Background of WUS

- **Wake-up stroke** is a condition, **affecting ≈ 8-25%** of patients with stroke.
- **It is a distinct but underprivileged subgroup** of patients with stroke.
- **a challenge** to acute stroke treatment
- Since the time window is unknown, the majority of patients with WUS are excluded from reperfusion treatment with IV thrombolysis or EVT.
- However, **a relevant number of these patients might benefit** from reperfusion treatment.
- There are some **brain imaging concepts guiding the reperfusion treatment** in patients with unknown time of symptom onset.
- Thrombolysis in selected patients with WUIS is feasible, and its outcomes are comparable with those thrombolysed with 0 to 4.5 hours.
- There are **limited data** on the risks and benefits of reperfusion therapies for WUS.

Treatment Concepts for Wake-Up Stroke and Stroke With Unknown Time of Symptom Onset. G.Thomalla, C. Gerloff. *Stroke. 2015;46:9 2707-2713*

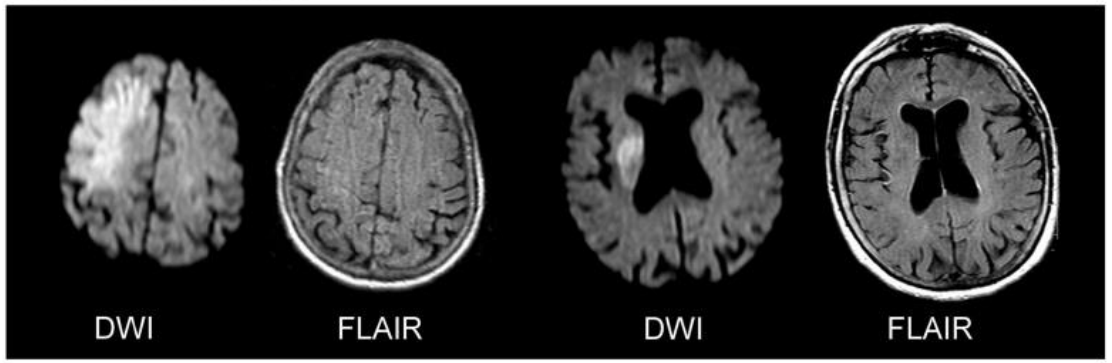
Reperfusion Therapies for Wake-Up Stroke. Systematic Review. Deborah Buck, Lisa C. Shaw, Christopher I. Price, Gary A. Ford, B Chir. *Stroke. 2014;45:6 1869-1875.*

Wake-up stroke: clinical characteristics, imaging findings, and treatment option – an update. *D. Leander Rimmele, G.Thomalla. Frontiers in Neurology.* March 2014; Vol 5; Article 35: 1-7.

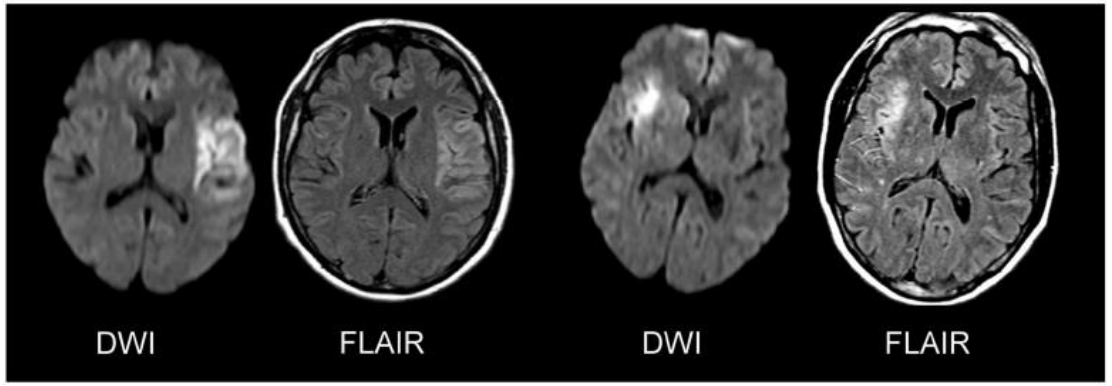
Neuroimaging is crucial to determine the candidates for EVT in late comers and WUS

DWI-FLAIR-mismatch was shown to identify patients within 3–4.5 h with high specificity and positive predicted value (PPV);

DWI-FLAIR-mismatch



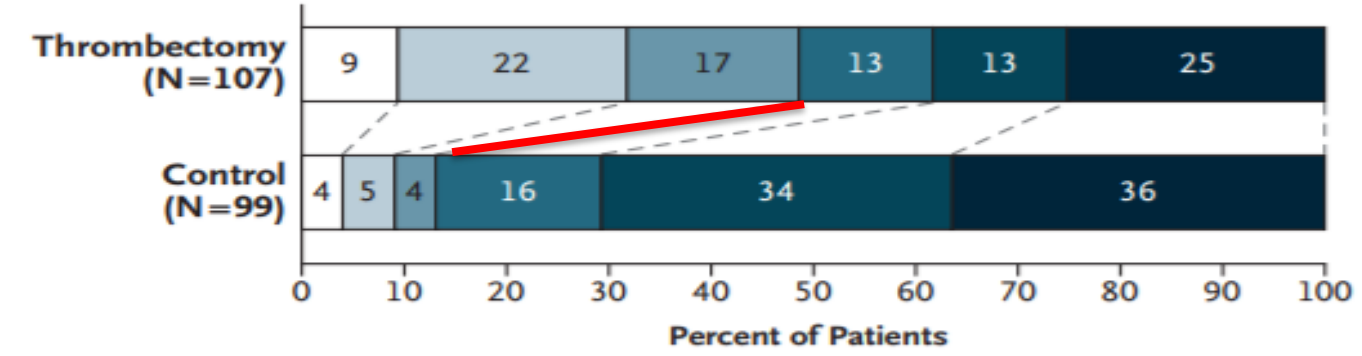
No DWI-FLAIR-mismatch



- In large multicenter studies (PRE-FLAIR:PRE-dictive value of FLAIR and DWI for the identification of acute ischemic stroke patients 3 and 4.5 h of symptom onset–a multicenter study including 643 patients (*Lancet Neurol* (2011) **10**:978–86.).
- The specificity of the DWI-FLAIR-mismatch to identify patients within the time frame of 4.5h was in this study 0.81 and the PPV 0.87.

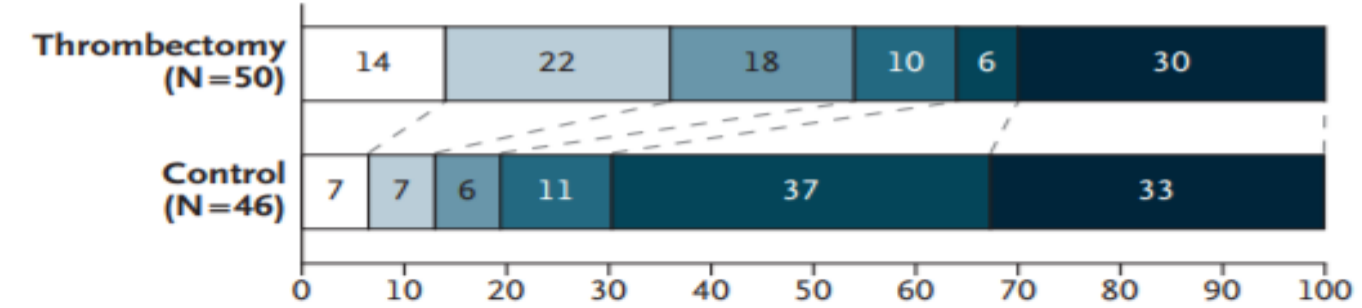
D. Leander Rimmele, G.Thomalla. Frontiers in Neurology. 2014; Vol 5; Art35: 1-7.

DAWN: Thrombectomy Effective Up to 24 Hours After Stroke

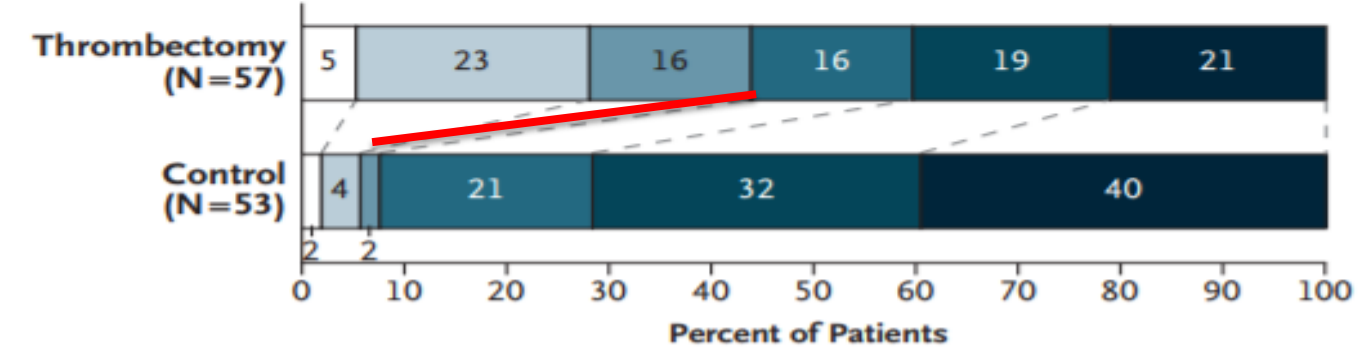


B Subgroups According to Time of Stroke Onset

Last Known to Be Well 6 to 12 Hr before Randomization

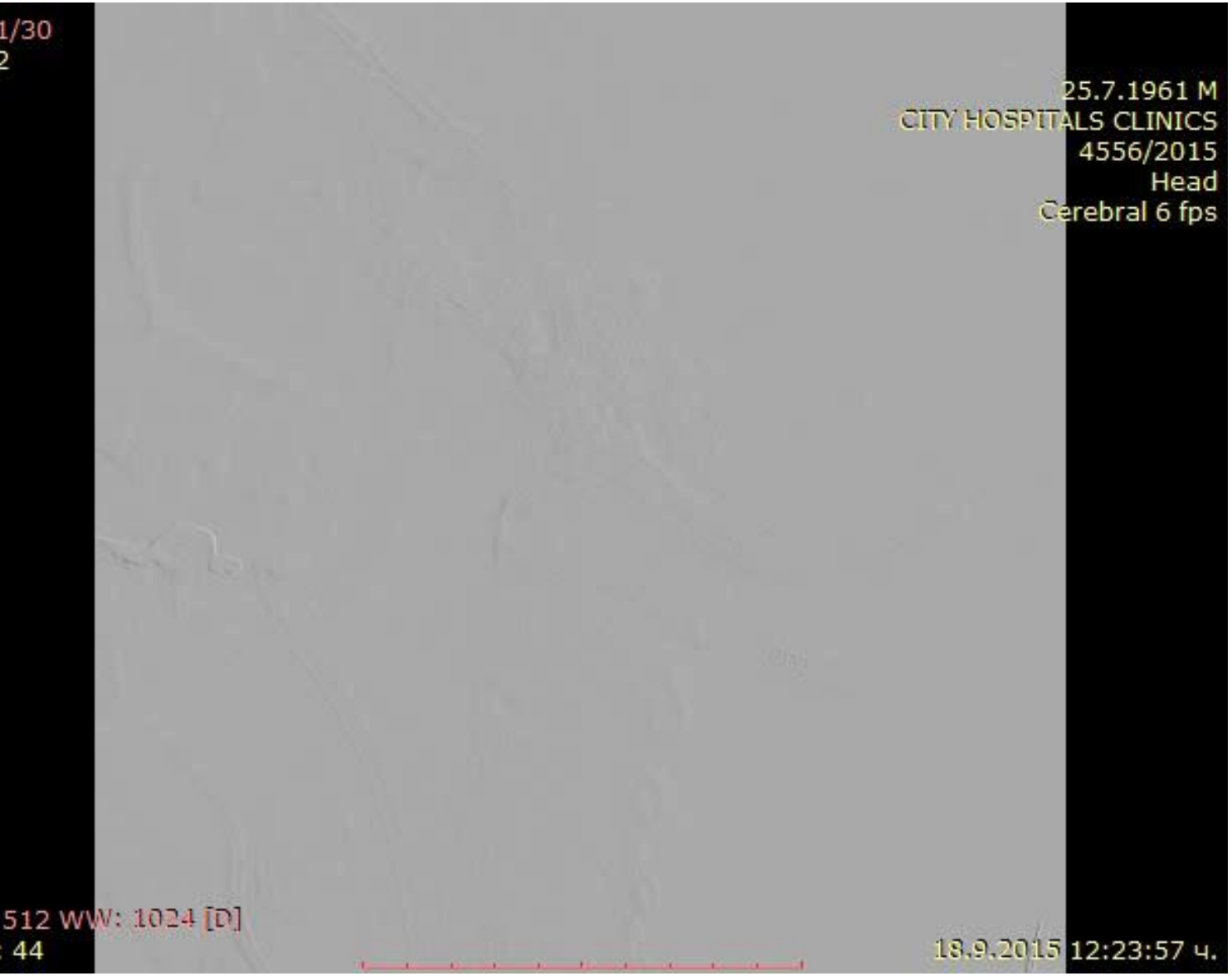


Last Known to Be Well >12 to 24 Hr before Randomization



omy	Posterior Probability	
	Benefit	Heterogeneity
(1.1 to 3.0)	>0.99	
		0.47
(0.3 to 4.2)	0.99	
(0.6 to 2.9)	>0.99	
(−0.6 to 5.5)	0.95	
		0.14
(0.2 to 3.2)	0.99	
(1.3 to 4.0)	>0.99	
		0.42
(0.8 to 2.8)	>0.99	
(0.3 to 4.2)	0.99	
		0.71
(1.0 to 3.7)	>0.99	
(0.6 to 3.1)	>0.99	
		0.77
(0.8 to 5.2)	>0.99	
(0.9 to 3.1)	>0.99	
		0.21
(1.0 to 3.6)	>0.99	
(0.5 to 5.9)	0.99	
(−0.5 to 3.2)	0.93	
		0.22
(0.4 to 3.4)	>0.99	
(1.1 to 3.6)	>0.99	
		0.70
(0.9 to 3.2)	>0.99	
(0.8 to 3.9)	>0.99	

Interventional EV Procedure: ADAPT



- “Carotid T-occlusion”
- Imitating occlusion of the carotid artery
- In fact is cause by an embolus sitting on the bifurcation

Interventional EV Procedure: ADAPT

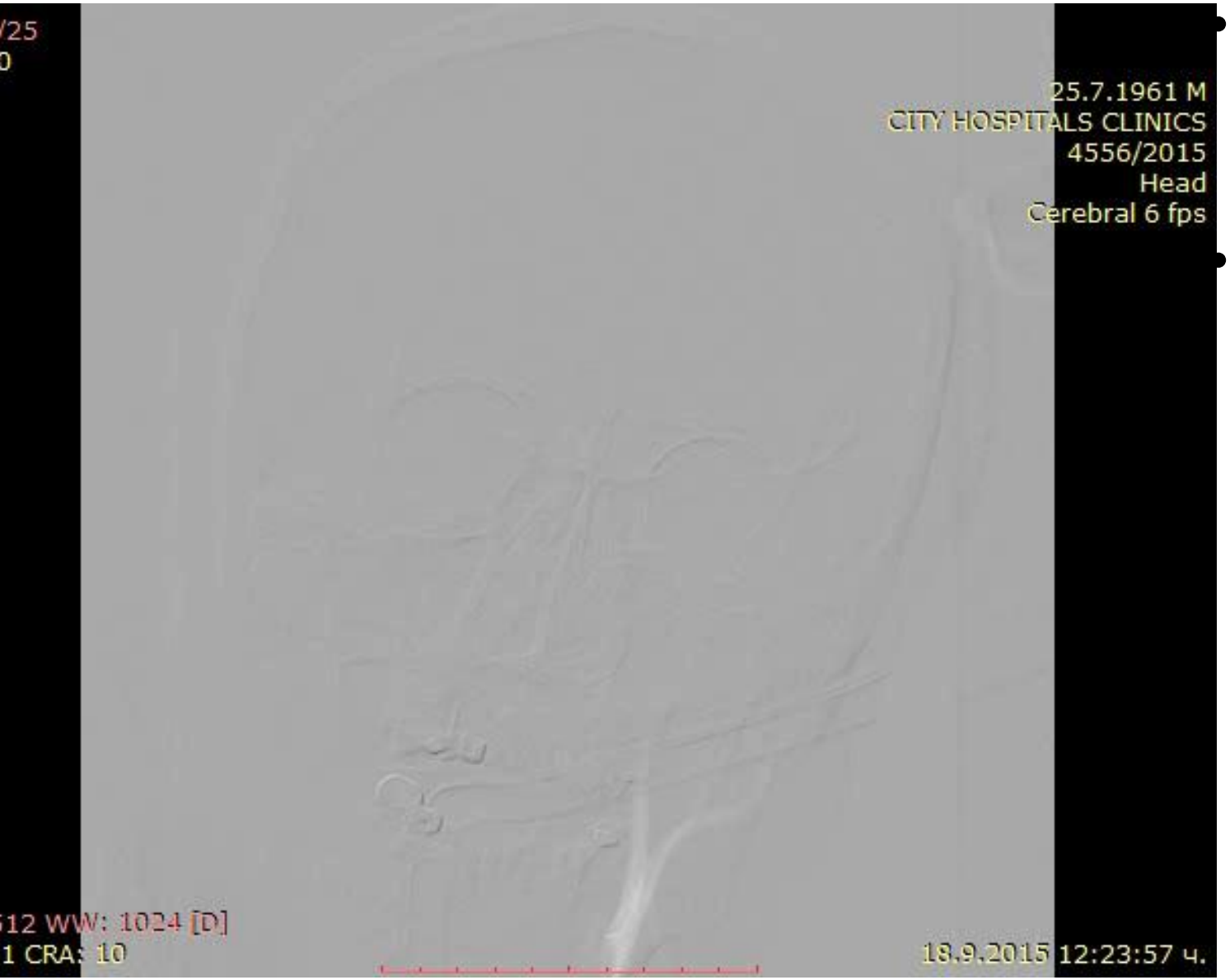
A selective cannulation of LCCA with 6 Fr catheter Benchmark was performed, followed by introduction of ACE catheter in proximal part of ICA.

Over a 0,014” wire catheter Neuron 5MAX as placed proximal to the occlusion.

Selective thromboaspiration was performed with Penumbra aspiration system.

Post aspirational angiography reveals no residual thrombosis with excellent angiographic result, TICI score 3.

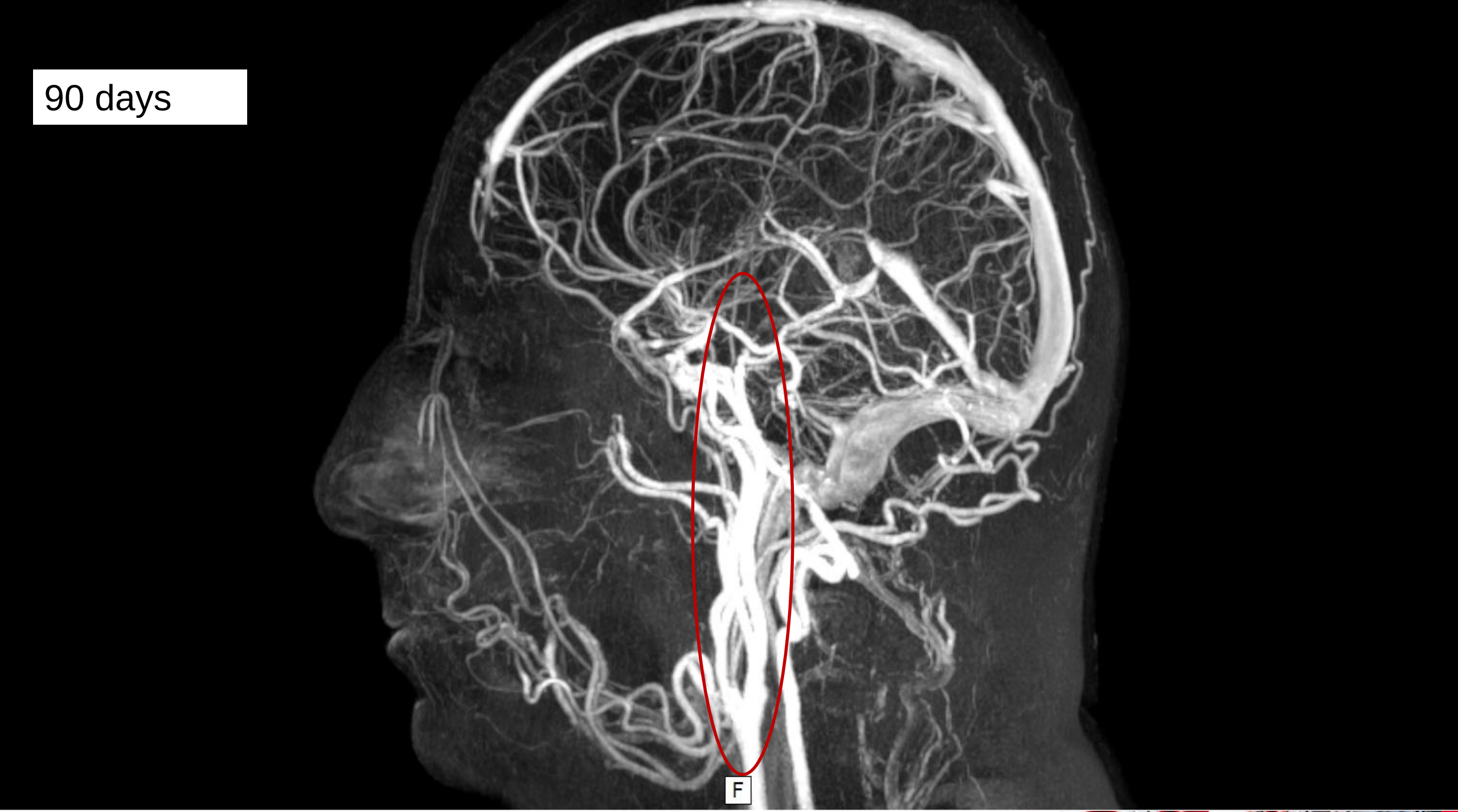
Interventional EV Procedure: ADAPT

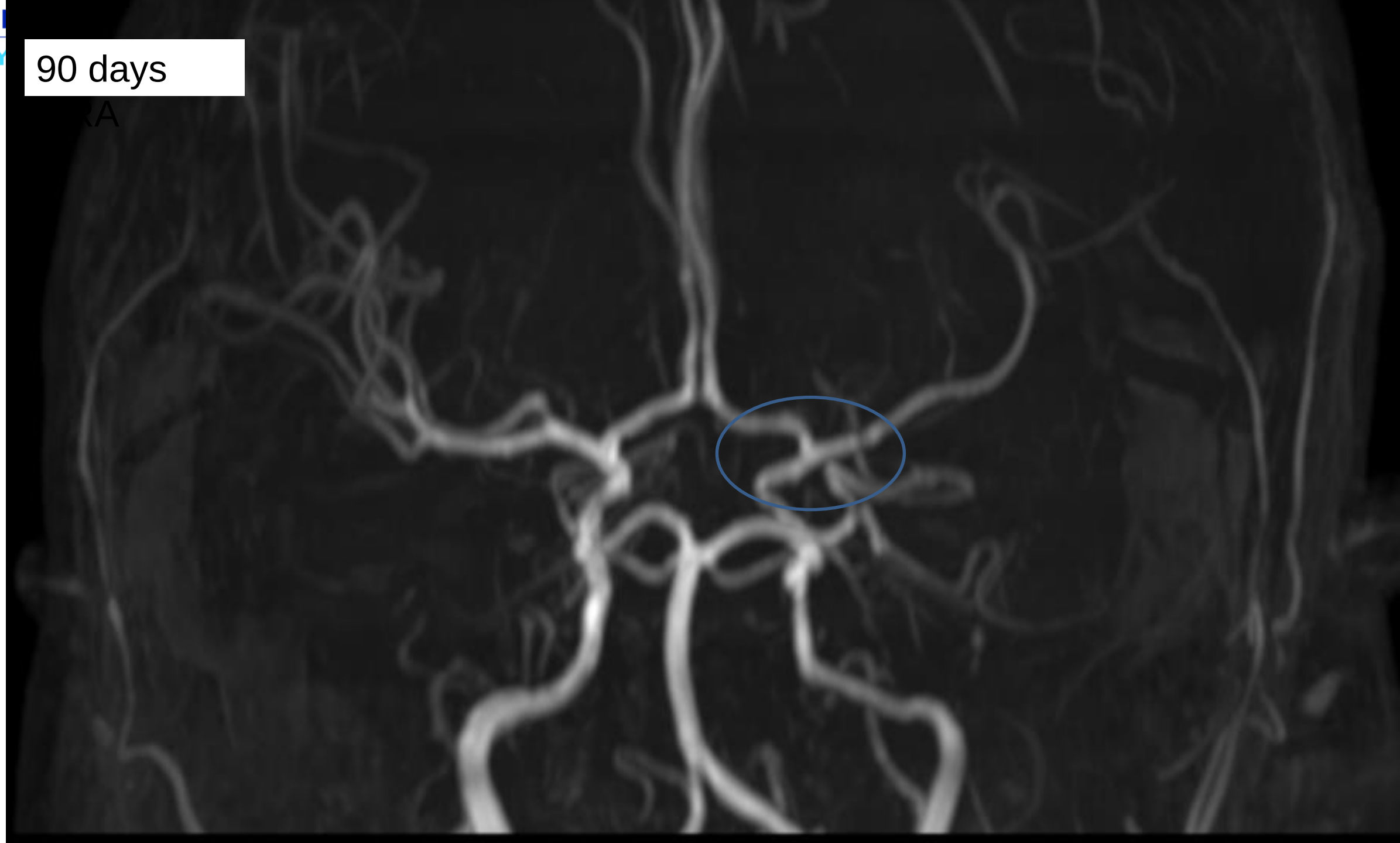


- After 3 aspirational passes with the 5 MAX
- Post aspirational angiography reveals no residual thrombosis with excellent angiographic result, TICI score 3.

Outcome

- The patient was discharged on the 12th post procedural day;
- The neurologic examination on the day the discharge reveals no motor deficit only persisting sensory aphasia. NIHSS = 5; mRS = 3
- 90 day mRS = 1


90 days
F


90 days

Case II

Gender: male, 66y., late acute stroke comer (Aphasic and right side hemiplegic since 25 hours, Systemic thrombolysis resulted inefective)

NIHHSS= 19 (Major stroke)

Concomitant disease:

- 2 vessel coronary disease, history of LAD PCI, 6 y. before
- Arterial hypertension II grade, dyslipidemia, smoker

Vascular access: ***Right femoral artery, Shuttle sheath 6F***

Target carotid artery: LICA- nearly full thrombosis

Primary distal protection system: *Spider 5.0 after recanalization with coronary microcatheter and distal confirmation*

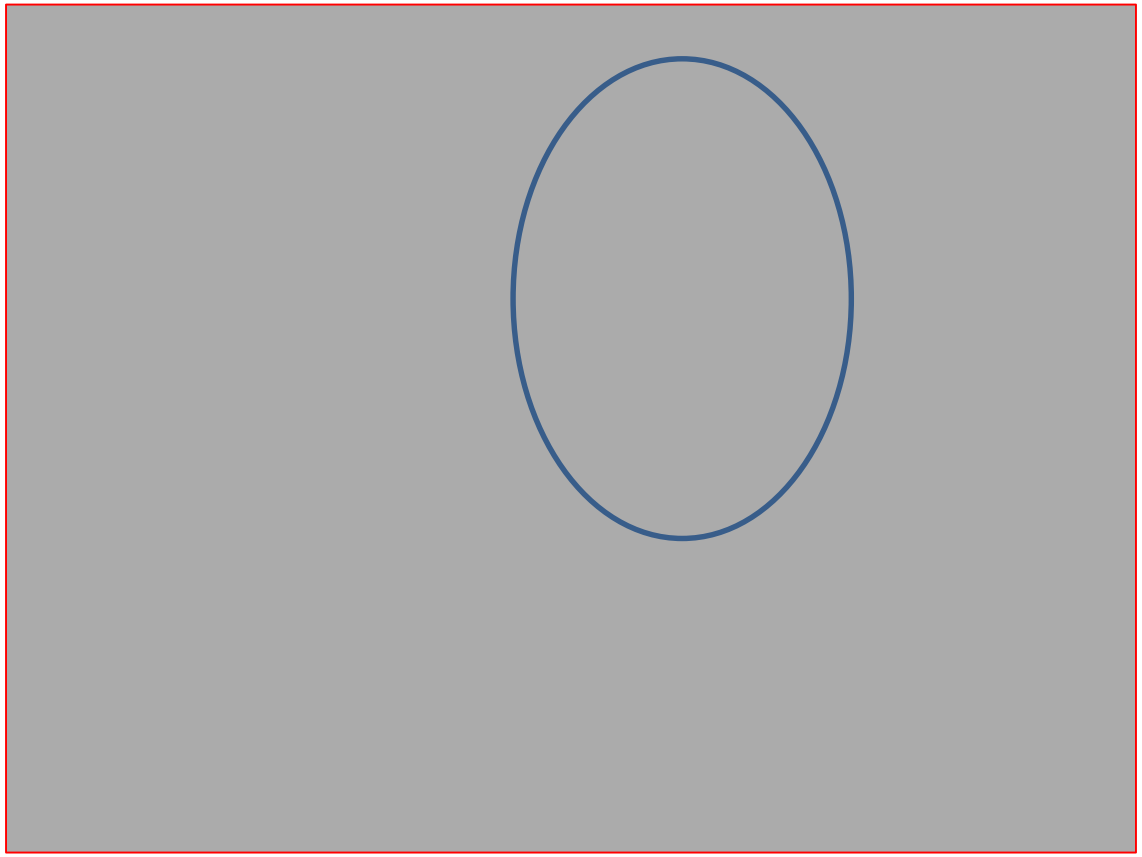
Implanted stent:

After predilatation Tapered X-Act 8-6/40mm.

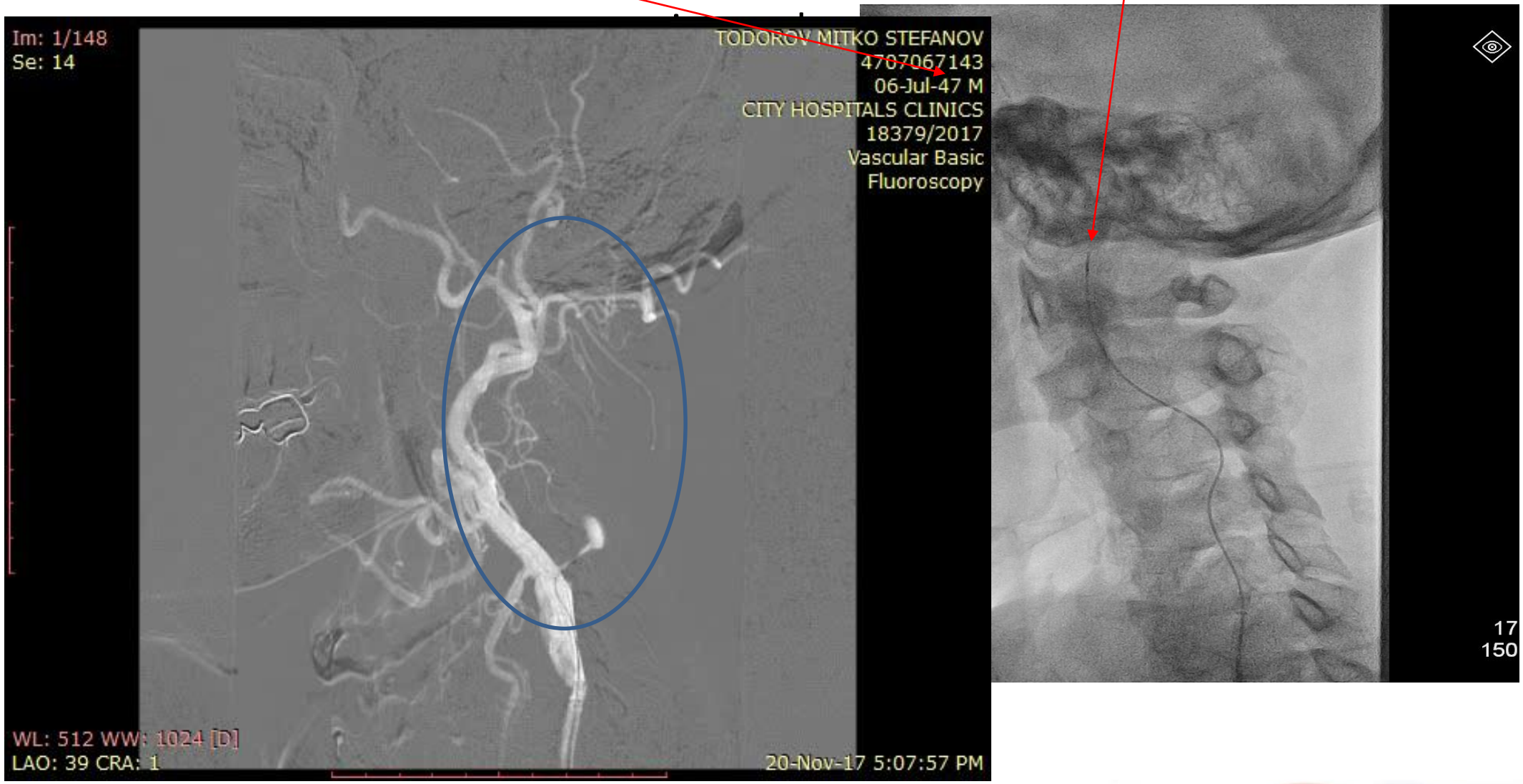
Postdilatation:

Double protection (thrombus containing lesion) + balloon Paladin 5.0/20 mm.

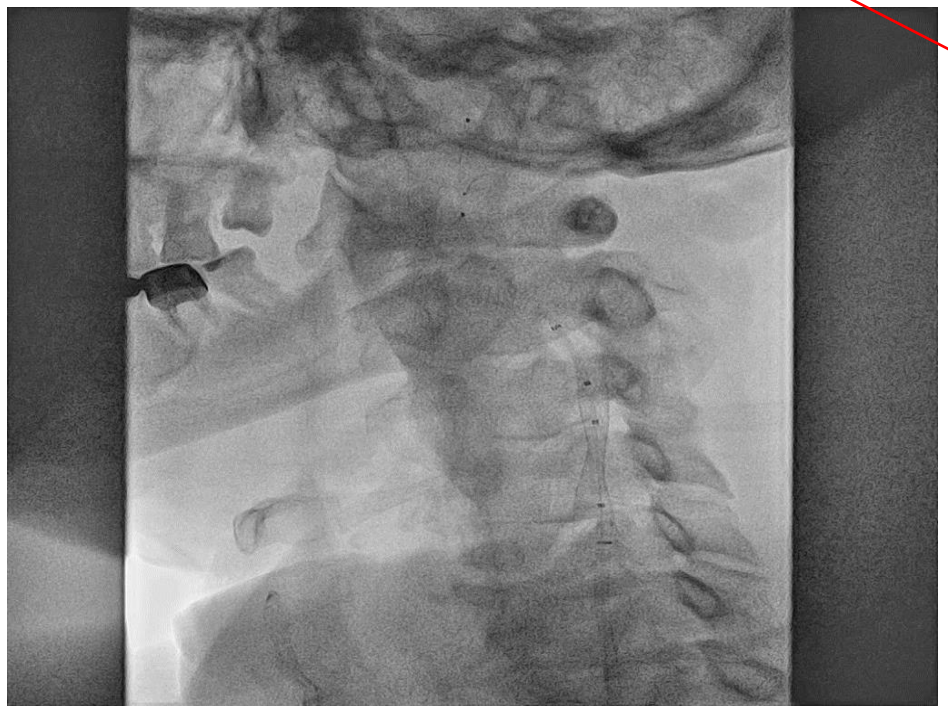
LICA near occlusion (subacute thrombosis)

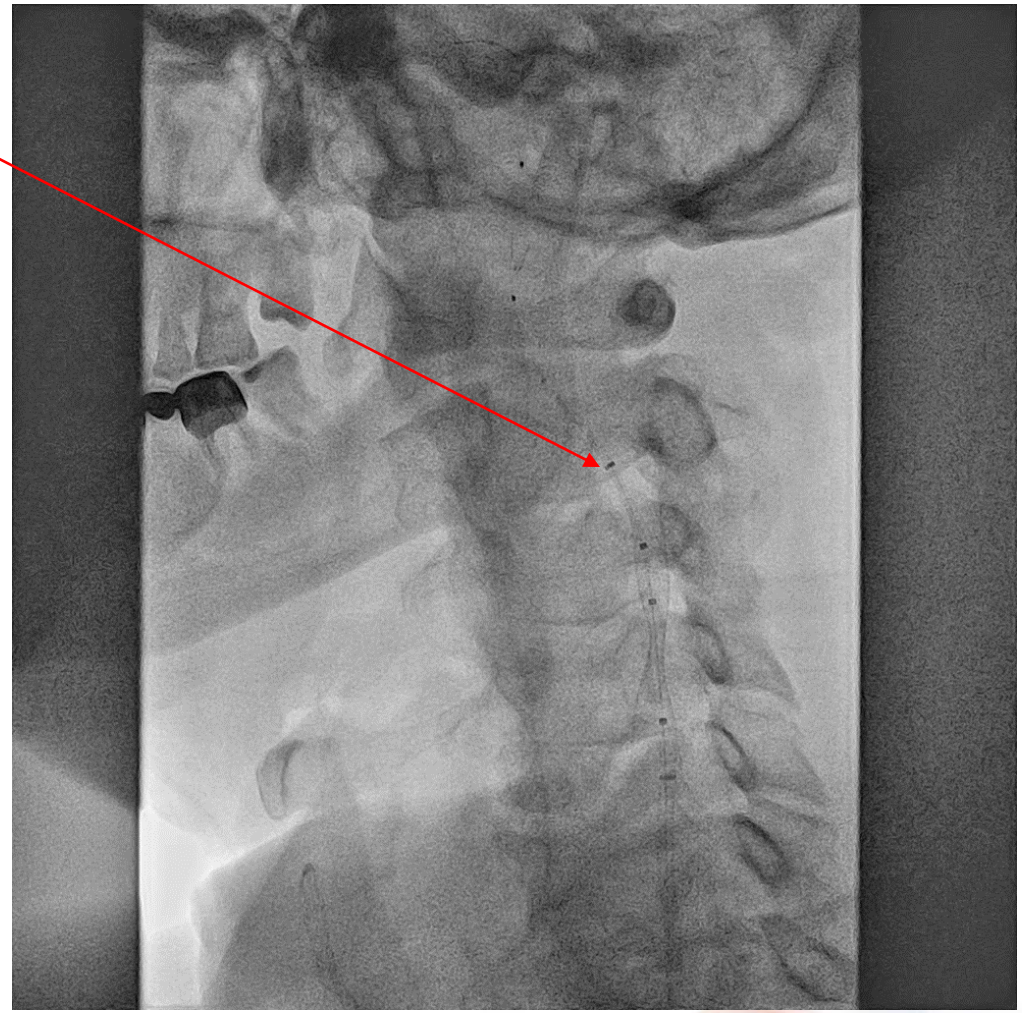


.014 Runthrough Hypercoat supported by FineCross

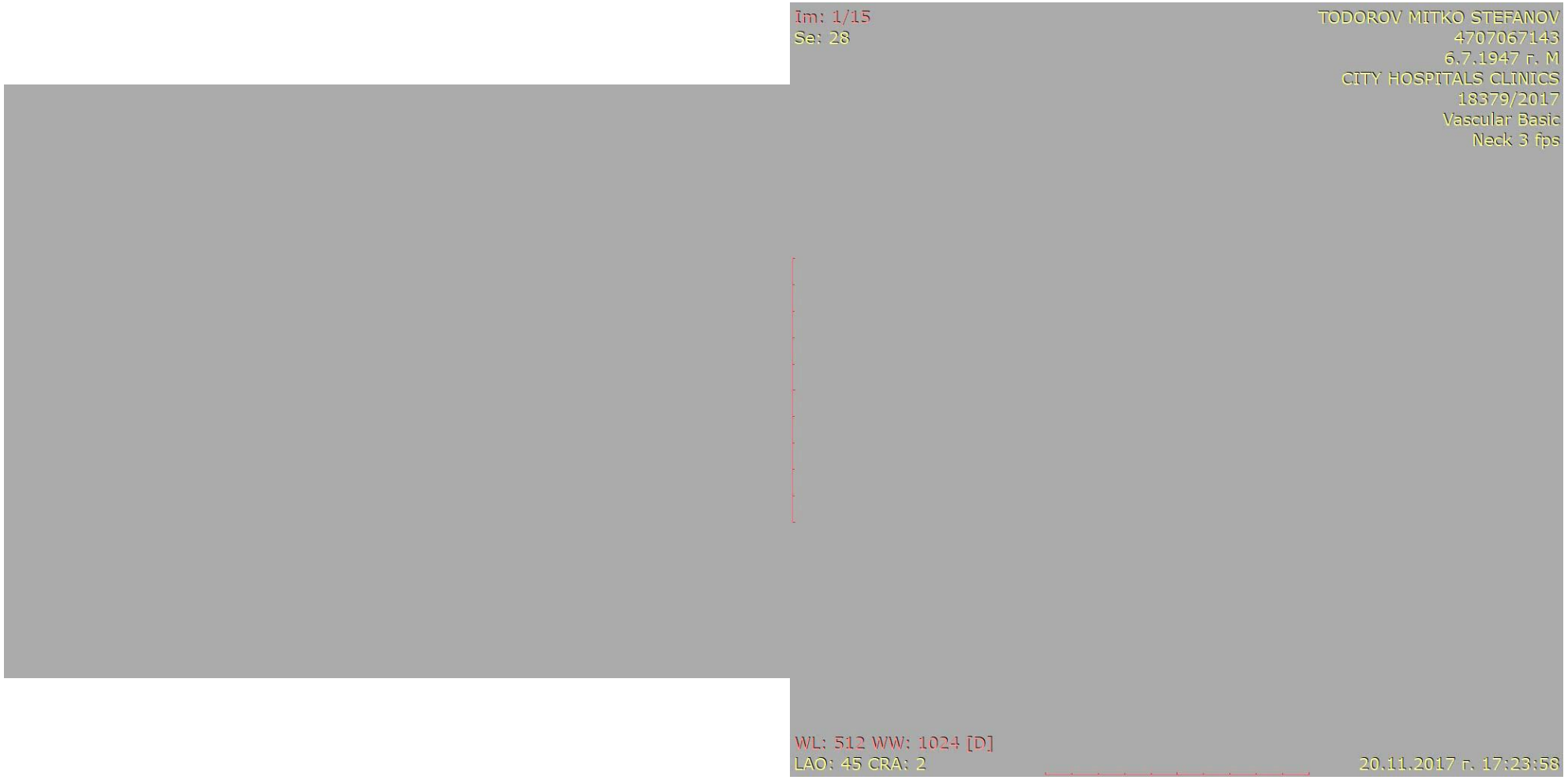


“Double filter” protection (thrombus containing lesion)
postdilation Paladin (Contego) 5.0/20mm:





TICI-3 flow restored



TICI-III flow with normalized parenchymal phase

Clinical course

- Speech restored immediately after intervention
- NIHSS= 4 at 30 days after (mild right hemiparesis and hemihypoestesia)

ACIBADEM CITYCLINIC

17years girl 3 days after open heart ASD surgical closure. Woke up with signs of stroke


Doncheva,Stanislava Nikolaeva
ID: 20190308/513
* 10.05.2001 , F
Study 8.0.44358849
08.03.2019
13:58:03
1010000 IMA 19 FRM 9
National Cardiology Hospital
Ref.: ,,,,
DFP-8000D
Coronary /Carotid
SINGLE PLANE\DSA\ACQ
CRA 3
RAO 23
W: 255
C: 128

Conclusions

- In AIS the transformation of Penumbra to core infarct is dependent on time and collaterals
- The clinical outcome is directly dependent on recanalization success
- Innovations in catheter based mechanical thrombectomy lead to significant improvement in recanalization rate
- In the updated guidelines (2018/2019) high level of indication for EVT of stroke is extended to patients with witnessed onset of symptoms within 6 to 24 hours and wake up stroke, meeting the necessary neuroimaging criteria for core/to ischemic tissue mismatch
- Strict regulations establishing multidisciplinary collaboration are crucial for the success of a local stroke/endovascular program

The most frequent cause for ischemic stroke is:

A. Atherosclerotic obstruction of carotid artery

B. Cardio-embolism

C. Aortic dissection

D. Hypertensive attack

Which statement is true:

A. Initial systemic thrombolysis is a contraindication for endovascular thrombectomy in patients with ischemic stroke

B. Systemic thrombolysis is likely to improve the final result of endovascular thrombectomy if undertaken within 6 hours of symptoms onset

C. Catheter based thrombectomy is a golden standard for treatment of patients with ischemic stroke between 6 and 24 hours after symptoms onset in case of positive neuroimaging criteria for cor to penumbra difference

D. Catheter based thrombectomy is a golden standard for treatment of all patients with ischemic stroke between 6 and 24 hours after symptoms onset

Which of the trials listed bellow did not enroll acute ischemic stroke patients beyond 6 hours of symptom onset?

- DEFUSE-3
- DAWN
- MR CLEAN
- REVASCAT