

Case-Based Learning Stroke



정근화

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Case 1

M/64, Lt. sided weakness
HT/DM, PAD on stent
Aspirin, cilostazol

left sided weakness worsening,
1D later

MES on TCD monitoring

Spontaneous MES(+)

Depth	Dist	Mean	PI	RI	Vessel
40	100	19	121	75	ROPHN
60	100	46	127	88	ROPHN
70	100	36	128	75	ROPHN
80	100	50	125	75	RCCA
90	100	42	132	75	RCCA
95	100	44	135	82	RCCA
98	100	52	88	87	ROBERT
100	100	29	88	88	ROBERT

Depth	Dist	Mean	PI	RI	Vessel
40	100	19	121	75	LOPHN
60	100	46	127	88	LOPHN
70	100	36	128	75	LOPHN
80	100	50	125	75	LCCA
90	100	42	132	75	LCCA
95	100	44	135	82	LCCA
98	100	52	88	87	LOBERT
100	100	29	88	88	LOBERT

Next step?

1. Anticoagulation
2. Addition of clopidogrel
3. Emergent angioplasty
4. Emergent CEA

Treatment

Aspirin 100mg
Cilostazol 100mg bid
Clopidogrel 75mg



치료 시기에 관한 연구

Stratify	Events / Patients	ARR (%)	95% CI
Time since last event (weeks)	Surgical	Medical	
<2	18/122	26/175	14.7 12.3-17.1
	27/213	42/224	15.9 8.9-23.5
	40/325	86/339	18.5 12.1-24.9
2-4	17/136	13/81	4.4 -5.5-14.2
	34/202	32/234	1.5 -4.9-8.0
	32/288	44/325	9.8 3.0-16.5
4-12	29/271	31/238	4.1 -2.0-10.2
	34/289	50/282	6.4 0.4-12.5
	83/560	82/498	5.5 1.2-9.8
>12	20/236	12/133	0.7 -6.8-8.0
	32/227	18/139	-9.1 -13.9-5.2
	41/373	31/232	0.8 -5.2-6.8
Total	175/1474	244/1284	8.5 5.6-11.3

Inclusion criteria: transient ischaemic attack, non-disabling ischaemic stroke, or a retinal infarction

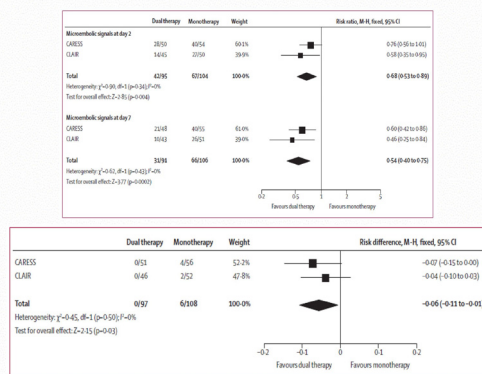
Rothwell, Lancet, 2004

- Pooled absolute risk of stroke and death of emergent op.
 - Stroke-in-evolution: 20.2%
 - Crescendo TIA: 11.4%
- Early vs. late surgery in TIA or minor stroke (p=0.13)

Rerkasem, Stroke, 2009

CARESS, Markus et al., Circulation, 2005
CLAIR, Wong et al., Lancet, 2010

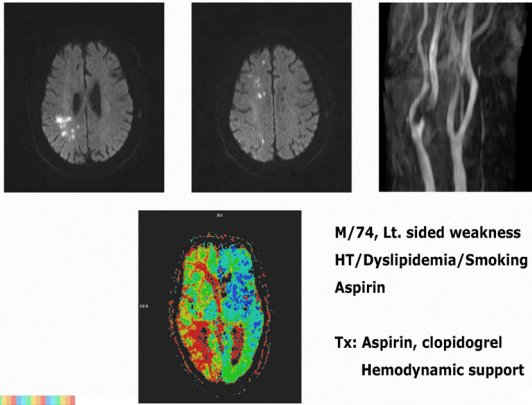
Symptomatic intracranial and extracranial artery stenosis ASA+CPD vs. ASA



국내진료지침 (2011.5)

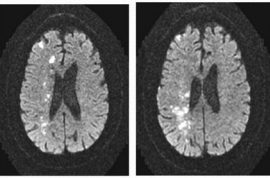
1. 최근 6개월 이내에 일과성 허혈발작이나 뇌경색이 있었던 심한 내경동맥 협착 환자(협착 정도 70-99%)는 경동맥 내막절제술을 하는 것이 권장된다. 경동맥 내막절제술 수술은 수술 전후의 이환율과 사망률이 6%미만인 의사가 시행하는 것이 권장된다. (근거수준Ib, 권고수준A)
2. 최근에 일과성 허혈발작이나 뇌경색이 있었던 중등도 내경동맥 협착(50-69%) 환자의 경우 환자의 연령, 성별, 동반된 질환, 처음 증상의 정도를 고려하여 경동맥 내막절제술을 시행할 수 있다. (근거수준Ib, 권고수준A)
3. 경도의 내경동맥협착(50% 미만) 환자에게는 내과적인 치료가 우선 권장된다. (근거수준Ib, 권고수준A)
4. 경동맥 내막절제술은 조기 수술의 금기사항이 없다면 허혈 증상이 발생한 뒤 2주 이내에 수술하는 경우 더 좋은 예후를 기대할 수 있다. (근거수준Ib, 권고수준B)
5. 유증상의 심한 내경동맥 협착(70% 이상)을 가진 70세 미만의 환자에서 6% 미만의 수술 전후 합병증이 예측되는 경우 스텐트 설치술이 내막절제술의 대체 치료로 고려될 수 있다 (근거수준Ib, 권고수준A)
6. 스텐트 설치술 직전과 수술 후 최소1개월 동안 클로피도그렐과 아스피린 병용투여를 유지하는 것이 추천된다. (근거수준Ib, 권고수준B)
7. 유증상 경동맥 협착 치료 과정에서 항혈소판제 및 statin계 지질저하제 사용, 위험인자의 적극적인 조절이 병행되어야 한다. (근거수준Ib, 권고수준B)

Case 2



M/74, Lt. sided weakness
HT/Dyslipidemia/Smoking
Aspirin

Tx: Aspirin, clopidogrel
Hemodynamic support



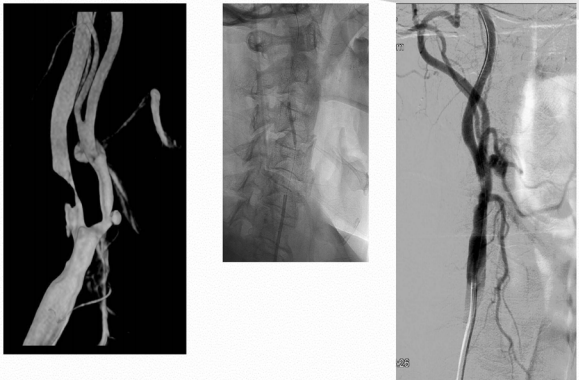
One day later,
Aggravation of left sided weakness
BP: 130/80

RIGHT					LEFT					
Depth	Peak	Mean	PI	Vessel	Depth	Peak	Mean	PI	Vessel	
(mm)	CBF (mL/100g/min)	CBF (mL/100g/min)			(mm)	CBF (mL/100g/min)	CBF (mL/100g/min)			
66	158	46	87	RMCA	66	157	53	86	LMCA	
56	158	46	83	RMCA1	56	157	54	102	LMCA1	
60	158	56	86	RMCA1	60	157	62	96	LMCA1	
50	158	33	82	RMCA2	46	158	64	81	LMCA2	
46	158	23	100	RMCA2	50	158	62	82	LMCA2	
66	158	30	83	RMCA1	72	158	59	85	LACA	
56	158	46	83	RMCA1	66	157	42	96	LPCA1	
40	158	12	82	ROPTH	66	157	59	100	LPCA2	
60	158	21	113	RS/PHON	46	157	15	127	LOPTH	
30	158	19	126	RCCA	70	158	59	100	LS/PHON	
30	158	240	40	15	RCA	50	158	38	102	LS/PHON
30	158	46	196	80	REGA	30	158	29	120	LOCA
66	158	19	88	RVEM1	30	158	36	100	LCA	
66	158	16	88	RVEM2	30	158	24	187	LECA	

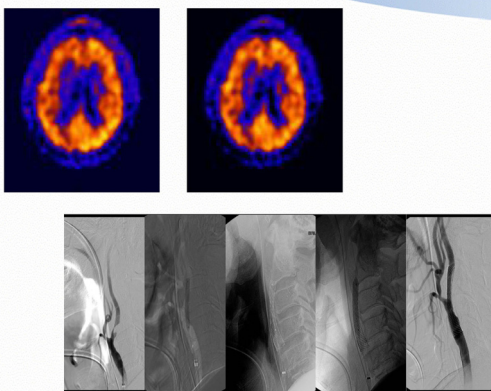
No MES

Next step?

1. Norepinephrine
2. Switch antiplatelet therapy or dose-up
3. Emergent angioplasty/stenting
4. Emergent CEA



Primary angioplasty

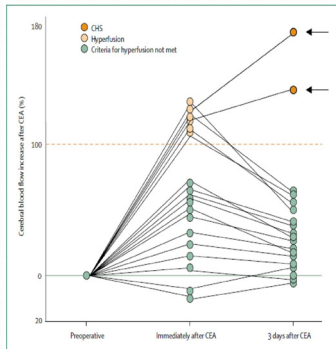


Staged stenting

RIGHT					LEFT					RIGHT					LEFT				
Depth	Peak	Mean	PI	Vessel	Depth	Peak	Mean	PI	Vessel	Depth	Peak	Mean	PI	Vessel	Depth	Peak	Mean	PI	Vessel
(mm)	CBF (mL/100g/min)	CBF (mL/100g/min)			(mm)	CBF (mL/100g/min)	CBF (mL/100g/min)			(mm)	CBF (mL/100g/min)	CBF (mL/100g/min)			(mm)	CBF (mL/100g/min)	CBF (mL/100g/min)		
66	158	46	87	RMCA	66	157	53	86	LMCA	66	157	54	87	RMCA	66	157	54	87	LMCA
56	158	46	83	RMCA1	56	157	54	102	LMCA1	56	157	55	82	RMCA1	56	157	55	82	LMCA1
60	158	56	86	RMCA1	60	157	62	96	LMCA1	60	157	62	96	RMCA1	60	157	62	96	LMCA1
50	158	33	82	RMCA2	46	158	64	81	LMCA2	46	158	64	81	RMCA2	46	158	64	81	LMCA2
46	158	23	100	RMCA2	50	158	62	82	LMCA2	50	158	62	82	RMCA2	50	158	62	82	LMCA2
66	158	30	83	RMCA1	72	158	59	85	LACA	72	158	59	85	RMCA1	72	158	59	85	LACA
56	158	46	83	RMCA1	66	157	42	96	LPCA1	66	157	42	96	RMCA1	66	157	42	96	LPCA1
40	158	12	82	ROPTH	66	157	59	100	LPCA2	40	158	12	82	RMCA2	66	157	59	100	LPCA2
60	158	21	113	RS/PHON	46	157	15	127	LOPTH	60	158	21	113	ROPTH	46	157	15	127	LOPTH
30	158	19	126	RCCA	70	158	59	100	LS/PHON	30	158	19	126	RS/PHON	70	158	59	100	LS/PHON
30	158	240	40	15	50	158	38	102	LS/PHON	30	158	240	40	15	50	158	38	102	LS/PHON
30	158	46	196	80	30	158	29	120	LOCA	30	158	46	196	80	30	158	29	120	LOCA
66	158	19	88	RVEM1	30	158	36	100	LCA	66	158	19	88	RVEM1	30	158	36	100	LCA
66	158	16	88	RVEM2	30	158	24	187	LECA	66	158	16	88	RVEM2	30	158	24	187	LECA

Hemodynamic improvement

Time frame of hyperperfusion phenomenon



van Mook et al, Lancet Neurol, 2005

Carotid endarterectomy

Author	Year	Patients (n)	Definition of hyperperfusion/CHS	Patients with hyperperfusion (%)	Patients with CHS (%)	Patients with ICH (%)
Ogasawara ⁴²	2007	1596	Acute neurological deterioration in the immediate postoperative period	n.d.	30/1596 (1.9%)	6/1596 (0.4%)
Malczon ⁴⁸	2007	100			14/100 (14%)	n.r.
Wagner ⁴⁹	2005	1602			6/1602 (0.4%)	3/1602 (0.2%)
Karapantziou ⁵⁰	2005	388			5/388 (1.3%)	4/388 (1%)
Fujimori ⁵¹	2004	95			12/95 (13%)	n.r.
Coats ⁵	2003	129			4/129 (3.1%)	1/129 (0.8%)
Fukuda ⁵¹	2007	70	CBF increase of 100% compared with preoperative values assessed by PWI	7/70 (10%)	2/70 (2.8%)	n.r.
Ogasawara ¹⁸	2005	67	CBF increase >100%, compared with preoperative values measured by PET in MCA by TCD or assessed by SPECT images	7/67 (10.4%)	2/67 (3%)	n.r.
Hosoda ¹⁸	2003	41	CBF increase >100%, compared with preoperative values assessed by SPECT images	4/41 (9.8%)	n.r.	0%
Yoshimoto ¹⁸	2005	18		7/18 (39%)	2/18 (11%)	n.d.
Suga ²⁸	2007	90		12/90 (13%)	2/90 (2.2%)	n.d.
Komurohata ⁷⁵	2006	89		10/89 (11%)	2/89 (2.2%)	n.d.
Ascher ⁷⁷	2003	404	Severe ipsilateral headache, seizures	n.r.	9/404 (2.2%)	n.d.
Total		4689	Increased ipsilateral ICA volume flow (>100%) compared with intraoperative values measured by TCD	47/375 (12.5%)	90/4648 (1.9%)	14/3756 (0.37%)

Moulakakis et al, J Vasc Surg 2009

Carotid stenting

Author	Year	Patients	Definition of hyperperfusion /CHS	Patients with hyperperfusion (%)	Patients with CHS (%)
Menezes ⁴⁸	2008	29	Neurological symptoms (homonymous or non homonymous) associated with hyperperfusion in brain SPECT scan and increased MCV in the ipsilateral MCA	n.d.	2/29 (6.9%)
Ogasawara ⁴²	2007	2008	Neurological symptoms (homonymous or non homonymous) associated with hyperperfusion in brain SPECT scan and increased MCV in the ipsilateral MCA	n.d.	31/2008 (1.5%)
Abou ⁴²	2007	536	Neurological symptoms (homonymous or non homonymous) associated with hyperperfusion in brain SPECT scan and increased MCV in the ipsilateral MCA	n.d.	5/536 (0.9%)
Kalish Zentgraf ⁴²	2006	92	Neurological symptoms (homonymous or non homonymous) associated with hyperperfusion in brain SPECT scan and increased MCV in the ipsilateral MCA	n.d.	3/92 (3.3%)
de Mont de Bachement ⁴²	2006	30	Neurological symptoms (homonymous or non homonymous) associated with hyperperfusion in brain SPECT scan and increased MCV in the ipsilateral MCA	n.d.	1/30 (3.3%)
Liak ⁴²	2005	17	Neurological symptoms (homonymous or non homonymous) associated with hyperperfusion in brain SPECT scan and increased MCV in the ipsilateral MCA	n.d.	2/17 (11.8%)
Liak ⁴²	2004	30	Neurological symptoms (homonymous or non homonymous) associated with hyperperfusion in brain SPECT scan and increased MCV in the ipsilateral MCA	n.d.	1/30 (3.3%)
Abou ⁴²	2004	610	Neurological symptoms (homonymous or non homonymous) associated with hyperperfusion in brain SPECT scan and increased MCV in the ipsilateral MCA	n.d.	2/610 (0.3%)
Coats ⁴²	2003	44	Neurological symptoms (homonymous or non homonymous) associated with hyperperfusion in brain SPECT scan and increased MCV in the ipsilateral MCA	n.d.	2/44 (4.5%)
Total		4446		7/47 (15%)	52/4446 (1.18%)

Moulakakis et al, J Vasc Surg 2009

Risk factors of hyperperfusion syndrome

- Comorbidity/medication**
- Diabetes mellitus
 - Longstanding hypertension
 - Pre-existing hypertensive microangiopathy
 - Minor stroke in the presenting history
 - Age ≥ 72 years
 - Recent (<3 months) contralateral CEA
 - High-grade carotid artery stenosis

Flow related

Preoperative

- Poor collateral flow
- Contralateral carotid occlusion
- Incomplete circle of Willis
- Preoperative hypoperfusion
- Diminished cerebrovascular reactivity or reserve
- Intracerebral steal (decrease of CBF after acetazolamide challenge)

Perioperative or postoperative

- Increased intraoperative CBF after clamp release
- Intraoperative distal carotid pressure of <40 mm Hg (measured through shunt)
- Persistence of hyperperfusion longer than several days postoperative
- Systemic hypertension

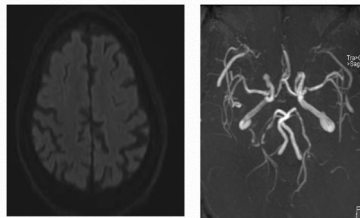
Miscellaneous

- Use of (high doses of) volatile halogenated hydrocarbon anaesthetics
- Use of anticoagulants or antiplatelet therapy
- Periprocedural cerebral infarction

van Mook et al, Lancet Neurol, 2005

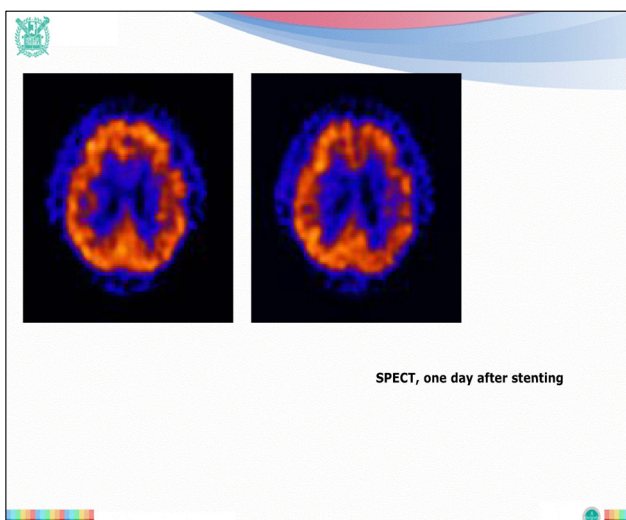
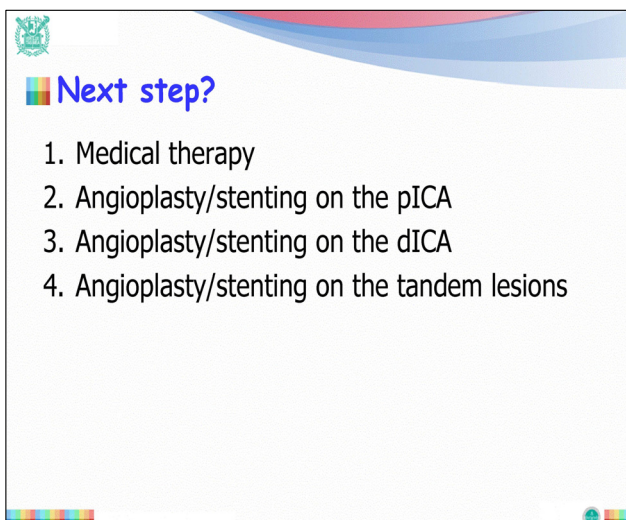
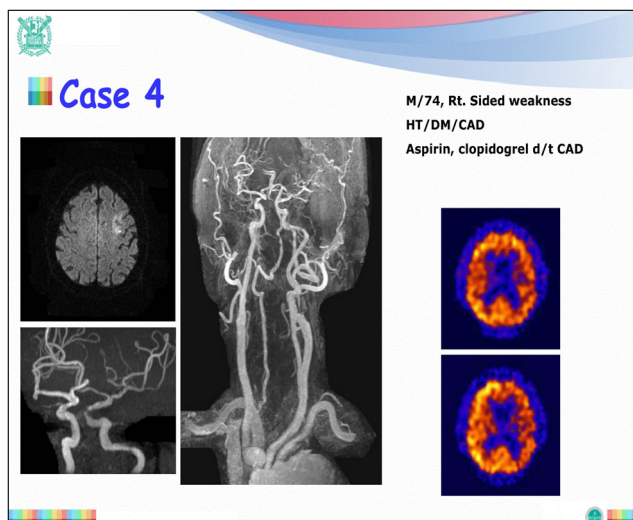
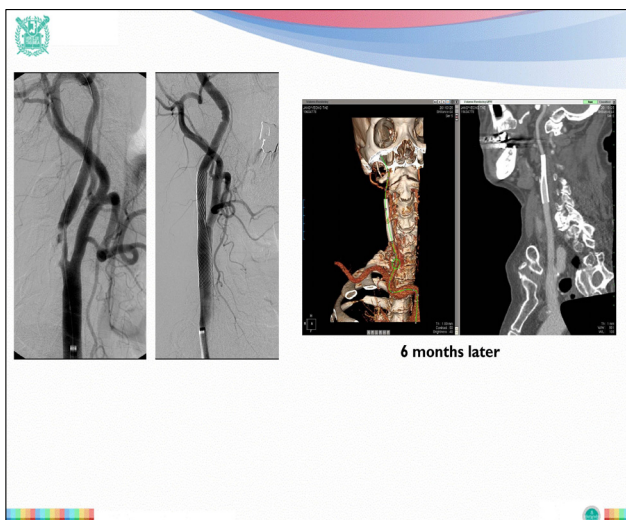
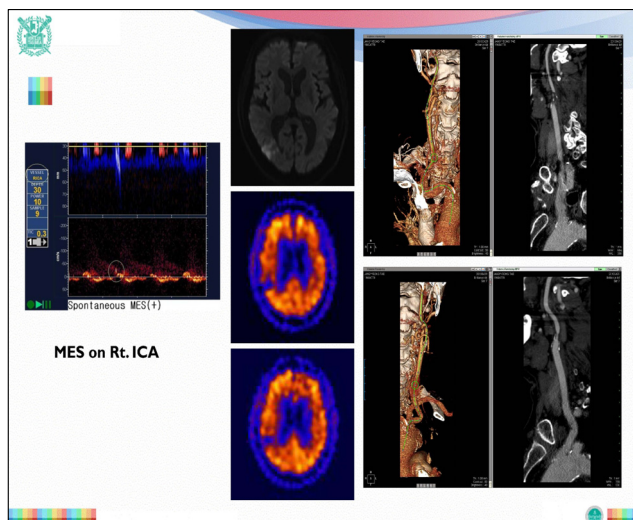
Case 3

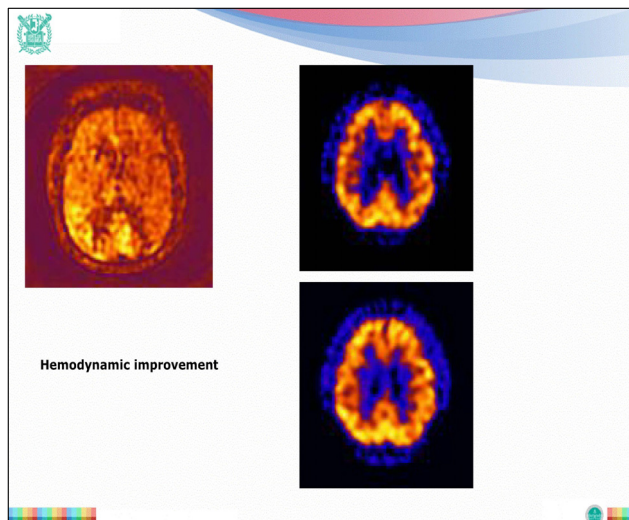
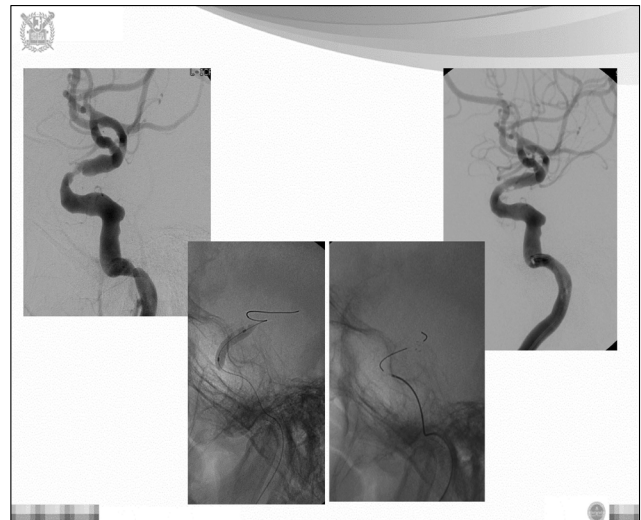
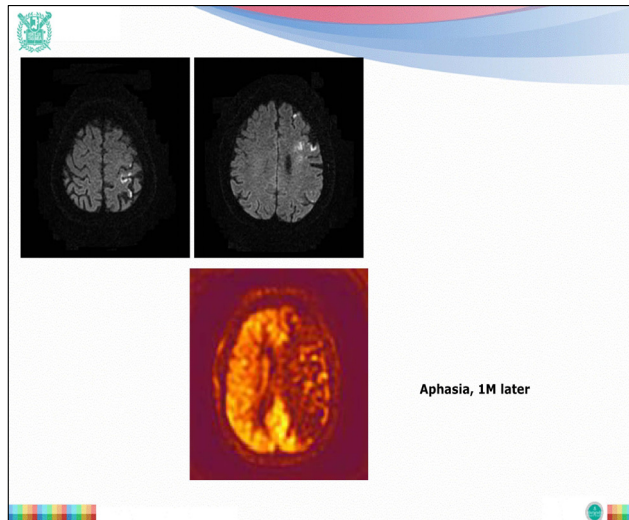
M/81, HT, dyslipidemia, on ASA
Transient dysarthria



Next step?

- 증상이 완전히 회복되었으므로 침습적인 검사, 치료보다는 보존적으로 치료한다.
- 재발 위험이 높은 상황으로 심해 보이는 쪽이 문제일 가능성이 높으므로 심한 쪽을 중재시술을 진행한다.
- 어느쪽 병변이 문제인지 모르므로 적극적인 항혈소판제 치료를 한다.
- 어느쪽 병변이 문제인지 모르므로 양쪽 경동맥 모두 중재시술을 고려한다.





Carotid disease

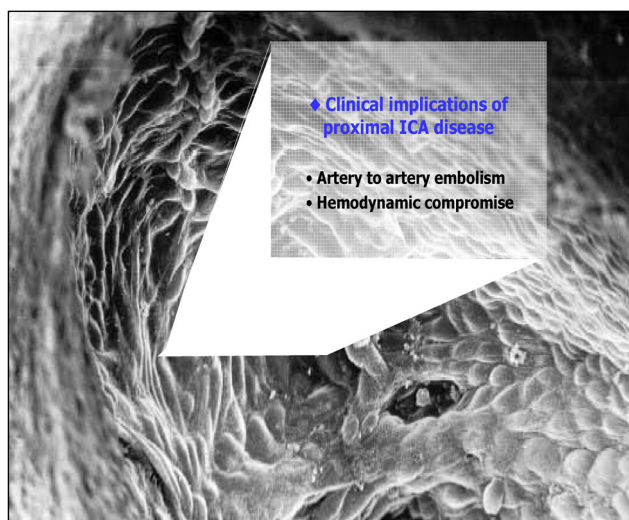
A

High Shear Region
Low Shear Region
Cross Section of Carotid Stenosis

External carotid artery
Internal carotid artery
Common carotid artery
Estimated position of carotid wall

NASCET: $\frac{A-B}{A}$
ECST: $\frac{C-B}{C}$

- Symptomatic
 - Occlusion: no benefit
 - 70%+: mandatory
 - 50%+: beneficial
 - 50%-: no benefit
- Asymptomatic
 - 70%+: beneficial
 - 50%+: no benefit



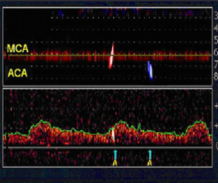
	10.01-12.03 11.03-30 mean 6 SD 37 mean 34 SD 24 P₁ 0.83	<table><tr><th>Condition</th><th>n</th><th>Pooled MFS-prevalence</th><th>Range (within studies)</th><th>Prognostic impact</th></tr><tr><td>ICA stenosis</td><td>844</td><td>42%</td><td>18-100%</td><td>++</td></tr><tr><td>Asymptomatic</td><td>1826</td><td>8%</td><td>2-29%</td><td>+</td></tr><tr><td>Acute symptomatic</td><td>183</td><td>30%</td><td>22-75%</td><td>(+)</td></tr><tr><td>Chronic symptomatic/asymptomatic</td><td>123</td><td>0%</td><td>0%</td><td>?</td></tr><tr><td>CAD</td><td>82</td><td>50%</td><td>36-75%</td><td>?</td></tr><tr><td>With stroke</td><td>16</td><td>13%</td><td>0-20%</td><td>?</td></tr><tr><td>With local symptoms</td><td>88</td><td>32%</td><td>13-48%</td><td>?</td></tr><tr><td>Aortic arch atherosclerosis</td><td></td><td></td><td></td><td></td></tr></table>	Condition	n	Pooled MFS-prevalence	Range (within studies)	Prognostic impact	ICA stenosis	844	42%	18-100%	++	Asymptomatic	1826	8%	2-29%	+	Acute symptomatic	183	30%	22-75%	(+)	Chronic symptomatic/asymptomatic	123	0%	0%	?	CAD	82	50%	36-75%	?	With stroke	16	13%	0-20%	?	With local symptoms	88	32%	13-48%	?	Aortic arch atherosclerosis				
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ICA stenosis	844	42%	18-100%	++																																											
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CAD	82	50%	36-75%	?																																											
With stroke	16	13%	0-20%	?																																											
With local symptoms	88	32%	13-48%	?																																											
Aortic arch atherosclerosis																																															

Table 1 Prevalence of MFS in different degrees of symptomatic carotid stenosis						
Author	0-30%	30-69%	70-99%	100%		remarks
	++	++	++	++		
Cannon [5]	0	0	0	20	30	0
Daffertshofer [6]	0	4	26	10	40	0
DeGrote [7]	0	0	0	5	12	0
Droste [11]	0	1	0	12	17	24
Eikel [14]	0	4	1	6	5	8
Georgiadis [18]	0	3	4	21	15	3
Grosvet [19]	0	0	0	20	0	0
Hutchinson [20]	0	0	0	13	12	0
Markus [26]	0	1	5	9	8	15
Mallory [29]	0	3	6	26	34	0
Seidler [36]	0	0	0	27	6	0
Slawka [29]	0	0	1	1	14	6
Valton [44]	0	0	0	11	19	0
van Zuijlen [46]	0	0	0	22	14	0
Overall	0	6	17	74	219	235
	0%	19%	48%	51%		

Chi² = 12.50, d.f. = 3, p < 0.0001

Table 2 Prevalence of MFS in different degrees of asymptomatic carotid stenosis						
Author	0-30%	30-69%	70-99%	100%		remarks
	++	++	++	++		
Alkott [1]	0	0	0	0	27	204
Daffertshofer [6]	0	0	0	10	1	11
Droste [11]	0	0	10	4	25	0
Eikel [14]	0	117	1	12	0	9
Georgiadis [18]	0	49	2	59	3	37
Markus [26]	0	0	0	12	1	15
Mallory [29]	0	0	1	8	11	22
Olsson [32]	0	0	0	9	75	0
Seidler [36]	0	0	0	9	54	0
Spence [40]	0	0	0	32	287	0
Stok [43]	0	0	0	5	33	0
Overall	0	66	4	111	102	772
	0%	3%	12%	36%		

Chi² = 23.2, d.f. = 3, p < 0.0001

Ritter et al., J Neurol, 2008

Table 2 Risk of combined recurrent stroke or TIA in patients with symptomatic carotid stenosis

Author	f-u	n	MES +	MES -	Events MES + (%)	Events MES - (%)
Babikian [2]	8	104	33	71	8 (24%)	1 (1%)
Censori [5]	17.4	50	20	30	6 (30%)	1 (3%)
Markus [25]	22.5	200	89	111	23 (26%)	8 (7%)
Overall		354	142	212	37 (26%)	10 (5%)

OR = 7.5 (3.6–15.4); p < 0.0001

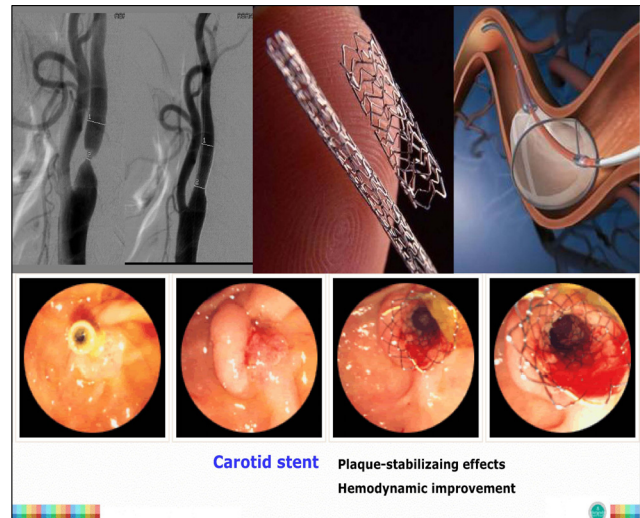
**MES → prognostic factor
stenosis, plaque nature?**

Table 4 Risk of TIA and stroke in asymptomatic carotid stenosis

Author	n	f-u	MES +	MES -	Events MES + (%)	Events MES - (%)	remarks
Abbott [1]	231	26	27	204	1 (3%)	5 (2%)	Final "MES-positivity" declared after up to six consecutive investigations. Only first six months of study used for calculation.
Molloy [29]	42	37	12	30	2 (14%)	0	
Orlandi [32]	84	26	9	75	5 (36%)	0	
Siebler [36]	64	72	8	56	3 (38%)	2 (4%)	> 1 MES = "MES-positive", maximum of two investigations scored
Spence [40]	319	52	32	287	9 (28%)	7 (2%)	> 2 MES = "MES-positive", only first year of follow-up considered
Overall	740	121	619	20 (17%)	14 (2%)		

OR = 13.4 (6.5–27.4); p < 0.0001

Ritter et al., J Neurol, 2008



When?

- 경동맥 내막절제술은 허혈 증상이 발생한 뒤 2주 이내에 시술하는 경우 더 좋은 예후를 기대할 수 있다.
- 단, 불안정한 상태의 환자의 경우에는 지연 시술이 합병증을 줄일 수 있다.
- Staged intervention: beneficial, but no insufficient evidence

How long dual antiplatelet treated?

- Early thromboembolic event
 - 1w
- In-stent thrombosis
 - <6m
- Longterm dual antiplatelet
 - No evidence

Messages

- MES monitoring
- Hemodynamic status, especially tandem lesion
- Careful consideration of intervention time
- Periprocedural antiplatelet management
- Staged angioplasty