



REPERFUZIJSKA TERAPIJA AKUTNOG ISHEMIJSKOG MOŽDANOG UDARA

USPJEŠNO LIJEČENJE ZA SVAKU ŽIVOTNU DOB

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Zavod za intenzivno liječenje i cerebrovaskularne bolesti Kliike za neurologiju KBC Zagreb

Specijalizirani centar za liječenje MU - ESO



Samo kao uvod:

- ❖ 16 milijuna ljudi u svijetu svake godine oboljeva od moždanog udara, a oko 6 milijuna oboljelih umire, projekcija za 2030 – 23 milijuna oboljelih/7.8 milijuna umrlih
- ❖ 2/3 oboljelih je starije od 75 godina, a 1/3 je starija od 80 godina
- ❖ Jedina uspješna terapija u akutnoj fazi je rekanalizacijska terapija
- ❖ Rekanalizacijska terapija nema dobne granice!

No:

1. Da li i stariji bolesnici dobivaju rekanalizacijsku terapiju u istom omjeru?
2. Da li su ishodi usporedivi
3. Da li u starijoj populaciji imamo isti postotak komplikacija?
4. Da li postoji “cost-benefit”?

Qureshi et al.: **Intraarterial Recanalization Techniques for Patients 80 Years or Older with Acute Ischemic Stroke: Pooled Analysis from 4 Prospective Studies.** AJNR 30, Jun-Jul 2009

Chandra et al.: **Clinical outcome after intraarterial Stroke therapy in the very elderly: why is it so heterogeneous?.** Frontiers in Neurology. April 2014 (5).

Alawieh et al.: **Outcomes of endovascular thrombectomy in the elderly: a real world multicenter study.** J. Neurointervent. Surg. 2018.



ČINJENICE:

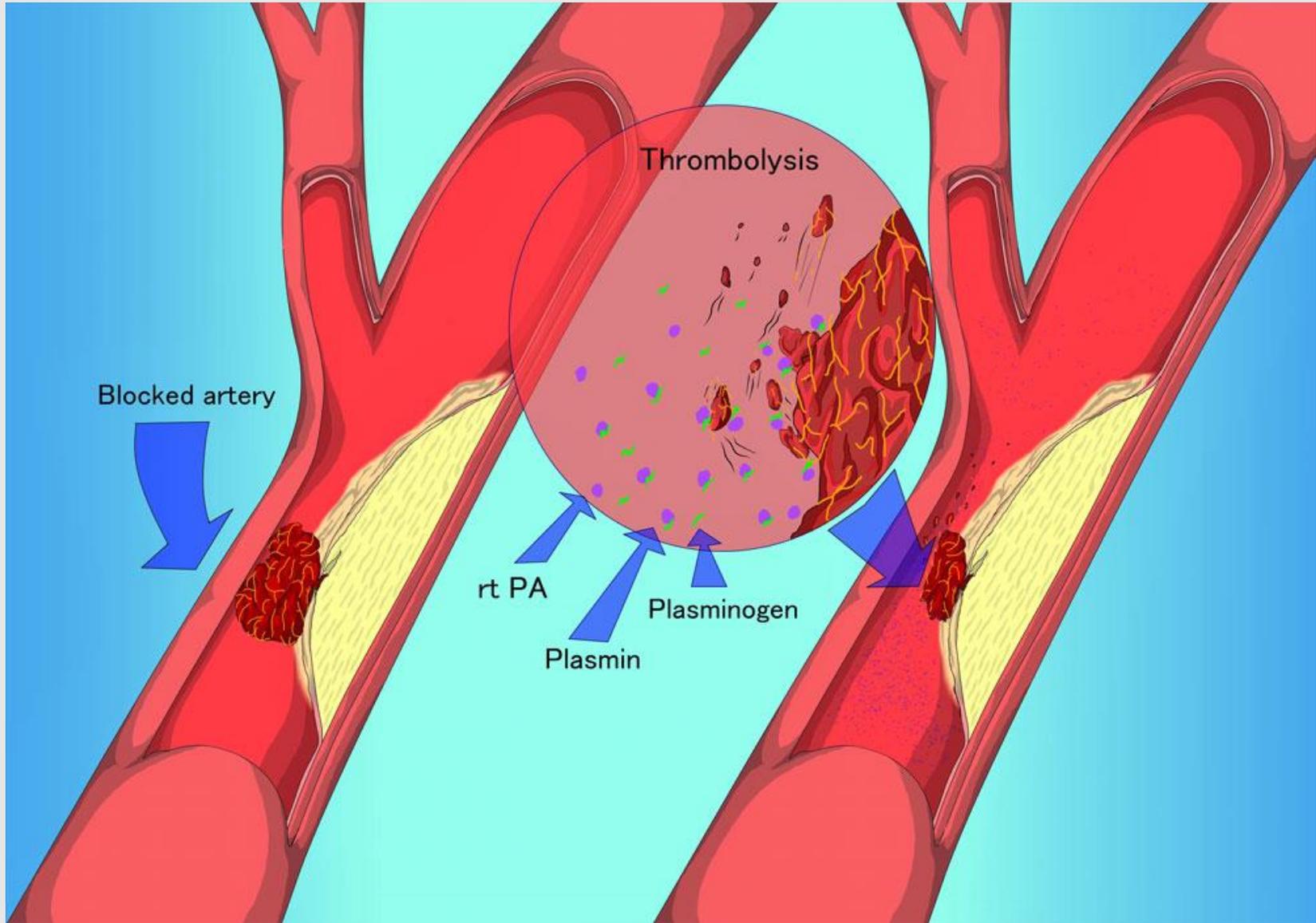
**KOLATERALE
LOKALNI ČIMBENICI – TROMBOZA “in situ”
KARDIOEMBOLIJSKI MU ČEŠĆI
KOMORBIDITETI
PREMORBIDNI FUNKCIONALNI STATUS**

TL: niži omjer dobrog funkcionalnog ishoda nego kod mlađih bolesnika, isti omjer komplikacija, pitanje TL i kardioembolijskog MU, veći inicijalni volumen infarciranog tkiva



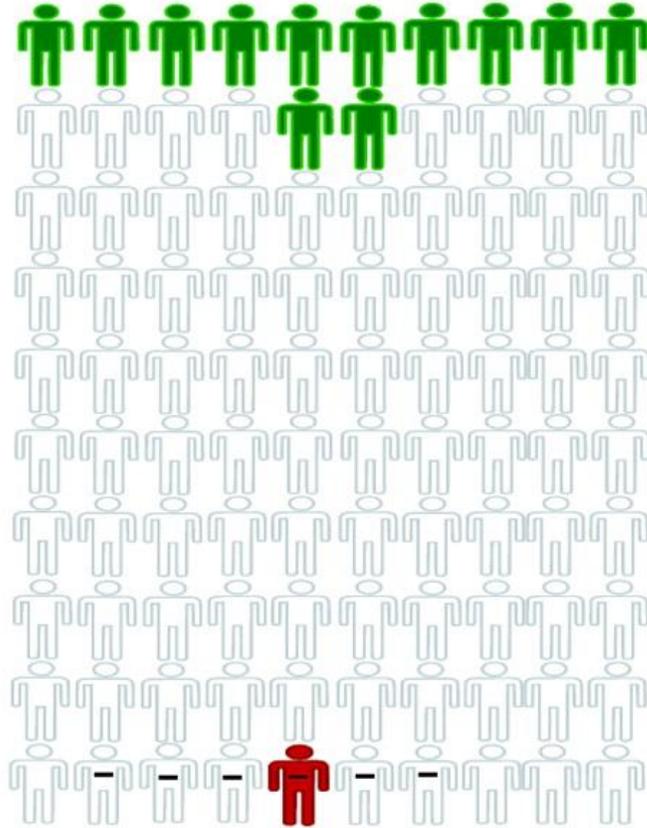
Conclusions— Aging of the population is a growing reality in Western societies and this translates into an increasing demand on healthcare systems. In our study, patients with stroke over 80 had higher risk-adjusted fatality, longer hospitalization, and were less likely to be discharged to their original place of residence. Strategies need to be implemented to facilitate equal access to specialized stroke care for the elderly.





TPA for Cerebral Ischemia within 3 Hours of Onset-Select Changes in Outcome Due to Treatment

A1



Changes in final outcome as a result of treatment:

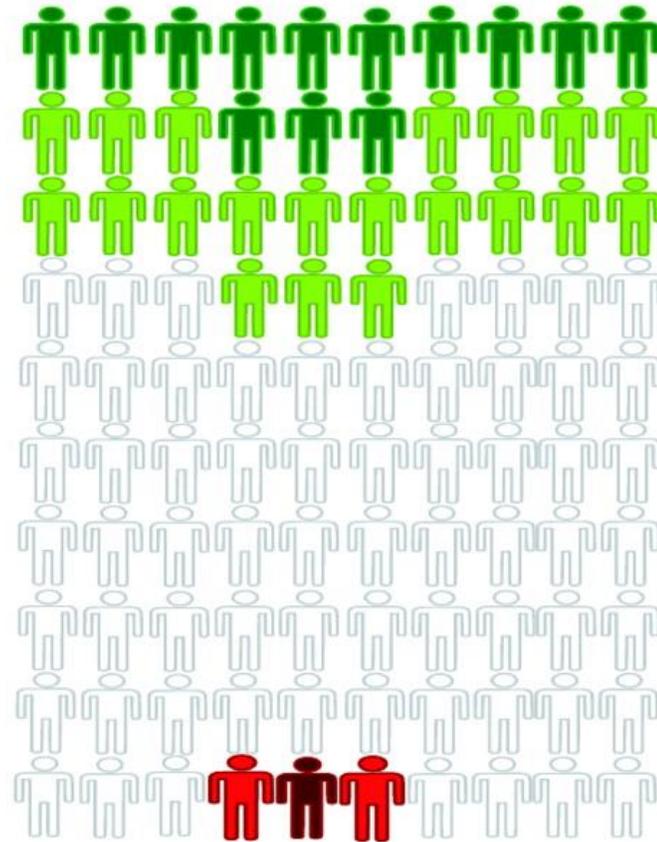
- Normal or nearly normal
- No major change
- Severely disabled or dead

Early course:

- No early worsening with brain bleeding
- Early worsening with brain bleeding

TPA for Cerebral Ischemia within 3 Hours of Onset- Changes in Final Outcome Due to Treatment

A2

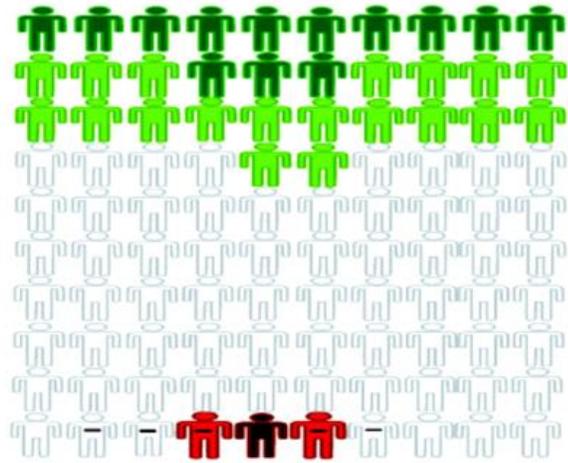


Changes in final outcome as a result of treatment:

- Normal or nearly normal
- Better
- No major change
- Worse
- Severely disabled or dead



Impact of Ischemic Stroke Treatment



Changes in final outcome as a result of tPA within 3 h

- Normal or nearly normal
- Better
- No major change
- Worse
- Severely disabled or dead

Early course:

- No early worsening with brain bleeding
- Early worsening with brain bleeding

Treatment	NNT	Benefit (%)
tPA 1-3 h *	3	32
Thrombectomy	2-3	40
tPA 3-4.5 h	6	16
IA lytics	7	14
Aspirin	77	1

For every 100 patients treated with IV tPA for stroke within 3 h *:

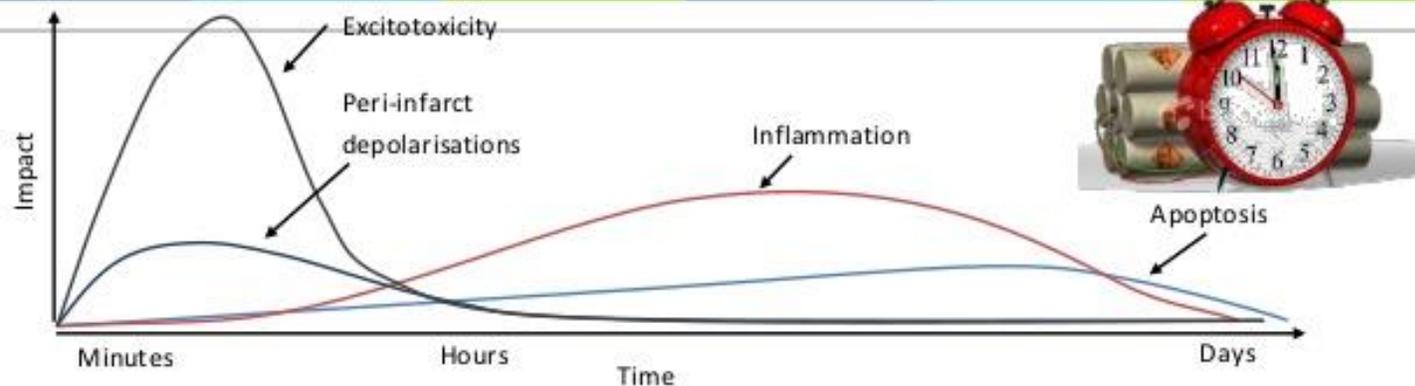
- 32** have better outcome
- 13** become normal or near normal
- 6** have ICH
- 3** become worse outcome or dead



@jackcfchong



“Time is brain”



Estimated Pace of Neural Circuitry Loss In Typical Large-Vessel Supratentorial Acute Ischaemic Stroke

	Neurons Lost	Synapses Lost	Myelinated Fibres Lost	Accelerated Aging
Per Stroke	1.2 billion	8.3 trillion	7140 km	36 y
Per Hour	120 million	830 billion	714 km	3.6 y
Per Minute	1.9 million	14 billion	12 km	3.1 wk
Per Second	32,000	230 million	200 m	8.7 h

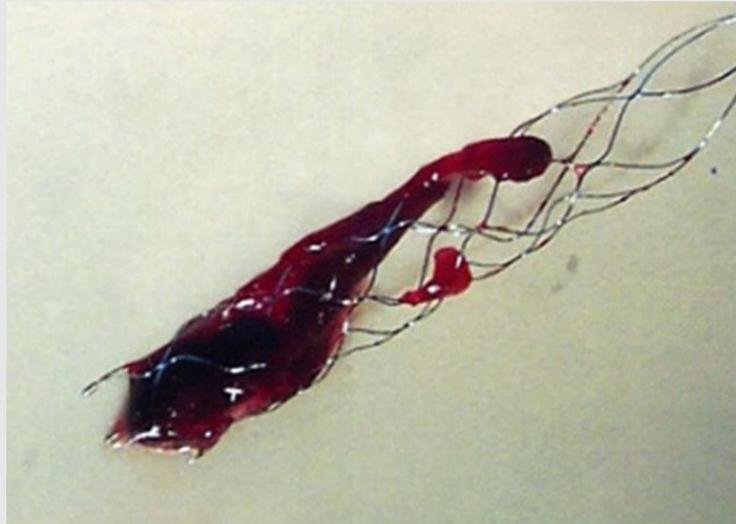
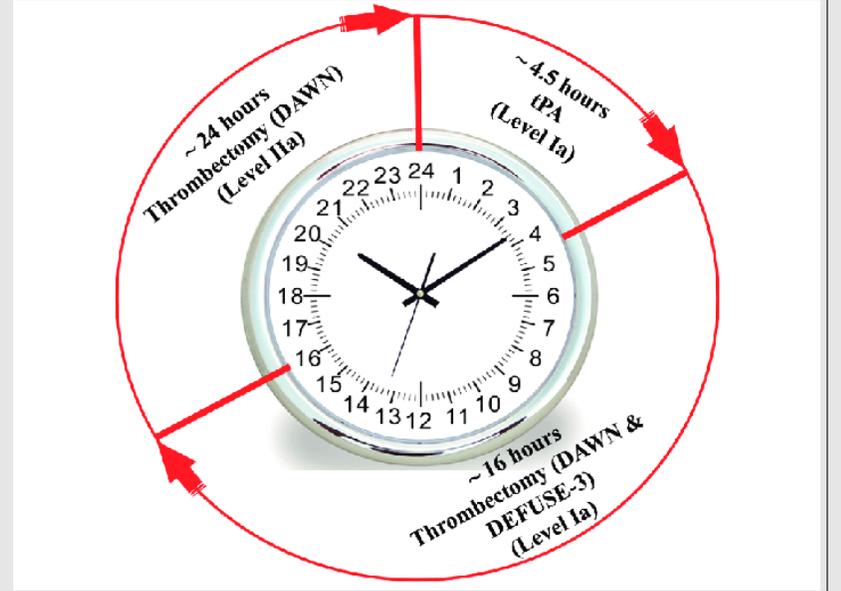
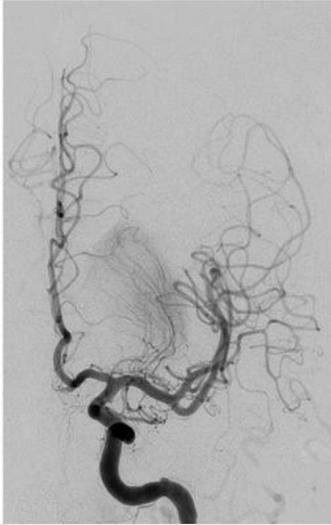
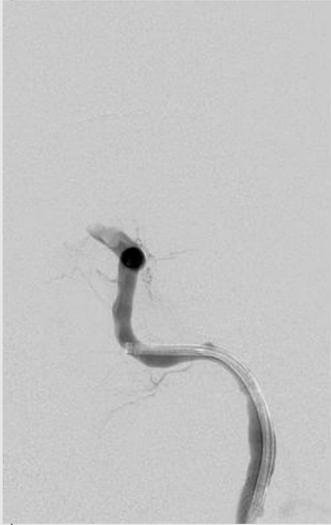
Saver. Stroke 2006;37:263-266.

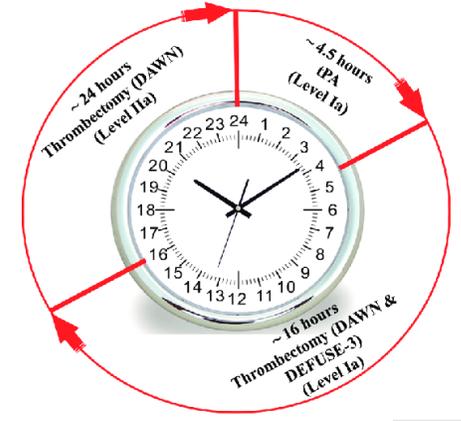
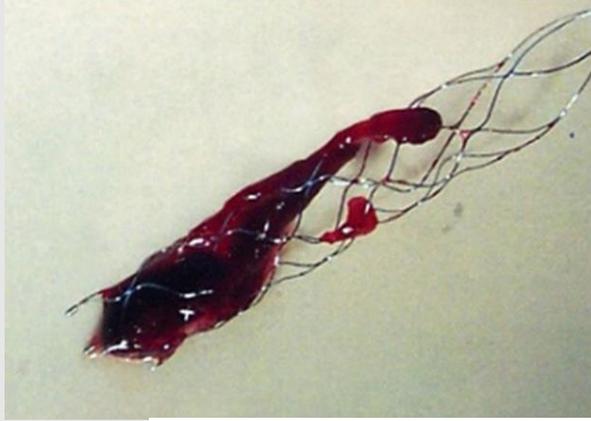


Višestruki mehanizmi oštećenja koji uključuju neurotoksičnost, upalne promjene, promjene KVB

Vrijeme ima presudan značaj – 1.9milijuna neurona/1 min







Bolesnici stariji od 80 godina imaju lošiju prognozu od mlađih bolesnika

ALI

Bolesnici kod kojih je provedena rekanalizacija imaju bolji ishod od onih koji su liječeni konzervativno

Oprezna selekcija ali dob nije granica!

Qureshi et al.: **Intraarterial Recanalization Techniques for Patients 80 Years or Older with Acute Ischemic Stroke: Pooled Analysis from 4 Prospective Studies.**

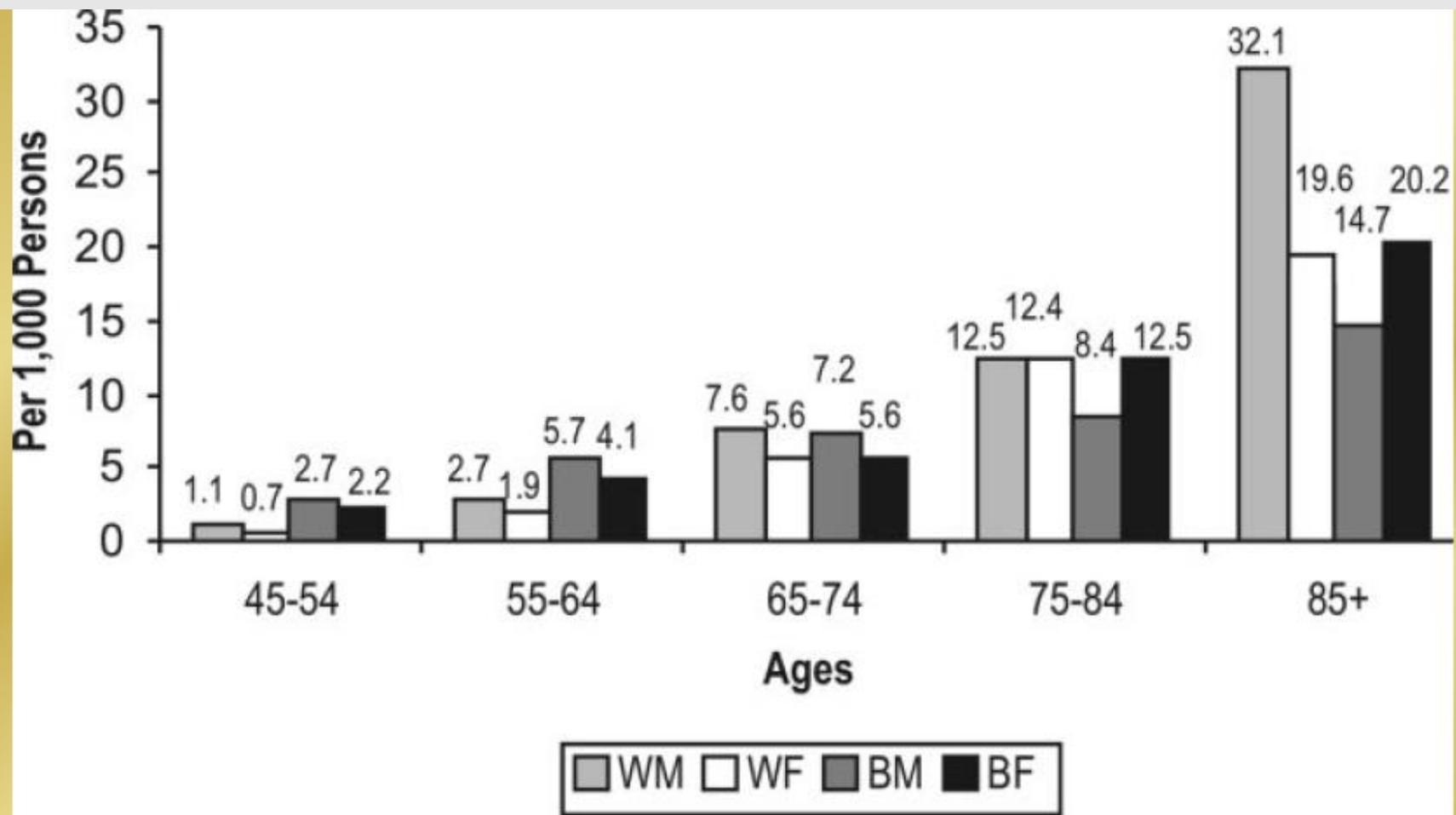
AJNR 30, Jun-Jul 2009

Chandra et al.: **Clinical outcome after intraarterial Stroke therapy in the very elderly: why is it so heterogeneous?** Frontiers in Neurology. April 2014 (5).

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UČESTALOST MU RASTE S DOBI



Vascular risk factors

	Age <80	Age ≥80
Diabetes	557 (38%)*	229 (29%)*
Hypertension	1187 (81%)*	686 (87%)*
Heart Disease	615 (42%)*	387 (49%)*
Atrial Fibrillation	205 (14%)*	331 (42%)*
Coumadin use	176 (12%)*	142 (18%)*
Statin use	762 (52%)*	347 (44%)*

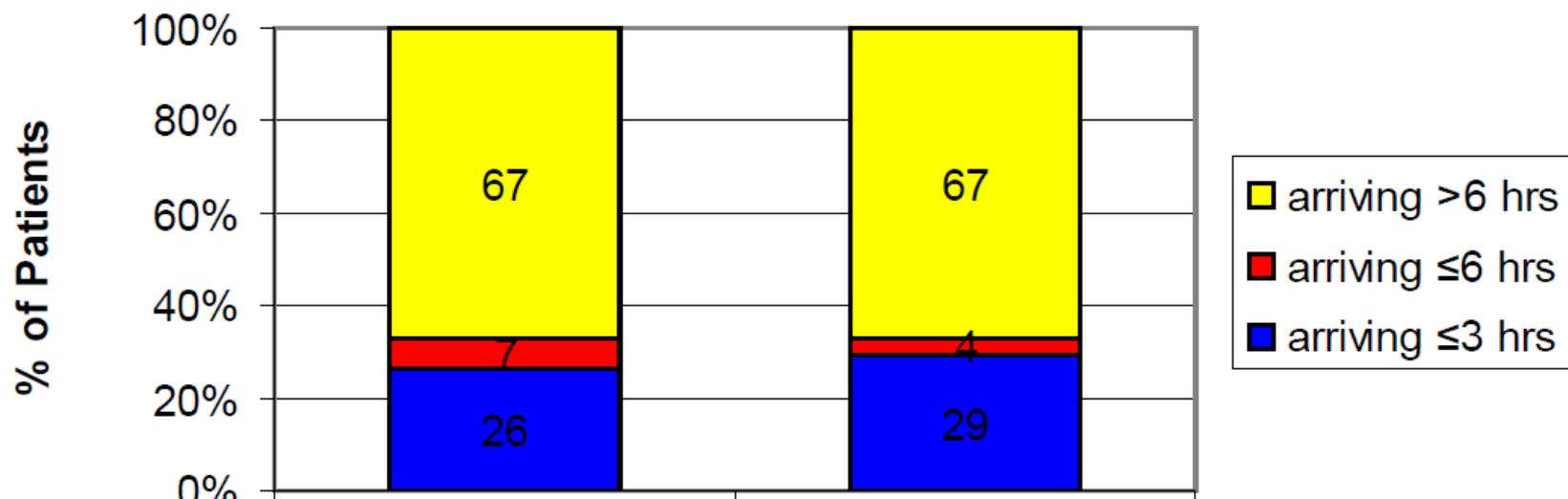
Figures in parentheses are percentages, * $p < 0.05$; χ^2 test.

Denti et al JAGS 2009;58:12-17

Simpson et al Stroke 2005;35:1771-5



Triage information for Patients Arriving to Hospital with AIS



VRIJEME DOLASKA U BOLNICU



Stroke Severity

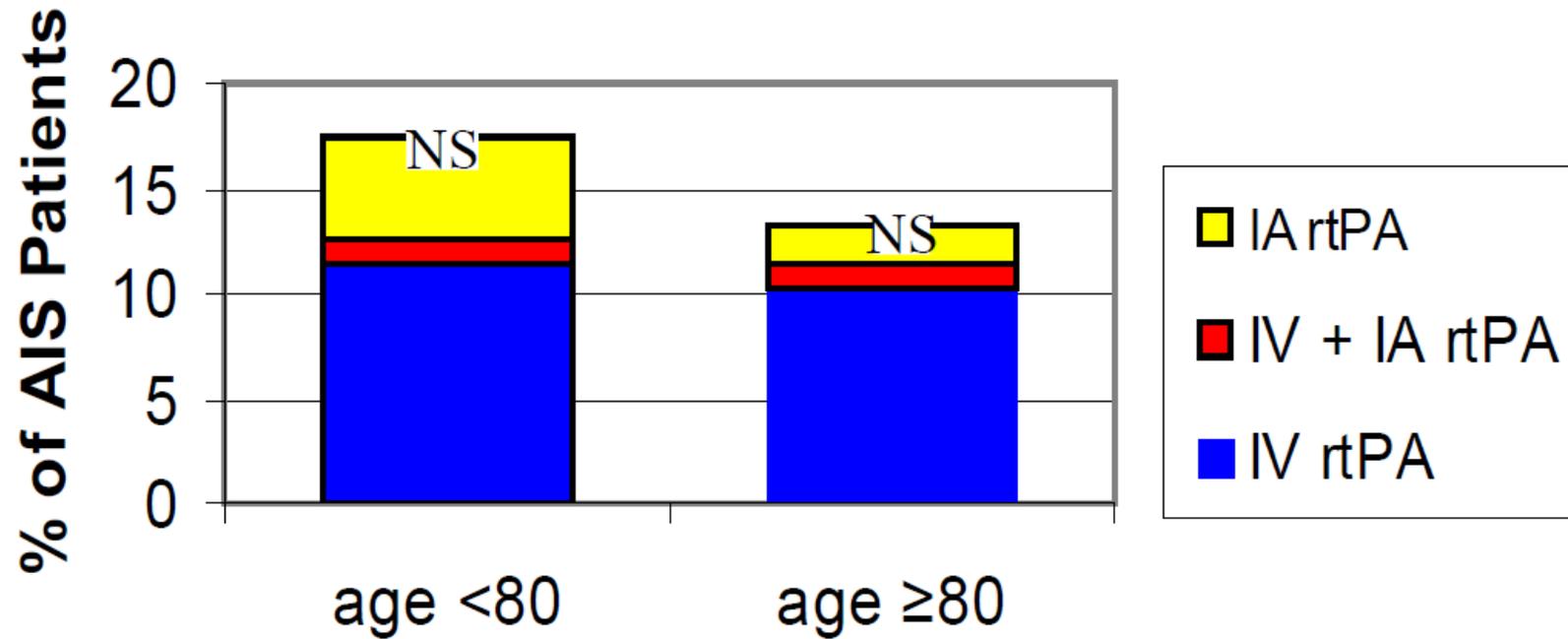
	Age <80	Age ≥80
Admission NIHSS	6.8 ± .36 *	9.3 ± .57 *
Male	6.5 ± .49	7.8 ± .86 *
Female	6.9 ± .56	10.2 ± .75 *

Figures in parentheses are percentages, ** p < 0.05; χ^2 test.

TEŽINA MOŽDANOG UDARA



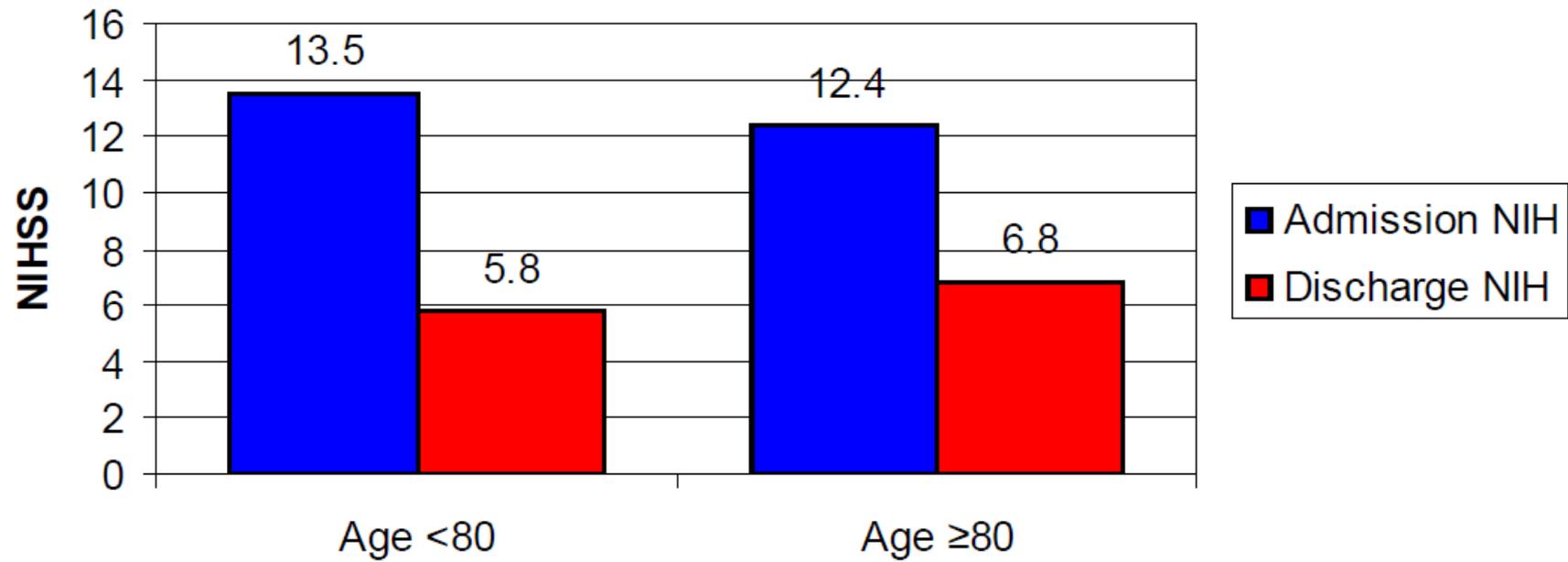
Rates of rtPA Use



PRIMJENA REKANALIZACIJSKE TERAPIJE



NIHSS on Admission and Discharge in Patients Receiving Thrombolytics



Symptomatic ICH

	IV rtPA	IA rtPA
age <80	8/166 (5.0%)	9/97 (9%)*
age ≥ 80	2/81 (2.2%)	7/31 (22%)*

Figures in parentheses are percentages, * $p < 0.05$; χ^2 test.

POSTOTAK KOMPLIKACIJA



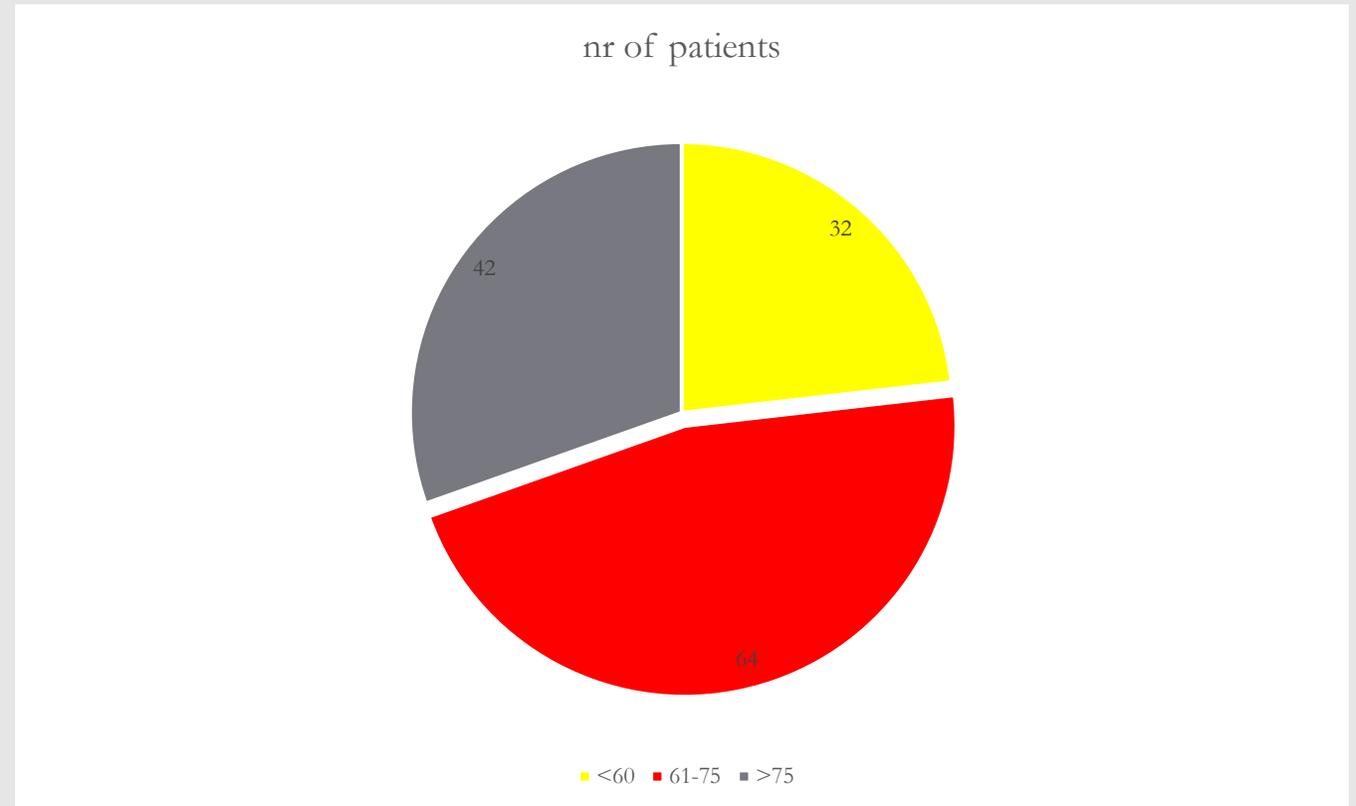
Retrospektivna studija u našem Centru

University Hospital Zagreb – Neurological Intensive Care
Unit, ESO Comprehensive Stroke Center

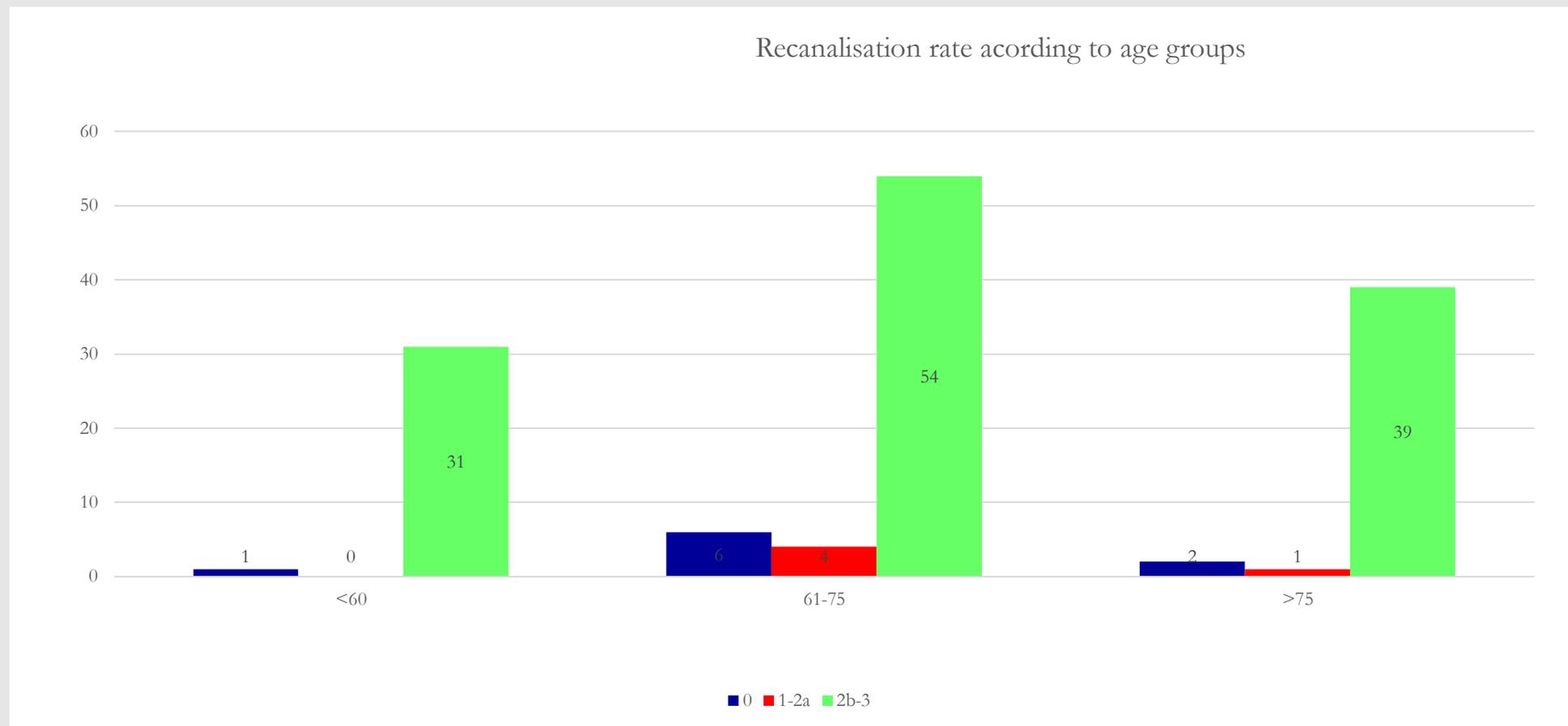
2019

Bolesnici s akutnim MU I LVO
Indikacija za trombektomiju

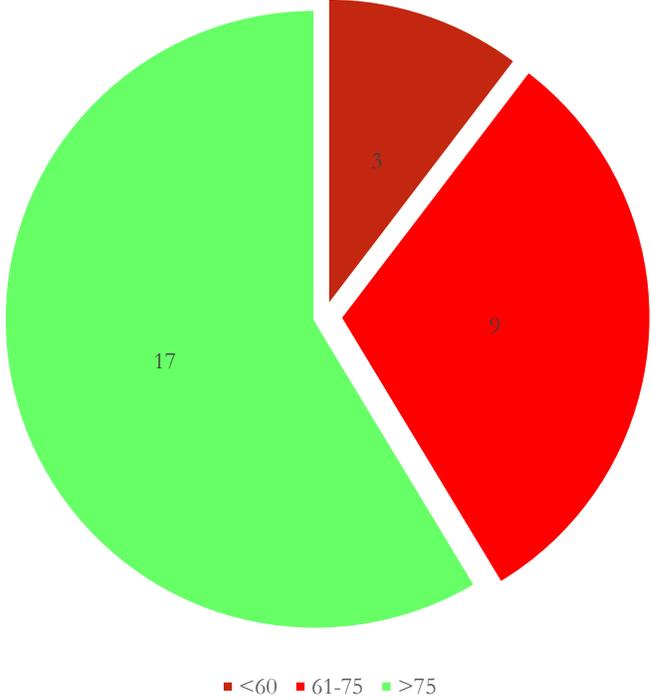
139 bolesnika TK (sa ili bez TL)
Standardno zbrinjavanje
Stopa rekanalizacije
Funkcionalni ishod (mRS) 90 dana



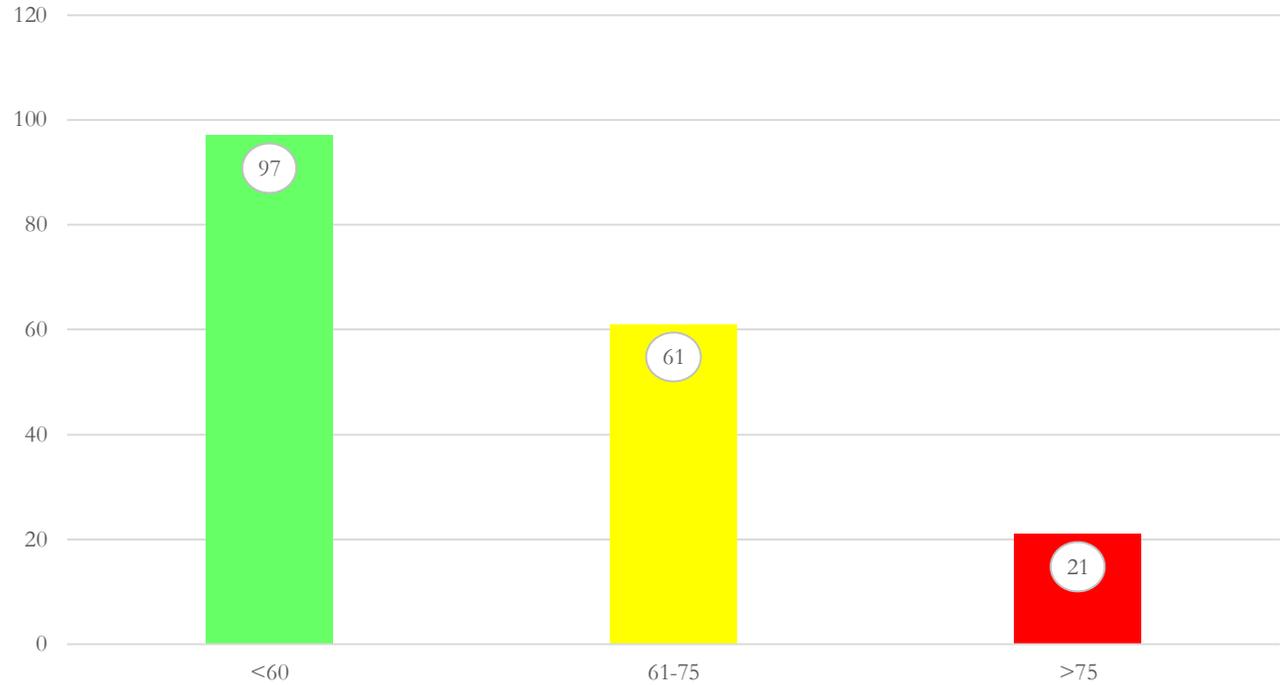
Rezultati



mortality rate for different age groups in percentage



mRS 0-3 (functionally independent) in percentage



Zaključci iz naše studije

Dob NIJE kontraindikacija za rekanalizacijsku terapiju bilo kojeg modaliteta

Ishod je općenito lošiji za starije od 75 nego za mlađe od 75

Ishod je značajno bolji za bolesnike koji su liječeni rekanalizacijskom terapijom nego za one koji to nisu

Komorbiditet i etiologija MU su glavni prediktori ishoda



ŠTO KAŽU DRUGI...

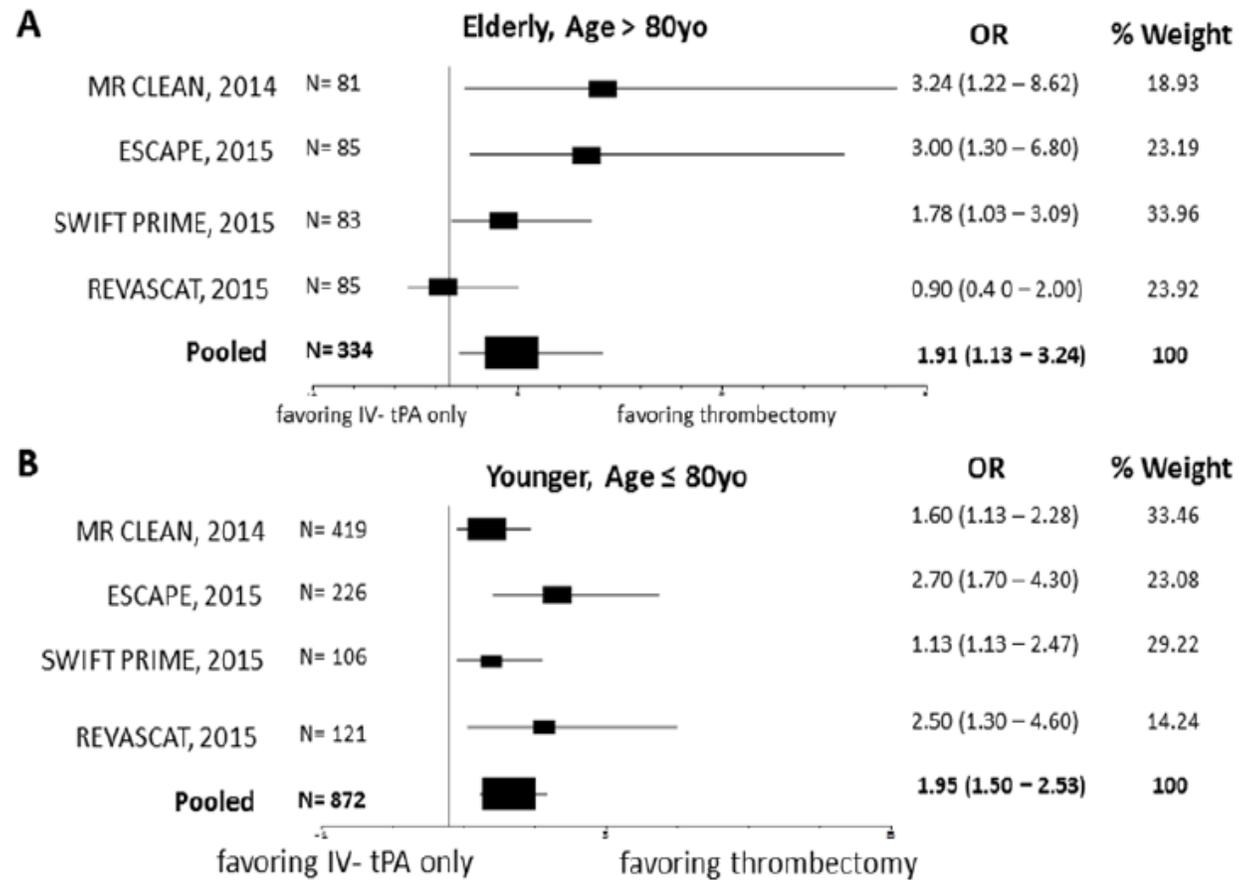
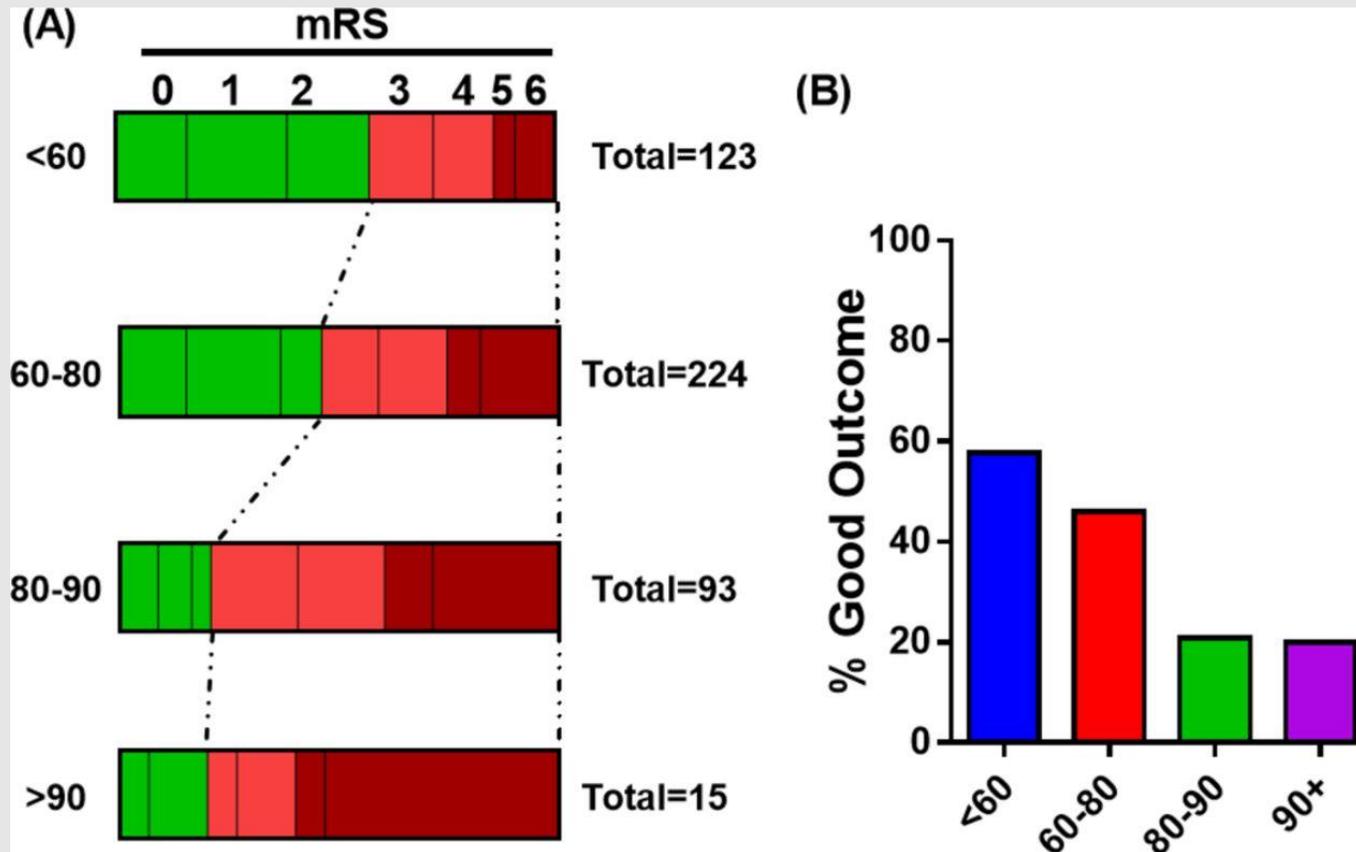


Figure 1: Adjusted odds ratio of improvement in modified Rankin Score (mRS) at 90 days, stratified by age.



ŠTO KAŽU DRUGI...



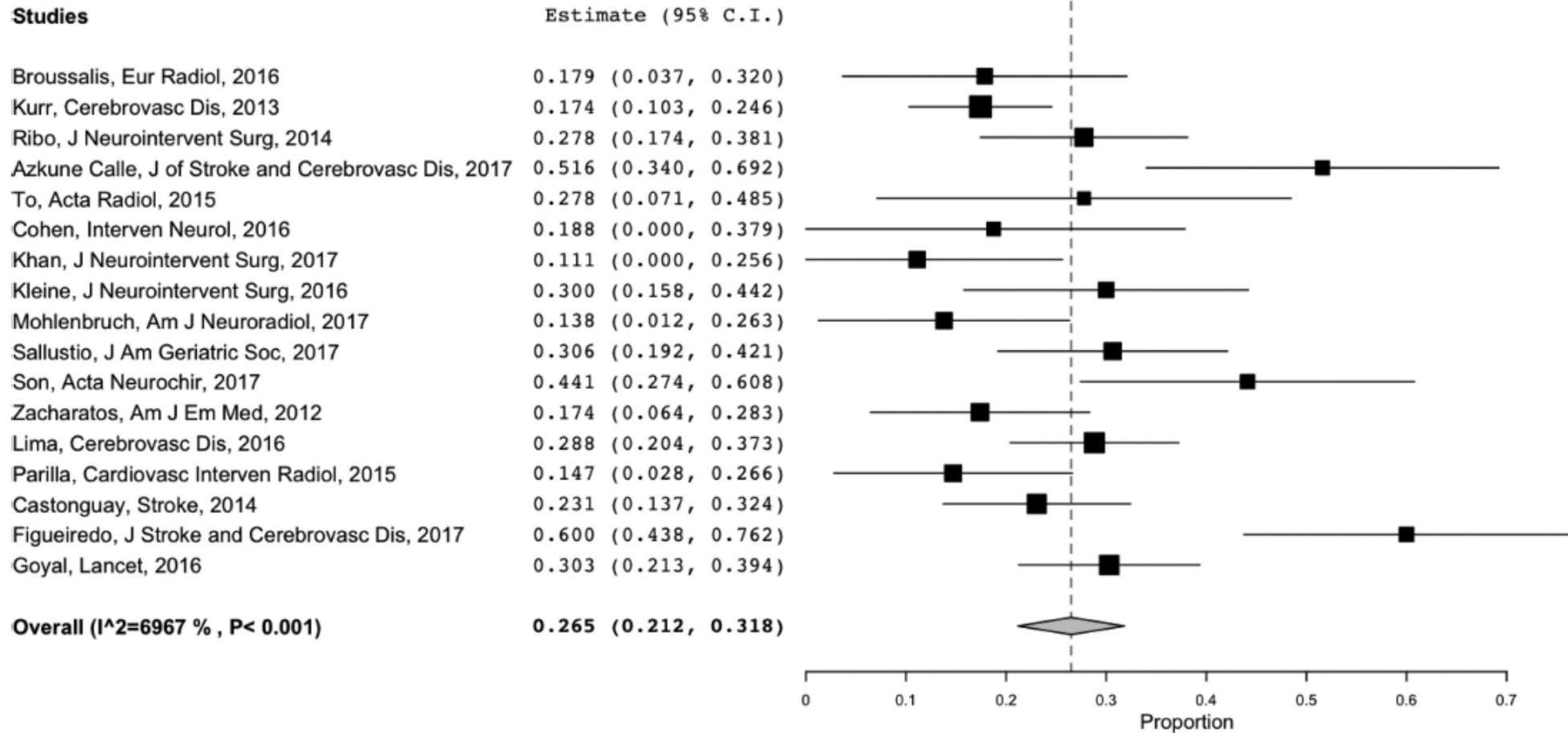


FIG 2. Meta-analysis forest plot for good functional outcomes at 3 months.



Summary of clinical outcomes

Outcome		Heterogeneity (I ²)
Good functional outcome at 3 mo	27% (95% CI, 21%–32%)	70%
Mortality within 3 mo	34% (95% CI, 23%–44%)	91%
Successful revascularization	78% (95% CI, 72%–85%)	83%
Procedure-related complication	11% (95% CI, 4%–17%)	56%
Any ICH	24% (95% CI, 15%–32%)	83%
Symptomatic ICH	8% (95% CI, 5%–10%)	61%
Time to groin (min)	251 (95% CI, 224–278)	88%
Procedure time (min)	99 (95% CI, 67–131)	98%

Note:—ICH indicates intracranial hemorrhage.

Najnoviji podaci

Meta analize, veliki broj bolesnika – bolji ishod s jednakim rizikom za komplikacije



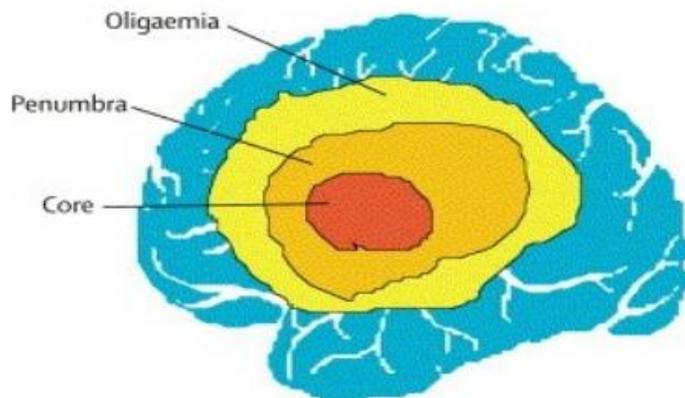


ZAŠTO MORAMO
LIJEČITI AKUTNI MU S
REKANALIZACIJSKOM
TERAPIJOM?



Penumbrae of Ischemic Stroke

60



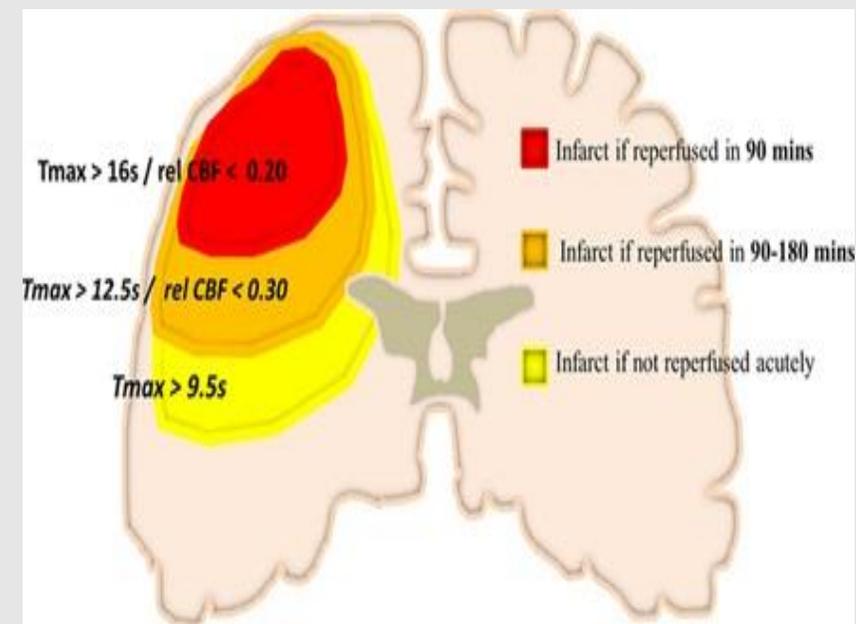
- Penumbrae is the target of any reperfusion therapy
- The fate of brain tissue depends on
 - Time
 - Cerebral blood flow
 - Occluded arterial flow
 - Collateral blood flow
- Time is brain

Cilj „spasavanja” je penumbra
Ishod ovisi o vremenu/kolateralama/???

CTP to recanalization time: the key for accurate determination of infarct core?

Luciana Catanese, MD

[d’Esterre CD, Boesen ME, Ahn SH, Pordeli P, Najm M, Minhas P, et al. Time-Dependent Computed Tomographic Perfusion Thresholds for Patients With Acute Ischemic Stroke. Stroke. 2015](#)



Modified Rankin score 0 1 2 3 4 5 Death

All patients



Age ≤80



Age >80



Mechanical Thrombectomy Procedural Overview



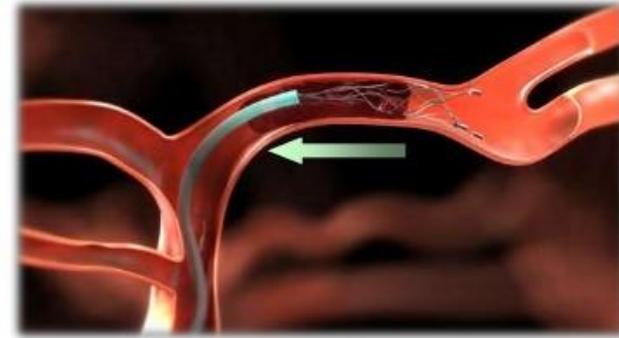
Deployment of stent in the clot:

Stent embedded in clot –
traps the clot within device mesh.

15

Allina Health

Mechanical Thrombectomy Procedural Overview



Positioning and Deployment of stent in the clot:

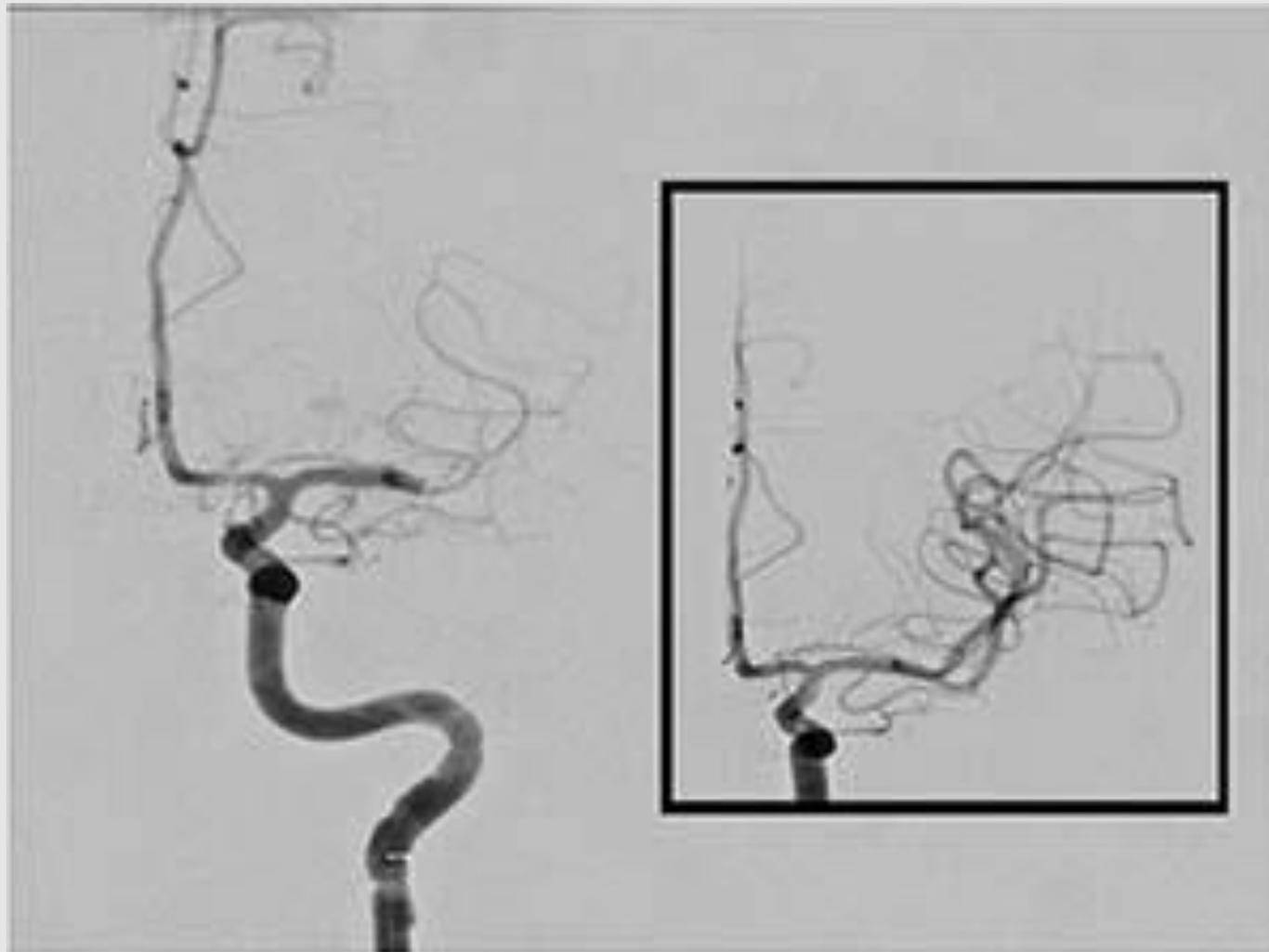
Catheter pulled back, stent deployed into clot.

14

Allina Health



Angiografija –
prije i poslije



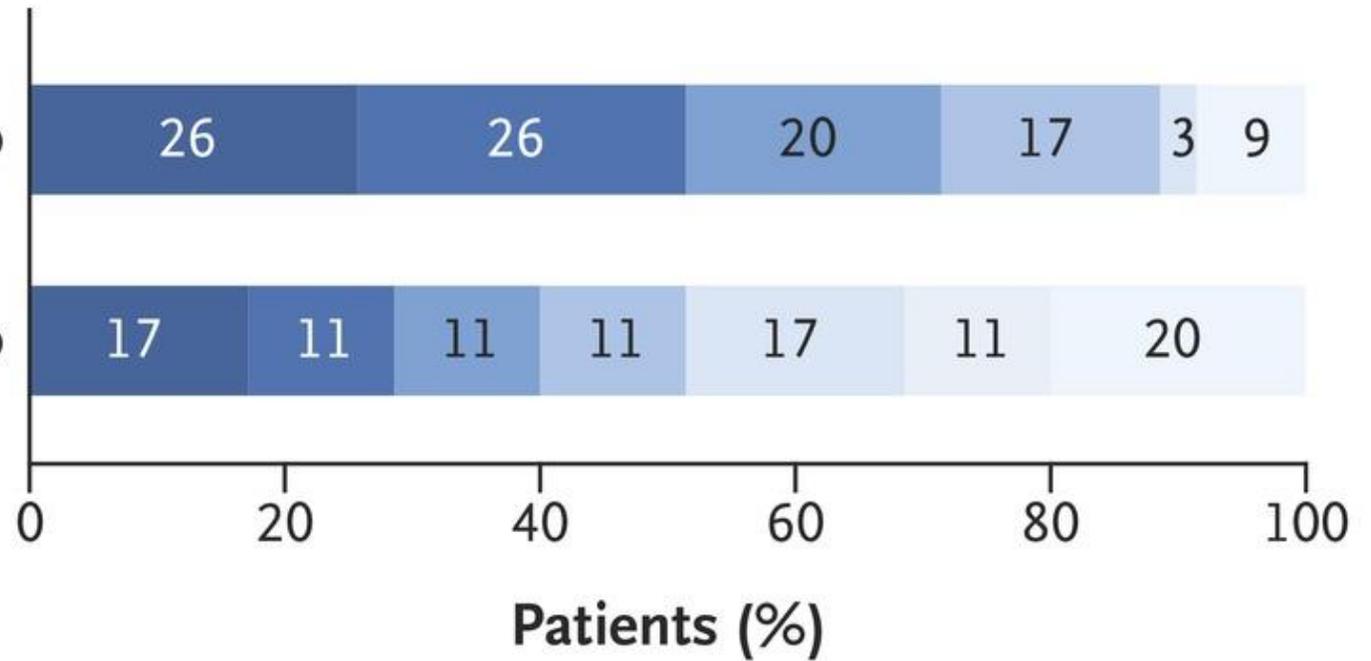
Score on Modified Rankin Scale

No symptoms ← → Death

■ 0 ■ 1 ■ 2 ■ 3 ■ 4 ■ 5 ■ 6

Endovascular-Therapy Group

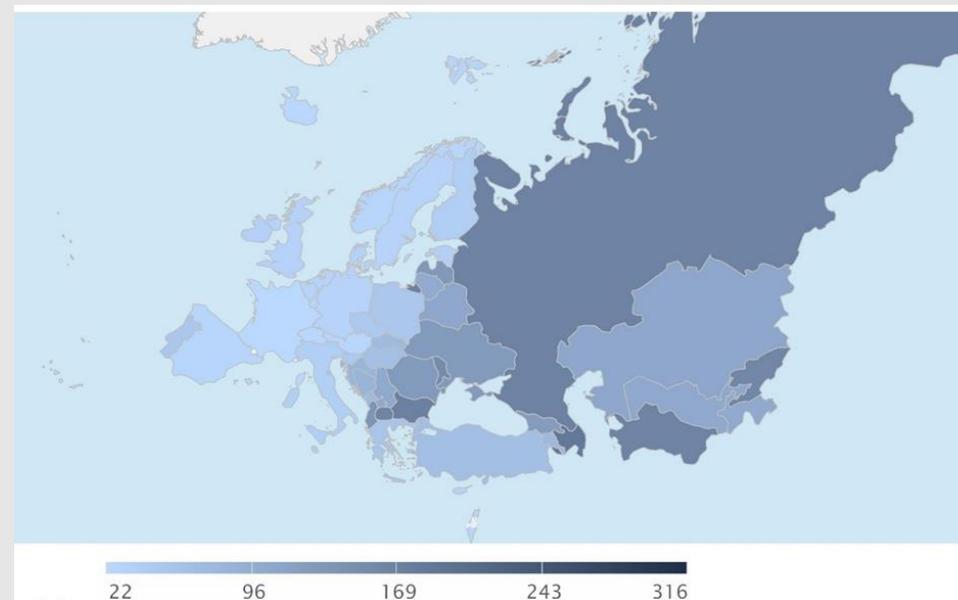
Alteplase-Only Group



Po mortalitetu od cerebrovaskularnih bolesti Hrvatska sa standardiziranom stopom smrtnosti od 81/100.000 spada među zemlje koje su iznad prosjeka europske regije. Prosjek za zemlje Europske regije iznosi 77/100.000, a za zemlje EU 42/100.000, a raspon stopa za zemlje EU je od 22-171/100.000. (Francuska-Bugarska)(slika 5). Usporedbom mortaliteta u dobi do 65 godina, Hrvatska sa standardiziranom stopom od 11,3/100.000 spada u zemlje koje su ispod prosjeka europske regije, a iznosi 16,6/100.000, a prosjek za zemlje EU je 7,0.(slika 6)

Incidencija 270 – 290 /100.000

Kako je kod nas?



NACIONALNA STRATEGIJA PREVENCIJE I LIJEČENJA MOŽDANOG UDARA

Prepoznaj simptome!

Utrnulost ruke

Jedna ruka pada i ne može se zadržati ispružena u visini ramena.



Disfunkcija govora

Govor postaje nerazumljiv.



Asimetrija lica

Jedna strana lica se objesi, osmijeh je iskrivljen.



Reagirajte odmah

Ako se naglo pojavi bilo koji od ovih simptoma radi se o moždanom udaru. Svaka minuta je dragocjena.



Nazovi odmah

Prepoznaj moždani udar! 112

Referentni centar za intenzivnu neurologiju i endovaskularno liječenje moždanog udara i krvotvornih malformacija središnjeg živčanog sustava MZRH



Rezultati nacionalnih strategija

Značajan pad mortaliteta (<15%)

Kvalitetno zbrinjavanje u Jedinicama za liječenje MU

Rekanalizacijska terapija (povećanje udjela tako liječenih bolesnika
za 2-3x)

Obaviještenost opće populacije

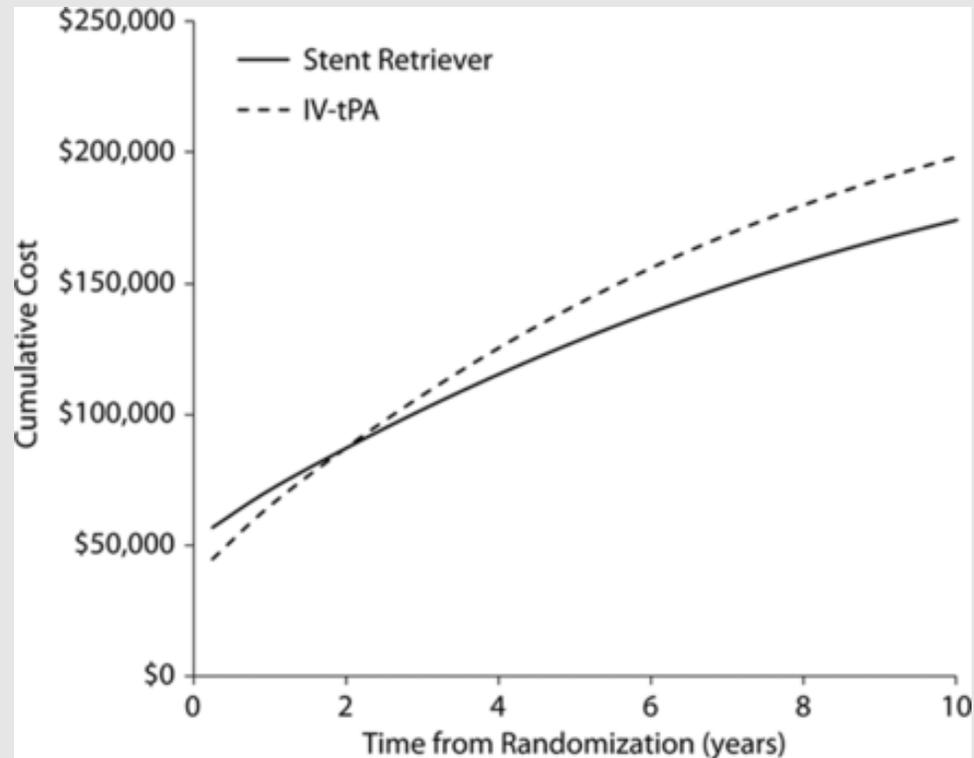
Ciljana rehabilitacija – specijalizirane ustanove

Izrada registra i kvalitetne dokumentacije s usporedivim podacima

Smanjenje izravnih i neizravnih troškova



Učinak rekanalizacijske terapije na troškove u zdravstvu



...mechanical thrombectomy using the solitaire stent retriever plus tPA is associated with higher initial treatment costs both in-hospital and over 90 days of follow-up. However, lifetime projections based on a combination of trial data and data from a large external cohort of stroke survivors demonstrated that the stent retriever strategy is an economically dominant strategy with substantial long-term cost savings and gains in both life-expectancy and quality-adjusted life-expectancy—results that were consistent in multiple sensitivity and subgroup analyses.



Liječenje moždanog udara u RH

24 bolničke ustanove
22 nrl odjela (80%)

	Ishemijski MU	ICH	SAH
Broj MU (5.136)	4.372	532	204
Postotak	86%	10%	4%
TL (193)	4.4%		
TK (80)	1.8%		





~50% JLMU, ali u ¼ JLMU <1% TL bolesnika
 TK u dva Centra (Zgb), ukupno <2%TK bolesnika u RH

- Endov
- NRL
- JLMU



Prepoznaj simptome!

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Referentni centar za intenzivnu neurologiju i endovaskularno liječenje moždanog udara i krvožilnih malformacija središnjeg živčanog sustava MZRH



Partneri projekta

