Ajuarteri trombektoomia – mis, kellele ja millal?

Kaarel Kärmas

V aasta resident

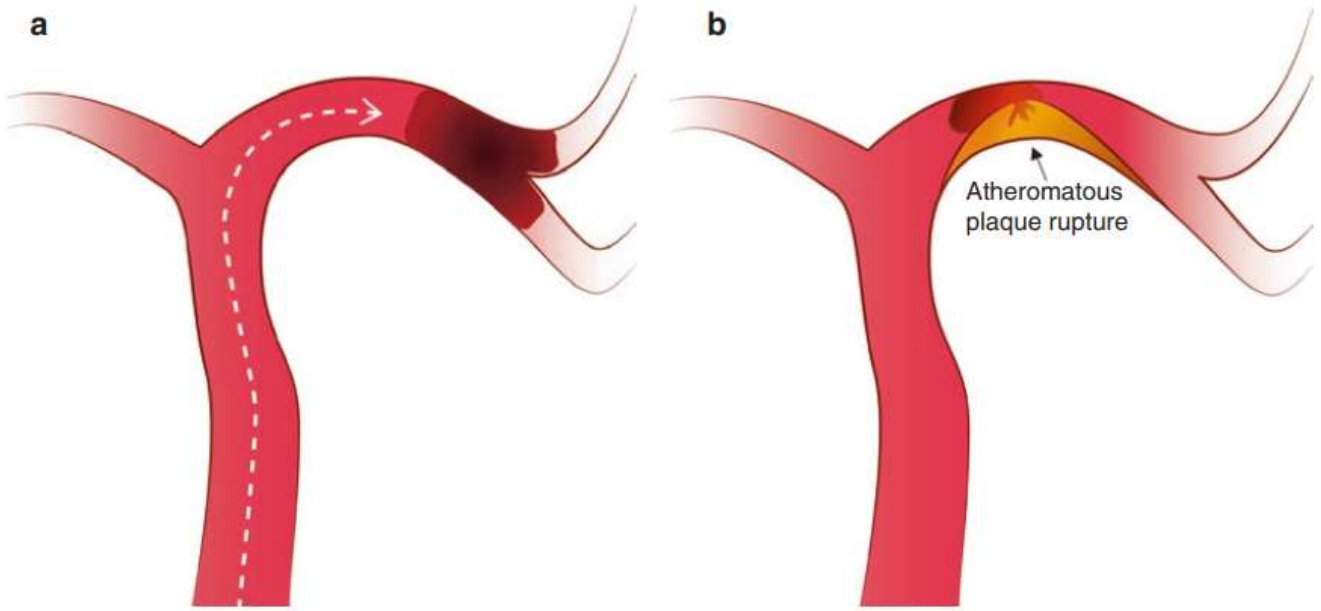
ERÜ talvine õppepäev
2019
Jaanihanso

Ettekande sisu

- Hetkeseis Eestis
- Ajuarteri trombektoomia protseduuri kirjeldus
- Lühiajalugu ja esimesed randomiseeritud uuringud
- Hiljutised nn „hilise ajaakna“ randomiseeritud uuringud

Ajuarteri trombektoomia

- Menetlusradioloogiline protseduur (DSA+fluoroskoopia), kus perifeerse arteri kaudu mehaaniliselt eemaldatakse suurest peaaju varustavast arterist tromb, kasutades selleks spetsiaalseid neurointerventsionaalseid seadmeid/vahendeid

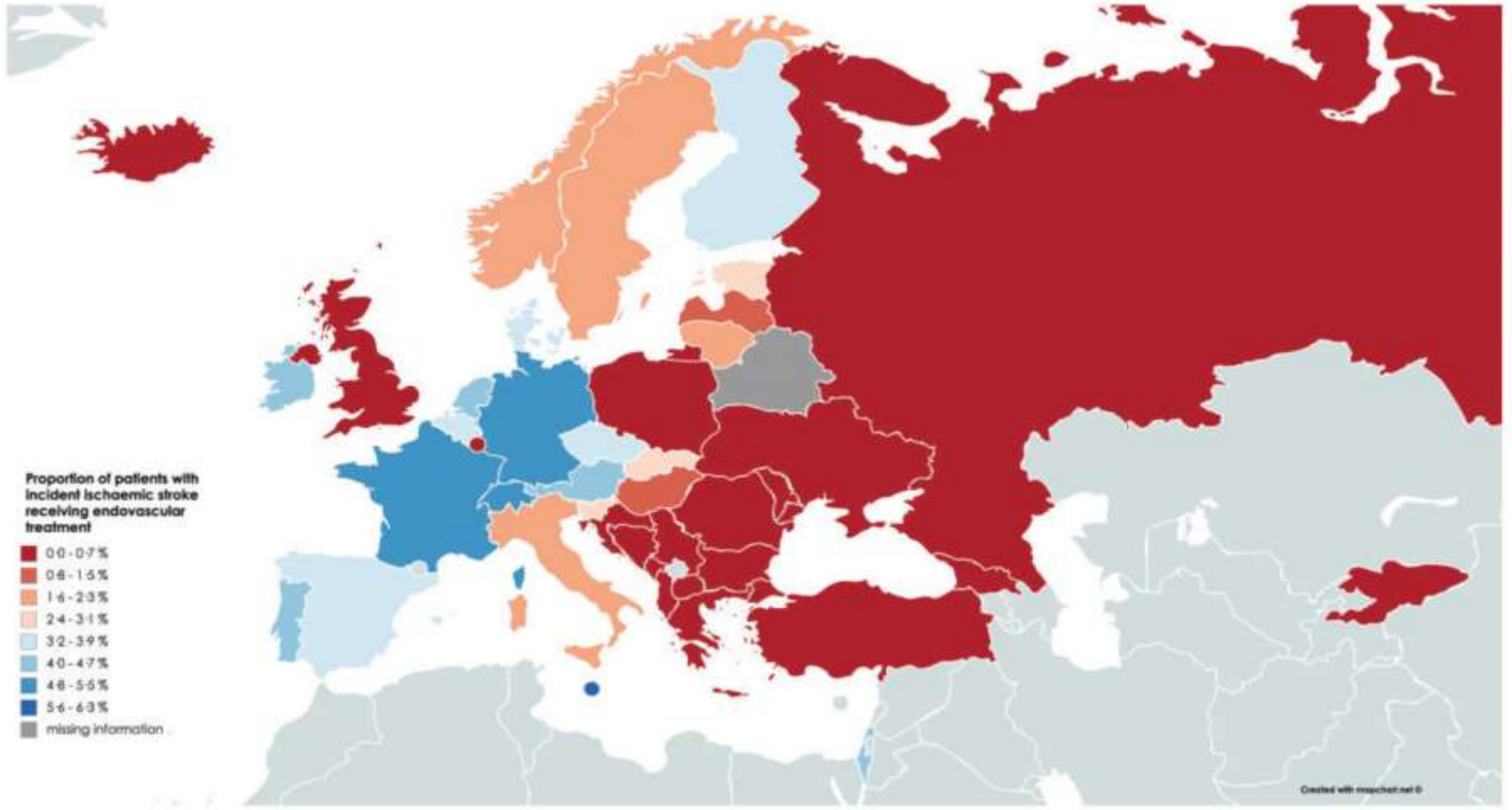


Hetkeseis Eestis

- 2015-2017*
  - PERH – 200 ajuarteri trombektoomiat
  - TÜK – 87 ajuarteri trombektoomiat
  - ITK – 42 ajuarteri trombektoomiat
- 2018
  - PERH – 98 ajuarteri trombektoomiat
- 2019
  - PERH – 112 ajuarteri trombektoomiat *(14.11.19 seisuga)*

**Eerik K et al. Insuldi revaskulariseeriva ravi hetkeseis Eestis. Eesti Arst 2018; 97(5):240–246*

Hetkeseis Eestis (2016-2017 andmed)



Aguiar de Sousa, D. et al. (2019) 'Access to and delivery of acute ischaemic stroke treatments: A survey of national scientific societies and stroke experts in 44 European countries', European Stroke Journal, 4(1), pp. 13–28

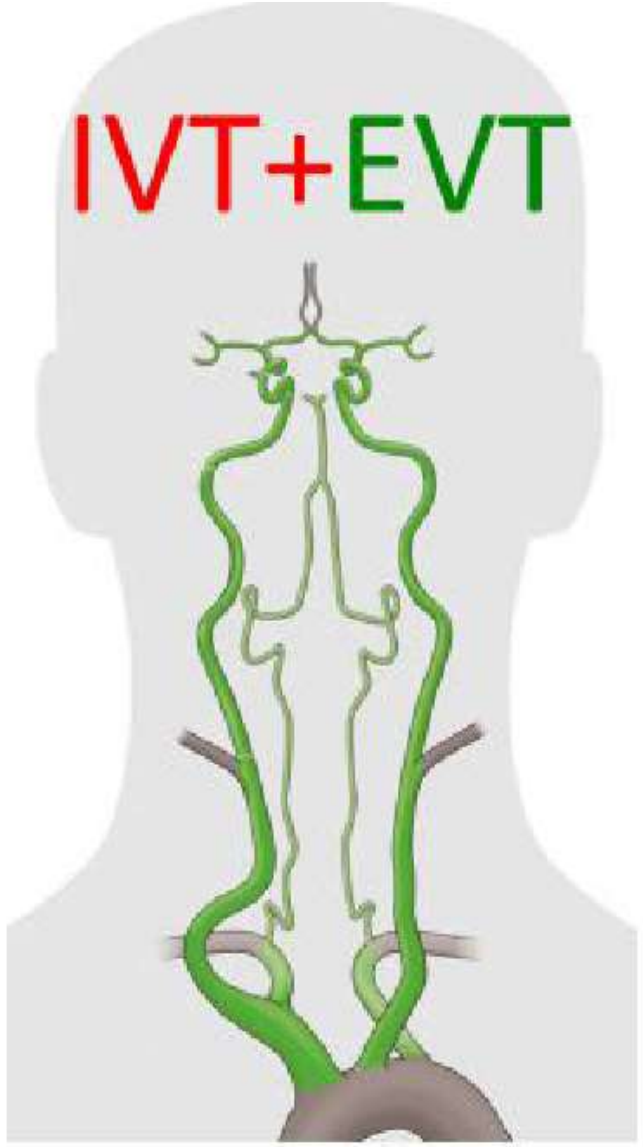
Figure 6. Choropleth map showing contemporary annual estimates of the proportion of patients with incident ischaemic stroke receiving endovascular treatment (EVT) in 42 European countries (mean 1.9%; 95% CI 1.3–2.5).

Suure soone sulgus (LVO)

- Anatoomiline lokalisatsioon on erinevates kliinilistes uuringutes erinevalt defineeritud

- 2018 a SNIS *(Society of Neurointerventional Surgery)* ravijuhend:
  - Iga arteri sulgus, mida on võimalik tänapäevaste neuroendovaskulaarsete seadmete/vahenditega selektiivselt ja ohutult kateteriseerida

- Praktikas eelkõige:
  - ICA intrakraniaalne osa/terminus (ja A1)
  - MCA M1 segment ja M2 segment
  - A.basilaris (ja P1)



Keskmine ajuarter (MCA)

- Normivariandid:
  - Suur MCA hargnemise variaabelsus
    - Varajane MCA hargnemine (M1 segment <1cm)
    - Bi- või trifurkatsioon
  - Tõelised anomaaliad on harvad
    - Aksessoorne MCA (lähtub ACAst)
    - MCA duplikatsioon (lähtub ICAst)
    - Fenestreerunud MCA

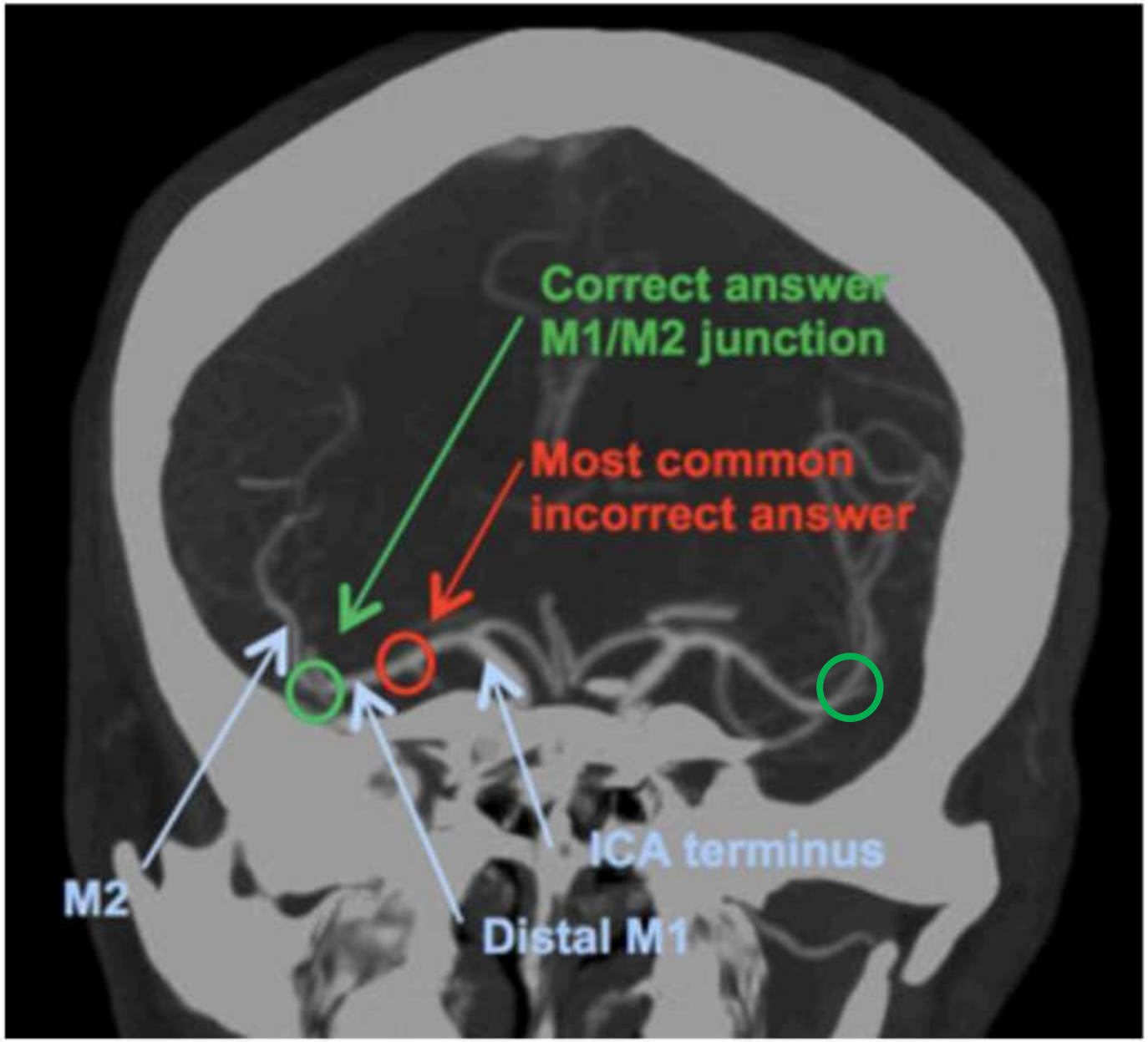


Fig. 2: CT Angiogram coronal head MIP image with arrows showing relevant anatomy and most common answers. The horizontal M1 segment transitions to M2 as it enters the Sylvian fissure, then it curves upwards (MCA genu)

Mitchell DP et al. Middle Cerebral Artery Anatomy: Do you know yours? Poster ECR 2016 / C-1360

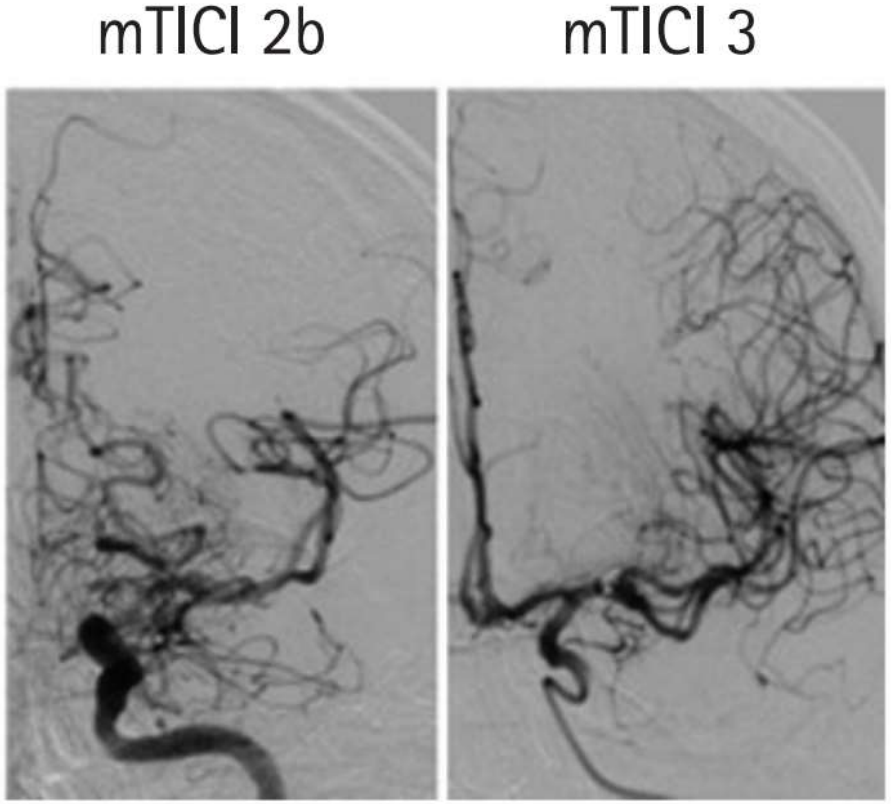
Ajuarteri trombektoomia

- Protseduur toimub eelistatult lokaalanesteesias
  - *„consious sedation“*
  - vajadusel intubatsioon ja üldnarkoos
- Vererõhu monitooring
  - ESO/ESMINT 2019:
    RR <180/105 mmHG protseduuri ajal ja järgneva 24 h jooksul
  - Samas SVR >150 mmHg ilmselt vajalik aju kollateraalide säilitamiseks
    (ASA/AHA 2018/2019)

Protseduuri eesmärk

- Võimalikult **ohutu** ja **kiire** ajukoe reperfusioon, defineeritud kui **mTICI** *(modified Treatment in Cerebral Infarction)* **2b või 3**
  - mTICI 2b – antegraadne verevool/reperfusioon rohkem kui 50% arteri varustusalast
  - mTICI 3 – täielik antegraadne verevool/reperfusioon arteri varustusalal

Raviajad (min)	Aasta 2015	2016	2017	p-väärtus
Aeg insuldi tekkest trombolüüsini	113,8 ± 53,4	120,6 ± 99,3	110,0 ± 63,1	0,692
Aeg insuldi tekkest femoraalarteri punktsioonini	231,8 ± 121,8	221,5 ± 97,3	193,1 ± 83,9	0,025
Aeg insuldi tekkest rekanalisatsioonini	278,4 ± 135,3	258,6 ± 110,9	236,3 ± 94,4	0,054
Aeg femoraalarteri punktsioonist rekanalisatsioonini	48,0 ± 29,2	40,7 ± 29,8	39,4 ± 29,1	0,129
Aeg trombolüüsist trombektoomiani	106,7 ± 73,6	100,8 ± 67,5	78,4 ± 46,9	0,016



Chamorro A. Journal of Stroke 2018;20(2):197-207

Perifeerne juurdepääs

- Perifeerse arteri punktsioon ja kateriseerimine Seldingeri järgi
  - *Eelistatud a.femoralis communis*
  - *Alternatiivselt a.carotis communis*
  - *Harva a.brachialis, a.radialis/ulnaris*

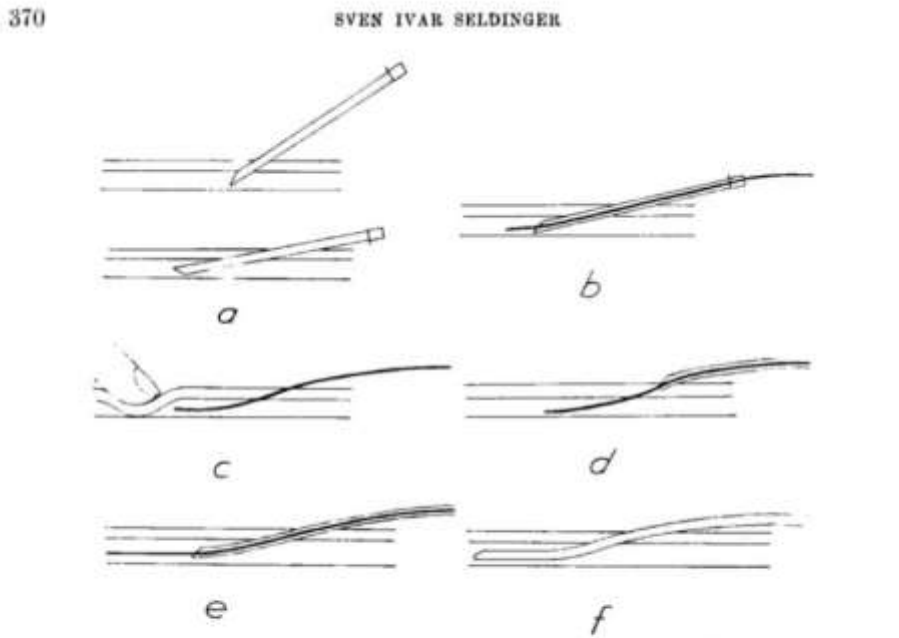
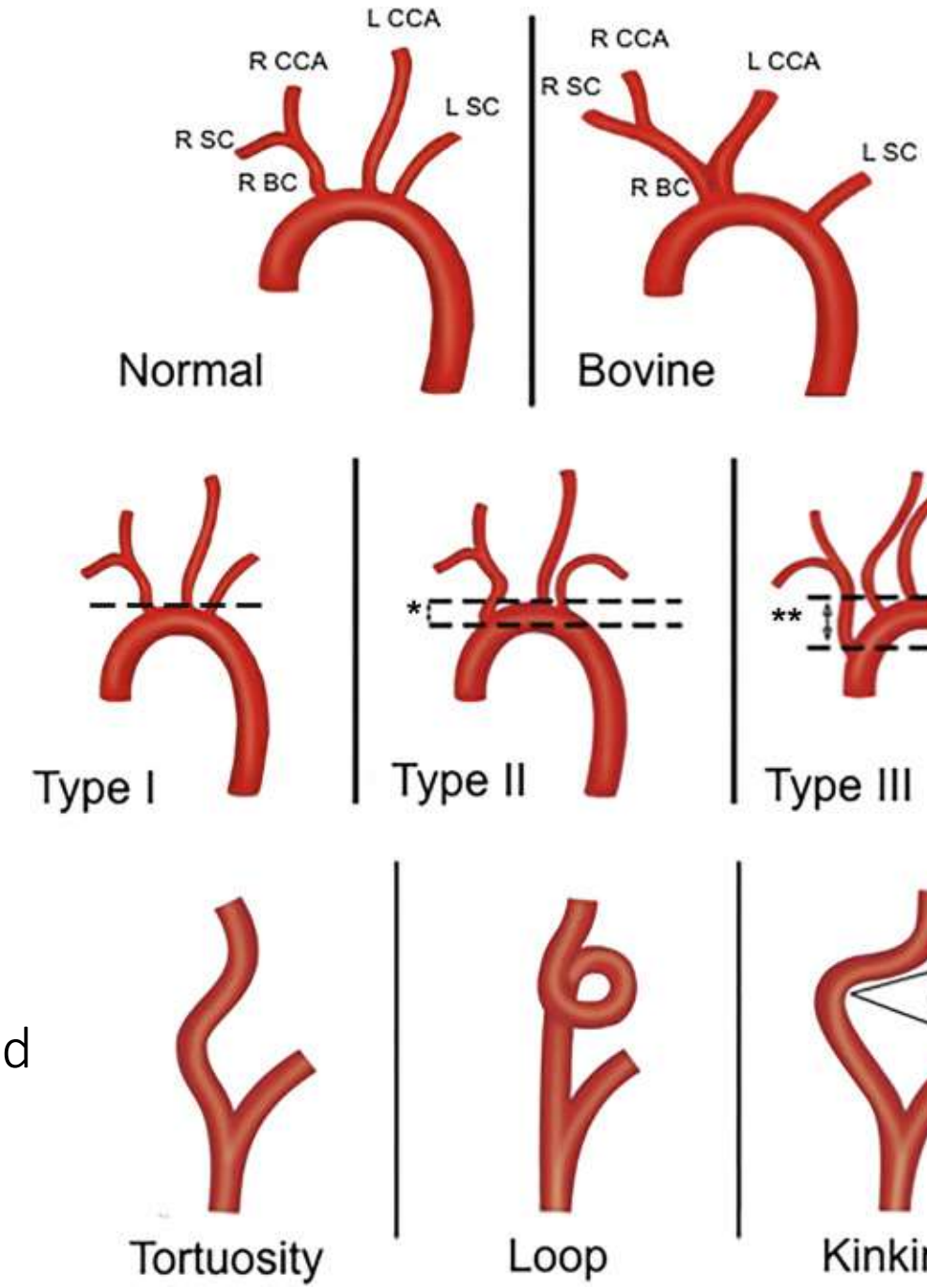


Fig. 2. Diagram of the technique used. a) The artery punctured. The needle pushed upwards. b) The leader inserted. c) The needle withdrawn and the artery compressed, d) The catheter threaded on to the leader. e) The catheter inserted into the artery, f) The leader withdrawn.

Acta Radiol 1953;39:370

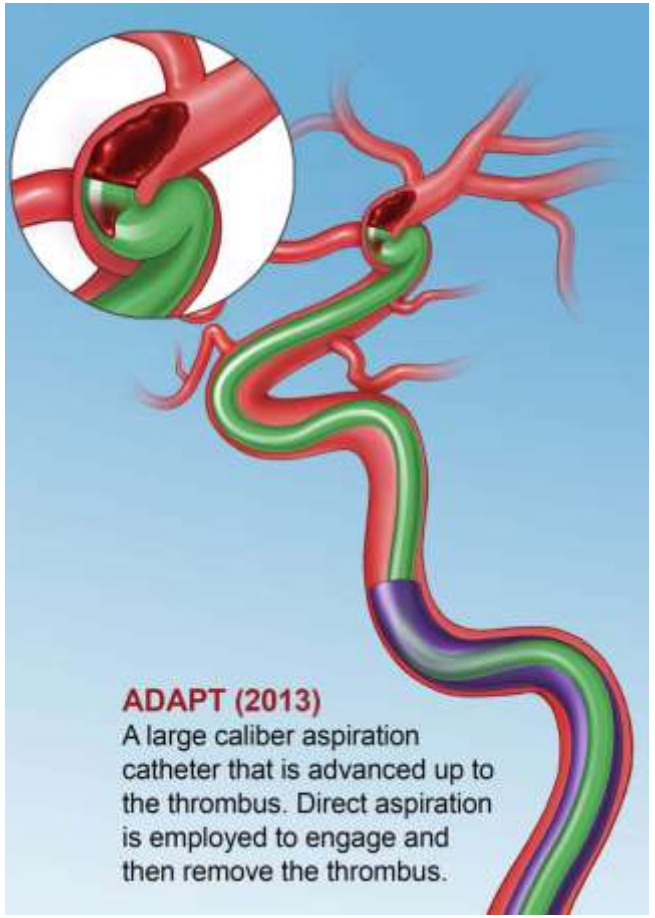
Perifeerne juurdepääs

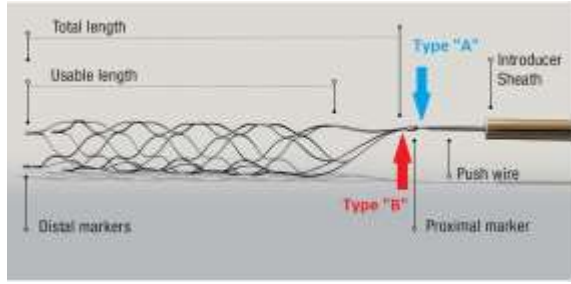
- Navigatsioon aordikaarel ja kaelaarterite kateteriseerimine
  - Oluline <u>eelinfo KT-angiograafiast</u>
    - Uuritav piirkond peaks katma lisaks kaelale ka aordikaare ja sellest väljuvad suured harud
  - Võimalik kaasuv kaelaarterite stenoos, oklusioon ja dissektsioon *(nn tandem lesioonid)*
  - Navigeerimisel kasutusel erinevat tüüpi diagnostilised kateetrid (4-5F), juhtekateetrid(6-9F), tugikateetrid, distaalse juurdepääsu kateetrid ja juhtetraadid (0.035“ profiil)



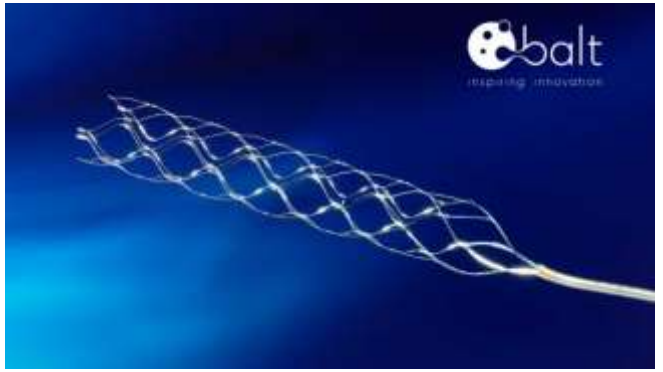
Protseduuri tehnika

- Stentriiver *(stent+retrieve)* tehnika
  - *Traadiga liidetud eridisainiga nitinoolstent:*
    Solitaire AB (EV3), Catch/Catch mini (Balt), Trevo (Stryker), Embotrap (Cerenovus),pREset/pREset LITE (Phenox), Aperio (Acandis)
  - *„Standard deployment“*
  - *„Push and Fluff“ tehnika*
- Direktse aspiratsiooni tehnika
  - *ADAPT – a direct aspiration first pass technique*
  - Suure valendikuga (0.064“- 0.072“) intrakraniaalsed aspiratsioonkateetrid:
    ACE68/ACE64 (Penumbra), Sofia (Microvention)
- *Hübriidtehnikad*
  - *Stentriiver + aspiratsioonkateeter (SOLUMBRA)*
  - *Stentriiver + aspiratsioon BGC-st (ballooniga juhtekateerter)*

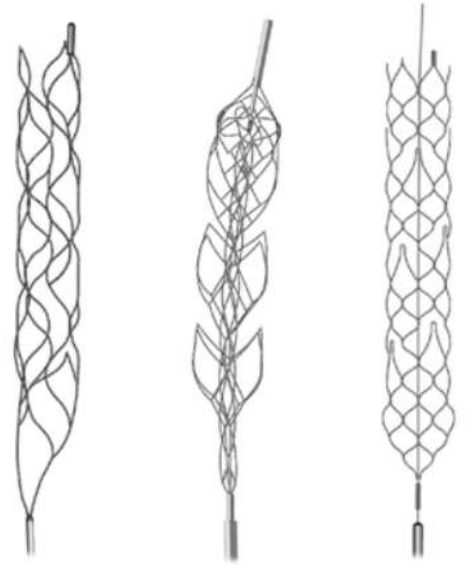




Solitaire AB



Catch



pREset Embotrap Aperio

Vastunäidustused

- Absoluutsed vastunäidustused
  - Neurokuvamisel leitud **intrakraniaalne hemorraagia**
  - Suuremahuline **väljakujunenud ajuinfrakt** sulgunud arteri varustusalal

- Suhtelised vastunäidustused
  - puuduvad eeldused heaks paranemiseks (protseduuri eelne mRS >2)
  - seoses kaasuvate haigustega on kaugprognoos halb (eeldatav elulemus <6 kuu)
  - Madal ASPECTS?

Näidustused

- Praegused patsientide selektsiooni kriteeriumid on eelkõige suurte randomiseeritud kliiniliste uuringute **sisse-arvamise kriteeriumid või nende kombinatsioonid**

- Käesolevalt täpsete kliiniliste selektsiooni kriteeriumite määratlemine mõnevõrra problemaatiline
  - Mõned patsientide rühmad praeguseks põhjalikumalt uuritud
  - Kiirelt lisanduvas teaduskirjanduses ka vastuolulist teavet

- Mõned eksperdid toovad välja, et praegused trombektoomia selektsiooni kriteeriumid on eelkõige insuldi prognoosi faktorid *(predictor of outcome)* mitte tõelised selektsiooni kriteeriumid ning nende range järgimise tulemus on **patsientide üleselektsioon**, mistõttu jäävad osad ägeda insuldiga patsiendid ravita *(Nogueira RG, Ribó M. Stroke. 2019;50(9):2612.)*

Vajalikud mõisted

- NIHSS - *National Institutes of Health Stroke Scale*
  - Insuldi raskusastme hindamise skaala
    - 1-6 punkti - vähese neuroloogilise defitsiidiga insult
    - 7-15 punkti - mõõduka neuroloogilise defitsiidiga insult
    - 16-42 punkti - raske neuroloogilise defitsiidiga insult
- mRS – *Modified Rankin Scale*
  - *mRS 0-2 = hea tulemus*
- ASPECTS – *Alberta Stroke Program Early CT Score*

Modified Rankin Scale

Score	Description
0	No symptoms at all
1	No significant disability despite symptoms; able to carry out all usual duties and activities
2	Slight disability; unable to carry out all previous activities, but able to look after own affairs without assistance
3	Moderate disability; requiring some help, but able to walk without assistance
4	Moderately severe disability; unable to walk without assistance and unable to attend to own bodily needs without assistance
5	Severe disability; bedridden, incontinent, and requiring constant nursing care and attention
6	Dead

Reproduced with permission from: Van Swieten JC, Koudstaa PJ, Visser MC, et al. Interobserver agreement for the assessment of handicap in stroke patients. Stroke 1988; 19:604. Copyright © 1988 Lippincott Williams & Wilkins.

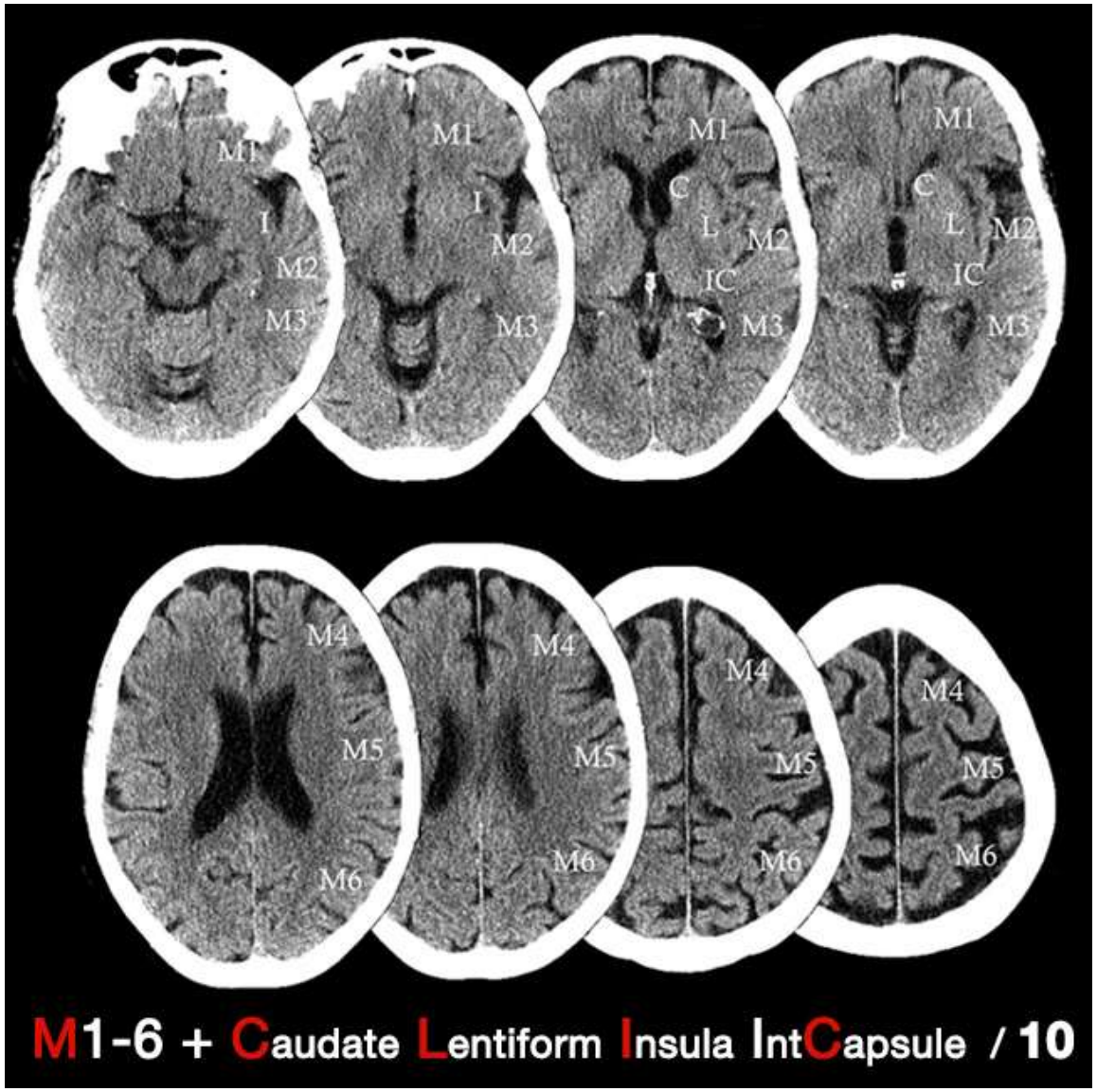
ASPECTS

Calculating the ASPECTS Score:

Each area of grey white loss constitutes 1 deduction point

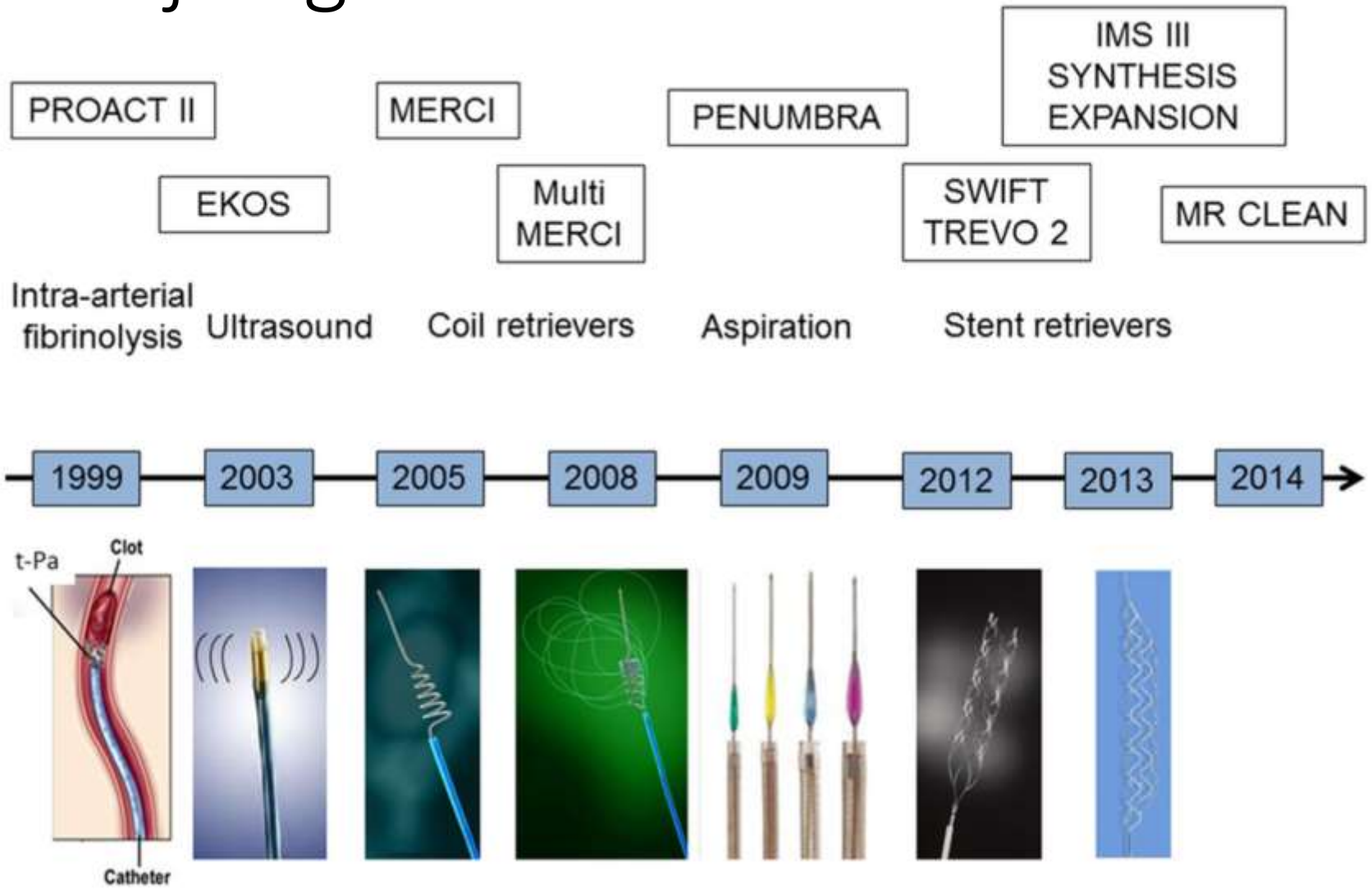
Subganglionic Nuclei:	
M1 - *Frontal operculum*	-1
M2 - *Anterior temporal lobe*	-1
M3 - *Posterior temporal lobe*	-1
Supraganglionic Nuclei:	
M4 - *Anterior MCA*	-1
M5 - *Lateral MCA*	-1
M6 - *Posterior MCA*	-1
Basal Ganglia:	
Caudate (C)	-1
Lentiform Nucleus (L)	-1
Insula (I)	-1
Internal Capsule (IC) *any part*	-1
Total ASPECTS Score.	**/10**

http://www.aspectsinstroke.com/



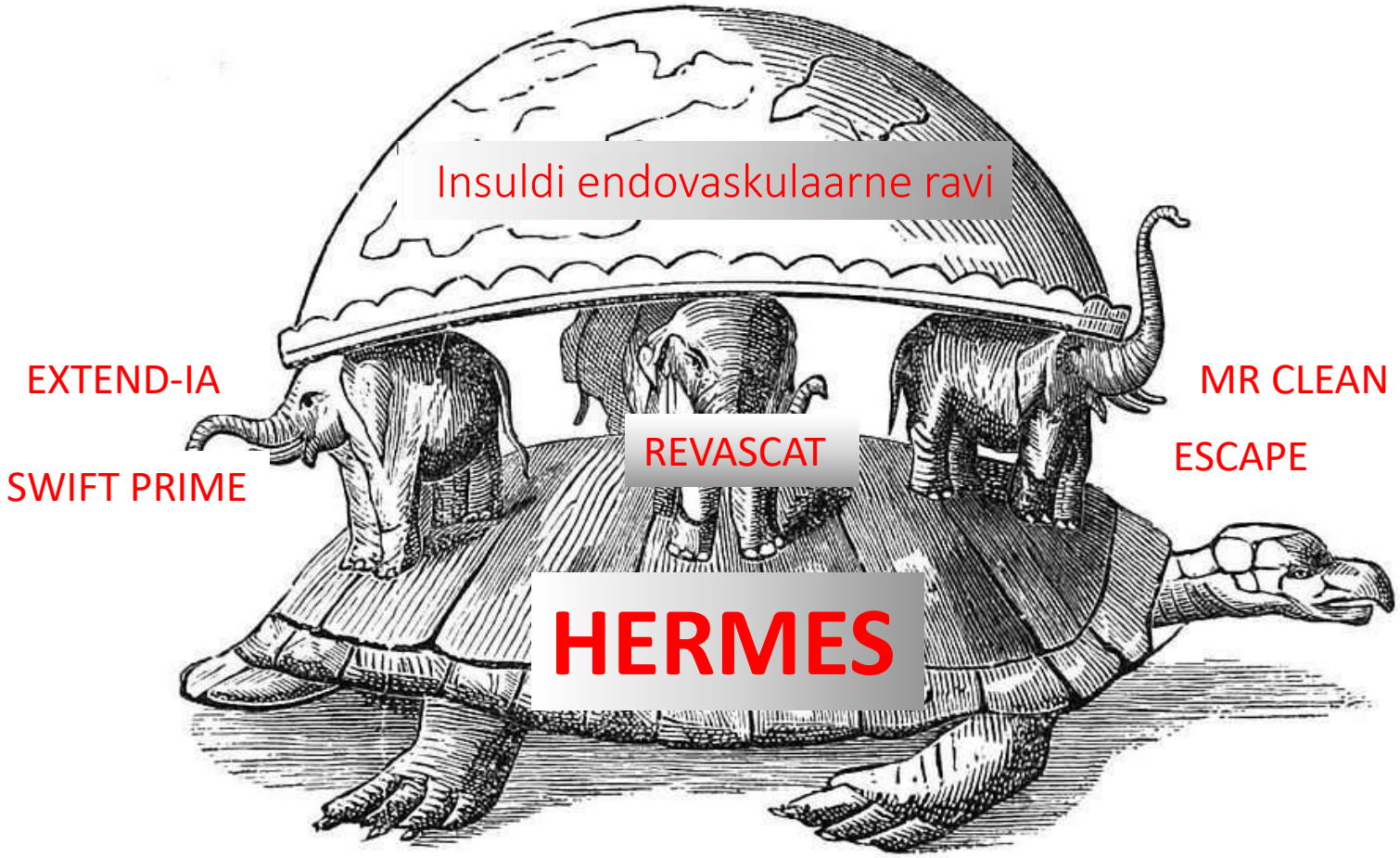
- Changes are **best identified at a scan window of** 50x30 [40 **x 40].** Avoid scoring ASPECTS at the standard window level of 80x30.
- It is important to **scroll through the entire scan** to identify these signs in deep gray regions and M1-6 MCA territories.

Lühike lähiajalugu



Pierot et al. Stroke. 2015;46:909-914.

Insuldi ravi paradigma muutus 2015 aastal



Randomiseeritud kliinilised uuringud 2014-2015

Trial	No of patients, total/IA (when applicable)	LVO location	Time window for thrombectomy, hours	Stroke severity (NIHSS score)	Imaging criteria	Treatment groups	mRS score=0–2 at 90 days
Randomized trials: Endovascular vs medical							
MR CLEAN[8]	500/223	ICA, M1, M2, A1, A2	0–6	≥2	No limit	Endovascular arm: stent retrievers in 97% of IA cases, 87% of IA-treated patients received IV rtPA first. Control arm: IV rtPA in 91% of patients	Endovascular group: 33% Control group: 19% NNT=7.1
ESCAPE[13]	215/165	ICA, M1, both (all) M2s	0–12	'Disabling' symptoms but no strict NIHSS limit	CT ASPECTS 6–10, moderate-to-good collateral status on mCTA	Endovascular arm: stent retrievers in 86% of all IA cases. 73% of IA-treated patients received IV rtPA first Control arm: IV rtPA in 79% of patients	Endovascular group: 53% Control group: 29% NNT=4.2
EXTEND-IA[9]	70/35	ICA, M1, M2	0–6	No limit	CTP/MRP core <70 mL	Endovascular arm: IV rtPA plus Solitaire stent retriever in all IA cases. Control arm: IV rtPA in all	Endovascular group: 71% NNT=3.2
SWIFT PRIME[10]	196/98	ICA, M1	0–6	8–29	CTP/MRP core ≤50 mL, CT/MRI ASPECTS 6–10	Endovascular arm: IV rtPA plus Solitaire stent retriever in all IA cases. Control arm: IV rtPA in all	Endovascular group: 60% Control group: 35% NNT=4
REVASCAT[12]	206/103	Anterior circulation LVO	0–8	≥6	CT ASPECTS 7–10, MRI DWI ASPECTS 6–10	Endovascular arm: Solitaire stent retriever thrombectomy. 68% of IA-treated patients received IV rtPA first. Control arm: IV rtPA in 78% of patients.	Endovascular group: 44% Control group: 28% NNT=6.3

Mokin M, Ansari SA, McTaggart RA et al. J NeuroIntervent Surg 2019;11:215–220.

2016 HERMES metaanalüüs

NNT = 2,6

	Intervention population	Control population	Risk difference (%)	Rate ratio (95% CI)	Odds ratio (95% CI)	Adjusted rate ratio (95% CI)	Adjusted odds ratio (95% CI)
mRS score reduction (shift analysis; primary outcome)*	..	..	..	..	2·26* (1·67–3·06); p<0·0001	..	2·49* (1·76–3·53); p<0·0001
mRS score 0–1 at 90 days	26·9% (170/633)	12·9% (83/645)	14·0	2·00 (1·54–2·60); p<0·0001	2·49 (1·84–3·35); p<0·0001	2·06 (1·59–2·69); p<0·0001	2·72 (1·99–3·71); p<0·0001
mRS score 0–2 at 90 days	46·0% (291/633)	26·5% (171/645)	19·5	1·7 (1·41–2·05); p<0·0001	2·35 (1·85–2·98); p<0·0001	1·73 (1·43–2·09); p<0·0001	2·71 (2·07–3·55); p<0·0001
NIHSS score 0–2 at 24 h	21·0% (129/615)	8·3% (52/630)	12·7	2·47 (1·79–3·41); p<0·0001	2·91 (2·06–4·12); p<0·0001	2·66 (1·92–3·67); p<0·0001	3·77 (2·49–5·71); p<0·0001
Early neurological recovery at 24 h	50·2% (309/616)	21·2% (134/633)	29·0	2·34 (1·91–2·87); p<0·0001	4·04 (2·75–5·93); p<0·0001	2·34 (1·91–2·87); p<0·0001	4·36 (3·03–6·27); p<0·0001

Data show the proportion of patients with outcome (n/N), unless otherwise stated. NIHSS=National Institutes of Health Stroke Scale. mRS=modified Rankin Scale. *Common odds ratio indicating the odds of improvement of 1 point on the mRS.

***Table 2*: Efficacy outcomes from the pooled data**

HERMES Collaborators

Highly Effective Reperfusion evaluated in Multiple Endovascular Stroke trials (HERMES)

ESCAPE REVASCAT MR CLEAN EXTEND-IA SWIFT PRIME

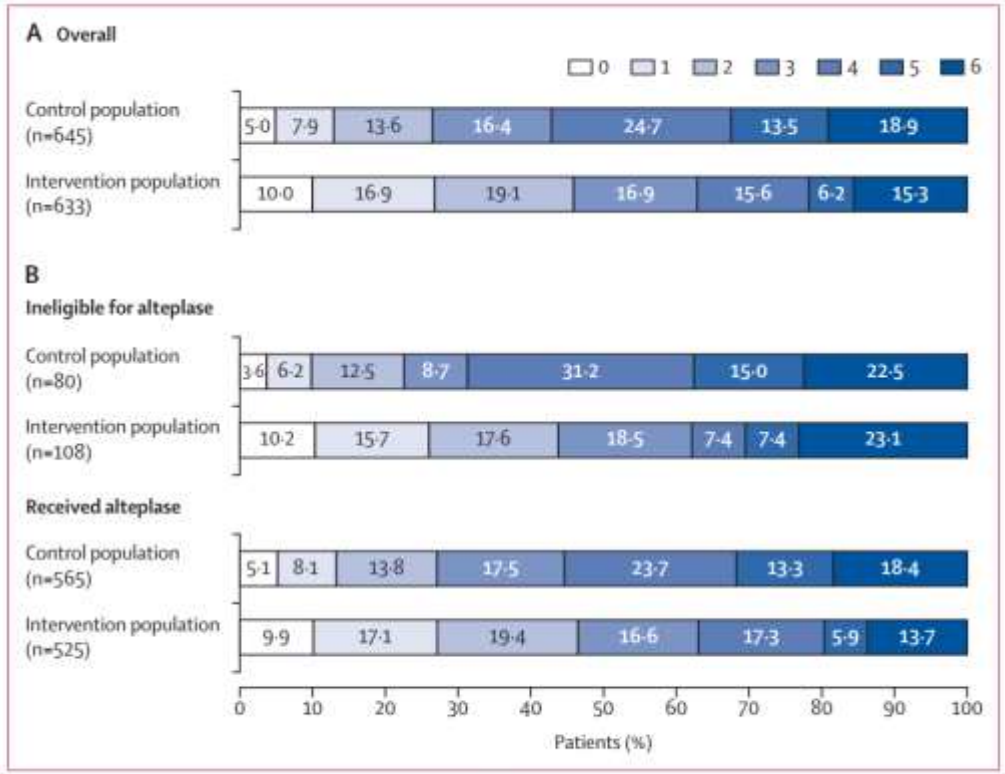


***Figure 1*: Scores on the modified Rankin Scale at 90 days**

Goyal M et al. Lancet 2016; 387: 1723–31

2016 HERMES metaanalüüs

HERMES Collaborators

Highly Effective Reperfusion evaluated in Multiple Endovascular Stroke trials (HERMES)

	Intervention population	Control population	Risk difference (%)	Rate ratio (95% CI)	Odds ratio (95% CI)	Adjusted rate ratio (95% CI)	Adjusted odds ratio (95% CI)
Symptomatic intracranial haemorrhage	4·4% (28/634)	4·3% (28/653)	0·1	1·06 (0·63–1·80); p=0·82	1·07 (0·62–1·83); p=0·81	1·07 (0·62–1·80); p=0·81	1·07 (0·62–1·84); p=0·81
Parenchymal haematoma type 2	5·1% (32/629)	5·3% (34/641)	−0·2	0·99 (0·61–1·61); p=0·97	0·99 (0·60–1·63); p=0·97	1·04 (0·64–1·69); p=0·88	1·04 (0·63–1·72); p=0·88
Mortality	15·3% (97/633)	18·9% (122/646)	−3·6	0·82 (0·63–1·07); p=0·15	0·77 (0·54–1·10); p=0·16	0·82 (0·62–1·08); p=0·15	0·73 (0·47–1·13); p=0·16

Data show the proportion of patients with outcome (n/N), unless otherwise stated.

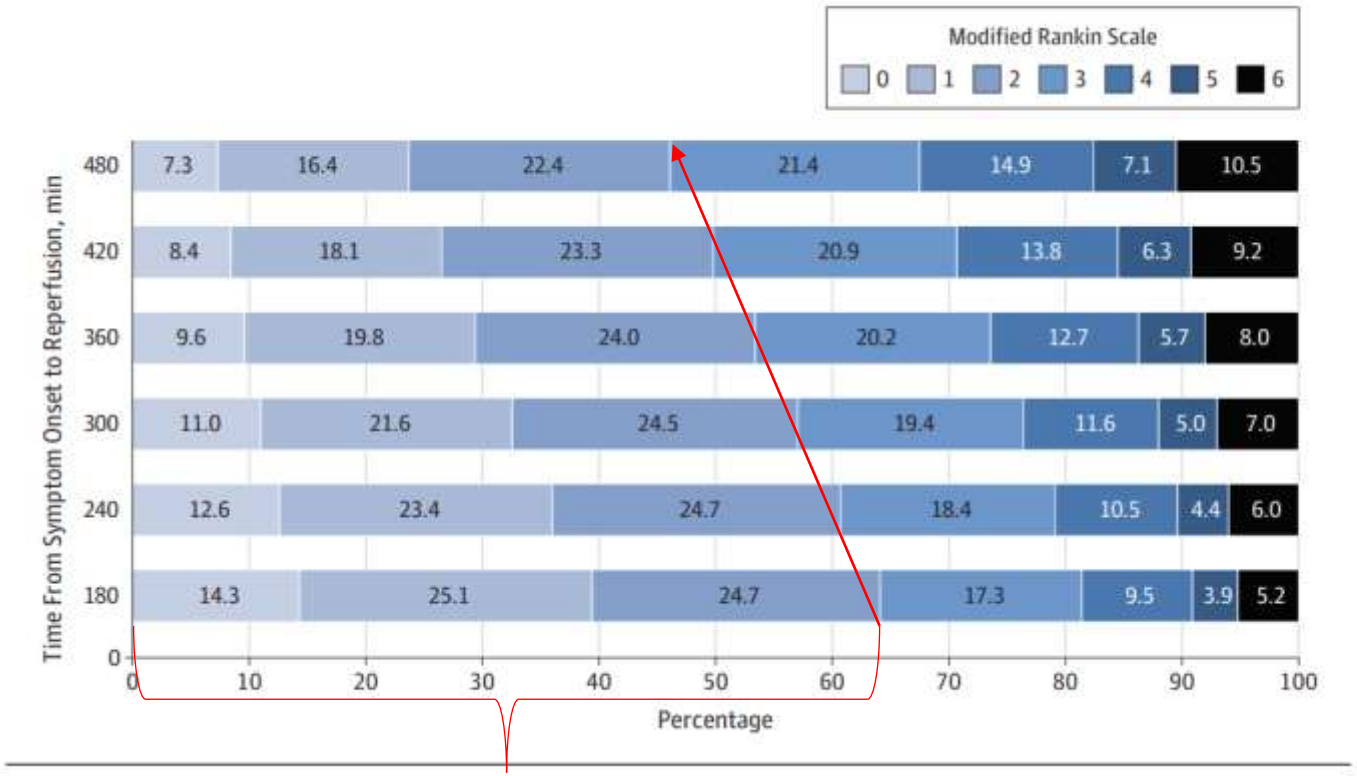
***Table 4*: Safety outcomes at 90 days**

Goyal M et al. Lancet 2016; 387: 1723–31

Insuldi ajaline kestvus ja TE ravitulemus

HERMES Collaborators

Highly Effective Reperfusion evaluated in Multiple Endovascular Stroke trials (HERMES)



mRS 0-2 = hea tulemus

„TIME IS BRAIN“

Data are from the 390 endovascular group patients in whom substantial reperfusion (modified Thrombolysis in Cerebral Infarction score of 2b or 3) was achieved. Rows are intercepts from a single model using all 390 patients, treating time as a continuous variable. Model adjusted for age, sex, baseline stroke severity (National Institutes of Health Stroke Scale), target occlusion location, and concomitant intravenous tissue plasminogen activator.

Saver JL, Goyal M, van der Lugt A, et al. Time to Treatment With Endovascular Thrombectomy and Outcomes From Ischemic Stroke: A Meta-analysis. *JAMA.* 2016

Patsientide selektsioon

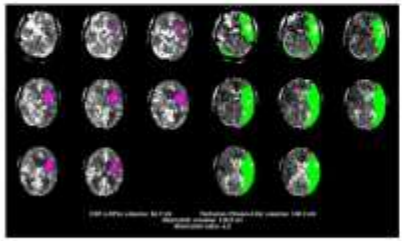
- Hüpoteetiline olukord:
- Kohort A
  - KT-perfusiooni kriteeriumite alusel selekteeritud patsiendid ravitulemustega NNT=3 ja 90-päeva mRS 0-2= 70%
  - *A la* EXTEND-IA, SWIFT PRIME

- Kohort B
  - Natiiv KT kriteeriumite alusel selekteeritud patsiendid ravitulemustega NNT=5 ja 90-päeva mRS 0-2= 35%
  - *A la* MR CLEAN, THRACE

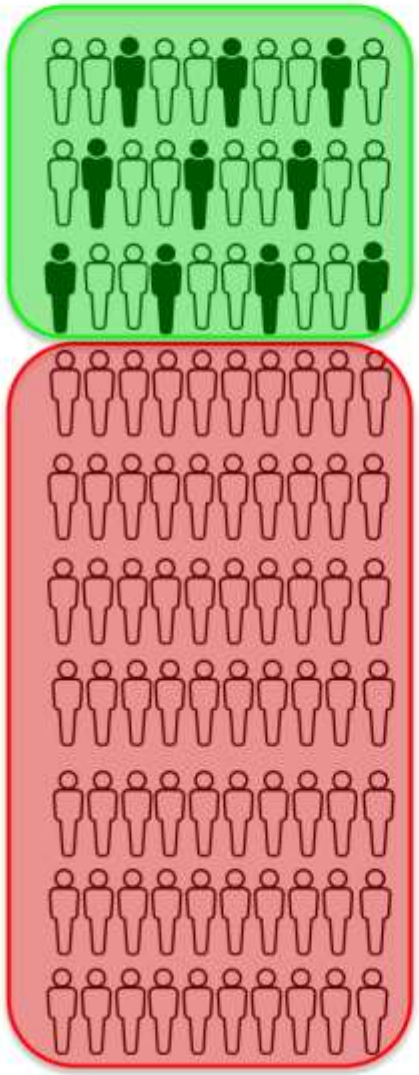
Pt.-de võimalik üleselektsioon

- Näitlikustatud situatsioon

Over-Selection

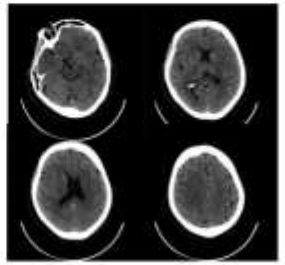


CT PERFUSION

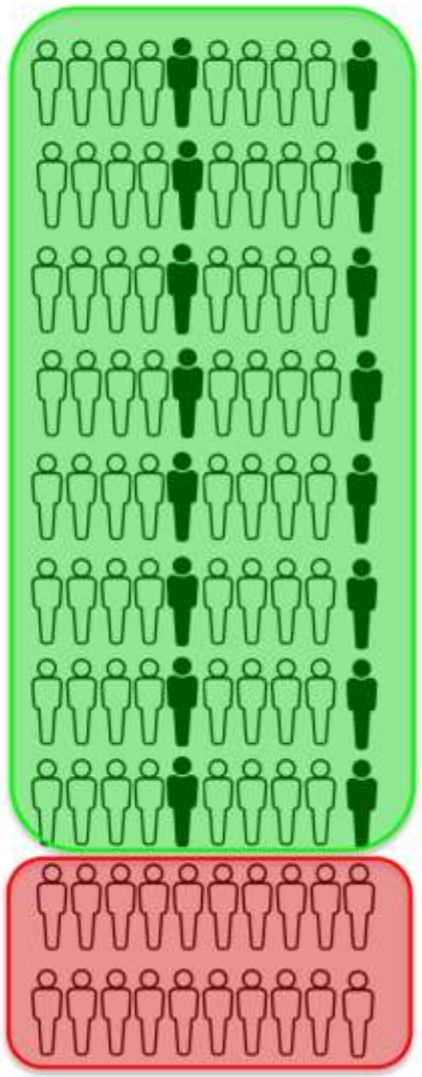


Treated Patients:
NNT = 3
90-Day mRS 0-2: 70%

Benefit in the Overall Population:
10:100 pts



NON-CONTRAST CT



Treated Patients:
NNT = 5
90-Day mRS 0-2: 35%

Benefit in the Overall Population:
16:100 pts

Raul G Nogueira. Late Window Treatment: DAWN, AURORA and the Effect of Time. Loeng ESO 2018 aastakonverents

2019 ASA/AHA ravijuhend

- Varajases ajaaknas (0-6 h) olevate patsientide radioloogiline selektsioon

2. When evaluating patients with AIS within 6 hours of last known normal with LVO and an Alberta Stroke Program Early Computed Tomography Score (ASPECTS) of ≥6, selection for mechanical thrombectomy based on CT and CTA or MRI and MRA is recommended in preference to performance of additional imaging such as perfusion studies.	**I**	**B-NR**	New recommendation.
Of the 6 RCTs that independently demonstrated clinical benefit of mechanical thrombectomy with stent retrievers when performed <6 hours from stroke onset, 4 trials (REVASCAT [Randomized Trial of Revascularization With Solitaire FR Device Versus Best Medical Therapy in the Treatment of Acute Stroke Due to Anterior Circulation Large Vessel Occlusion Presenting Within Eight Hours of Symptom Onset], SWIFT PRIME [Solitaire With the Intention for Thrombectomy as Primary Endovascular Treatment], EXTEND-IA [Extending the Time for Thrombolysis in Emergency Neurological Deficits–Intra-Arterial], and ESCAPE)[105–108] used some form of advanced imaging to determine eligibility, whereas 2 (THRACE [Trial and Cost Effectiveness Evaluation of Intra-Arterial Thrombectomy in Acute Ischemic Stroke] and MR CLEAN)[109,110] required only NCCT and demonstration of LVO. Because the last 2 studies independently demonstrated benefit in the treated group, the role of additional imaging-based eligibility criteria is not well established and could lead to the exclusion of patients who would benefit from treatment and are therefore not indicated at this time. Further RCTs may be helpful to determine whether advanced imaging paradigms using CTP, CTA, and MRI perfusion and diffusion imaging, including measures of infarct core and penumbra, are beneficial for selecting patients for reperfusion therapy who are within 6 hours of symptom onset and have an ASPECTS <6.			See Table XVII in online Data Supplement 1.

2018 ASA/AHA ravijuhend

- Ei muudetud 2019 uuenduses *(30.10.19)*

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
6. Although its benefits are uncertain, the use of mechanical thrombectomy with stent retrievers may be reasonable for patients with AIS in whom treatment can be initiated (groin puncture) within 6 hours of symptom onset and who have prestroke mRS score >1, ASPECTS <6, or NIHSS score <6, and causative occlusion of the internal carotid artery (ICA) or proximal MCA (M1). Additional randomized trial data are needed.	IIb	B-R

2019 ESO/ESMINT ravijuhend

PICO question	Recommendations
PICO 1: For adults with LVO related acute ischemic 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 ischemic stroke presenting within 6 hours after symptom onset, we recommend MT plus BMM, including IVT whenever indicated, over best BMM alone to improve functional outcome. Quality of evidence: High ⊕⊕⊕⊕ Strength of recommendation: Strong ↑↑

Expert opinion
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 MT 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.

2018 ASA/AHA ravijuhend

- Ei muudetud 2019 uuenduses (30.10.19)

2. In patients under consideration for mechanical thrombectomy, observation after IV alteplase to assess for clinical response should not be performed.	**III: Harm**	**B-R**

Hiljutised randomiseeritud kliinilised uuringud

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Thrombectomy 6 to 24 Hours after Stroke with a Mismatch between Deficit and Infarct

R.G. Nogueira, A.P. Jadhav, D.C. Haussen, A. Bonafe, R.F. Budzik, P. Bhuva, D.R. Yavagal, M. Ribo, C. Cognard, R.A. Hanel, C.A. Sila, A.E. Hassan, M. Millan, E.I. Levy, P. Mitchell, M. Chen, J.D. English, Q.A. Shah, F.L. Silver, V.M. Pereira, B.P. Mehta, B.W. Baxter, M.G. Abraham, P. Cardona, E. Veznedaroglu, F.R. Hellinger, L. Feng, J.F. Kirmani, D.K. Lopes, B.T. Jankowitz, M.R. Frankel, V. Costalat, N.A. Vora, A.J. Yoo, A.M. Malik, A.J. Furlan, M. Rubiera, A. Aghaebrahim, J.-M. Olivot, W.G. Tekle, R. Shields, T. Graves, R.J. Lewis, W.S. Smith, D.S. Liebeskind, J.L. Saver, and T.G. Jovin, for the DAWN Trial Investigators*

This article was published on November 11, 2017, at NEJM.org.

DOI: 10.1056/NEJMoa1706442

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Thrombectomy for Stroke at 6 to 16 Hours with Selection by Perfusion Imaging

G.W. Albers, M.P. Marks, S. Kemp, S. Christensen, J.P. Tsai, S. Ortega-Gutierrez, R.A. McTaggart, M.T. Torbey, M. Kim-Tenser, T. Leslie-Mazwi, A. Sarraj, S.E. Kasner, S.A. Ansari, S.D. Yeatts, S. Hamilton, M. Mlynash, J.J. Heit, G. Zaharchuk, S. Kim, J. Carrozzella, Y.Y. Palesch, A.M. Demchuk, R. Bammer, P.W. Lavori, J.P. Broderick, and M.G. Lansberg, for the DEFUSE 3 Investigators*

This article was published on January 24, 2018, at NEJM.org.

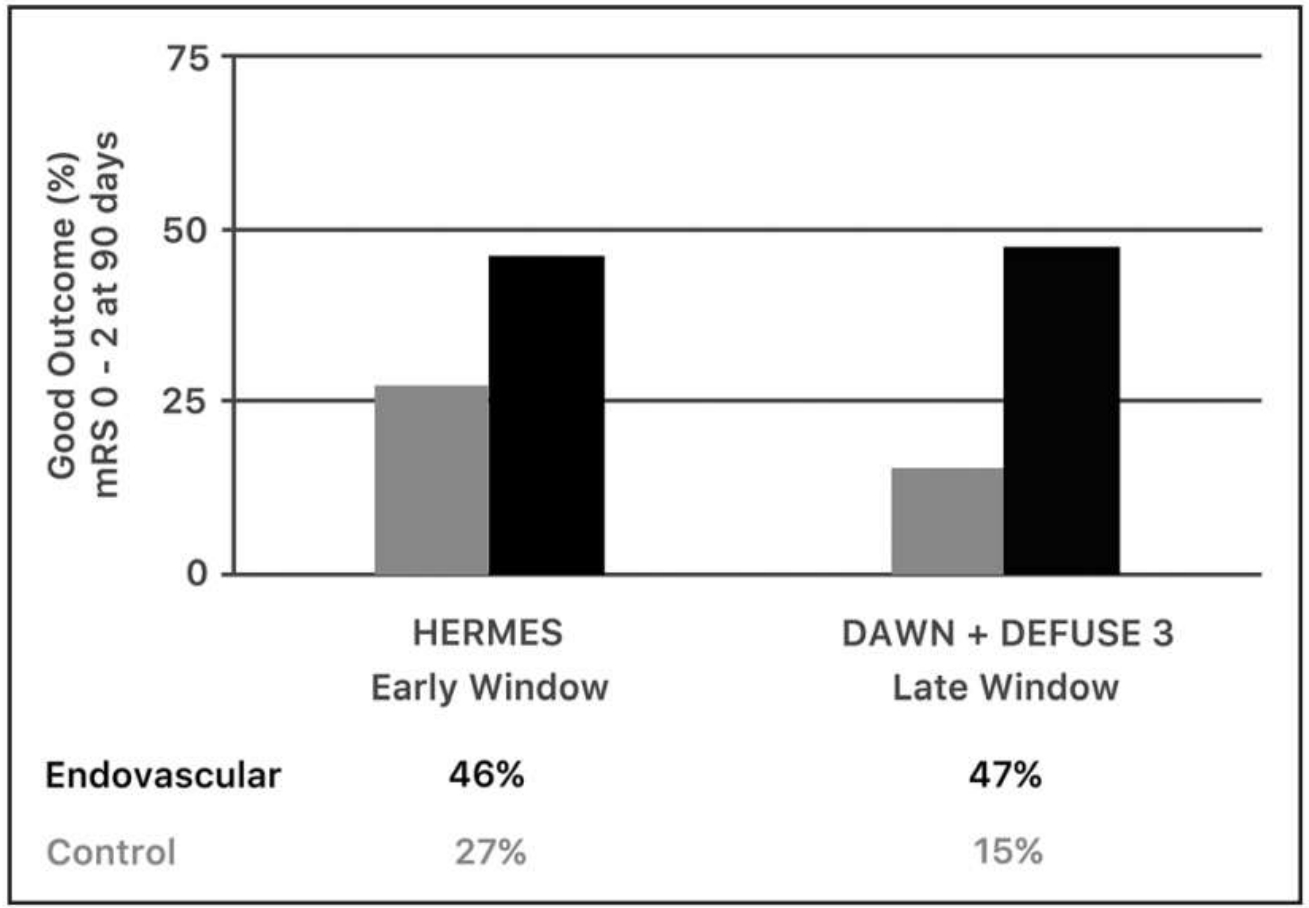
DOI: 10.1056/NEJMoa1713973

Hiljutised randomiseeritud uuringud

Trial	No of patients, total/IA (when applicable)	LVO location	Time window for thrombectomy, hours	Stroke severity (NIHSS score)	Imaging criteria	Treatment groups	mRS score=0–2 at 90 days
Randomized trials: Endovascular vs medical							
DAWN[16]	206/107	ICA, M1	6–24	≥10	CTP, MRP Group A: age ≥80, core <21 mL Group B: ag e<80, NIHSS ≥10, core <31 mL Group C: age <80, NIHSS ≥20, core <51 mL	Endovascular arm: Trevo stent retriever Control arm: medical management (antiplatelets)	Endovascular group: 49% Control group: 13%
DEFUSE 3[15]	182	ICA, M1	6–16	≥6	CTP/MRP core <70 mL, Penumbra/ core ≥1.8 mL	Endovascular arm: direct aspiration without stent retriever in 27%, stent retrievers were used in 80% of IA interventions. Control arm: medical management (antiplatelets)	Endovascular group: 45% Control group: 17%

Mokin M, Ansari SA, McTaggart RA et al. J NeuroIntervent Surg 2019;11:215–220.

Hilise ajaakna paradoks



Raviefekt 19% 32% (p=0.006)

- „TIME IS BRAIN??“

Albers G W. Late Window Paradox. Stroke 2018

Hilise ajaakna paradoks

- *DEFUSE 2 (2012)*

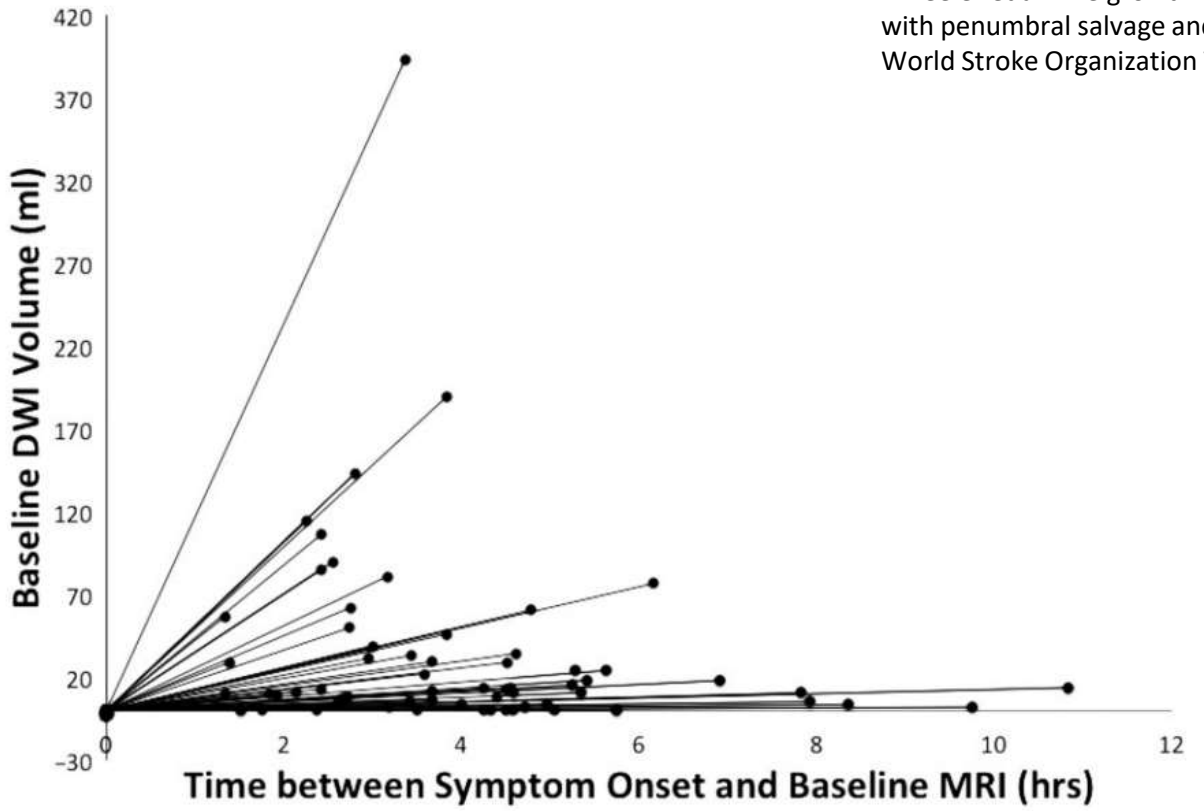


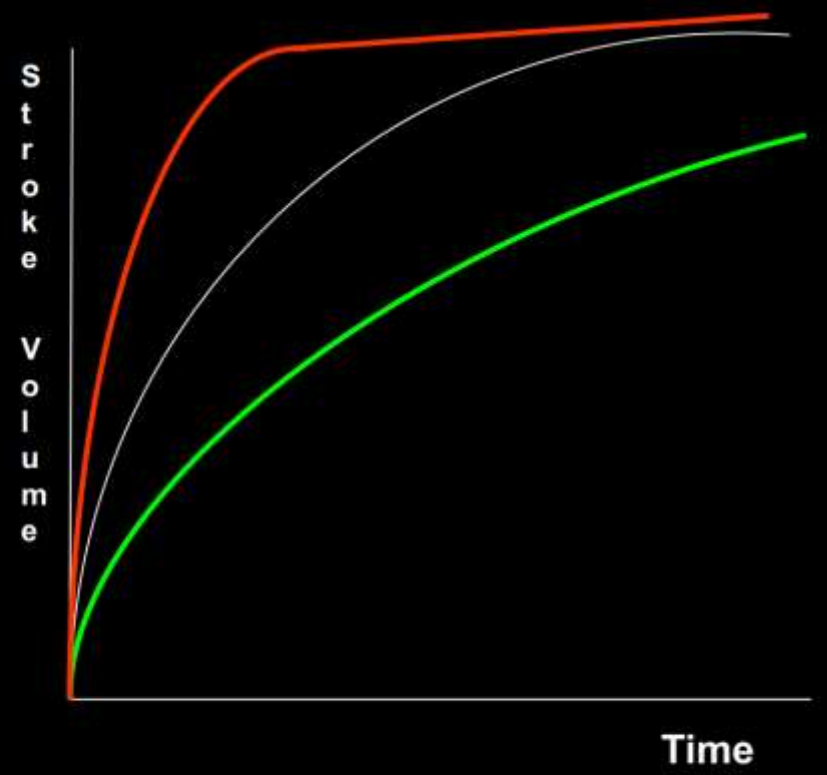
Fig. 2 Initial DWI growth rate for the 65 patients with known time of stroke onset. Graphed based on the assumption of infarct volume of 0 ml just prior to symptom onset and linear growth (based on initial findings in Part I of this study). Overall, median initial growth rate was 3·1 ml/h, with a range from 0 ml/h to 117 ml/h. DWI, diffusion-weighted imaging; MRI, magnetic resonance imaging.

Wheeler et al. The growth rate of early DWI lesions is highly variable and associated with penumbral salvage and clinical outcomes following endovascular reperfusion. World Stroke Organization Vol 10, July 2015, 723–729

Different Brains Have Different Time Profiles!

The pace of stroke progression appears to be highly variable and is likely dependent of multiple factors other than the duration and intensity of ischemia including:

- Collateral flow (via Circle of Willis and/or leptomeningeal collaterals)
- Ischemic preconditioning
- Cerebral perfusion pressure
- Cerebral blood volume
- Serum glucose
- Body temperature
- Oxygen delivery capacity



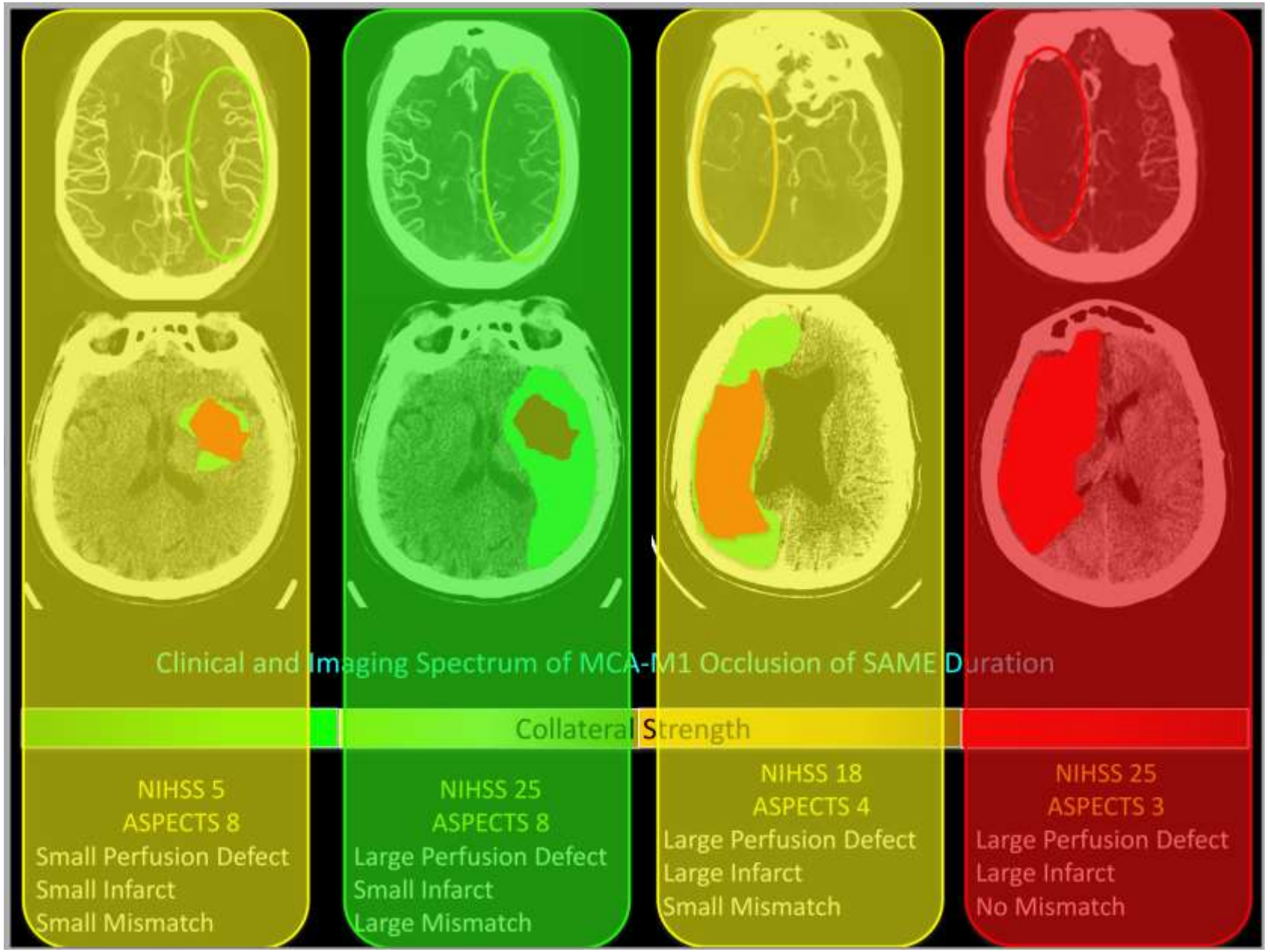
Raul Nogueira, MD

EMORY UNIVERSITY

Raul G Nogueira. Late Window Treatment: DAWN, AURORA and the Effect of Time. Loeng ESO 2018 aastakonverents

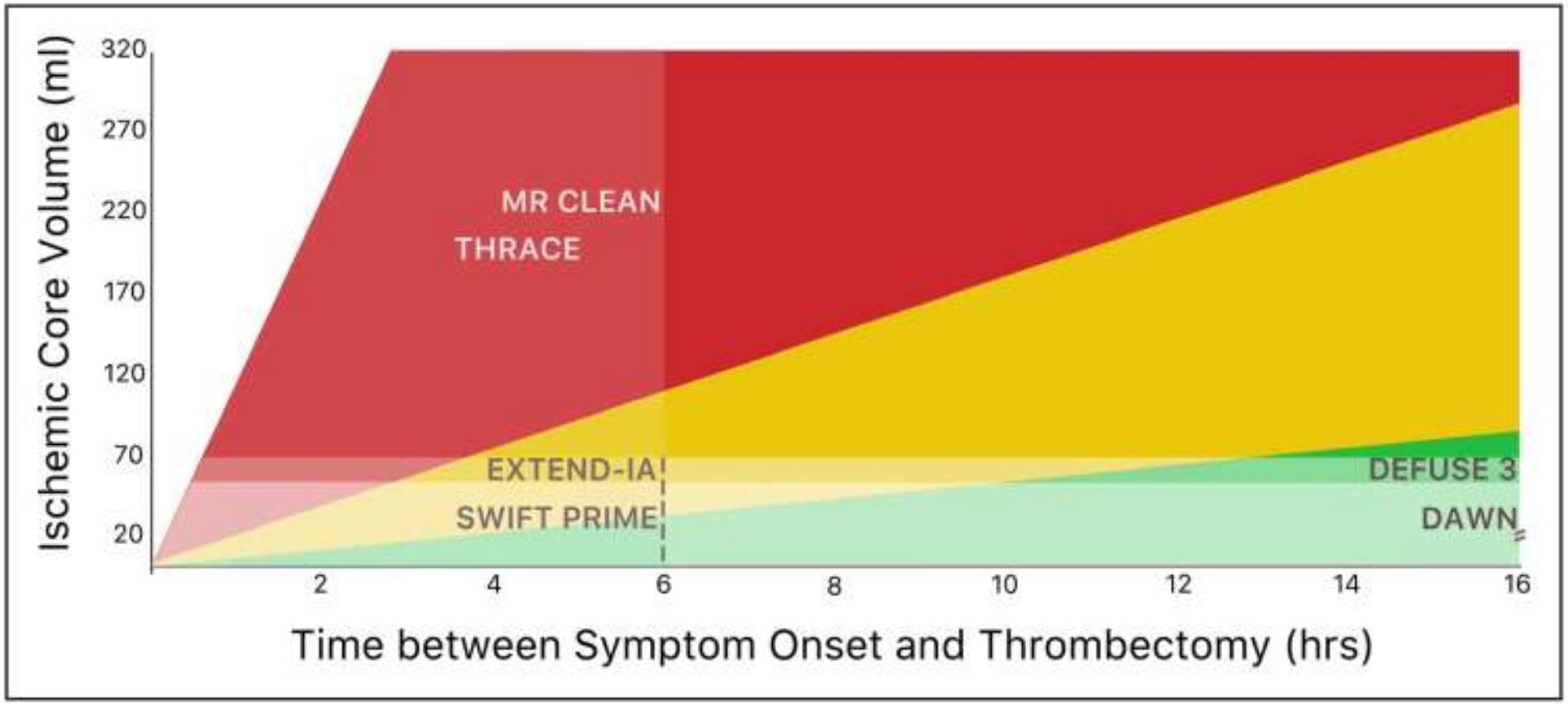
Hilise ajaakna paradoks

- Insuldi erinevad profiilid



Raul G Nogueira. Late Window Treatment: DAWN, AURORA and the Effect of Time. Loeng ESO 2018 aastakonverents

Hilise ajaakna paradoks



Albers G W. Late Window Paradox. Stroke 2018

Hilise ajaakna insult ja TE

- ASA/AHA 2018 ja 2019 ravijuhis

3.7.3. 6 to 24 Hours From Onset	COR	LOE	New, Revised, or Unchanged
1. 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**	New recommendation.
2. 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**	New recommendation.
The DAWN trial used clinical-core mismatch (a combination of NIHSS score and imaging findings on CTP or DW-MRI) as eligibility criteria to select patients with large anterior circulation vessel occlusion for treatment with mechanical thrombectomy between 6 and 24 hours from last known normal. This trial demonstrated an overall benefit in function outcome at 90 days in the treatment group (mRS score 0–2, 49% versus 13%; adjusted difference, 33% [95% CI, 21–44]; posterior probability of superiority >0.999).[51] In DAWN, there were few strokes with witnessed onset (12%). The DEFUSE 3 trial used perfusion-core mismatch and maximum core size as imaging criteria to select patients with large anterior circulation occlusion 6 to 16 hours from last seen well for mechanical thrombectomy. This trial showed a benefit in functional outcome at 90 days in the treated group (mRS score 0–2, 44.6% versus 16.7%; RR, 2.67 [95% CI, 1.60–4.48]; *P*<0.0001).[52] Benefit was independently demonstrated for the subgroup of patients who met DAWN eligibility criteria and for the subgroup who did not. DAWN and DEFUSE 3 are the only RCTs showing benefit of mechanical thrombectomy >6 hours from onset. Therefore, only the eligibility criteria from one or the other of these trials should be used for patient selection. Although future RCTs may demonstrate that additional eligibility criteria can be used to select patients who benefit from mechanical thrombectomy, at this time, the DAWN or DEFUSE 3 eligibility should be strictly adhered to in clinical practice.[51,52]			See Table XVII in online Data Supplement 1.

Hilise ajaakna insuldi selektsiooni kriteeriumid

DAWN trial eligibility require all of the following:

- Treatment (femoral puncture) can start within 6 to 24 hours of time last known to be well
- Failed or contraindicated for IV tPA
- A deficit on the NIHSS of ≥10 points
- No significant prestroke disability: Baseline mRS score ≤1
- Baseline infarct involving <1/3 of MCA territory
- Intracranial occlusion of the ICA or M1 segment of the MCA
- A clinical-core mismatch according to age:
  - Age ≥80 years: NIHSS ≥10 and infarct volume <21 mL
  - Age <80 years: NIHSS 10 to 19 and infarct volume <31 mL
  - Age <80 years: NIHSS ≥20 and infarct volume <51 mL

Vajalik minimaalselt MRT-DWI, võimalik ka KTP/MRP

DEFUSE 3 trial eligibility require all of the following:

- Treatment (femoral puncture) can start within 6 to 16 hours of time last known to be well
- A deficit on the NIHSS of ≥6 points
- Only slight or no prestroke disability: Baseline mRS score ≤2
- Occlusion of the cervical or intracranial ICA (with or without tandem MCA lesions) or the M1 segment of the MCA
- Age 18 to 90 years
- A target mismatch profile on CT perfusion or MRI defined as:
  - An ischemic core volume <70 mL, and
  - A mismatch ratio (the volume of the perfusion lesion divided by the volume of the ischemic core) >1.8, and
  - A mismatch volume (volume of perfusion lesion minus the volume of the ischemic core) >15 mL

Vajalik KT-perfusioon või MRT-perfusioon

UpToDate®

Hilise ajaakna insuldi selektsiooni kriteeriumid

Eligibility for Endovascular Trial Enrollment in the 6- to 24-Hour Time Window

Analysis of a Single Comprehensive Stroke Center

Ashutosh P. Jadhav, MD, PhD; Shashvat M. Desai, MD; Cynthia L. Kenmuir, MD, PhD; Marcelo Rocha, MD, PhD; Matthew T. Starr, MD; Bradley J. Molyneaux, MD, PhD; Bradley A. Gross, MD; Brian T. Jankowitz, MD; Tudor G. Jovin, MD

Conclusions—Of all patients with acute ischemic stroke presenting to a single comprehensive stroke center, 1.7% of patients qualified for DAWN clinical trial enrollment with an additional 0.6% to 1% qualifying for the DEFUSE-3 trial. These data predict an increase in thrombectomy utilization with important implications for comprehensive stroke center resource optimization and stroke systems of care. **(*Stroke*. 2018;49:1015-1017. DOI: 10.1161/STROKEAHA.117.020273.)**

Kas hilises ajaaknas insuldi endovaskulaarse ravi näidustuse määramisel on täiendavad kuvamismeetodid ilmtingimata vajalikud?

Raul G Nogueira. Late Window Treatment: DAWN, AURORA and the Effect of Time. Loeng ESO 2018 aastakonverents

„Natiiv KT-peast on nagu hea vein – läheb ajaga ainult paremaks“

Raul G Nogueira. Late Window Treatment: DAWN, AURORA and the Effect of Time. Loeng ESO 2018 aastakonverents

Table 1 Interobserver reliability of ASPECTS scoring on NCCT and CTASI in different time categories from stroke onset

	NCCT		CTASI	
Time	Intraclass correlation	95% CI (lower, upper)	Intraclass correlation	95% CI (lower, upper)
0–90	0·48*	0·28–0·71	0·96*	0·93–0·98
91–180	0·80	0·66–0·90	0·94	0·89–0·97
181–360	0·81	0·69–0·91	0·87	0·78–0·94
>360	0·89	0·81–0·95	0·89	0·80–0·95
Overall	0·78	0·69–0·84	0·93	0·90–0·95

*Comparison of the intraclass correlation at 0–90 mins vs. 90 mins or greater, $P = 0{\cdot}0001$ for NCCT and $P = 0{\cdot}178$ for CTASI.
ASPECTS, Alberta Stroke Program Early CT Score; NCCT, noncontrast computed tomography; CTASI, CT angiography source image; CI, confidence interval.

Bal et al. International Journal of Stroke. Vol 10, January 2015, 55–60

Kokkuvõte

- Ajuarteri trombektoomia on väga efektiivne ja suhteliselt ohutu ägeda insuldi ravimeetod
- Hiljutiste kliiniliste uuringute valguses ei ole nö ravi ajaaken enam ainuke reperfusioonravi kriteerium

- Insuldi ravi põhiprintsiibid ei ole siiski muutunud:

> waste no time assembling the requisite focused clinical stroke history and examination, waste no time imaging the brain and blood vessels, waste no time synthesizing the clinical and radiological pictures, waste no time declaratively diagnosing, and waste no time offering definitive fast treatment.

Schellinger PD et al. Stroke. 2018;49:2559-2561.

Tänan tähelepanu eest!

Suur tänu Äli Roose, Dmitry Maksin, Vladislav Malikov, Kalle Põder!