

ARCS 2020

ARTERIAL RECANALIZATION IN CEREBRAL STROKE

**뇌졸중 재개통 심포지엄 및
대한뇌혈관내치료의학회
2020 추계보수교육**

2020년 9월 19일(토)
스위스 그랜드 호텔(구 그랜드 힐튼)
컨벤션센터 4층 컨벤션홀C



ARCS 2020

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뇌졸중 재개통 심포지엄 및 대한뇌혈관내치료의학회
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모시는 글

존경하는 대한뇌혈관내치료의학회 회원 여러분 !

코로나바이러스 감염증이 지속되는 가운데 환자 진료를 위해 헌신 하고 계신 회원 여러분의 노고에 존경과 경의를 표합니다. 향후 상당 기간 지속될 것으로 예상되는 코로나 시대를 맞아 본 학회에서는 추계 보수교육을 과거와는 다른 형태로 진행하려고 합니다. 방역지침 을 철저히 따르면서 제한된 인원만 학회장에 입장할 수 있도록 하고 참석이 어려운 회원을 위해 온라인으로 학회장을 실시간 중계하려고 합니다. 처음에는 어색할 수 있지만 포스트 코로나시대에는 일상이 될 수도 있을 것입니다.

뇌혈관질환은 10년전까지만 해도 암을 제외하고 성인 사망 원인 1위를 차지하던 질환이었으나, 치료 결과가 향상되면서 심장질환, 폐렴에 이어 성인 사망 4위를 차지하는 질환이 되었습니다. 이렇게 치료 결과가 호전되어 OECD 평균보다 훨씬 낮은 사망률을 기록하게 된 이유는 일선에서 환자를 진료하고 시술을 담당하는 회원 여러 분들이 환자에 대한 열정과 사명감을 갖고 24시간 365일 불철주야 노력 하기 때문일 것입니다. 특히, 중증도가 높은 급성기 뇌혈관 폐색 환자는 제한시간 내에 기계적 혈전제거술로 재개통을 하지 못하면 예후가 불량하고 사망률이 높기 때문에 이들 환자를 잘 치료하는 것이 매우 중요합니다. 2018년 한 해 동안 국내에서 약 4000례에 달하는 기계적 혈전제거술이 시행되었으며 이는 5년전에 비해 두 배 이상 증가한 수치입니다. 이렇게 급속도로 늘어나는 응급 시술을 적은 인력으로 감당하고 계신 회원 여러분들의 노고에 감사드립니다.

이번 추계보수교육은 급성기 뇌경색의 표준치료로 자리잡은 기계적 혈전제거술에 대해 비용대비 효율이라는 키워드를 적용할 때 흡인 우선이 좋을지, 스텐트 우선이 좋을지에 대한 토론과 실제 임상 현장 에서 치료 제한 시간을 넘어서 오는 환자를 어떻게 치료하는 것이 좋을 지에 대한 발표가 있을 것이며, 한국인에서 비교적 흔한 두개강 내 뇌혈관 협착과 관련된 급성 뇌혈관 폐색에 대한 혈전제거술에 대해 심도 있는 논의가 이루어질 것입니다.

제2회 ARCS 및 추계보수교육을 통해 급성기 뇌경색 환자 치료 역량을 한층 더 강화할 수 있을 것이며, 이는 우리나라 국민들의 뇌졸중 치료 결과 향상으로 이어질 것입니다. 마지막으로 본 프로그램 램을 기획하고 준비해 주신 김태곤 수련교육 이사과 학회장을 준비 하고 온.오프라인 세팅을 하느라 수고해 주신 박석규 총무이사께 감사드리며, 회원 여러분의 많은 관심과 참여 부탁드립니다.

감사합니다.

대한뇌혈관내치료의학회 회장 윤석만

2020~2021 대한뇌혈관내치료의학회 임원진

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2020~2021 대한뇌혈관내치료의학회 임원진

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	정영진	영남대학교병원



[PROGRAM]

10:00-11:20	Session I. Mechanical Thrombectomy in Acute Ischemic Stroke 좌장: 박석규 (순천향대), 신승훈 (차의과학대)	
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10:40-11:00	Mechanical thrombectomy in tandem occlusion of extracranial ICA and MCA 이동훈 (가톨릭대)	23
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12:00-12:20	Is less better? (Controversies in imaging for endovascular treatment candidates): Yes or No 오재상 (순천향대)	38
12:20-12:40	The never-ending story: Patients not within the DAWN/DEFUSE 3 criteria should not be treated with endovascular thrombectomy in the extended time window 김종훈 (영남대)	44
12:40-13:00	Recent trends for AIS (Review of articles) 박상규 (연세대)	50
13:00-13:10	Photo time & Break	
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13:10-13:30	Pathophysiology and risk factors of ICAS in Asia 장철훈 (영남대)	57
13:30-13:50	Imaging and diagnosis of ICAS 김의중 (경희대)	67
13:50-14:10	Discussion	
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14:30-14:50	Endovascular mangement of ICAS with large vessel occlusion 유승훈 (울산대)	81
14:50-15:10	Surgical mangement of ICAS 최석근 (경희대)	82
15:10-15:30	Coffee break	
15:30-16:50	Session V. Interesting or Complicated Cases Presentation in Mechanical Thrombectomy 좌장: 권현조 (충남대), 정진영 (연세에스병원)	
15:30-15:50	Case Presentataion 1 장인복 (한림대)	85
15:50-16:10	Case Presentataion 2-Periprocedural vessel injury complication during late-window thrombectomy 김상욱 (명지성모병원)	92
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16:50	Closing remark 김태곤 (대한뇌혈관내치료의학회 수련교육이사)	



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뇌졸중 재개통 심포지엄 및 대한뇌혈관내치료의학회
2020 추계보수교육

Session I. Mechanical Thrombectomy in Acute Ischemic Stroke

좌장 : 박석규 (순천향대), 신승훈 (차의과학대)

Mechanical thrombectomy: Does contact aspiration first strategy become a standard?

Mechanical thrombectomy in vertebrobasilar occlusion: Are there 6hr time window?

Mechanical thrombectomy in tandem occlusion of extracranial ICA and MCA

Mechanical thrombectomy in M2 or M3 occlusion

고준경 (부산대)

강현승 (서울대)

이동훈 (가톨릭대)

최재형 (동아대)

Mechanical thrombectomy: Does contact aspiration first strategy become a standard?

고 준 경

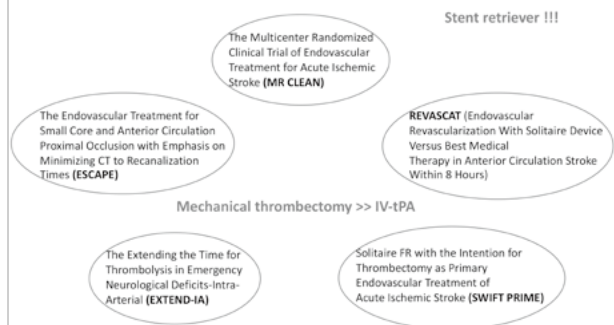
부산대병원 신경외과

Mechanical thrombectomy: Does contact aspiration first strategy become a standard?

고준경



NEW RCTs OF ENDOVASCULAR STROKE TREATMENT (2015)



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

3.7. Mechanical Thrombectomy (Continued)

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.

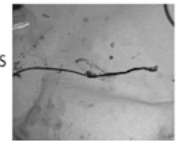
COR	LOE
I	A

Recommendation revised from 2015 Endovascular.

ORIGINAL RESEARCH

ADAPT FAST study: a direct aspiration first pass technique for acute stroke thrombectomy

NeuroIntervent Surg 2014



5MAX (Penumbra) or 5MAX ACE (Penumbra)

98 prospectively identified AIS (100 occluded large cerebral vessels)

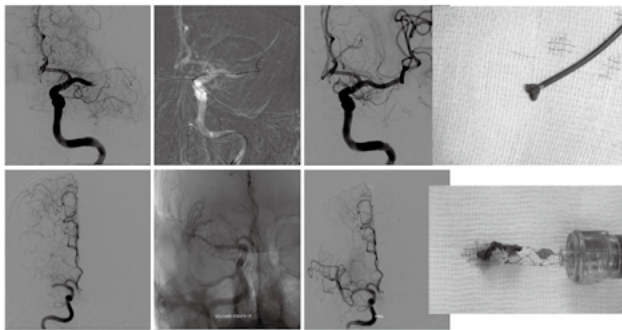
at six institutions were included in the study.

(Medical University of South Carolina, Swedish Medical Center, Vanderbilt University, Stony Brook University, Erlanger Medical Center, and University of Buffalo.)

	ADAPT FAST (n=100)	SWIFT trial (n=89)	TREVO trial (n=88)	STAR study (n=202)	NASA registry (n=354)	Solitaire data* (n=355)	Trevo data* (n=221)
TICI 2a/2b/3 (%)	N/A	83/1	90	N/A	87.5	82	83
Device TICI 2b/3 (%)	78	75.9/	68/	79/	72.5	NR	NR
		91/	91/	91/			
Final TICI 2b/3 (%)	95	75.9/	68/	85	72.5	82	83
mRS 0-2 (%)	40	36	40	55	42	47	51
Mortality (%)	20	17	34	19	36.2	14	31
Time to final revascularization (min)	37	NR	NR	NR	50%	NR	NR
Device related complications (%)	2	8.6	9	7.5	NR	6	5
Symptomatic ICH (%)	0	2	7	4	9.9	6	8

ADAPT is a fast, simple, efficient, and safe strategy

Two current mainstreams among such mechanical thrombectomy techniques, "stent retriever thrombectomy" and "direct clot aspiration"



JAMA | Original Investigation

Effect of Endovascular Contact Aspiration vs Stent Retriever on Revascularization in Patients With Acute Ischemic Stroke and Large Vessel Occlusion

The ASTER Randomized Clinical Trial

Bertrand Laperque, MD, PhD; Raphael Blanc, MD, MSc; Benjamin Gory, MD, PhD; Julien Labreuche, EST; Alan Duhamel, PhD; Gaudier Marlet, MD; Suzanne Saleme, MD; Vincent Costalat, MD, PhD; Serge Bracard, MD; Hubert Desat, MD, PhD; Mikael Maugris, MD, PhD; Anthony Gervais, MD; Michel Petit, MD, PhD; for the ASTER Trial Investigators

JAMA August 1, 2017

- Randomized, multicenter, open-label, blinded end-point clinical trial
- Contact aspiration technique(192) vs the standard Stent retriever technique(189)
- Conducted in 8 comprehensive stroke centers in France (October 2015-October 2016)
- Superiority design

The hypothesis of this trial was that use of first-line contact aspiration would increase the rate of successful revascularization by 15% compared with a first-line stent retriever

Flow of Patients Through the ASTER Trial



Operators were required to perform at least 3 attempts at revascularization using the assigned endovascular technique before switching to another endovascular procedure (rescue therapy)

- rescue therapy
1. Stent retriever
 2. Combined stent retriever with contact aspiration
 3. Contact aspiration
 4. Balloon angioplasty with or without stenting

A retrospective study comparing aspiration and stent retriever techniques

Events	No./Total (%)	First-Line Contact Aspiration (n = 192)	First-Line Stent Retriever (n = 189)
All-cause mortality at 3 mo	35/181 (19.3)	35/182 (19.2)	35/182 (19.2)
Intracranial hemorrhage at 24 h ^{a,b}	87/188 (46.3)	85/188 (45.2)	85/188 (45.2)
Hemorrhagic infarction	58/188 (30.9)	49/188 (26.6)	49/188 (26.6)
Type 1 ^c	23/188 (12.2)	24/188 (13.0)	24/188 (13.0)
Type 2 ^c	35/188 (18.6)	25/188 (13.6)	25/188 (13.6)
Pericranial hematoma	24/188 (12.8)	33/188 (17.4)	33/188 (17.4)
Type 1 ^c	17/188 (9.0)	19/188 (10.3)	19/188 (10.3)
Type 2 ^c	7/188 (3.7)	14/188 (7.6)	14/188 (7.6)
Intraventricular hemorrhage	6/188 (3.2)	2/184 (1.1)	2/184 (1.1)
Remote intracranial hemorrhage	1/188 (0.5)	1/184 (0.5)	1/184 (0.5)
Symptomatic intracranial hemorrhage at 24 h	10/188 (5.3)	12/188 (6.5)	12/188 (6.5)
Procedure-related adverse events ^b	31/192 (16.2)	30/189 (15.9)	30/189 (15.9)
Embolization in a new vascular territory	7/192 (3.7)	5/189 (2.7)	5/189 (2.7)
Arterial perforation	5/192 (2.6)	3/189 (1.6)	3/189 (1.6)
Arterial dissection	5/192 (2.6)	2/189 (1.1)	2/189 (1.1)
Vasospasm	5/192 (2.6)	12/189 (6.4)	12/189 (6.4)
Subarachnoid hemorrhage	13/188 (6.9)	13/188 (7.1)	13/188 (7.1)
New ischemic stroke in a different vascular territory	10/188 (5.3)	16/188 (8.5)	16/188 (8.5)

No significant differences between groups

technique for the treatment of acute ischemic stroke: >24h. (PT) vs stent retrievers for acute stroke therapy: an - technique for acute stroke thrombectomy.

ss of a direct aspiration first pass technique (ADAPT) for the te stroke.

Primary and Secondary Efficacy Outcomes

Outcomes	No./Total (%) ^a	First-Line Contact Aspiration (n = 192)	First-Line Stent Retriever (n = 189)	Risk Difference, % (95% CI) ^b	Odds Ratio (95% CI)	P Value
Primary Efficacy Outcome						
Successful revascularization at the end of all procedures						
mTICI score of 2b or 3 assessed by core laboratory ^c						
Intention-to-treat analysis ^d	154/192 (80.4)	157/189 (83.1)	2.4 (-5.4 to 9.7)	1.20 (0.68-2.10)	.53	
Per-protocol analysis ^e	140/153 (91.5)	140/145 (96.6)	6.8 (-0.6 to 14.1)	1.91 (0.93-3.91)	.08	
mTICI score of 2b or 3 assessed at study site ^f	163/192 (84.9)	163/189 (86.2)	-1.4 (-8.3 to 5.5)	0.90 (0.50-1.59)	.71	
Secondary Angiographic Efficacy Outcomes						
Complete revascularization at the end of all procedures						
mTICI score of 1 assessed by core lab ^g	72/192 (37.5)	73/189 (38.6)	-1.1 (-11.0 to 9.0)	0.95 (0.62-1.45)	.82	
mTICI score of 2 or 3 assessed by core lab ^h	121/192 (63.0)	128/189 (67.7)	-4.7 (-13.8 to 4.4)	0.81 (0.53-1.24)	.34	
mTICI score of 3 assessed by core lab ⁱ	55/192 (28.7)	67/189 (35.5)	-6.8 (-16.2 to 2.5)	0.73 (0.54-1.13)	.16	
mTICI score of 2c or 3 assessed by core lab ^j	83/192 (43.2)	94/189 (49.7)	-6.5 (-16.4 to 3.3)	0.77 (0.51-1.16)	.21	
Use of rescue treatment	63/192 (32.8)	45/189 (23.8)	9.0 (-0.9 to 18.1)	1.57 (0.99-2.47)	.05	
Clinical Efficacy Outcomes						
Change in NIHSS score at 24 h, mean (95% CI) ^k	-4.8 (-6.1 to -3.6) ^h	-5.2 (-6.5 to -3.9) ^h	0.38 (-1.42 to 2.18) ^h	NA	.68	
Functional independence at 3 mo ^l	82/181 (45.3)	91/182 (50.0)	-4.6 (-14.7 to 6.1)	0.83 (0.54-1.26)	.38	
Modified Rankin Scale score at 3 mo, median (interquartile range)	3.0 (1.0 to 5.0)	2.5 (1.0 to 5.0)	NA	0.76 (0.53-1.10) ^h	.15	

there were no significant differences between groups

Outcomes	No./Total (%) ^a		Risk Difference, % (95% CI) ^b	Odds Ratio (95% CI)	P Value
	First-Line Contact Aspiration (n = 192)	First-Line Stent Retriever (n = 189)			
Successful revascularization after first-line strategy alone					
mTICI score of 2b or 3 assessed by core laboratory ^c	121/192 (63.0)	128/189 (67.7)	-4.7 (-13.8 to 4.4)	0.81 (0.53-1.24)	.34
mTICI score of 3 assessed by core laboratory ^d	55/192 (28.7)	67/189 (35.5)	-6.8 (-16.2 to 2.5)	0.73 (0.54-1.13)	.16
mTICI score of 2c or 3 assessed by core laboratory ^e	83/192 (43.2)	94/189 (49.7)	-6.5 (-16.4 to 3.3)	0.77 (0.51-1.16)	.21
Use of rescue treatment	63/192 (32.8)	45/189 (23.8)	9.0 (-0.9 to 18.1)	1.57 (0.99-2.47)	.05
Clinical Efficacy Outcomes					
Change in NIHSS score at 24 h, mean (95% CI) ^k	-4.8 (-6.1 to -3.6) ^h	-5.2 (-6.5 to -3.9) ^h	0.38 (-1.42 to 2.18) ^h	NA	.68
Functional independence at 3 mo ^l	82/181 (45.3)	91/182 (50.0)	-4.6 (-14.7 to 6.1)	0.83 (0.54-1.26)	.38
Modified Rankin Scale score at 3 mo, median (interquartile range)	3.0 (1.0 to 5.0)	2.5 (1.0 to 5.0)	NA	0.76 (0.53-1.10) ^h	.15

even though there was no statistical significance.....

First-line strategy analysis : stent retriever group is better

Clinical efficacy outcomes : stent retriever group is better

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

3.7. Mechanical Thrombectomy (Continued)	COR	LOE	Note, Revised, or Unchanged
12. The use of mechanical thrombectomy devices other than stent retrievers as first-line devices for mechanical thrombectomy may be reasonable in some circumstances, but stent retrievers remain the first choice.	IIb	B-R	Recommendation revised from 2015 Endovascular.
The ASTER trial (Contact Aspiration vs Stent Retriever for Successful Revascularization) compared the contact aspiration technique and the standard stent retriever technique as first-line EVT for successful revascularization within 6 hours among patients with acute anterior circulation ischemic stroke and LVO. The proportion of patients with successful revascularization at the end of all interventions was 85.4% (n=154) in the contact aspiration group versus 83.1% (n=157) in the stent retriever group (OR, 1.20; 95% CI, 0.68–2.10; P=0.53; difference, 2.4%; 95% CI, –5.4 to 9.7%). The secondary clinical and point of mRS score of 0 to 2 at 90 days was achieved by 82 of 181 (45.3%) in the contact aspiration group versus 91 of 182 (50.0%) in the stent retriever group (OR, 0.83; 95% CI, 0.54–1.26; P=0.38). The primary end point in ASTER was technical (successful) revascularization after all interventions, and the trial was not powered to detect a smaller yet potentially clinically important difference between groups. Given its superiority design to detect a 15% difference in the primary end point, this trial was not designed to establish noninferiority. ¹⁹			

A Direct Aspiration First Pass Technique vs Standard Endovascular Therapy for Acute Stroke: A Systematic Review and Meta-Analysis

Neurosurgery. 2018 Jul 1;83(1):19–28. doi: 10.1093/neuros/nyx386.

TABLE 1. Study Characteristics for Included Studies on ADAPT Strategy in Endovascular Therapy (EVT) Employed in Selected Randomized Controlled Trials							
First author (ADAPT)	Year	Study Period	Region	n	Guide catheter	Aspiration catheter	Aspiration
Kang ¹⁸	2015	R, OS	South Korea	22	Shuttle Guide	Penumbra	20 mL syringe
Turk ¹⁹	2014	R, OS	USA	98	Neuron 188 (Penumbra)	MAX (Penumbra), MAX ACI (Penumbra)	20 or 60 mL syringe, or Penumbra aspiration pump
Turk ¹⁹	2014	R, OS	USA	37	Neuron 188 (Penumbra)	MAX (Penumbra), MAX ACI (Penumbra)	20 or 60 mL syringe, or Penumbra aspiration pump
Jankowitz ²⁰	2015	R, OS	USA	112	Neuron 188 (Penumbra)	MAX (Penumbra), MAX ACI (Penumbra)	20 mL syringe
Kim ²¹	2015	R, OS	South Korea	70	BF guide cath	Penumbra	20 mL syringe
Hungerford ²²	2016	R, OS	USA	104	NI	NI	NI
Kabaneck ²³	2016	R, OS	Germany	38	BF guide catheter	SCPA	20 mL syringe
Kwon ²⁴	2016	R, OS	Germany	34	Neuron 188 (Penumbra)	MAX (Penumbra), MAX ACI (Penumbra)	Penumbra aspiration pump
Muscarello ²⁵	2016	R, OS	USA	76	Neuron 188 (Penumbra), Shuttle Guide, Carotid Street (Flow) (Penumbra)	MAX (Penumbra), MAX ACI (Penumbra)	Penumbra aspiration pump
Miyata ²⁶	2016	R, OS	Japan	43	NI	MAX (Penumbra), MAX ACI (Penumbra)	NI
Nou ²⁷	2016	R, OS	Spain	6	Neuron 188 (Penumbra)	MAX (Penumbra)	Penumbra aspiration pump
Park ²⁸	2016	R, OS	South Korea	12	BF guide catheter	MAX (Penumbra)	20 mL syringe
Roman ²⁹	2016	R, OS	Italy	71	NI	MAX (Penumbra), MAX ACI (Penumbra)	20 or 60 mL syringe
Roman ²⁹	2016	R, OS	Italy	102	NI	MAX (Penumbra), MAX ACI (Penumbra)	20 or 60 mL syringe
Singh ³⁰	2016	R, OS	South Korea	86	Shuttle Guide	MAX (Penumbra), MAX ACI (Penumbra)	20 mL syringe
Stump ³¹	2016	R, OS	Germany	135	BF guide catheter	MAX (Penumbra), MAX ACI (Penumbra)	20 or 60 mL syringe
Vargha ³²	2016	R, OS	USA	191	Neuron 188 (Penumbra)	MAX (Penumbra), MAX ACI (Penumbra)	Penumbra aspiration pump
First author (EVT)	Year	Study Period	Region	n	Endovascular therapy type		
EXTEND ³³	2015	R, CT	Canada, USA, South Korea, Europe	185	Various		
EXTEND 1+ ³⁴	2015	R, CT	Australia, New Zealand	25	Various		
MR CLEAN ³⁵	2015	R, CT	Europe	233	Various		
RESCUE 1 ³⁶	2015	R, CT	Europe	103	Various		
SWIFT-PRIME ³⁷	2015	R, CT	USA, Europe	98	Various		

Abbreviations: ADAPT, aspiration and direct aspiration, first pass; BF, balloon forward; CT, computed tomography; EXTEND, extended time to reperfusion; MAX, MAX (Penumbra); MAX ACI, MAX ACI (Penumbra); NI, not indicated; OS, open surgery; R, randomized; SCPA, Solitaire (Medtronic); Shuttle Guide, Shuttle Guide (Penumbra); Turk, Turk (Penumbra); Vargha, Vargha (Penumbra).

R, retrospective; OS, observational study; RCT, randomized controlled study; USA, United States of America; n, number of patients included.

TICI 2b-3

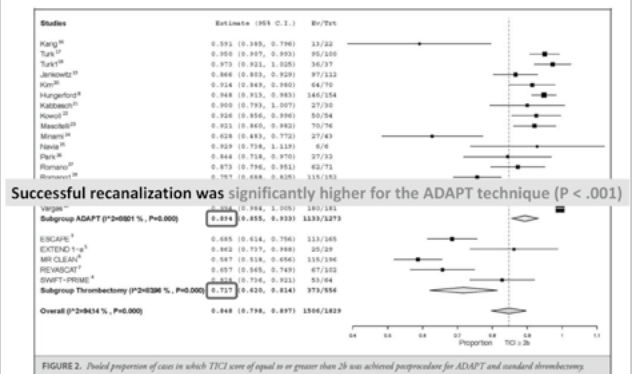


FIGURE 2. Proportion of cases in which TICI score of 2b or greater was achieved postprocedure for ADAPT and standard thrombectomy.

90-d mRS 0 to 2 for functional outcome

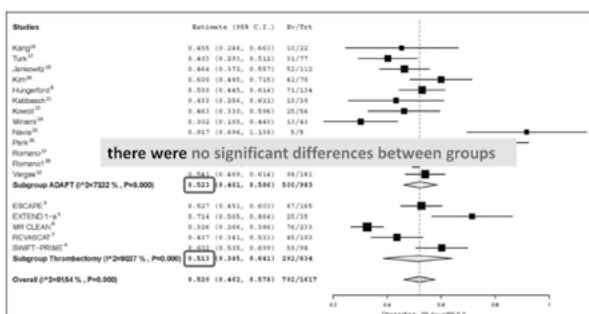


FIGURE 3. Proportion of patients with a 90-d mRS score of 0 to 2 for ADAPT and standard thrombectomy.

Symptomatic Intracerebral Hemorrhage

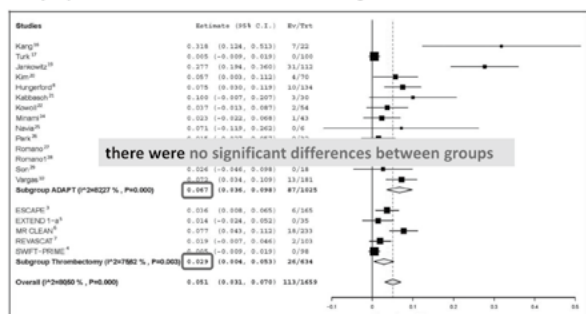
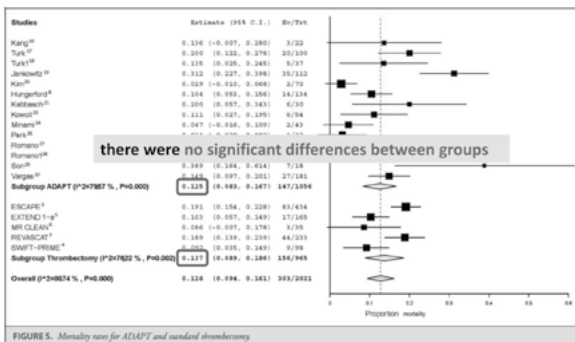


FIGURE 4. Proportion of patients with sICH for ADAPT and standard thrombectomy.

Mortality



Conclusion of this Meta-analysis

APADT is

- Cost-effective
- Comparable with recent RCTs.



Aspiration thrombectomy versus stent retriever thrombectomy as first-line approach for large vessel occlusion (COMPASS): a multicentre, randomised, open label, blinded outcome, non-inferiority trial

Aquila S, Turk B, Adnan Siddiqi, Johanna T Fik, Ronda A De Lencastre, David J Fiorillo, Eugene Gu, Elad I Levy, Kenneth V Snyder, Riccardo A Hanel, Amin Aghaiehsheini, B Keith Woodward, Harry R Hixon, Mohamed (Chaudry), Alejandro M Spiccia, Anwar T Rai, Donald Frei, Joana E Delgado Alvarado, Mike Kelly, Adam Arthur, Blake Rastor, Joay English, Italo Linfante, Kyle M Fargen, J Mocco

Randomized Controlled Trial | Lancet. 2019 Mar 9;393(10175):998-1008.

- Randomized, multicenter, open-label, blinded outcome
- Aspiration first pass(134) vs Stent retriever first line(136)
- Conducted in 15 comprehensive stroke centers in USA & Canada (June 2015-July 2017)
- Non-inferiority design

The null hypothesis of this trial was that patients treated with aspiration as first pass achieve inferior outcomes compared with those treated with a stent retriever first line approach.

Efficacy endpoints

	Aspiration first pass thrombectomy (n=134)	Stent retriever first line thrombectomy (n=136)	Odds ratio (95% CI)	p-value
Primary efficacy endpoint				
Modified Rankin scale score of 0-2 at 90 days	69 (52%)	67 (50%)	NA	0.004
Secondary efficacy endpoints				
Median time to TICI 2b or greater (min)	22 (19-28)	33 (28-37)	NA	0.004
90-day global disability modified Rankin shift			0.98 (0.64-1.51)	0.954
0	27 (20%)	24 (18%)		
1	26 (20%)	32 (24%)		
2	35 (26%)	9 (7%)		
3	7 (5%)	14 (10%)		
4	20 (15%)	17 (13%)		
5	6 (5%)	4 (3%)		
6	30 (23%)	30 (22%)		
TICI 2b or greater within 45 min	50% (65/130)	44% (59/134)	1.1 (0.8-1.5)	0.298
TICI 2 within 45 min	34% (45/130)	27% (37/134)	1.7 (1.0-3.0)	0.046
Secondary efficacy outcomes				
TICI 2b or greater on first pass	57% (75/131)	51% (69/136)	1.32 (0.9-1.9)	0.32
TICI 2b or greater within 45 min of access	74% (97/131)	68% (92/136)	1.46 (0.9-2.3)	0.17
Occurrence of emboli in a new territory	3% (4/131)	2% (3/136)	2.08 (0.50-15.54)	0.44
Presence of vasospasm involving the accessed vascular tree	8% (10/131)	7% (10/136)	1.02 (0.40-2.55)	1.00
90-day global disability utility weighted modified Rankin shift	0.58 (0.4-1.33)	0.57 (0.4-1.30)**	NA	0.76
Improved (lower) mRS at 24h	7.5 (9.5-11.2)	7.3 (9.8-12.1)	NA	0.86
Improved (lower) mRS at 7 days post-treatment or post-discharge	13.0 (8.5-17.0)	10.1 (8.7-12.1)	NA	0.42
Stroke Impact Score				
Strength	35.8 (4.7)	36.1 (4.3)	NA	0.79
Memory	30.4 (5.8)	30.5 (5.1)	NA	0.95
Mood	33.7 (5.9)	32.8 (5.5)	NA	0.37
Communication	33.8 (5.2)	31.6 (5.1)	NA	0.27
ADL or IADL	42.8 (10.4)	43.1 (10.8)	NA	0.82
Mobility	36.1 (10.4)	37.1 (9.7)	NA	0.57
Hand function	20.1 (6.4)	21.1 (5.9)	NA	0.54
Social participation	21.1 (9.5)	21.1 (9.4)	NA	0.74

Cost analysis

	Aspiration first pass thrombectomy (n=134)	Stent retriever first line thrombectomy (n=136)	p value
Data primary, list price secondary (\$)			
Mean	9540 (7962)	14081 (4797)	<0.0001
Median	6633 (5937-9823)	12790.40 (11723-15181)	<0.0001
Data secondary, list price primary (\$)			
Mean	10084 (8873)	15158 (5223)	<0.0001
Median	6848 (6113-9764)	13686 (12715-16548)	<0.0001

Table 6: Aggregate supply chain cost analysis

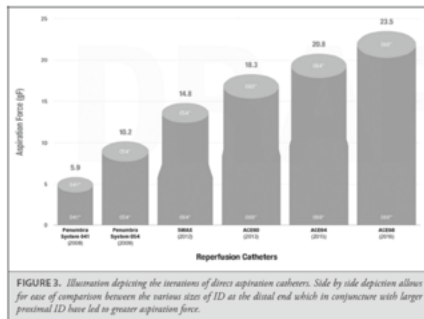
Conclusion of COMPASS

APADT is

- non-inferior functional outcome at 90 days
- cost effective compared with the stent retriever first line.

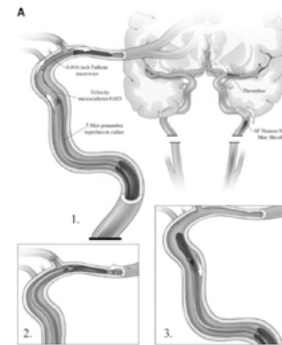
This findings might directly affect current stroke treatment guideline recommendations.

The larger ID, the better outcome



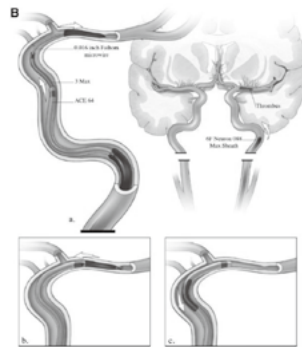
Neurosurgery. 2020 Jan 1;86(1):61-70. doi: 10.1093/neuros/nyy444.

Clot engaged at the distal catheter tip



Neurosurgery. 2020 Jan 1;86(1):61-70. doi: 10.1093/neuros/nyy444.

Clot ingestion



Neurosurgery. 2020 Jan 1;86(1):61-70. doi: 10.1093/neuros/nyy444.

ORIGINAL RESEARCH

Larger ACE 68 aspiration catheter increases first-pass efficacy of ADAPT technique

Josser E Delgado Almandoz,¹ Yasha Kayan,¹ Adam N Wallace,¹ Ronald M Tarrel,² Jennifer L Fease,¹ Jill Marie Scholz,¹ Anna M Milner,¹ Pezhman Roohani,² Maximilian Mulder,¹ Mark L Young¹

J Neurointerv Surg. 2019 Feb;11(2):141-146. doi: 10.1136/neurintsurg-2018-013957.



Figure 1 Time of release and specifications of ACE 60, 64 and 68 aspiration catheters (reproduced with permission from Penumbra, Inc.)

Table 1 Baseline clinical and radiological patient characteristics

	All patients, n=152 (%)	ACE 60, n=57 (%)	ACE 64, n=35 (%)	ACE 68, n=60 (%)	P values
Mean age, years	68.1	67.4	68.7	68.3	0.65*/0.71†
Sex					0.05†
Female	70 (46)	21 (37)	22 (63)	27 (45)	
Male	82 (54)	36 (63)	13 (37)	33 (55)	
Atrial fibrillation	61 (40)	22 (39)	12 (34)	27 (45)	0.56
Diabetes mellitus	32 (21)	12 (21)	8 (23)	12 (20)	0.95
Hypertension	93 (61)	34 (60)	21 (60)	38 (63)	0.91
Mean NIHSS	18.5	18.2	18.8	18.4	0.6*/0.62†
IV tPA administration	81 (53)	31 (54)	18 (51)	32 (53)	0.96
Mean baseline mRS ASPECTS	9	9.3	8.7	8.9	0.015*/0.08†
Thrombus location					
ICA	43 (28)	14 (25)	11 (31)	18 (30)	0.72
MCA M1	78 (51)	25 (44)	20 (57)	33 (55)	0.36
MCA M2	26 (17)	14 (25)	3 (9)	9 (15)	0.12
MCA M3	5 (3)	4 (7)	1 (3)	0	0.1
LtF side	86 (57)	31 (54)	17 (49)	38 (63)	0.34
Tandem ICA origin occlusion	22 (15)	8 (14)	7 (20)	7 (12)	0.5
Mean cervical tortuosity, degrees	244.8	255.8	263.6	223.8	0.81*/0.28†
Sevenscore [‡]	41 (27)	19 (33)	10 (29)	12 (20)	0.26
Mean time LKW to groin puncture, min	262	226.1	302.3	274.4	0.028*/0.11†

*P value for the difference between ACE 60 and ACE 64 using Student's t test.

†P value for the difference between ACE 60 and ACE 68 using Student's t test.

‡ASPECTS, Alberta Stroke Program Early CT Score; CT, computed tomography; ICA, internal carotid artery; IV tPA, intravenous tissue plasminogen activator; LKW, last known well.

mRS, modified Rankin Scale; MCA, middle cerebral artery; N, number of patients; NIHSS, National Institutes of Health Stroke Scale; mRS, modified Rankin Scale; mRS, modified Rankin Scale.

Table 2 Efficacy of the ADAPT technique with larger-bore ACE aspiration catheters

	All cases, n=152 (%)	ACE 60, n=57 (%)	ACE 64, n=35 (%)	ACE 68, n=60 (%)	P values
Mean time puncture to reperfusion, minutes	34.5	44.4	30.2	27.7	0.02*/0.003†
Median time puncture to reperfusion, minutes	24	30	26	19.5	n/a
Mean number of ADAPT passes	2.3	2.3	2.5	2	0.6*/0.81†
Median number of ADAPT passes	2	2	2	1	n/a
Overall successful reperfusion	137 (90)	50 (88)	32 (91)	55 (92)	0.74
Successful reperfusion using ADAPT only	122 (80)	38 (67)	31 (89)	53 (88)	0.005
Successful reperfusion after first ADAPT pass	64 (42)	19 (33)	13 (37)	32 (53)	0.07*/0.04†
Stent-retriever rescue	22 (14.5)	15 (26)	1 (3)	6 (10)	0.004
Mean number of ADAPT passes before stent-retriever rescue	3.3	2.6	3	5	0.8*/0.029†
Successful reperfusion after stent-retriever rescue	15 (88)	12 (80)	1 (100)	2 (33)	0.09

*P value for the difference between ACE 60 and ACE 64 using Student's t test.

†P value for the difference between ACE 60 and ACE 68 using Student's t test.

‡Defined as thrombolysis in cerebral infarction 2b, 2c, or 3.

n/a, not applicable.

Table 3 Complications of the ADAPT technique with larger-bore ACE aspiration catheters

	All cases, n=152 (%)	ACE 60, n=57 (%)	ACE 64, n=35 (%)	ACE 68, n=60 (%)	P values
Embolic to new territory	5 (3.3)	3 (5.3)	1 (2.9)	1 (1.7)	0.5
Intracranial vascular injury	4 (3.3)	1 (1.8)	2 (5.7)	3 (5)	0.5
Vessel perforation	3 (2)	1 (1.8)	1 (2.9)	1 (1.7)	0.9
Aneurysm perforation	1 (0.7)	0	0	1 (1.7)	0.5
Intracranial dissection	1 (0.7)	0	0	1 (1.7)	0.9
Carotid cavernous fistula	1 (0.7)	0	1 (2.9)	0	0.2
SRH	7 (4.6)	1 (1.8)	2 (5.7)	4 (6.7)	0.4
Intraparenchymal	3 (2)	1 (1.8)	0	2 (3.3)	0.5
Subarachnoid	4 (2.6)	0	2 (5.7)	2 (3.3)	0.23
All SR rescue cases, n=22 (%)	SR rescue after ACE 60, n=19 (%)	SR rescue after ACE 64, n=11 (%)	SR rescue after ACE 68, n=14 (%)	P values	
SRH after stent retriever rescue	3 (13.6)	0	1 (100)	2 (33.3)	0.005
Intraparenchymal	1 (4.5)	0	0	1 (16.7)	0.23
Subarachnoid	2 (9.1)	0	1 (100)	1 (16.7)	0.003

SRH=symptomatic intracranial hemorrhage, SR: stent retriever.

Table 4 Independent predictors of successful reperfusion

	Patients with successful reperfusion after first ADAPT pass (%)	Patients with successful reperfusion with ADAPT only (%)	P values*
ACE catheter used			0.016/0.0016
ACE 60, n=57	19 (33)	38 (67)	
ACE 64, n=35	13 (37)	31 (89)	
ACE 68, n=60	32 (53)	53 (88)	
Thrombus location			0.013/0.048
ICA, n=43	5 (12)	27 (63)	
MCA M1, n=78	47 (60)	70 (90)	
MCA M2, n=26	11 (42)	23 (88)	
MCA M3, n=5	1 (20)	2 (40)	

*P value from multivariate logistic regression analysis for successful reperfusion after first ADAPT pass/successful reperfusion with ADAPT only.
ICA, internal carotid artery; MCA, middle cerebral artery.

Table 5 Independent predictors of a good clinical outcome at 90 days (mRS 0-2)

	Patients with good clinical outcome (%)	P values*
Successful reperfusion after first ADAPT pass		0.0004
Yes, n=64	41 (64)	
No, n=88	29 (33)	
NIHSS ≤21		0.0076
Yes, n=104	57 (55)	
No, n=48	13 (27)	
History of hypertension		0.026
No, n=59	34 (58)	
Yes, n=93	36 (39)	

*P value from multivariate logistic regression analysis.
mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale.

Conclusion

The use of the ACE 68 aspiration catheter led to

- shorter groin puncture to reperfusion time,
- a higher rate of successful reperfusion after the first ADAPT pass,
- and a lower rate of stent-retriever rescue in our cohort.

•CASE series

Take home messages

- ADAPT provide the benefits of faster recanalization times and lower procedural cost.
- The larger-bore aspiration catheter, the better outcome.

Thank you for your attention!



Mechanical thrombectomy in vertebrobasilar occlusion: Are there 6hr time window?

강 현 승

서울대병원 신경외과

ARCS 2020 KoNES 추계보수교육 2020.9.19.(토) 스위스그렌드힐튼 컨벤션센터

Mechanical thrombectomy in vertebrobasilar occlusion: Are there 6hr time window?

강현승 (서울대)

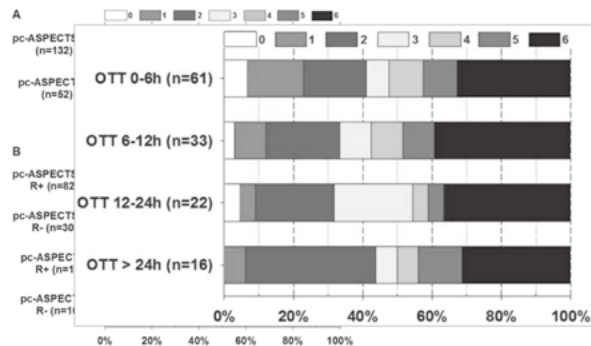
CRCS guideline

- 뇌바닥동맥 (basilar artery) 폐색과 같은 뒷순환계 뇌졸중 환자에서 동맥내 혈전용해술을 기관내 기준에 따라 치료 방법으로 사용할 수 있다. (근거수준 III, 권고수준 B) 2013.2. 추가

*Clinical Research Center for Stroke 뇌졸중임상연구센터 <http://www.stroke-crc.or.kr/>

Basilar Artery Occlusion: What is special here?

- Associated with **high mortality** (85%–95%) if recanalization does not occur.
- Negligible likelihood of good outcome (2%) in the absence of recanalization, but reaching at least **partial recanalization** increased the odds of favorable outcome to **38%**. [Lindsberg & Mattie 2006 Stroke]
- In the Helsinki IVT cohort (n=184), favorable outcome (mRS 0–3) was achieved
 - in **39%** of those treated within 6 hours
 - in **36%** within 6–12 hours
 - in **36%** above 12 hours. [Strbian et al. 2013 Ann Neurol]
 - Recanalization took place in 82%, 70%, and 75%, respectively.
- If patients with extensive infarction already at baseline are excluded, at least 50% reached mRS 0–3 even when treated beyond 12 hours.



Time window for recanalization in basilar artery occlusion: Speculative synthesis

- Most centers apply recanalization therapies for BAO up to **12–24 hours** after symptom onset.
- Distinct features of the posterior circulation might sustain **brittle patency of brainstem perforators** in the face of stepwise growth of the thrombus
 - ✓ highly developed, persistent **collateral arterial network**
 - ✓ **reverse filling** of the distal basilar artery
 - ✓ delicate **plasma flow** siding the clot

Lindsberg, et al. 2015 *Neurology*

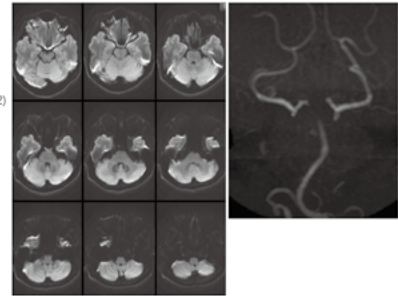
F45 Dizziness, Lt face/hand numbness "치과 마취가 덜 풀린 느낌"
h/o rheumatic MS/MR, Afib, Renal infarction; WFR (prev PT INR 2.57)

LNT=FAT 3:40 AM
EVT 5:40

INIHSSS **4** (Limb ataxia 2, Sensory 2)
PT INR, 1.38

MR 6:13
IV TPA, 7:07

Id. 47014419 LeeMH

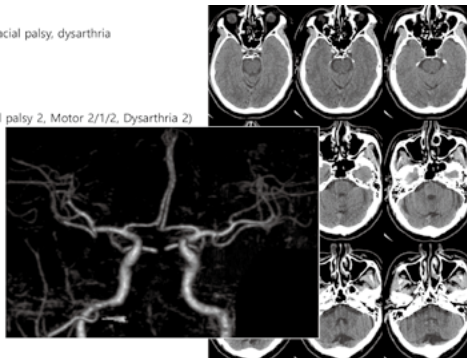


M63 Rt hemiparesis, Lt facial palsy, dysarthria
h/o HT Afib; ASA CPG

LNT 7 PM
FAT 8 PM
EVT 8:30 PM
INIHSSS **10** (LOC 1, Facial palsy 2, Motor 2/1/2, Dysarthria 2)

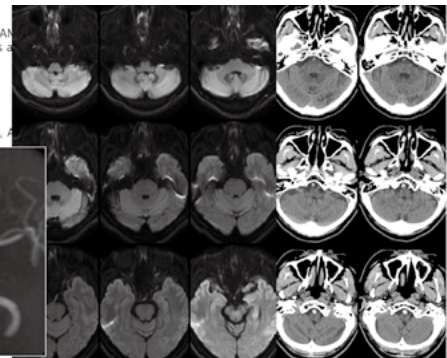
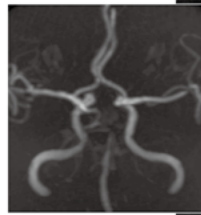
IV TPA, 9:36 PM
IA 10:25 PM

Id. 48131975 KimNH



M69 dizziness, dysarthria (7AM)
h/o cerebral infarction (3wks),
ASA CPG; HT

LNT 14:00
FAT 14:30
EVT 14:51
INIHSSS **13** (FP2, LUE3, LLE4, ...)

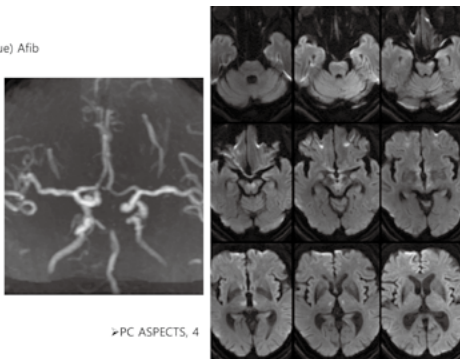


F85 altered mentality
h/o HT; CABG AVR (tissue) Afib
ASA

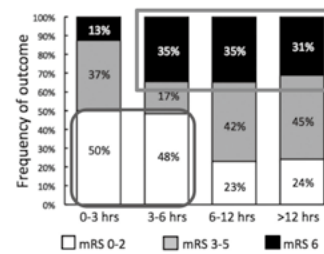
LNT 20:00
FAT 22:30
EVT 00:18
INIHSSS **25**

Id. 26124357 LeeCD

>PC ASPECTS, 4



Clinical outcomes & Time from symptom onset to procedure



Mokin et al. 2016 *Stroke*

Acute Basilar Artery Occlusion and 6hr Time Window to Recanalization

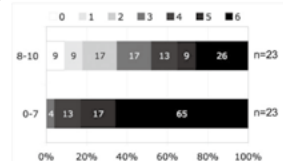
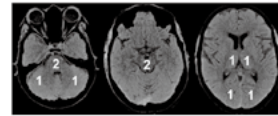
- 231 patients with acute BAO treated with endovascular treatment
- Good outcome (mRS 0-2), **29.5%**
- Overall mortality, **36.8%**
- ✓ **Time to reperfusion beyond 6 h**, more than half fold decreased chance of good outcome [OR **0.47** 95% CI (0.23-0.95) $p < 0.05$]
- ✓ Odds for good outcome, reduced by almost 2/3 with **post-interventional intracerebral hemorrhage** [OR **0.28** 95% CI (0.08-0.98)]
 - ✓ Unfavorable outcome, 100% with symptomatic ICH
- Risk for death, reduced by more than 80% if **collaterals** were present [0.16 95% CI (0.03-0.87)] and if recanalization was successful (TICI 2b-3) [OR 0.19 95% CI (0.05-0.78)]
- Odds for survival, 5-fold higher in patients with no post-interventional hemorrhages present [OR 5.35 95% CI (2.2-1.58)]

Revindren et al. 2019 Front Neurol

Extent of Hypoattenuation on CT Angiography Source Images Predicts Functional Outcome in BAO

- CTA SI pc-ASPECT* score & favorable functional outcome
- **52%** (12/23) with a score ≥ 8
- **4%** (1/23) with a score < 8 (RR **12.1**; 95% CI, 1.7 to 84.9)

*Acute Stroke Prognosis Early CT



Puetz et al. 2008 Stroke

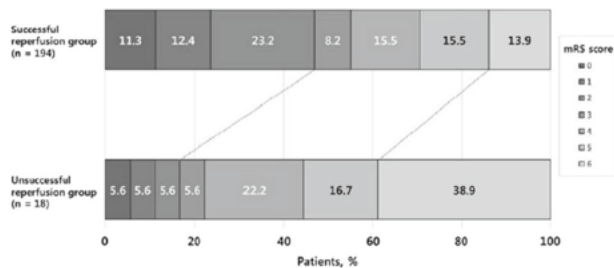
Endovascular Thrombectomy for Acute Basilar Artery Occlusion: A Multicenter Retrospective Observational Study

- n=212, 3 centers
- Reperfusion, 91.5%; Favorable outcome, **44.8%**
- Symptomatic hemorrhage, 1.9%; Mortality, **16%**
- Younger age, lower NIHSS on admission, absence of DM and parenchymal hematoma

Kang DH, Jung C, Yoon W et al. 2018 Stroke

Indication

- **eligible for thrombectomy** if the thrombectomy could be started within **12 hours** of the estimated time of stroke onset
- **excluded from thrombectomy** when pretreatment imaging showed **extensive ischemic changes in the brain stem** or the stroke was considered mild, based on an admission NIHSS score of 3 or less



Kang DH, Jung C, Yoon W et al. 2018 Stroke

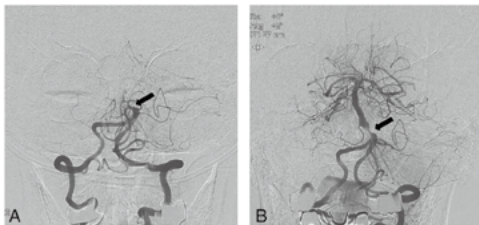
Occlusion sites				
Proximal	52 (24.5%)	25 (26.3%)	27 (23.1%)	0.586
Middle	48 (22.6%)	18 (18.9%)	30 (25.6%)	0.247
Distal	112 (52.8%)	52 (54.7%)	60 (51.3%)	0.616
Time from onset to groin puncture, min, median (IQR)	242 (167.5-357)	223 (150-340)	270 (182.5-371)	0.435
Procedure duration, min, median (IQR)	40 (25-69.75)	36 (22-58)	45 (28.5-81.5)	0.037
Time from onset to reperfusion, min, median (IQR)	295 (224-423.75)	280 (195-375)	319 (239-446.5)	0.206
Baseline NIHSS, median (IQR)	17 (19-23.75)	12 (7-20)	20 (14.5-25.5)	<0.001
First-line thrombectomy technique				
Stent-retriever	145 (68.4%)	68 (71.6%)	77 (65.8%)	0.369
Contact aspiration	67 (31.6%)	27 (28.4%)	40 (34.2%)	

Acute basilar artery occlusion: differences in characteristics and outcomes after endovascular therapy between patients with and without underlying severe atherosclerotic stenosis

- 62 patients with acute BAO - stent retriever thrombectomy
- **24%**, intracranial angioplasty and stenting for atherosclerotic stenosis
- **Proximal** occlusion, related to atherosclerosis (60% vs 6.4%, $P < .001$)
- **Distal** occlusions, more likely thromboembolic (91.5% vs 26.7%, $P < .001$)
- Bilateral thalamic infarction, less common in pts with athero. stenosis (0% vs 27.7%, $P = 0.027$).

Lee YY et al. 2017 AJNR

	All Patients (n = 62)	Patients with ICAS (n = 15)	Patients without ICAS (n = 47)	P Value
Age (mean) (yr)	69.6 ± 11.95	67.1 ± 10.03	70.3 ± 12.50	.205
Male sex (No.) (%)	36 (58.1)	12 (80.0)	24 (51.1)	.048
Risk factor (No.) (%)				
Hypertension	37 (59.7)	11 (73.3)	26 (55.3)	.216
Diabetes mellitus	14 (22.6)	4 (26.7)	10 (21.3)	.727
Dyslipidemia	16 (25.8)	6 (40.0)	10 (21.3)	.182
Smoking	15 (24.2)	5 (33.3)	10 (21.3)	.489
Coronary artery disease	5 (8.1)	0 (0.0)	5 (10.6)	.323
IV thrombolysis (No.) (%)	17 (27.4)	7 (46.7)	10 (21.3)	.094
Occlusion sites (No.) (%)				
Proximal	12 (19.4)	9 (60.0)	3 (6.4)	<.001
Middle	3 (4.8)	2 (13.3)	1 (2.1)	.143
Distal	47 (75.8)	4 (26.7)	43 (91.5)	<.001
Bilateral thalamic infarction (No.) (%)	13 (21.0)	0 (0.0)	13 (27.7)	.027
Baseline NIHSS score (mean)	12.4 ± 6.23	12.7 ± 5.95	12.3 ± 6.37	.773
pc-ASPECTS (median) (IQR)	7 (6-8)	7 (6-8)	7 (6-8)	.794
Time to procedure (mean) (min)	289.6 ± 129.68	309.3 ± 139.65	283.3 ± 127.60	.531
Procedure time (mean) (min)	30.9 ± 17.76	39.0 ± 19.47	28.3 ± 16.56	.006
Time to revascularization (mean) (min)	321.0 ± 136.22	348.3 ± 143.84	312.2 ± 134.12	.459



	All Patients (n = 62)	Patients with ICAS (n = 15)	Patients without ICAS (n = 47)	P Value
mTICI 2b or 3 (No.) (%)	60 (96.8)	15 (100.0)	45 (95.7)	NS
mRS 0-2 (No.) (%)	33 (53.2)	9 (60.0)	24 (51.1)	NS
Symptomatic hemorrhage (No.) (%)	1 (1.6)	0 (0.0)	1 (2.1)	NS
Mortality (No.) (%)	10 (16.1)	2 (13.3)	8 (17.0)	NS

Inclusion criteria

- Presentation within **12** hours of stroke onset
- Baseline NIHSS score of ≥ 4
- No ICH
- No bilateral diffuse pontine ischemia on DWI
- Premorbid mRS score of ≤ 2

Lee YY et al. 2017 AJNR

Post. Circulation Stroke: Time window for IAT

- Time window depends on various factors
- Without recanalization, chance of fav outcome is extremely limited.
 - < 6hrs of symptom onset: Fav outcome in ~50%
 - > 6hrs of symptom onset: Fav outcome in ~one fourth
 - > 3hrs of symptom onset: Mortality in ~one third
- Without diffuse bilateral pontine ischemia: Fav outcome in ~50%
- **PC ASPECT score** ≥ 6 (hopefully ≥ 8)
- Without extensive infarction at baseline, at least 50% reach mRS 0-3 even when treated beyond 12 hours.

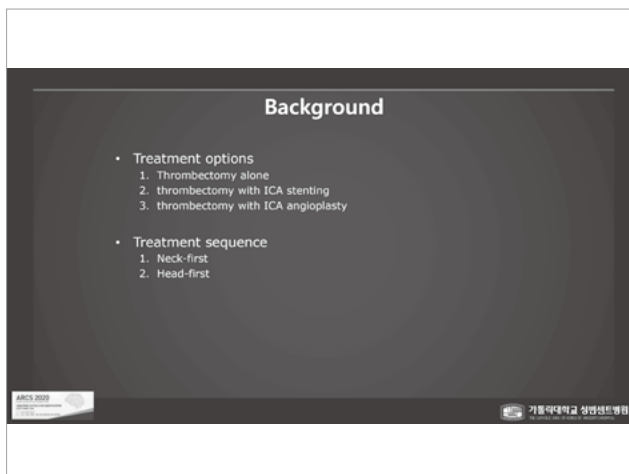
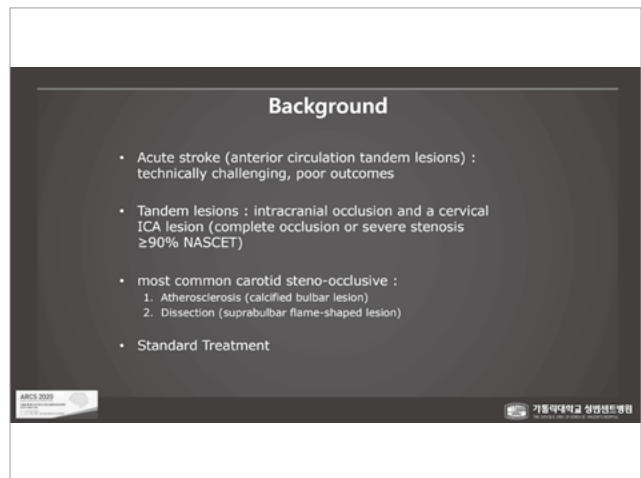
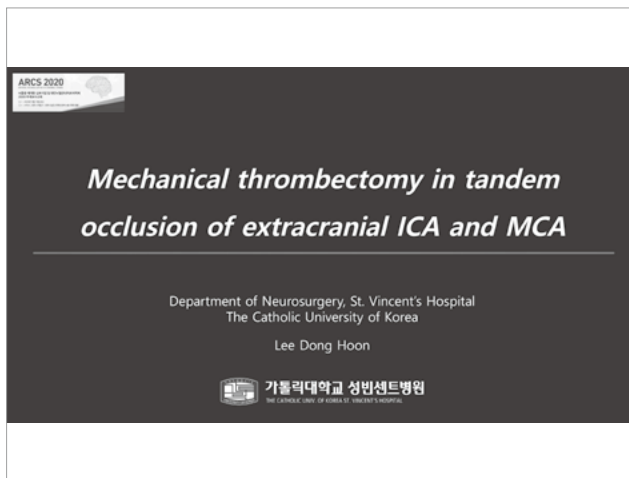


힘든 시기입니다.
모두 기운내세요!

Mechanical thrombectomy in tandem occlusion of extracranial ICA and MCA

이 동 훈

가톨릭대 성빈센트병원 신경외과

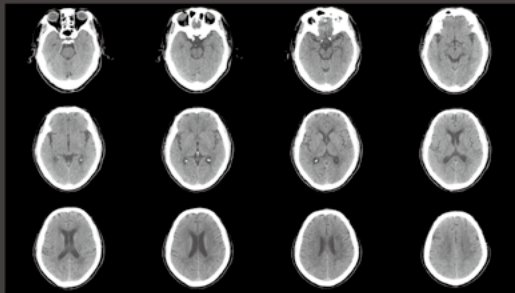


Result

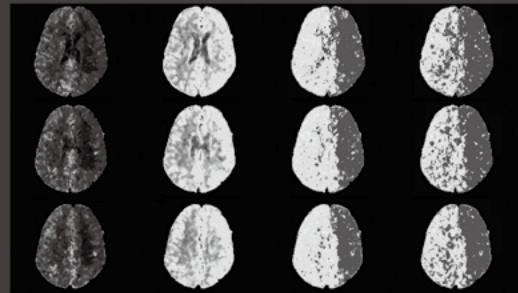
- Successful recanalization (TICI $\geq 2b$) : 19
- Symptomatic ICH : 1
- 3month mRS (≤ 2) : 15

Case

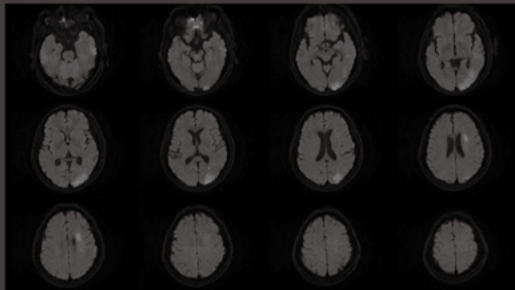
- M/74
- Rt. Side weakness III



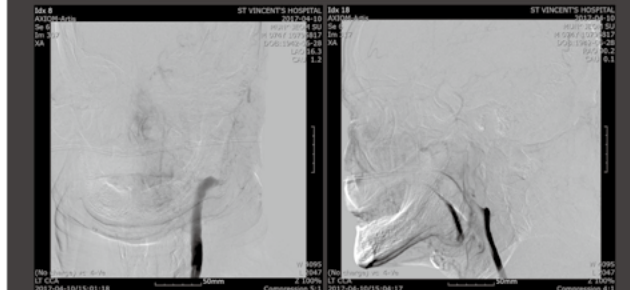
Non-enhance CT



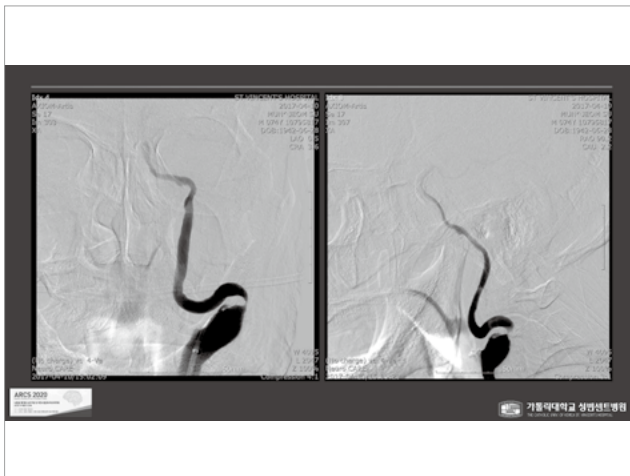
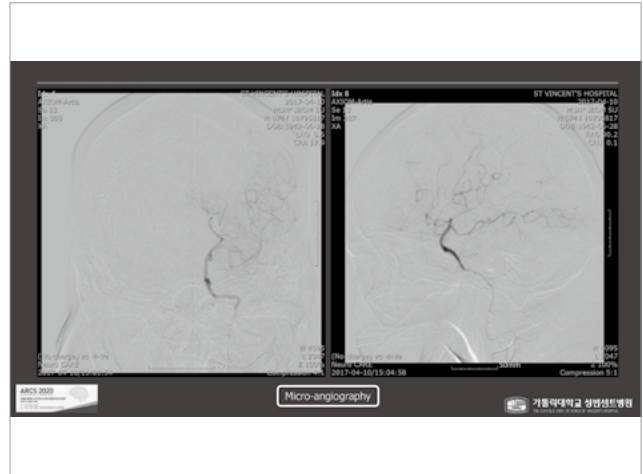
perfusion CT

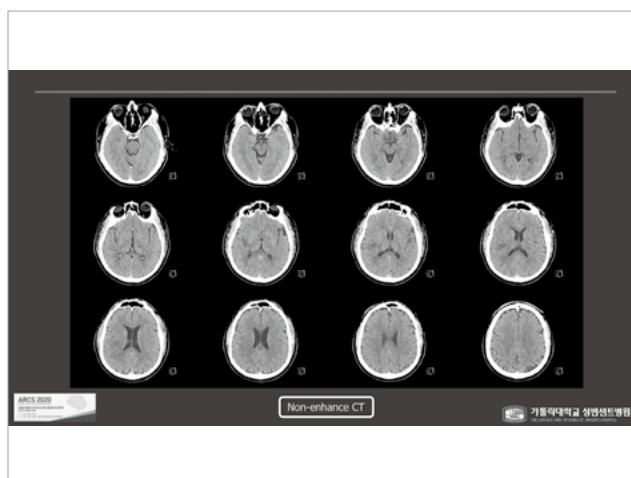
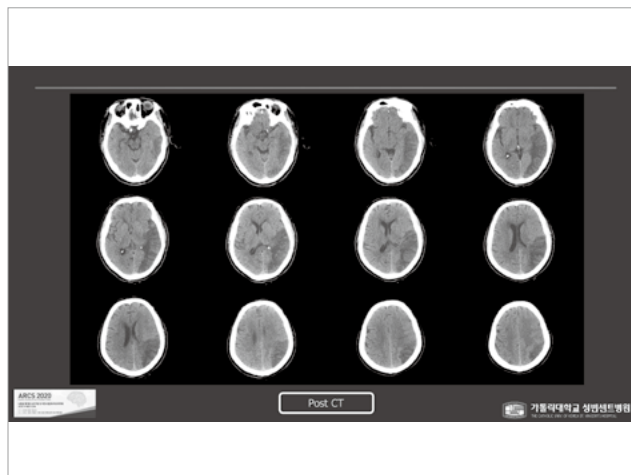


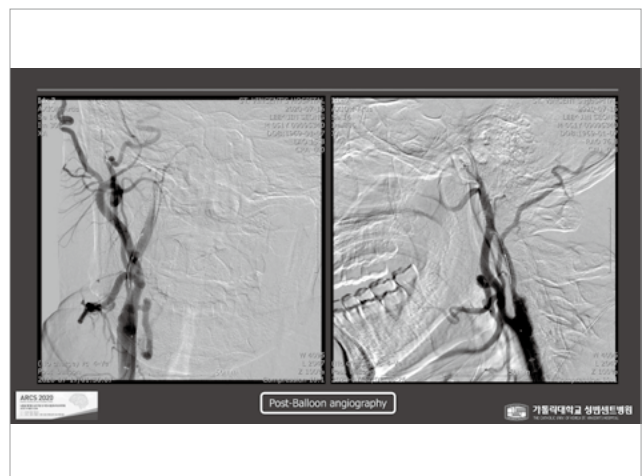
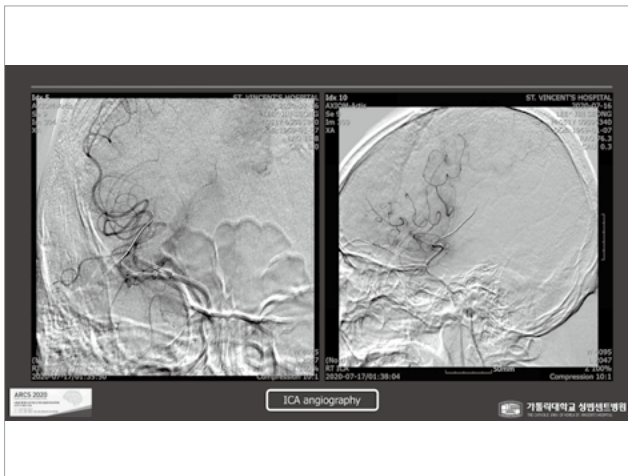
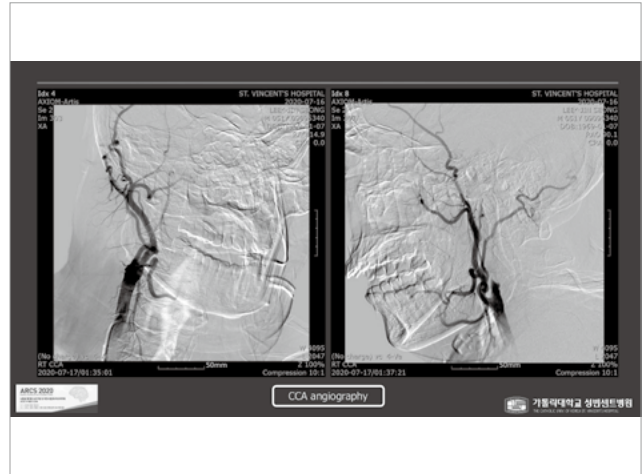
Diffusion MRI

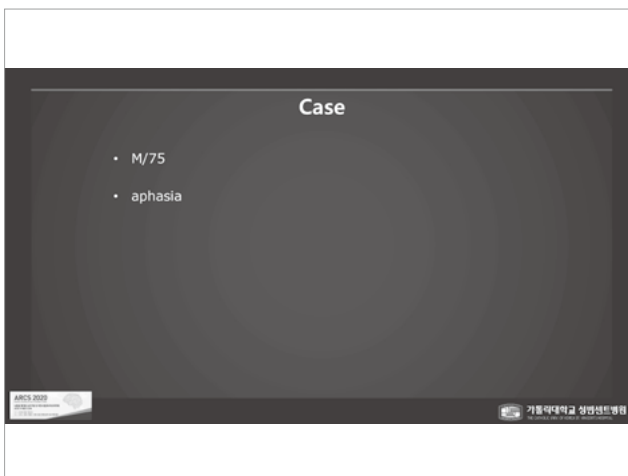
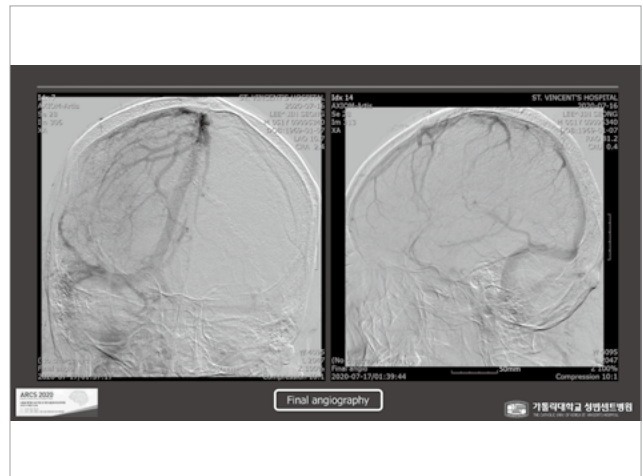
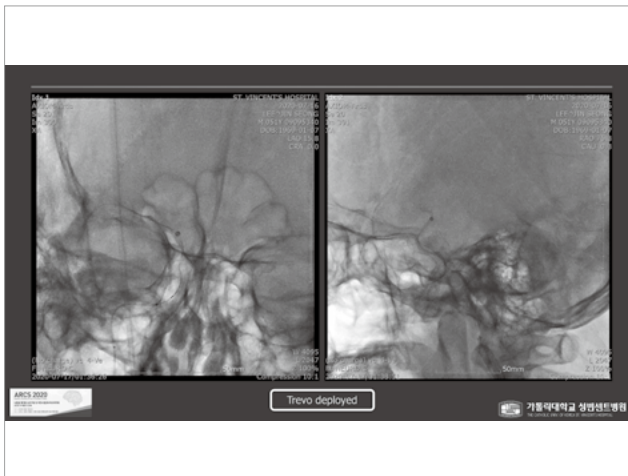
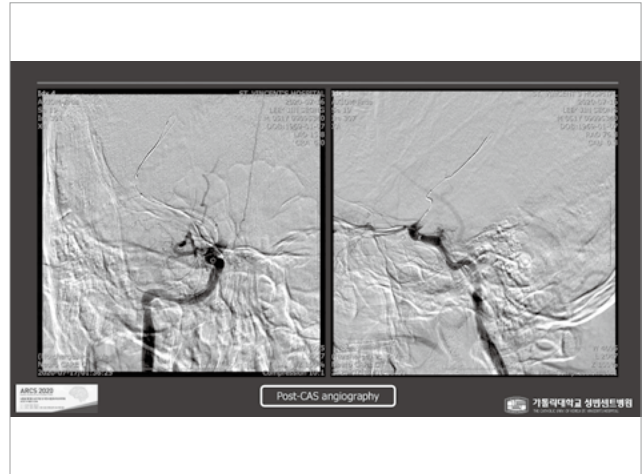
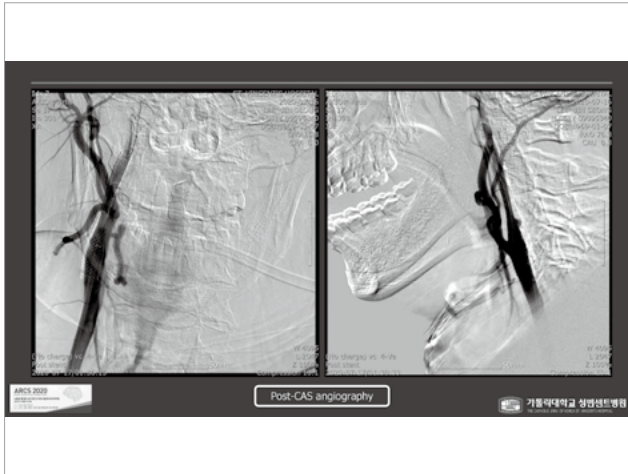


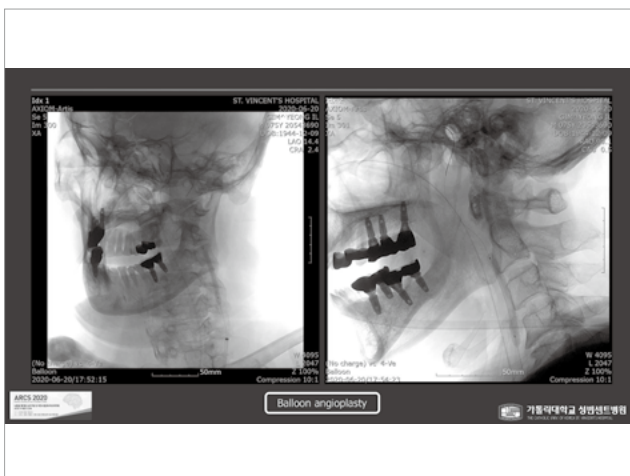
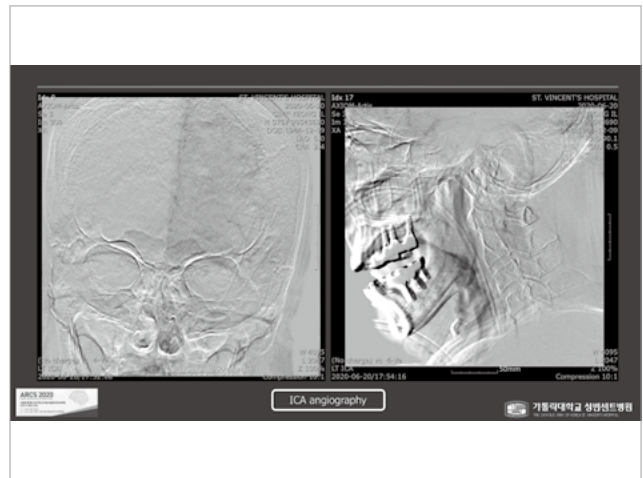
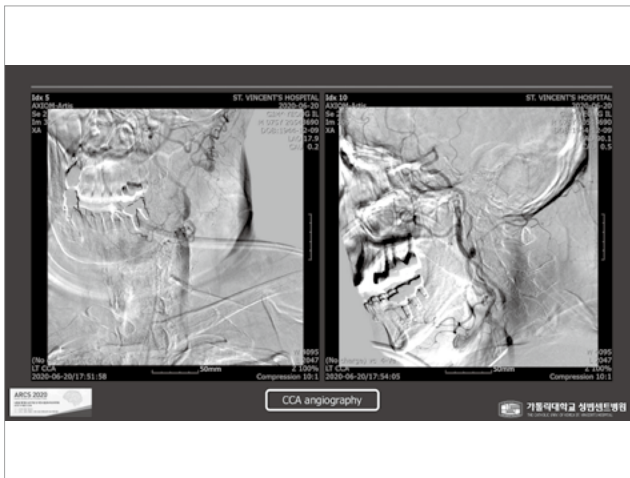
Initial DSA

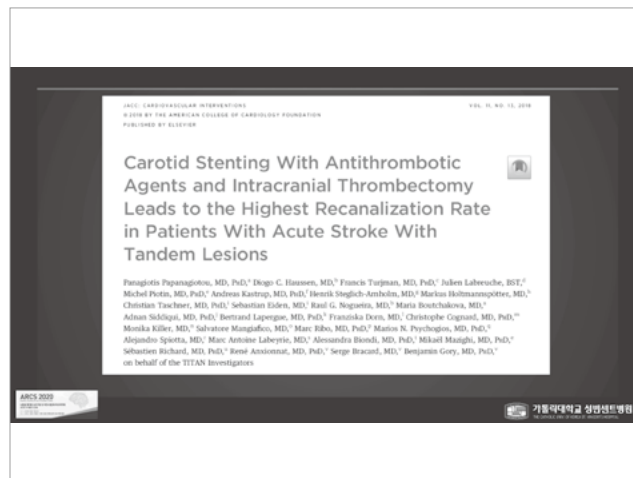
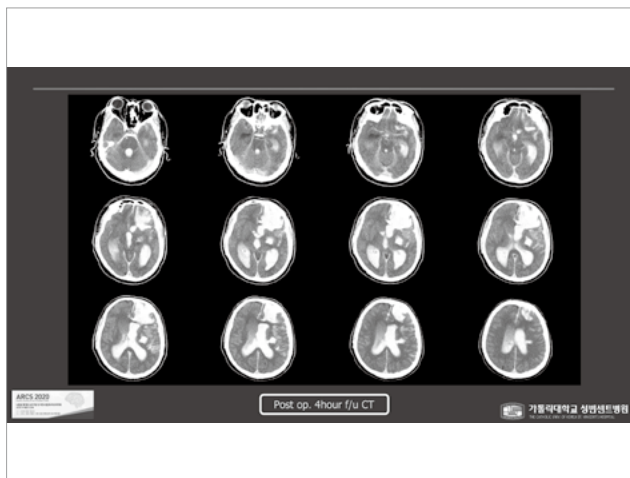












Emergent Management of Tandem Lesions in Acute Ischemic Stroke

Analysis of the STRATIS Registry

Adhishank P. Jadhav, MD, PhD; Osama O. Zaidat, MD; David S. Liebeskind, MD; Dilpreet R. Yavagal, MD; Diego C. Haussen, MD; Frank R. Hellinger Jr, MD, PhD; Reza Jahan, MD; Madhusudan A. Janna, MD; Viktor Storch, MD, PhD, MS; Raul G. Nogueira, MD; Tyler G. Jovic, MD

Background and Purpose—Although intracranial thrombectomy represents the standard treatment approach for anterior circulation tandem occlusions, whether the extracranial lesion requires acute stenting remains unclear. One aim was to investigate differences in clinical and procedural outcomes related to stenting extracranial lesions in a registry of patients undergoing thrombectomy for acute stroke.

Methods—Data were analyzed from the STRATIS registry (Randomized Evaluation of Patients Treated With Neurothrombectomy Devices for Acute Ischemic Stroke)—a prospective, nonrandomized study of patients undergoing neurothrombectomy with the Solitaire device. A total of 994 patients treated at 79 sites were analyzed. Univariate and multivariable logistic regression was used to assess relationship between outcome and procedural technique.

Results—Of 147 (14.9%) patients with tandem lesions treated, stenting of the extracranial lesion during thrombectomy was performed in 80 patients and withheld in 67 patients. There were no differences between groups with respect to age, ASPECTS (American Stroke Program Early CT Score), or intravenous tPA (tissue-type plasminogen activator) use. However, the patients in the stenting group had lower baseline National Institutes of Health Stroke Scale (18 versus 17.9; $P=0.07$), shorter time to arterial puncture time (13.8 versus 15.4 minutes; $P=0.04$), and lower rates of distal thrombolysis (0.7% versus 2.4%; as compared to the nonstenting group). Good outcomes (modified Rankin Scale 0–2) at 90 days were higher in the stenting group (48.5% versus 42.2%; $P=0.001$) with no difference in mortality or symptomatic hemorrhage. After adjustment for covariates, stenting continued to be associated with superior outcomes.

Conclusions—Acute stenting of an extracranial carotid stenosis during neurothrombectomy can be achieved with rapid safety compared with no stenting. Careful stenting in the acute phase may lead to better outcomes that should ideally be confirmed by randomized trials. (Stroke. 2019;50:428–433. DOI: 10.1161/STROKEAHA.118.021053.)

Key Words: arterial thrombolysis • carotid stenosis • intracranial hemorrhage • stroke • stroke • thrombectomy

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Conclusion

Tandem Occlusion: If You See It, Stent It



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Thank you



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Mechanical thrombectomy in M2 or M3 occlusion

최 재 형

동아대병원 신경외과

Mechanical thrombectomy (MT) using newer generation devices had evolved substantially and become the standard treatment for acute ischemic stroke patients with internal carotid artery or proximal middle cerebral artery (MCA) (M1 segment) occlusion. However, the role of MT for patient with distal occlusion of MCA (M2 segment) was underrepresented and still the benefit of MT for distal MCA occlusion remains uncertain and further evidence is warranted. Here, to investigate the efficacy and safety of MT for M2 occlusion, we review the evidences of MT for M2 segment occlusion, natural course of M2 occlusion, clinical outcome of MT for M2 occlusion compared with best medical treatment, thrombectomy result of M1 and M2 occlusion, and treatment outcomes by device type used for MT of M2 occlusion.

Key words: intervention, middle cerebral artery, stroke, thrombectomy



ARCS 2020

ARTERIAL RECANALIZATION IN CEREBRAL STROKE

뇌졸중 재개통 심포지엄 및 대한뇌혈관내치료의학회
2020 추계보수교육

Session II. Acute Ischemic Stroke in the real World (Controversies in Endovascular Stroke Treatment)

좌장: 권순찬 (울산대), 김대원 (원광대)

Optimizing imaging for patients with suspected LVO

Is less better? (Controversies in imaging for endovascular treatment candidates):
Yes or No

The never-ending story: Patients not within the DAWN/DEFUSE 3 criteria should not
be treated with endovascular thrombectomy in the extended time window

Recent trends for AIS (Review of articles)

장동규 (가톨릭대)

오재상 (순천향대)

김중훈 (영남대)

박상규 (연세대)

Optimizing imaging for patients with suspected LVO

장 동 규

가톨릭대 인천성모병원 신경외과

Rapid recognition of a suspected LVO is very important for improving the patients outcome with acute ischemic stroke. The development of field triage stroke scales such as the Cincinnati Prehospital Stroke Severity Scale (CP-SSS), Los Angeles Motor Scale (LAMS), Rapid Arterial Occlusion Evaluation (RACE), FAST (Face, Arms, Speech Test), EMS Vision Aphasia Neglect (VAN) score, Field Assessment Stroke Assessment for Emergency Destination (FAST-ED), and Ambulance Clinical Triage for Acute Stroke Treatment (ACT-FAST) has allowed for faster triage of patients with suspected LVO. However, a recently published meta-analysis reported that no scale could accurately determine presence or absence of LVO with either high sensitivity or specificity. While individual sensitivities and specificities were as high as 87% and 90%, overall positive predictive values are not high. To expedite diagnosis and rapid triage, mobile stroke units (MSUs) have equipped with imaging capabilities (CT and CT angiography) and potential to provide IV-tPA en route to an advanced stroke center. In hospital workflow, use of supplemental radiological data (CT, CT angiography, and CT perfusion) to determine final activation or deactivation is optimal because NIHSS criteria alone to determine thrombectomy candidacy has proven to be inaccurate, missing up to 30% and 60% of anterior and posterior circulation ischemic strokes, respectively. Therefore, it is essential for any automated stroke diagnostic tool to integrate both clinical and radiological data. Another major limitation is the time delay from initial image acquisition of a suspected LVO patient (CT, CTA, CTP) and final notification of the interventional team owing to the need for radiographic interpretation by a stroke specialist and inefficient communication process from initial LVO diagnosis to activation of the interventional team. Teleradiology has emerged as a valuable adjunct in stroke care such as tablet-based radiology platforms and proliferation of MSUs with basic imaging capacity (CT or CTA). Without imaging capabilities in the field, new devices such as the volumetric impedance phase shift spectroscopy (VIPS) device (Cerebrotech, Pleasanton, CA) and SONAS device (BURL Concepts, San Diego, CA) using transcranial US and microbubble intravenous contrast to identify potential LVOs. In hospital situation, development of CT scan and biplane angiography hybrid technology with further improve overall times to treatment. Hybrid imaging systems such as the Siemens MIYABI Angio-CT

(Siemens, Munich, Germany) can expedite thrombectomy when identified on screening imaging (CT/CTA). Helsinki model in expediting thrombolysis eliminated time waste in the preintervention workflow, by physically co-locating CT and angiography. However, in most comprehensive stroke centers, stroke-ready interventional suite may be the standard of care. Incorporating noninvasive angiographic and perfusion imaging (CTA/CTP) would expedite acute stroke care. To maximize efficiency in the preintervention workflow, rapid recognition of a potential LVO in the field with the adoption of MSUs with imaging capacity (especially CTA) and prehospital notification of incoming LVO. Rapid radiological processing and interpretation of imaging is mandatory.

Cerebral imaging is the only way to ascertain the presence of LVO and exclude a hemorrhagic stroke.

1. Computed Tomography : noncontrast CT scan is the most valuable initial investigation excluding hemorrhagic stroke within seconds of evaluation. The head CT scan may be normal within the first few hours of stroke onset. Hyperdense vessel sign suggests acute arterial occlusion with 19% to 40% of MCA stroke cases. Hyperdense sign of ICA, basilar artery, and proximal PCA can be found.
2. Alberta Stroke Program Early CT Score : A score of <6 indicates high ischemic burden. Patients with ASPECTS of 0 to 5 showed a trend toward improved outcomes with EVD. The addition of CTP may help in stratifying low ASPECT patients. ASPECTS decay by interhospital transfer can be found 1 of every 3 patients becoming ineligible for thrombectomy. Therefore, repeating imaging when a transferred patient with neurological decline may be prudent.
3. ASPECTs for Non-MCA territory infarcts : ACA or posterior circulation occlusion account for 1-2% and 10-20%, respectively. There are still neither reliable scoring system nor consensus for imaging predictors of posterior stroke outcomes.
4. MRI : Highly sensitive for the detection of early ischemia but less readily available and needs clearance to exclude certain implants, and takes longer imaging time. To decrease the acquisition times, limited number of sequences, ie, DWI, FLAIR, and GE can be performed. Changes seen on the DWI are sometimes reversible. Some centers use MRI for stroke screening with MR perfusion (MRP) imaging to assess the area of irreversible ischemic change. After MRI scan, IV tPA decision can be complicated because there are no guidelines for the safety of tPA in the presence of microbleeds, cerebral amyloid angiopathy, and cavernous malformation.
5. CTA and MRA : Detection and localization of the occlusion site with CTA or MRA. CTA is critical for planning thrombectomy revealing the anatomy of the aortic arch, cervical tortuosity, severe stenosis, or occlusion and the extent of thrombus affecting the choice of vascular access, thrombectomy devices, and adjunct tools. MRA can benefit patients who have an allergy to

iodinated contrast. Typically an NIHSS score of 6 is taken as the cut-off for performing CTA or MRA since there is limited evidence to support the use of EVT in patients with NIHSS scores of <6 despite the evidence that LVO can be present in patients with NIHSS <6.

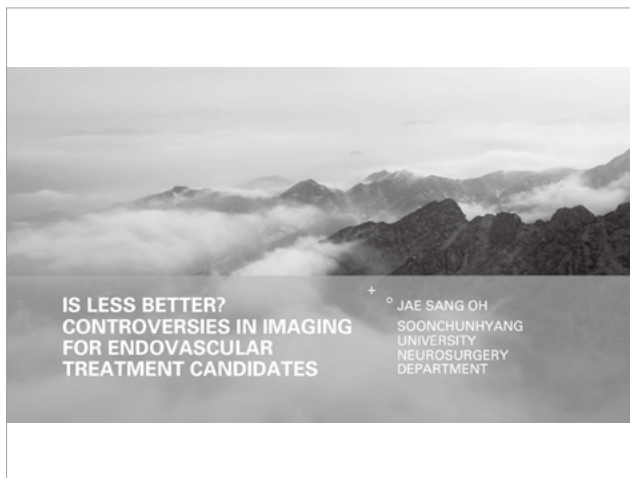
6. Multiphase CTA : Evaluation of intracranial collateral vessels. Multiphase CTA can help in the identification of a distal or small vessel occlusion.
7. Perfusion Imaging : MR- and CT-based perfusion studies are useful to assess irreversible infarct core and potentially salvageable tissue at risk (ischemic penumbra). CTP is preferred over MRP due to only minimal delay of only 4 to 5 minutes. Routine use of CTP/MRP is highly variable depending on the center or physician preference. Sometimes it is reserved for unclear or challenging cases such as awake stroke or late presentation whereas other centers perform it routinely.
8. Imaging for Late-Presenting Strokes : DAWN trial and DEFUSE 3 trial had used clinical imaging mismatch (combination of NIHSS score and imaging findings on CTP or DWI MRI). CTP, DW-MRI, and perfusion MRI are recommended in the AHA guidelines those who present after 6h of LKW time and meet the selection criteria for either trial. This recommendation can increase 30% of the number of thrombectomy-eligible patients.

In conclusion, according to individual center's circumstance, optimization of imaging modalities can improve early recognition and rapid recanalization, leading to better clinical outcome with suspected LVO.

Is less better? (Controversies in imaging for endovascular treatment candidates): Yes or No

오 재 상

순천향대 천안병원 신경외과



All you need ..

- Time is Brain
- Early time, late time
- What do you want?



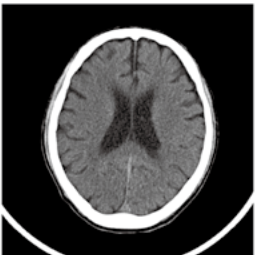
Making decision

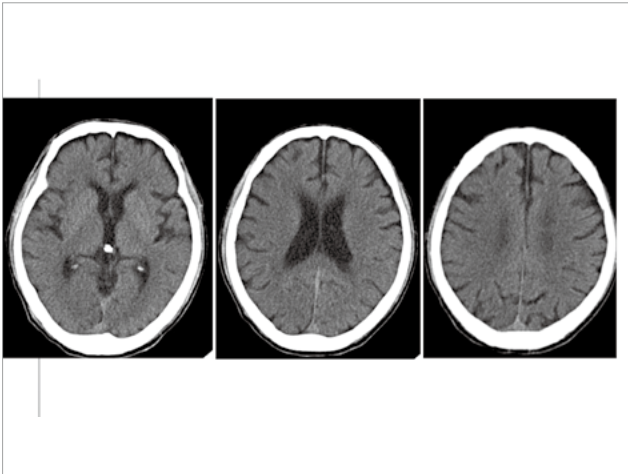
- Information of patient's clinical status
- Brain image
 - CT
 - CTA
 - MRI & MRA
 - DWI / FLAIR
 - Perfusion MRI



Case 1

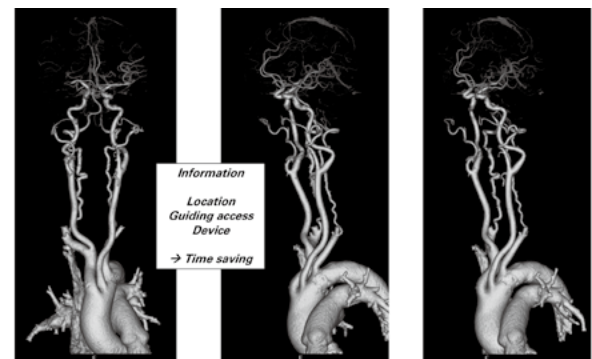
- M/74
- C/C) Lt. hemiparesis
- Past Hx.) HTN, DM, CVD(s/p PCI), HCC
 - 07.21 HCC : RFA
 - 07.22 항혈전제 재복용
- Onset to door 20min





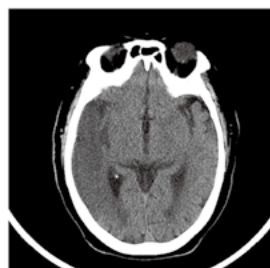
Next Step?

- First , IV tPA vs Brain angio CT vs DWI vs MRA
- If, IV tPA injection
- 2020.07.25 NR IV tPA
- Second,
Immediately IA MT vs Brain angio CT vs DWI vs MRA



Case 2

- F/86
- C/C) Lt. hemiparesis
- Past Hx.) HTN
- Unknown onset
- Wake up stroke





Next Step?

- First, if No IV tPA

Immediately IA MT vs Brain angio CT vs DWI vs MRA

- NS call "improved hemiparesis gt 3 → 4+"

- Next?
- Immediately IA MT vs Medical management
- Brain angio CT vs DWI vs MRA

Clinical Trials

Different Clinical Criteria & Different Image Criteria

- MR CLEAN
- ESCAPE
- EXTEND-IA
- REVASCAT
- SWIFTPRIME
- THRACE
- THERAPY
- DEFUSE-3
- DAWN

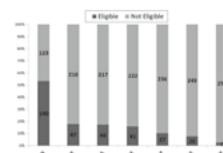
Tawil et al. European Stroke Journal 2016 1(4):264-271

Study	Clinical criteria			CTA criteria		Tissue selection criteria		
	Age	Pre-stroke function	Max time from onset to endovascular therapy	NIHSS	Patients ineligible for IV tPA	Baseline NCCT	Perfusion criteria	Collaterals
MR CLEAN ¹	≥18	Any	6h	≤3	No	ICA, M1, M2, A1, A2	Not used for selection	Not used for selection
ESCAPE ²	≥18	Barthel index > 90	12h	>5	Included	ICA, M1, M2 equivalent (two or more PG occlusions)	ASPECT score > 5	Not used for selection
EXTEND-IA ³	≥18	mRS ≤ 2	6h	Any	No	ICA, M1 or M2	Hypodensity more than one third of MCA territory	Not used for selection
REVASCAT ⁴	18-85	mRS ≤ 1	6h	≤4	Included	ICA or M1	ASPECT > 6 for patients < 80 years	Not used for selection
SWIFTPRIME ⁵	18-80	mRS ≤ 1	6h	≤8-30	No	ICA or M1	ASPECT > 6	Not used for selection
THRACE ⁶	18-80	Any	6h	≤10-25	No	ICA, M1, upper third of basilar	Not used for selection	Not used for selection
THERAPY ⁷	18-85	mRS ≤ 0	Within local thrombolysis window	≤8 or aphasia	No	Large artery thrombolysis occlusion in anterior circulation	Hypodensity more than 1/3 of the MCA territory	Not used for selection

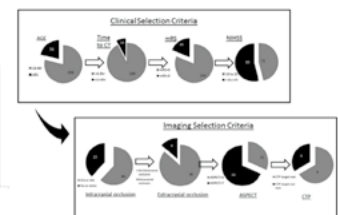
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EXTEND-IA ³	≥18	mRS ≤ 2	6h	Any	No	ICA, M1 or M2	Hypodensity more than one third of MCA territory	Not used for selection
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THERAPY ⁷	18-85	mRS ≤ 0	Within local thrombolysis window	≤8 or aphasia	No	Large artery thrombolysis occlusion in anterior circulation	Hypodensity more than 1/3 of the MCA territory	Not used for selection

Seven RCT

- 263 patients

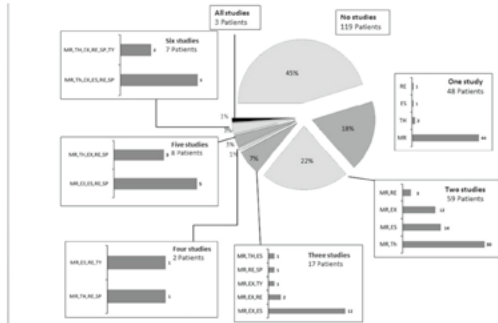


Meeting criteria for each of studies
IA eligibility 53% on MR CLEAN
17% for EXTEND-IA

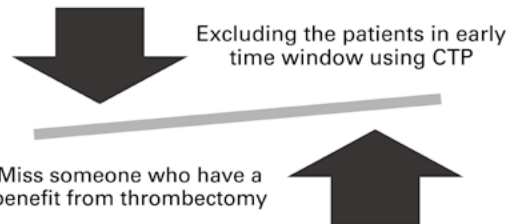


Different clinical and imaging selection criteria

El Tawil et al. European Stroke Journal 2016;1(4):264-271



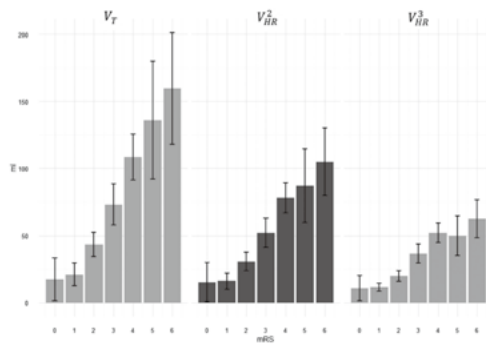
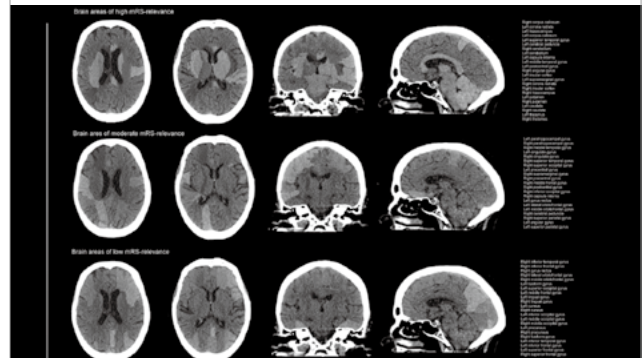
IA Thrombectomy indication ?



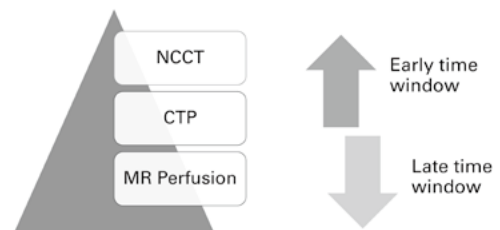
NCCT is enough?

- Ischemic lesion between ..
 - Noncontrast computed tomography (NCCT)
 - Modified Rankin Scale (mRS)
- MR CLEAN 500 patients
- Ischemic lesion on NCCT
- Different outcome according to different ischemic lesion

M. Ernst et al. Stroke 2017;48:2426-2433



TMI.... In early time window

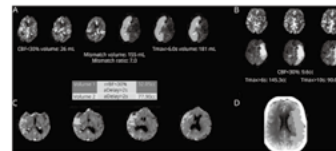


Only time is not brain

- Image is also brain..
- DAWN & DEFUSE 3

Automatic CT perfusion for AIS

- DAWN : NIHSS and Ischemic core
- DEFUSE : Tmax > 6 secs
- T max, MTT, CBF (mL/100g/min), CBV



Achala Vagal et al. Neurology 2018;93:1-11

Pitfalls and pearls of automated CTP

1. Patient motion
2. Poor contrast bolus
3. Brain coverage
4. Excessive radiation for CTP
5. Underestimation of the ischemic core
6. Core volumes calculation using a set threshold
7. Penumbral misclassification
8. Posterior fossa and lacunar strokes
9. Variation in CTP results across Vendors
10. Stroke mimics

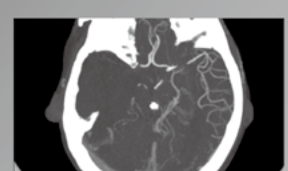
Misclassification of penumbral mismatch

- Overestimated penumbral zone
 - Chronic infarction
 - Carotid stenosis
 - Chronic occlusion
 - Cardiac arrhythmia
 - Aortic dissection
- Not reliable to
 - ...posterior fossa, lacune infarction, severe white matter disease



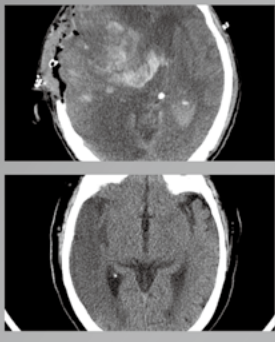
Which is worst?

- Within one hour
- Unknown onset



Which is worst?

- Within one hour
- Unknown onset



Final result

- Within one hour
→ mRS 6
- Unknown onset
→ mRS 3

Conclusion

- Each study had a different inclusion criteria.
- NCCT is sometime enough in early time window.
- Other studies could give a benefit in late time window.
- But it is not always correct.

The never-ending story: Patients not within the DAWN/DEFUSE 3 criteria should not be treated with endovascular thrombectomy in the extended time window

김 종 훈

영남대병원 신경외과



The never-ending story

Patients not within the DAWN/DEFUSE 3 criteria should not be treated with EVT in the extended time window

영남대병원 신경외과
김종훈

ORIGINAL RESEARCH

Real-world stent retriever thrombectomy for acute ischemic stroke beyond 6 hours of onset: analysis of the NASA and TRACK registries

Maxim Mokin,¹ Alex Abou-Cheik,² Alicia C Castonguay,³ Raul G Nogueira,⁴ Joey D English,⁵ Hamed Farid,⁶ Rishi Gupta,⁷ Coleman Martin,⁸ William Edward Holloway,⁹ Diogo C Hausman,¹⁰ Nils Mueller-Kronast,⁹ Osama O Zaidat,¹⁰ on behalf of the NASA and TRACK Investigators.

Mokin M, et al. *J Neurointerv Surg* 2019;11:334-337.

- Specifically, in patients with occlusion of the ICA or M1, 34% arrived at the hospital beyond the first 6 hours from symptom onset, including wake-up strokes.
- Patients with unknown time of onset stroke, including wake-up stroke (WUS) and those who had late presentations: These patients are estimated to account for up to 40% of AIS with LVOs in the anterior circulation.

YU MC 영남대학교의료원

Evolution of endovascular reperfusion therapy



1999: PROACT II

2005: MERCI

2007: MELT

2009: Penumbra pivotal trial, 1st Solitaire case

2011: MAIA MERCI

2012: SYNTHESIS MR RESCUE

2013: SYNTHESIS MR RESCUE

2015: MR CLEAN, ESCAPE, EXTEND-IA, REVASCAT, SWIFT prime

2016: THRACE, THERAPY

2017: DEFUSE 3

2018: DEFUSE 3

Benefit of EVT (difference of 3M mRS)

Mechanical Thrombectomy beyond 6 Hour

New Era of Acute Stroke Care

DAWN and DEFUSE 3 trial



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

Reviewed for evidence-based integrity and endorsed by the American Association of Neurological Surgeons and Congress of Neurological Surgeons

Endorsed by the Society for Academic Emergency Medicine

William J. Powers, MD, FAHA, Chair; Alejandro A. Rabinstein, MD, FAHA, Vice Chair; Teri Ackerson, BSN, RN; Opeolu M. Adeoye, MD, MS, FAHA; Nicholas C. Bambakidis, MD, FAHA; Kyra Becker, MD, FAHA; José Biller, MD, FAHA; Michael Brown, MD, MSc; Bart M. Demaerschalk, MD, MSc, FAHA; Brian Hoh, MD, FAHA; Edward C. Jauch, MD, MS, FAHA; Chelsea S. Kidwell, MD, FAHA; Thabele M. Leslie-Mazwi, MD; Bruce Ovbiagele, MD, MSc, MAS, MBA, FAHA; Phillip A. Scott, MD, MBA, FAHA; Kevin N. Sheth, MD, FAHA; Andrew M. Southerland, MD, MSc; Deborah V. Summers, MSN, RN, FAHA; David L. Tirschwell, MD, MSc, FAHA; on behalf of the American Heart Association Stroke Council

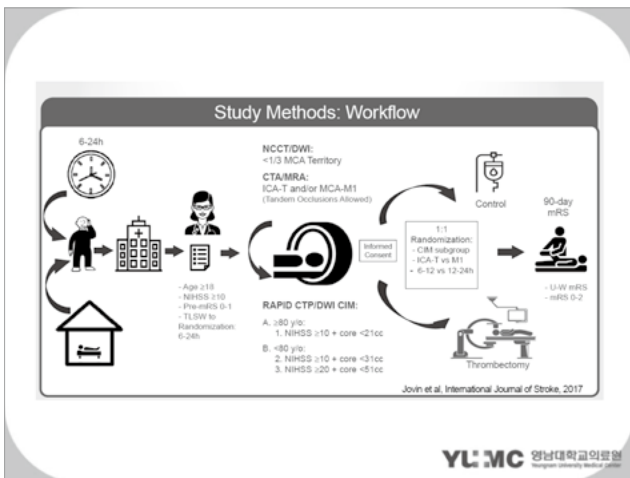
3.7. Mechanical Thrombectomy (Continued)	COR	LOE	New, Revised, or Unchanged
7. In selected patients with AIS within 6 to 16 hours of last known normal who have LVO in the anterior circulation and meet other DAWN eligibility criteria, mechanical thrombectomy is recommended.	I	A	New recommendation.
8. In selected patients with AIS within 6 to 24 hours of last known normal who have LVO in the anterior circulation and meet other DAWN eligibility criteria, mechanical thrombectomy is reasonable.	Ia	B-R	New recommendation.
The DAWN trial used clinical imaging mismatch as 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).¹⁰⁸ 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; $P < 0.0001$).¹⁰⁹ 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 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 and DEFUSE-3 eligibility should be strictly adhered to in clinical practice.			
9. The technical goal of the thrombectomy procedure should be reperfusion to a modified Thrombolysis in Cerebral Infarction (mTICI) 2b/3 angiographic result to maximize the probability of a good functional clinical outcome.	I	A	Recommendation reworded for clarity from 2015 Endovascular. See Table LXXVIII in online Data Supplement 1 for original wording.

DAWN Study

DWI or CTP Assessment with clinical mismatch in the triage of Wake up and late presenting strokes undergoing Neurointervention

A multi-center, phase II/III, prospective, randomized, open-label, blinded outcome (PROBE) trial

Patient	AIS Subjects with the followings inclusion criteria
Intervention	Trevo thrombectomy plus medical management
Comparison	Medical management alone
Outcome	Average weighted mRS score / proportion of good functional outcome at 90 days
Inclusion criteria	- Clinical signs and symptoms consistent with the diagnosis of an acute ischemic stroke - Age ≥ 18 - Baseline NIHSS ≥ 10 (assessed within 1 hour prior to measuring core infarct volume) - Can be randomized between 6 to 24 hours after time last known well - Pre-stroke mRS must be 0 or 1
Imaging inclusion criteria	<1/3 MCA territory involved, as evidence by CT or MRI - Occlusion of the intracranial ICA and/or MCA-M1, as evidence by MRA or CTA - Clinical imaging mismatch defined as one of the following on RAPID MR-DWI or CTP-CBF maps: 0-20 cc core infarct and NIHSS ≥ 10 (and age ≥ 80 years old) 0-30 cc core infarct and NIHSS ≥ 10 (and age < 80 years old) 31-50 cc core infarct and NIHSS ≥ 20 (and age < 80 years old)



DEFUSE 3 Study

Diffusion and perfusion imaging Evaluation For Understanding Stroke Evolution

A multicenter, phase III, prospective, randomized, open-label, blinded outcome (PROBE) trial

Patient	AIS Subjects with the followings inclusion criteria
Intervention	Endovascular therapy plus medical management
Comparison	Medical management alone
Outcome	Ordinal score on the mRS at 90 days
Inclusion criteria	- Clinical signs and symptoms consistent with the diagnosis of an acute ischemic stroke - Age 18-85 years - Baseline NIHSS ≥ 6 and remains ≥ 6 immediately prior to randomization - Endovascular treatment can be initiated between 6 to 16 hours after time last known well - Pre-stroke mRS must be 0 or 2
Imaging inclusion criteria	- Occlusion of the ICA or MCA-M1, as evidence by MRA or CTA - Target Mismatch Profile on CT perfusion or MRI - Ischemic core volume < 70 ml - Mismatch ratio > 1.8 - Mismatch volume ≥ 15 ml

Comparison the study design and enrolled criteria

	DAWN	DEFUSE 3
Study design	Phase II/III PROBE	Phase III PROBE
Locations	26 centers in US, Canada, Europe and Australia	38 centers in US
Recruiting period	2014.09-2017.02 (2y5m)	2014.05-2017.05 (3y)
Recruited patients No.	296	182
Intervention group	107	52
Control group	99	50
Clinical inclusion criteria		
Age	≥ 18	18-85
Baseline NIHSS	≥ 10	≥ 6
Time window	6-24 hrs after LST	6-16 hrs after LST
Pre-stroke mRS	0-1	0-2
Imaging inclusion criteria		
Occlusion site	Intracranial ICA and/or M1	ICA or M1
Mismatch profile	Clinical imaging mismatch	Target mismatch on CT/MRI
Core volume	<21 (acute), <31 (age 18-79) or 31-50 (NIHSS ≥ 20 and age < 80)	< 70 ml
Mismatch ratio	None	> 1.8
Mismatch volume	None	> 15 ml

- DEFUSE 3 trial enrolled a broader patient population than the DAWN trial except time window.
- 62% of DEFUSE 3 patients met DAWN eligibility criteria.

"Time is Brain"

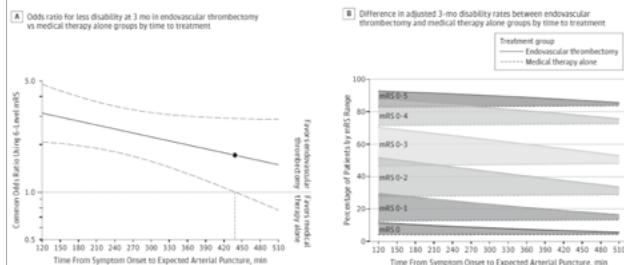


Time is brain, that is for sure

JAMA | Original Investigation

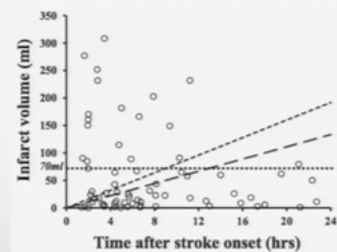
Time to Treatment With Endovascular Thrombectomy and Outcomes From Ischemic Stroke: A Meta-analysis

JAMA September 27, 2016 Volume 316, Number 12



Time does not explain everything !

68 consecutive patients with MCAO or distal ICAO within 24 hours from onset



Replicated from Copen, Radiology, 2009.

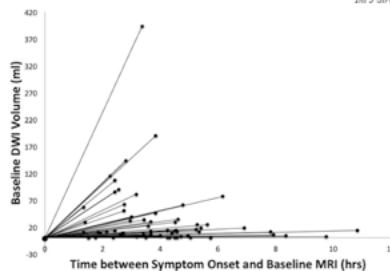
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Time does not explain everything !

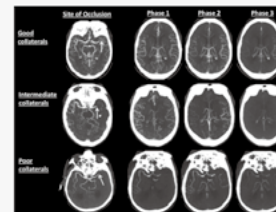
The Growth Rate of Early DWI Lesions is Highly Variable and Associated with Penumbra Salvage and Clinical Outcomes Following Endovascular Reperfusion

Hayley W Wheeler, BS, Michael Mlynash, MD MS, Marouf Inoue, MD PhD, Aaryani Tigmisi, MS, John Liggins, MS, Roland Bammer, PhD, Maarten O Lenoir, MD PhD, Stephanie Kemp, BS, Greg Zaharchuk, MD PhD, Matus Straka, PhD, Gregory W Albers, MD, and On behalf of the DEFUSE 2 Investigators
Stanford Stroke Center, Stanford University School of Medicine, Stanford, CA 1215 Welch Road, Modular D Stanford, CA 94305 USA

Int J Stroke. 2015 July; 10(5): 723-729. doi:10.1111/ij.12436.



- Initial DWI growth rate for the 65 patients with known time of stroke onset.
- Overall, median initial growth rate was 3.1 ml/hr, from 0 ml/hr to 117 ml/hr.

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mCTA Collateral Score and Description

- Score: Modified T-Map
- When compared with the asymptomatic control template, there is no flow and/or no flow is increased posteriorly of the asymptomatic control template.
 - When compared with the asymptomatic control template, there is a flow of one phase in flow in of posterior vessels, but anterior and middle is the same.
 - When compared with the asymptomatic control template, there is a flow of two phases in flow in of posterior vessels and one phase in flow in of anterior vessels.
 - When compared with the asymptomatic control template, there is a flow of three phases in flow in of posterior vessels and one phase in flow in of anterior vessels.
 - When compared with the asymptomatic control template, there is a flow of four phases in flow in of posterior vessels and one phase in flow in of anterior vessels.
 - When compared with the asymptomatic control template, there is a flow of five phases in flow in of posterior vessels and one phase in flow in of anterior vessels.
 - When compared with the asymptomatic control template, there is a flow of six phases in flow in of posterior vessels and one phase in flow in of anterior vessels.
 - When compared with the asymptomatic control template, there is a flow of seven phases in flow in of posterior vessels and one phase in flow in of anterior vessels.
 - When compared with the asymptomatic control template, there is a flow of eight phases in flow in of posterior vessels and one phase in flow in of anterior vessels.
 - When compared with the asymptomatic control template, there is a flow of nine phases in flow in of posterior vessels and one phase in flow in of anterior vessels.
 - When compared with the asymptomatic control template, there is a flow of ten phases in flow in of posterior vessels and one phase in flow in of anterior vessels.
 - When compared with the asymptomatic control template, there is a flow of eleven phases in flow in of posterior vessels and one phase in flow in of anterior vessels.
 - When compared with the asymptomatic control template, there is a flow of twelve phases in flow in of posterior vessels and one phase in flow in of anterior vessels.
 - When compared with the asymptomatic control template, there is a flow of thirteen phases in flow in of posterior vessels and one phase in flow in of anterior vessels.
 - When compared with the asymptomatic control template, there is a flow of fourteen phases in flow in of posterior vessels and one phase in flow in of anterior vessels.
 - When compared with the asymptomatic control template, there is a flow of fifteen phases in flow in of posterior vessels and one phase in flow in of anterior vessels.
 - When compared with the asymptomatic control template, there is a flow of sixteen phases in flow in of posterior vessels and one phase in flow in of anterior vessels.
 - When compared with the asymptomatic control template, there is a flow of seventeen phases in flow in of posterior vessels and one phase in flow in of anterior vessels.
 - When compared with the asymptomatic control template, there is a flow of eighteen phases in flow in of posterior vessels and one phase in flow in of anterior vessels.
 - When compared with the asymptomatic control template, there is a flow of nineteen phases in flow in of posterior vessels and one phase in flow in of anterior vessels.
 - When compared with the asymptomatic control template, there is a flow of twenty phases in flow in of posterior vessels and one phase in flow in of anterior vessels.

- The status of collaterals : the most important factor in differentiating 'fast progressors' from 'slow progressors'

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Time does not explain everything !

- The aim of reperfusion therapy : to reverse ischemic process by salvaging the penumbra, limit the final infarct size
- Current selection criteria for reperfusion therapy use strict time windows.
- This is based on the assumption that : the ischemic process evolves in time is similar in all individuals
- However, due to significant variability in collateral capacity : this process occurs at different speeds in different individuals
- a physiological rather than chronological approach to patient selection

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Comments and Opinions

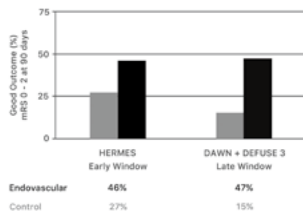
Late Window Paradox

Gregory W. Albers, MD

(Stroke. 2018;49:768-771. DOI: 10.1161/STROKEAHA.117.020206.)

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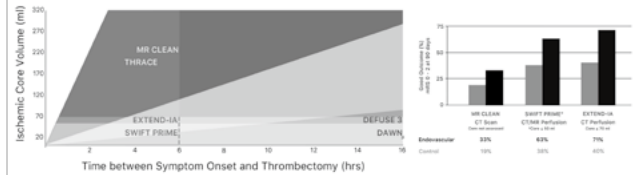
Larger Benefits With Later Treatment (Late window paradox)



- Absolute increase in mRS of 0-2
19% early window vs 32% late window
($P=0.006$, Breslow-Day test)

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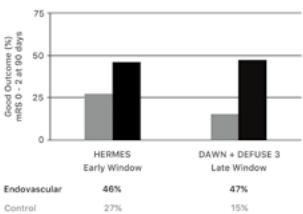
Variable growth rate of early DWI lesions



- DWI growth rates in patients with MCA or ICA occlusion
 - Rapid early growth rates (red zone) : ~20% with growth rates of 15-100mL/h
 - Intermediate growth (yellow zone) : ~30% with growth rates of 3-10mL/h
 - Slow growth (green zone) : ~50% with very high rate of stable DWI volumes during the early hours after stroke

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Late Window Paradox



- Very poor outcome in control groups in these late window trials
 - No IV-tPA therapy (with 35-40% reperfusion rate)
 - Eventually, the collateral circulation fails and infarcts evolve into the region of critical hypoperfusion in these control groups with large volume of tissue at risk

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Explaining the Paradox by Understanding Stroke Evolution

- a substantial percentage of patients with LVOs have very slow growth of the ischemic core for up to 12 hours or longer.
 - Although some fortunate patients never develop a large infarct despite a persistent large artery occlusion : the vast majority of the slow growers with LVOs will eventually develop an extensive infarction
 - Typically takes 3 days for the maximum DWI volume to be achieved in non-reperused patients.
- Therefore, late arriving patients with LVOs and small infarct core volumes can have extremely robust treatment effects.

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Late Window Paradox

- Only a minority (probably <10%) of these patients have collaterals that are adequate to assure a favorable outcome in the absence of reperfusion
- The bottom line is the absolute benefit was larger in the late window studies.

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Neuroradiology (2019) 61:115-117
<https://doi.org/10.1007/s00234-018-2122-1>

EDITORIAL

Treatment of ischemic stroke beyond 3 hours: is time really brain?

Rüdiger von Kummer¹

- Neurons can tolerate CBF below 10 ml/100g/min for a maximum of 30 min, and can survive ischemic CBF values above 18 ml/100g/min for an indeterminate period of time.
- Modern brain imaging with DWI and PWI confirmed these findings in IS patients showing no infarct growth and persistence of penumbra over 24 hours.

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Is time really brain ?

- Time does not mean progressive loss of brain tissue after each IS, and there is a stroke population that *can recover* with arterial recanalization and restoration of blood supply far beyond 3 hours.
- The pathological conditions that enable or inhibit benefit from reperfusion therapy are *still widely unknown*.
- And the question which LVO strokes should not be treated remains *unanswered*.

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Is time really brain ?

- It is believed that in the *presence of LVO and severe neurological deficit*, a small core is usually associated with a large area of tissue at risk (penumbra), with *small core being the strongest predictor of favorable outcome following reperfusion therapy*.
- Safety concerns remain and are likely to represent the *main reason why physicians are reluctant to treat patients beyond 24 h*.
- Device, technique, Indication...

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Endovascular Treatment of Acute Ischemic Stroke May Be Safely Performed With No Time Window Limit in Appropriately Selected Patients

Alex Abou-Chebl, MD

Background and Purpose—The traditional time window for acute ischemic stroke intra-arterial therapy (IAT) is <6 hours, which is based on pharmacological thrombolysis without penumbral imaging. This study was conducted to determine the safety of patient selection for IAT based on perfusion mismatch rather than time.

Methods—A cohort of consecutive patients treated with IAT was identified by database review. Patients were selected for IAT based on the presence of perfusion mismatch using CT perfusion or MRI regardless of stroke duration. Thrombolysis was minimized after 6 hours in favor of mechanical embolectomy or angioplasty ± stenting. Outcomes (National Institutes of Health Stroke Scale, modified Rankin Scale) were assessed by independent examiners. A multivariate analysis was performed to compare those treated <6 hours (early) with those treated >6 hours (late).

Results—Fifty-five patients (mean National Institutes of Health Stroke Scale=19.7±5.7) were treated, 34 early and 21 late, with mean time-to-intervention of 3.4±1.6 hours and 18.6±16.0 hours, respectively. Thrombolysis in Myocardial Ischemia 2 or 3 recanalization was achieved in 82.8% early and 85.7% late patients ($P=1.0$). Intracerebral hemorrhage occurred in 25.5% overall, but symptomatic intracerebral hemorrhage occurred in 8.8% of the early and 9.5% of the late patients ($P=1.0$). Thirty-day mortality was similar (29.4% versus 23.8%, $P=0.650$). At 3 months, 41.2% and 42.9%, respectively, achieved a modified Rankin Scale ≤2 ($P=0.902$). Only presenting National Institutes of Health Stroke Scale was a predictor of modified Rankin Scale ≤2 (OR 0.794[95% CI 0.68 to 0.92], $P=0.009$) and death (adjusted OR 1.29[95% CI 1.04 to 1.59], $P=0.019$).

Conclusions—In appropriately selected patients, IAT for acute ischemic stroke can be performed safely regardless of stroke duration. The concept of an acute ischemic stroke treatment window for IAT should be re-evaluated with a clinical trial selecting patients with perfusion mismatch. (Stroke. 2018;41:1996-2000.)

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No Time Window Limit

Table 2. Procedural Outcomes and Complications

No. (%)	Early	Late	Overall	P
Recanalization				
TIM 2 or 3	28 (82.8%)	18 (85.7%)	46 (84%)	1
TIM 3	14 (41.2%)	10 (47.6%)	24 (43.6%)	0.783
Intracerebral Hemorrhage*				
All	9 (25.5%)	5 (23.8%)	14 (25.5%)	0.905
Asymptomatic	3 (8.8%)	2 (9.5%)	5 (9.1%)	1
Postoperative change in NIHSS	8.1±6.7	5.5±5.9	7±6.4	0.19
Death at 30 days	10 (29.4%)	5 (23.8%)	15 (27.3%)	0.65
Modified Rankin Scale ≤2 at 3 months				
All	14 (41.2%)	9 (42.9%)	23 (41.8%)	0.902
Survivors	14 (80.9%)	9 (56.2%)	23 (57.5%)	0.096

- This study showed that : multimodal IAT may be *safely* used to treat patients who present *beyond* the traditional *6-hour* time window if they are selected based on the *presence of perfusion mismatch*.

- In appropriately selected patients, IAT for AIS can be performed *safely regardless of stroke duration*.

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CLINICAL AND POPULATION SCIENCES

Endovascular Thrombectomy for Acute Ischemic Stroke Beyond 6 Hours From Onset

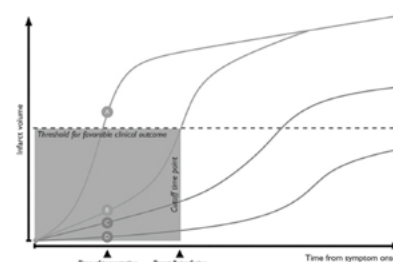
A Real-World Experience

Stroke. 2020;1-12011-2021 July 2020

CONCLUSIONS—This *real-world study* suggests that in patients with large vessel occlusion selected on the basis of CT perfusion and collateral circulation assessment, endovascular treatment *beyond 6 hours* is feasible and safe with no increase in symptomatic intracranial hemorrhage.

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Effect of time-to-perfusion on clinical outcome based on collateral state



"Time clock"
(uniform criteria)

"Tissue clock"
(individualized criteria)

AJNR Am J Neuroradiol 36:495-500 Mar 2015
Hwang Mar 2015 www.ajnr.org

Tissue-clock (individualized criteria)

- In AIS due to emergent LVO, *target mismatch* may persist after the traditional "time-window" up to 10 days.
- EVT decided* upon the "tissue-clock" may be feasible and efficacious.
- RCT based on only the "tissue-clock" is warranted.

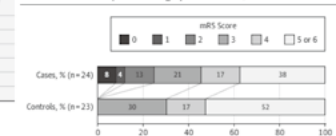
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EVT appears to benefit patients with large core and large mismatch profiles (Baseline infarct core ≥ 50 mL)

Table 2. Outcomes for Patients With Baseline Ischemic Cores Greater Than 50 mL*

Outcome	Cases (n = 28)	Controls (n = 28)	P Value
Pericerebral hematoma Type 2	2 (7)	1 (4)	>.99
Hemicraniectomy	2 (7)	6 (21)	.10
Final ischemic volume, mean (SD), mL	86.59 (76.94)	241.99 (120.35)	<.001
90-d mRS score			.04
0-2	6 (21) ^a	0	.04
3-5	11 (40) ^a	7 (25) ^a	.77
6	4 (17) ^a	4 (17) ^a	>.99
90-d Mortality	9 (38) ^a	14 (52) ^a	.15
	7 (28) ^a	11 (48) ^a	.75

Figure. Functional Outcomes at 90 Days According to the Score on the Modified Rankin Scale (mRS) (Baseline Ischemic Core ≥ 50 mL on Computed Tomographic Perfusion)



Shift analysis by Wilcoxon signed rank test, $P = .04$.

JAMA Neurology January 2017 Volume 74, Number 1

Strategy proposal of patients with LVO with late window

- Find patients who are likely to get worse
 - internal borderzone infarction
 - poor collateral
 - severely decreased perfusion
- Check the patients often (NICU, Stroke Unit)

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2018 Guidelines for the Early Management of Patients With AIS warned the overuse of EVT

3.7. Mechanical Thrombectomy (Continued)	COR	LOE	New, Revised, or Unchanged
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	New recommendation.
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	New recommendation.

The DAWN trial used clinical imaging mismatch (a combination of mRS 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, 36%; 95% CI, 21-44; posterior probability of superiority >0.999).¹⁰ 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 known normal 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; $P < 0.0001$).¹¹ 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 exclusively adhere to in clinical practice.

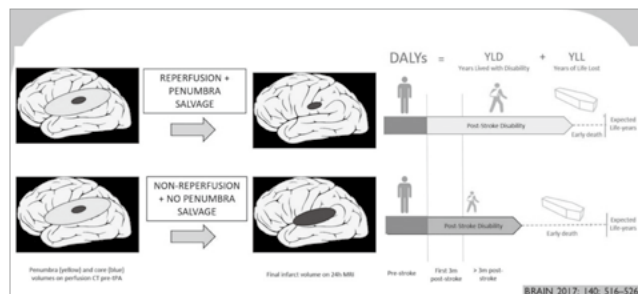
See Table XXX in online Data Supplement 1.

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Conclusion

- SAVE THE PENUMBRA
- Although RCTs remain the gold standard in the assessment of intended effects of interventions, observational studies can be useful for providing important information under everyday circumstances.

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For each of 100 patients, 7.2 days of disability-adjusted life-year days were saved (95% CI, -10.4 to -4.1 days, $p < 0.001$).

Each "min" of earlier onset-to-treatment time resulted in a saving of 4.4 disability-free days after stroke (1.3-7.5 days).

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Recent trends for AIS (Review of articles)

박 상 규

연세대 강남세브란스병원 신경외과

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Recent Trend fo AIS

Review of articles

Sang Kyu Park, M.D., Ph.D.

Associate Professor, Cerebrovascular & Endovascular Surgery,
Department of Neurosurgery, Stroke Center, Gangnam Severance Hospital

Severance

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Ischemic Core vs Penumbra

Figure 1. Regions of Cerebral Hypoperfusion Following Acute Ischemic Stroke

2,000,000 neuronal loss/min
↓
10hr = 26 yrs normal aging

JAMA April 14, 2015; Volume 313, Number 14
Sever JL. Time is brain-quantified. Stroke. 2006;

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tPA

Table 1. Summary of the NINDS and ECASS-3 Trials

	No. (%)	IV rtPA	Placebo	P Value
NINDS, 1995¹⁰				
No. enrolled	312	312		
Median baseline NIHSS score ^a	14	15		
Favorable 90-d outcome, mRS 0-1	133 (42.6)	83 (26.6)		<.01
Symptomatic intracranial hemorrhage ^b	20 (6.4)	2 (0.6)		<.01
ECASS-3, 2008¹¹				
No. enrolled	418	403		
Median baseline NIHSS score ^a	9	10		
Favorable 90-d outcome, mRS 0-1	219 (52.4)	182 (45.2)		.04
Symptomatic intracranial hemorrhage ^b	33 (7.9)	14 (3.5)		<.01

¹⁰ Tissue plasminogen activator for acute ischemic stroke. *N Engl J Med* 1995;333(24):1581-1587.

¹¹ Hackett W, Kaste M, Bluhmki E, et al. Thrombolysis with alteplase 3 to 4.5 hours after acute ischemic stroke. *N Engl J Med* 2008;359(13):1217-1226.

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THE LANCET

Volume 375, Issue 9727, 15-21 May 2015, Pages 1695-1703

Articles

Time to treatment with intravenous alteplase and outcome in stroke: an updated pooled analysis of ECASS, ATLANTIS, NINDS, and EPITHET trials

Meta-analysis
2775 pts,
odds ratios (ORs)

0-90 min: 2.55
91-180 min: 1.64
181-270 min: 1.34
>270 min: no benefit

symptomatic hemorrhage: 5.37 (5.2% vs 1.0%)

Prof Kennedy R, Lees FRCP¹, R. W. Erich Bluhmki PhD², Prof Rüdiger von Kummer MD³, Prof Thomas G Smith MD⁴, Prof Danilo Toni MD⁵, Prof James C Grotta MD⁶, Prof Gregory W Albers MD⁷, Prof Marika Kaste MD⁸, John R Marler MD⁹, Scott A Hamilton PhD¹⁰, Prof Barbara C Tilley PhD¹¹, Prof Stephen M Davis¹², Prof Geoffrey A Donnan¹³, Prof Werner Hacke MD¹⁴, for the ECASS, ATLANTIS, NINDS and EPITHET rt-PA Study Group Investigators[†]



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tirofiban

Intra-Arterial Prourokinase

for Acute Ischemic Stroke

The PROACT II Study: A Randomized Controlled Trial

Anthony Furlan, MD

Donald H. Johnston, MD

Lawrence W. Steiner, MD

Michael Gass, PhD

Howard Rowley, MD

Carl E. Sizer, MD

Michael Proctor, MD/PhD

Seung Hwang, MD

Fred Colquhoun, MD

Wayne M. Clark, MD

Frank Silver, MD

Tim Winters, MD

See also PROACT II Symposium

Interfering with thrombus formation and/or thrombolysis after acute ischemic stroke but must be given within 3 hours of onset. (no randomized trials have failed to show overall benefits for fibrinolytic therapy must be within 6 hours of stroke onset)^{1,2} A number of factors have contributed to this failure. But stroke heterogeneity has been cited as a major cause.^{3,4} A broad-based trial of a homogeneous case population provides an alternative to the traditional trial, randomized, con-

Control: Intravenous tissue-type plasminogen activator can be beneficial to some patients when given within 3 hours of stroke onset, but many patients present later after stroke onset and alternative treatments are needed.

Objective: **Proven**—improvement in efficacy and safety of intra-arterial (IA) recombinant prourokinase (alteplase) in patients with acute ischemic stroke.

Design: PROACT II (Prolytic in Acute Cerebral Thrombolysis II), a randomized, controlled, multicenter, open-label clinical trial with blinded follow-up conducted between February 1996 and August 1996.

Setting: Fifty-four centers in the United States and Canada.

Patients: A total of 180 patients with acute ischemic stroke of less than 6 hours' duration caused by angiographically proven occlusion of the MCA and without hemorrhage or major early infarction signs, on computed tomographic scans.

Intervention: Patients were randomized to receive 1 mg of IA tPA + p-tissue plasminogen activator (alteplase) or 1 mg of saline (n = 90).

Main Outcome Measures: The primary outcome, evaluated by intention-to-treat, was based on the proportion of patients with slight or no neurological decline at 90 days as defined by a modified Rankin score of 2 or less. Secondary outcomes included MCA recanalization, the frequency of intracerebral hemorrhage with neurological deterioration, and mortality.

Results: For the primary analysis, 46% of intracerebral p-tPA and 26% of control patients had a modified Rankin score of 2 or less (P = .04). Mortality was 28% for the p-tPA group and 27% for the control group. The recanalization rate was 44% for the p-tPA group and 18% for the control group (P < .001). Intracerebral hemorrhage with neurological deterioration within 24 hours occurred in 2.2% of intracerebral p-tPA and 2.2% of control patients (P = .96).

Conclusions: Despite an increased frequency of early symptoms, intracerebral hemorrhage, treatment with IA + p-tPA within 3 hours of the onset of acute ischemic stroke caused by MCA occlusion significantly improved clinical outcome at 90 days.

JAMA. 1996;276:2021-2027

www.jama.com

[illegible]

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IA thrombolysis								
RCTs of IA Thrombolysis With Control Group (IV v/PA Alone or No Treatment)								
	PROACT II 1999 ^{13,14}	MULT 2007 ^{15,16}	SYNTHESIS EXP. 201 ^{16,18}					
No. of centers (sites by country)	54 (US and Canada)	57 (Japan)	24 (Italy)					
No. analyzed	IA, 121 control, 59 [*]	IA, 57 control, 57 [*]	IA v EV, 181 IV vPA, 181					
Median baseline NIHSS score ^a	IA, 17 control, 17	IA, 14 control, 14	IA v EV, 13 IV vPA, 13					
Time from onset to initiation of IA treatment, h ^b	IA, 4.7 control, 5.1	IA, 3.3 control, 3.4	NR					
Time from onset to reperfusion, h	IA, 5.3	NR	IA v EV, 3.8					
Final reperfusion grade (TICI grade 2 or 3), No. (%)	IA, 71 (100) (65.7) control, 9/50 (18.0)	IA, 42 (73.3) control, NR	NR					
P-value	<.01							
Feasible 90-d outcome (mRS 0-2), No. (%) ^c	IA, 48 (39.7) control, 15 (25.4)	IA, 38 (66.7) control, 22 (38.6)	IA v EV, 137 (75.7) IV vPA, 152 (84.0)					
P-value	.04	.35	.07					
Symptomatic intracranial hemorrhage, No. (%)	IA, 10 (100) (10.2) control, 1/54 (1.8)	IA, 5 (8.8) control, 1 (1.8)	IA v EV, 10 (5.5) IV vPA, 10 (5.5)					
P-value	.06	.21	.99					

Imaging based patient selection



NIH Public Access
Author Manuscript

Published in final edited form as:

Lancet Neurol. 2012 October ; 11(10): 849-857. doi:10.1016/S1473-4462(12)70200-X.

Magnetic Resonance Imaging Profile and Response to Endovascular Reperfusion: Results of the DEFUSE 2 Prospective Cohort Study

Favorable penumbra pattern

:penumbra to infarct core

> 1.8

-> mRS 0-2: 56.5% vs 31.3%

THE NEW ENGLAND JOURNAL OF MEDICINE

ORIGINAL ARTICLE

A Trial of Imaging Selection and Endovascular Treatment for Ischemic Stroke

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Favorable penumbra pattern

-> mRS 0-2: 25.0% vs 22.2%

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

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ABSTRACT

BACKGROUND: Thrombectomy is currently recommended for eligible patients with stroke who are treated within 6 hours after the onset of symptoms.

DESIGN: We conducted a multicenter, randomized, open-label trial, with blinded outcome assessment, of thrombectomy in patients 6 to 16 hours after they were last known to be well and who had remaining ischemic brain tissue that was not yet infarcted. Patients with proximal middle-cerebral-artery or internal-carotid-artery occlusions, an initial infarct size of less than 70 mL, and a ratio of the volume of ischemic tissue on perfusion imaging to infarct volume of 1.8 or more were randomly assigned to endovascular therapy (thrombectomy) plus standard medical therapy (endovascular-therapy group) or standard medical therapy alone (medical-therapy group). The primary outcome was the infarct score on the modified Rankin scale (range, 0 to 5, with higher scores indicating greater disability) at day 90.

RESULTS: The trial was conducted at 18 U.S. centers and terminated early for efficacy after 142 patients had undergone randomization (70 in the endovascular-therapy group and 72 in the medical-therapy group). Endovascular therapy plus medical therapy, as compared with medical therapy alone, was associated with a favorable shift in the distribution of functional outcomes on the modified Rankin scale at 90 days (odds ratio, 2.75 [95% CI, 1.01 to 7.41]) and a higher percentage of patients who were functionally independent, defined as a score on the modified Rankin scale of 0 to 2 (48% vs. 17%, $P=0.002$). The 90-day mortality rate was 14% in the endovascular-therapy group and 20% in the medical-therapy group ($P=0.16$), and there was no significant between-group difference in the frequency of symptomatic intracranial hemorrhage (7% and 4%, respectively; $P=0.75$) or of serious adverse events (45% and 51%, respectively; $P=0.18$).

CONCLUSIONS: Endovascular thrombectomy for ischemic stroke 6 to 16 hours after a patient was last known to be well plus standard medical therapy resulted in better functional outcomes than standard medical therapy alone among patients with proximal middle-cerebral-artery or internal-carotid-artery occlusion and a region of tissue that was ischemic but not yet infarcted. (Funded by the National Institutes of Neurological Disorders and Stroke [DEFUSE 3 Clinical Trials.gov number, NCT02586453].)

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Endovascular Trial Comparison

Table 3. Study Outcome Summary

Study	Year	Patients n	Hours to Intervention	Disability Benefit	Number Needed to Treat
IMS – III	2013	658	3	No difference	–
MR RESCUE	2013	118	8	No difference	–
SYNTHESIS	2013	181	6	–	–
MR CLEAN	2015	500	6	15.5% benefit	7
ESCAPE	2015	316	12	23.7% benefit	4
EXTEND-IA	2015	70	4.5	31% benefit	3
SWIFT PRIME	2015	196	6	25% benefit	12
REVASCAT	2015	206	8	15.5% benefit	7
THRACE	2016	414	5	11% benefit	9
THERAPY	2016	108	4.5	No difference	–
DAWN	2017	206	24	36% benefit	3
DEFUSE 3	2018	182	16	28% benefit	4

mRS = modified Rankin score; NNT = number needed to treat.

* The THERAPY trial did not have statistically significant difference in disability benefit between treatment arms.

Endovascular Trial Comparison

SYNTHESIS EXP, 2013 ^{28,9}	IMS III, 2013 ²²	MR RESCUE, 2013 ²⁹	MR CLEAN, 2014 ³⁰	ESCAPE, 2015 ³¹	EXTEND-IA, 2015 ³²	SWIFT PRIME, 2015 ³³
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1. thrombectomy device

-> SYNTHESIS, IMS III, MR RESCUE: IA tPA infusion, MERCI, Penumbra

-> MR CLEAN, ESCAPE, EXTEND-IA, SWIFT PRIME: predominantly stent

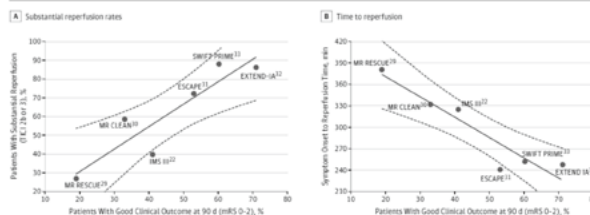
2. time to perfusion was lower in recent trial

-> ESCAPE (4hr), EXTEND-IA (4.1hr) vs IMS III (5.4hr)

Endovascular Trial Comparison

SYNTHESIS EXP, 2013 ^{28,9}	IMS III, 2013 ²²	MR RESCUE, 2013 ²⁹	MR CLEAN, 2014 ³⁰	ESCAPE, 2015 ³¹	EXTEND-IA, 2015 ³²	SWIFT PRIME, 2015 ³³
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Figure 3. Rate of Reperfusion and Time to Reperfusion Compared With Percentage of Good Outcomes in the 6 Trials Comparing Endovascular Treatment to Medical Treatment Alone



Endovascular Trial Comparison

SYNTHESIS EXP, 2013 ^{28,9}	IMS III, 2013 ²²	MR RESCUE, 2013 ²⁹	MR CLEAN, 2014 ³⁰	ESCAPE, 2015 ³¹	EXTEND-IA, 2015 ³²	SWIFT PRIME, 2015 ³³
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1. thrombectomy device

-> SYNTHESIS, IMS III, MR RESCUE: IA tPA infusion, MERCI, Penumbra

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2. time to perfusion was lower in recent trial

-> ESCAPE (4hr), EXTEND-IA (4.1hr) vs IMS III (5.4hr)

3. proximal artery occlusion confirmed via CTA

-> homogenous enrollment to show benefit





ARCS 2020

ARTERIAL RECANALIZATION IN CEREBRAL STROKE

뇌졸중 재개통 심포지엄 및 대한뇌혈관내치료의학회
2020 추계보수교육

Session III. Luncheon Seminar on Intracranial Atherosclerosis (ICAS)

좌장 : 윤석만 (순천향대), 고준석 (경희대)

Pathophysiology and risk factors of ICAS in Asia

Imaging and diagnosis of ICAS

장철훈 (영남대)

김의종 (경희대)

Pathophysiology and risk factors of ICAS in Asia

장 철 훈

영남대병원 신경외과

Pathophysiology & Risk Factors of Intracranial Atherosclerotic Stenosis(ICAS) in Asia

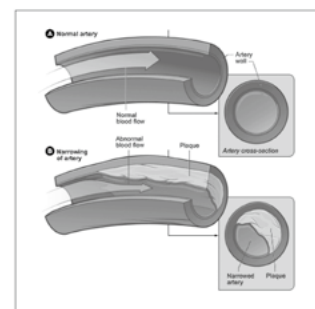
영남의대
신경외과 장 철 훈

Contents

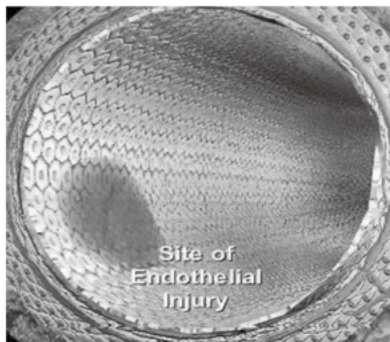
- Atherosclerosis
- Pathology in ICAS
- ICAS in ischemic stroke
- Risk factors of ICAS
- Conclusion

Atherosclerosis

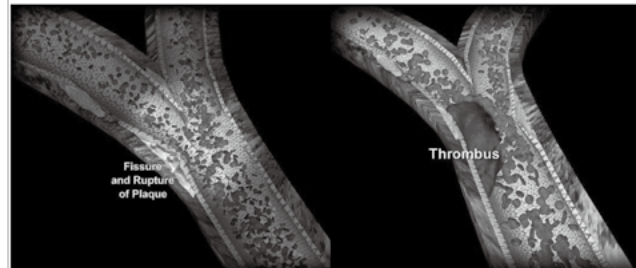
A disease in which the inside of artery narrows due to the build up of plaque



Atherosclerosis



Atherosclerosis



plaque

- Original three components
 - 1) cell
 - 2) connective tissue extracellular matrix
 - 3) Intra- and extracellular lipid
- In advanced, it was complex with calcification & hemosiderin deposition
- Vulnerability of plaque

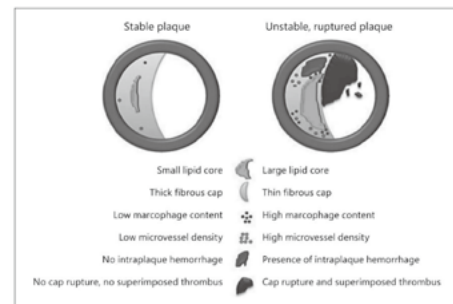


Fig. 3. Schematic overview of a stable atherosclerotic plaque (left) and an unstable atherosclerotic plaque (right). With permission [92].

(van Lammeren GW et al. Atherosclerotic plaque bio-markers: beyond the horizon of the vulnerable plaque. Curr Cardiol Rev. 2011; 7:22–27.)

The morphological features of plaques associated and not associated with infarcts in the MCA territory. With permission [93]

	Plaques associated with infarct (n = 46)	Plaques not associated with infarct (n = 65)	p value	95% confidence interval
Degree of area stenosis, %	62.2±16.8	52.4±10.5	0.001	-15.4 to -4.19
Fibrous cap	1.59±0.83	1.46±0.69	0.403	-0.42 to 0.17
Lipid core	2.48±0.91	1.98±0.82	0.004	-0.83 to -0.16
Intraplaque hemorrhage	14/46	10/65	0.066	0.958 to 6.045
Intraplaque neovasculation	13/46	5/65	0.008	1.549 to 14.423
Intraplaque thrombus	7/46	1/65	0.008	1.361 to 96.932
Intraplaque calcification	16/46	15/65	0.202	0.770 to 4.107
CD45RO	2.38±0.78	1.79±0.81	0.007	-0.968 to 0.158
CD68	3.07±0.64	2.58±0.70	0.009	-0.849 to -0.130

(Chen XY, et al. Middle cerebral artery atherosclerosis: histological comparison between plaques associated with and not associated with infarct in a postmortem study. Cerebrovasc Dis. 2008; 25:74–80.)

ICAS vs ECAS on pathology

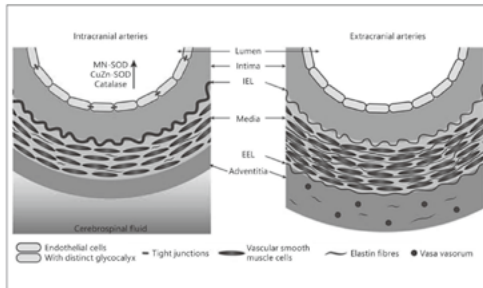


Fig. 1.

Major structural characteristics of intracranial and extracranial arteries. Intracranial arteries tend to be muscular arteries with a thin media and adventitia, few elastic medial fibers, thicker and denser internal elastic lamina (IEL), and lacking external elastic lamina (EEL) and vasa vasorum. With permission [91].

Autopsy Series during 1960s

- Atherosclerotic changes started from 1st to 2nd decades and progressing with age
- Advance atherosclerotic lesions were almost non-existent up to 4th decade
- Relatively **linear progression** in ECAS
- **Late onset** of ICAS d/t higher level of antioxidant enzyme in intracranial vessel at a young age

Autopsy Study

- Occurred later & was less severe than aortic or coronary lesions in Japan, a nation-wide autopsy study in 1988 (1 months ~ 39 yrs. old)

(Tanaka K et al. A nation-wide study of atherosclerosis in infants, children and young adults in Japan. *Atherosclerosis*. 1988; 72:143–156.)

- ICAS was more severe in Hong Kong Chinese than ECAS, that shown in Japan and white population

(Leung SY, et al. Pattern of cerebral atherosclerosis in Hong Kong Chinese. Severity in intracranial and extracranial vessels. *Stroke*. 1993; 24:779–786.)

Autopsy Study

- **Mainly early lesion** (63%) & a few advanced lesion (15%)

(Ritz K, et al. Cause and mechanisms of intracranial atherosclerosis. *Circulation*. 2014; 130:1407–1414.)

- Macrophage infiltration was relatively low

(Narula J, et al. Histopathologic characteristics of atherosclerotic coronary disease and implications of the findings for the invasive and noninvasive detection of vulnerable plaques. *J Am Coll Cardiol*. 2013; 61:1041–1051.)

- Hemorrhage, ulceration and calcification were less frequent

(Moossy J. Cerebral infarcts and the lesions of intracranial and extracranial atherosclerosis. *Arch Neurol*. 1966; 14:124–128.)

Distribution of atherosclerosis in autopsy Study

- **In American & European**
ICA > VA > BA > MCA > PCA > ACA
- **In Asian**
MCA > ICA > BA > VA > PCA > ACA
- **In all cohorts**
cerebellar & communicating arteries were rarely affected
ICA, from cavernous Seg.
BA, upper & lower regions

Intracranial atherosclerotic stenosis (ICAS)

Intracranial atherosclerotic stenosis (ICAS)

- Major cause of **ischemic stroke**
- Associated with **high risk of recurrent stroke** (up to 25~30% within 2yrs in China)
- **Higher prevalent in Asian**, black, Hispanic & Indian than Caucasian populations but the causes of racial differences remain **unknown**

Epidemiology

- **Stroke associated with ICAS**
5 ~ 10% in white
15 ~ 29% in black
30 ~50% in Asian

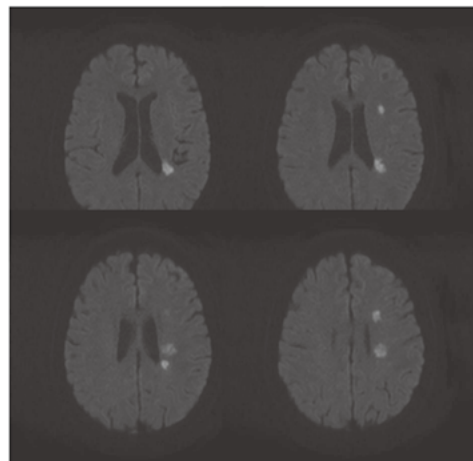
Mechanism of stroke in ICAS

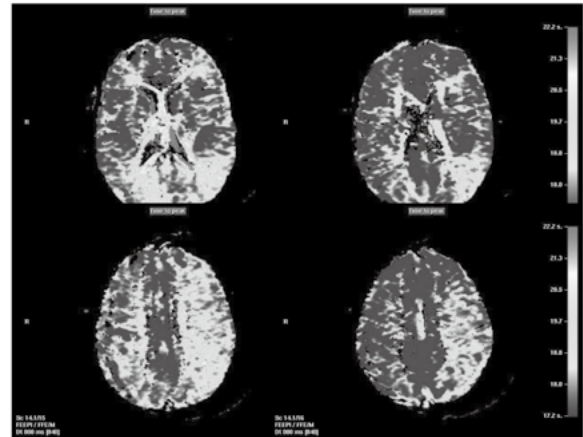
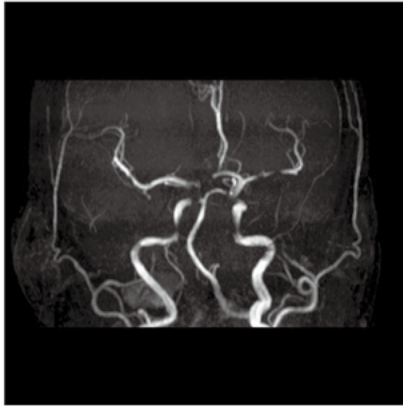
- **3 major hypothesized mechanism**
 - 1) hypoperfusion
 - 2) artery-to-artery embolism
 - 3) plaque extension over small penetrating artery ostia (branch atheromatous disease)
- Combination of theses

Hypoperfusion

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- Progressive Rt-side hemiparesis (upper >> lower) for 3days
- DM

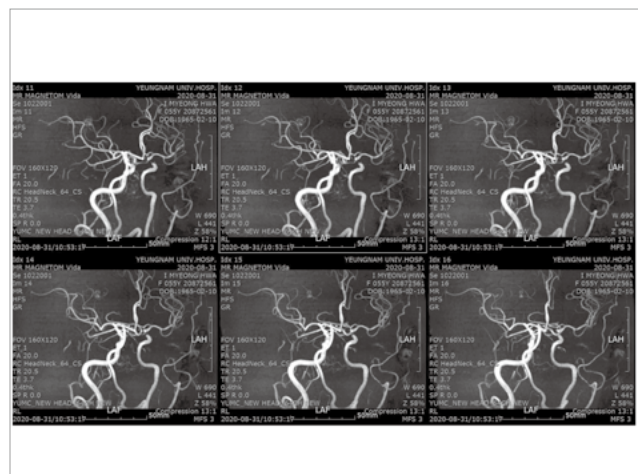
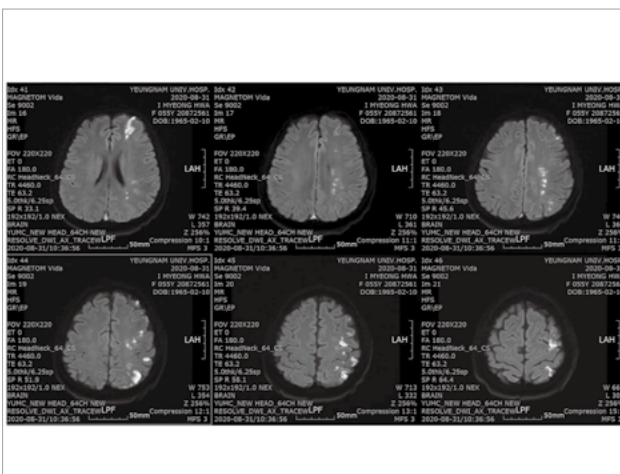




Artery- to Artery embolism

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- Lymphoma → Chemotherapy
- Rt. Hand motor weakness after chemotherapy (4days later)
- Thrombocytopenia (50 ~33K) & D-dimer; WNL



■TCD Studies : (TCD Monitoring for 30MIN)

For the TCD embolus detection, evaluation of the recanalization or occlusion of the MCA, or additive effect in the thrombus dissolution, the right and left MCA main stems were simultaneously insonated through the temporal windows with head band. For all studies, the same transcranial pulsed Doppler ultrasound device with 2-MHz multi-gate transducers was used. The following definition for microemboli was used: typical visible and audible (click, chirp, whistle), short-duration, high-intensity signal within the Doppler flow spectrum with a time delay in the two channels within each side. Complete occlusion was defined by absent or minimal TCD signals, partial occlusion by blunted or dampened signals, and complete recanalization by normal or low-resistance stenotic signals implying unobstructed flow distal to any residual lesion.

■Result :

There are some microembolic singnals during TCD monitoring.

Lt - 3(1',18') Rt - 0

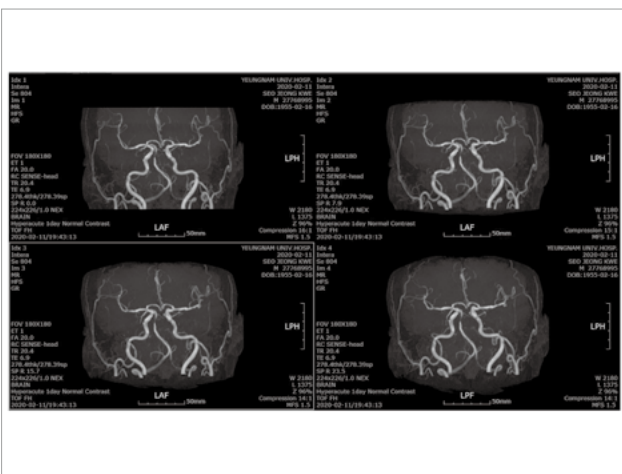
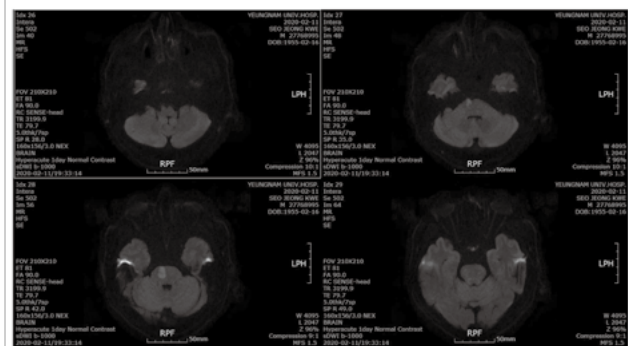
■Conclusions :

■Recommendation :

Branch atheromatous disease

M / 64

- Lt-side hemiparesis
- HTN, DM, MetS



Risk Factors

Risk factor (Age / Sex)

- More prevalent in old age than ECAS (decreased antioxidant level with age)
- Sex ; M>F but controversial (more prevalent in women ≤ 45 yrs)

Risk factor (Hypertension)

- strong risk factor
- ICAS > ECAS d/t more vulnerable to hemodynamic stress (smaller diameter, thinner media & adventitia, fewer elastic media fiber)

Risk factor (Diabetics mellitus)

- strong risk factor
- ICAS > ECAS
(higher level of antioxidant in intracranial vessel, **depletion of antioxidant level** d/t metabolic syndrome)

The incidence of DM is more frequent in western

In Asians,
lower body mass index, a younger onset age, and a higher visceral adiposity
→ increased fatty acid influx to the liver, altered adipokine production, fatty liver, and insulin resistance.
→ Excessive insulin resistance may lead to increased vulnerability to free radical toxicity, preferentially affecting intracranial arteries.

Risk factor (Hypercholesterolemia)

- ICAS < ECAS (the only convention risk factor than ICAS)
- An inherent resistance to the toxic hypercholesterolemia effects in monkeys and rabbits following an atherogenic diet

Risk factor (smoking)

- ICAS = ECAS
- More correlated with ICAS in **younger men** (well not known but deletes antioxidant enzyme level)

Risk factor (Metabolic Syndrome(Mets))

- Compilation of risk factors, abdominal obesity, elevated triglyceride level, hypertension, and impaired fasting glucose level
- ICAS > ECAS in eastern & western population

Risk factor (Metabolic Syndrome(Mets))

- associated with insulin resistant & vulnerability to oxidative stress ↑
- Resistin ↑ ; LDL-chol. uptake ↑
- Adiponectin ↓ ; a protective effect against atherosclerosis ↓ (ApoA ↓, ApoB/ApoA ↑)
- Obstructive sleep apnea

Risk factor (vascular tortuosity)

- Increased vascular tortuosity
→ local turbulence & abnormal shear stress in vessel wall
→ generation of atherosclerosis
- ICAS = ECAS
- Associated with vascular elastin & elastin metabolism (it seemed racial difference)

Maximum MCA angle & tortuosity

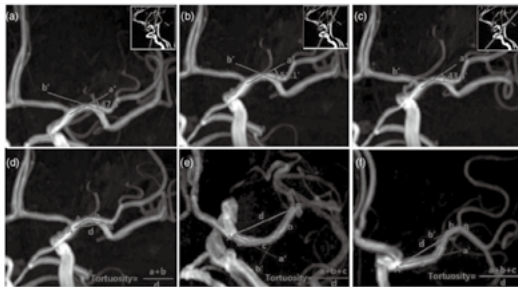


Fig. 1 Measurement of the middle cerebral artery (MCA) tortuosity. The angles are serially measured from the adjacent planes (represented in the small, right upper box in each panel) of the 3D-reconstructed MCA (a, b, and c) to identify the slice where the maximum angle (51.1°) is shown (slice B in this case). The tortuosity of the MCA (arc-chord ratio × 100) is measured from the slice B as (a + b/c) × 100 (d). In cases of multiple angles, the tortuosity is measured as (a + b + c/d) × 100 (e and f).

(BJ Kim, et al. Vascular tortuosity may be related to intracranial artery atherosclerosis Research. 2015; 1081-1086)

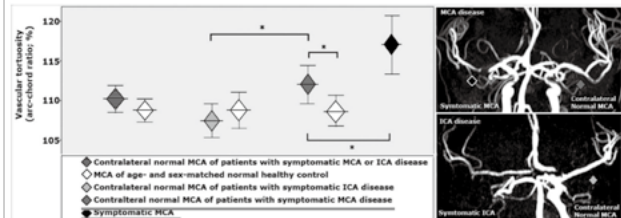


Fig. 2 Vascular tortuosity of middle cerebral artery (MCA) in each group with the representative cases; healthy normal control (white), patients with ischemic stroke (stripes), contralateral normal-looking MCA (cMCA) in patients with symptomatic proximal internal carotid artery (pICA) disease (light-gray), cMCA in patients with symptomatic MCA disease (dark-gray), and symptomatic MCA (black). Asterisk (*) represents significant difference ($P < 0.05$). The range represents 95% confidence interval.

(BJ Kim, et al. Vascular tortuosity may be related to intracranial artery atherosclerosis Research. 2015; 1081-1086)

Table 3 Factors independently associated with symptomatic MCA disease (vs. ICAS disease)

	Univariate analysis		Multivariate analysis	
	OR	P	Adjusted OR	P
Age	0.973	0.05	0.947	0.002
Male	0.195	<0.001	0.153	<0.001
Hypertension	1.075	0.83		
Diabetes	0.452	0.02	0.443	0.04
Hyperlipidemia	0.861	0.53		
Smoking	0.804	0.48		
Coronary artery disease	0.198	0.02		
Previous stroke history	0.522	0.05		
Proximal MCA diameter (mm)	0.325	0.005	0.229	0.002
Distal MCA diameter (mm)	0.461	0.07		
Length of MCA (mm)	1.002	0.95		
Minimal distance between the ends (mm)	0.969	0.33		
Tortuosity of MCA	1.047	0.01	1.060	0.003

Variables with potential association with MCA disease ($P < 0.10$) from univariate analyses were used for multivariate analysis. Variables entered into multivariate analysis: age, male, diabetes, coronary artery disease, previous stroke history, proximal MCA diameter, and tortuosity of MCA. ICAS, intracranial atherosclerosis; MCA, middle cerebral artery.

(BJ Kim, et al. Vascular tortuosity may be related to intracranial artery atherosclerosis Research. 2015; 1081-1086)

In conclusion (Why tortuosity?)

- Independent risk factor, except age
- Associated with atherosclerosis frequently
- Higher degree atherosclerosis is not associated with increasing tortuosity over-time
- Vascular tortuosity in cMCA was detected in patients with symptomatic MCA disease but not in pICA lesion even if risk factors were similar
- Small caliber of pMCA is independent risk factor

Table 1. Summary of studies investigating the risk factors for ICAS and ECAS patients

Reference	Race	Vascular characteristics	Assessment	No. of cases	Evaluation site	Risk factors for ICAS	Risk factors for ECAS	Comment
Hayden et al. ¹⁰	Mixed	symptomatic	CA	115	115		Hypertension	
	105 Whites			23 PCA	CCA, PCA		CAD	
	15 Blacks			85 CCA			peripheral artery disease	
				7 both				
Isotani et al. ⁴	Mixed	symptomatic	CA	1367	ICA, PCA	Black	White	
	1058 Whites			1022 ICA		Asian		
	86 Blacks			108 PCA				
	223 Asians			237 both				
	(Taiwanese, Japanese)							
Yasaka et al. ¹¹	Asian	symptomatic	CA	154	ICA, PCA, BA	PCA	ICA and BA	Comparison of
	(Japanese)			75 ICA		advanced hypertension	CAD, DM, Hyperlipidemia	ICA, PCA, and BA associated risk factors
				47 PCA				
				32 BA				
Sacco et al. ³	Mixed	symptomatic	Duplex, TCD	428	All	Black and Hispanics	White	No direct comparison between
	46% Hispanics			40 ECAS		young age (vs. non-ethers)	Hyperlipidemia (vs. non-ethers)	ICAS and ECAS
	33% Blacks			33 ICAS		DM (vs. non-ethers)	diabetes (vs. non-ethers)	
	19% Whites			365 non-ethers				
Wright et al. ¹²	Mixed	symptomatic	CA, duplex	274	All	Male	Whites	No risk factors difference
	42% Blacks			TCD, MRA				ICAS from ECAS

(continued)

Table 1. Continued

Reference	Race	Vascular characteristics	Assessment	No. of cases	Evaluation site	Risk factors for ICAS	Risk factors for ECAS	Comment
	29% Whites		CA			DM (OR for ICAS 10.8, ECAS 4.3 vs. control)		No direct comparison between
	22% Blacks					MetS (OR for ICAS 4.6, ECAS 3.3 vs. control)		ICAS and ECAS
	49% Hispanics							
Park et al. ¹³	Asian	symptomatic		464	All	Ins. apolipoprotein ratio		No direct comparison between
	(Korean)			208 ICAS				ICAS and ECAS
				48 ECAS				
				28 both				
				188 non-ethers				
Kim et al. ⁵	Asian	symptomatic	MRA, CTA, CA	1300	All	MetS (posterior ICAS)	Age, male	
	(Korean)			688 ICAS			hyperlipidemia	
				371 ECAS				
				41 both				
Lopez-Garcia et al. ¹⁴	White	symptomatic	MRA, TCD, duplex	933	CCA	DM, MetS	Male, hypertension, smoking	
				57 ICAS		intracranial artery		
				404 ECAS				
				23 both				
				408 non-ethers				
Lei et al. ¹⁵	Asian	symptomatic	MRA, CTA, CA	1192	All	DM, LDL	Age, male	No direct comparison between
	(Chinese)			493 ICAS		(vs. non-ethers)	(vs. non-ethers)	ICAS and ECAS

(continued)

Table 1. Continued

Reference	Race	Vascular characteristics	Assessment	No. of cases	Evaluation site	Risk factors for ICAS	Risk factors for ECAS	Comment
				79 ECAS				
				124 both				
				561 non-ethers				
Chen et al. ¹⁶	Asian	symptomatic	MRA, TCD, CA	155	ICA	Hypertension	smoking	
	(Chinese)			80 intracranial ICA				
				75 extracranial ICA				
Sung et al. ¹⁷	Asian	symptomatic	MRA, Duplex, TCD	13,529	All	DM (vs. non-ethers)		Patients who were referred
	(Taiwanese)			112 ICAS				to ultrasound laboratory
				121 ECAS (extracranial carotid stenosis)				No direct comparison between
				128 both				ICAS and ECAS
				733 non-ethers				
Li et al. ¹⁸	Asian	symptomatic	CTA	412	All	Low Apo A1		
	(Chinese)			137 ICAS				
				44 ECAS				
				24 both				
				157 non-ethers				

CA: carotid angiography; TCD: transcranial Doppler; MRA: magnetic resonance angiogram; CTA: computed tomography angiogram; PCA: middle cerebral artery; CCA: common carotid artery; ICA: internal carotid artery; PCA: middle cerebral artery; BA: basilar artery; ECAS: extracranial atherosclerosis; ICAS: intracranial atherosclerosis; DM: diabetes mellitus; MetS: metabolic syndrome; LDL: low-density lipoprotein; CAD: coronary artery disease.

Table 2. Explanations for racial differences in cerebral atherosclerosis location

Observation	Possible explanations	Comments
ICAS is more common in the East	Hypercholesterolemia less common in Asians ^a	Intracranial artery resistant against hypercholesterolemia
	Advanced, untreated hypertension more common in Asians ^b	Intracranial artery prone to hemodynamic stress due to its histologic characteristics
	Differences in intracranial vascular tortuosity ^b	Intracranial arterial tortuosity seems to be associated with atherosclerosis, but differences in arterial tortuosity across ethnicities have not yet been studied
	Contamination of ICAS cases with non-atherosclerotic disease cases ^c	Intracranial non-atherosclerotic diseases (e.g., MMD, dissection) are more common among Asians
	Genetic differences ^b	Variant in ring finger protein 213 gene is common in Asians
	Ethnic differences in the nature of or host-response to diabetes mellitus or MetS ^d	Antioxidant depletion makes the intracranial artery vulnerable to MetS
ICAS is more common in older subjects in the West	Age-related decrease in antioxidant level in intracranial arteries ^a	
ICAS is more common in young subjects in the East	Contamination of ICAS cases with non-atherosclerotic disease cases ^c	Intracranial non-atherosclerotic disease (e.g., MMD, dissection) is common in young Asians
	Cigarette smoking may be more correlated with ICAS in young subjects than in old subjects ^b	Cigarette smoking is more prevalent in young Asian men
ICAS is more common in women in the East	Contamination of ICAS cases with non-atherosclerotic disease cases ^c	MMD or vasculitis is more common in Asian women

Note: ICAS: intracranial atherosclerosis; MMD: moyamoya disease; MetS: metabolic syndrome.

^aSome evidence from previous studies.

^bTolerance not yet sufficient.

Conclusions of ICAS lesion in Asia

- More prevalent
- Late onset
- More early lesion
- Hypertension, DM, MetS
- Hypercholesterolemia (An inheritent resistance to the toxic hypercholesterolemia)
- Contamination with non-atherosclerotic disease (esp. in younger, female patients)
- Ethnic difference to DM & MetS

Conclusions (more prevalence of ICAS lesion in Asia)

- **Higher antioxidative enzyme level** in ICA
➔ late onset
- **Depletion of antioxidante level** in DM, Mets patients (racial difference)
- More vulnerable to **hemodynamic stress** in aging process, HTN, vascular tortuosity (d/t small caliber, thin media & adventitia, fewer elastic fiber in media)
- More **non-atherosclerotic lesion** (eg. MMD)

Review

International
Journal of Stroke
WSO**Location of cerebral atherosclerosis:
Why is there a difference between
East and West?**

Jong S Kim, Yeon-Jung Kim, Sung-Ho Ahn and Bum J Kim

Abstract

Intracranial atherosclerosis is more prevalent in Asian patients, whereas extracranial atherosclerosis is more common in individuals from western countries. The reasons for this discrepancy remain unknown. We reviewed the relevant literature and discussed the currently available information.

Although the study population, diagnostic modality, and risk factor definitions differ between studies, hypercholesterolemia is more correlated with extracranial atherosclerosis than intracranial atherosclerosis. The difference in hypercholesterolemia prevalence is one of the main reasons for racial differences. Intracranial arteries contain higher antioxidant level than extracranial arteries and may be more vulnerable to risk factors for antioxidant depletion (e.g., metabolic syndrome and diabetes mellitus). Intracranial arteries may be vulnerable to factors associated with hemodynamic stress (e.g., advanced, salt-retaining hypertension and arterial tortuosity) because of a smaller diameter, thinner media and adventitia, and fewer elastic medial fibers than extracranial arteries. Additionally, non-atherosclerotic arterial diseases (e.g., moyamoya disease) that commonly occur in the intracranial arteries of East Asians may confound the reports of intracranial atherosclerosis cases. Genes, including RNF 213 or those associated with high salt sensitivity, may also explain racial differences in atherosclerotic location.

To understand racial differences, further well-designed studies on various risk and genetic factors should be performed in patients with cerebral atherosclerosis. Additionally, improvements in diagnostic accuracy via advancements in imaging technologies and increased genetic data will aid in the differentiation of atherosclerosis from non-atherosclerotic intracranial diseases.

Keywords

Intracranial atherosclerosis, risk factor, metabolic syndrome, gene, Asia

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SAGE



Imaging and diagnosis of ICAS

김 의 종

경희대병원 영상의학과

죽상경화성(atherosclerotic) 두개강내 혈관 협착은 아시아에서 서구인들 보다 허혈성 뇌졸중의 중요 원인으로 알려져 있고 아시아 특히 극동 아시아인의 허혈성 뇌졸중 중 약 30-50%의 주요 원인이라 알려져 있다.

두개강내 동맥질환을 진단하기 위하여 CT angiography, MR angiography 및 Digital subtraction angiography(DSA)등 이 사용될 수 있고 Intracranial atherosclerosis(ICAS)는 DSA를 통하여 협착의 정도, 길이, 궤양의 유무를 판단할 수 있으며 이를 통하여 치료방침을 결정하는데 많은 도움을 얻을 수 있다. 이런 영상들은 진단과 치료 방침 결정에 많이 이용되고 있으나 혈관내강을 영상화하는 것으로 조영제가 차있는 혈관 또는 high flow가 지나가는 곳의 영상을 보여주는 것(arterial luminal images)이고 주된 병소가 있는 혈관벽은 잘 나타내지 못하는 단점을 가진다. 그래서 때로는 혈관이 좁아지는 병소들과의 감별이 어려울 때가 있고 치료방침 결정에 혼돈이 생길 수 있다.

오래전 부터 혈관벽의 병소를 영상화하는 노력이 있어 왔고 이전에 경동맥의 혈관벽영상(Vessel Wall Image: VWI)에 대한 관심과 연구가 진행되고 더불어 두개강내 혈관의 VWI가 대두되게 되었다. 시간이 지나면서 고사양의 MRI들의 개발과 더불어 많은 technique을 적용시킨 영상이 소개 되고 연구되기 시작하면서 현재 많은 기관에서 허혈성 뇌졸중 환자의 일부에서 혈관벽영상(VWI)을 얻고 질환의 상태를 파악하고 치료방침 결정에 많은 도움을 받고 있다. 아울러 high risk plaque feature를 확인하여 재발되는 뇌졸중을 예측할 수도 있다.

VWI는 고해상도를 요구하기에 삼차원(3D)기법이 선호되고 여러방향의 영상(multiplanar images: axial, coronal, sagittal)을 얻는다. 주위조직을 suppression 하면서 대조해상도를 높이기 위하여 Black Blood Technique을 적용하고 여기에 여러 technique을 적용하여 혈관영상(SPAC, CUBE, VISTA)을 얻게 된다. T1, T2강조영상을 얻고 때로는 Proton density 강조영상을 얻기도 한다. 여기에 조영제 주입후 T1강조영상을 얻어 VWI를 완성한다.

ICAS의 VWI는 plaque의 focal eccentric wall thickening, outward remodeling, variable enhancement의 소견과 intraplaque hemorrhage를 보일 수 있다.

조영증강은 염증, macrophage infiltration, Vasa vasorum과 관계된다고 알려져 있고, 급성뇌졸중과 관계된다고 알려져 있다.

Symptomatic lesion은 좀 더 조영증강되고, outward remodelling, plaque surface irregularity와 intraplaque hemorrhage를 보인다. Intraplaque hemorrhage는 symptomatic lesion 에서 좀 더 보이기는 하나 두개강내의 병변보다는 덜 보이는 경향이 있고 T1 high signal intensity를 보인다.

ICAS와 감별이 필요한 질환은 Dissection, Moyamoya disease, Vasculitis, Reversible cerebral vasoconstrictive syndrome(RCVS)이 포함되고 이 중 dissection과의 감별이 중요한데 두질환 모두 출혈을 영상에서 보여줄 수 있기 때문이다. ICAS에서는 plaque내 출혈을 확인하는 게 중요하고 이것은 T1, T2강조영상에서 모두 확인한다. Dissection의 경우 출혈을 좀 더 많은 빈도수에서 보이고 double lumen등의 소견을 동반하고 Wall내에 출혈이 보인다. Dissection에서 MR angiography의 source image를 통하여 double lumen, flap등을 확인할 경우 감별이 용이 할 수 있다. 그러나 실제 비슷한 영상 소견을 보일 수 있는데 그런 경우는 임상증상을 참고하여 감별하는게 중요하다. 아울러 dissection의 경우 막히지 않은 경우 추적검사에서 정상과 유사하게 회복될 수 있다.

moyamoya disease, vasculitis, RCVS는 concentric thickening의 소견을 보이고 호발 부위가 다른 점, 증상이 다른점으로 구별하고 기존의 CTA, MRA 및 DSA로 감별이 가능하다.

MRI의 발전 및 MR기법의 발전과 더불어 이 형태의 영상은 더욱 발전할 것으로 보이고 이런 질환들의 연구가 진행됨에 따라 환자 치료 및 예후 판정에 많은 도움이 되리라 사료된다.



ARCS 2020

ARTERIAL RECANALIZATION IN CEREBRAL STROKE

뇌졸중 재개통 심포지엄 및 대한뇌혈관내치료의학회
2020 추계보수교육

Session IV. Management of Intracranial Atherosclerosis

좌장 : 장경술 (가톨릭대), 김문철 (에스포항병원)

Medical management of ICAS

Endovascular mangement of ICAS with large vessel occlusion

Surgical mangement of ICAS

이종영 (한림대)

유승훈 (울산대)

최석근 (경희대)

Medical management of ICAS

이 종 영

한림대 강동성심병원 신경외과

Medical Management of Intracranial Stenosis

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College of Medicine, Hallym University, Seoul, Korea.

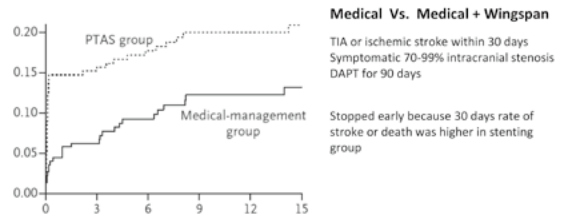
Risk factors of Atherosclerosis

Non Modifiable	Modifiable, Major	Modifiable
- Increasing age - Male - Genetic abnormalities	- HTN - Dyslipidemia - DM - Smoking	- Obesity - Physical inactivity - Stress - Lipoprotein (a) - Inflammation - Alcohol - Hyperhomocysteinemia

Managements for ICAS

- First off, medications for ICAS
 - The lesson in SAMMPRIS trial
- Antiplatelets
 - Antiplatelet Vs. anticoagulant
 - Mono. Tx. Vs. Dual Tx.
- Statin
 - High Intensity Vs. other intensity

SAMMPRIS, 2011



Aggressive management of ICAS

- Medical managements in SAMMPRIS trial
 - 90 days Dual Antiplatelets(ASA+clopidogrel)
 - High dose statin (Rosuvastatin 20mg to 40mg)
- Aggressive risk factor approach in SAMMPRIS trial
 - Systolic blood pressure ≤ 140 mmHg
 - ≤ 130 mmHg if diabetic
 - LDL cholesterol < 70 mg/dL
 - Secondary targets
 - Non-HDL cholesterol < 100 mg/dL, HbA1c $< 7.0\%$, smoking cessation
 - Weight management, BMI < 25 kg/m²; if initial BMI > 27 kg/ m², 10% weight loss
 - Physical activity: Moderate intensity activities, at least 3 times per week for 30 minutes

Antithrombotics

- 1960s, • Anticoagulation
- Anticoagulation with warfarin
 - severe occlusive disease in the VB artery and recurrent ischemic stroke despite antiplatelet treatment

Stroke 1977;8:150-175.

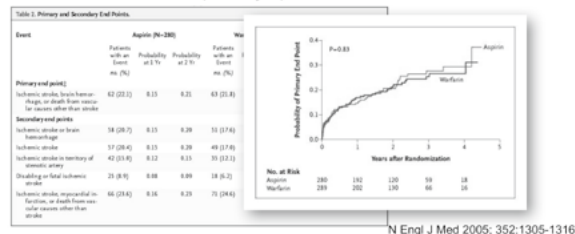
Antithrombotics

- 2005 • Warfarin-Aspirin Symptomatic Intracranial Disease
- 50 to 99 % stenosis
 - N=569
 - Mean FU of 1.8 Yrs

N Engl J Med 2005; 352:1305-1316

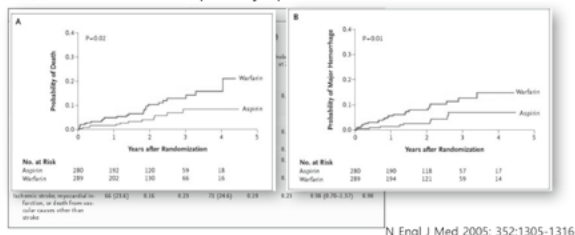
Antithrombotics

- 2005 • Warfarin-Aspirin Symptomatic Intracranial Disease



Antithrombotics

- 2005 • Warfarin-Aspirin Symptomatic Intracranial Disease



Antithrombotics

- 2005 • Warfarin-Aspirin Symptomatic Intracranial Disease
- Warfarin is not widely used
 - not more effective than aspirin and a high risk of bleeding
- 2001 EFFECTS OF CLOPIDOGREL IN ADDITION TO ASPIRIN IN PATIENTS WITH ACUTE CORONARY SYNDROMES WITHOUT ST-SEGMENT ELEVATION
- THE CLOPIDOGREL IN UNSTABLE ANGINA TO PREVENT RECURRENT EVENTS TRIAL INVESTIGATORS*
- 2002 Early and Sustained Dual Oral Antiplatelet Therapy Following Percutaneous Coronary Intervention A Randomized Controlled Trial

Steven R. Steinhilber, MD, Peter S. Berger, MD, J. T. Li, MD, et al.

N Engl J Med 2001; 345:494-502
 JAMA. 2002;288(19):2411-2420

Antithrombotics

- 2005
- Warfarin-Aspirin Symptomatic Intracranial Disease
 - Warfarin is not widely used
 - not more effective than aspirin and a high risk of bleeding
 - ASA only Vs. Dual antiplatelet
 - If ASA alone in symptomatic ICAS
 - **Annual rate of recurrent stroke: 4–19%**

Journal of Stroke 2017;19(3):261-270

Antithrombotics

- 2005
- Warfarin-Aspirin Symptomatic Intracranial Disease
 - Warfarin is not widely used
 - not more effective than aspirin and a high risk of bleeding

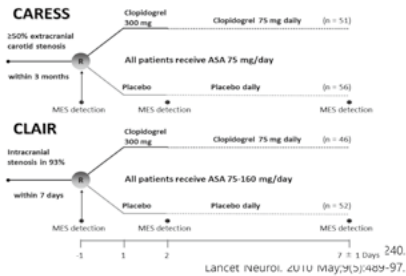
Dual Antiplatelet Therapy With Clopidogrel and Aspirin in Symptomatic Carotid Stenosis Evaluated Using Doppler Embolic Signal Detection
The Clopidogrel and Aspirin for Reduction of Emboli in Symptomatic Carotid Stenosis (CARESS) Trial

Clopidogrel plus aspirin versus aspirin alone for reducing embolisation in patients with acute symptomatic cerebral or carotid artery stenosis (CLAIR study): a randomised, open-label, blinded-endpoint trial

40.
37.

Antithrombotics

A to A embolism
Microembolic signal



Antithrombotics

Meta-analysis of two studies

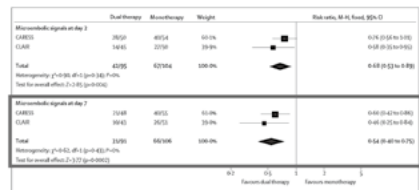


Figure 2: Meta-analysis of number of patients with at least one microembolic signal in CARESS and CLAIRE. M-H, Mantel-Haenszel.

Circulation 2005;111:2233-2240.
Lancet Neurol. 2010 May;9(5):489-97.

Antithrombotics

Meta-analysis of two studies

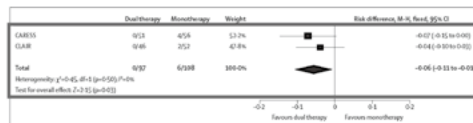


Figure 3: Meta-analysis of number of patients with recurrent stroke in CARESS and CLAIRE. M-H, Mantel-Haenszel.

Circulation 2005;111:2233-2240.
Lancet Neurol. 2010 May;9(5):489-97.

Antithrombotics

Characteristics	CARESS		CLAIRE	
	Dual Therapy (n=51)	Monotherapy (n=56)	Dual therapy (n=46)	Monotherapy (n=52)
Any bleeding	2 (3.9)	1 (1.8)	0	0
Life-threatening bleeding	0	0	0	0
Major bleeding including intracranial bleeding	0	0	0	0
Minor bleeding	2 (3.9)	1 (1.8)	2	0
Any recurrent vascular event	5 (9.8)	12 (21.4)	4	6
TIA/ischemic stroke	4 (7.8)	11 (19.6)	1	2
TIA/ischemic stroke ipsilateral to the qualifying stenosis	0	4 (7.1)	0	1
Myocardial infarction	1 (2.0)	0	0	0

Circulation 2005;111:2233-2240.
Lancet Neurol. 2010 May;9(5):489-97.

Antithrombotics, Dual antiplatelets

	MATCH, 2004	CHARISMA, 2006	CHANCE, 2013	POINT, 2018
Comparison	DAPT vs. Clopidogrel	DAPT vs. ASA	DAPT vs. ASA	DAPT vs. ASA (Clopidogrel 600mg)
Inclusion criteria	within 3 months	within 5 years	within 24 hours	within 12 hours
Length of Treatment	Long term	Long term	Short term, (21 days)	Short term, (90 days)
Primary outcome	No benefits of DAPT	No benefits of DAPT	Benefits of DAPT	Benefits of DAPT
Hemorrhagic complications	More	More	No difference	A little bit more

Antithrombotics

Dual antiplatelet therapy in stroke and ICAS

Subgroup analysis of CHANCE

Table 2 Efficacy and safety outcomes of patients with and without ICAS*

Outcome	Without ICAS (n = 808)		With ICAS (n = 481)		p Value*
	Placebo plus aspirin (n = 308)	Clopidogrel plus aspirin (n = 300)	Placebo plus aspirin (n = 200)	Clopidogrel plus aspirin (n = 281)	
Efficacy outcomes					
Primary efficacy outcome, stroke	17 (5.5)	16 (5.3)	34 (13.4)	26 (11.3)	<0.0001
Secondary efficacy outcomes					
Composite efficacy outcome*	19 (6.2)	16 (5.3)	34 (13.4)	26 (11.3)	0.0001
Ischemic stroke	17 (5.5)	16 (5.3)	34 (13.4)	26 (11.3)	<0.0001
Hemorrhagic stroke	0 (0)	0 (0)	0 (0)	0 (0)	NA
Myocardial infarction	2 (0.7)	0 (0)	0 (0)	0 (0)	0.208
Vascular death	1 (0.3)	0 (0)	0 (0)	0 (0)	0.374
Death from any cause	1 (0.3)	1 (0.3)	0 (0)	0 (0)	0.208
TIA	7 (2.3)	5 (1.7)	9 (3.4)	4 (1.7)	0.425
mRS score at 90 d					<0.0001
0-2	299 (97.4)	287 (96.6)	221 (88.6)	204 (89.5)	
3-6	9 (2.6)	10 (3.4)	29 (11.4)	24 (10.5)	

Neurology 2015;85:1154-1162

Antithrombotics

Dual antiplatelet therapy in stroke and ICAS

Subgroup analysis of CHANCE

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Hemorrhagic stroke	0 (0)	0 (0)	0 (0)	0 (0)	NA
Myocardial infarction	2 (0.7)	0 (0)	0 (0)	0 (0)	0.208
Vascular death	1 (0.3)	0 (0)	0 (0)	0 (0)	0.374
Death from any cause	1 (0.3)	1 (0.3)	0 (0)	0 (0)	0.208
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Neurology 2015;85:1154-1162

Antithrombotics, TOSS I

Cilostazol Prevents the Progression of the Symptomatic Intracranial Arterial Stenosis

The Multicenter Double-Blind Placebo-Controlled Trial of Cilostazol in Symptomatic Intracranial Arterial Stenosis

- 135 Korean patients with acute symptomatic ICAS
- ASA+Cilostazol Vs. ASA
- 6 months MRA and TCD FU

TABLE 3. The Outcome of Symptomatic Stenosis Measured by MRA and TCD, and Outcome of Asymptomatic Stenosis Measured by MRA

	Cilostazol (%)	Placebo (%)	Total (%)	P
MRA outcome of symptomatic stenosis				0.018
Regression	11 (24.4)	8 (15.4)	19 (19.6)	
Stationary	31 (65.8)	29 (55.8)	60 (61.9)	
Progression	3 (6.7)	15 (28.8)	18 (18.6)	
TCD outcome of symptomatic stenosis				0.004
Regression	12 (26.6)	8 (15.7)	20 (21.5)	
Stationary	29 (60.0)	30 (58.8)	59 (63.4)	
Progression	1 (2.4)	13 (25.5)	14 (15.1)	
MRA outcome of asymptomatic stenosis				0.339
Regression	4 (10.3)	7 (13.7)	11 (12.2)	
Stationary	34 (67.2)	40 (76.4)	74 (82.2)	
Progression	1 (2.6)	4 (7.8)	5 (5.5)	

Stroke. 2005;36:782-786

Antithrombotics, TOSS I

Cilostazol Prevents the Progression of the Symptomatic Intracranial Arterial Stenosis

The Multicenter Double-Blind Placebo-Controlled Trial of Cilostazol in Symptomatic Intracranial Arterial Stenosis

- 135 Korean patients with acute symptomatic ICAS
- ASA+Cilostazol Vs. ASA
- 6 months MRA and TCD FU

TABLE 6. The Outcome of the Symptomatic Stenosis According to the Severity of Stenosis on Initial MRA

	Normal to Mild Stenosis (n=45)	Moderate to Severe Stenosis (n=49)
Regression (%)	6 (12.5)	13 (26.5)
Stationary (%)	34 (70.8)	26 (53.1)
Progress (%)	8 (16.7)	10 (20.4)

Stroke. 2005;36:782-786

Antithrombotics, TOSS II

Efficacy and Safety of Combination Antiplatelet Therapies in Patients With Symptomatic Intracranial Atherosclerotic Stenosis

- 457 patients with acute symptomatic ICAS (M1 and BA)
- ASA+Cilostazol vs. ASA+Clopidogrel
- 7 months MRA FU

The overall change in the stenosis was **more favorable (less progression and more regression) in the cilostazol group (P=0.049)**

Table 2. Primary and Secondary End Points

Outcome	Cilostazol (n=232)	Clopidogrel (n=225)	P
Primary end point			
Progression of symptomatic ICAS*	20 of 202 (9.3)	32 of 207 (15.5)	0.082
Secondary end points			
Regression of symptomatic ICAS*	61 of 202 (30.2)	49 of 207 (23.7)	0.139
Progression of asymptomatic ICAS*	8 of 404 (2.0)	13 of 414 (3.1)	0.306
Regression of asymptomatic ICAS*	26 of 404 (6.4)	15 of 414 (3.6)	0.068
New ischemic lesions on follow-up MRA*	34 of 182 (18.7)	23 of 191 (12.0)	0.078
New ischemic lesions in the territory of ICAS*	22 of 182 (12.0)	17 of 191 (8.9)	0.321

Stroke. 2011;42:2883-2890.

Risk factor control

Relationship between risk factor and vascular events in the SAMMPRIS

Risk factor measure	Target	No. patients with available data	Percentage of patients in target overall
Primary risk factors			
Systolic blood pressure	<140 mm Hg (1-130 if diabetic)	227	53
LDL-C	<70 mg/dL	225	47
Secondary risk factors			
Non-HDL-C	<100 mg/dL	225	60
HbA1c*	<7.0%	113	42
Smoking	Cessation	227	65
Weight management	For initial BMI of 25-27 kg/m ² : target BMI <25 kg/m ² For initial BMI >27 kg/m ² : target 10% weight loss	227	19
Physical activity	PACE score of 4-8*	227	44

Neurology® 2017;88:379-385

PACE score for Physical activities

PACE Score	PACE Qs
1	No regular vigorous or moderate exercise now, and not start in the next 6 months
2	No regular vigorous or moderate exercise now, but think of starting in the next 6 months.
3	Trying to start doing vigorous or moderate exercise, but not regularly
4	Vigorous exercise less than 3 times per week (or) moderate exercise less than 5 times per week
5	30 minutes a day of moderate exercise 5 or more days per week for the last 1-5 months.
6	30 minutes a day of moderate exercise 5 or more days per week for the last 6 months or more.
7	Vigorous exercise 3 or more days per week for the last 1-5 months
8	Vigorous exercise 3 or more days per week for the last 6 months or more

Risk factor control

Relationship between risk factor and vascular events in the SAMMPRIS

Risk factor measure	Target	No. patients with available data	Percentage of patients in target overall
Primary risk factors			
Systolic blood pressure	<140 mm Hg (1-130 if diabetic)	227	53
LDL-C	<70 mg/dL	225	47
Secondary risk factors			
Non-HDL-C	<100 mg/dL	225	60
HbA1c*	<7.0%	113	42
Smoking	Cessation	227	65
Weight management	For initial BMI of 25-27 kg/m ² : target BMI <25 kg/m ² For initial BMI >27 kg/m ² : target 10% weight loss	227	19
Physical activity	PACE score of 4-8*	227	44

Neurology® 2017;88:379-385

Risk factor control

Medically Treated Patients in SAMMPRIS and WASID

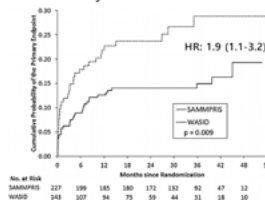


Table 1. Probability of the SAMMPRIS Primary End Point for SAMMPRIS Medical Patients and SAMMPRIS-Eligible WASID Patients

Months After Randomization	SAMMPRIS (n=227), Probability of Primary End Point (95% CI)	WASID (n=143), Probability of Primary End Point (95% CI)
1	5.8% (3.4%-9.7%)	10.5% (6.5%-16.9%)
6	8.9% (5.9%-13.5%)	17.9% (12.5%-25.4%)
12	12.6% (8.9%-17.8%)	21.9% (15.8%-29.9%)
24	14.1% (10.1%-19.4%)	23.7% (17.4%-31.9%)
36	14.9% (10.7%-20.6%)	28.9% (21.1%-38.8%)
P-value*	0.009	

Stroke. 2015;46:2562-2567.

Risk factor control

Medically Treated Patients in SAMMPRIS and WASID

Table 2. Baseline Characteristics for the SAMMPRIS Medical Group Versus SAMMPRIS-Eligible WASID Patients

Characteristic	SAMMPRIS Medical Group (n=227)	WASID (n=143)	P-value*
Age, y	59.5±11.8	62.5±10.0	0.009
History of hypertension	203 (89%)	109 (76%)	0.001
Not using statin at enrollment	31 (14%)	56 (39%)	<0.0001
Old infarcts in the territory of the symptomatic artery	75/222 (34%)	26/130 (20%)	0.015
Categories of percent stenosis of symptomatic artery			0.0004
70% to 79%	102 (45%)	94 (66%)	
80% to 89%	97 (43%)	40 (28%)	
90% to 99%	28 (12%)	9 (7%)	
Systolic BP, mm Hg	146.8±21.8	139.1±17.8	0.0002
Diastolic BP, mm Hg	82.3±12.0	78.5±9.5	<0.0001
BMI, kg/m ²	30.7±8.3	30.1±8.3	0.548
LDL, mg/dL	97.7±36.6	125.4±39.7	<0.0001
HDL, mg/dL	38.8±10.1	43.8±13.4	0.0004

Stroke. 2015;46:2562-2567.

Risk factor control

ICAD under Modern Medical Therapy

- aspirin 80mg and clopidogrel 75mg
Total of 4 weeks, followed by aspirin 80mg/day
- Statin, lifestyle modifications
 - LDL level < 70 mg/dl
 - HbA1c < 6.5%
 - Systolic blood pressure < 140mmHg
 - Abstinence from smoking

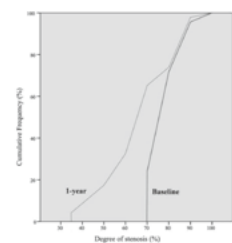


FIGURE 1. Cumulative frequency curves of the angiographic outcome. [Color figure can be viewed in the online issue, which is available at www.annalsneurology.org.]

ANN NEUROL 2015;77:478-486

Risk factor control

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Total of 4 weeks, followed by aspirin 80mg/day

• Statin, lifestyle modifications

- LDL level < 70 mg/dl

- HbA1c < 6.5%

Stenosis changes	%
Regression (stenosis reduced >10%)	49%
Quiescence (stenosis same or ±10%)	43%
Progression (stenosis increased >10%)	8%

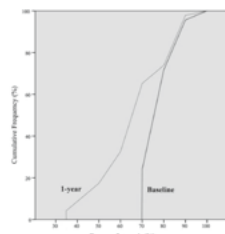


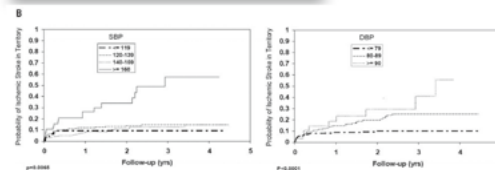
FIGURE 1. Cumulative frequency curves of the angiographic outcome. (Color figure can be viewed in the online issue, which is available at www.annalsneurology.org.)

ANN NEUROL 2015;77:478-486

Risk factor control-Blood Pressure

Relationship Between Blood Pressure and Stroke Recurrence in Patients With Intracranial Arterial Stenosis

Tanya N. Tumm, MD, George Cizic, MD, Michael J. Lynn, MD, Suman Chaturvedi, MD, Marc Chaturvedi, MD, Chih, for the Warfarin-Aspirin Symptomatic Intracranial Disease (WASID) Trial Investigators



Circulation. 2007;115:2969-2975.

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Table 2. HRs and 95% CIs According to Average SBP and DBP for Any Ischemic Stroke and Stroke in Territory

Blood Pressure, mm Hg	Sample Size, n	Stroke in Territory			Stroke in Territory		
		Events, n (%)	HR (95% CI)	P	Events, n (%)	HR (95% CI)	P
SBP							
<119	32	3 (9)	...	...	...	...	...
120-139	268	35 (13)	1.4 (0.4-4.5)	0.590	1.3 (0.4-4.1)	0.704	
140-159	218	22 (10)	1.1 (0.3-3.7)	0.881	0.8 (0.2-2.9)	0.796	
≥160	49	17 (35)	4.7 (1.4-16.0)	0.014	3.9 (1.1-14.1)	0.040	
DBP							
<79	348	32 (9)	...	...	...	...	...
80-89	185	36 (19)	2.2 (1.4-3.6)	0.001	2.2 (1.3-3.7)	0.004	
≥90	34	9 (26)	3.5 (1.7-7.3)	0.0009	5.1 (2.1-12.4)	0.0003	

*HRs and probability values are for comparisons between the lowest blood pressure category and each of the higher blood pressure categories.

Circulation. 2007;115:2969-2975.

Risk factor control-Blood Pressure

Association of Systolic Blood Pressure with Progression of Symptomatic Intracranial Atherosclerotic Stenosis

Jong-Ho Park, Bruce Chellogale, Kwon-Nil Hong, Sun-Il Kwon

Department of Neurology, Severance Hospital, Yonsei University, Seoul, Korea
Department of Neurology, Medical University of South Carolina, Charleston, SC, USA
Department of Neurology, Rancho Los Amigos Hospital, Torrance, California, USA
Department of Neurology, Rancho Los Amigos Hospital, Torrance, California, USA

Table 3. Outcomes of baseline sICAS across mean SBP category

sICAS outcome	<120 (n=26)	120 to 139 (n=233)	≥140 (n=18)
Regression	9 (32.1)	62 (26.6)	14 (77.8)
Quiescence	13 (46.4)	146 (62.7)	14 (77.8)
Progression	6 (21.4)	25 (10.7)	0 (0)

Values are presented as number (%) of patients.

sICAS, symptomatic intracranial atherosclerotic stenosis; SBP, systolic blood pressure.

* χ^2 test.

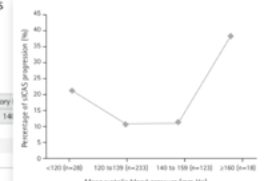


Figure 2. Percentage of sICAS progression by mean systolic blood pressure category among patients with an ICAS stroke. sICAS, symptomatic intracranial atherosclerotic stenosis.

Journal of Stroke 2017;19(3):304-311

Risk factor control-Blood Pressure

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Supplementary Table 1. Severity of baseline sICAS across SBP category

sICAS severity	<120 (n=26)	120 to 139 (n=233)	140 to 159 (n=123)	≥160 (n=18)	P
Mild (<50%)	6 (21.4)	81 (34.8)	40 (32.5)	7 (38.9)	0.509
Moderate (50% to 69%)	9 (32.1)	75 (32.2)	43 (35.0)	9 (50.0)	
Severe (70% to 99%)	13 (46.4)	74 (31.8)	38 (30.8)	2 (11.1)	
Occlusion	0 (0)	3 (1.3)	2 (1.6)	0 (0)	

Values are presented as numbers (%) of patients.

sICAS, symptomatic intracranial atherosclerotic stenosis; SBP, systolic blood pressure.

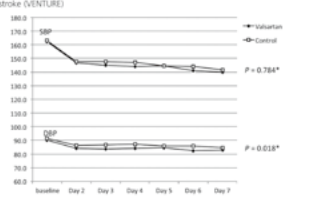
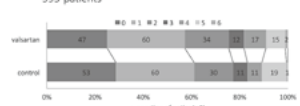
Journal of Stroke 2017;19(3):304-311

BP reduction in acute ischemic stroke

Modest blood pressure reduction with valsartan in acute ischemic stroke: a prospective, randomized, open-label, blinded-end-point trial

M. Sun Oh, Kyung-Ho Yu, Kwon-Sik Hong, Dong-Wook Kang, Jong-Moo Park, Hee-Joon Baek, Jeong-Kook, Junyoung Lee, Byung-Chul Lee, and on behalf of the Valsartan Efficacy on Modest Blood Pressure Reduction in Acute Ischemic Stroke (VENTURE) study group

BP reduction with valsartan within 48 h after symptom onset
multicenter, prospective, randomized, open-label, blinded-end-point trial
393 patients

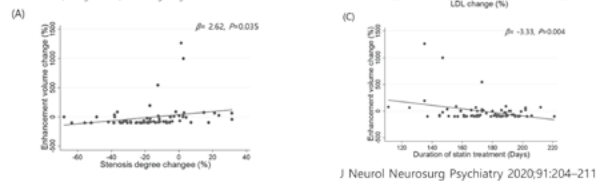


Int J Stroke 2015;10:745-751.

Plaque stabilization-Statin

Intensive Statin Treatment in Acute Ischaemic Stroke Patients with Intracranial Atherosclerosis: a High-Resolution Magnetic Resonance Imaging study (STAMINA-MRI Study)

Jong-Won Chung¹, Jihoon Cha², Mi-Ji Lee³, In-Wu Yu⁴, Moo-Seok Park⁵, Woo-Keun Seo⁶, Sung-Tae Kim⁷, Oh Young Bang⁸



J Neurol Neurosurg Psychiatry 2020;91:204-211

Atherosclerosis in CV risk-free

Normal LDL-Cholesterol Levels Are Associated With Subclinical Atherosclerosis in the Absence of Risk Factors

Leticia Fernández-Fernández, MD, PhD^{1,2,3,4}, Valentín Pastor, MD, PhD^{1,2,3,4}, Beatriz López-Medrano, MD, PhD^{1,2,3,4}, Belén Oliva, MD^{1,2,3,4}, José M. García-Ruiz, MD^{1,2,3,4}, José Mendigueren, MD^{1,2,3,4}, Víctor Bravo, MD, PhD^{1,2,3,4}, Stuart Pocock, MD, PhD^{1,2,3,4}, Jorge Balboa, MD, PhD^{1,2,3,4}, Antonio Fernández-Ortiz, MD, PhD^{1,2,3,4}, Javier Sano, MD^{1,2,3,4}

Progression of Early Subclinical Atherosclerosis (PESA) study (n=4,184) without conventional CVRFs (n=1,779)

• middle-aged population between 40 and 54 years

1) untreated SBP >140 mmHg and DBP >90 mmHg

2) untreated fasting plasma glucose >126 mg/dL

3) untreated total cholesterol >240 mg/dL, LDL-C >160 mg/dL, and HDL-C <40 mg/dL

4) no current smoking status

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TABLE 1 Baseline Characteristics of the CVRF-Free PESA Study Population Based on Presence of Atherosclerosis

Baseline characteristics	CVRF-Free Population (n = 1,779)	No Atherosclerosis (n = 899)	Atherosclerosis (n = 880)	p-Value
Age, yrs	45.0 ± 4.1	44.0 ± 3.7	46.0 ± 4.2	<0.001
Male	884 (49.7)	349 (38.8)	535 (60.8)	<0.001
10-yr ASCVD	0.99 (0.50-2.00)	0.73 (0.40-1.30)	1.40 (0.68-3.70)	<0.001
30-yr FHS	0.09 (0.06-0.10)	0.07 (0.05-0.12)	0.12 (0.07-0.17)	<0.001
Family history of CVD ^a	248 (13.9)	100 (11.1)	148 (16.8)	0.466
Weight, kg	71.8 ± 12.4	69.4 ± 12.9	71.9 ± 12.6	<0.001
Height, cm	169.3 ± 8.7	168.2 ± 8.7	169.3 ± 8.7	<0.001
BMI, kg/m ²	24.9 ± 3.3	24.3 ± 3.3	25.3 ± 3.4	<0.001
Cholesterol	138 (7.8)	57 (6.3)	81 (9.2)	0.034
SBP, mm Hg	112.6 ± 10.4	103.9 ± 10.3	114.4 ± 10.2	<0.001
DBP, mm Hg	69.8 ± 7.7	68.7 ± 7.5	70.8 ± 7.8	<0.001
LDL-C, mg/dL	87 (9.0)	86 (9.0)	89 (10.0)	<0.001
HDL-C, mg/dL	53 (5.4)	53 (5.4)	54 (5.4)	<0.001
LDL-C/HDL-C	4.3 (2.4-6.0)	4.3 (2.4-6.0)	4.4 (2.4-6.0)	0.058
Total cholesterol, mg/dL	190.7 ± 24.0	187.0 ± 24.4	194.4 ± 22.9	<0.001
LDL-C, mg/dL	120.5 ± 20.3	107.4 ± 21.7	120.7 ± 20.1	<0.001
Cholesterol, mg/dL	46.0 ± 12.4	44.8 ± 12.8	47.2 ± 12.9	<0.001
HDL-C, mg/dL	54.4 ± 10.4	55.4 ± 10.6	53.5 ± 10.1	<0.001
Triglycerides, mg/dL	61 (5.0)	61 (5.0)	68 (5.0)	<0.001
Lipoprotein (a), mg/dL	163 (5.4-42.0)	163 (5.4-42.0)	163 (5.4-42.0)	0.980
apoB, mg/dL	100.0 ± 8.9	101.7 ± 8.8	100.0 ± 8.0	<0.001
apoA, mg/dL	61.0 ± 10.1	61.0 ± 10.1	61.0 ± 10.1	0.127
apoB/apoA	0.08 (0.04-0.10)	0.08 (0.04-0.10)	0.07 (0.04-0.10)	0.459
VCAM-1, ng/mL	619.8 (500.4-760.8)	609.9 (485.9-739.8)	626.5 (502.8-776.7)	0.018
Fibrinogen, mg/dL	284.1 ± 43.0	284.1 ± 43.0	284.1 ± 43.0	0.999
Platelets, mg/dL	120.2 ± 18.7	120.2 ± 18.7	120.2 ± 18.7	<0.001

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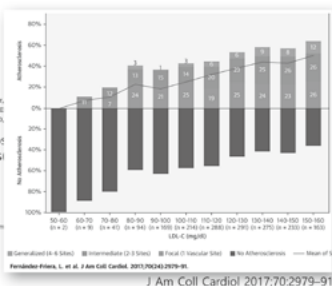
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J Am Coll Cardiol 2017;70:2979-91

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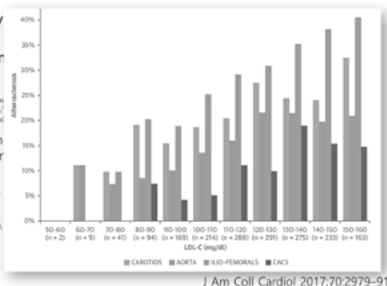
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J Am Coll Cardiol 2017;70:2979-91

Summary of Medical management

- Medical management of ICAS
 - Standard Treatment
 - Optimal antiplatelet therapies and lifestyle modifications
 - Antiplatelet medications
 - Additional risk reduction on top of medical treatment consisting of BP, blood glucose, cessation smoking
 - Aggressive LDL reduction with high-dose statins
 - Physical activities
 - Even if CV risk-free, LDL cholesterol is independently associated with the presence and extent of early systemic atherosclerosis.

Endovascular mangement of ICAS with large vessel occlusion

유 승 훈

울산대 강릉아산병원 신경외과

최근 여러 연구에서 Intracranial large vessel occlusion (LVO) 에 대한 Thrombectomy 가 기존의 치료와 비교하여 월등한 성적을 보이면서 현재는 Endovascular Treatment 가 하나의 표준적인 치료방법으로 자리잡고 있다. 그러나 그 과정에서 새로이 부각되는 문제가 이러한 치료가 Intracranial atherosclerotic stenosis (ICAS) 가 동반된 LVO 의 경우에도 동일한 효과가 있는 지에 대한 문제이다. 이에 대한 연구는 아직까지 충분치 않기는 하나 치료의 실제에서 적지 않게 만나게 되는 문제들을 위치 또는 치료전략 차원에서 분류하여 정리해 보고자 한다.

첫째는 치료전략 선택의 문제이다. 이는 병변의 상태에 대한 판단의 문제일 것이다. 우선, MRA 또는 CTA 에서 Occlusion 으로 보이기는 하였으나 TFCA 에서는 Severe Stenosis 와 compromised distal flow 가 보일 경우이다. 이 때 병변 주변으로 Thrombus filling 이 있다면 Thrombectomy 를 먼저 시행한 후 그 다음 수순을 진행하는 것이 바람직하겠지만, 만약 Thrombus 가 거의 없는 상태라면 first line 으로 Angioplasty 를 고려하는 것도 좋은 Option 이 될 수 있을 것이다. 물론, 이러한 경우는 비교적 드문 경우이며 대부분의 경우에는 Complete Occlusion 으로 확인되어 Thrombectomy 를 시행하였으나 한 두 차례를 시도하여도 Occlusion 이 지속되거나 또는 일시적으로 flow 가 재개되었다가 다시 막히는 경우이다. 이러한 경우가 대표적인 ICAS-related LVO 의 전형적 소견이며 이를 감별하기 위하여 병변의 위치에 따른 구별방법이 제시될 수 있기는 하나 Thrombus filling 이 병변 앞뒤로 되어 있는 경우에는 구별이 쉽지 않다. 그러나, 많은 경우에 있어서는 병변에 Stentriever 를 deploy 한 상태에서 angiogram 을 확인해 보면 구별이 용이한 경우가 많다. 이러한 Atherosclerotic lesion 에 Thrombectomy 를 반복하는 것은 그 자체로 plaque inflammation 을 자극하기 때문에 확인이 된 경우라면 바로 이어서 Angioplasty 를 시도하는 것이 도움이 될 수 있다. 이 때, Balloon Angioplasty 만 할 것인가 또는 Stent Angioplasty 까지 진행할 것인가의 여부는 Lesion 의 상태나 시술자의 선택에 달린 문제이기도 하나, LVO 가 발생한 환자들의 상당수가 Antiplatelet medication 이 되지 않은 상태가 많고 시술 후에도 Reperfusion hemorrhage 또는 Infarction 부위의 Malignant swelling 이 발생하여 Craniectomy 등의 2차적인 수술이 필요할 수도 있기 때문에 Stent Angioplasty 를 우선적으로 고려하는 것에는 신중할 필요가 있을 것이다. 물론, Balloon Angioplasty 를 진행한 후에 또 다시 Reocclusion 이 발생하는 경우라면 이는 Inflamed plaque 에 의한 Reocclusion 이기 때문에 이 때에는 Stent apply 가 거의 유일한 해결이 될 수 있다는 것은 분명할 것이다. 그리고 이러한 고려는 전술한 Direct Angioplasty 를 고려할 때에도 동일하게 적용될 수 있을 것이다.

두번째는 이러한 치료전략에서 가장 중요한 것으로 어느 시점에서 전략변화를 결정할 것인가 하는 문제이다. 예를 들어 반복적인 Thrombectomy 시도에도 불구하고 Occlusion 이 지속되는 경우라면 다른 대안이 없기 때문에 Angioplasty 를 선택하는 것에 별다른 이견이 없겠지만, Faint flow 가 유지되고 있다면 IA Antiplatelet injection 을 먼저 시도하고 필요하다면 IV injection 으로 유지시키는 방법을 사용할 지, 아니면 Angioplasty 를 바로 진행할 지 여부가 고민스러울 수 있다. 이에 대해서는 각각의 경우에 대한 반론의 여지가 있는 것은 분명하나 저자의 의견으로서는 중요한 기능점은 definite 한 flow compromise 의 여부라고 생각한다. Flow compromise 가 definite 할 때에는 상당수에서 Reocclusion 이 발생하는 경우가 많기 때문에 그러할 경우에는 적당한 Angioplasty 를 하는 것이 효과적일 것이라고 생각한다. 그리고 IA 또는 IV Antiplatelet injection 이 가지는 hemorrhagic risk 역시 중요한 고려사항이 될 수 있다.

세번째는, 금번 발표의 주제인 ICAS-related LVO 는 아니지만 ECAS-related LVO 인 경우 역시 치료에 있어서 일반적인 Thrombectomy 와는 많은 차이가 있는 것을 반드시 고려하여야 할 것이다. 대표적으로 Proximal ICA Stenosis 가 원인이 되어 Occlusion 이 된 경우이며 이 경우에는 특별히 고려할 사항들이 있다. 우선 현재 일반적으로 사용되고 있는 Proximal Occlusion Balloon Catheter 의 경우에는 Proximal ICA 에 거치하는 용도이며 이를 CCA distal 에 거치시킨 후 사용할 경우에는 ECA 로부터의 retrograde flow 로 인해 그 효과를 충분히 발휘하기 어려운 단점이 있다. 물론, 이러한 경우 MoMa 와 같은 Dual Balloon equipped Catheter 가 ECA와 CCA 를 동시에 Occlusion 시킬 수 있기 때문에 유용한 대안이 될 수 있으며 이미 ICA Occlusion 이 있는 상태이기 때문에 Emergency 가 아닌 경우에 발생할 수 있는 Ischemic Intolerance 에 대해 크게 우려할 바가 아니어서 나름의 편의성도 있다. 하지만, Proximal ICA Steno-occlusive lesion 에 대한 Carotid Angioplasty 를 하고 나서 발생할 수 있는 distal embolus 에 의한 2차적인 Occlusion 이나, 처음부터 Intracranial Occlusion 이 동시에 발생한 경우에는 2차적으로 Thrombectomy 를 하여야 하는데 이 경우에는 이 device 가 최적화되어 있지 않은 단점이 있기는 하다. 그래서 각 상황에 맞추어 신중한 선택이 필요하다. 또 다른 경우는 Vertebro Basilar system 의 Occlusion 이 발생한 상태에서 Vertebral artery orifice stenosis (VAOS) 가 동반되어 있는 경우이다. 이러한 경우에는 그 이전 상 Embolic occlusion 이라기 보다는 대부분 Stenosis 의 악화로 발생하는 경우이기 때문에 VAOS 를 먼저 해결해야 하나 유의할 것은 VAOS 의 해결 후에 2차적인 또는 처음부터 동반되어 있는 Thromboembolism 에 의한 Occlusion 을 해결해야 하는 상황을 고려하여 처음부터 Stent-Angioplasty 를 하기 보다는 일단 Balloon Angioplasty 를 하여 device engagement 가 가능하게 한 후 distal problem 을 정확히 확인 및 해결한 후에 필요할 경우 Stent-Angioplasty 를 고려하여야 할 것이다.

주지하다시피 ICAS-related LVO 에 대한 Endovascular Treatment 역시 Successful Recanalization 과 그에 이르는 시간이 성공적인 치료의 기능점이다. 따라서 그 발생 이전에 있어 Emboli LVO 와의 차이점과 그에 따라 치료에 대한 반응이 다른 점을 고려하여 치료의 시작 전부터 발생할 수 있는 여러 상황에 대한 충분한 고려 후에 적절한 대처를 하여야 할 것이다.

Surgical mangement of ICAS

최 석 근

경희대병원 신경외과

Intracranial atherosclerosis (ICAS)는 재발성 뇌졸중의 가장 대표적인 위험요소라고 할 수 있다. 이의 치료 방법으로는 첫째, 항혈소판 제제, 둘째, endovascular treatment가 일반적으로 가장 먼저 고려 되고 있다. 위 두 치료법이 동시에 적용이 가능 할 때 어떤 치료법이 바람직한가에 대한 연구논문들은 이미 많이 나와 있으며 지속적인 논쟁거리이다.

ICAS에 대한 수술적인 치료는 약물치료로만으로 환자의 혈류를 정상화 할 수 없고 지속적인 혈류 부전이 초래되는 상황, 여기에 endovascular treatment만으로 치료하기 힘든 경우에 적용 될 수 있는 치료방법이다. 당연히 이러한 환자 군의 연령이 비교적 연령이 높은 군에 속하므로 치료방법은 두개강 내외의 혈관을 서로 직접 문합해 주는 방법을 많이 사용하게 된다. 수술적인 방법은 소아의 모야모야병에서 이루어지는 수술 술식보다는 가능한 직접 혈관 문합술을 사용하게 되는 것이 일반적이다. 이는 아마도 성인의 경우 소아처럼 간접 문합술을 사용하였을 경우 정상 혈류내에 신생혈관 생성인자의 분비가 차이가 있고 혈관의 생성을 기대하기 힘든 부분이 있을 것이고 또한 성인의 ICAS는 가능한 조기에 혈류가 보전되는 치료방법이 효과적이기 때문일 것이다.

수술적인 치료의 evidence를 평가하기 위한 연구에서는 항상 문제가 되는 부분(bias)이 있다.

첫째, 치료의 난이도인데 실제 약물 치료에 비해서 수술적인 치료는 기술적인 부분에 있어서 수술자마다 숙련도의 차이가 있기 때문에 발생하는 오류(bias)이다. 이는 결과에 악영향을 미치게 된다. 즉 수술이 잘될 경우 눈으로 느껴지는 효과를 보게 됨에도 불구하고 숙련되지 않은 수술자들이 연구에 포함되면서 수술의 효과에 대해서 위음성의 결과를 초래하게 한다.

두번째, ICAS라는 질환은 실제 질환 자체가 그냥 하나의 진단명으로 표현하기에는 아주 다양성을 가진 질환이다. 똑같은 부위의 혈관 협착이라고 하여도 collateral flow나 hemodynamics는 서로 상이하다. 그리고 혈류의 속도나 혈류 요구량 등은 같은 진단을 할지라도 개개인마다 차이가 나게 마련이다. 즉 ICAS라고 할지라도 실제 연구대상군에 속한 환자들은 모든 환자들이 필연적으로 heterogenous하게 마련이다. 이는 일반화의 오류(bias)가 필연적이게 된다.

그래서 환자의 평가나 치료방법은 환자 개개인의 혈류 역학적인 특성에 따라서 다 다른 판단을 해야한다. 수술적인 치료는 약물 치료나 endovascular treatment 보다는 일반적이지 않기때문에 높은 수준의 evidence를 확보하고 있지는 못하다.

수술적인 치료의 적응은 일반적으로 endovascular treatment의 적응증과 유사하다고 할 수 있으며 endovascular treatment보다 차선책으로 고려되는 것이 일반적이다. 두 치료 모두 현재보다는 앞으로 혈류 장애에 의한 뇌손상이 진행될 거라고 보는 검사결과일때 치료를 고려하게 된다.



ARCS 2020

ARTERIAL RECANALIZATION IN CEREBRAL STROKE

뇌졸중 재개통 심포지엄 및 대한뇌혈관내치료의학회
2020 추계보수교육

Session V. Interesting or Complicated Cases Presentation in Mechanical Thrombectomy

좌장 : 권현조 (충남대), 정진영 (연세에스병원)

Case Presentataion 1

Case Presentataion 2

Case Presentataion 3

Case Presentataion 4

장인복 (한림대)

김상욱 (명지성모병원)

진선탉 (에스포항병원)

박정현 (한림대)

Case Presentataion 1

장 인 복

한림대 성심병원 신경외과

Interesting or complicated cases
presentation in mechanical
thrombectomy

Chang In Bok

Department of Neurosurgery
Institute of Neuroscience
Hallym University Medical Center

Case 1

Tandem lesion (thrombectomy & CAS)

IV tPA & thrombectomy

M/74

c/c: left side motor weakness(GII/GIII)
disarthria

NIHSS:11

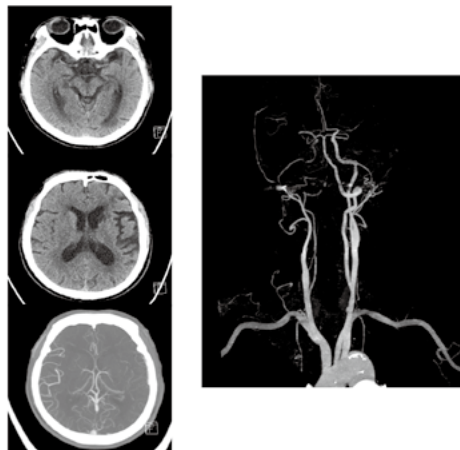
Delay time: 48m

Onset to needle time: 74m

Door to needle time: 26m

Door to puncture time:107m

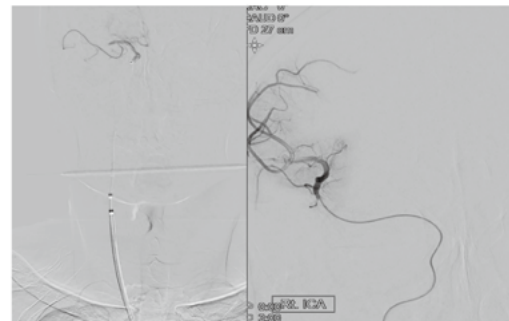
Puncture to recanalization:40m



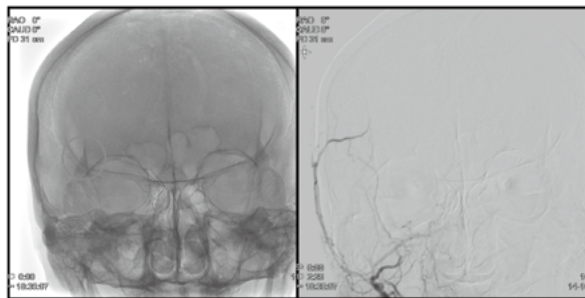
Cello 9Fr. & aspiration



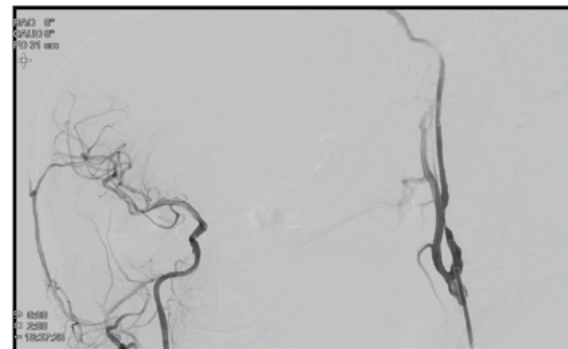
Rt. M1 occlusion



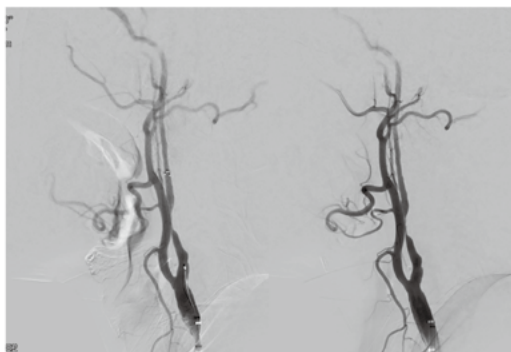
Solitaire stent (6x30mm)



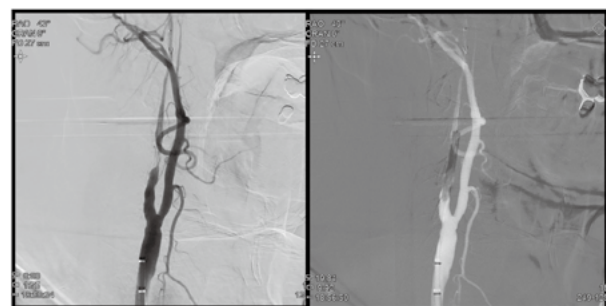
Rt. M1 recanalization & ICA proximal stenosis



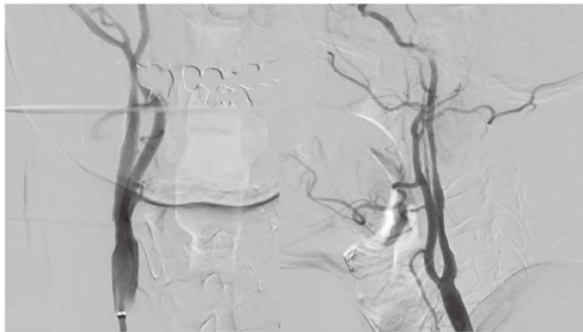
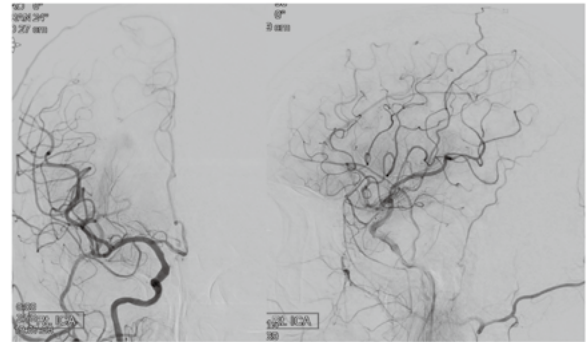
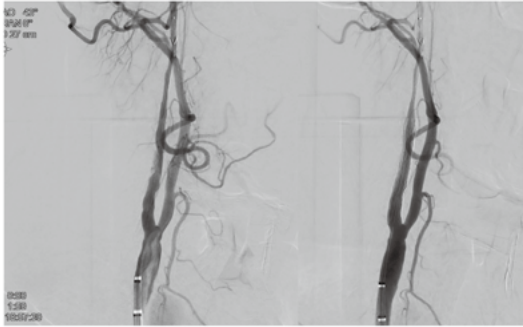
Thrombectomy Trial with Solitaire stent



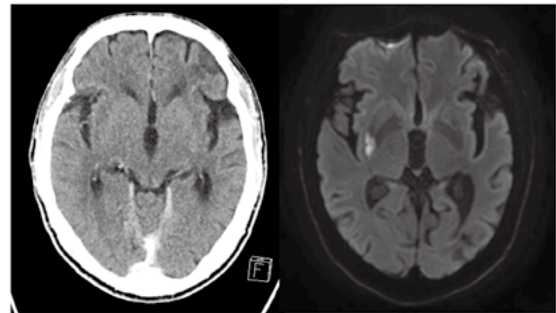
CAS (Acculink 6-8x40mm)



CAS (Acculink 6-8x40mm)



NIHSS(11->2)



Case 2

Tandem lesion (CAS & thrombectomy)

Thrombectomy, IV tPA (-)
M/81
c/c: left side motor weakness(GIII/GIV)
Sick sinus syndrome- pacemaker insertion
Old CVA (2019)- Rt. Thalamic infarction
HTN/DM +/-
NIHSS:7
Delay time: 301m, unclear onset
Door to puncture time:84m
Puncture to recanalization:80m

Rt. ICA proximal stenosis



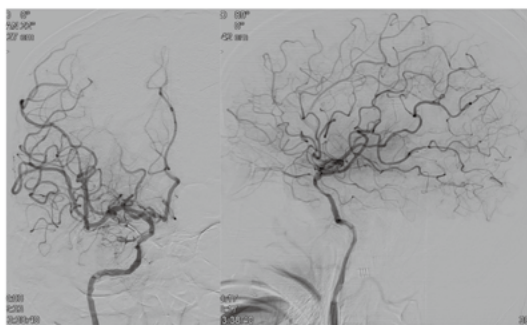
Rt. M1 occlusion



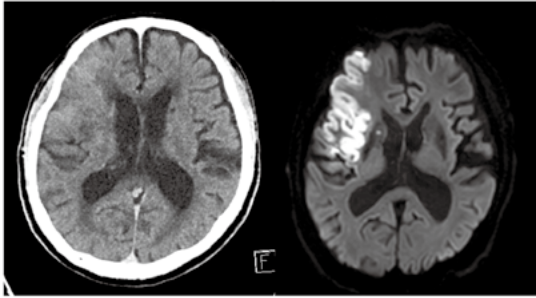
CAS (Wall stent, 7x50)



Thrombectomy (Solitaire 4x20)



NIHSS (7->4)



Case 3

Rt. ICA occlusion (radial approach)

IV tPA + thrombectomy

M/58

c/c: left side motor weakness(GII/GIII)

Thoracic aorta dissection, descending: stent insertion

Carotid artery bypass: Rt-Lt bypass graft & Lt. CCA- Lt. SCA graft

HTN/DM +/-

NIHSS:11

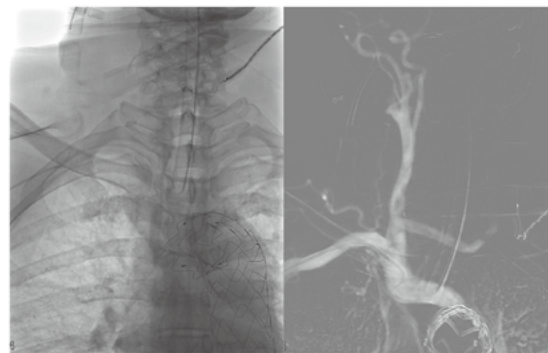
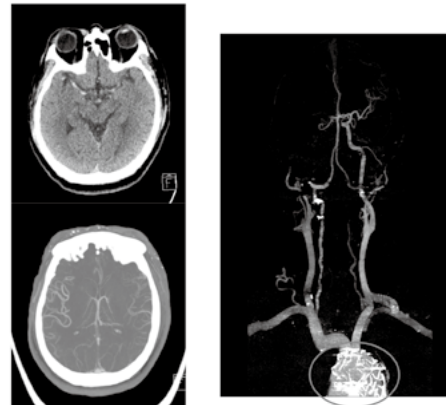
Delay time: 35m

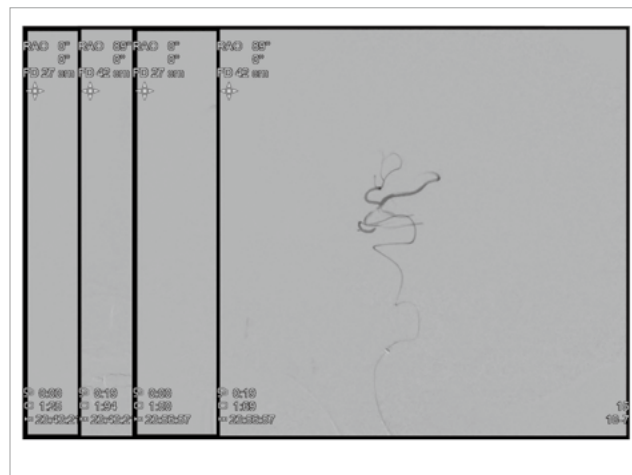
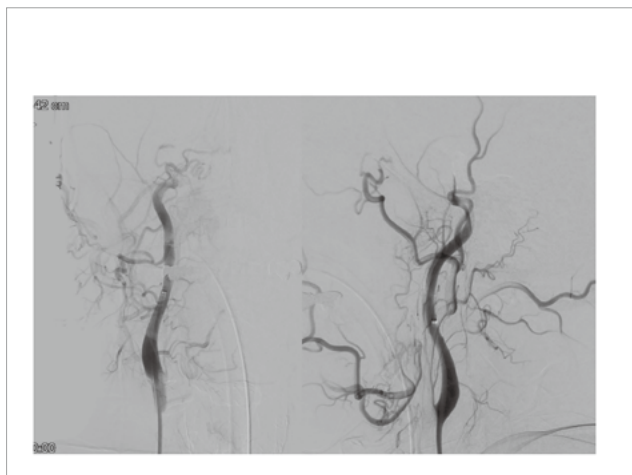
Onset to needle time: 98m

Door to needle time: 63m

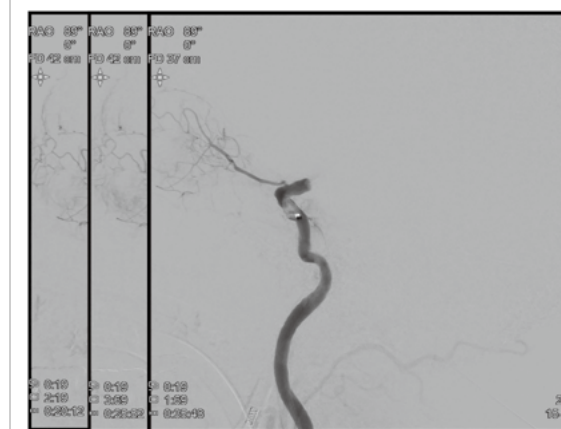
Door to puncture time:189m

Puncture to recanalization:106m

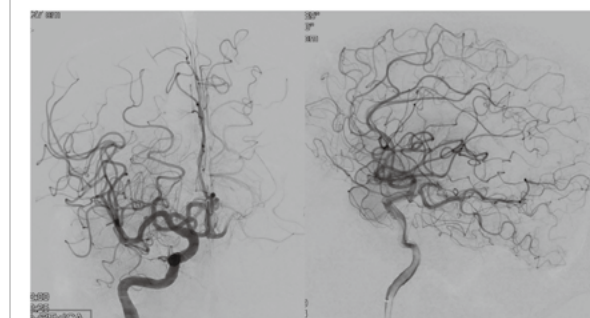
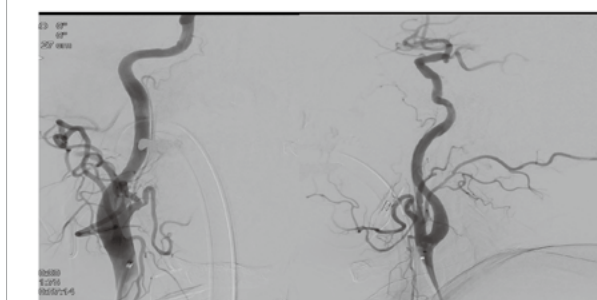




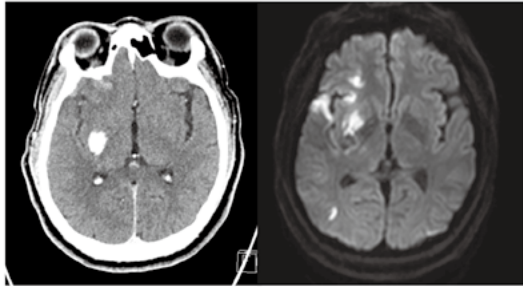
Solitaire (6x30)



Navien (058) & marksmen withdrawal



NIHSS (11->2)



감사합니다.

Case Presentataion 2—Periprocedural vessel injury complication during late—window thrombectomy

김 상 욱

명지성모병원 신경외과

Background: Recent studies such as DAWN, and DEFFUS 3, demonstrated that the benefits of endovascular therapy in the extended time window in patients with anterior circulation large vessel occlusion ischemic stroke and favorable imaging profile, and 2019 Stroke guidelines suggested that mechanical thrombectomy with a stent retriever is reasonable in selected acute stroke patients within 6 to 24 hours. We report a case of complication that occurred during thrombectomy in a late time window.

Case Description: A 60-year old man presented with left side subjective weakness 1 month ago. However, recently his symptoms were aggravated even though taking dual antiplatelets. MRI shows embolic infarctions with ICA occlusion and perfusion—diffusion mismatch. The trans-femoral cerebral angiography (TFCA) identified near occlusion due to multiple thrombi, and mechanical thrombectomy was performed immediately. Several attempts of mechanical thrombectomy with a retriever stent were unsuccessful, and CCF occurred due to damage to the vessels in the cavernous segment during the procedure. Multiple stents were successfully placed in the lesion, and CCF and ICA occlusion were resolved simultaneously. And the patient's symptoms were recovered.

Conclusion: Mechanical thrombectomy may be attempted in patients with a late time window, but it needs to pay attention to complications such as vessel injury during the procedure.

Case Presentataion 3—Interesting case of mechanical thrombectomy in PSSH

진 섣 탁

에스포항병원 신경외과

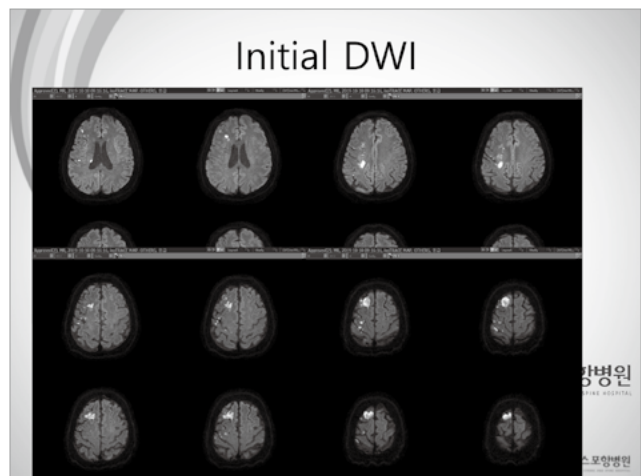
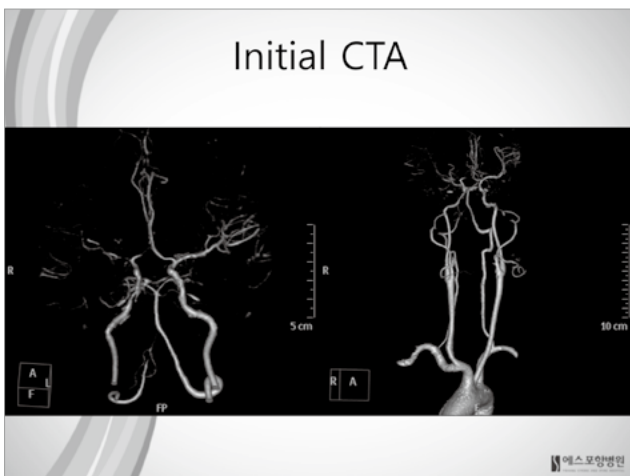


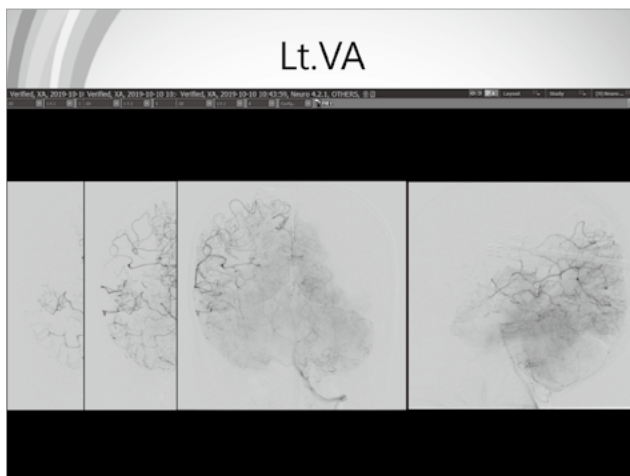
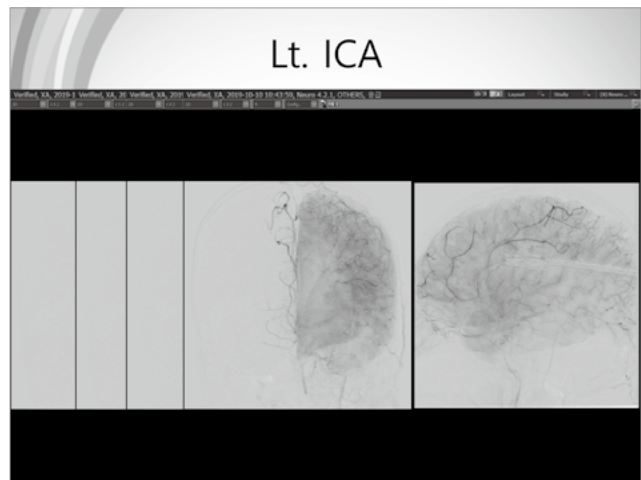
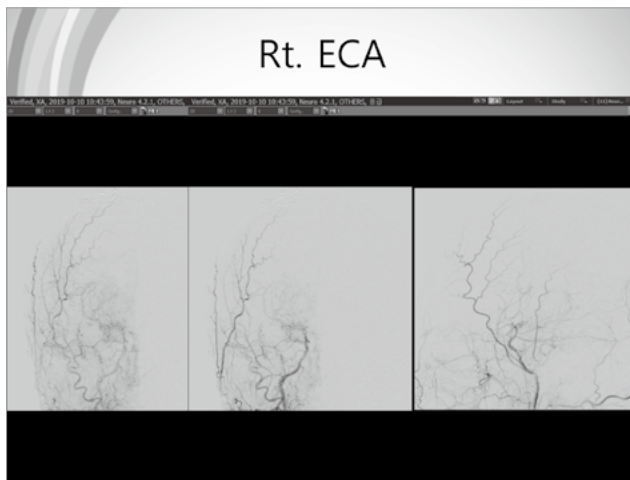
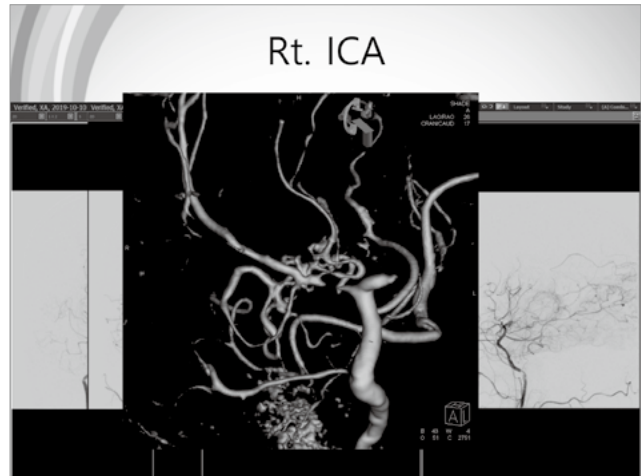
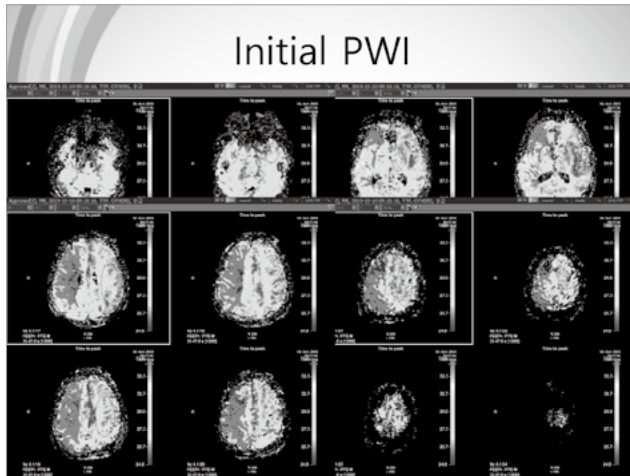
Case review

- M / 56
- 내원 24시간전 발생 후 진행되는 Lt. hemiparesis (G1/G3)
- 내원당시 NIHSS 6
- P.Hx : none
- HbA1c 11.6 / TG 318 / LDL 137
-> uncontrolled DM & lipidemia

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에스포항병원



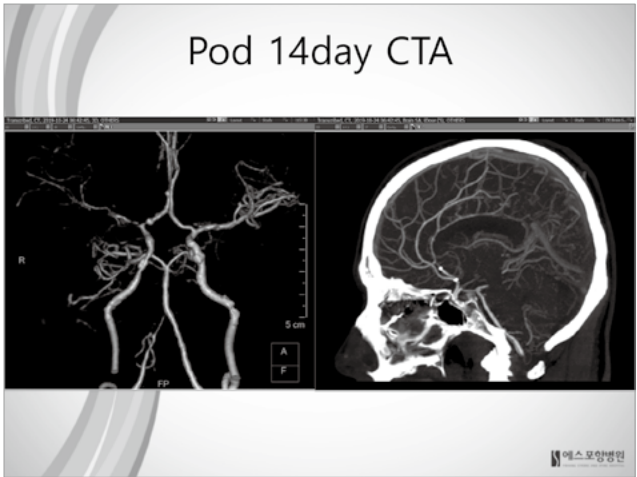
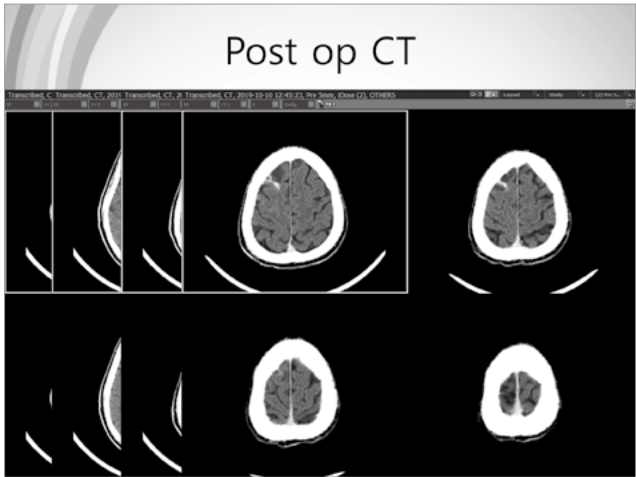
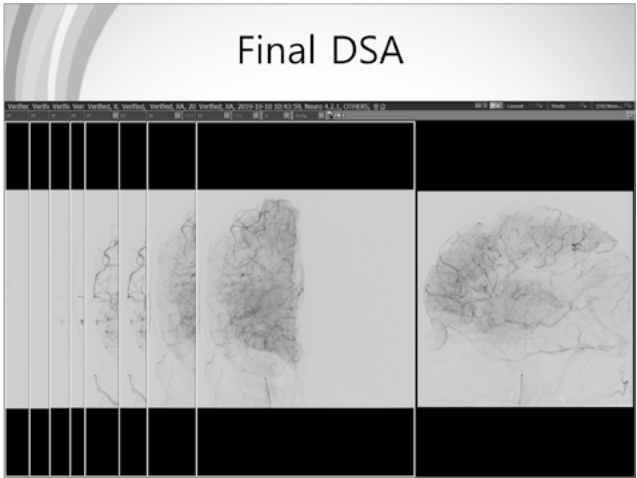
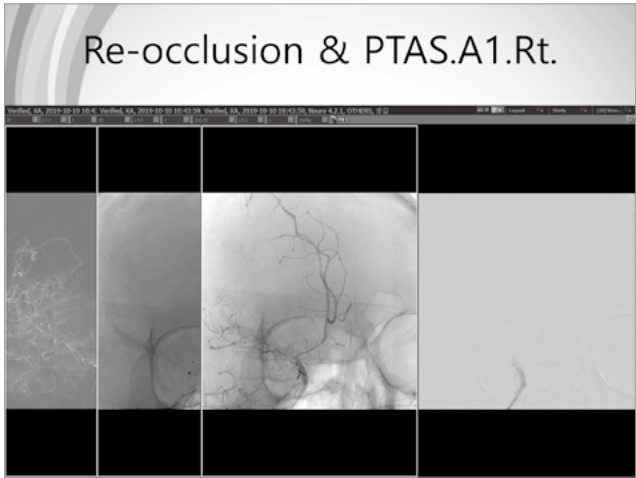
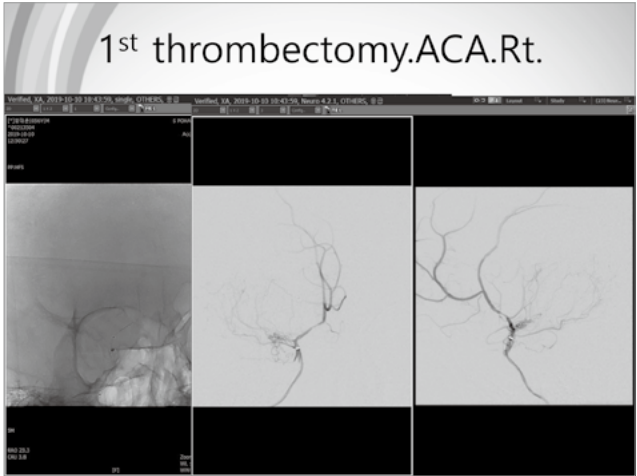
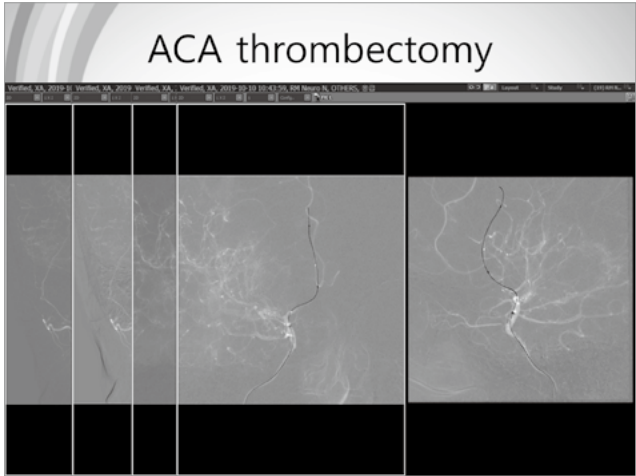


Thrombectomy ? Where?

- Acute MCA infarction c D/P mismatching
-> MCA thrombectomy ?
- But maybe chronic occlusion.MCA & Acute A1 occlusion
-> MCA-STA bypass?
- Or -> ACA thrombectomy?

에스포항병원
FORWARD STROKE AND SPINAL HOSPITAL

에스모항중원



Post op

- NIHSS 6
- Alert / Lt.motor G1/G3 – 변화 없음
- 1M D/C NIHSS 5
- Lt. motor G3/G4 호전되었으나 자가보행은 힘든 상태
- 2M OPD 지팡이 보행 내원 mRS 3

에스포항병원
POHANG STROKE AND SPIKE HOSPITAL에스포항병원
POHANG STROKE AND SPIKE HOSPITAL

Discussion

Case Reports | World Neurosurg. 2019 Mar;123:86-88. doi: 10.1016/j.wneu.2018.11.236. Epub 2018 Dec 8.

Distal Thrombectomy for Acute Anterior Circulation Stroke with Chronic Large Vessel Occlusion

Jin Zhang ¹, Xiao Zhang ², Jingjing Zhang ³, Yun Song ⁴, Ju Han ⁵

Affiliations → expand

PMID: 30517546 DOI: 10.1016/j.wneu.2018.11.236

Abstract

Background: Endovascular therapy has been increasingly recommended for the treatment of acute ischemic stroke with large vessel occlusion of the anterior circulation. However, occlusions of the distal cerebral artery are not uncommon and may cause clinical deficits, especially when combined with ipsilateral chronic large vessel occlusion. Therefore in this patient population, the recognition of chronic occlusion and recanalization of the distal occlusive artery might be of great value for flow compensation.

Case description: A 59-year-old male with a history of stroke was transferred to the emergency department with a severe right hemiplegia and aphasia syndrome. Head computed tomography demonstrated an old infarction focus of the left basal ganglia, and digital subtraction angiography revealed an occlusion of the left middle cerebral artery (MCA). After careful attempts, the microguidewire could not pass through the left MCA. On consideration of the patient's previous stroke history and the angiographic neovascularization, the left MCA was recognized as a chronic occlusion and its territory was supposed to be partly compensated by the ipsilateral anterior cerebral artery (ACA). A super selective angiography of the left ACA demonstrated an occlusion of the callosomarginal artery. After a mechanical thrombectomy with a stent retriever, an angiogram showed complete recanalization and good antegrade reperfusion of the ACA supplying the partial MCA territory. The patient had a positive prognosis.

Conclusions: The recognition of chronic occlusion is crucial during acute mechanical thrombectomy, and distal thrombectomy may be beneficial after a careful full-scale assessment.

에스포항병원
POHANG STROKE AND SPIKE HOSPITAL에스포항병원
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Discussion

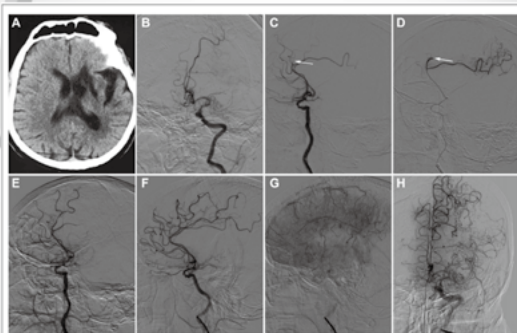


Figure 1. Cerebral imaging of the mechanical thrombectomy. (A) Axial CT scan showing the old infarction focus of the left basal ganglia. (B) Digital subtraction angiography (DSA) showing the occlusion of the left middle cerebral artery (MCA). (C) DSA showing the occlusion of the left MCA. (D) DSA showing the occlusion of the left MCA. (E) DSA showing the occlusion of the left MCA. (F) DSA showing the occlusion of the left MCA. (G) DSA showing the occlusion of the left MCA. (H) DSA showing the occlusion of the left MCA.

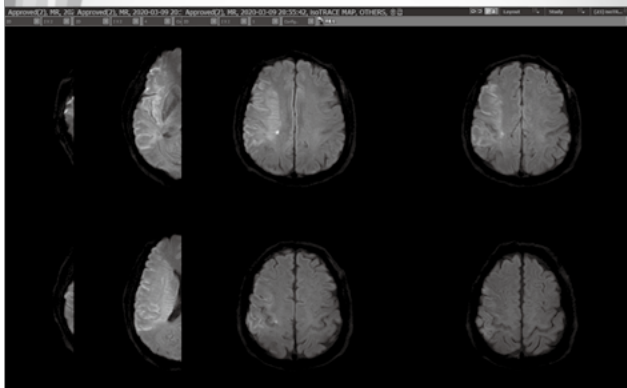
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Case review

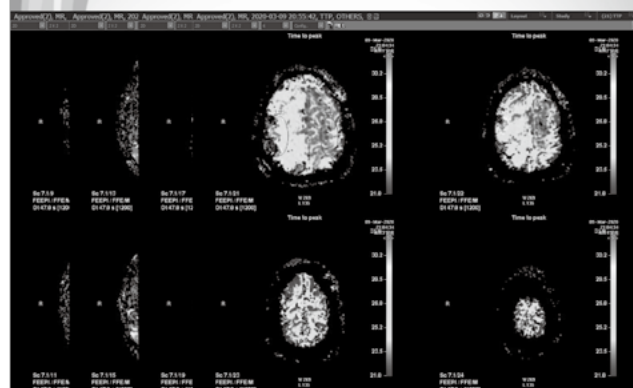
- M/48
- P.Hx) HTN
- 내원 40분전 차에서 목격된 Lt. hemiplegia
- LNT : 1시간40분전 당구장(7pm)
- NIHSS 11
- Drowsy / Dysarthria / Facial palsy Lt.hemiplegia(G1/G1)

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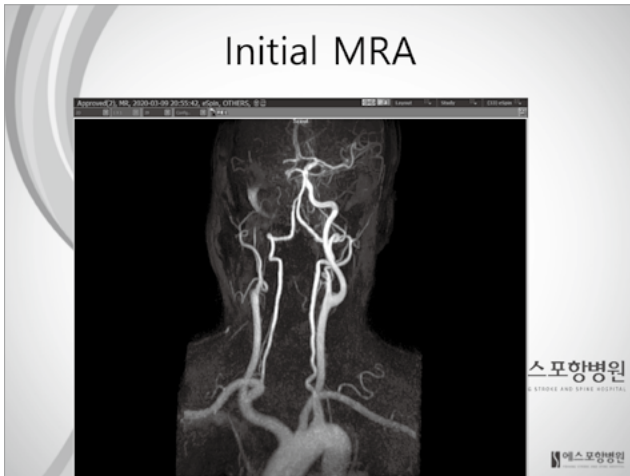
Initial DWI



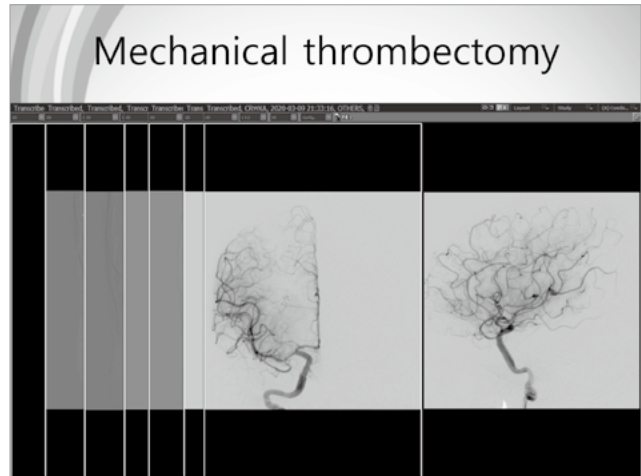
Initial PWI



Initial MRA



Mechanical thrombectomy

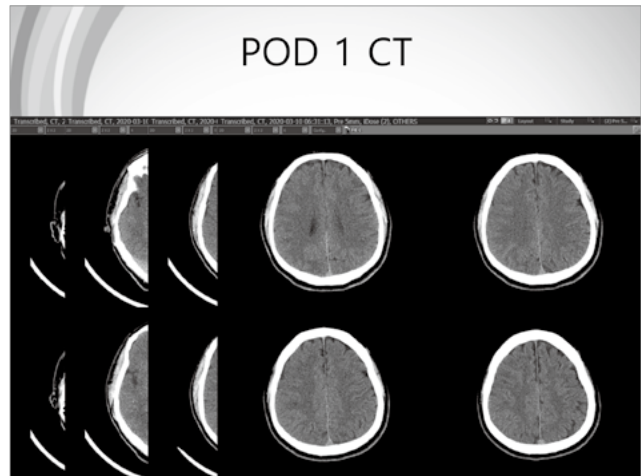


Post op N.ex

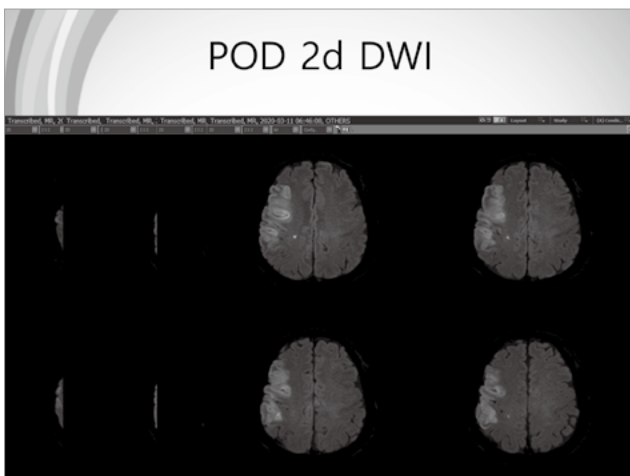
- Door to Puncture time: 1시간 13분
- Puncture 후 recanalization time: 49분
- Near alert
- Mild dysarthria
- Lt. hemiparesis G4+/G4+



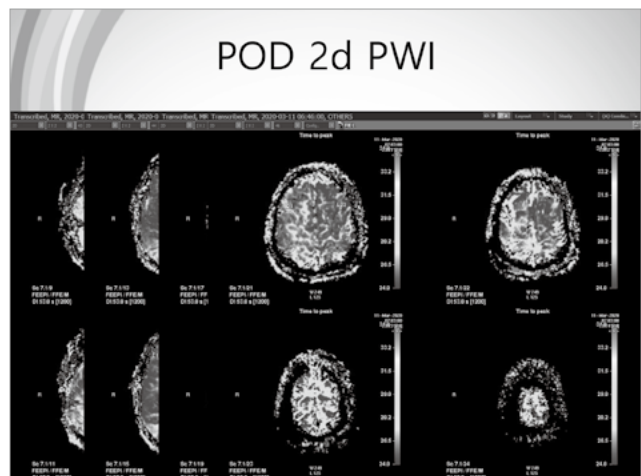
POD 1 CT



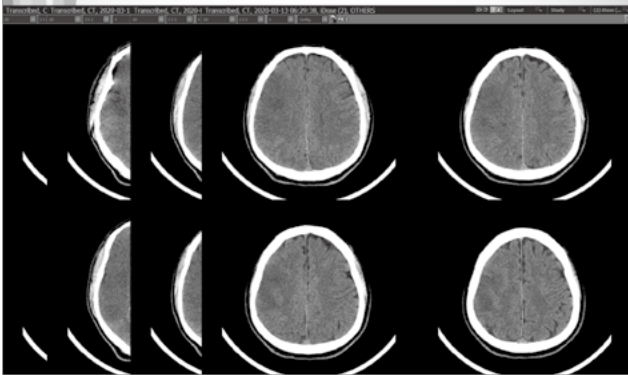
POD 2d DWI



POD 2d PWI



POD 5d CT



Discussion

- 발생 1시간 이내 도착한 환자
- D/P matched total MCA infarction
- NIHSS 11 / motor G1/G1
- MT? or Decompression?

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Discussion

- 48yr / motor G1/G1
- If I can do very fast & successful MT or if not ?
- Maybe can recover
- Maybe not to do decompression
- Maybe make hemorrhage

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Discussion

- Still I don't know should I do thrombectomy for D/P matched patients.
- But, if Young & arrived earlier & poor Px.
- How about doing thrombectomy very fast.

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POHANG STROKE AND SPINE HOSPITAL

Case Presentataion 4

박 정 현

한림대 동탄성심병원 신경외과

MCA Occlusion with ICA Dissection

Case 1. 58 Yr / male. Crossfit activity

Case 2. 70 Yr / female. C2 fracture

Cervical trauma would induce ICA dissection

Carotid stent with mechanical thrombectomy would be the treatment

Should take attention for thrombectomy stent with carotid stent

ARCS 2020 ARTERIAL RECANALIZATION IN CEREBRAL STROKE
뇌졸중 재개통 심포지엄 및 대한뇌혈관내치료의학회 2020 추계보수교육

인 쇄 2020년 9월 17일

발 행 2020년 9월 19일

발 행 처 대한뇌혈관내치료의학회

회 장 윤 석 만

총무이사 박 석 규

수련교육이사 김태곤, 유승훈

주 소 서울시 서초구 서초대로 350 (서초동 동아빌라트 2타운) 407호

제 작 엘에스커뮤니케이션즈

주 소 서울특별시 동대문구 천호대로85길 17 압구정빌딩 6층
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REPAIR.**



†January 2020 Finance Report. Data on file at Abbott

*On Nov. 8, 1993, the first (Perclose) patent was filed for the percutaneous suture vascular closure device. The Perclose portfolio includes all percutaneous suture closure devices. Data on file at Abbott.

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소중한 환자의 건강한 혈관을 위해

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Safety
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Cilostazol + Ginkgo biloba ext. 복합 서방정 혈전생성 억제¹와 신경보호²를 동시에



Renexin CR

1일 1회 복용으로 복약순응도 향상 기대³

기존 IR 대비 이상사례 발현 유의하게 개선⁴

Renexin CR Tab.

Cilostazol 200mg,
Ginkgo Biloba ext. 160mg

[References] 1. Ryu KH, et al. Ginkgo biloba extract enhances antiplatelet and antithrombotic effects of cilostazol without prolongation of bleeding time. *Thrombo Res.* 2009;124:328-334 2. Kwak PA, et al. Supra-Additive Neuroprotection by Renexin, a Mixed Compound of Ginkgo Biloba Extract and cilostazol, Against Apoptotic White Matter Changes in Rat after Chronic Cerebral Hypoperfusion. *J Clin Neurol.* 2012 Dec; 8(4): 284-292 3. Bae JP, et al. Adherence and dosing frequency of common medications for cardiovascular patients. *Am J Manag Care.* 2012 Mar;18(3):139-46 4. SID142 임상3상, Data on file, SK케미칼. [Updated 2019.04.09]

리넥신서방정 제품요약정보

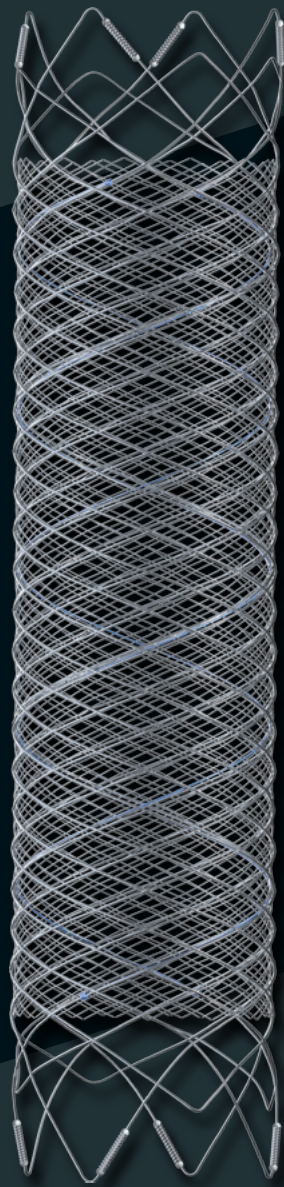
【제품명】 리넥신서방정 **【원료약품 및 그 분량】** 이 약 1정 중 유효성분 : 실로스타졸(UP)···200 mg, 은행엽건조엑스(생규)···160 mg **【성상】** 연두색의 타원형 서방성 필름코팅정 **【효능·효과】** 다음 질환에 대하여 실로스타졸 단독요법으로 효과가 불충분한 경우, 실로스타졸과 은행엽건조엑스 제제의 병용요법에 대한 대체요법 1. 만성동맥폐색증(허벅지병, 폐색성 동맥경화증, 당뇨병성 말초혈관병증 등)에 따른 괴양, 동통 및 냉감 등 허혈성 증상상의 개선 2. 뇌경색(심인성 뇌색전증 제외) 발증 후 재발억제 **【용법·용량】** 이 약은 서방정 정제이므로 분쇄하거나 분할 또는 씹지 않고 전체를 복용하며, 식사를 피하여 공복 상태에서 복용한다. 이 약은 1회 용량으로 실로스타졸 100밀리그램과 은행엽건조엑스 80밀리그램을 1일2회 병용투여시 효과가 충분한 성인 환자에 대하여 대체요법으로 투여한다. 통상 성인에 대하여 1일1회, 1회 1정을 경구 투여한다. **【사용상의주의사항】** 1. 경고, 이 약은 실로스타졸 투여로 인해 맥박수가 증가하여 협심증이 발현될 수 있으므로 협심증의 증상(가슴통증 등)에 대한 문진을 주의깊게 실시한다(뇌경색 재발 억제효과를 검토하는 시험에서, 장기간에 걸쳐 PRP(pressure rate product)를 의미있게 상승시키는 작용이 인정되었다. 또한, 실로스타졸 투여군에서 협심증이 발현된 증례가 나타났다). 2. 다음 환자에는 투여하지 말 것. 1) 출혈(혈우병, 모세혈관 취약증, 두개내출혈, 상부소화관출혈, 요로출혈, 객혈, 초저체출혈 등) 또는 그러한 소인(활동성 소화궤양, 최근 6개월 이내에 출혈성뇌졸중, 3개월 이내에 외과수술, 증식당뇨망막병증, 조절되지 않는 고혈압)이 있는 환자(출혈을 조장할 우려가 있다) 2) 울혈성심부전 환자(증상을 악화시킬 우려가 있다) 3) 이 약 및 이 약의 구성성분에 과민반응의 병력이 있는 환자 4) 임부 또는 임신하고 있을 가능성이 있는 여성 및 수유부 3. 다음 환자에는 신중히 투여할 것. 1) 항응고제(와파린 등), 항혈소판제(아스피린, 티클로피딘 등), 혈전용해제(유로키나제, 알테플라제 등), 프로스타글란딘 E1 제제 및 그 유도체(알프로스타딜, 리마프로스트 알파엑스 등)를 투여중인 환자 2) 월경기간 중인 환자(출혈을 조장할 우려가 있다) 3) 관동맥 협착의 합병증 환자(이 약의 투여에 의한 맥박수 증가로 협심증을 유발할 가능성이 있다) 4) 중증 신장에 환자(크레아티닌 청소율 ≤ 25 mL/분)(이 약의 대사물의 혈중농도가 상승될 수 있다) 5) 중등도 또는 중증 간장에 환자(이 약의 혈중농도가 상승될 수 있다) 6) 당뇨병 또는 내당능 장애가 있는 환자(출혈성 유해증상이 발현하기 쉽다) 7) 지속적으로 혈압이 상승하고 있는 고혈압 환자(약성고혈압 등) 8) 심방이나 심실전위 환자, 심방세동이나 조동 환자, 심실빈맥, 심실세동 또는 다초점성심실이상성박동 환자, QT간격의 연장이 있는 환자 9) S자형 심실 중격이 있거나 위험이 있는 환자(특히 고령자) : S자형 심실 중격 환자에서 좌심실 유출로 폐쇄가 보고되었다. 실로스타졸 복용 시작 후 새로운 수축기 잡음 혹은 심장 증상의 발생 여부를 모니터링 한다. **【제조자】** 에스케이케이미칼(주) 충청북도 청주시 흥덕구 신단로 149 **【판매자】** 에스케이케이미칼(주) 경기도 성남시 분당구 판교로 310 2020.03.24

※ 처방하시기 전 제품설명서 전문을 참고하십시오. 최신 허가사항에 대한 정보는 '식약품안전센터 의약품안전나라 (<https://nedrug.mfds.go.kr/index>)'에서 확인할 수 있습니다.

Reference. 리넥신서방정 허가정보, 의약품안전나라 [Cited 2020.03.25] Available from : <https://nedrug.mfds.go.kr/>

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