Korean Society
of Cerebrovascular Surgeons
대한뇌혈관외과학회

대한뇌혈관내수술학회
SKEN
Society of Korean Endovascular Neurosurgeons

대한뇌혈관외과학회 | 대한뇌혈관내수술학회

KSCVS-SKEN 합동 연수강좌

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주관 : 대한신경외과학연구재단

2016년도 대한뇌혈관외과학회 임원진

■ 실행이사회

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전임회장	김한규	분당제생병원
전임회장	나형균	가톨릭대학교 여의도성모병원
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재 무	장철훈	영남대학교병원
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제4, 5대	권도훈	울산대학교 서울아산병원
제6대	안성기(작고)	(전) 한림대학교 성심병원
제7대	신용삼	가톨릭대학교 서울성모병원
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제9대	김범태	순천향대학교 부천병원

인 사 말

갈수록 어려워지는 의료 환경 속에서도 우리나라 뇌혈관 질환의 치료와 예방뿐만 아니라 관련분야 연구에 매진하시는 양 학회 회원 여러분께 경의를 표합니다.

금년은 양 학회가 의기투합하여 공동으로 연수강좌를 개최한 지 7번째 되는 해입니다.

의학의 발전은 과거의 직관적 의학에서 근거 중심을 뛰어넘어 맞춤 정밀의학의 단계로 이행하고 있는 듯합니다. 지난 3월 알파고를 통하여온 국민이 인지하게 된 인공지능은 질병의 진단과 치료에도 성큼 다가오게 될 것으로 보입니다. 이에 대비하기 위하여 IBM의 왓슨 기술고객 자문 배영우 상무님을 모시고 진료와 연구 현장에서의 인공지능 활용에 대하여 알아보는 시간을 마련하였고, 미국의 NIH에 해당되는 국립보건연구원의 박현영 심혈관 희귀질환과 과장님을 모시고 국립 보건연구원의 임상연구 지원부분에 대한 특강을 듣도록 하였습니다.

또한 뇌혈관 질환의 카테터를 이용한 혈관 내 수술과 개두술을 통한 미세혈관 수술에서 늘 쟁점이 되어왔던 주요한 주제뿐만 아니라 약물치료와 영상의학 부분에서도 궁금하였던 여러 주제를 다룰 예정입니다.

봄의 막바지에서 여름으로 가는 문턱에서 환자진료와 연구를 잠시 뒤로하고 뇌혈관 질환에서의 최근 이슈들을 즐겨보는 여유를 가져보시기 바랍니다.

2016년 5월 27일

대한뇌혈관외과학회 회장 **박현선**

대한뇌혈관외과학회 및 대한뇌혈관내수술학회 회원 여러분 안녕하십니까?

금번 2016년 합동연수강좌를 세심하게 준비하여 주신 대한뇌혈관외과학회 박현선 회장님과 이사진 여러분의 노고에 깊이 감사드립니다.

급작스런 발병과 예기치 못한 경과가 특징적인 뇌혈관질환을 동물적인 감으로 신속 정확히 진단하고 성공적으로 치료하여 환자분들에게 좋은 결과를 선사해 드리려면, 우리 스스로가 항상 새로운 지식과 술기에 눈과 귀를 열고 있어야만 합니다. 이런 의미에서 매년 개최되는 양 학회의 합동연수강좌는 모든 회원님들에게 놓쳐서는 안 될 must see, must hear의 귀한 기회라고 생각됩니다.

우리 신경외과 의사들은 뇌혈관질환 치료의 최선봉이자 최후의 보루가 되어왔다고 자부합니다. 세계와 어깨를 나란히 할 수준의 개두수술, 혈관내수술 성적을 낼 수 있었던 근본은 온갖 역경을 극복하고 노력을 아끼지 않았던 선배 의료진의 각고의 노력이었습니다. 이제, 훨씬 현대화된 기구와 기계, 축적된 경험은 젊은 young gun 후학들의 열정을 기다리고 있습니다.

아무리 의료환경이 척박해지고, 불합리한 점이 많더라도, 생명을 구하기 위하여 묵묵히 수술실에서, 혈관촬영실에서 밤을지새우는 우리 모두의 의지와 노력은 결코 폄하될 수 없습니다.

“손에 쟁기를 들고 가는 사람은 뒤를 돌아보면 안 된다”는 말이 있습니다. 우리 모두의 집중력, 판단력과 세심한 술기가 항상 최고의 상태로 유지될 수 있도록, 비록 하루 동안의 짧은 일정이지만 최선을 다하여 준비한 본 합동연수강좌에 양 학회 회원 여러분 모두를 초대합니다.

대단히 감사합니다.

2016년 5월 27일

대한뇌혈관내수술학회 회장 **성재훈**

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－고려대학교 경영대학원 경영학 석사 (MBA)
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경력 정보

－한국아이비엠㈜ 고객기술자문 상무[2013~]
－한국생산성학회 산학이사 [2013~]
－서비스사이언스전국포럼 및 서비스사이언스 학회 운영위원 [2007~2012]
－한국아이비엠㈜ 기술영업 혁신팀 실장[2012~2013]
－한국아이비엠㈜ 연구소 전략기획 및 헬스케어 솔루션 연구개발 실장 [2008~2012]
－한국아이비엠㈜ 유비쿼터스 컴퓨팅 연구소 실장 [2004~2008]
－u헬스협회 운영위원 [2011]
－유비쿼터스컴퓨팅사업단 총괄기획위원 [2005~2010]
－지식경제부 통합기술청사진 기획위원 [2008]
－정보통신부.IBM 국제공동연구 헬스케어과제 관리책임 [2008]
－정보통신부.IBM 국제공동연구 텔레매틱스과제 연구책임 [2004~2007]
－정보통신연구진흥원 텔레매틱스 과제기획위원 [2003~2006]
－IBM Pervasive Computing 제품개발 및 텔레매틱스 연구개발 [2001~2007]
－IBM Pervasive Computing 디바이스 관리 제품개발 (일본IBM 연구소 파견) [2000]
－한국어 음성인식 소프트웨어 연구개발 (IBM ViaVoice) [1999~2001]
－IBM OS/2, JavaOS 및 IBM AIX 시스템 S/W개발 [1991~1998]
－한국아이비엠㈜ 소프트웨어 개발 연구소 입사 [1991]

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	1995	연세대학교 의과대학	의학	석사
	2000	연세대학교 의과대학	의학(내과학)	박사
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WSO oversight committee (since 2012)

저서 ; 22권 (including chapter authors)

1. Kim JS. Sensory System Dysfunction
   In, Bogousslavsky J, Fisher M, eds, Textbook of Neurology, Butterworth Heinemann, Boston, 1998
2. 김종성, 최스미. 뇌졸중의 모든 것 (정담) 1998
3. 김종성. 뇌에 관해 풀리지 않는 의문들 (지호) 2000
4. Kim JS. Sensory abnormality.
   In Bogousslavsky J, Caplan L, eds, Stroke syndromes, Cambridge University Press, 2nd ed., 2001.
5. 김종성. 뇌졸중 119 (가림), 2001
6. 이태규,김종성. 두통 (의학출판사) 2002
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10. 김종성. 신경학 (군자출판사) 2007
11. Kim JS, Caplan LR, Wong KS. Intracranial atherosclerosis (Wiley−Blackwell) 2008
12. 김종성. 뇌졸중 (e−public), 2009
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14. 김종성. 뇌과학 여행자 (사이언스 북스) 2011
15. Kim JS. Sensory abnormality, Stroke Syndrome, (3rd ed) Caplan LR, van Gijn J (ed), Cambridge University Press. 2012
16. Kim JS, Medullary infarcts and hemorrhages, Stroke Syndrome, (3rd ed) Caplan LR, van Gijn J (ed), Cambridge University Press. 2012
17. Kim JS. Disturbances of the Voluntary Control of Emotional Expression In Ferro J ed. Neuropsychiatric symptoms of cerebrovascular diseases. 2014
18. Kim JS. Pathophysiology of TIA and ischemic stroke. In Norrving B (ed). Stroke/Cerebrovascular Disease. Oxford Press, 2014
19. Kim JS. Symptoms of TIA. In Uchiyama S, Amaranco P, Minematsu K, Wong KSL (eds) TIA as Acute Cerebrovascular Syndrome 2014
20. Kim JS. Posterior Cerebral Artery Disease. In Grotta JC (ed). Stroke : Pathophysiology, Diagnosis and Management. 6th ed. 2015
21. Kim JS, Caplan LR. Vertebrobasilar Artery Disease In Grotta JC (ed). Stroke : Pathophysiology, Diagnosis and Management. 6th ed. 2015
22. Kim JS, Caplan LR, Posterior Circulation Diseases. In Caplan's Stroke : A Clinical Approach, 5th ed.

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미국신경과학회 (American Academy of Neurology) : 회원
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International Journal of Stroke
(Official Journal of International Stroke Society, since 2006)
Cerebrovascular disease
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학술 논문 ; 439 편

국외 SCI 논문 ; 328편
국내 논문 ; 110편

대한뇌혈관외과학회 | 대한뇌혈관내수술학회

KSCVS-SKEN 합동 연수강좌

일 시 : 2016년 5월 27일(금)
장 소 : 울산대 서울아산병원 연구원 지하 대강당
주 최 : 대한뇌혈관외과학회, 대한뇌혈관내수술학회
주 관 : 대한신경외과학연구재단
평 점 : 6점

08 : 30 Registration
08 : 40—08 : 50 Opening Remarks 박현선(대한뇌혈관외과학회장), 성재훈(대한뇌혈관내수술학회장)
08 : 50—09 : 00 Congratulatory Address 임영진(대한신경외과학회 이사장)

09 : 00—10 : 20 Scientific session I — 좌장 : 허승곤(연세대), 백민우(뉴고려병원)

Para—clinoid aneurysm

1. Radiological work-up 박근영(연세대) / 18
2. Endovascular treatment 정진영(동의의료원) / 22
3. Surgical treatment 한영민(가톨릭대) / 26
4. Current recommendation and literature review 주성필(전남대) / 32

10 : 20—10 : 40 Coffee break

10 : 40—11 : 40 Special lecture I — 좌장 : 박현선(인하대), 성재훈(가톨릭대)

1. 인공지능과 의료의 미래 배영우(전 한국IBM(주) 고객기술자문 상무, 현 아이메디씬(주) CTO) / 34
2. 국립보건연구원 임상연구지원현황 박현영(국립보건연구원 심혈관 희귀질환 과장) / 38

11 : 40—12 : 10 Special lecture II — 좌장 : 오창완(서울대)

Update MR imaging for cerebral hemorrhage 최현석(가톨릭대 서울성모병원 영상의학과) / 46

12 : 10—13 : 10 Lunch

13 : 10—14 : 10 Scientific session II — **좌장 : 홍승철(성균관대), 김범태(순천향대)**

Dural—AVF

1. Etiology and pathogenesis and diagnosis — 신동성(순천향대) / 48
2. Endovascular treatment — 권순찬(울산대) / 56
3. Surgical treatment — 안재성(울산대) / 57
4. Current recommendation and literature review — 임용철(아주대) / 63

14 : 10—14 : 50 Special lectureIII — **좌장 : 권병덕(울산대)**

MCA steno—occlusion, classification & management — 김종성(울산대 서울아산병원 신경과) / 68

14 : 50—15 : 10 Coffee break

15 : 10—16 : 40 Workshop by video for beginner — **좌장 : 김한규(분당제생병원), 권오기(서울대)**

1. How to clip of ICA aneurysm — 정영균(인제대) / 80
   MCA aneurysm — 박인성(경상대) / 86
   ACA aneurysm — 박익성(가톨릭대) / 93
2. How to coil assisted by STENT — 김성림(가톨릭대) / 98
   Balloon — 윤석만(순천향대) / 100
   Multiple catheter — 강현승(서울대) / 102

16 : 40—18 : 00 Scientific session III — **좌장 : 나형균(가톨릭대), 고준석(경희대)**

Update in the management of intracranial stenosis

1. Medical management and follow up — 이종영(한림대) / 104
2. Endovascular treatment — 이재일(부산대) / 113
3. Surgical treatment — 김정은(서울대) / 123
4. Current recommendation and literature review — 정승영(을지대) / 128

18 : 00 Closing Remarks — 박현선(대한뇌혈관외과학회장), 성재훈(대한뇌혈관내수술학회장)

Scientific session I

좌장 : 허승곤(연세대), 백민우(뉴고려병원)

Para-clinoid aneurysm

1. Radiological work-up — 박근영(연세대)
2. Endovascular treatment — 정진영(동의의료원)
3. Surgical treatment — 한영민(가톨릭대)
4. Current recommendation and literature review — 주성필(전남대)

Paraclinoid Aneurysms Radiologic Evaluation

Keun Young Park

Department of Neurosurgery, Severance Hospital, Yonsei University College of Medicine

2016 KSCVS-SKEN 합동연수강좌

Paraclinoid Aneurysms -Radiologic Evaluation-

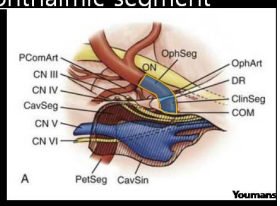
Keun Young Park

Department of Neurosurgery, Severance Hospital, Yonsei University College of Medicine

Paraclinoid Aneurysm

"Clinoidal segment" + "Ophthalmic segment"

- ✓ Benign natural course
- ✓ Surgically challenging lesion



Before treatment, radiologic evaluation is mandatory.

Radiologic Evaluation

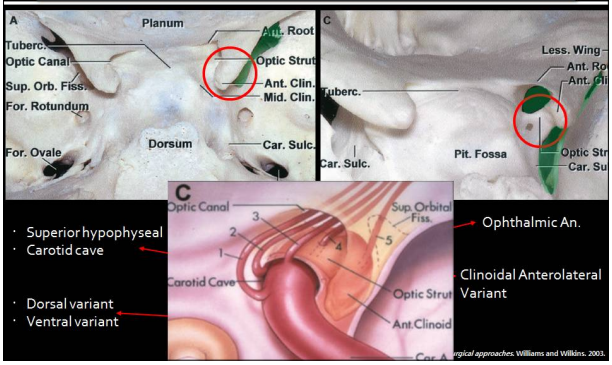
CONTENTS

- ✓ Anatomical Relationship
  - Bone
  - Dura
  - Nerve
- ✓ Characteristics of Aneurysm
  - Aneurysm Direction
  - Thrombus, Intramural hemorrhage
  - Calcification
- ✓ Collateral Evaluation
  - Compression study
  - Balloon Test Occlusion
  - ECA/Radial artery evaluation

RADIOLOGIC TOOLS

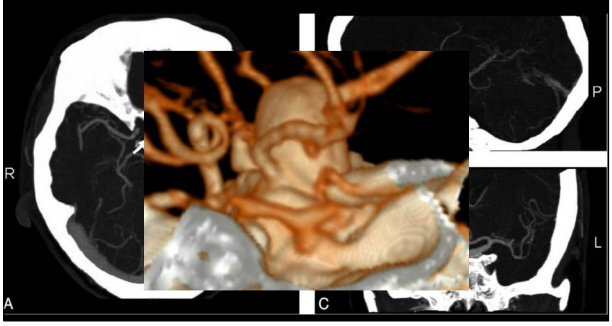
- ✓ Simple X-ray
- ✓ CT & CT angiography
- ✓ MRI
- ✓ Catheter Angiography

Anatomical Relationship -Bony Structure



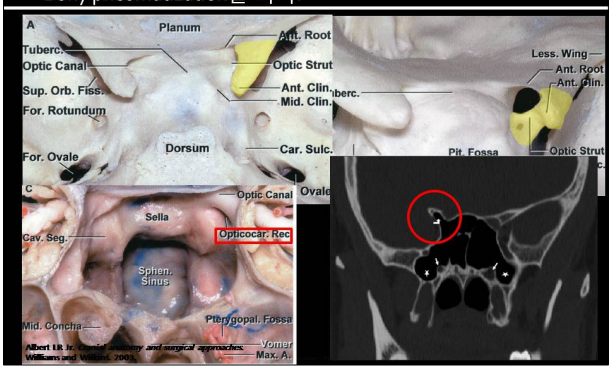
CT & CT angiography

Aneurysm과 Bony structure 사이의 관계 및 거리 등을 추정.



CT & CT angiography

Bony pneumatization을 파악.

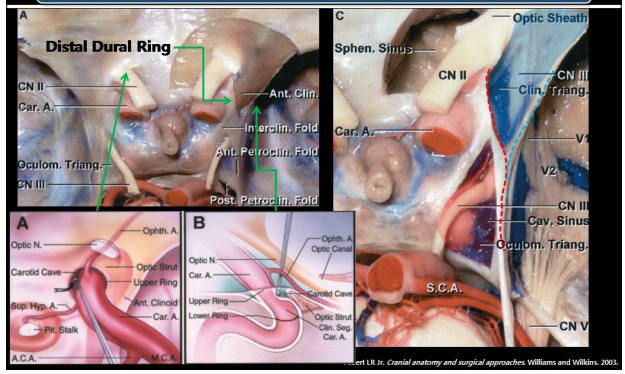


Anatomical Relationship -Dura

Aneurysm과 Dura와의 관계를 파악하는 것은 왜 중요한가?

- Treatment Indication (*Extradural* vs *Intradural*)
- Treatment Option

Anatomical Relationship -Dura



Albert LR Jr. *Cranial anatomy and surgical approaches.* Williams and Wilkins. 2003.

Anatomical Relationship -Dura

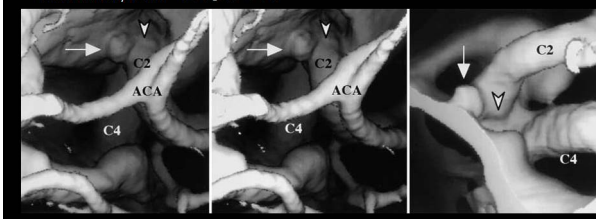
- Ophthalmic artery
  Punt J: Some observations on aneurysms of the proximal internal carotid artery. J Neurosurg 51:151–154, 1979
- Anterior Clinoid Process
  Taptas JN: Intradural and extradural ICA. J Neurosurg 51:877–878, 1979.

Anatomical Relationship -Dura

CT

직접 dura를 보여주기는 어려움.

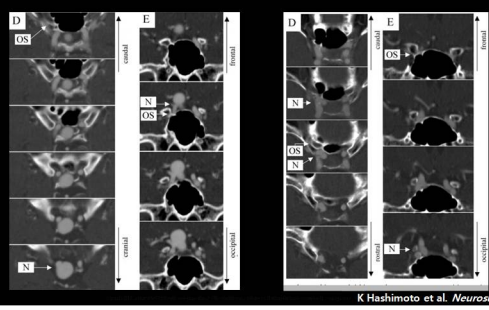
ICA concavity: Dura가 ICA 붙는 부위.



Y Murayama et al. *JNS.* 2001.

Anatomical Relationship -Dura

Optic Strut 을 PDR의 landmark로 이용



K Hashimoto et al. *Neurosurgery.* 2006.

Anatomical Relationship -Dura

MR proton density (MR PD)

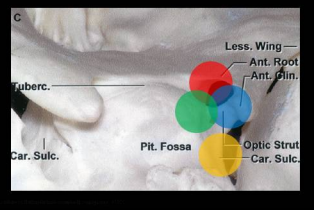
	Short TE (<20 ms)	Long TE(> 80 ms)
Short TR (<700 ms)	T_1-weighted	Not commonly used
Long TR (>2000 ms)	Proton density-weighted	T_2-weighted

Yoon SJ et al. *JCEN.* 2015.

Characteristics of Aneurysm -Direction

Based on Angiography

- ✓ Superior
- ✓ Medial
- ✓ Lateral
- ✓ Inferior/Posterior



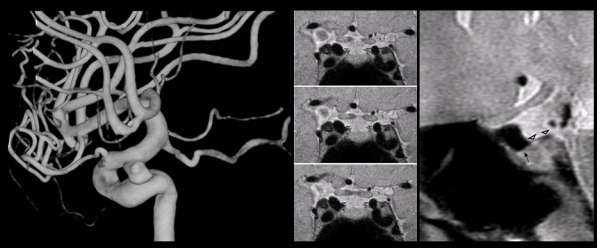
Characteristics of Aneurysm -Direction

- ✓ Surgical Approach 시 중요.
- ✓ Intradural/Extradural lesion

Location	Projection				
	Superior	Inferior/posterior	Medial	Lateral	Total
Extradural	0	14(73.7%)	31 (63.3%)	3 (75.0%)	48 (63.2%)
Transdural	1 (25.0%)	4 (21.0%)	5 (10.2%)	0	10 (13.2%)
Intradural	3 (75.0%)	1 (5.3%)	13 (26.5%)	1 (25.0%)	18 (23.7%)
Total	4 (5.3%)	19 (25.0%)	49 (64.5%)	4 (5.3%)	76

Yoon SJ et al. *JCEN*. 2015.

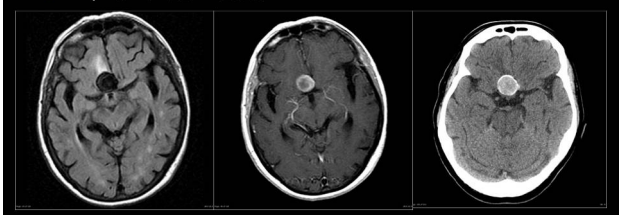
F/52
Incidental paraclinoid aneurysm, inferior/posterior projection
Size: 5.0 mm



Characteristics of Aneurysm -Calcification

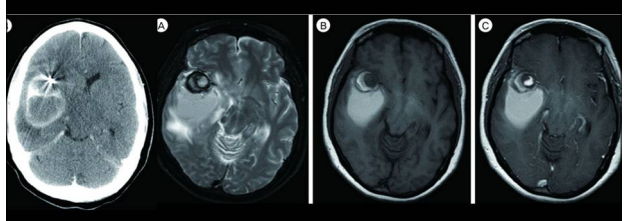
CT가 유용.

- ✓ Wall degeneration
- ✓ Clip이 어려울 가능성



FLAIR T1 GD CT

Characteristics of Aneurysm -Intramural hemorrhage

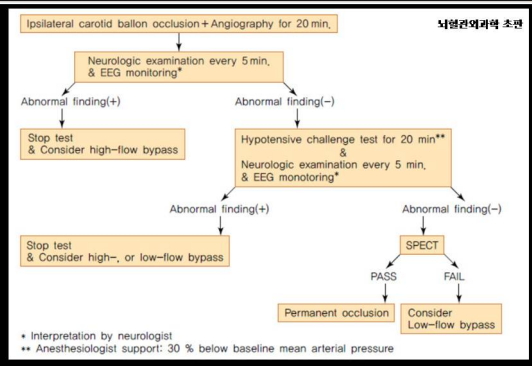


Kim HJ et al. JCEN. 2015.

Collateral Evaluation

- ✓ Cross-Compression Study
- ✓ Alcock Test
- ✓ Balloon Test Occlusion
  - Major collaterals
  - Ophthalmic artery collateral

Collateral Evaluation



Collateral Evaluation

J Neurointerv Surg. 2015 Jun 25. pii: neurintsurg-2015-011800. doi: 10.1136/neurintsurg-2015-011800. [Epub ahead of print]

Endovascular treatment of unruptured ophthalmic artery aneurysms: clinical usefulness of the balloon occlusion test in predicting vision outcomes after coil embolization.

Kim B[1], Jeon P[2], Kim K[2], Yang N[2], Kim S[2], Kim H[2], Byun H[2], Jo KI[2].

AJNR Am J Neuroradiol. 2014 Nov-Dec;35(11):2146-52. doi: 10.3174/ajnr.A3999. Epub 2014 Jun 26.

Endovascular treatment of ophthalmic artery aneurysms: assessing balloon test occlusion and preservation of vision in coil embolization.

Ahn JH[1], Cho YD[2], Kang HS[3], Kim JE[3], Cho WS[3], Jung SC[4], Kim CH[5], Han MH[6].

BTO를 통해 ECA-OA collateral을 확인 후, OA occlusion을 시도할 수 있다.

Conclusions

- ✓ Paraclinoid aneurysm은 benign natural course를 보인다.
- ✓ 반면에, 치료를 요하는 paraclinoid aneurysm은 surgically challenging한 경우가 대부분이다.
- ✓ 따라서, 충분한 radiologic evaluation을 통해, 주변 구조물과의 관계 및 동맥류의 특징을 살펴야, 불필요한 치료를 피하고, 합병증을 최소화할 수 있을 것이다.

Paraclinoid Aneurysms ; Endovascular treatment

정진영
동의의료원 신경외과

Introduction

ICA paraclinoid segment에 위치한 동맥류의 endovascular treatment는 다양한 동맥류의 방향, carotid siphon의 tortuosity에 의해 때로는 매우 치료가 어려운 상황을 만날 수 있으므로 이 위치의 동맥류를 치료하기 위한 기술적 이해가 필요하다.

Paraophthalmic 또는 paraclinoid aneurysm의 endovascular treatment시 balloon 또는stent 등을 이용한 adjuvant technique 을 사용한다 하더라도 혈관의 해부학적 구조에 적합한 모양의 microcatheter를 이용하여야 시술이 진행되는 동안 안정적이고 안전한 coil packing이 이루어 질 수 있으며 이것이 가장 선행되어야 할 중요한 부분이다.

1. Shapes of Microcatheters

일반적으로 국내에서 사용되는 aneurysm용 microcatheters

ExcelsiorSL-10(Stryker), Prowler 14(Codmann), Echelon-10(Coviden), Headway(Microvention)가 있으며 제품 군에 따라 차이가 있지만 대개 aneurysm을 selection 하는 distal end가 preshaped("45," "90," "J," "C," and "S"(Figure 1)) 되어 있는 형태를 갖추고 있으며 이를 이용하면 좀 더 안정적인 microcatheter stability를 손쉽게 얻을 수 있다.

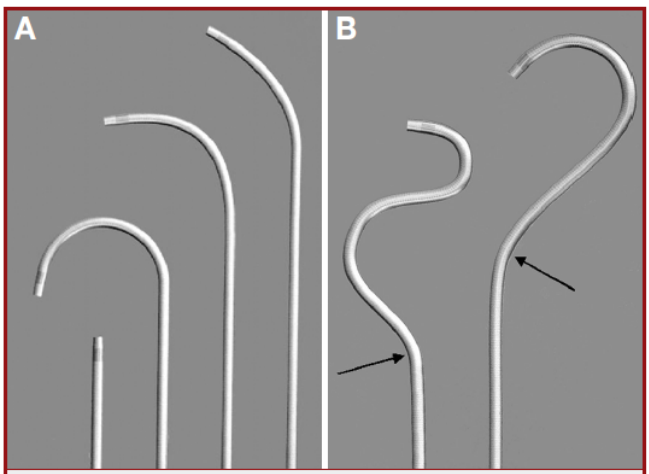


FIGURE 1. *Photographs of preshaped microcatheters: straight, J, 90, and 45 (A), and S and C (B) presented in order. The S and C shapes have an additional small obtuse curve at the beginning of the shapes (arrows).*

2. Steam shaping of microcatheters

제조 시부터 preshaped 된 제품을 쓰면 가장 안정적인 microcatheter stability 를 얻을 수 있겠지만 특히 paraclinoid/paraophthalmic aneurysm의 치료 시에는 이 만으로는 불충분 한 경우가 많으므로 개별 혈관의 모양에 따른 tailored shape 의 microcatheter 를 steam에 의한 열을 이용해 상황에 맞추어 만들어야 할 때가 종종 있다.

특이 paraclinoid/paraophthalmic aneurysm 치료 시 사용되는 대표적인 모양은 다음과 같다.

1) Pig tail shape (simple, right and left)

2) S-shape (simple, right and left)

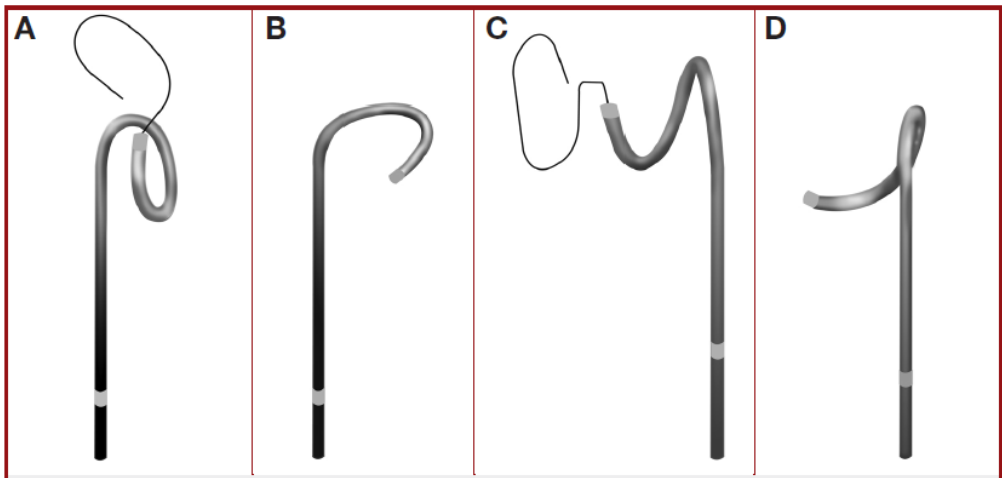


FIGURE 2. *Diagram of "pigtail" shape before and after steaming. A, diagram of 2-dimensional "Pigtail-simple" shape shows curling at the tip portion with a shaper for steaming. Steaming usually takes 30 to 40 seconds and steamed microcatheters are soaked in normal saline for 30 seconds or more. B, diagram poststeam reveals the less curling tip portion without the shaper. "Pigtail-left" shape presteam (C) and poststeam (D) are shown on diagrams. This shape has a 3-dimensionally coiled curve on the left side, which is designed to be suitable for placement in abruptly arising sidewall aneurysms. The side, left vs right (not shown), is determined with the relative direction of the shaped tip to the main shaft of the microcatheter.*

Pig tail shape을 만드는 방법

제품 속에 들어있는 mandrel을 이용하여 원하는 모양의 2배정도를 구부린 후 steam으로 30초에서 40초 간 가열한 후 차가운 normal saline에 담그고(20-30초), 이 과정을 2-3회 혹은 수 차례 반복하여 mandrel을 제거하면 shaping 한 mandrel에 가까운 모양의 microcatheter를 얻을 수 있다. Right or left pig tail shape은 이를 기본으로 동맥류의 방향에 따라 distal end에 방향성을 주어 좀 더 응용하여 mandrel 모양을 만듦.

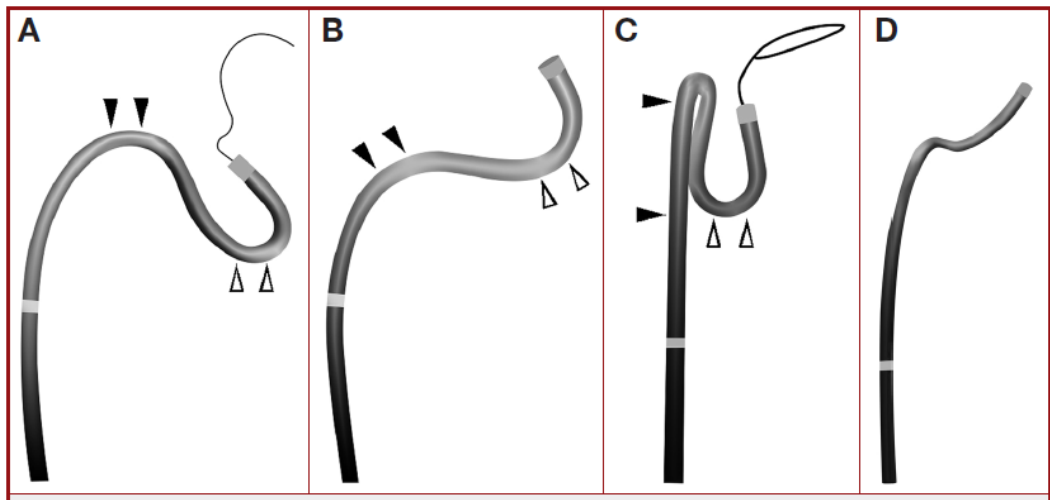


FIGURE 3. *Diagram of "S" shape before and after steaming. Presteam (A) and poststeam (B) diagrams of 2-dimensional "S-simple" shape show the superior (open arrowheads) and inferior (black arrowheads) curves of the character "S." Varying the size and length of each curve provides the most appropriate "S" shape for a specific aneurysm. "S-right" shape presteam (C) and poststeam (D) are demonstrated on diagrams. This shape is 3-dimensional and the superior curve (open arrowheads) is perpendicular to the inferior curve and main shaft (black arrowheads) before steaming. The side, right vs left (not shown), is determined with the relative direction of the superior curve to the main shaft of the microcatheter.*

S-shape shape을 만드는 방법

mandrel을 S shape으로 만든 후 동일한 방법으로 steam shaping하면 simple S-shape을 얻을 수 있다. 이러면 proximal 과distal part에 superior, inferior 방향으로 두 개의 curve 가만들어 지고 혈관의 모양에 맞추어서 이 curve의 정도를 달리하면 좀더 안정적인 microcatheter stability를 유지할 수 있다. 이 기본 모양에 동맥류의 방향을 고려하여 distal end 부분을 오른쪽, 또는 왼쪽으로 shaping을 하면 혈관과 동맥류의 방향을 모두 만족시키는 3차원 구조의 응용된 microcatheter shape을 얻을 수 있다.

3. Navigating methods of Microcatheters

1) Shaping된 microcatheter 자체만을 microguide wire의 도움 없이 advance하거나 목표지점을 지난 후 withdrawal 하며aneurysm을 selection 하는 방법 (가장 안전하고 이상적인 microcatheter shape이 이루어 졌을 때 가능).
2) Wire-steering method : shaping된 microguide wire를 microcatheter의 distal end 부위에 위치시킨 후 aneurysm 입구에서 steering하여 microcatheter를 aneurysm 내로 navigation 하는 방법
3) Looping method : 급격한 angle의 방향을 가진 동맥류의 경우 microcatheter를 looping 시킨 상태에서 aneurysm을 지난 후 pulling 하면서 aneurysm 내로 navigation.
4) Coil 또는 microguide wire를 이용하여 직접 aneurysm 내로 navigation.

4. To increase intra-aneurysmal stability ofmicrocatheters during coiling

Paraclinoid aneurysm의 성공적인 coiling을 위해서는 microcatheter를 aneurysm 내로 positioning 시키는 것뿐만 아니라 indwelling 시킨 microcatheter의 stability를 유지하는 것이 매우 중요하다. Micro-guide wire 등을 이용하여 강제로 aneurysm을 superselection하더라도 microcatheter의 모양이 해부학적 구조와 일치하지 않으면 coiling이 진행되

는 동안 microcatheter의 kick back을 유발시키고 불완전한 치료나 치료관련 합병증으로 이어질 가능성을 높이게 된다. 그러므로 각각 동맥류의 방향 및 혈관 모양에 맞는 microcatheter의 shaping은 navigation 및 positioning을 쉽게 해주고 coil이 진행되는 동안 microcatheter stability 도 유지할 수 있게 해주는 중요한 요소이다.

Coil이 진행되는 동안 microcatheter stability를 좋게 유지하기 위해서는 **microcatheter가 동맥류 반대쪽 ICA wall에 지지할 수 있도록 모양을 만들어야 한다.** 대부분의 para-ophthalmic aneurysm처럼 superior projection 의aneurysm 의 경우, S-shape microcatheter의 첫 번째 curve와 두 번째 curve 사이 부분이 aneurysm 반대 쪽 ICA inferior wall 에 위치할 수 있도록 shaping을 하면 안정적인 coiling을 하는데 큰 도움을 얻을 수 있다. Paraclinoid aneurysm의 가장 흔한 형태인 medical projection 의aneurysm을 pig tail shape의 proximal widening part가 ICA lateral wall을 지지할 수 있도록 디자인 되면 또한 안정적인 microcatheter support을 유지할 수 있다.

5. Shapability and shape-retention of various catheters

Non-braided 또는 fiber-braided microcatheter가 stainless-steel-braided microcatheters (ex, Excelsior SL-10) 보다 shapability 가 우월한 것으로 보고되고 있으또 다른 test 에서는 steam-shaped Proweler 14 microcatheter (platinum, larger pitch-coiled design)가Excelsior SL-10 microcatheter 보다 shapability 와 shape-retention 능력이 부족하나 preshaped Proweler 14 microcatheter는 SL-10 microcatheter 와 동등한 결과를 보여준다.

6. Conclusion

Paraclinoid or paraophthalmic aneurysm의 coiling을 계획할 때 동맥류의 방향을 고려하여 steam shaping 된 microcatheter 를 이용하면 aneurysm을 selection 하는데 있어서 불필요한 노력과 시간을 줄일 수 있고 coiling 이 진행되는 과정에서도 안정적인 packing을 얻을 수 있다.

7. Reference

1) Kwon BJ[1], Im SH, Park JC, Cho YD, Kang HS, Kim JE, Han MH.
Neurosurgery. 2010 Jul ; 67(1) : 34-40 ;
Shaping and navigating methods of microcatheters for endovascular treatment of paraclinoid aneurysms.

2) Abe Tet al
AJNR Am J Neuroradiol. 2004 Jun-Jul ; 25(6) : 1058-61
Distal-tipshape-consistency testing of steam-shaped microcatheters suitable for cerebral aneurysm coil placement.

3) Kiyosue H et al
AJNR Am J Neuroradiol. 2005 Nov-Dec ; 26(10) : 2610-6.
Shapability, memory, and luminal changes in microcatheters after steam shaping : a comparison of 11 different microcatheters.

Surgery for paraclinoid aneurysms :

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Surgery for paraclinoid aneurysms:

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1.Anatomical classification
2.Surgical technique
3.Microsurgical experiences
4.Avoidance of complication

Introduction (1): Classification

Classification based on anatomical location
very important for microsurgical clipping
less important for endovascular procedures

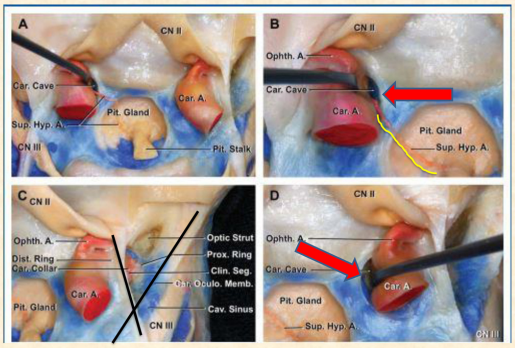
Branching vessel	Anatomical relationship
Carotid-ophthalmic	Paraclinoid dorsal/ventral variant
superior hypophyseal artery	carotid cave intra-cavernous
paraopthalmic	juxta-dural ring

Introduction (2): Indication for intervention

1) **Iihara et al.** had advocated treatment for **aneurysms >5 mm**, and had recommended **direct surgery for superiorly projecting unruptured aneurysms.**

2) **De Jesus et al.** had recommended treatment for **all aneurysms >4 mm with an extension into the subarachnoid space**, if the patient was in **good physiological condition and was expected to live at least 10 more years.**

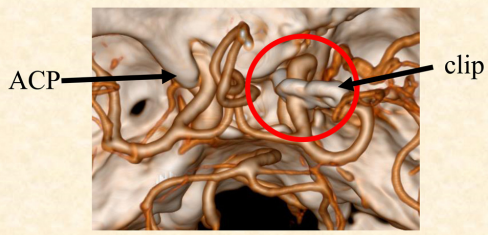
Introduction (3): Complex anatomy



Microsurgical Anatomy of the Carotid Cave, Neurosurgery 2012

Aim of this Presentation

1) Microsurgical experience in patients with ***pararclinoid aneurysms.***
2) Outcome assessment based on a ***Modified Classification (propose a New Classification System)***



Clinical materials and methods (1)

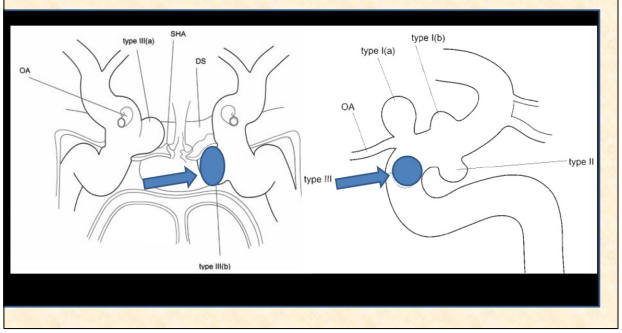
42 Patients (Jan. 2008 ----- May 2015)
Aneurysms aring from **C5 and C6 segments** of the ICA
Size: **< 10 mm**

	Ruptured (n = 7, An. = 8)	**Un-ruptured (n = 35, An. = 37)**
Sex (F/M)	6/1	30/5
Age	52.3 years old (21 ---71ys)	45.8 years old (25 ---- 62 ys)

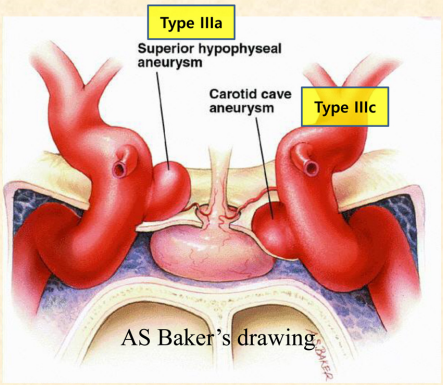
Relative contraindications to endovascular treatment
(wide neck, difficulty in catheter access, incorporation of the artery, giant, artherosclerotic, thrombosed an.)

Clinical materials and methods (2)

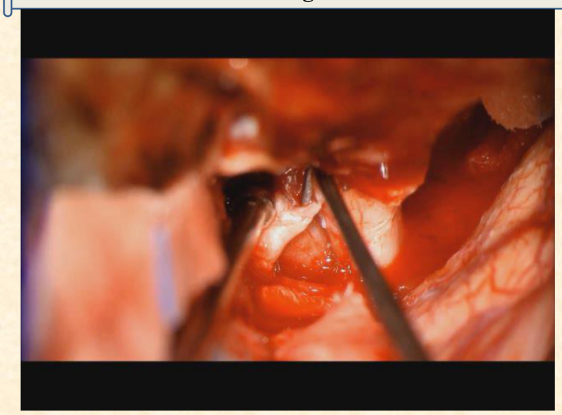
Classification of Aneurysms based on Barami, Day and Kobayashi proposal



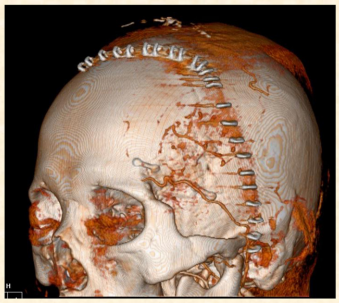
Clinical materials and methods (3)



Inter-dural origin of the OA

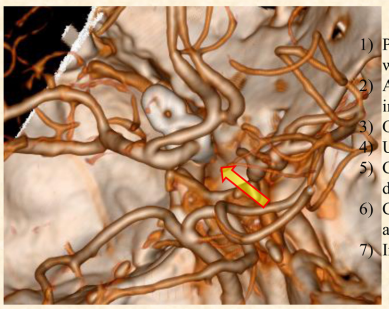


Method (5), Surgical technique



1) Pterional approach with or without orbitotomy
2) ACP resection (extradurally or intradurally)
3) Opening of the sylvian fissure
4) Un-roofing of the optic canal
5) Circumferential resection of the distal dural ring
6) Clip applied parallel to the long axis of the ICA
7) Intra-operative monitoring

Method (6), Surgical technique



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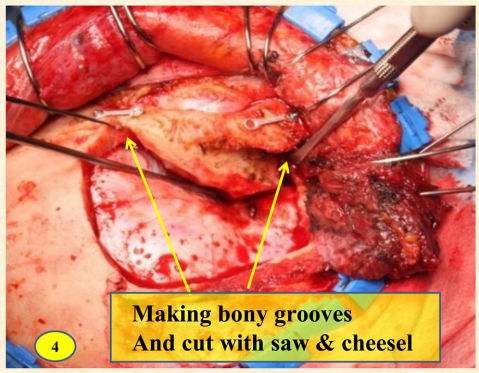
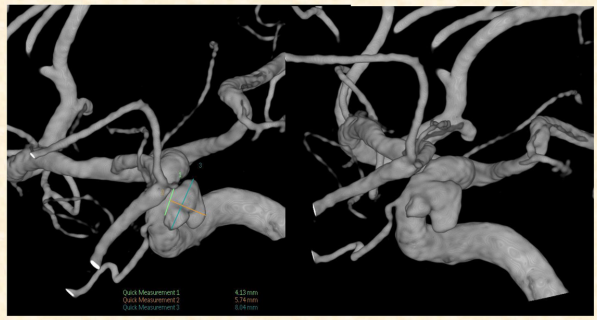
Surgical technique (Rt. O-P approach)

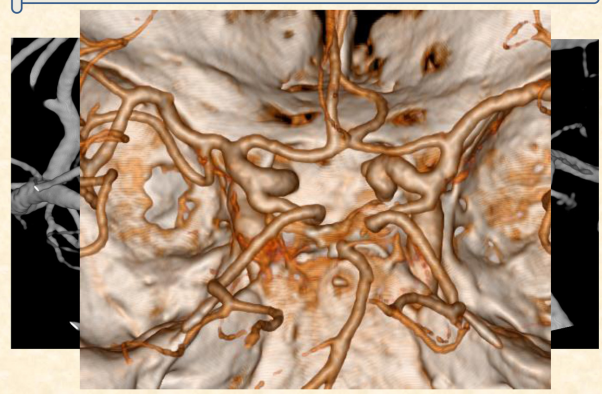


Surgical technique (Rt. O-P approach)

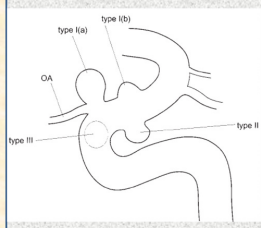
Method (7), Surgical technique (M/67, SHA)



Method (8), Surgical technique (M/67, SHA)



Results (1) Classification of aneurysms

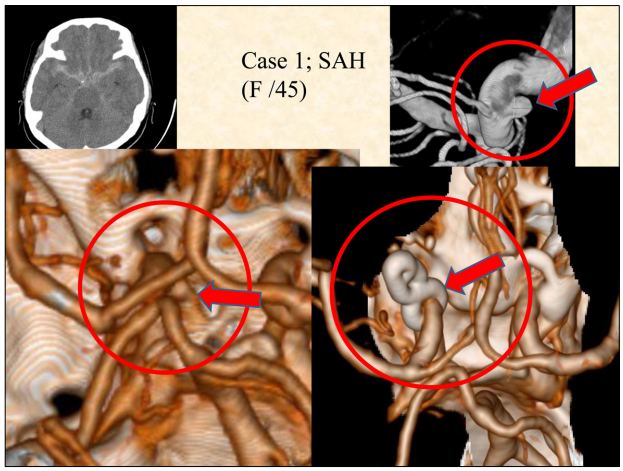


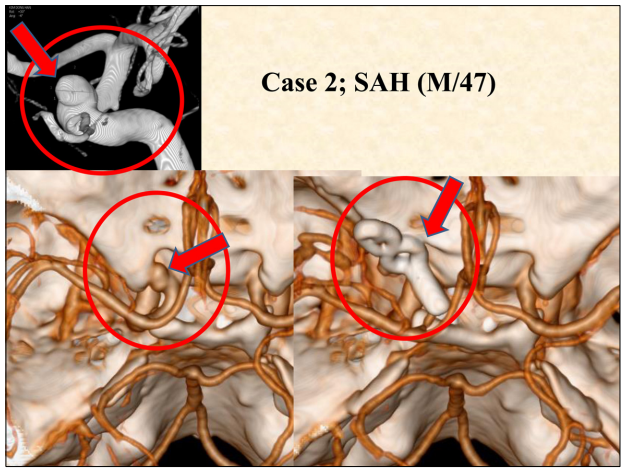
Number of aneurysm

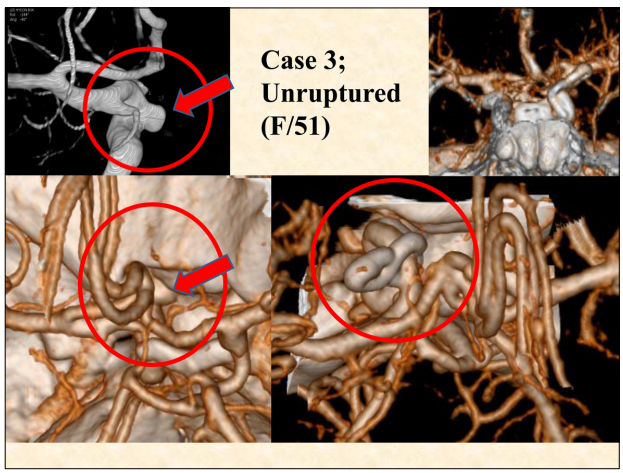
Type I a: 8 (17.7%)
Type I b: 3 (6.6%)
Type II: 3 (6.6%)
Type III a: 11 (24.4%) **SHA**
Type III b: 2 (4.4%)
Type III c: 17 (37.5%) **Cave**
Type IV: 1 (2,2%)

Modified Barami's classificaiton

Illustrative cases







Results (2) Clinical outcome

Modified Rankin Scale (6 months after the operation)

mRS	Ruptured (n=7) (number of patients)	Un-ruptured (n=35) (number of patients)
O	2 (28,5%)	29 (82.6%)
1	2 (28.5%)	5 (14.3%)
2	0	1 (2.9%)
3	1 (14.3%)	0
4	0	0
5	0	0
6	2 (28.5)	0

Results (3) Clinical Events

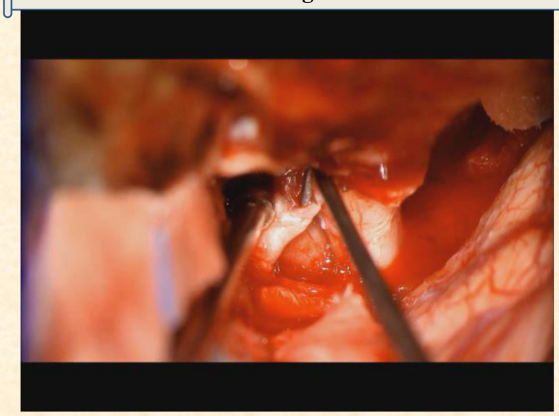
Event	Ruptured (n=7) (number of patients)	Un-ruptured (n=35) (number of patients)
Chewing discomfort	5 (71.4%)	10 (28.6%)
Visual impairment	0 (0%)	3 (8%)
Frontal numbness	6 (85.7%)	16 (45.7%)
Hyposmia	1 (14.2%)	2 (5.7%)
Infection	1 (14.2%)	1 (2.8%)
CSF leak	0 (0%)	0 (0%)
Transient 3rd N. palsy	1 (14.2%)	1 (2.8%)

Avoidance of complications (1)

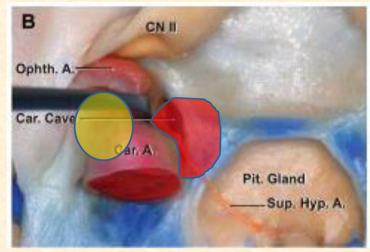
Causes of visual loss in this series
all patients with cave aneurysms
during the resection of the DDD

1) Excessive manipulation of the optic nerve (none)
2) Delayed inflammation: **1 case**
3) Anatomical variance (inter-dural origin of the opthalmic artery, tight arachnoid attached to the DDD) : **2 cases**
4) **Compromise of the sup. hypophyseal artery**
----- No visual impairement, but careful

Inter-dural origin of the OA



Procedures needed

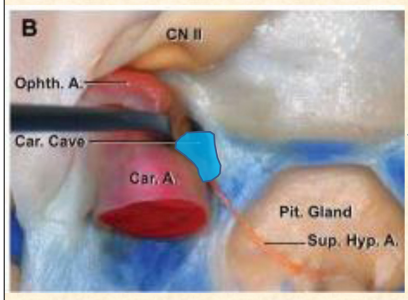


Type 1, 2
Sup. (Dorsal)
direction

Type 3
Sup. Hypoph
yseal artery

1) ACP resection
2) Release the falciform ligament
3) Opening the Distal Dural Ring
(partially, near completely)
4) Optic nerve manipulation
5) Visualization (cave aneurysm; hidden area)

Procedures needed



Type 1, 2
Sup. (Dorsal)
direction

Type 3
Sup.
Hypo-physeal
artery

Type 3 c
Sub-group

Carotid cave

Procedures needed

Type I, 2 (dorsal, ophthalmic aneurysm: partial resection of the DDD, relatively easier)

Type 3 a (SHA: Partial resection of the DDD)

Type 3b, 3c (cave), 4 (hidden, near complete resection of the DDD: relatively difficult)

Discussion :

Natural history of Un-ruptured aneurysms

A retrospective analysis on the natural history of
incidental small paraclinoid unruptured aneurysm

J Neurol Neurosurg Psychiatry 2014

Annual rupture of 0.12% and
an annual growth of 1.01%.

Risk factors; Size, Hypertension, Branch-related
Other Known risk factors: Smoking etc.

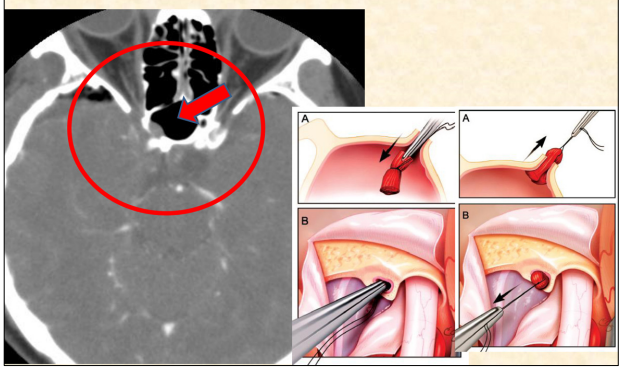
Conclusion

- Using a Modified Barami's Classification,
  We can predict surgery-related morbidities.
- To avoid complications, accurate knowledge of the
  surrounding neurovascular and osseous anatomy is essential.
- Un-ruptured small paraclinoid aneurysm is a benign lesion,
  if risk factors controlled carefully.

Surgery for paraclinoid aneurysms is an effective method to prevent fatal SAH.

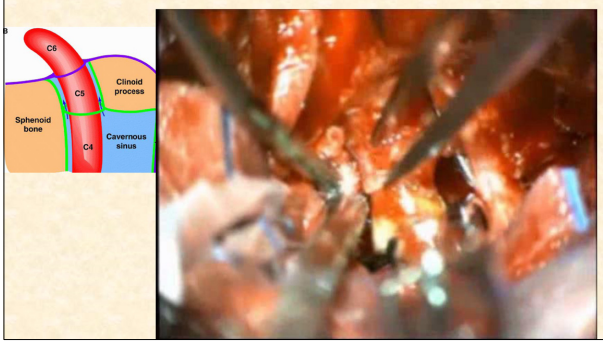
Avoidance of complications

Yoyo technique with muscle plug to prevent from CSF leak



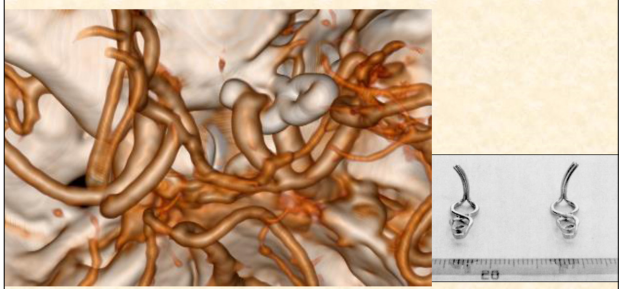
Avoidance of complications

Bleeding from the cavernous sinus
Bleeding from the carotid collar (R/O Arterial bleeding)



Avoidance of complications (5)

Clip application parallel to the axis of the ICA



Curved fenestrated clip may be useful

Paraclinoid Aneurysm : Current recommendation and literature review

Sung pil Joo

Department of Neurosurgery, Chonnam National University Hospital and Medical School, Gwangju, Republic of Korea

In the literatures, paraclinoid aneurysm accounted for approximately 1.5—11% of all intracranial aneurysm. Paraclinoid aneurysms have been defined as intracranial aneurysms that arise from the internal carotid artery (ICA) between the site of its exit from the roof of the cavernous sinus and the origin of the posterior communicating artery. These aneurysms are classified on the basis of complex relationships among theaneurysm sac, dura, branch arteries, and anterior clinoid process. Because of the close relationship to the complexity of adjacent structures such as skull base including anterior clinoid process (ACP), cavernoussinus and critical cranial nerves, surgical treatment of paraclinoid aneurysms remains a technical challenge to many neurosurgeons. Advances in endovascular treatment (EVT) have greatly improved the treatment outcomes of paraclinoid aneurysms. However, EVT had the shortcoming of durability and thromboembolic complications. As well, surgical treatment of paraclinoid aneurysms is still challenging due to the complexity of adjacent structures. Some reports presented a multidisciplinary approach of micro—surgery and EVT for the treatment of paraclinoid aneurysms. Considering the procedure related risks of unruptured paraclinoid aneurysms, it is important to identify the proper indication as well as to select safe and effective methods for treatment. The purpose of the present presentation is to assess the outcomes under the multidisciplinary treatment based on current literature review.

Special lecture I

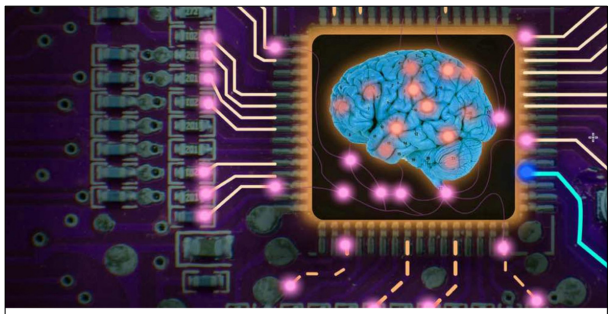
좌장 : 박현선(인하대), 성재훈(가톨릭대)

1. 인공지능과 의료의 미래
   배영우(전 한국IBM(주) 고객기술자문 상무, 현 아이메디씬(주) CTO)
2. 국립보건연구원 임상연구지원현황 박현영(국립보건연구원 심혈관 희귀질환 과장)

인공지능과 의료의 미래

배영우

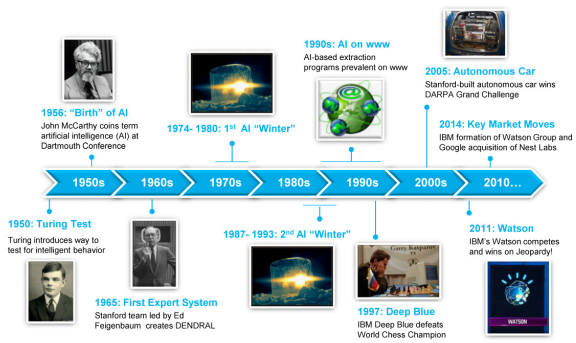
전 한국IBM(주) 고객기술자문 상무, 현 아이메디씬(주) CTO



인공지능과 의료의 미래

How A.I. changes the way we live and work

인공지능의 발전...



2

인공지능 (AI)

- "기계를 인간 행동의 지식에서와 같이 행동하게 만드는 것"

  "The science and engineering of making intelligent machines"

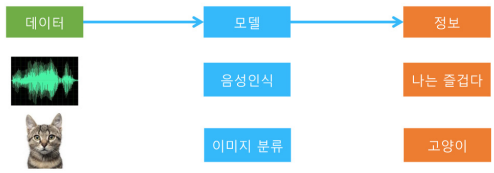
  – 존 매카시(John McCarthy)

➢기계가 어떤 문제를 실제로 사고하고 해결할 수 있는 지능
➢기계가 진짜 지능을 갖추지는 못했지만 미리 정의된 규칙의 모음을 이용해서 지능을 흉내내는 컴퓨터 프로그램

3

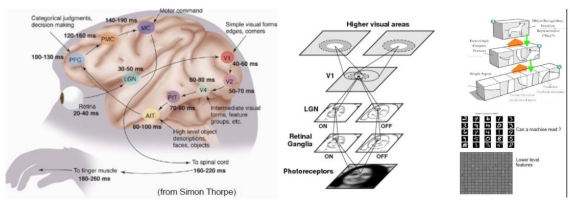
기계학습 (Machine Learning)

- 지도학습(Supervised): 값을 예측(Regression) vs. 값을 기반으로 선택(Classification)
- 비지도학습(Unsupervised)



4

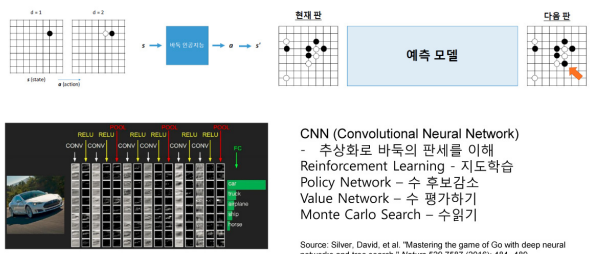
딥러닝 (Deep Learning) – 기계학습의 유형



5

알파고 (AlphaGo) – 바둑 인공지능

- **정돈된(Clean) 게임영역에 초점**



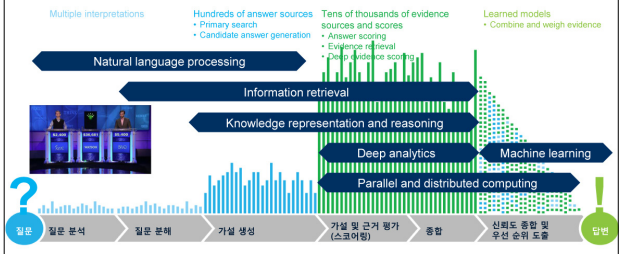
CNN (Convolutional Neural Network)
- 추상화로 바둑의 판세를 이해
Reinforcement Learning - 지도학습
Policy Network – 수 후보감소
Value Network – 수 평가하기
Monte Carlo Search – 수읽기

Source: Silver, David, et al. "Mastering the game of Go with deep neural networks and tree search." *Nature* 529.7587 (2016): 484–489.

6

왓슨(Watson) – Deep Q&A, 인지컴퓨팅

- **혼돈된(Messy) 과제에 초점**
- **3초 만에 질문 분석, 가설 생성, 가설 및 근거 평가를 완료하고 신뢰도와 함께 답변 도출**



인지(Cognitive) 컴퓨팅 – **추론**하고, **학습**하고, **인간과 상호작용**을 통해 계속 **진화**하는 컴퓨팅 기술로 인간의 인지능력을 확장

"확장지능"

인간의 언어로 상호작용
음성인식, 이미지 인식, 시각화 기술 등 인간의 방식으로 상호작용하며, 이 상호작용을 통해 계속 학습하면서 진화

인공지능과 기계학습의 결합
감지하고 예측하고, 생각할 수 있도록 하는 인공지능과 기계학습을 통해 훈련되는 학습 시스템

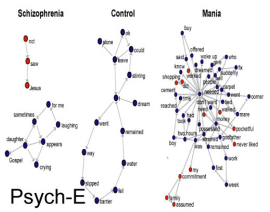
전문지식으로 의사결정 향상
언어, 전문용어 등 전문분야에 대한 지식을 쌓고 이를 통해 최적의 데이터를 만들어 의사결정을 지원

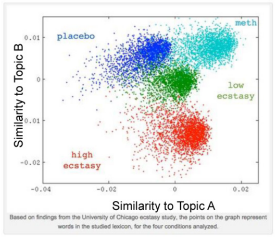
새로운 기반 과학기술의 발전:
Embodied Cognition, Approximate Computing, Neuromorphic Computing, Computational Neuroscience 등

8

Computational Neuroscience

- Psych-E 도구는 인지상태를 음성 및 텍스트 분석을 통해 평가 (정신 분열증, 아스퍼거, 열광)





9

인공지능 선도 기업과 다섯 가지 주요 상용화기술

인공지능 선도 기업과 용어

"Cognitive Computing" *"Artificial Intelligence"* *"Machine Intelligence"* *"Machine Learning"* *"Smart Machines"*

IBM Google Bloomberg Microsoft Gartner

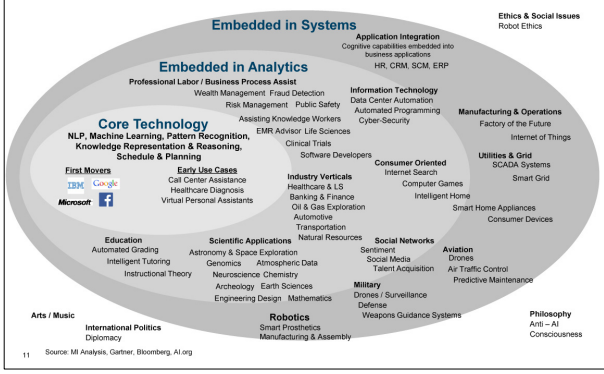
다섯 가지 주요 기술

1. **자연어처리 (Natural Language Processing)**
2. **기계학습 (Machine Learning)**
3. **패턴인식 (Pattern Recognition)**
4. **지식설명 및 추론 (Knowledge Representation & Reasoning)**
5. **일정 및 계획 (Schedule & Planning)**

Source: Jim Sporher, Director IBM Cognitive Systems Institute, aitopics.org

10

인공지능의 상용화에따른 비즈니스 확장 영역



Source: MI Analysis, Gartner, Bloomberg, AI.org

11

인공지능 분야의 기업은 주류기업, 스타트업, 시스템통합, 신규 비즈니스 개척에 중점을 둔 비주류기업 그리고 하드웨어와 클라우드 인프라를 제공하는 기반기술기업으로 분류

주류 기업
플랫폼 서비스
인공지능 기업인수, 스타트업 지원,
제품개발을 위한 인재영입, VR 및 Robotics영역 확장
대표기업: IBM Microsoft hp Google Baidu facebook

스타트업 기업
특정분야에 집중하여 기술개발,
솔루션가능성을 보여주는 데모에 능숙
대표기업: KENSHO Numenta Cycorp Palantir

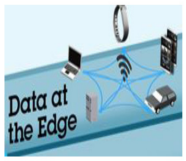
시스템통합 기업
파트너십으로 기존 고객을 위한 솔루션 제공에
집중하면서 새로운 고객 확보를 위한 구축 역량 강화
대표기업: accenture Deloitte Capgemini EY TATA WIPRO

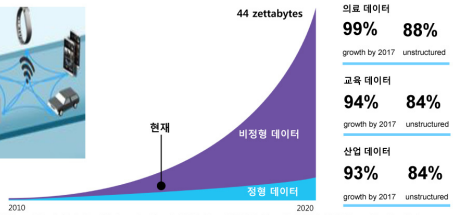
비주류 기업
자체 솔루션 개발을 위한 인원 확충,
기존 솔루션의 경쟁력강화를 위해 인공지능 역량강화
대표기업: IBM Siemens GE

기반기술 기업
인공지능 구축에 필요한 기반 기술 제공
대표기업: NVIDIA QUALCOMM Microsoft Azure amazon protege TRIFACTA

12

2020년이 되면 매일 1 인당 143GB를 생성하며 그 중 85%가 비정형 데이터일 것으로 예측



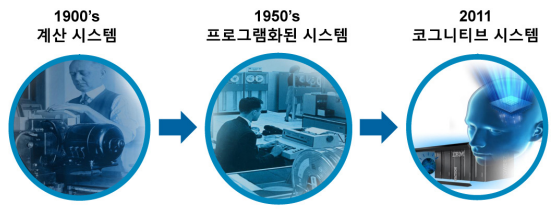


	의료 데이터	교육 데이터	산업 데이터
growth by 2017	99%	94%	93%
unstructured	88%	84%	84%

'Edge 데이터' : 기존 데이터와는 달리 보다 빠르게 생성되는 비정형적이고 임시적인 태블릿, 스마트폰, 센서 등에서 생성되는 새로운 형태의 데이터

13

새로운 인지(Cognitive) 컴퓨팅의 시대



14

인지컴퓨팅은 기존 검색의 한계를 초월한 의사결정지원

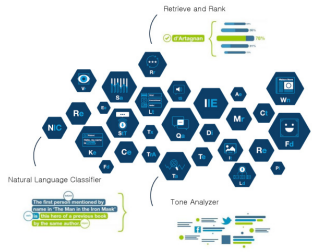
검색엔진	vs.	Watson (인지컴퓨팅)
질문		사람에게 질문 하듯 자연어로 질문
2-3 개의 키워드로 요약		질문을 이해
키워드가 포함된 문서를 찾음		가능성 있는 대답 추론
인기도를 기준으로 결과를 나열		근거를 분석
검색결과 및 관련 문서 읽기		신뢰도를 계산
답을 찾음		답, 근거 및 신뢰도를 같이 전달
관련 근거 정보 검토 및 분석		제시된 답과 근거를 검토

15

Watson API 는 28개로 확대되었으며 월간 API call 수는 30억건 도달

Watson's APIs are the cognitive building blocks that harness our data.

Message Resonance
Concept Expansion
Face Detection
Natural Language Classifier
Speech to Text
Text to Speech
Language Translation
Language Detection
Sentiment Analysis
Dialog
Retrieve and Rank
Image Link Extraction
Tradeoff Analytics
Entity Extraction
Tone Analyzer
Personality Insights
Taxonomy
Author Extraction
Concept Tagging
Relationship Extraction
Concept Insights
Relationship Extraction
Question & Answer
Feed Detection
Keyword Extraction
Visual Recognition
Image Tagging
Text Extraction



16

36개국, 29개 산업 에 걸쳐 100여개의 선도적인 기업들이 Watson과 함께 Cognitive Business를 시작

29 Industries	**36** Countries	**80K** Developers building with Watson
50,000 Students in Melbourne	**1.1M** Patients at Bumrungrad	**5.5M** Citizens in Singapore
5 Languages Learned by Watson	**160** Universities offering Watson courses	**400+** Partners Powered by Watson

17

Watson을 통해 고객 및 직원과 적극적으로 소통 하고, 방대한 정보로부터 새로운 통찰력을 찾아내 최적의 의사결정을 수행

18

Watson 인지컴퓨팅을 적용한 '암' 치료의 혁신

3명 중 한 명
암으로 사망

3배
암 치료 비용 증가율이 일반 질환 치료비용 증가율의 3배
연 15-18% 더 증가

20%
암 진단 시 조기 오진 비율
높은 경우는 44%에 달함

$2,638억
(268조 원)
2010년 한 해 미국의 암 치료 관련 총비용

$$$$$$$$$$$$
$$$$$$$$$$$$
$$$$$$$$$$$$
$$$$$$$$$$$$

(출처 : 전미 암 협회)

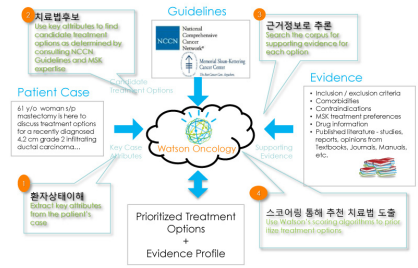
IBM Watson Oncology
Built with Memorial Sloan Kettering

의사들이 MSK 암센터의 방대한 임상 정보, 공개된 연구 자료, 의료적 증거, 환자 신상 정보를 활용해, 암 환자에게 가장 효과적인 치료법 제시.
암전문의가 Watson을 가르치는데 5천시간.
Watson은 60만 건이상의 사례 및 2백만 페이지 이상의 의학 저널 학습.

MSK 암센터, MD Anderson암센터, 웰 포인트 보험사와 암 치료 혁신을 위한 솔루션 연구개발

19

Watson 온콜로지 의료진단지원 과정



20

Watson을 적용한 신약연구개발 혁신 사례

Watson Discovery Advisor (WDA) for Life Sciences
- 신약 개발 지원, 약물 안전성 및 독성 연구 지원
- 과학 학술 문서 이해 및 학습

Watson Discovery Advisor의 혁신적 가치
- 약물 적용 대상 확인 및 검증
- 약물 화합물 발견 및 최적화
- 약물 안전성 및 독성 예측분석
- 약물 용도 변경 및 경쟁정보 (Competitive Intelligence)
- 과학적 사실 인용, 논리적 추론 그리고 생물학적 경로 및 화학적 생물학적 관련성 전반에 걸친 추론
- 가설 생성 그리고 신규 바이오 마커에 대한 성공가능성 향상
- 독성 및 안전성에대한 이해도 향상을 위한 관련 정보 검색, 발췌 및 정규화를 자동으로 수행
- 본격적인 투자를 결정하기 전에 초기 대상 선정 및 신속한 결과 확인을 통한 위험감소

Johnson & Johnson 존슨앤드존스

- 신약 효능 연구의 70%가 자료 검색, 분석에 소요
- 왓슨을 활용하여 어떤 경우에 부작용이 생기고, 어떤 약품과 상호작용 하는지 연구

21

Watson Health

IBM은 Watson Solution에 기반한 헬스케어 전담 조직을 신설하고, Watson Cloud 와 개방형 헬스케어 플랫폼을 발표

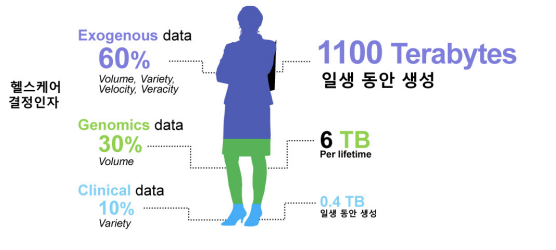
explorys PHYTEL MERGE Healthcare

Watson Health 파트너십

Johnson & Johnson Medtronic

22

헬스케어 빅 데이터 – 외생 데이터의 중요성



Source: "The Relative Contribution of Multiple Determinants to Health Outcomes", Lauren McGover et al., *Health Affairs, 33, no.2 (2014)*

Watson Health Cloud: 헬스케어 생태계의 중심

24

국립보건연구원 임상연구지원현황

박현영

국립보건연구원 심혈관 희귀질환과 과장

국립보건연구원 임상연구지원현황

NIH 국립보건연구원

질병관리본부 국립보건연구원
심혈관·희귀질환과/임상연구지원TF 박현영

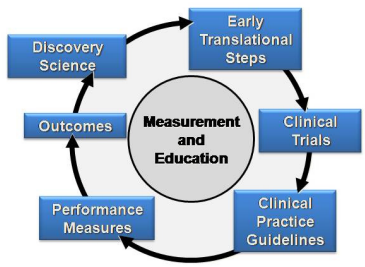
목차

- 임상연구 개요와 현황
- 임상연구등록과 자료관리
- 국립보건연구원 임상연구현황

임상연구(시험)개요와 현황

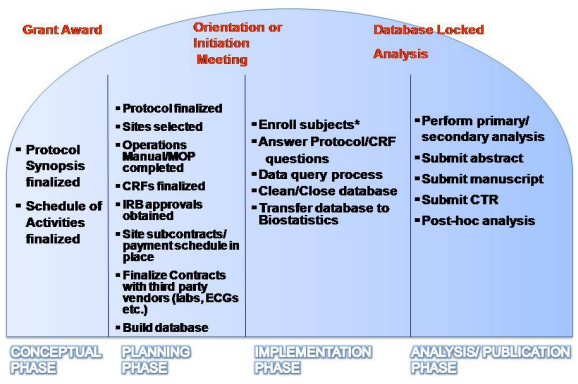
Clinical Research: "Learning health systems"

Generating Evidence to Inform Policy

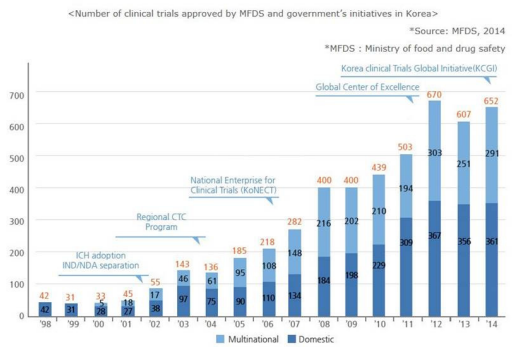


Califf RM et al, Health Affairs, 2007

Life Cycle of a Clinical Research



Clinical Trials



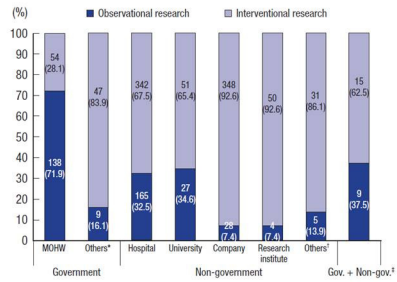


Fig. 2. Classification of research types of registered clinical research by funding source. Data are expressed as No. (%). *The other government funding sources were included except the MOHW; †Non-profit organizations and academic associations were included; ‡The researches were funded both by government source(s) and non-government source(s). MOHW, Ministry of Health and Welfare.

Choi EK et al., J Korean Med Sci 2016; 31: 1-8

Table 3. Three most frequently studied disease categories among the registered clinical researches

No.	Total (n = 1,323)	Research type		Gender			Age (yr)	
		Observational (n = 385)	Interventional (n = 938)	Male only (n = 129)	Female only (n = 93)	Both (n = 1,101)	< 18 only (n = 50)	≥ 65 only (n = 16)
1	Digestive 173 (13.1)	Nervous 74 (19.2)	Digestive 117 (12.5)	Circulatory 20 (15.5)	Neoplasm 13 (14.0), Endocrine 13 (14.0), Genitourinary 13 (14.0)	Digestive 169 (15.3)	Mental 5 (10.0), Skin 5 (10.0)	Nervous 3 (18.8), Neoplasm 3 (18.8)
2	Nervous 125 (9.4)	Digestive 56 (14.5)	Musculoskeletal 100 (10.7)	Genitourinary 17 (13.2)	-	Nervous 122 (11.1)	-	-
3	Musculoskeletal 121 (9.1)	Circulatory 36 (9.4)	Circulatory 79 (8.4)	Endocrine 10 (7.8)	-	Musculoskeletal 108 (9.8)	Nervous 4 (8.0)	Circulatory 2 (12.5), Blood & Immune 2 (12.5)

Data are expressed as the disease category and No. (%).

Choi EK et al., J Korean Med Sci 2016; 31: 1-8

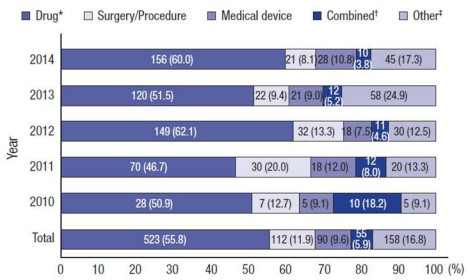
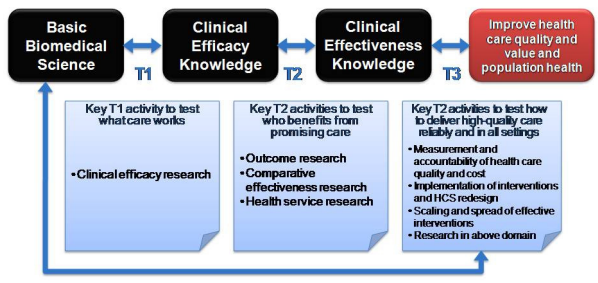


Fig. 3. Classification of the registered research by intervention. Data are expressed as No. (%). *Drug includes biological and vaccine; †Combined intervention includes more than two interventions; ‡Others include behavioral therapy, dietary supplement, radiation therapy and non-listed interventions.

Choi EK et al., J Korean Med Sci 2016; 31: 1-8

Translational research
The 3T's Road Map



JAMA 2008;299(19):2320

↔ Essential need for feedback between and across the parts of the transformation framework.

임상연구등록과 자료관리

헬싱키선언

- 2000년, 워싱턴 개정
  - ✓ 모든 연구의 디자인이 공개적으로 접근이 되어야 하는 원칙
  - ✓ The design of all studies should be publicly available
- 2008년, 서울
  - ✓ 모든 임상시험은 첫 참여자의 모집 전에 공개적으로 접근이 되는 데이터베이스에 등록되어야 함
  - ✓ Every clinical trial must be registered in a publicly accessible data base before recruitment of the first subject

Legal Requirement

Food and Drug Administration (FDA) Modernization Act of 1997

- In November 1997, Congress included a provision in the Food and Drug Modernization Act to mandate that the National Institutes of Health (NIH) establish, maintain, and **operate a public resource for information on efficacy studies of drugs, including biological drug products**, to treat serious or life-threatening diseases and conditions conducted under the FDA's investigational new drug (IND) regulations (21 CFR parts 312 and 812).
- Section 113 of the Modernization Act required that the **Clinical Trials Data Bank** contain the following information: (1) **Information about Federally and privately funded clinical trials for experimental treatments** (drug and biological products) for patients with serious or life-threatening diseases or conditions, (2) a description of the **purpose of each experimental drug**, (3) patient **eligibility criteria**, (4) a description of the **location of clinical trial sites**, and (5) a **point of contact** for patients wanting to enroll in the trial, all in a form that could be readily understood by the public.

임상연구정보 등록

- 임상연구대상자 보호 강화, 연구수행의 투명성 및 결과의 객관성 확보 등을 위하여 보건의료기술연구개발사업 임상연구과제의 연구정보 등록
- 질병관리본부 국립보건연구원에 구축된 임상연구정보서비스 (Clinical Research Information Service, CRIS, http://cris.nih.go.kr)에 연구비지원과제와 관련된 임상연구정보를 등록
- 성과보고 시, 임상연구 성과는 CRIS 등록 승인번호를 기재

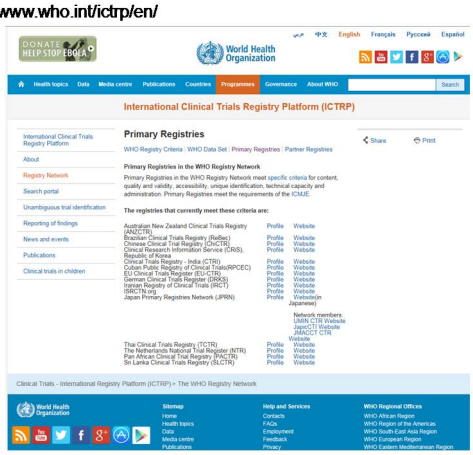
<보건의료기술 연구개발사업 관리규정> 제26조의2

주관연구기관의 장은 연구개발정보를 제26조제1항에 따라 전문기관의 장이 운영하는 보건의료기술 종합시스템에 등록하여야 한다. 다만, 보건복지부장관이 지정한 **임상연구과제의 경우에는 그 연구개발 정보**를 보건복지부장관이 지정한 전담기관에도 등록하여야 한다.

14

http://cris.nih.go.kr

ICPRT - http://www.who.int/ictrp/en/



등록항목

Table 1. Required data elements for research registration with the CRIS

Items	Data element
1. Background	- Unique protocol ID, Public/Brief title, Scientific title, Acronym, MFDS regulated study, IND/IDE protocol, Other registry if applicable (name, registration number)
2. Institutional Review Board/Ethics Committee*	- Board approval status, Board approval number, Approval date, Name of Board, Data Monitoring Committee
3. Contact details	- Name, Title, Telephone, email, Affiliation of the following persons: Contact person for principal investigator/scientific queries, Contact person for public queries, Contact person for updating information
4. Study status	- Overall recruitment status: Study site, Date of first enrollment, Status of first enrollment, Target sample size, Primary completion date, Study completion date - Recruitment status by participating study site: Name of study site, Recruitment status, Date of first enrollment, Status of first enrollment
5. Source(s) of monetary/material support	- Organization name, Organization type, Project ID
6. Sponsor organization(s)	- Organization name, Organization type
7. Study summary	- Summary
8. Study design	- Interventional study: Study purpose, Phase, Intervention model, Blinding/masking, Allocation, Intervention type, Intervention description, Arm label, Target sample size, Arm type, Arm description - Observational study: Observational study model, Time perspective, Target sample size, Cohort/group label, Cohort/group description, Biospecimen collection & Archiving, Biospecimen description
9. Subject eligibility†	- Condition(s)/disease(s), Rare disease, Inclusion/Exclusion criteria
10. Outcome measure(s)	- Type of primary outcome, Primary outcome, Secondary outcome
11. Publication information	- If applicable, Author, Title, Journal name, Publication year

Source: https://cris.nih.go.kr/cris/en/images/explain_en.pdf. *Approval letter should be uploaded; †Registrant selects the disease category according to the ICD-10 classification and then enters the details. CRIS, Clinical Research Information Service; MFDS, Ministry of Food and Drug Safety; IND/IDE, Investigational New Drug/Investigational Device Exemption.

등록절차

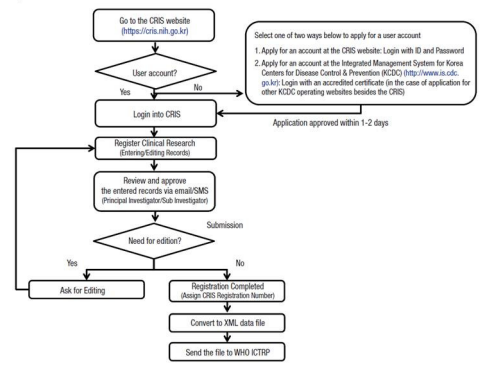
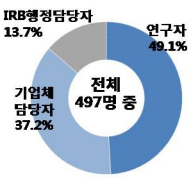


Fig. 1. Registration process in the CRIS and information sharing with WHO ICTRP. CRIS, Clinical Research Information Service; WHO ICTRP, World Health Organization International Clinical Trials Registry Platform.

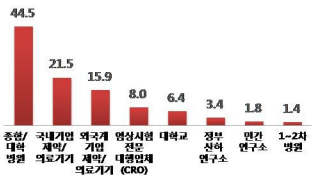
임상시험등록제 연구를 위한 인식도 조사

2014, 식품의약품안전평가원 임상연구과

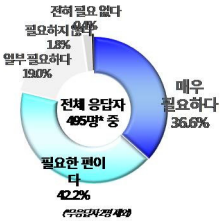
조사 대상자



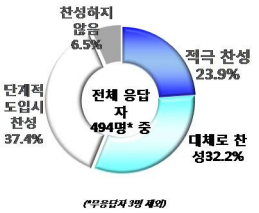
근무기관 (복수 응답) (단위 : %)



식약처 허가 국내 임상시험 등록의무화 도입 필요성



임상시험 결과까지 등록을 의무화하는 제도에 대한 의견



2014, 식품의약품안전평가원 임상연구과

MEDICAL NEWS & PERSPECTIVES

Clinical Trials Registry Expands

Bridget M. Kuehn JAMA. 2009;302(1):22

Note for the media/WHO 4
14 April 2015

WHO Calls for Increased Transparency in Medical Research

14 APRIL | 2015 GENEVA -WHO today issued a public statement calling for the **disclosure of results from clinical trials for medical products, whatever the result**. The move aims to ensure that decisions related to the safety and efficacy of vaccines, drugs and medical devices for use by populations are supported by the best available evidence.

"Our intention is to promote the sharing of scientific knowledge in order to advance public health," said Dr. Marie-Paule Kieny, WHO Assistant Director General for Health Systems and Innovation. "It underpins the principal goal of medical research: to serve the betterment of humanity."

"Failure to publicly disclose trial results engenders misinformation, leading to skewed priorities for both R&D and public health interventions," said Kieny. "It creates indirect costs for public and private entities, including patients themselves, who pay for suboptimal or harmful treatments."

Note for the media/WHO 4
14 April 2015

WHO Calls for Increased Transparency in Medical Research

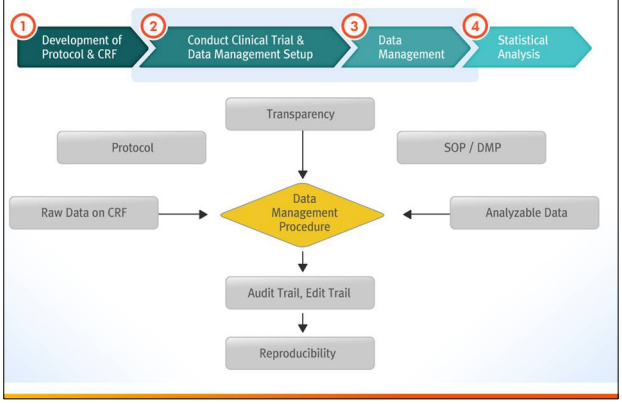
...

For example, in a study that analysed reporting from large clinical trials (more than 500 participants) registered on clinicaltrials.gov and completed by 2009, 23% had no results reported. These unreported trials included nearly 300 000 participants. Among clinical trials of vaccines against five diseases registered in a variety of databases between 2006-2012, **only 29% had been published in a peer-reviewed journal by the WHO recommended deadline of 24 months following study completion**.

...WHO's call for disclosure includes older unreported clinical trials, the results of which may still have an important bearing on scientific research today. WHO also reaffirms the need for all clinical trials to be registered on a WHO primary clinical trial registry so that they can be accessible through the International Clinical Trials Registry platform. This will ensure transparency as to which clinical trials have occurred, and allow verification of compliance with public disclosure requirements.

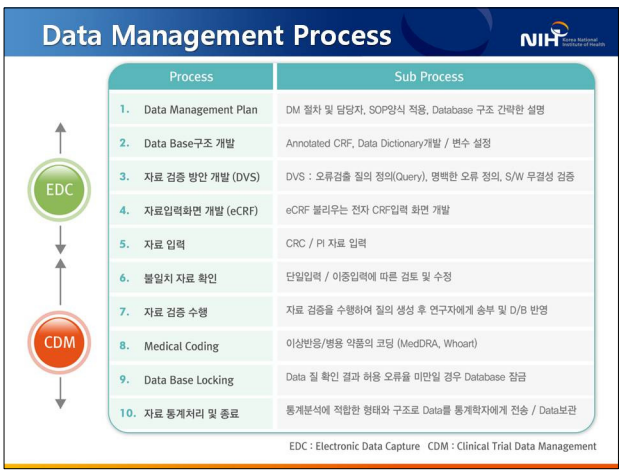
임상연구자료관리: process

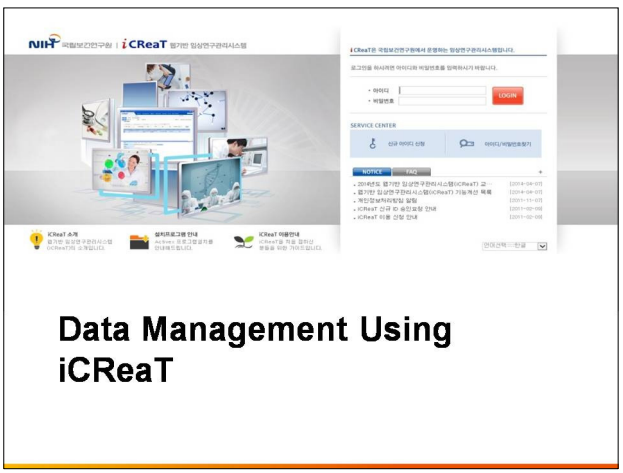
NIH

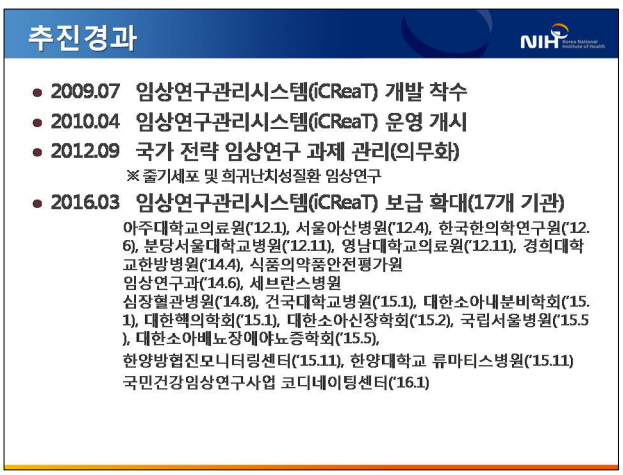


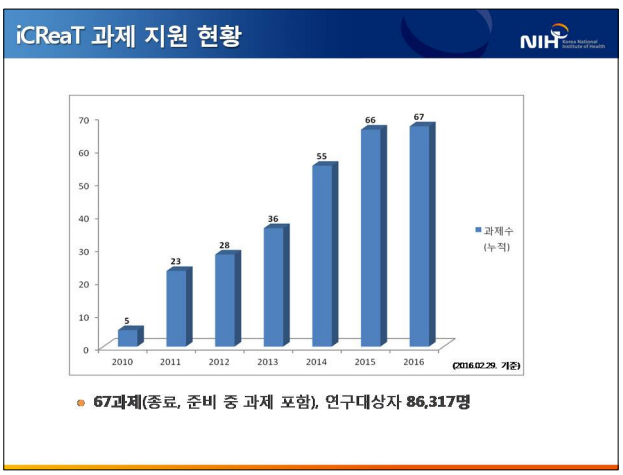

I. Global Regulation
4. 임상시험 전자자료처리 및 관리를 위한 가이드라인 (2010.10)
목적
이 가이드라인은 의약품 및 의료기기 임상시험을 실시하고자 할 때, 임상시험 의뢰자, 임상시험 실시기관, 임상시험 수탁기관을 포함하여 임상시험 자료를 생성,처리 및 관리하는 모든 기관을 위한 임상시험 전자자료처리 및 관리에 관한 지침을 제공하는 것을 목적으로 한다.
임상시험의 근거자료는 임상시험을 재현 및 평가하기 위한 근거이므로 이 가이드라인은 전자자료와 문서의 신뢰성, 품질, 무결성을 보장하기 위한 지침으로 개발하였다.
이 가이드라인은 규정이 아닌 현행규정을 토대로 현 시점에서 식약청의 임상시험 전자자료 처리 및 관리에 대한 운영 방향에 대한 권고사항이며, 다른 법률에서 별도로 정하는 경우에는 해당 법률을 따라야 한다.
범위
모든 컴퓨터시스템에 적용
자료의 생성방식에 무관
종이문서에 기재하였다가 컴퓨터시스템에 입력 / 컴퓨터시스템에 입력 자동화된 장비에서의 전송
임상시험 전자 자료처리 및 관리 가이드라인
제 1 장 목적
제 2 장 용어정의
제 3 장 범위
제 4 장 표준작업지침서
제 5 장 컴퓨터 시스템 검증
제 6 장 변경이력
제 7 장 날짜 및 시간 기록
제 8 장 자료보관
제 9 장 권한 관리
제 10 장 전자서명
제 11 장 시스템 접근 및 보안
제 12 장 시스템 기본 기능 및 문서
제 13 장 시스템 변경관리
제 14 장 시스템 백업과 복구
제 15 장 비상계획
제 16 장 참여자 교육 및 훈련


I. Global Regulation
3. KGCP : 자료의 처리
제28조(자료의 처리) 제1항 제1호~제6호, 제2항
전자화된 임상시험 자료처리 방법이나 원거리 전자자료시스템을 이용할 경우 의뢰자는 다음 각호의 사항을 준수하여야 한다.
전자 자료처리시스템의 완전성, 정확성, 신뢰성 및 일관되게 의도한 대로 작동하는 정도가 의뢰자가 설정한 요구사항에 일치하는지에 대한 확인 및 문서화 (시스템검증) } System Validation, Data Validation
전자 자료처리시스템의 사용에 대한 문서화된 SOP 유지 } SOP
자료의 수정과정이 기록되고 일단 입력된 자료에 대한 삭제가 이루어지지 않는 방식으로 자료의 수정이 가능하도록 전자자료처리시스템이 설계되었다는 사실의 확인 (점검기록, 자료기록, 편집기록 등) } Audit trail, System Qualification
인가되지 않은 자에 의한 자료의 접근이 허용되지 않도록 보안시스템의 유지 자료를 수정할 수 있도록 인가된 자의 명단 유지 } Security Management
자료의 적절한 복사본(backup) 유지 } Backup
자료가 처리과정에서 변화되는 경우에는 원래의 자료(관찰)와 처리된 자료의 비교가 항상 가능하여야 한다. } Data Validation


Data Management Process
NIH
Process
Sub Process
1. Data Management Plan
DM 절차 및 담당자, SOP양식 적용, Database 구조 간략한 설명
2. Data Base구조 개발
Annotated CRF, Data Dictionary개발 / 변수 설정
3. 자료 검증 방안 개발 (DVS)
DVS : 오류검출 질의 정의(Query), 명백한 오류 정의, S/W 무결성 검증
4. 자료입력화면 개발 (eCRF)
eCRF 불리우는 전자 CRF입력 화면 개발
5. 자료 입력
CRC / PI 자료 입력
6. 불일치 자료 확인
단일입력 / 이중입력에 따른 검토 및 수정
7. 자료 검증 수행
자료 검증을 수행하여 질의 생성 후 연구자에게 송부 및 D/B 반영
8. Medical Coding
이상반응/병용 약품의 코딩 (MedDRA, Whoart)
9. Data Base Locking
Data 질 확인 결과 허용 오류율 미만일 경우 Database 잠금
10. 자료 통계처리 및 종료
통계분석에 적합한 형태와 구조로 Data를 통계학자에게 전송 / Data보관
EDC
CDM
EDC : Electronic Data Capture CDM : Clinical Trial Data Management


NIH
iCReaT
Data Management Using iCReaT


추진경과
NIH
2009.07 임상연구관리시스템(iCReaT) 개발 착수
2010.04 임상연구관리시스템(iCReaT) 운영 개시
2012.09 국가 전략 임상연구 과제 관리(의무화)
※ 줄기세포 및 희귀난치성질환 임상연구
2016.03 임상연구관리시스템(iCReaT) 보급 확대(17개 기관)
아주대학교의료원('12.1), 서울아산병원('12.4), 한국한의학연구원('12.6), 분당서울대학교병원('12.11), 영남대학교의료원('12.11), 경희대학교한방병원('14.4), 식품의약품안전평가원
임상연구과('14.6), 세브란스병원
심장혈관병원('14.8), 건국대학교병원('15.1), 대한소아내분비학회('15.1), 대한핵의학회('15.1), 대한소아신장학회('15.2), 국립서울병원('15.5), 대한소아베뇨장애야뇨증학회('15.5),
한양방혈진모니터링센터('15.11), 한양대학교 류마티스병원('15.11)
국민건강임상연구사업 코디네이팅센터('16.1)


iCReaT 과제 지원 현황
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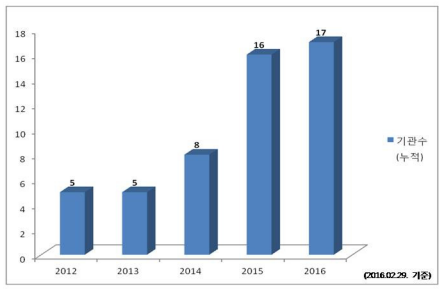
2016
과제수 (누적)
(2016.02.29. 기준)
67과제(종료, 준비 중 과제 포함), 연구대상자 86,317명

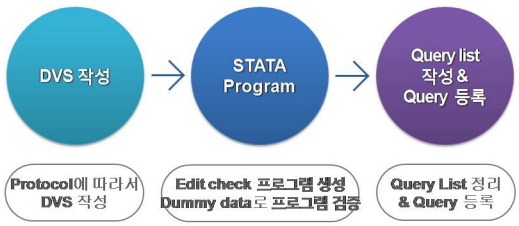
iCReaT 기관 단위 보급 현황



기관 단위 보급 : 17기관, 35과제(종료, 준비 중 과제 포함)

웹기반 임상연구관리시스템(iCReaT) 관리

Process of Data Validation



국립보건연구원 임상연구현황

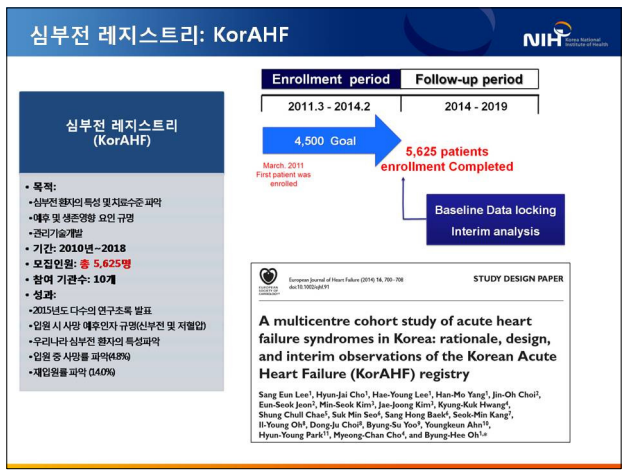
2013년~2015년 학술, 정책, 내부 과제 현황

	학술 (KNIH)	정책 (KNIH)	학술 (KCDC)	정책 (KCDC)	내부 (KNIH)	KNIH (학술+정책)	합계
2013	33	83	1	69	106	116	292
2014	47	86	7	79	109	133	328
2015	72	77	7	96	111	149	363
합계	152	246	15	244	326	398	983

연구과제 추진절차

	학술연구용역과제
연구계획 수립	◦ 연구과제시행 및 성과관리계획 제출
⇩	
선정 및 평가	◦ 과제 제안 심의 (중복성 검토) (연구사업심의위원회) ◦ 학술연구용역과제평가 (연구기획과/내·외부전문가)
⇩	
계약 및 진도관리	◦ 학술연구용역과제계약 (질병관리본부 총무과) ◦ 진도관리(사업부서/연구기획과)
⇩	
평가	◦ 과제결과 평가 및 정산 (연구기획과/내·외부전문가)
⇩	
연구성과 활용	◦ 성과사후관리(5년) (연구기획과)

발주센터	발주부서	연구과제명
생명의과학센터	심혈관·희귀질환과	조직구증식증 임상연구 네트워크 구축 및 운영
		아밀로이드증의 조기진단과 예후인자 발굴을 위한 연구
		국내유전성가족성 부정맥질환 임상네트워크 구축 및 운영
		국내 전신성홍반성 루푸스 임상네트워크 구축 및 운영
		국내 시신경척수염 임상네트워크 구축 및 운영
		국내 크론병 임상연구 네트워크 구축 및 운영
		국내 극소저체중아 관리지표 생산을 위한 레지스트리 구축 및 운영
		가임기여성 건강설문조사
		경년기여성에서 신체정신건강상태 및 위험요인 규명을 위한 전향적 연구
		임신합병증 유병률조사 및 위험인자 발굴
		심뇌혈관질환 고위험군(노인) 예방관리코호트 구축 및 운영
		급성심근경색환자 예후 및 관리지표발굴을 위한 전향적 추적관찰 연구
		심부전(Heart Failure)질환 Registry구축 및 관리
		장기이식 코호트 구축 및 운영
	뇌질환과	알츠하이머병 생물학적지표 기반 진단표준화 연구
	호흡기·알레르기질환과	소아 호흡기알레르기질환 장기추적 코호트
		실내외 환경변화가 영유아 알레르기질환 발생에 미치는 영향의 전향적연구
유전체센터	유전체역학과	도시기반 코호트 사업
		농촌기반 코호트 사업
		지역사회 기반 코호트 심층조사사업(안산)
		지역사회 기반 코호트 심층조사사업(안성)



Special lecture II

좌장 : 오창완(서울대)

Update MR imaging for cerebral hemorrhage

최현석(가톨릭대 서울성모병원 영상의학과)

Update MR imaging for cerebral hemorrhage

최현석

가톨릭의대 서울성모병원 영상의학과

1. CT

조영증강 전 CT에서 hemorrhage는 electron density의 증가로 bright density을 보인다. 최근 소개된 dual energy CT는 hemorrhage와 iodine 조영제의 구분이 가능하다. 조영증강 후 CT에서는 active bleeding focus을 발견 할 수 있는 경우가 있다.

2. MRI

A. GRE

MRI sequence중 고전적인 방법이다. hemorrhage는 자성(paramagnetism)을 띄고 있기 때문에 MRI 자장 환경에서 국소 자장을 변화시킨다.

B. FLAIR

CSF신호를 억제하는 T2영상기법으로 SAH나 subdural hemorrhage의 발견에 유용하다.

C. T1 and T2-weighted image of evolution of hemorrhage

Oxy-hemoglobin, Deoxy-hemoglobin, Met-hemoglobin, ferritin, hemosiderin등의 상태에 따라 다양한 신호 강도를 보이므로 hemorrhage의 stage을 평가할 수 있다.

D. SWI and QSM

최근 임상적으로 사용되는 SWI는 GRE와 비교하여 high resolution, flow compensation, less distortion의 장점이 있으며, QSM(quantitative susceptibility mapping)을 통하여 정량적 분석이 가능하다.

3. Clinical application : 다양한 질환의 영상 소견의 소개 및 토의

A. Hypertensive ICH

B. AVM

C. Aneurysm and SAH

D. Traumatic brain injury

Scientific session II

좌장 : 홍승철(성균관대), 김범태(순천향대)

Dural—AVF

1. Etiology and pathogenesis and diagnosis — 신동성(순천향대)
2. Endovascular treatment — 권순찬(울산대)
3. Surgical treatment — 안재성(울산대)
4. Current recommendation and literature review — 임용철(아주대)

Etiology and Pathogenesis and Diagnosis
Etiology and pathogenesis of dAVF

신동성
순천향대 부천병원

DAVFs make up 10% to 15% of intracranial vascular malformations and are abnormal connections between dural arteries and dural venous sinuses, meningeal veins, or cortical veins.dAVFs have been associated with history of trauma, previous craniotomy, or dural venous sinus thrombosis. In the setting of interrupted normal sinus outflow and elevated local venous pressures, it is hypothesized that tiny physiologic shunts may enlarge, or neoangiogenic factors may promoted the formation of pathologic connections. Multiple dAVFs may occur secondary to thrombosis of the involved sinus. Once the malformation is present in a dural structure, the shunted flow might cause turbulence and reversal of the normal venous flow, which could lead to stagnation and thrombosis away from the original malformation. Second malformation might then develop by recanalization.

Adult dAVFs, which constitute the majority of lesions, are most common at the transverse, sigmoid, and cavernous sinus. There is also a subset of pediatric lesions that can often involve the torcula, superior sagittal sinus, and large venous lakes.

Awad at el.[1], described to natural history of dAVF. Authors suggest the presence of several stage in the natural history of lesions (Fig). Microscopic communications between arteries and veins exist in normal dura mater ant the proximity of venous sinus. Trauma, surgery, sinus thrombosis, or other factors might initiate the genesis of a true dAVF.

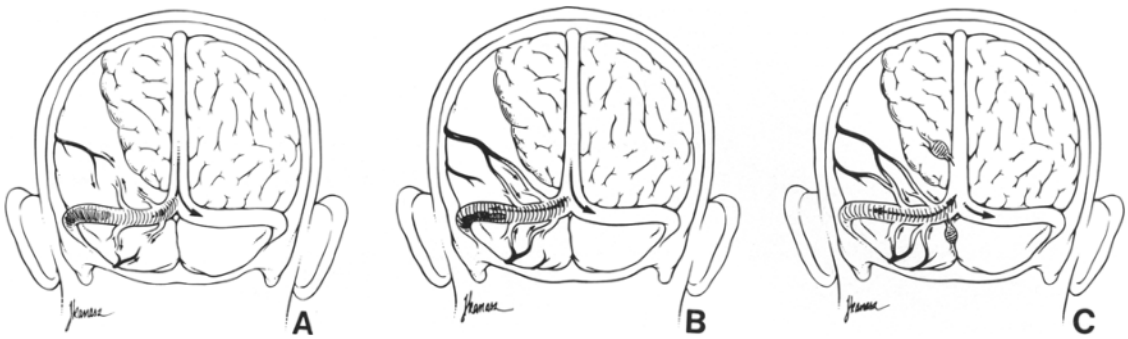


FIG. 4. Artist's illustration of three possible stages in the natural history of a dural arteriovenous malformation (AVM). A: Sinus thrombosis and engorged dural venous collaterals with opening of embryonic arteriovenous communications. B: Arteriovenous shunting favors recruitment of arterial feeders into the nidus (sump effect) with secondary venous hypertension. C: Venous hypertension favors leptomeningeal retrograde venous drainage and predisposes such channels to become varicose and aneurysmal. These three stages can be clearly documented in dural AVM's from our experience and from the literature.

Development of acquired AVF due to venous hypertension

Terada, et al.[2], reported on a rat model of AVF, and they stated that venous hypertension without sinus or venous thrombosis can induce a d AVF. They proposed that exposure of the vessel to venous hypertension may result in the dilation of the vessels and loss of sphincter control in arterioles. Increased intraluminal pressure in the vessels stimulates angiogenesis, and direct connections to the sinus or vein might from, resulting in the development of dural fistulas.

NIshijima et al.[3], illustrated few microscopic finding of dAVF specimen. They observed "No direct communication between dural arteries and venous sinuses ; in serial section (Fig).

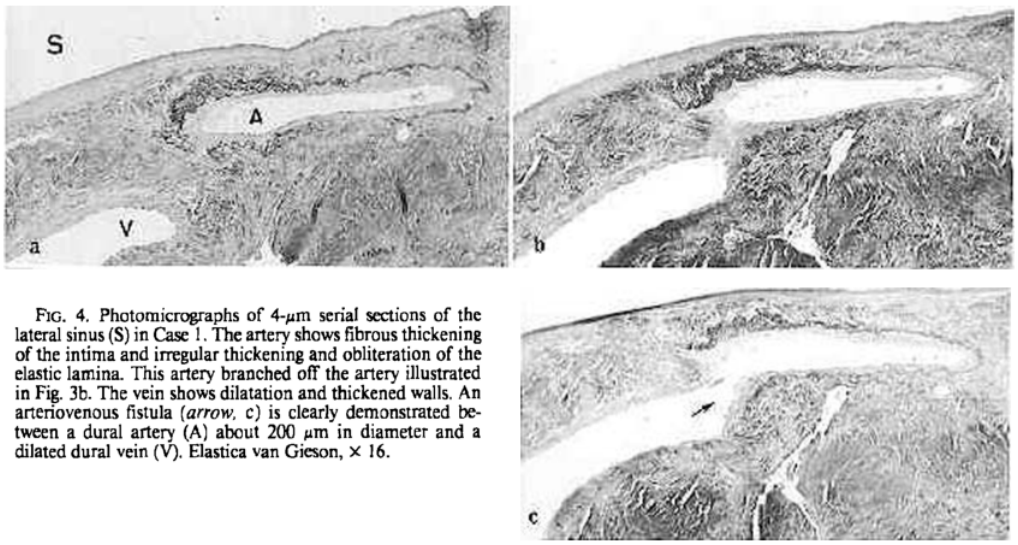


FIG. 4. Photomicrographs of 4-μm serial sections of the lateral sinus (S) in Case 1. The artery shows fibrous thickening of the intima and irregular thickening and obliteration of the elastic lamina. This artery branched off the artery illustrated in Fig. 3b. The vein shows dilatation and thickened walls. An arteriovenous fistula (*arrow, c*) is clearly demonstrated between a dural artery (A) about 200 μm in diameter and a dilated dural vein (V). Elastica van Gieson, × 16.

These AVF were present in the dura near the venous sinuses but not in their intima" and speculated that the mechanisms of the progression of dural AVF are as follow ; a single AVF formed in the dural near a venous sinus may become dilated because the blood flow increases due to a marked reduction in the peripheral vascular resistance. Once the fistula has formed arterial blood gathers around it via the well-developed vascular system. Dural veins dilate and become thickened. The influx of arterial blood induces thrombogensesis and injury to the intima into the sinus. Thrombus formation progress by repetition of above process. Venous sinus pressure increases, and organized thrombi with fibrous thickening of the sinus intima. Even more remarkable change take place in the dural veins, arteries, and the AVF themselves. In this vicious circle, new AVF develop.

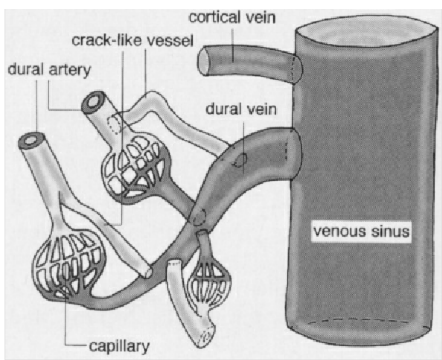


FIGURE 6. Illustration showing anastomosis between dural arteries and venous sinus through crack-like vessels.

Hamada et al.[4], mentioned that sinus hypertension caused by stenoocclusive disease of the venous sinuses and arterial hypertension force abnormal connection to open between arteries and veins in the dura mater, which may result in increasingly dilated venules and the formation of a dAVF. The direction of venous drainage from the fistula might be described by anatomic communication and pressure between crake-

like vessels of the dura meter, the sinus, and the cortical vein(fig).

Relationship between dAVF to sinus thrombosis

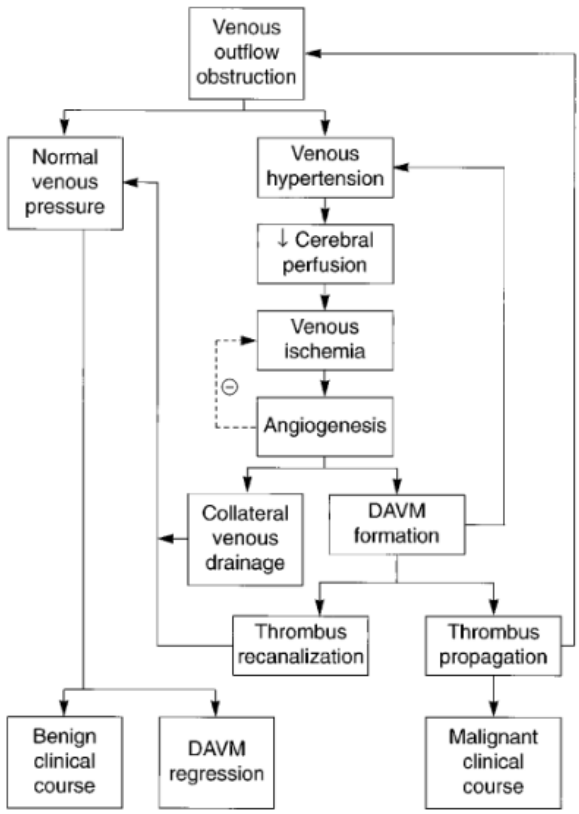
In several clinical and experimental studies, the most important factor related to the pathogenesis of dAVF is thought to be sinus thrombosis and venous or intra-sinus hypertension. Additionally, some investigators have suggested that sinus thrombosis does not always lead to the development of dAVF, but that venous hypertension is needed to form a dAVF

Sakaki, et al.[5], stressed the importance of secondary sinus thrombosis or thrombophlebitis, or late intrasinus hypertension for the genesis of dAVF following sacrifice of the sigmoid sinus.

Herman et al.[6], reported on a rat model subjected to various hemodynamic stresses. They suggested the importance not only of sinus thrombosis but also of sinus hypertension in the development of dAVF., based on the result in their rat model, in which the rate for new dAVFs was higher in rats with sinus thrombosis and venous hypertension than in those with venous hypertension only.

Angiogenesis and dAVF

Uranishi et al.[7], investigated the expression of the angiogenic factors(basic fibroblastic growth factor ; bFGF, vascular endothelial growth factor ; VEGF) in dAVF obtained from surgical specimens. They observed the expression of bFGF and VEGF in the dAVF. The factors stimulating bFGF and VEGF in the dAVF are not known, but it might be possible that tissue hypoxia or intraluminal shear stress resulting from venous hypertension stimulates the expression of these angiogenic growth factors.



Lawton et al.[8], established hypothesis of dAVF formation(fig). Briefly, venous hypertension induced by an obstruction to venous outflow, such as a sinus thrombus, would initiate the pathogenesis of dAVF. Venous hypertension reduces cerebral perfusion and might produce ischemia. Tissue hypoxia normally stimulates angiogenesis in an attempt to reverse the ischemia. Aberrant angiogenic activity by dural blood vessels would then lead to arteriovenous shunting into the dural sinuses and to dAVF formation. Arterialization of the venous sinuses exacerbates venous hypertension and outflow occlusion, thereby creating a vicious circle that would enlarge the dAVF and lead to a more dangerous clinical course.

Classification of dAVF

The first comprehensive classificationof intracranial dAVFs based on radiological anatomy was proposed by Djinjkian and colleagues in 1977 ; it has subsequently been modified by Connard, et al,(Cognard classification). In their series of 204 patients, Cognard, et al., were able to show a relationship between type and aggressive presentation. In the Cognardreport, type I dAVFs had a benign course,in type II, reflux into the sinus induced intracraninal hypertension in 20% of cases, and reflux into cortical veins induced hemorrhage in 10%. Hemorrhage was present in 40% of cases of type III dAVFs and 65% of type IV. Type V produced progressive myelopathy in 50% of cases.

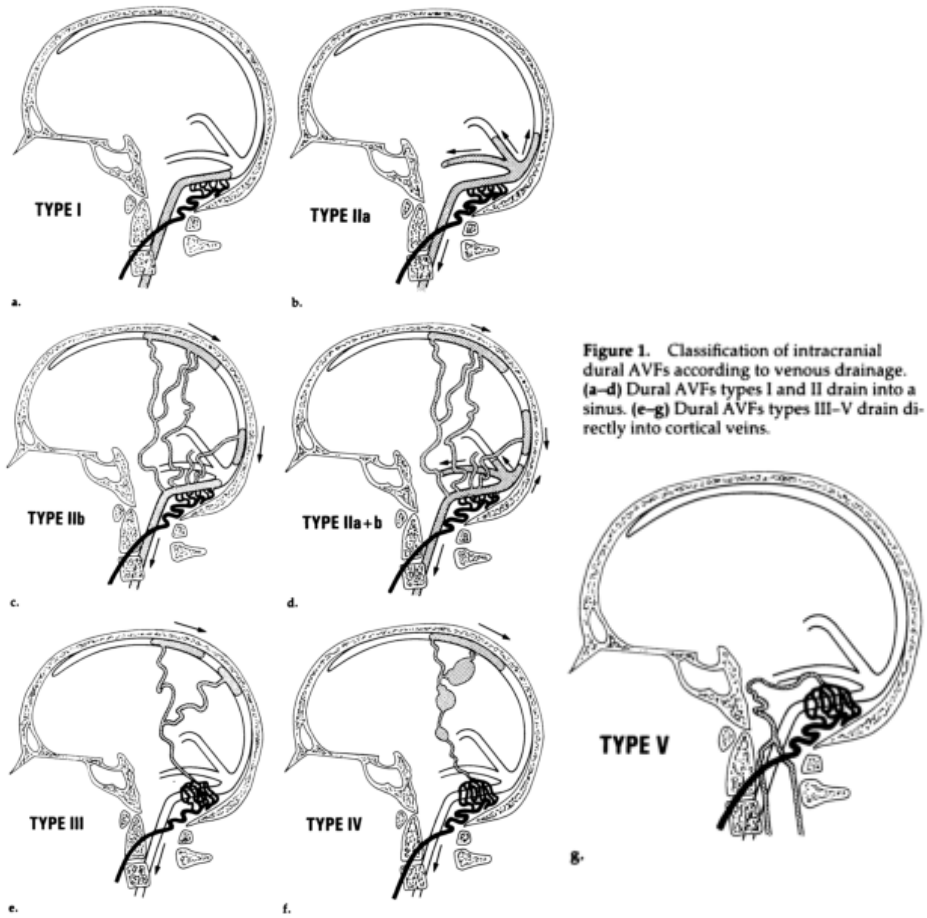


Figure 1. Classification of intracranial dural AVFs according to venous drainage. **(a–d)** Dural AVFs types I and II drain into a sinus. **(e–g)** Dural AVFs types III–V drain directly into cortical veins.

Borden Classification of Dural Arteriovenous Fistulas	
Type I	Anterograde drainage into the dural sinus/meningeal vein
Type II	Anterograde drainage into dural sinus & retrograde drainage into cortical veins
Type III	Isolated retrograde drainage: 1. Drains directly into cortical veins 2. Trapped segment of sinus with reflux into cortical veins 3. Venous varix/ dural lake with reflux into cortical veins

A similar, but simplified, version of this classification was proposed by Borden, et al.(Borden classification). They used five cases to demonstrate how their classification might be applied, suggesting its efficacy as a mode of predicting lesion behavior and how it might serve as a rationale for treatment.

Accurate diagnosis and classification of dAVFs is essential in identifying patients with high-risk lesions and to triage them toward appropriated therapies. The Borden and Cognard classification schemes, which have been well substantiated as predictors of dAVF behavior, both emphasize the relationship between cortical venous drainage (CVD) and increased risk of hemorrhage or nonhemorrhagicneurologic deficits. The absence of CVD (Borden I ; CognardIIa) is associated with a benign natural history. The presence of CVD (Borden II, III ; CognardIIb-V) indicates a more aggressive lesion.

Davies, et al.[9], investigated validity of classification for clinical presentation of intracranial dAVF. They propose that the term "retrograde leptomeningeal venous drainage" most accurately describes that single most important feature, although the term "cortical venous drainage" used by most authors (cognard, borden). Retrograde leptomeningeal venous drainage was most often seen in the dienchephalon involving the deep system only(fig)

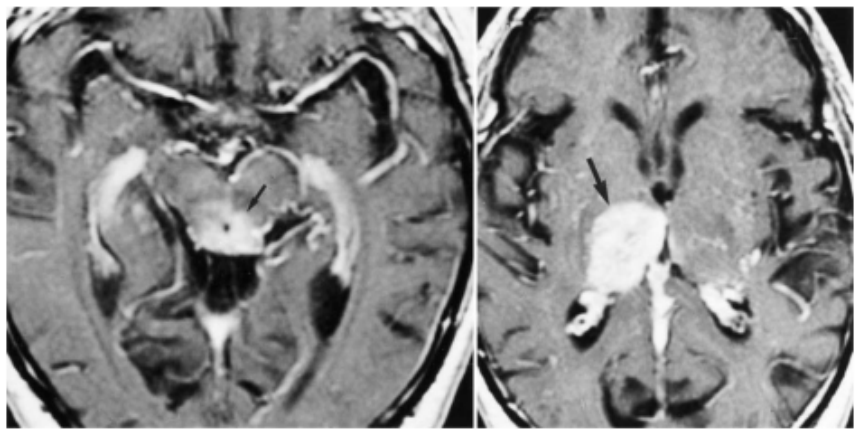


FIG. 2. Contrast-enhanced T_1-weighted axial magnetic resonance images demonstrating contrast enhancement in the territory of leptomeningeal veins in the deep system subjected to retrograde flow from an intracranial dural arteriovenous fistula. *Left:* Dorsal midbrain *(arrow)*. *Right:* Right thalamus *(arrow)*.

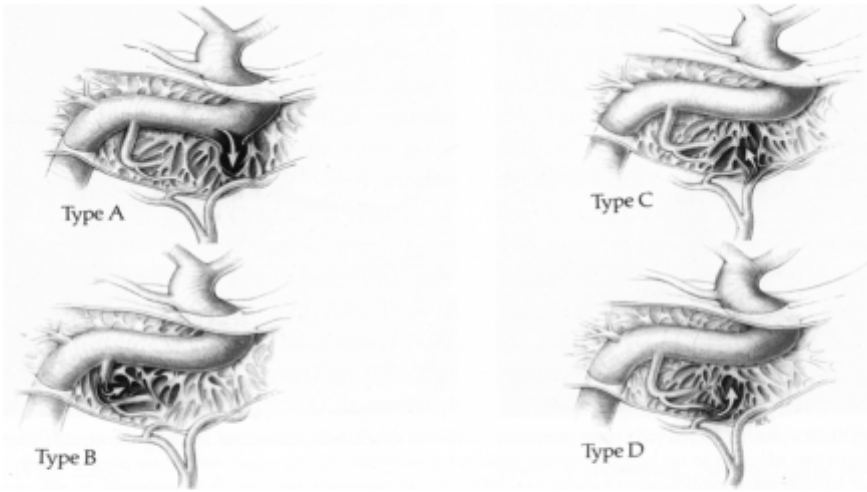
They proposed that the poor prognosis of lesion in "dangerous" locations in purely a function of their possession of a more dangerous venous anatomy : that is, regional venous anatomy enhances the possibility or mandates retrograde leptomeningeal venous drainage in some location.

Carotid Cavernous fistulae (CCF)

CCF arising from a defect in the cavernous segment of the ICA are called direct fistulae because the drainage into the cavernous sinus(CS) arises directly via the ICA. CCF resulting from dAVF supplied by ECA and ICA dural branches are traditionally call indirect, or dural, fistulae (dAVF of the cavernous sinus)

According with Barrow's classification, CCF could be classified in two groups : direct and indirect. Barrow's classification of CCF is based on the pattern of arterial supply. Barrow type A(direct) usually present a single connection between the internal carotid artery and the ipsilateral cavernous sinus. This type CCF usually show high flow and it is frequently caused by facial trauma. In contrast, indirect CCF are divided into 3 type : b, C and D. Barrow type B usually shows a connection between meningeal branches of the internal carotid and the sinus. Barrow type C is characterized by connections between meningeal branches of the external carotid and the sinus. Finally, Barrow type D is characterized by connections between meningeal branches of the internal and external carotid and the sinus.

Direct CCF are usually caused by severe head injuries or ruptured of cavernous aneurysms. In addition, they have also been linked with other surgical trauma such as rhinoplasty, orbital floor fractures reductions, partial maxillectomy, nasopharyngeal biopsy and Le Fort 1 osteotomy. In contrast, the etiology of most indirect CCF is idiopathic.



Classification of spontaneous carotid cavernous fistulas (CCFs) after Barrow 1985 (Barrow Neurologic Institute Quarterly, 1991;7:2).
Type A, direct fistula through a hole in the wall of the ICA (high -flow)
Type B, DCSF, indirect fistula supplied by ECA-feeder (low-flow)
Type C, DCSF, indirect fistula supplied by ICA-feeder (low-flow)
Type D, DCSF, indirect fistula supplied by ECA and ICA-feeder (low-flow)

TABLE 1. Proposed Venous Drainage–Based Classification System for Carotid Cavernous Fistulae

Type	Venous Drainage
1	Posterior/inferior drainage only[a]
2	Posterior/inferior and anterior drainage
3	Anterior drainage only[b]
4	Retrograde drainage into cortical veins ± other routes of venous drainage[c]
5	High-flow direct shunt between cavernous internal carotid artery and cavernous sinus (Barrow type A) ± multiple routes of venous drainage

[a]Posterior/inferior drainage: inferior petrosal sinuses, superior petrosal sinus, pterygoid, and parapharyngeal plexus.
[b]Anterior drainage: superior and inferior ophthalmic veins.
[c]Cortical drainage: superficial middle cerebral veins, perimesencephalic, and cerebellar venous system.

Thomas, et al.[10], proposedto venous drainage—based classification system for CCF. Angioarchitecture of the arterial side of the fistula determines the Barrow type, the most widely adopted system to classify CCF. However, the Barrow classification is not very practical from clinical and therapeutic standpoint, as symptomatology and current treatment approach are influenced largely by venous drainage.

Posterior/inferior drainage was defined as drainage that occurred primarily through the superior and inferior petrosal sinuses, pterygoid and parapharyngeal plexus. Anterior drainage defines drainage through the superior and inferior ophthalmic veins. Cortical drainage was defined as filling of the superficial middle cerebral veins, perimesencephalic, and cerebellar venous system.

Diagnosis of dAVF

The diagnosis of dAVFs at an early stage may be difficult because of nonspecific clinical and imaging findings. The goal of imaging is not only to determine the presence or absence of a dAVF but also to clarify the pattern of venous drainage.

Conventional cross-sectional imaging

Although the diagnosis of dAVFs has traditionally been by DSA, many of these lesions are now first detected or suspected on cross-sectional imaging. Noncontrast brain CT is often used as an initial screening tool to determine the presence of hemorrhage or edema from venous congestion. MRI can demonstrate engorged vessels, dilated venous pouches, or abnormal vascular enhancement in the presence of a dAVF. Venous hypertension in high-grade lesions is also thought to contribute to abnormalities such as white matter T2 hyperintensity, intracranial hemorrhage, or venous infarction. Low-grade lesions may exhibit only flow-void clustering, engorged veins, or proptosis. The presence of any suspicious findings on MRI should warrant further imaging evaluation with dynamic CTA, MRA, or DSA for clarification of lesion grade and management decision making.

Susceptibility-Weighted imaging

SWI can accurately depict retrograde CVD associated with dAVF. In the setting of dAVF there is impaired venous drainage and increased venous pressure, resulting in cortical venous engorgement, as well as prolonged venous stagnation, leading to increased venous oxygen extraction. These factors are thought to result in increased prominence of cortical veins on SWI in the setting of retrograde CVD with dAVF. SWI can depicts dilated superficial veins involving the ipsilateral cerebral hemisphere in dAVF with retrograde CVD.

MR angiography

3D TOF MRA is limited in the evaluation of dAVFs because of the lack of hemodynamic information. Lesions with smaller and multiple arterial feeders and draining veins, as commonly seen in carotid cavernous fistulas, are also more difficult to visualize precisely. Recently, whole-head time resolved MRA(trMRA) have study as a screening and surveillance tool.

CT angiography

dAVFs can be obscured by overlapping osseous structures on conventional CTA, reducing the sensitivity of the modality to as low as 15.4% in some studies. The advent of 320-detector-row CT scanners has also opened investigations into 4D dynamic CTA for the evaluation of dAVF. The appeal of this technology is similar to that of trMRA, as a potential tool to replace DSA for primary diagnosis and follow-up in patients who would otherwise require repeat DSA studies.

2D DSA and C-arm cone-beam CT

Despite advancements in noninvasive imaging modalities, conventional DSA remains the gold standard for detection and classification of dAVFs. DSA allow detection of small lesions that may be missed by other modalities. Ability to perform selective injections allow for precise identification of early dural venous sinus filling or cortical venous reflux. The 3d cone-beam CT, also called flat detector CT had a high spatial resolution and can clearly delineate venous structures that are often obscured by the effects of contrast dilution or motion artifact on DSA. These advantages allow it to accurately demonstrate fistulous points and visualize even very small arterial feeders or drain veins without the need for additional selective DSA injections.

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Dural AVF, Endovascular treatment

권순찬
울산대학교병원

Endovascular treatment is the primary treatment modality for dural arteriovenous shunts (DAVSs). With advancements of endovascular techniques, numerous routes of access and different occlusion methods are available. Endovascular strategies must be carefully tailored to the individual patientThe approach toan individual DAVSs is dictated by a variety of factors including operator's preference for a specific embolic agent, angio-architecture of the fistula, clinical symptoms, and routes of access available.

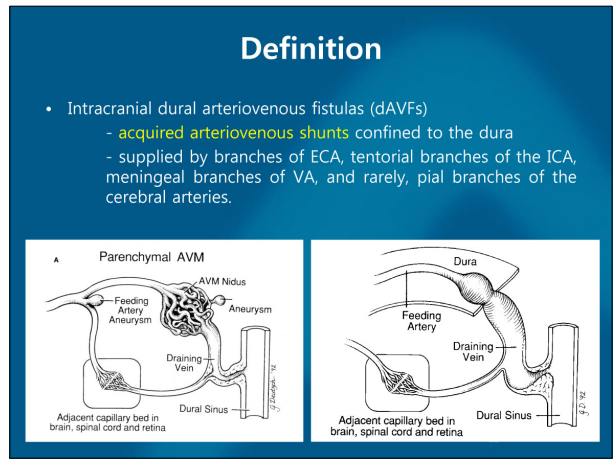
Endovascular treatment strategies can be divided into trans-arterial and trans-veous approach. Generally trans-arterial embolization alone has limited effectiveness, more often palliative or preparative treatment before more definite therapy. But, with the availability of Onyx as new highly penetrable embolic agent, there has been a resurgence of interest in trans-arterial approaches. Under appropriate circumstances, trans-venous embolization is highly effective to achieve curative obliteration of high-risk DAVSs.

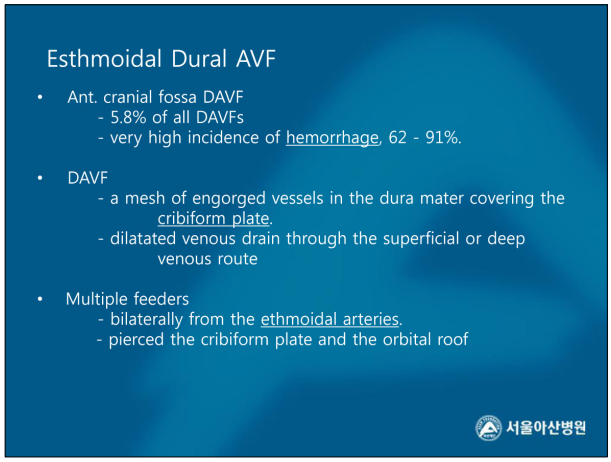
I would like to review endovascular approaches for DAVSs by Topology, and share our limited experiences during the last 5 years.

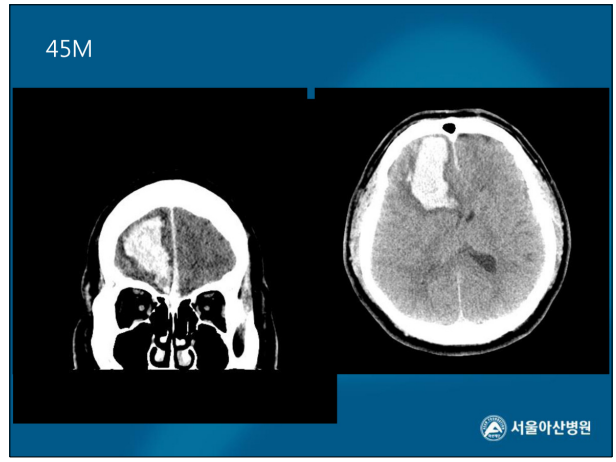
Surgical treatment

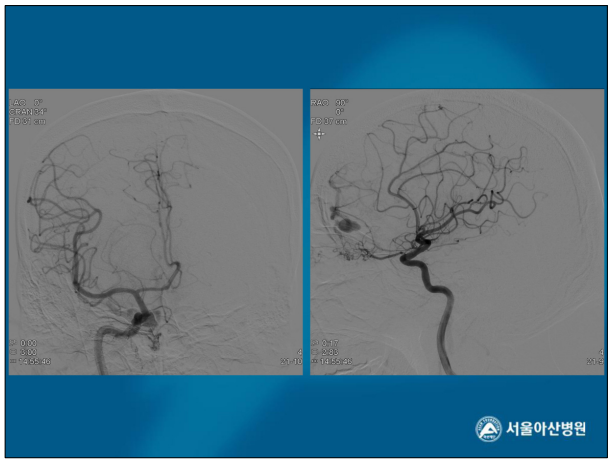
안재성, 양구형, 정재우

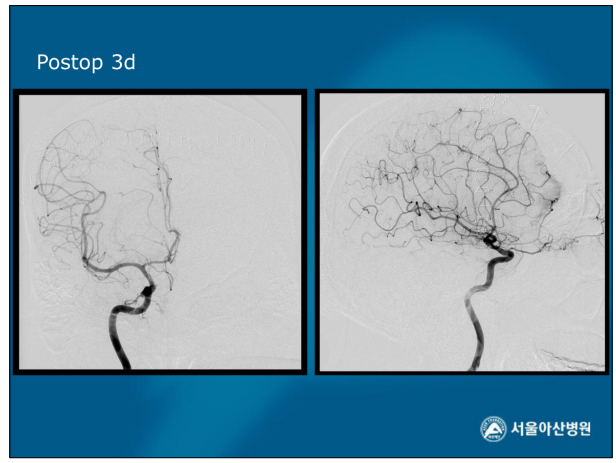
울산대학교 서울아산병원 신경외과

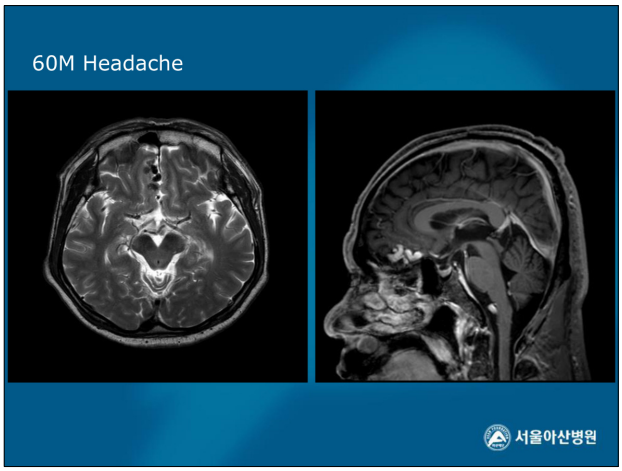


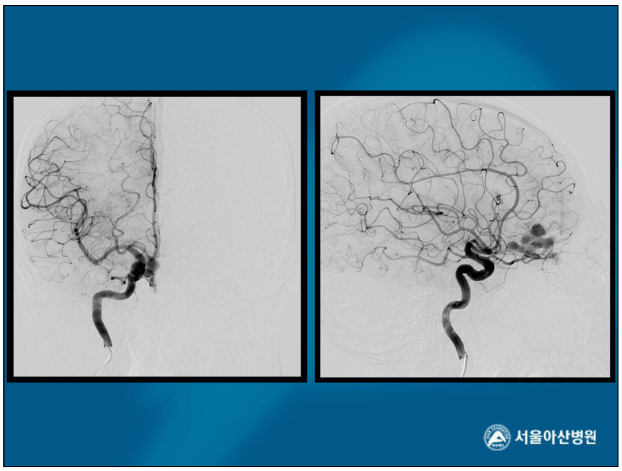









60M Headache
서울아산병원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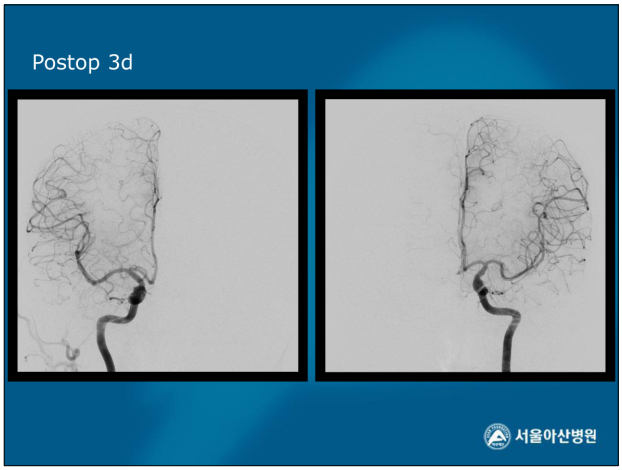
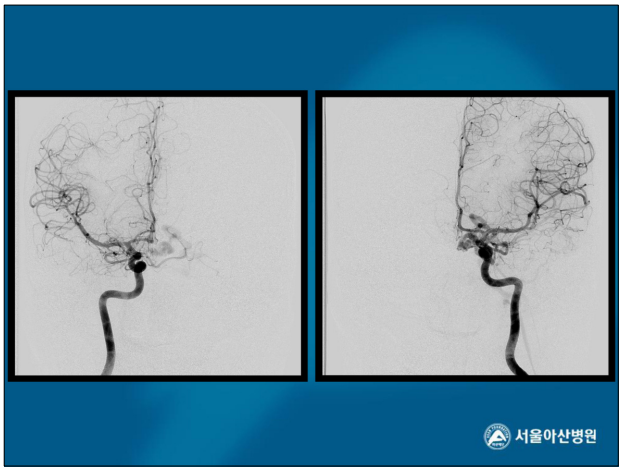

Postop 3d
서울아산병원


45M Headache
서울아산병원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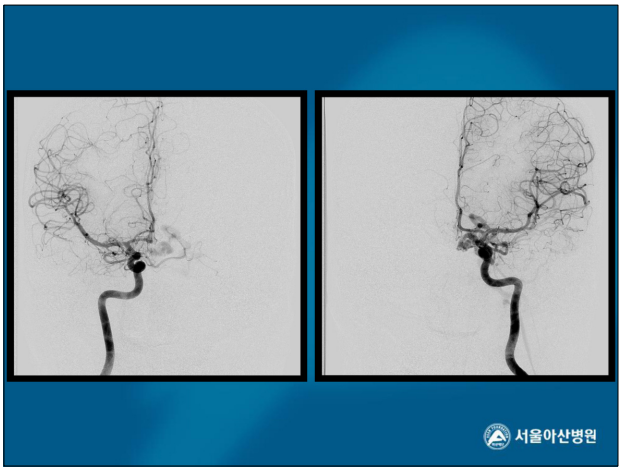
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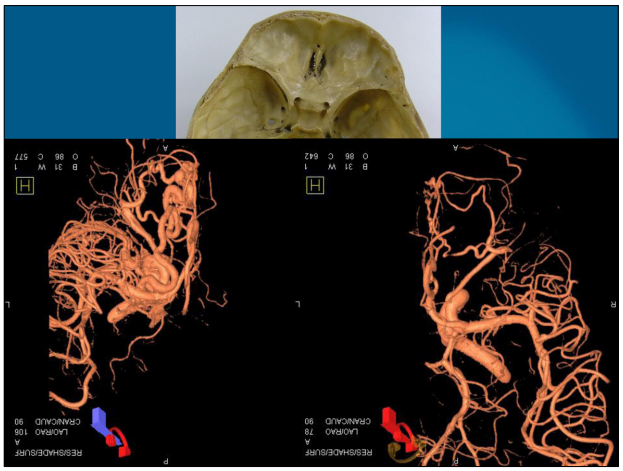

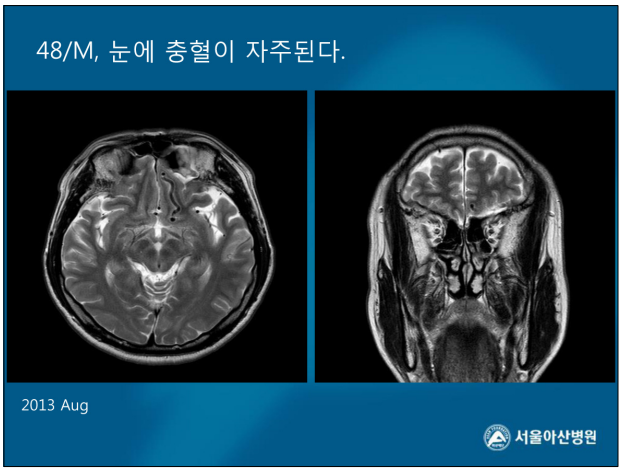
48/M, 눈에 충혈이 자주된다.
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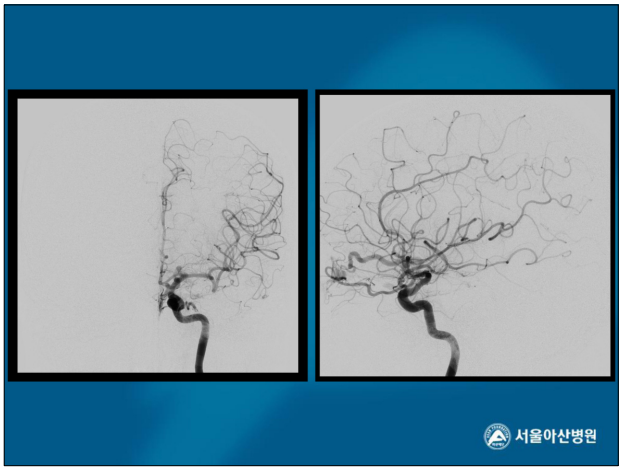
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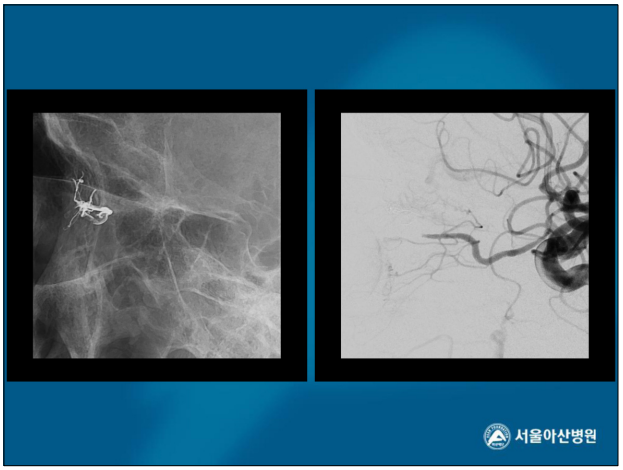
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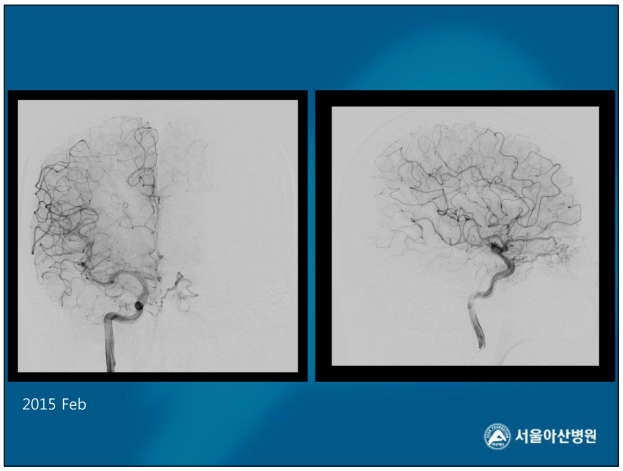
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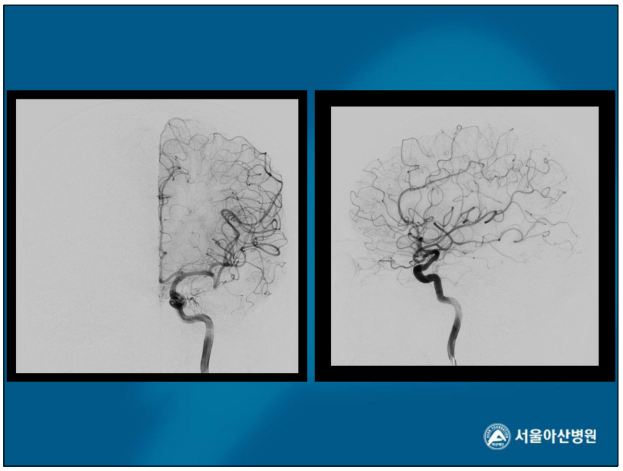
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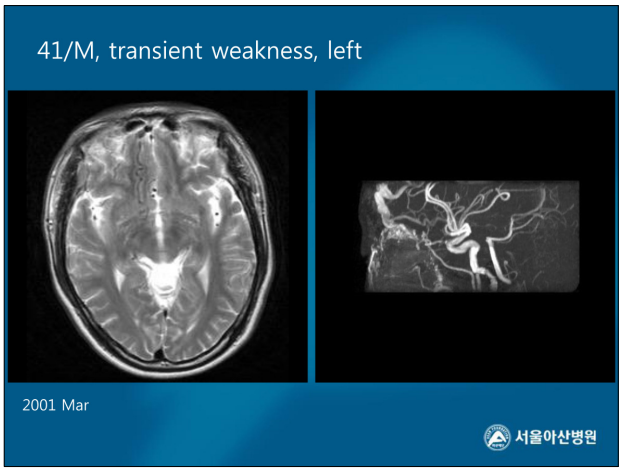
41/M, transient weakness, left
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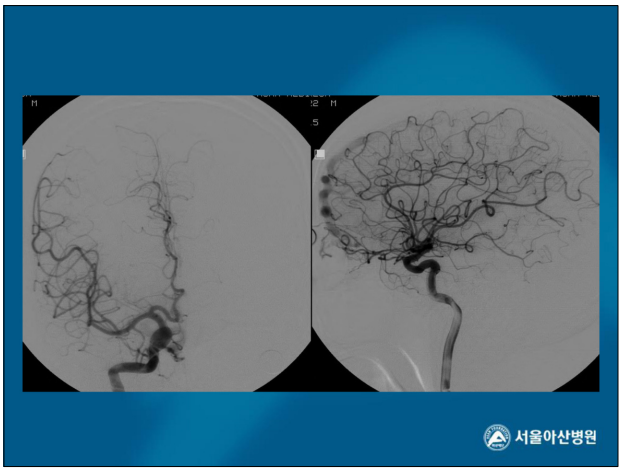
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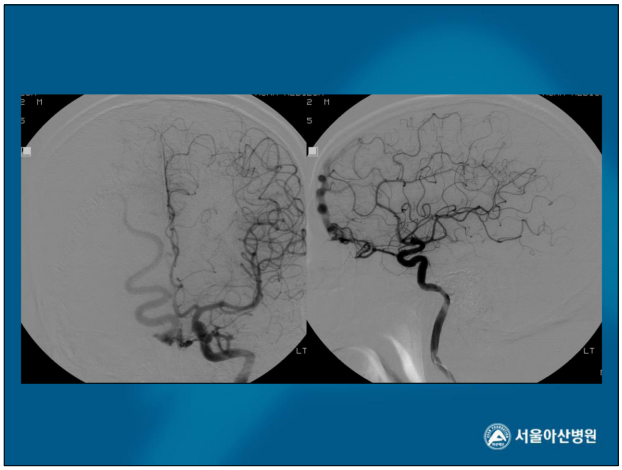
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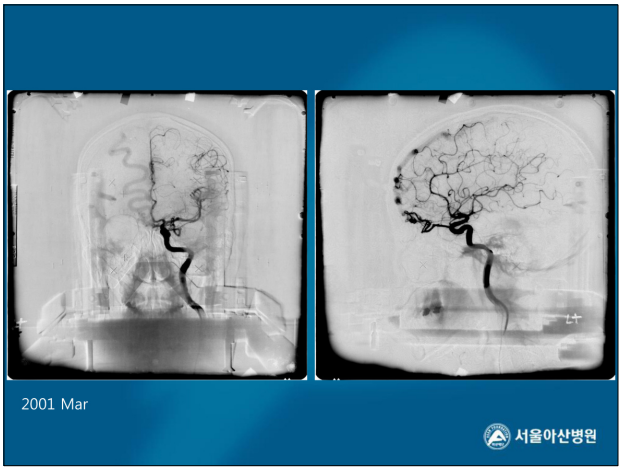
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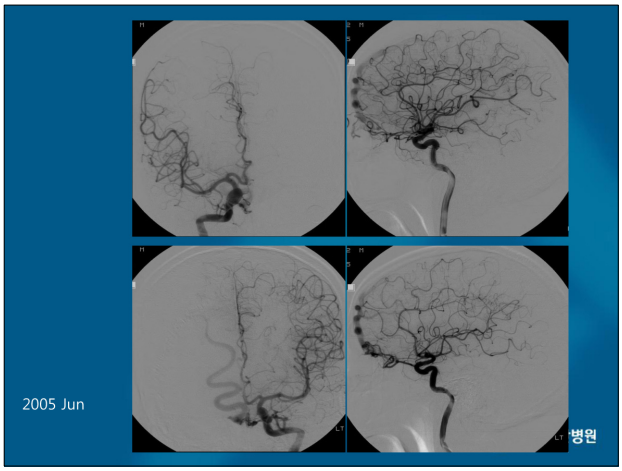
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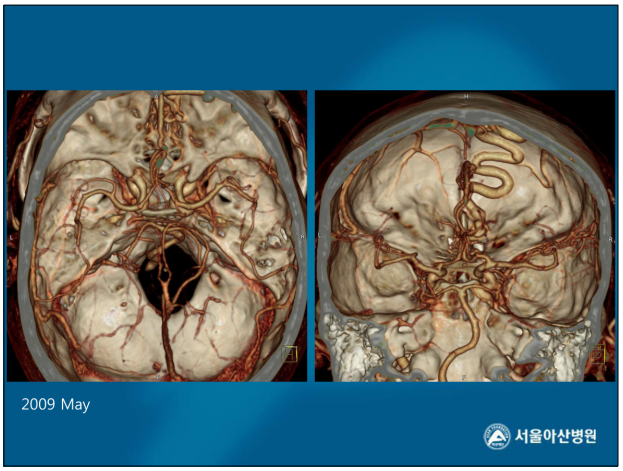

2009 May
서울아산병원

Therapeutic options

- Microsurgery
- Embolization
  - has a difficulty to access and a high risk of visual impairment
  - often did not achieve complete occlusion & higher recurrence rate than microsurgery.
- Radiosurgery
  - a latency period untill occlusion is crucially not acceptable.

서울아산병원

AMC series, 2011 Jan ~ 2016 April

		presentation	ICA feeder	ECA feeder	Cortical venous reflux	Drainage	6 mo outcome (GOS)
Case 1	57M	ICH/SAH	Bilateral Ethmoidal a. (non-dominant)	No	Lt. frontal : Present	Single Lt. : pterygoid V. plexus	GOS 5
Case 2	45M	headache	Bilateral Ethmoidal a. (Lt.-dominant)	No	Rt. frontal : Present	Single Rt. : sagittal sinus spheno-parietal sinus	GOS 5
Case 3	52M	headache	Bilateral Ethmoidal a. (non-dominant)	Bilateral ECA (STA/MMA)	Rt. frontal : Present	Bilateral Rt. dominant : sagittal sinus	GOS 5
Case 4	71M	ICH/SAH	Bilateral Ethmoidal a. (Rt. dominant)	No	Rt. frontal : Present c venous aneurysm	Bilateral Rt. dominant : basal vein	GOS 5
Case 5	49M	Decreased vision acuity	Bilateral Ethmoidal a. (Lt. dominant)	No	Lt. frontal : Present	Single Lt. : Lt. Cavernous Sinus	GOS 5
Case 6	55M	Subjective motor weakness	Bilateral Ethmoidal a.	No	Lt. frontal : Present	Single Lt. : sagittal sinus	GOS 5
Case 7	46M	ICH/SDH	Bilateral Ethmoidal a.	No	Lt. frontal : Present	Multiple cortical v. d/t occlusion of SSS	GOS 5
Case 8	57M	ICH	Bilateral Ethmoidal a.	Bilateral ECA (sphenopalatine a.)	Rt. frontal : Present	Single Rt. : sagittal sinus	GOS 5
Case 9	52Y	Dizziness, Diplopia Nausea, Headache	Bilateral Ethmoidal a.	Bilateral ECA (internal maxillary a.)	Lt. frontal : Present	Single Lt. : sagittal sinus	(GOS 5)
Case 10	60M	Asypmtomatic	Bilateral Ethmoidal a.	Bilateral ECA (sphenopalatine a.)	Rt. frontal : Present	Bilateral Rt. dominant : sagittal sinus	(GOS 5)
Case 11	45M	Headache	Bilateral Ethmoidal a.	Bilateral ECA (internal maxillary a. / MMA)	Lt. frontal : Present	Single Lt. : Lt. Cavernous Sinus	(GOS 5)

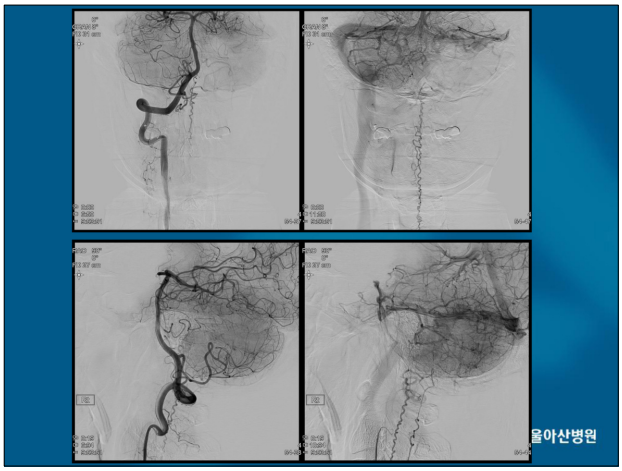
Post fossa dural AVF

서울아산병원

64/M, 대소변이 보기 힘

2014 Apr : 좌측 다리가 저리다
2015 Mar : 지팡이 사용
Apr : embo fail
휠체어 사용, 대소변 보기 힘들다

서울아산병원



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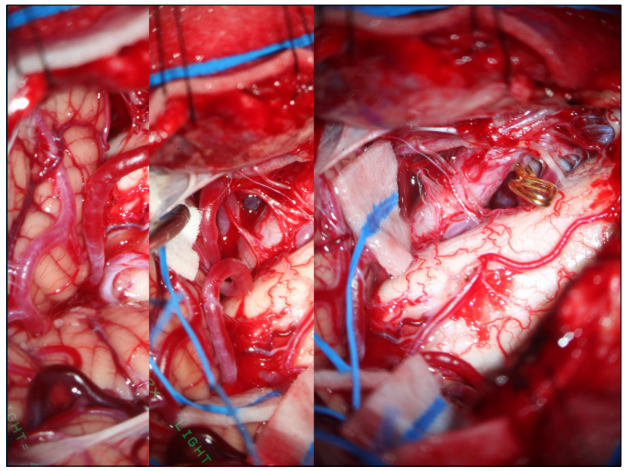
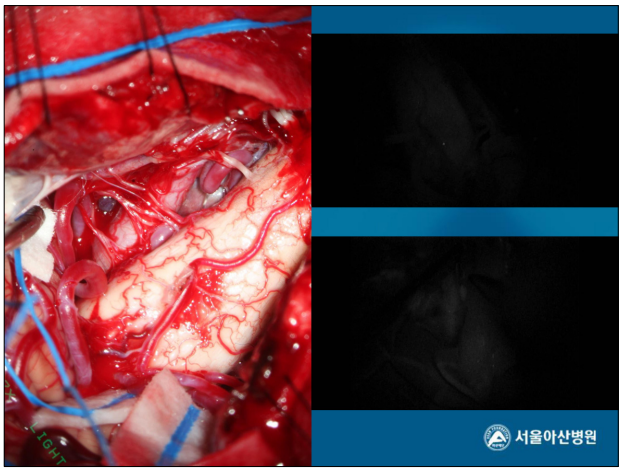




Conclusion

- Although the ant. cranial fossa ethmoidal DAVF has high incidence of hemorrhage (50%), microsurgical treatment with bilateral subfrontal appoach showed good GOS.
- Intraoperative ICG angiography ensure good radiological obliteration to help clarifying the arterialized venous drain and confirming the disconnection of fistula.
- It is important that we should confirm the disconnection of fistula bilaterally during operation, because some cases (50% in our cases) showed bilateral venous drain (dominant and non dominant occulted drainage). If not, recurrence can occur.

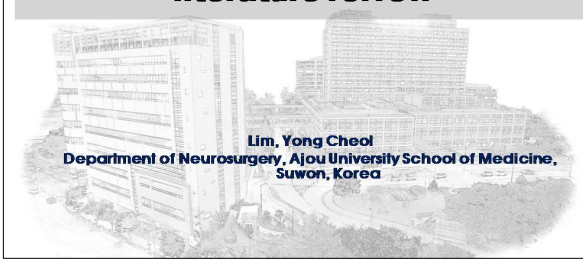
ASAN Medical Center

Dural-AVF Current recommendation and literature reivew

Lim, Youn Cheol

Deparlment of Neurosurgery, Ajou Universiiy School of Medicine, Suwon, Korea

Dural-AVF Current recommendation and literature reivew



Lim, Yong Cheol
Department of Neurosurgery, Ajou University School of Medicine, Suwon, Korea

Introduction

- Rare
  - 0.16-0.29/10,000/year
  - 7%(95% CI 4%-12%) of intracranial AVM
  - limited clinical course, outcome of managements
- Long-term Morbidity d/t
  - intracranial hemorrhage (ICH)
  - nonhemorrhagic focal neurological deficit (NFND)
  - epilepsy
  - visual and orbital disorders
  - headache
  - tinnitus

- Classification of dAVFs

Borden classification	Cognard classification	Lalwani classification	Barrow classification
I Venous sinus drainage, anterograde flow	I Main sinus drainage, anterograde flow	1 No restriction with normal antegrade flow	A Direct internal carotid-cavernous fistula
II Venous sinus drainage, retrograde flow into leptomeningeal veins	II Main sinus grainage, reflux into: a Sinus b Leptomeningeal veins a+b Sinus and leptomeningeal veins	2 Antegrade and retrograde venous drainage, with or without cortical drainage	B indirect shunts between the ICA and the cavernous sinus
III Drainage into leptomeningeal veins	III Direct leptomeningeal venous drainage without venous ectasia	3 Retrograde and cortical venous drainage without antegrade drainage	C indirect shunts between the meningeal branches of the ECA and the cavernous sinus
	IV Direct leptomeningeal venous drainage with venous ectasia	4 Only cortical venous drainage	D indirect shunt between the meningeal branches of the ECA, ICA and the cavernous sinus

Lalwani classification: venous restriction grade
Barrow classification: cavernous sius dAVF
Venous ectasia: venous diameter>5mm

Management Options

- Conservative Management
  - reasonable situation
    - ✓ asymptomatic
    - ✓ minimally symptomatic Borden Type I
    - ✓ without evidence of cortical venous drainage
  - spontaneous regression
    - ✓ reported in up to 73%
    - ✓ intermittent manual compression
    - ✓ cavernous sinus or transverse-sigmoid dAVF
- Endovascular techniques
  - most effective Tx. of dAVFs: occlusion of draining vein
  - transvenous embolization(TVE): highest success rate
  - transarterial embolization(TAE)
    - ✓ embolic material is pushed through the nidus into the venous side
    - ✓ if only feeding arteries are occluded, not draining vein
      - collateral vessel developed (recruitment of a. supply)
      - redirection of venous outflow
      - increase risk of hemorrhage
    - ✓ use only palliative
  - preserve normal venous drain system
    - ✓ avoid venous hyperlension and hemorrhage

- Surgery
  - techniques
    - ✓ simple ligation of feeding a.
      - success rates: 0-8%
    - ✓ blood-soaked fistula resection and packing of the venous sinus
    - ✓ interruption of the draining v.
  - standard Tx. for anterior fossa dAVFs
  - hybrid surgical/endovascular procedures
    - ✓ surgical exposure of the SOV for embolization of the cavernous dAVFs
    - ✓ craniectomy with direct puncture of venous sinus
- Radiosurgery
  - preliminary reports: encouraging
  - combined with embolization
  - overall occlusion rate: 58-83%
    - ✓ higher obliteration rate with embolization followed by radiosurgery (83%) compared to radiosurgery alone (67%)

A systemic review and meta-analysis : prognosis & treatment

Int J Stroke 2014 9: 670-677

- Association between dAVFs anatomy and ICH or FND at presentation
  - retrograde leptomeningeal venous drainage (Cognard grades III-V, Borden grade III*)
  - 'pseudophlebitic' pattern of venous drainage (dilated, engorged, serpiginous morphology)
- "aggressive symptoms"
  : ICH, FND, seizure, venous infarction, intracranial hypertension, myelopathy, cognitive dysfunction
  - any type of leptomeningeal venous drainage (Cognard grades IIb, IIa+b, III-V)
  - tentorial dAVFs
  - tranverse/sigmoid/superior sagittal sinus location
  - male sex

Int J Stroke 2014 9: 670-677

- Untreated clinical course
  - death (2.6%), ICH (3.3%)
  - risk of ICH in the future
    : presence of venous varix
    : presence of ICH in another
  - annual rate of ICH (1.8%)
    : in cortical venous drainage or reflux (3.7%)
    : ICH at presented (7.4%), without ICH at presented (1.5%)
- Treatment outcome
  - mortality: 1.2% (0.6-1.8%)
  - nonfatal ICH: 0.7% (0.3-1.4%)
  - nonfatal infarction: 0.7% (0.3-1.4%)
  - combined risk: 2.5% (1.4-3.9%)

Transverse-Sigmoid (Lateral) Sinus dAVFs

- Clinical features
  - female>male, Lt. > Rt.
  - Borden Type I
    - ✓ female 79%, median age of Sx. onset 54yrs
    - ✓ unilateral pulsatile tinnitus
    - ✓ normal MRI
  - associated with Meningioma
- Anatomy
  - Feeders
    - ✓ ECA: OA, PAA, APA, MMA, accessory MA, STA
    - ✓ ICA: MHT, ILT
    - ✓ VA: posterior MA, cerebellarfalcine a, muscular branches
  - Venous drainage
    - ✓ TS, SS: stenotic or occluded in significant percentage
    - ✓ retrograde venous flow --> occipital, parietal cortical veins

- Presentation
  - ✓ Hemorrhage, intracranial venous hypertension: 11%
  - ✓ Sx. without hemorrhage
    - pulsatile tinnitus
    - headache
    - visual disturbance
    - mastoid pain/otalgia
    - dizziness
    - hydrocephalus
    - trigeminal neuralgia
- Management
  - General information
    - often benign
    - frequently treat only to alleviate symptoms
    - aggressive characteristics: should be treated
    - meta-analysis (1997): combined Tx. (EV+Surgical Tx): significantly more effective
  - Manual compression
    - Technique: compress the pulsatile OA, 30min TID
    - Results
      - 25% of complete thrombosis may occur within 4-6 wks
      - transient relief from dAVFs-associated headaches

Surgery
- early surgery technique: complete excision coupled with packing of the SS --> blood loss
- surgical disconnection of the draining veins: good results

Embolization
- Venous embolization
  - ✓ suitable venous anatomy
    - » compromised, no longer contribute to drainage of normal tissues
    - » Parallel venous channel
    - » separate from, but in communication with the TS or SS
  - ✓ approaches
    - » femoral venous access
    - » direct puncture of the IJV
    - » craniectomy with direct puncture of a venous sinus

- Arterial embolization
  - rarely curative
  - palliation, adjunct to VE or surgery
- Results
  - angiographic cure rate: 55-87.5%
  - symptom improvement: 90-96%
  - transient complications: 10-15%
  - permanent complications: 0-5%
- Venous sinus angioplasty and stenting
- Radiosurgery
  - angiographic cure rates: 55-87.5%
  - symptom improvement or resolution: 74-96%
  - no neurologic complications

Cavernous Sinus dAVFs

- Clinical features
  - incidence
    - ✓ F>M, 60-70th decade, Lt. > Rt.
  - Anatomy
    - ✓ feeders
      - bilateral
      - ECA: branches of IMA, MMA, accessory MA, APA
      - ICA: cavernous segment branches
    - ✓ venous drainage
      - variable
      - impaired venous drainage
      - enlargement of SOV
      - cortical venous drainage: 31-34%
    - ✓ inferior petrosal sinus dAVF
      - variant of CS dAVFs
      - 3% of intracranial dAVFs
      - similar clinical presentation of CS dAVFs

- Presentation
  - ✓"Red-eyed shunt syndrome"
  - ✓common finding
    - chemosis (94%)
    - exophthalmos (87%)
    - cranial nerve palsy (54%)
    - increased IOP (60%)
    - diplopia (51%)
    - impaired vision (28%)
    - pulsatile tinnitus
  - ✓bruit: >50%
  - ✓"white-eye" CC dAVFs
    - posterior venous drainage predominant
    - painful ocular motor nerve palsy
    - without congestive orbital features

- Management
  - treatment indications
    - ✓ visual deterioration
    - ✓ obtrusive diplopia
    - ✓ intolerable bruit or headache
    - ✓ malignant proptosis with untreatable corneal exposure
    - ✓ retrograde cortical venous drainage
  - meta-analysis (1997)
    - ✓ overall success rates: TVE 78%, TAE 62%
  - Manual compression
    - Technique
      - ✓ compress to locate the pulse of the carotid artery in the mid-neck region just lateral to the trachea
      - ✓ gradually increasing pressure until the pulse is stopped
      - ✓ 10-15s at a time, 2-3 times an hour
    - contraindication
      - ✓ cervical carotid artery disease: atherosclerosis, dissection
      - ✓ sick sinus syndrome
      - ✓ poor patient compliance
    - Results
      - ✓ 30% of cases closure: within 41 days

- Embolization
  - TVE
    - ✓IPS route
      - successful embolization: 64%
      - thrombosed IPS can be traversed in some cases: 0.035" guidewire use
    - ✓SOV route
      - surgical exposure
      - success rate: 92-100%
      - higher than trasfemoral route
      - percutaneous puncture of the SOV
    - ✓Alternative techniques for access
      - direct puncture of the IJV
      - transfemoral facial v. approach
      - superior petrosal sinus
      - sylvian v.
      - Pterygoid plexus
      - frontal v.

  - TAE: rarely curative, palliation in selective case
  - embolic material
    - detachable coil
    - NBCA
    - Onyx
  - Results (2 large recent series)
    - complete cure: 90-94.5%

- Radiosurgery
  - several reports
  - the results are generally favorable: obliteration rates>80%
  - wide variety of techniques used (dose, embolization, anatomy)

Tentorial (superior petrosal) dAVFs

- general information
  - location: petrous ridge, involves superior petrosal sinus
  - prone to be hemorrhage
  - difficult Tx. by surgery or embolization
  - all or nearly all, Borden type II or III
  - Picard classification
    - ✓Tentorial marginal type
      - along the free edge of the tentorium
    - ✓Tentorial lateral type
      - adjacent to the lateral venous sinuses
    - ✓Tentorial medial type
      - adjacent to the straight sinus and torcula

- Clinical features
  - Anatomy
    - ✓Feeders
      - bilateral, multiple fine feeders
      - MMA, MHT, PCA, OA, Posterior MA, SCA
    - ✓Venous drainage
      - retrograde in all cases
      - cerebral, cerebellar veins
      - Basal vein of Rosenthal
      - Pontine, paramesencephalic veins
      - cervical paramedullary spinal veins
  - Presentation
    - ✓hemorrhage, hemorrhage history: 80-90%
    - ✓pulsatile tinnitus, hemi-facial spasm, myelopathy visual problems, trigeminal neuralgia, hemisensory disturbance

- Management
  - general information
    - ✓aggressive nature
      - should be obliterated when feasible
      - incomplete obliteration should be avoid
      - late f/u angiography should be done
    - ✓No single Tx. strategy
  - Surgery
    - ✓most effective
    - ✓single, surgically accessible draining vein
    - ✓Technique
      - resection of the nidus: not necessary
      - coagulation, division of the arterialized draining veins
      - interruption of the draining vein
      - interruption of the arterial supply

- Embolization
  - ✓TVE
    - difficult or impossible
      - tortuous leptomeningeal drainage is not connected to a venous sinus
  - ✓TAE
    - NBCA (choice), Onyx (good alternative)
    - temporary balloon-occlusion of the ICA when a microcatheter is placed in the tentorial artery
      - stabilize microcatheter
      - flow arrest during injection of embolic agent
      - prevent reflux into the ICA
    - "reversible asystole"
      - trigeminocardiac reflex during TAE
- Radiosurgery
  - ✓risk to adjacent structures: brainstem, cranial nerve
  - ✓successful obliteration has been reported

Superior Sagittal Sinus dAVFs

- general information
  - M=F
  - Mid-portion of SSS
- Clinical features
  - Anatomy
    - ✓feeders: MMA, OA, STA, VA, PAA, anterior falx artery
    - ✓venous drainage
      - 2 pattern
        - » directly into the SS
        - » into cortical v.
  - Presentation
    - ✓hemorrhage: 30%<, SAH, ICH, SDH
    - ✓venous hypertension Sx: mental change, headache
    - ✓misdiagnosis: acute SS thrombosis

- Management
  - Surgery
    - ✓fairly straightforward and effective
    - ✓technique
      - skeletonization of SSS (disconnection of arterialized veins)
      - surgical exposure followed by direct puncture for embolization
    - ✓surgical obliteration: should be avoided d/t venous infarction
  - Embolization
    - ✓TVE
      - "angiographically remote"
    - ✓TAE
      - combined with surgery and radiosurgery
      - small series reported: cure 50%
  - Radiosurgery
    - ✓small series reported

Anterior Fossa dAVFs

- General information
  - always have retrograde leptomeningeal venous drainage: high risk hemorrhage
  - frequently supplied anterior ethmoidal branchies: difficult to EVT
  - M>F
- Clinical features
  - Anatomy
    - ✓feeder
      - anterior ethmoidal branchies: 84%
      - bilateral: 50%
      - others: IMA, MMA, STA, ACA
    - ✓drainage
      - intradural frontal veins (all)
  - Presentation
    - ✓hemorrhage: 62%
    - ✓visual loss, proptosis, chemosis
    - ✓diminished olfactory sensation, taste
    - ✓intracranial venous hypertension, dementia

- Management
  - Surgery
    - ✓first-line Tx.
    - ✓technique
      - pterional, low frontal craniotomy
      - interruption of fistulous connection between the arteries perforating the dura around the cribriform plate, drain veins
      - coagulation and division of connecting veins
      - excision of the dura
    - ✓Results
      - rate of obliteration: 95%
      - no surgical complications were reported
  - Embolization
    - ✓TVE
      - direct puncture of the IJV
    - ✓TAE
      - problematic: the proximity of the central retinal artery
        - » the microcatheter tip should be positioned distal to the origin of the central retinal artery
        - » provocative test: amytal, lidocaine
        - » embolic particle: 400micrometer< (the average diameter of the central retinal artery)
      - successful embolization was reported
  - Radiosurgery
    - ✓successful radiosurgery has been reported

Special lecture III

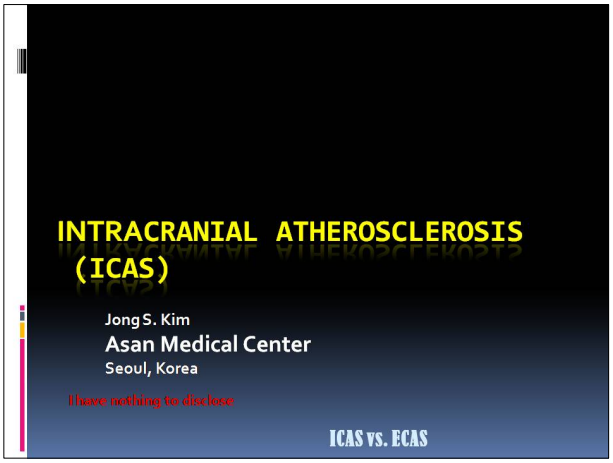
좌장 : 권병덕(울산대)

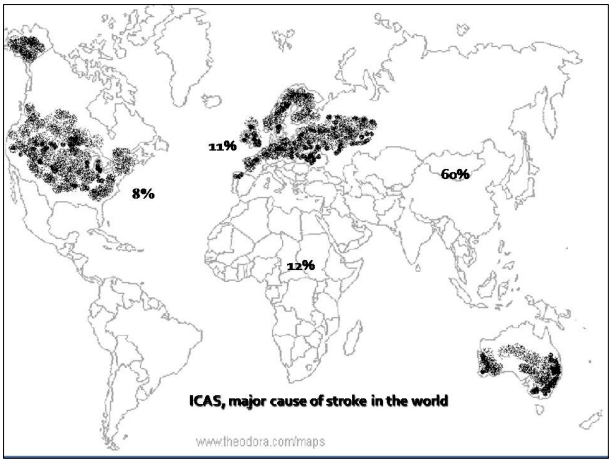
MCA steno-occlusion, classification & management

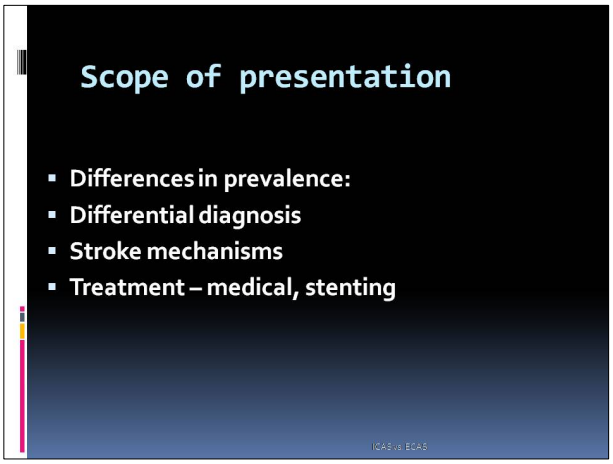
김종성(울산대 서울아산병원 신경과)

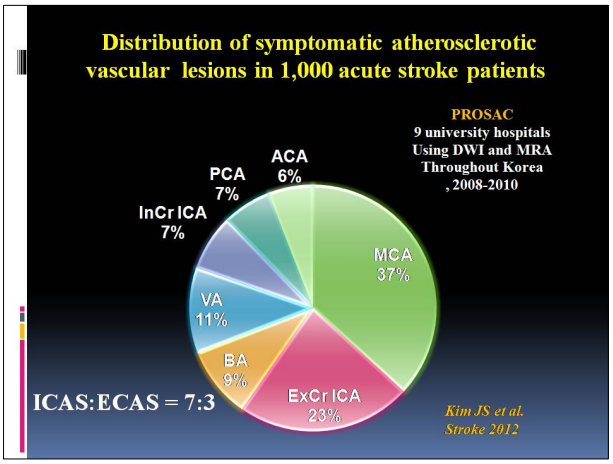
Intracranial Atherosclerosis(ICAS)

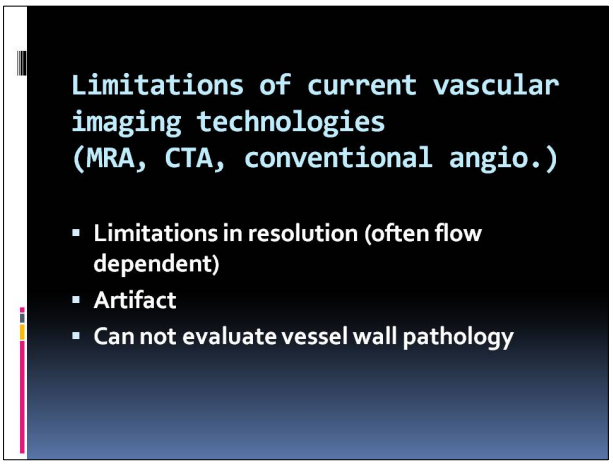
Jong S. Kim
Asan Medical Center Seoul, Korea











45-yr old man without risk factors -- Diagnosis ?

High-resolution vessel wall MRI (HR-MRI)

- T1-/T2-weighted imaging, proton-density imaging, contrast-enhanced T1-weighted imaging with turbo/fast spin-echo sequences or black-blood techniques
- For intracranial vessels, resolution of <1 mm (0.2-0.9 mm in 1.5-3 T MRI), a reconstructed 3D transverse imaging plane perpendicular to the arterial course, and the black-blood technique to suppress the arterial blood or cerebrospinal fluid signals

Choi et al. High resolution MRI
J Stroke 2015;17(3):1-18

High resolution vessel wall MRI

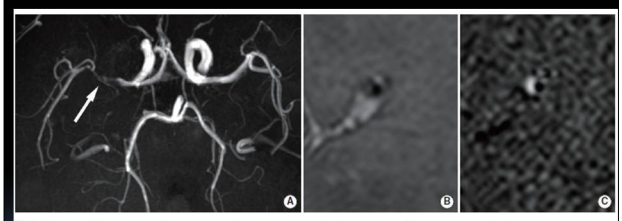


Figure 1. Intracranial atherosclerosis. A 49-year-old female patient presented with left-side weakness and four atherosclerotic risk factors. (A) Time-of-flight magnetic resonance angiograph showing severe stenosis in the right middle cerebral artery (arrow). (B) Proton-density image showing eccentric wall thickening and atherosclerotic plaques with a remodeling index of 1.47. (C) Contrast-enhanced T1-weighted image showing strong enhancement in eccentric atherosclerotic plaques.

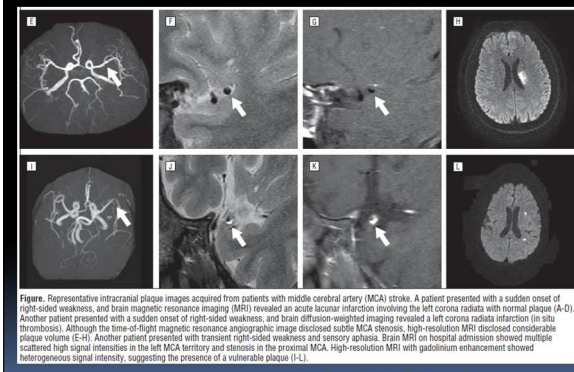


Figure. Representative intracranial plaque images acquired from patients with middle cerebral artery (MCA) stroke. A patient presented with a sudden onset of right-sided weakness, and brain magnetic resonance imaging (MRI) revealed an acute lacunar infarction involving the left corona radiata with normal plaque (A-D). Another patient presented with a sudden onset of right-sided weakness, and brain diffusion-weighted imaging revealed a left corona radiata infarction (in situ thrombosis). Although the time-of-flight magnetic resonance angiographic image disclosed subtle MCA stenosis, high-resolution MRI disclosed considerable plaque volume (E-H). Another patient presented with transient right-sided weakness and sensory aphasia. Brain MRI on hospital admission showed multiple scattered high signal intensities in the left MCA territory and stenosis in the proximal MCA. High-resolution MRI with gadolinium enhancement showed heterogeneous signal intensity, suggesting the presence of a vulnerable plaque (I-L).

Kim JM et al, Arch Neurol 2012

Table 1. Predominant HR-MRI characteristics of intracranial artery disease

	Atherosclerosis	Dissection	Moyamoya	Vasculitis	RCVS
Shape	Eccentric	Eccentric or combined	Concentric	Concentric (sometimes eccentric)	Concentric
Distribution	Any artery	Any artery (most common, VA)	Terminal ICA, proximal MCA, ACA	Medium- to small-sized vessels	Medium- to small-sized vessels
Signal intensity	Dependent on components (lipid, T1W iso/T2 hypo to iso; fibrous tissue, T1W/T2W iso; calcification, T1W/T2W dark)	Various (intramural hematoma, T1W hyper)			
Enhancement	Dependent on stage (+++ → +)	+/-	++/+	Dependent on stage (+++ → -)	Dependent on stage (+ → -)
Outer diameter	Positive or negative remodeling	Dependent on stage (Positive remodeling → restoration)	Negative remodeling		
Others	Intraplaque hemorrhage	Intimal flap, double lumen, intramural hematoma, or aneurysmal dilatation	Basal collaterals	Exclusive diagnosis	Exclusive diagnosis
Follow-up (resolution)	<30%	37.4%-75%	Progressive	Resolution with medication	Spontaneous reversibility

HR-MRI, high-resolution magnetic resonance imaging; RCVS, reversible cerebral vasoconstriction syndrome; VA, vertebral artery; ICA, internal carotid artery; MCA, middle cerebral artery; ACA, anterior cerebral artery.

Choi et al. High resolution MRI
J Stroke 2015;17(3):1-18

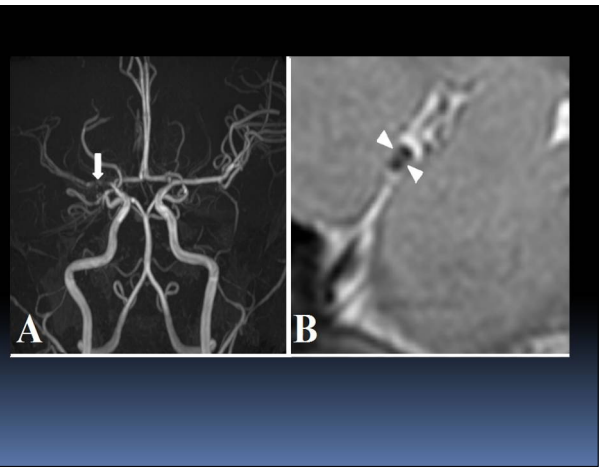
Impact of High resolution vessel wall MRI on differential diagnosis of MCA disease

- Patients who visited AMC with
- (1) unilateral MCA disease (≥50% stenosis or occlusion), (2) were ≤55 years old and had no or minimal (≤1) atherosclerotic risk factors (3) suspected as having ICAS on MRA
- We excluded patients with a confirmed diagnosis
- HR-MRI performed

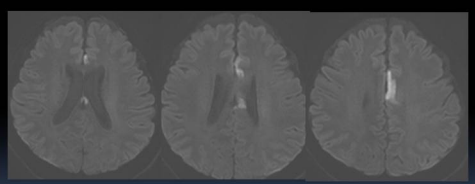
Ahn SH, Kim JS et al, Stroke 2015

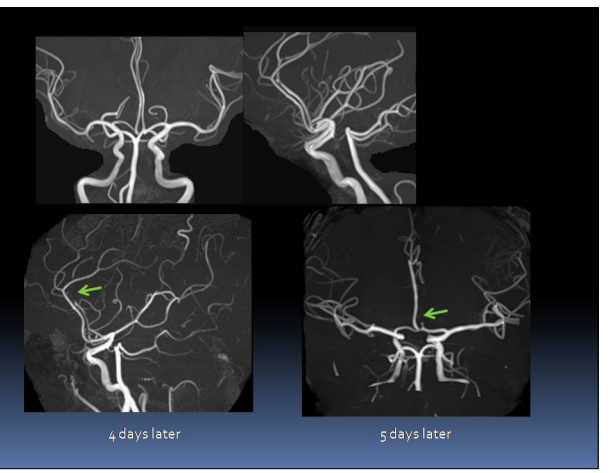
Table 1. Comparison of Clinical Variables Between HR-Athero and HR-Nonathero Patients

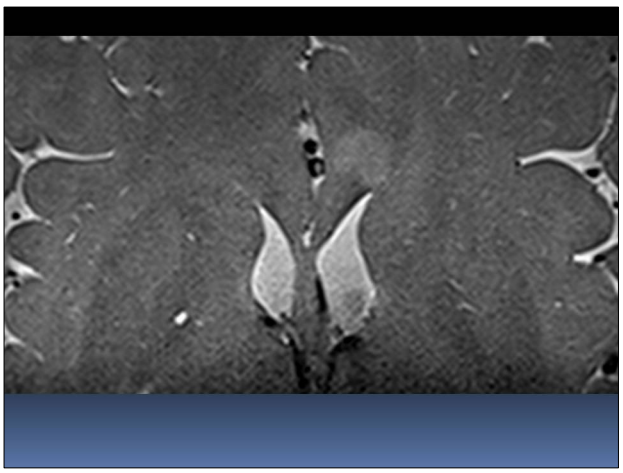
Variables	HR-Athero (N= 26)	HR-Nonathero (N=69)	*P* Value	HR-Nonathero			*P* Value*
				HR-MMD (n=29)	HR-Dissection (n=22)	HR-Vasculitis (n=18)	
Age, y	43.6±6.7	40.4±10.0	0.079	42.7±9.2	41.1±10.5	36.1±10.0†	0.045
Male	18 (69.2)	25 (36.2)	0.004	6 (20.7)‡	10 (45.5)	9 (50.0)	0.004
Risk factors							
No/Yes	18 (69.2)	45 (65.2)	0.712	18 (62.1)	13 (59.1)	14 (77.8)	0.592
Hypertension	8 (30.8)	11 (15.9)	0.107	7 (24.1)	1 (4.5)	3 (16.7)	0.112
Diabetes mellitus	3 (11.5)	4 (5.8)	0.340	2 (6.9)	2 (9.1)	0 (0.0)	0.553
Hyperlipidemia	8 (30.8)	25 (36.2)	0.618	7 (24.1)	12 (54.5)	6 (33.3)	0.142
Current smoking	13 (50.0)	17 (24.6)	0.018	6 (20.7)	4 (18.2)	7 (38.9)	0.052
F.Hx of stroke	8 (30.8)	21 (30.4)	0.975	9 (31.0)	6 (27.3)	6 (33.3)	0.989
Headache			0.265				0.185
New	3 (11.5)	16 (23.2)		5 (17.2)	3 (13.6)	3 (11.5)	
Chronic	2 (7.7)	10 (14.5)		10 (34.5)	4 (18.2)	2 (7.7)	
Degree of stenosis			0.125				0.001
Stenosis	22 (84.6)	46 (66.7)		13 (44.8)†	20 (90.9)	13 (72.2)	
Occlusion	4 (15.4)	23 (33.3)		16 (55.2)	2 (9.1)	5 (27.8)	
Pattern of stenosis			0.003				<0.001
Focal	17 (65.4)	19 (27.5)		3 (10.3)†	12 (54.5)	4 (22.2)	
Segmental	5 (19.2)	21 (30.4)		6 (20.7)	8 (36.4)	7 (38.9)	
Total	4 (15.4)	29 (42.0)		20 (69.0)	2 (9.1)	7 (38.9)	
Concomitantly involved vessel							
Ipsilesional distal ICA	2 (7.7)	17 (24.6)	0.086	10 (34.5)	5 (22.7)	2 (11.1)	0.077
Contralesional MCA	9 (34.6)	17 (24.6)	0.331	12 (41.4)	2 (9.1)	3 (16.7)	0.038
A1 portion of ACA			0.116				0.064
Ipsilesional A1	8 (30.8)	15 (21.7)		6 (20.7)	4 (18.2)	5 (27.8)	
Both A1	1 (3.8)	14 (20.3)		9 (31.0)	1 (4.5)	4 (22.2)	



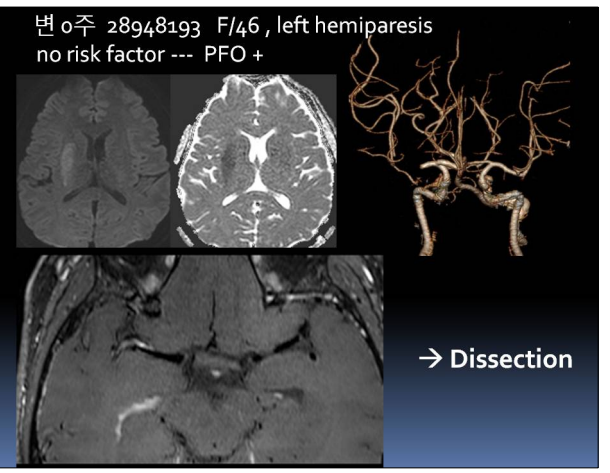
김o권 M/54 49778308 sudden right leg weakness
– improving –then worsening







변 o주 28948193 F/46 , left hemiparesis
no risk factor --- PFO +



→ Dissection

Dissection causing ischemic stroke and TIA

Total Dissection (n=135)
Intracranial dissection (n=89)
Extracranial dissection (n=44)

Table 2
Stroke mechanisms according to the location of dissection.

Location	Number [symptomatic]*	Stroke mechanism			
		In situ thrombotic occlusion	Artery to artery embolism	Local branch occlusion	Hemodynamic impairment
Vertebral artery	77 [63]		38 (60.3)	24 (38.1)	0
Intracranial	39 [32]	0	8 (25)	24 (75)	0
Extracranial	38 [31]	0	30 (96.7)	0	0
Internal carotid artery	29 [23]	3 (12.5)	16 (69.5)	2 (8.3)	1 (4.2)
Intracranial	13 [12]	3 (25)	5 (41.7)	2 (16.7)	1 (8.3)
Extracranial	16 [11]	0	11 (100)	0	0
Middle cerebral artery	24 [19]	2 (10.5)	6 (31.6)	2 (10.5)	6 (31.6)
Basilar artery	12 [12]	0	2 (16.7)	9 (75)	0
Posterior inferior cerebellar artery	8 [8]	3 (37.5)	5 (62.5)	0	0
Anterior cerebral artery	5 [3]	0	1 (33.3)	2 (66.7)	0
Posterior cerebral artery	4 [4]	1 (25)	1 (25)	2 (50)	0

Kwon JY, Kim NY, and Kim JS, J Neurol Sci 2015

A 64-year old woman
-- mild quadriparesis, paresthesia below the T5 and urinary retention.
No vascular risk factors
N/E: mild symmetric 4 extremities weakness and sensory loss below T5 dermatome, especially vibration sense and proprioception. Increased deep tendon reflex and bilateral Babinski`s sign

Spinal cord MRI: multiple cord signal change in T2 weighted image and Diffuse leptomeningeal thickening with enhancement from the lower medulla to the thoracic cord

6 months later, -- right hand weakness and right homonymous hemianopsia. MRI/MRA: left PCA infarction

A 57-year old male developed
transient dysarthria and left weakness (TIA).
-- HT, DM, SM
DWI negative for stroke,
MRA: Rt MCA stenosis on MRA

Tx: aspirin, clopidogrel, statin

6 months later,
he developed right thalamic infarction

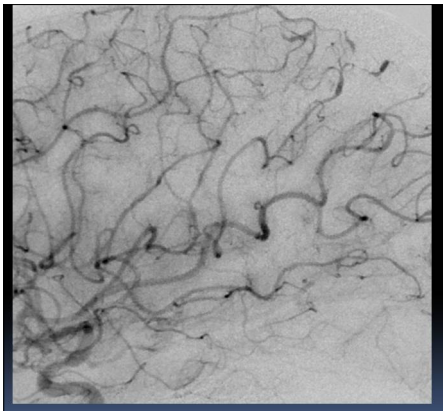
	Patient 1	Patient 2
Age	64	57
Sex	F	M
Vascular risk factors	none	HTN, DM, HL, SM
Initial Serum RPR	1:128	1:128
CSF profile		
WBC(/uL)	113(Lyphocyte81%)	31(Lymphocyte 88%)
Protein(mg/dl)	148.0	105.5
Glucose(mg/dl)	48/serum 96	74/ serum 126
CSF VDRL	1:64	1:4
Treatment(IV Penicillin) at 1st visit	yes	no
Time interval	6 months	2 months
Involved vessels	Bilateral MCA, ACA, left PCA, right PCom	Bilateral MCA, right PCA

(RPR=Rapid plasma Reagin)

Neurosyphilis

F/52 no risk factors

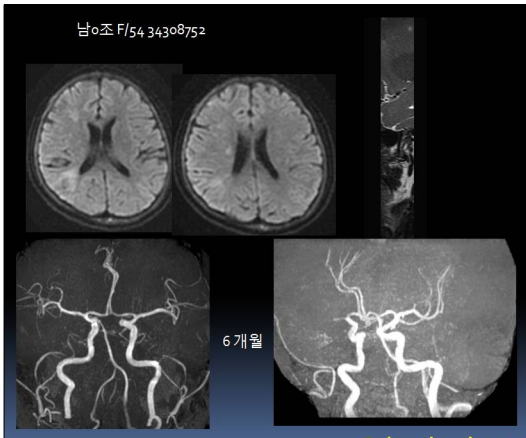
Sudden severe headache



2014 9 26

Reversible cerebral vasoconstriction syndrome (RCVS)

남0조 F/54 34308752



6 개월

Polycythemia vera

We need more ----

genetic studies ??

Ringer finger 213 (RNF 213) gene variation:
a polymorphism in c.14576G>A in RNF213 identified
in 95% of familial MMD and 79% of sporadic MMD

Fujimura et al. J Stroke 2014

RNF gene variant +

Advanced imaging and gene tests- Are you happy with these ?

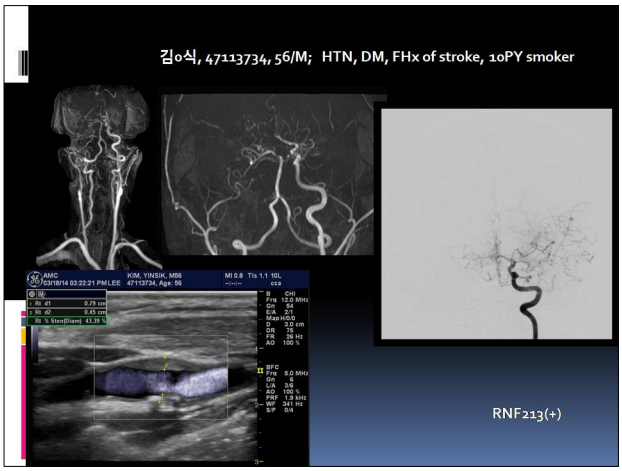
352 symptomatic MCA diseases in Korea

Table 2. Factors predicting the genetic variant of *RNF213* associated with MMD among 352 patients with intracranial arterial stenosis.

	RNF213			Univariate		Multivariate	
	present	absent	P-value	OR (95% CI)	P-value	OR (95% CI)	P-value
Age	46.5 ± 12.2	57.4 ± 14.9	<0.001	0.977 (0.956–0.999)	0.040	0.980 (0.960–1.000)	0.052
Female gender	121 (67.2%)	149 (50.3%)	<0.001	1.148 (0.677–1.948)	0.607		
Family history of MMD	14 (7.8%)	4 (1.4%)	<0.001	2.905 (0.831–10.159)	0.095	2.828 (0.824–9.707)	0.099
Vascular risk factors							
Hypertension	85 (47.2%)	161 (54.4%)	0.129	1.226 (0.713–2.108)	0.460		
Diabetes	21 (11.7%)	78 (26.4%)	<0.001	0.349 (0.178–0.684)	0.002	0.368 (0.192–0.704)	0.003
Dyslipidemia	51 (28.3%)	96 (32.4%)	0348	1.025 (0.585–1.795)	0.931		
Angiographic findings							
Distal ICA involvement	138 (76.7%)	91 (30.7%)	<0.001	1.569 (0.866–2.842)	0.137		
Basal collaterals	134 (74.4%)	57 (19.3%)	<0.001	3.027 (1.714–5.346)	<0.001	3.529 (2.066–6.026)	<0.001
Bilateral involvement	128 (71.1%)	65 (22.0%)	<0.001	2.625 (1.510–4.564)	0.001	3.072 (1.825–5.170)	<0.001
No. diagnostic criteria met*			<0.001				
0	16 (20.0%)	64 (80.0%)		Ref		Ref	
1	20 (28.6%)	50 (71.4%)		1.542 (0.701–3.388)	0.281	1.529 (0.699–3.348)	0.228
2	41 (57.7%)	30 (42.3%)		4.834 (2.244–10.412)	<0.001	4.797 (2.236–10.289)	<0.001
All 3	99 (75.6%)	32 (24.4%)		9.753 (4.687–20.294)	<0.001	10.214 (4.952–21.068)	<0.001

* Model 2, including age, gender, family history of MMD, vascular risk factors, and number of angiographic diagnostic criteria met.

Bang et al, PlosOne Adult moyamoya disease, 2015

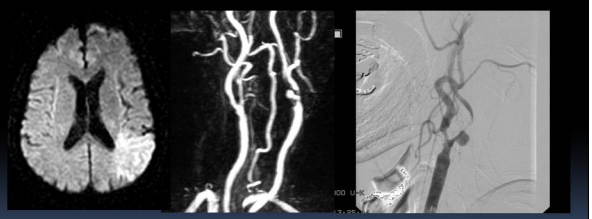


Atherosclerosis >

- Age, male
- Risk factor (including smoking in young men)
- Focal stenosis
- Atherosclerosis in other vessels
- RNF 213 polymorphism negative

Stroke mechanisms of ECAS

Mostly, artery to artery embolism
Vulnerable plaque, platelet aggregation
Inflammation
& Hemodynamic- not major stroke



Platelet aggregation ++

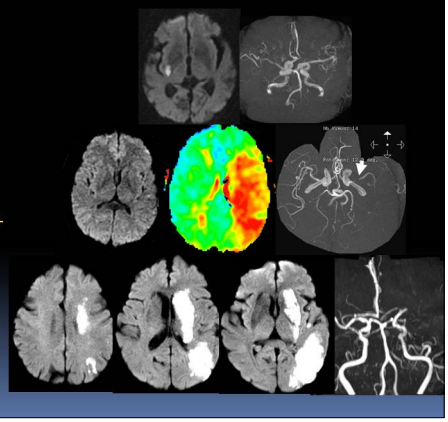
Mechanisms of stroke in ICAS

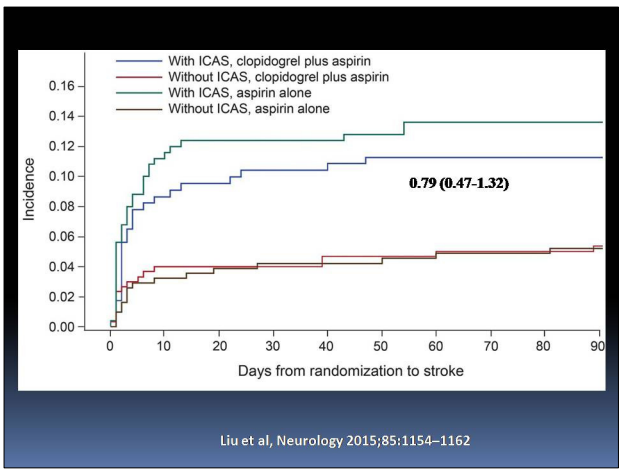
Perforator (branch) occlusion

Artery to artery embolism

Platelet aggregation ++

In situ Thrombotic occlusion

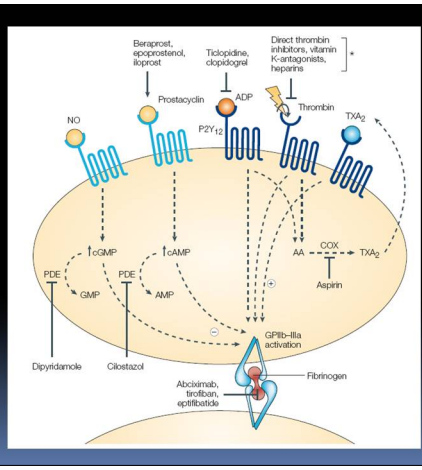




Treatment Options for ICAS

- Warfarin was not superior than aspirin increase in bleeding Risk (WASID, *NEJM* 2005).
- The risk of recurrent stroke with aspirin is still high
  Progression of ICAS is high with aspirin
- Dual antiplatelets may be needed
  In risky patients, in risky period

Antiplatelets



Combination therapy

- **Asp+clopidogrel**
  -- strong antiplatelet function
  Pros: CARESS: reduced microembolism in symptomatic ICA disease
  CHANCE: effective when administered early
  Cons: significantly increased bleeding risk (MATCH)
- **Asp+cilostazol**
  Pros:
  Diverse mechanism including effects on vessel wall – may not increase bleeding risk
  Cons: may not have early strong antiplatelet action

Study Design of TOSS 1 and TOSS II

– Patients with symptomatic ICAS (MCA, BA)
– MRA outcome (degree of stenosis)

Asp 100 mg/day (TOSS 1)
Asp + clopidogrel (TOSS 11)

Asp+ Cilostazol (TOSS 1 and 11)

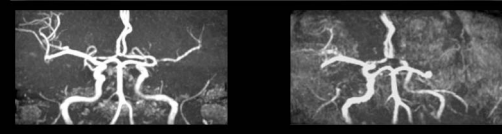
0 month
MRA
TCD

6 months
MRA
TCD

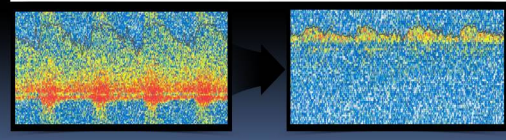
TOSS I Trial

Primary and Secondary Endpoint of TOSS I

Primary endpoint: progression of symptomatic stenosis on MRA



Secondary endpoint: progression of symptomatic stenosis on TCD

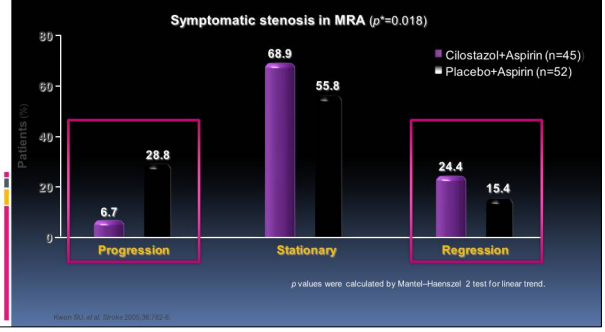


Kwon SU, et al. Stroke 2005;36:782-6.

TOSS I Trial

Cilostazol Efficacy in ICAS

Progression was significantly less frequent in the cilostazol group than in the placebo group (TOSS I)



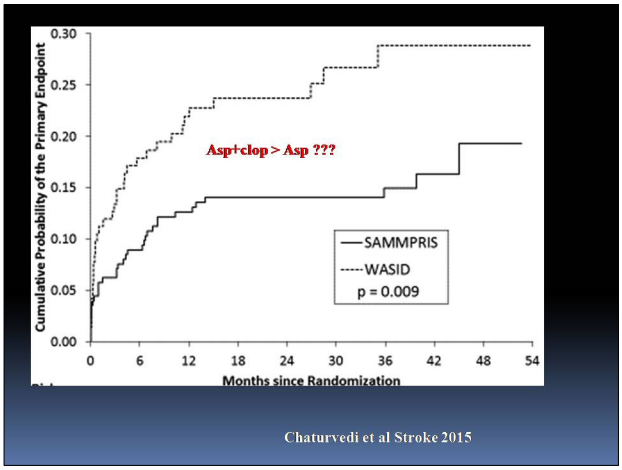
Kwon SU, et al. Stroke 2005;36:782-6.

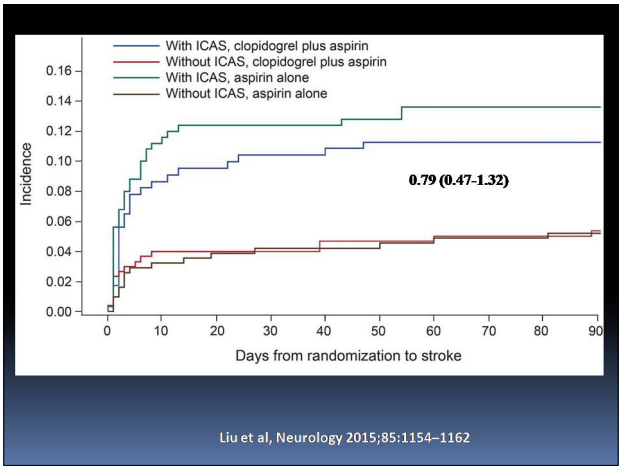
USA guideline

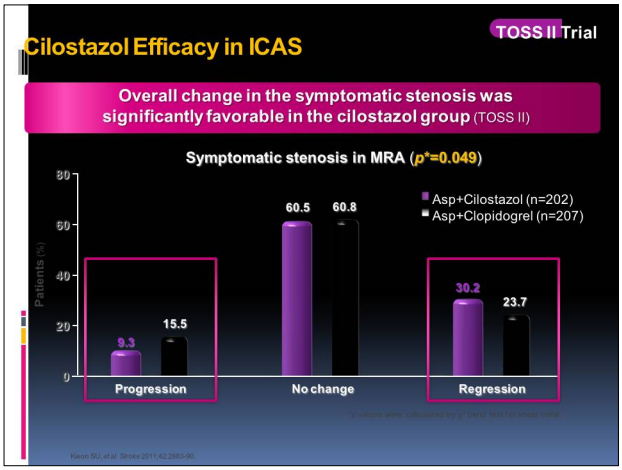
- For patients with recent stroke or TIA (within 30 days) attributable to severe stenosis (70%–99%) of a major **intracranial artery, the addition of clopidogrel 75 mg/d to aspirin for 90 days might be reasonable** (Class IIb; Level of Evidence B)" and that: "For patients with stroke or TIA attributable to 50% to 99% stenosis of a major intracranial artery, the data are insufficient to make a recommendation regarding the usefulness of clopidogrel alone, the combination of aspirin and dipyridamole, or cilostazol alone (Class IIb; Level of Evidence C).For patients

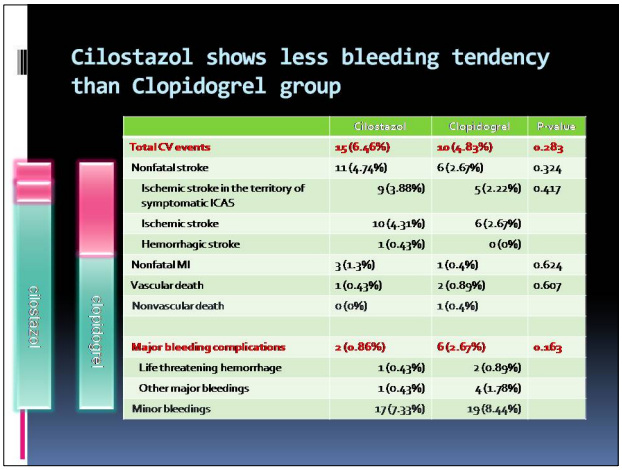
Kernan et al. Stroke 2014

ICAS vs. ECAS









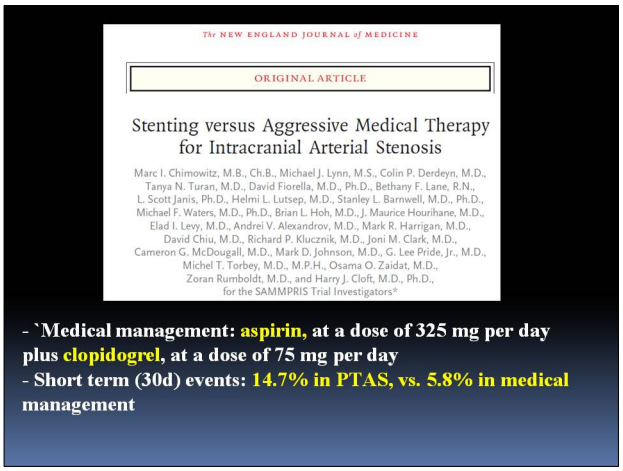
	Cilostazol	Clopidogrel	P-value
Total CV events	15 (6.46%)	10 (4.83%)	0.283
Nonfatal stroke	11 (4.74%)	6 (2.67%)	0.324
Ischemic stroke in the territory of symptomatic ICAS	9 (3.88%)	5 (2.22%)	0.417
Ischemic stroke	10 (4.31%)	6 (2.67%)	
Hemorrhagic stroke	1 (0.43%)	0 (0%)	
Nonfatal MI	3 (1.3%)	1 (0.4%)	0.624
Vascular death	1 (0.43%)	2 (0.89%)	0.607
Nonvascular death	0 (0%)	1 (0.4%)	
Major bleeding complications	2 (0.86%)	6 (2.67%)	0.163
Life threatening hemorrhage	1 (0.43%)	2 (0.89%)	
Other major bleedings	1 (0.43%)	4 (1.78%)	
Minor bleedings	17 (7.33%)	19 (8.44%)	

Conclusions

- Rigorous risk factor controls
- For symptomatic cases;
  Asp+cilostazol or asp+clopidogrel for 1-3 months, statin
- According to the timing ? Dual → mono
  stroke mechanisms ?
- and
  Burden of athero. in other vascular beds ,
  Bleeding tendency, cost, etc.

Interventional therapy in ICAS

- Elective angioplasty/stenting
- Acute endovascular intervention



- `Medical management: **aspirin**, at a dose of 325 mg per day plus **clopidogrel**, at a dose of 75 mg per day
- Short term (30d) events: **14.7% in PTAS, vs. 5.8% in medical management**

Author/yr	Design	Enrol. P	No.	Ethn.	Mean age (male)	HT	DM	SM	HL	CH	Deg.	Short term (30-day) events
East												
Suh 08	registry	2002.2–2007.4	100	Korean	61 (34-80)	71	33	36	26	15	≥70	10 (10%) (in 6 mo)
Yu 11	registry	ND	57	Chinese	64 (34-84)	N	N	N	N	N	≥50	3 (5.3%).
Jiang 11	registry	2007.1–2009.2	100	Chinese	53 (ND)	72	32	68	83	N	≥70	5 (5%)
Kim, 12	registry	2004.3-2010.4	77	Korean	61 (37-77)	N	N	N	N	N	>50	5 (6.5%)
Mohammadian, 12	nonrandomized	2008.9-2011.12	63	Iranian							≥70	1 (2.9%) in PTAS, 1 (3.4%) in MM
	control		34 PTAS		68 (N)	71	71	35	12	32		
			29 MM		79 ((N)	69	59	52	21	48		
Zhang 13	registry	2007.3-2010.12	61	Chinese	58 (41-74)	59	21	43	38	7	≥70	3 (5.0%)
Alurkar 13	registry	2004.4–2012.5	182	Indian	ND (18-75)	N	N	N	N	N	≥70	11 (5.6%) major 9 (4.6%) minor
West												
Chimow.	randomized	2008.11-2011.4	451	Caucasian 71%							≥70	14.7% in PTAS, 5.8% in MM
11	control		224 PTAS		61 (57%),	90	47	24	87	21		
			227 MM		60 (64%)	89	45	30	90	26		
Gandini 13	registry	2008.7-2011.5	21	Caucasian	71 (56-85)	76	57	57	67	38	>70	1 (4.8%)

Reasons for difference

- ICAS patients are younger
- Less often have dyslipidemia, diabetes, obesity, and atherosclerotic proximal vessels (aorta, carotid artery)
- ICAS more common → more experienced in large centers

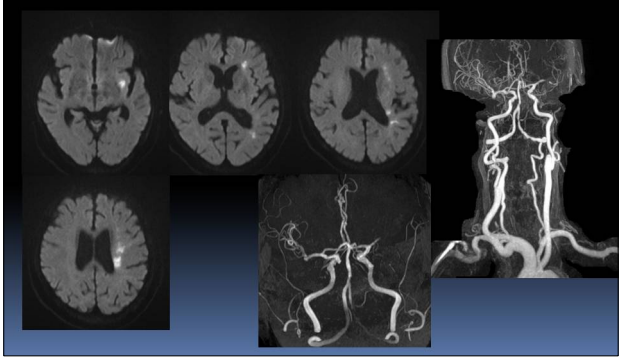
Our current practice

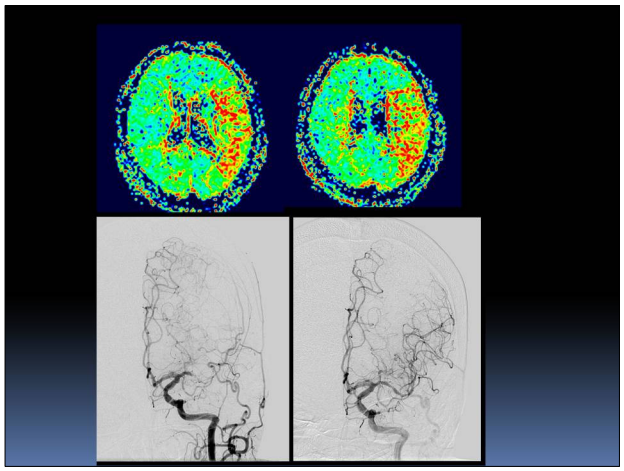
-- We don't do this routinely
But, we still do in selected patients

M/58
HT, dyslipidemia, smoking, coronary disease (CABG)
Dysarthria, Mild (IV) weakness, ataxia on right limbs

F/83

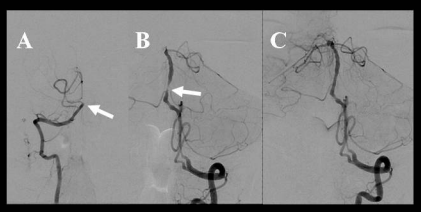
HT, dysarthria, mild right limb weakness
- fluctuating and gradually progressive for 3 days
- aphasia developed





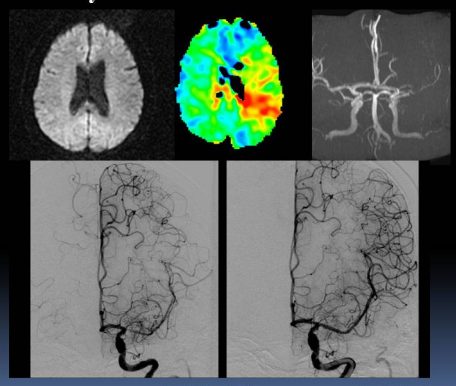
Our current practice

-- Select patients with potentially poor outcome
Progressive and unstable condition with hemodynamic instability in acute/subacute stage ?
Degree of stenosis, perfusion status
Lesion pattern
Amenable lesion (vascular tortuosity, athero. degree, age, etc)
-- should be performed in large, experienced center
-- should need multi-departmental approach - strict indication, objective/independent assessment



A 45–year-old man with HT, DM heart disease developed recurrent attacks of dizziness, diplopia, and gait instability that lasted usually for a few minutes. MRI showed no abnormal findings

Hemodynamic mechanism

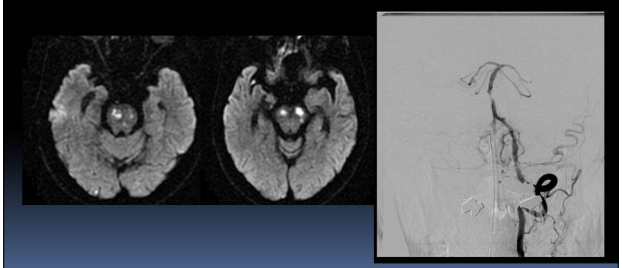


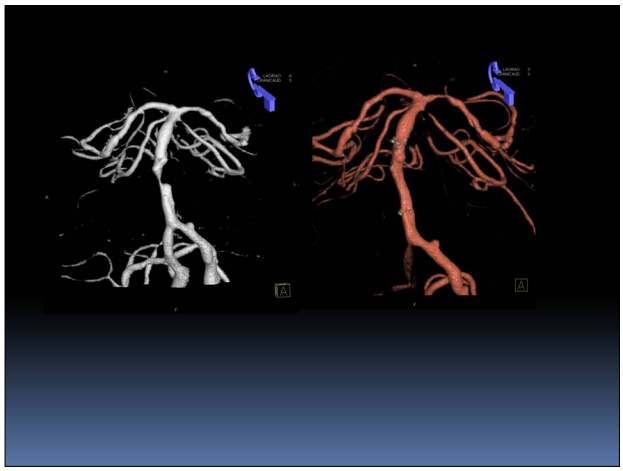
KKH, F/74 recurrent, brief, right hemipresis

Stenting/angioplasty in the acute setting

F/69 40207119 headache, ataxia, -→ confusion

M/71 40938336
Dysarthria Rt limb ataxia
-- progress to bilateral ataxia and weakness (IV)





Conclusions

- MCA atherosclerosis, common in Asians
- But, other MCA disease is also common
- Different pathogenic mechanism
- High risk of recurrent stroke in symptomatic cases
- Best medications (dual anitplatelets, statin) and rigorous risk factor controls
- Routine use of stenting/angioplasty not acceptable
- But, may be needed in highly selected patients: unstable condition with hemodynamic instability, amenable lesion especially in the acute/subacute stage
- Bypass surgery may be needed in selected patients

Workshop by video for beginner

좌장 : 김한규(분당제생병원), 권오기(서울대)

1. How to clip of ICA aneurysm	정영균(인제대)
MCA aneurysm	박인성(경상대)
ACA aneurysm	박익성(가톨릭대)
2. How to coil assisted by STENT	김성림(가톨릭대)
Balloon	윤석만(순천향대)
Multiple catheter	강현승(서울대)

How to clip the ICA aneurysm

정영균

인제대학교 부산백병원

2016년 5월 26일 대한뇌혈관외과학회-대한혈관내수술학회 합동연수강좌
서울 아산병원 연구원 대강당

How to clip the ICA aneurysm

정영균
인제대학교 부산백병원

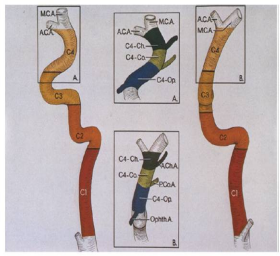
1. Paraclinoid aneurysms
2. Posterior communicating artery aneurysms
3. Anterior choroidal artery aneurysms
4. Blood blister like aneurysms

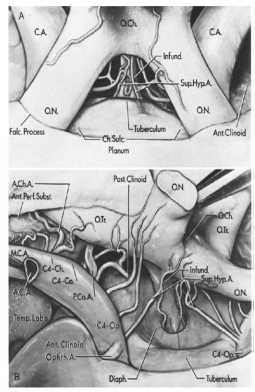
Microsurgical anatomy of the supraclinoid portion of the internal carotid artery

HIROHIKO GIBO, M.D., CARLA LENKEY, M.S., AND ALBERT L. RHOTON, JR., M.D.

Department of Neurosurgery, University of Florida Health Center, Gainesville, Florida

J Neurosurg 55:560–574, 1981





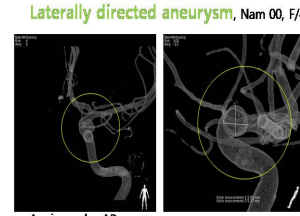
Paraclinoid aneurysms

1. Small aneurysms
   1. **Medial** direction : superior
      inferior : carotid cave
   2. **Anterior** direction
   3. **Anteromedial** direction: **ON compresion** +/-
   4. **Anterolateral** direction
   5. **Lateral** direction
   6. **Posterior** direction
   7. **Ophthalmic artery** aneurysm

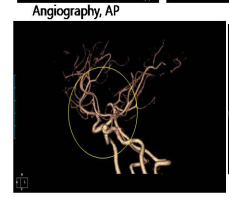
2. Large aneurysms

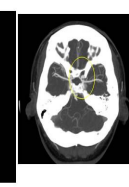
3. Giant aneurysms
4. Multiple paraclinoid aneurysms
   1. Same ICA
   2. Bilateral ICA
5. Bypass surgery

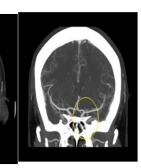
Laterally directed aneurysm, Nam 00, F/45



Angiography, AP



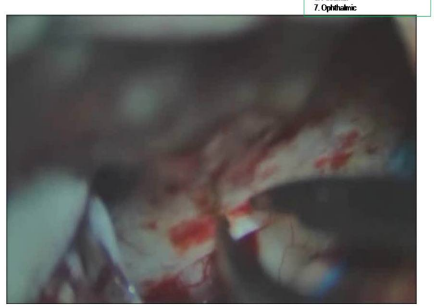




Laterally directed paraclinoid aneurysm

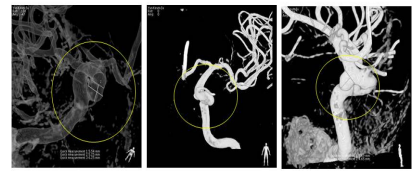
Small Paraclinoid aneurysms

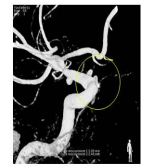
1. Medial : Superior
   Inferior
2. Anterior
3. Anteromedial: ON compression +/-
4. Anterolateral
5. Lateral
6. Posterior
7. Ophthalmic



Multiple aneurysm, **left paraclinoid**, **P-com** artery aneurysms
right ophthalmic a aneurysm

Yun 00, F/62





Left **paraclinoid** and **P-com aneurysm**

Right **ophthalmic** a aneurysm

Paraclinoid aneurysms

1.Small aneurysms
2. Large aneurysms
3. Giant aneurysms
4. Multiple aneurysm
   Same ICA
   Bilateral ICA
5. Bypass surgery
6. High speed drill or sonopet

Left ipsilateral approach to left posterior directed paraclinoid aneurysm & P-com
Contralateral approach to right ophthalmic artery aneurysm

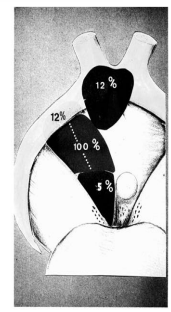
Posterior communicating artery

- Average diameter : 1.8 ± 0.7 mm
- Average length : 16 ± 4.3 mm

- PcoA branches : 2 groups
  - Inner group : 3-11 branches supplying the hypothalamus
  - Outer group: 2-7 branches

- Fetal type
- Padget's stage 3 (5-6 mm in length, 31 days)
  - ICA provide the blood supply fot the posterior territory
- Padget's stage 4 (7-12 mm in length, 33 days)
  - Formation of the vertebral arteries
  - Involution is variable : fetal, intermediate, and adult
  - : PcoA is larger than the PCA : 15-40%
- The anterior thalamoperforating brs of the PcoA
- Posterior thalamoperforating brs of the PCA

Microsurgical Anatomy of the Cisternal Course of the Perforating Branches of the Posterior Communicating Artery



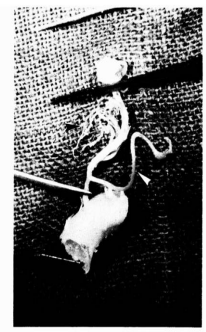


FIG. 6. After the ICA (*larger in size*) and P1 have been cut, the two groups of PcoA branches are well displayed: a medial group (*black arrowhead*), formed by 3 to 11 tiny hypothalamic branches, and a lateral group, formed by 2 to 7 branches, among which a main stem (*white arrowhead*) is constantly found. It corresponds to the premamillary artery.

Microsurgical Relations between Internal Carotid Artery–Posterior Communicating Artery (ICA-PComA) Segment Aneurysms and Skull Base: An Anatomoclinical Study

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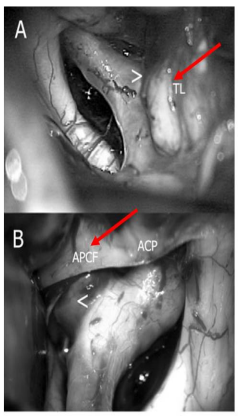
J Neurol Surg B 2012;73:337–341.



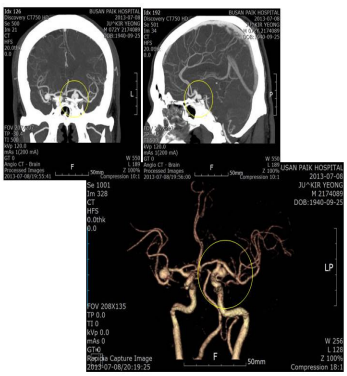
Surg Neurol Int. 2010; 1: 86.
Published online Dec 22, 2010. doi: 10.4103/2152-7806.74147
PMCID: PMC3011114

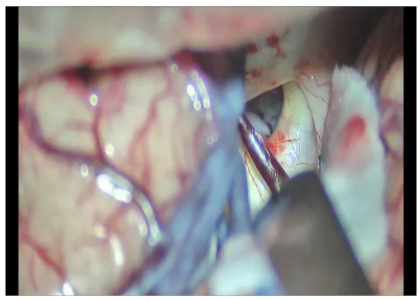
A review of the management of posterior communicating artery aneurysms in the modern era

Kiarash Golshani, Andrew Ferrell,[1] Ali Zomorodi, Tony P. Smith, and Gavin W. Britz[1]

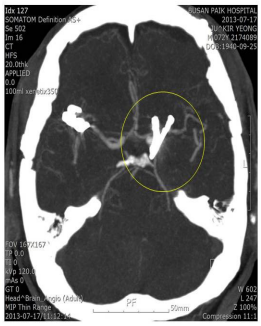
- The incidence of the fetal PCOM : 4-29%
- The direction of dome
  - Anterolaterally
    - The origin of PCOM artery may be hidden by the aneurysm
  - Superolateral fundus : temporal lobe
  - Posterolateral inferior fundus
  - Posteromedial inferior :rarely

주 00, M/73, left P-com aneuyrsm, right MCA aneurysm





주 00

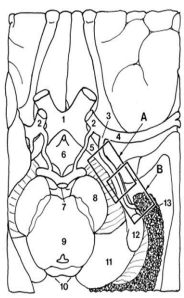


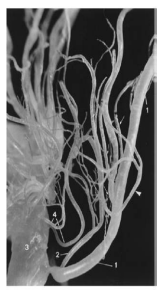
Anterior choroidal artery aneurysms

THE SURGICAL ANATOMY OF THE PERFORATING BRANCHES OF THE ANTERIOR CHOROIDAL ARTERY

Slobodan Matsitskovic, M.D., Ph.D.,* Hirohiko Gibo, M.D., Ph.D.,† Luciano Brigante, M.D.,‡ Ivana Nikoljčević, M.D., and Predrag Petrović, M.D.* *Institute of Anatomy, School of Medicine, University of Belgrade, Belgrade, Yugoslavia; †Neurosurgical Service, Shizuoka-Sogo General Hospital, Kosugaya City, Japan; and ‡Department of Neurosurgery, Catanzaro Hospital, Trieste, Italy

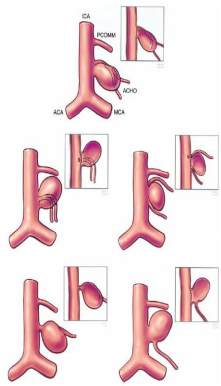
Surg Neurol 1999;52:30–6





The perforators : 1-4 or 1-10
2-9

- 2-5% of all intracranial aneurysms
- Anterior Choroidal Syndrome
  - Hemiplegia, hemianesthesia, and hemianopsia
  - Foix, et al. in 1925 in a pater of the Societe d'Ophthalmologie



Ischemic complications of surgery for anterior choroidal artery aneurysms

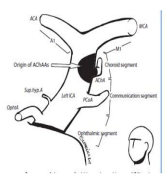
Jonathan A. Friedman, M.D., Mark A. Pichelmann, M.D., David G. Piepgras, M.D., John L. D. Atkinson, M.D., Cormac O. Maher, M.D., Fredric B. Meyer, M.D., and Kirstine K. Hansen, R.N.
Department of Neurological Surgery, Mayo Clinic, Rochester, Minnesota

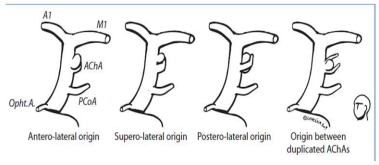
J Neurosurg 94:565-572, 2001

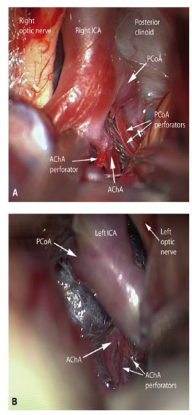
- Diameter of the AChA : 0.5 to 2.0 mm
- Rhoton et al. : a single trunk 50 hemispheres
- Yasargil : 2-4 vessels in 30%
- AChA : 2 segments
  - Cisternal segement
  - Plexal (choroid) segment
- Venous structures
  - Superficial middle and anterior cerebral veins→ the sphenoparietal or cavernous sinus
  - The deep venous system : anterior and deep middle cerebral veins and the basal vein of Rosenthal : inferior aspect of the ICA bifurcation.

Microneurosurgical Management of Anterior Choroid Artery Aneurysms

Martin Lehecka[1], Reza Dashti[1], Aki Laakso[1], Jouke S. van Popta[1], Rossana Romani[1], Ondrej Navratil[1], Leena Kivipelto[1], Riku Kivisaari[1], Mansoor Foroughi[1], Jouji Kokuzawa[1], Hanna Lehto[1], Mika Niemelä[1], Jaakko Rinne[2], Antti Ronkainen[2], Timo Koivisto[2], Juha E. Jääskeläinen[2], Juha Hernesniemi[1]



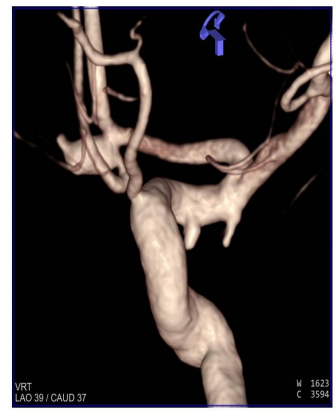




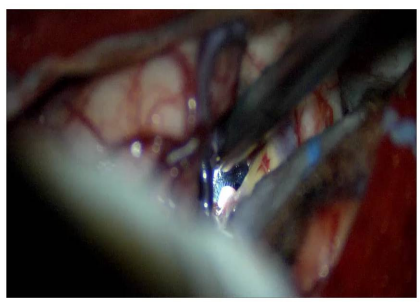
M/ 71

Multiple aneurysms

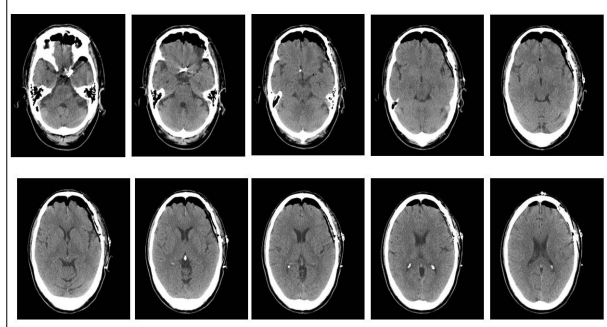
A-com aneurysm
Left P-com and
Anterior choroidal artery aneurysm



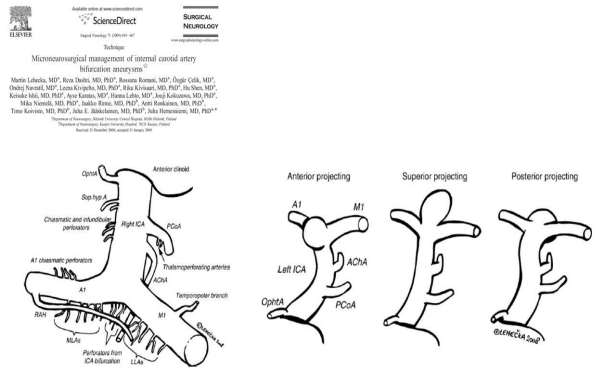
Using 70 degree endoscope



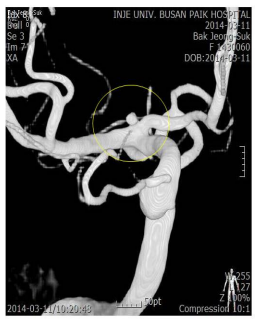
Postoperative brain CT

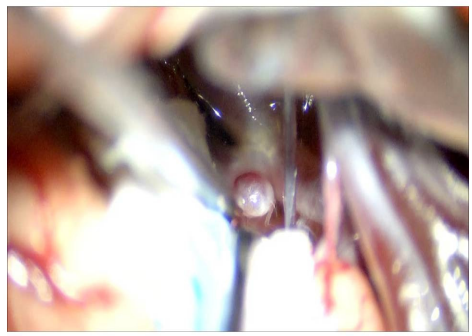


- ICA bifurcation aneurysms
  - 2-9% of all Ias
  - The venous structures
  - The perforators of ICA bifurcation may be adherent to the dome
    a. retraction, b. dissection, c. coagulation, d. kinking, e. compression for hemostasis, f. temporary occlusion, g. final clipping
  - 2 most common rupture before clipping
    - Lifting the frontal lobe and dislocation of the ICA

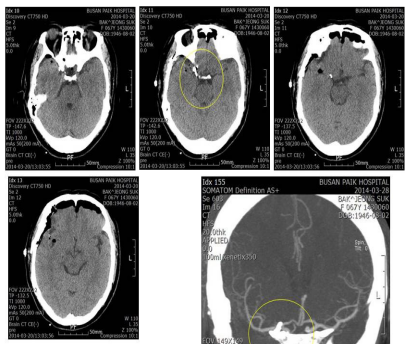


박 00, F/67, right ICA bifurcation aneurysm



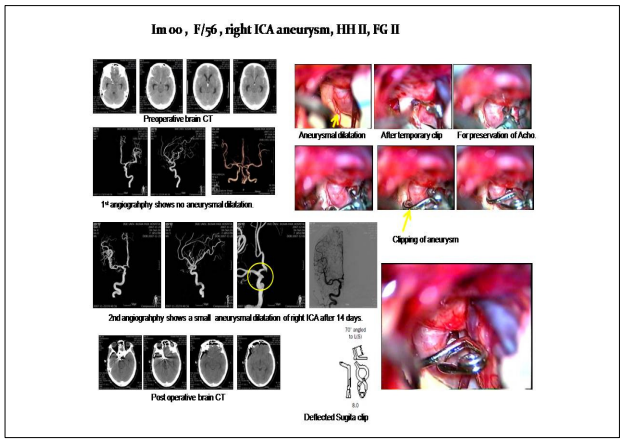


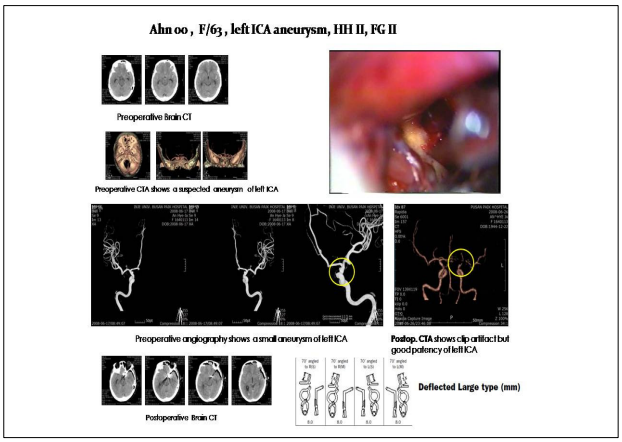
박 00



Postop brain CT & follow up CTA

- Blood blister like (BBL) aneurysms
- 16 patients from 2008 to 2015 May
- 3 male and 13 females
- 7 surgical methods
  - Simple clipping in 4 cases, clipping with fenestrated clips in 3 cases ICA trap and STA-MCA bypass in 3 cases, STA-MCA bypass and clip with fenestraed clip in 1 case, wrapping and clipping in 3 cases, wrapping and clip with STA-MCA bypass in 1 case, and ICA trap and ECA-RA-MCA bypass in 1 case





Conclusions

- Microsurgical anatomy
- Good Mentor
- Strategy to aneurysm or proximal control
- Perforators
- If possible avoid perforation, sharp dissection, temporary clip or tentative clip or trapping
- Venous structure , especially deep sylvian venous system
- Until your satisfaction, (자꾸 쪼물락 거리지 마라)

How to clip of MCA aneurysm

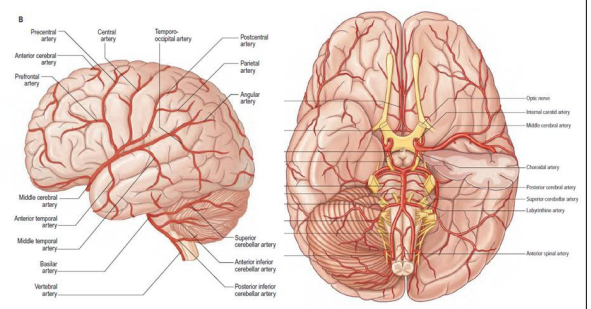
In Sung Park MD, PhD

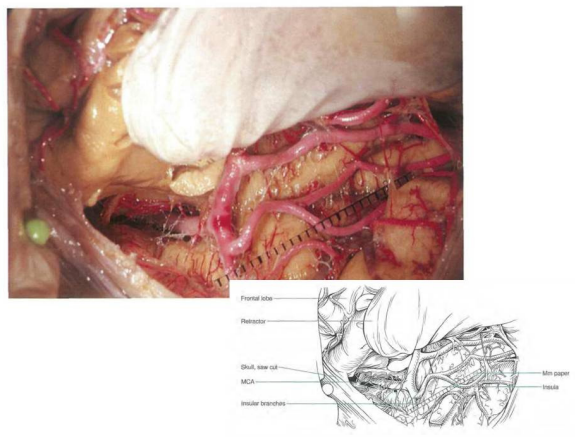
Departrnent of Neurosurgery Gyeongsang National University School of Medicine and Gyeongsang National University Hospital

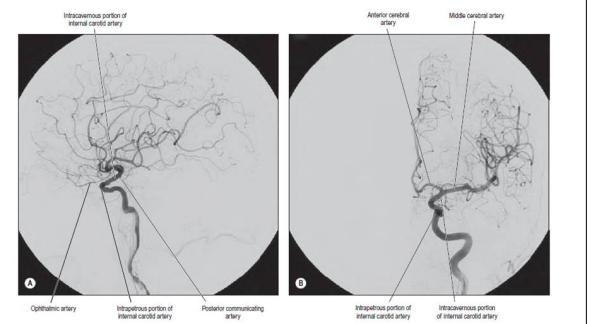
How to clip of MCA aneurysm

In Sung Park MD, PhD
Department of Neurosurgery
Gyeongsang National University School of Medicine
and Gyeongsang National University Hospital

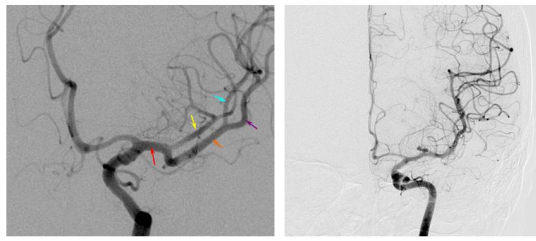
Anatomy

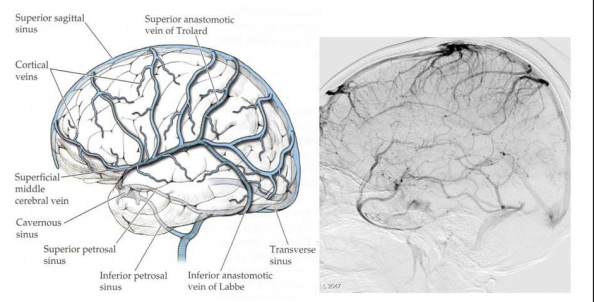




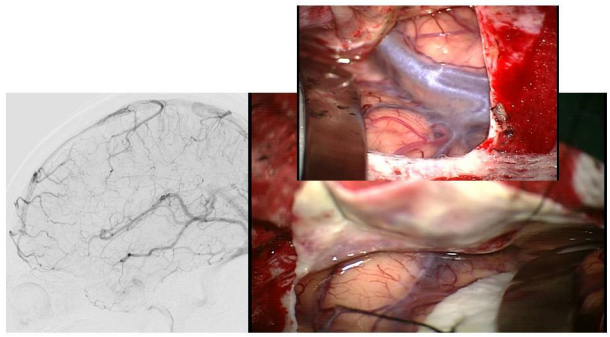


Short M1

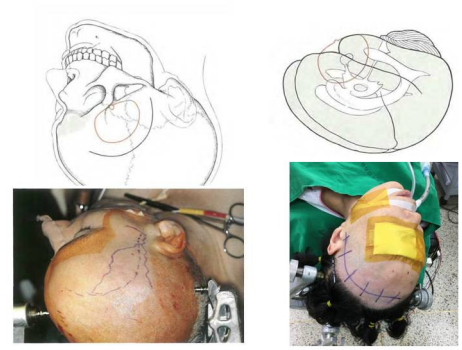




Hypoplastic superficial sylvian vein

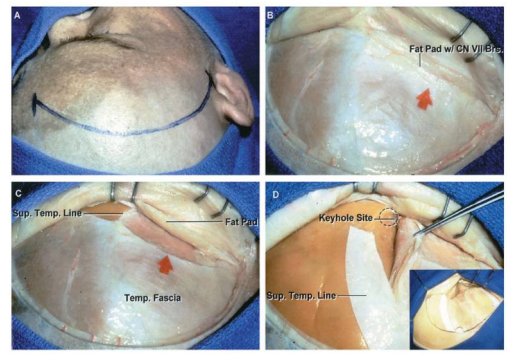


Pterional Approach

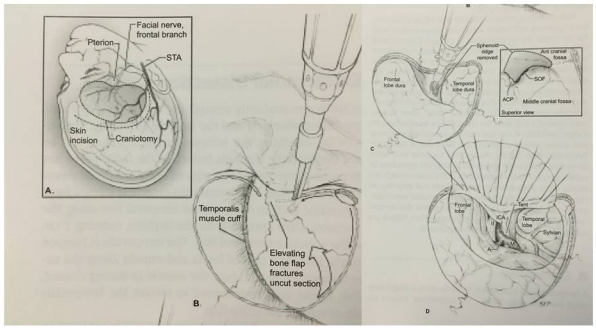


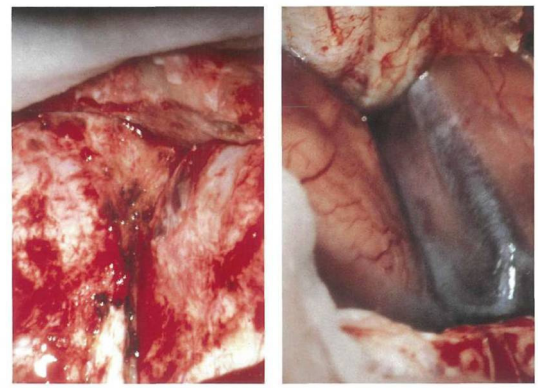
Intraoperative Monitoring

Skin incision

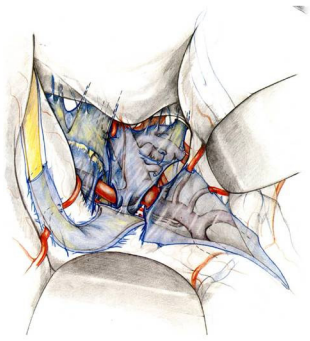


Crainotomy & Dura incision





Subarachnoid dissection



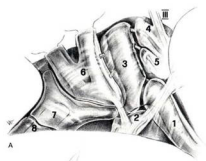
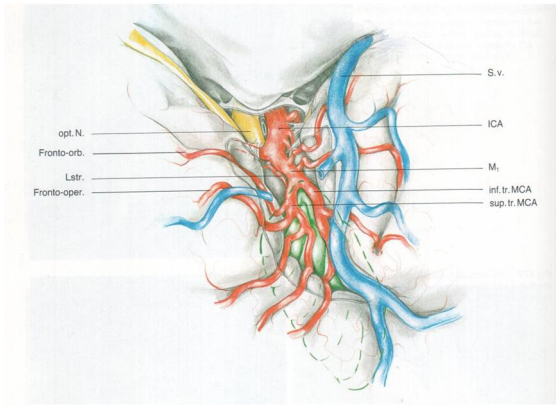


Fig 8A–B The parachiasmatic cisterns as recognized under the operating microscope from the pterional approach.
1 Sylvian cistern with middle cerebral artery
2 Olfactory cistern (base) with olfactory tract
3 Carotid cistern with internal carotid artery
4 Interpeduncular cistern (lateral recess) with posterior communicating artery
5 Crural cistern with anterior choroidal artery
6 Chiasmatic cistern with chiasm
7 Lamina terminalis cistern with anterior cerebral and anterior communicating artery
8 Callosal cistern (ant. part) with distal anterior cerebral artery A_2



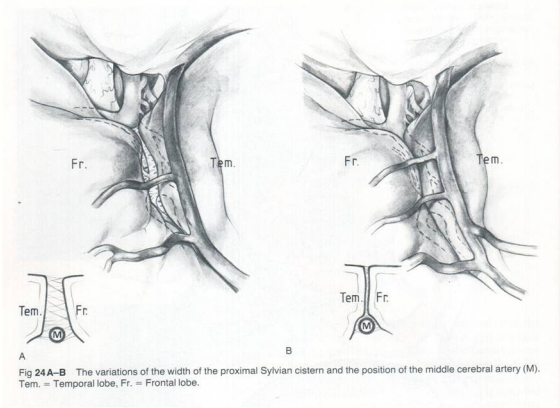


Fig 24A–B The variations of the width of the proximal Sylvian cistern and the position of the middle cerebral artery (M). Tem. = Temporal lobe, Fr. = Frontal lobe.

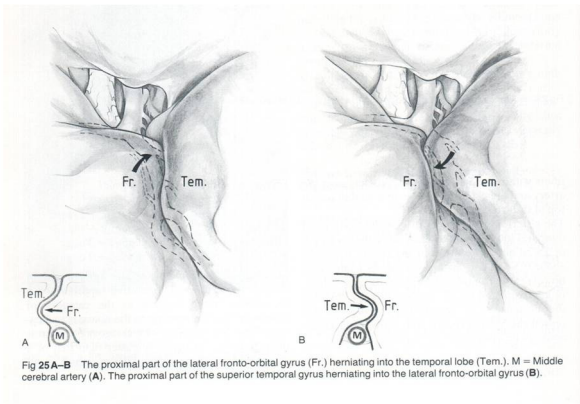
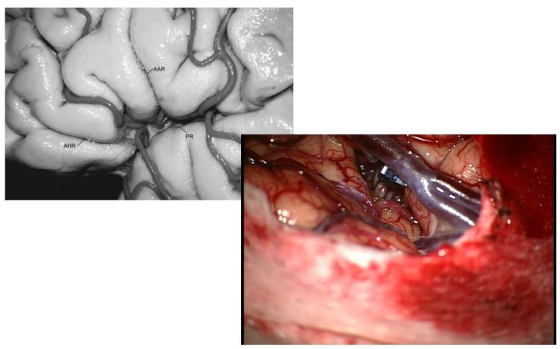
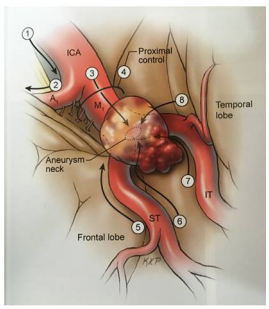


Fig 25A–B The proximal part of the lateral fronto-orbital gyrus (Fr.) herniating into the temporal lobe (Tem.). M = Middle cerebral artery (**A**). The proximal part of the superior temporal gyrus herniating into the lateral fronto-orbital gyrus (**B**).

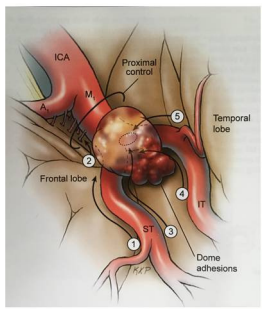
Landmark of Sylvian dissection



Proximal control

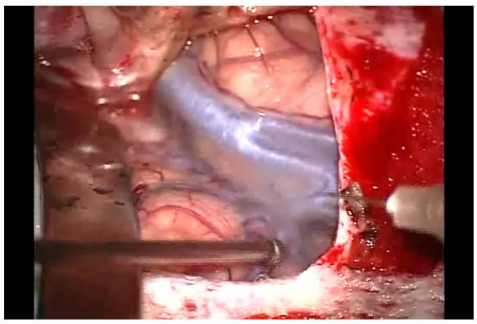


Proximal to Distal dissection

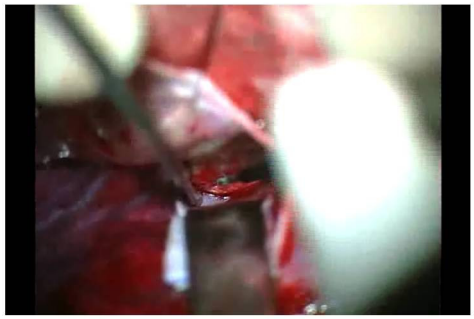


Distal to Proximal dissection

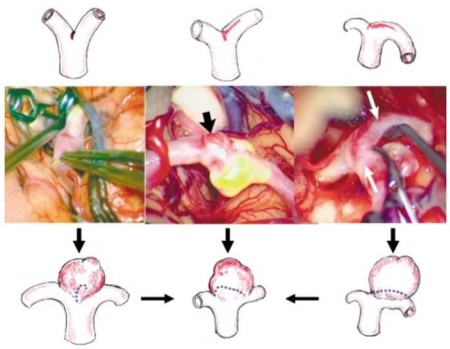
Lateral Sylvian dissection

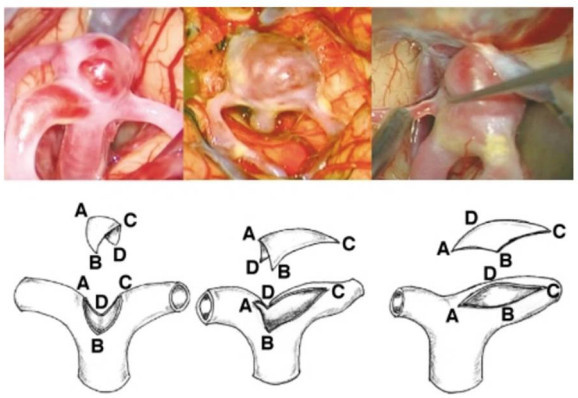


Medial Sylvian dissection



How to clipping of aneurysm





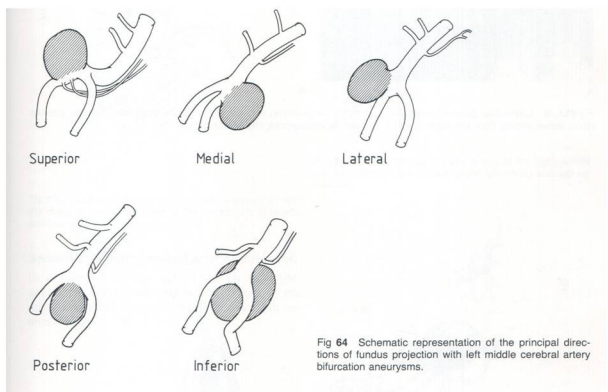
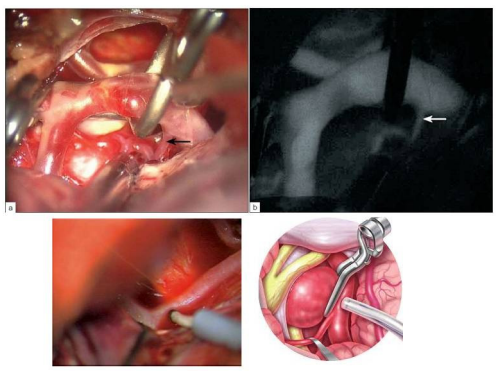
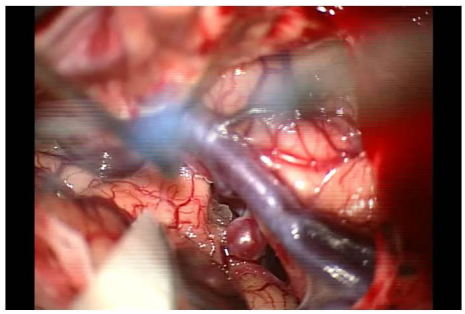


Fig 64 Schematic representation of the principal directions of fundus projection with left middle cerebral artery bifurcation aneurysms.

Intraoperative ICG & Doppler

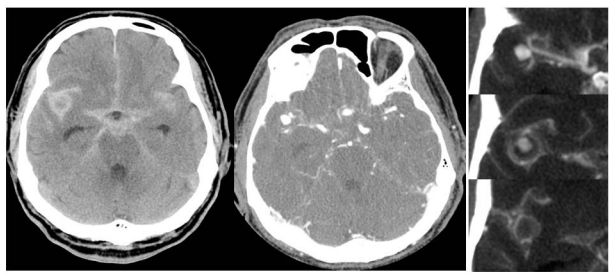


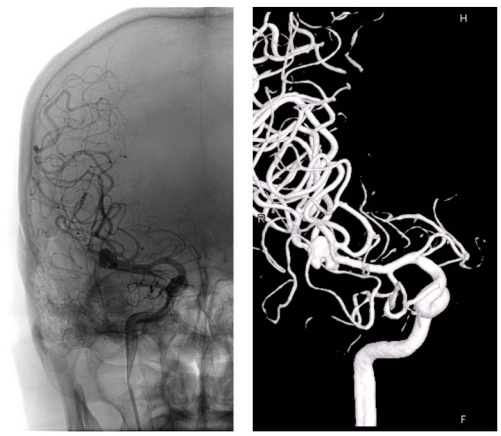
Permanent Clipping

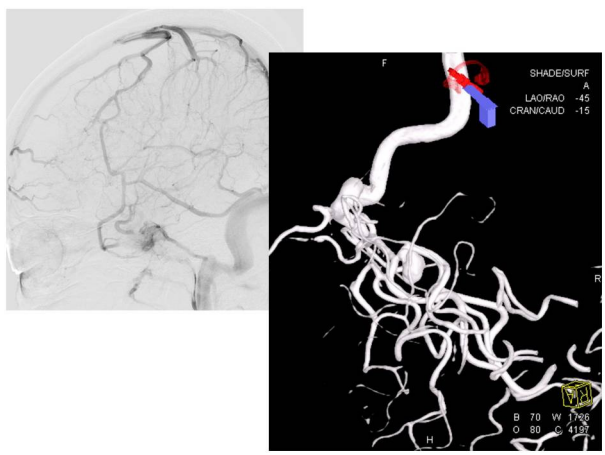


CASE

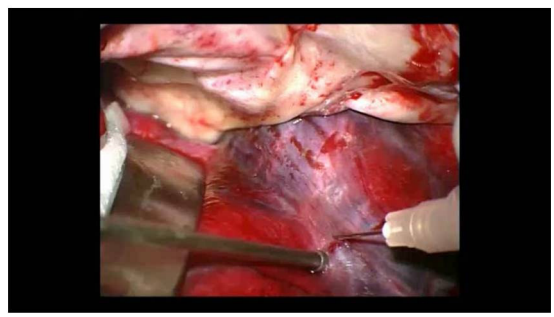
- M/70
- Brief Hx. : Sudden Onset HA (H-H Gr. 2)







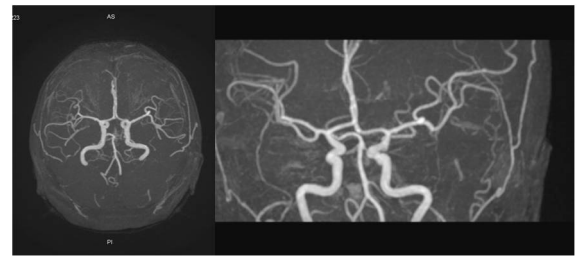
OP



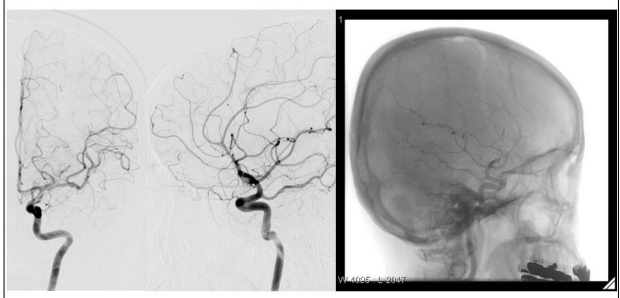
CASE

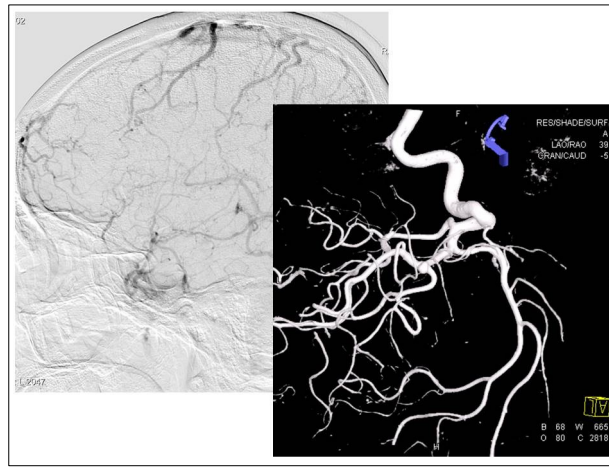
F/50

- Incidental An
  - Lt. MCA bifurcation An. On MRA



TFCA





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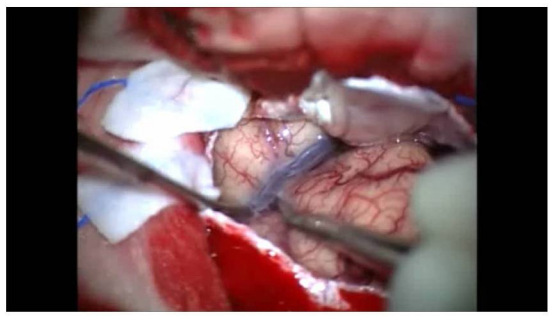
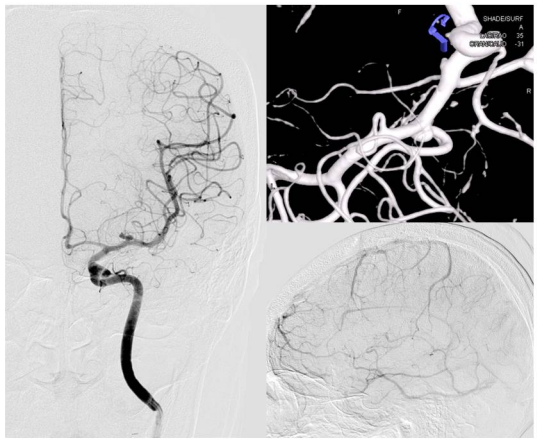
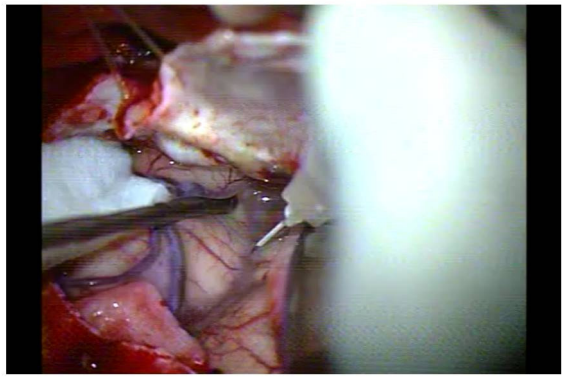
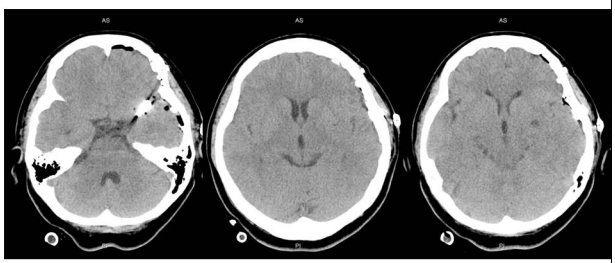
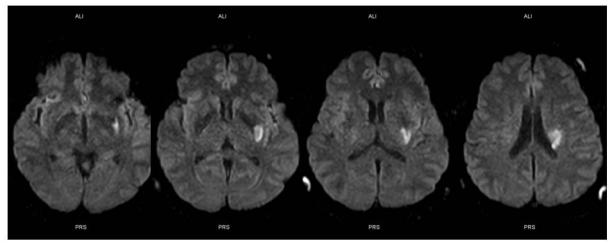


Complication CASE









Thank you for your attention

How to Clip of ACA aneurysm

박익성

가톨릭대학교 부천성모병원

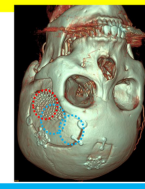
How to Clip of ACA Aneurysm

가톨릭대학교 부천성모병원

박익성

Aneurysm location and Approach

Frontotemporal Approach → A1 segment

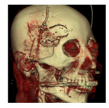


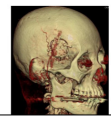
Anterior communicating artery

Interhemispheric approach → Distal ACA

Frontotemporal Approach

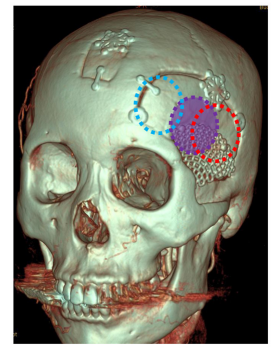
- Trans-eyebrow Approach
  - Suprarobital
  - Superciliary
  - Trans-ciliary
  - Eyebrow incision
  - Lateral subfrontal
- Lateral supraorbital A.
- Pterional Trans-sylvian A.



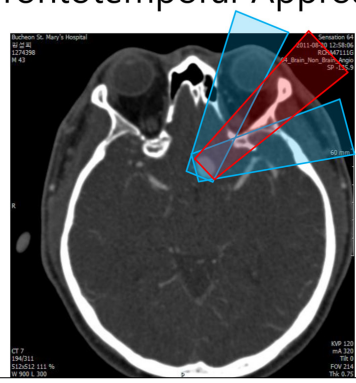


Frontotemporal Approach

- Trans-eyebrow Approach
- Lateral supraorbital A.
- Pterional Trans-sylvian A.

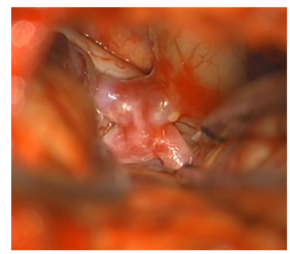


Frontotemporal Approach

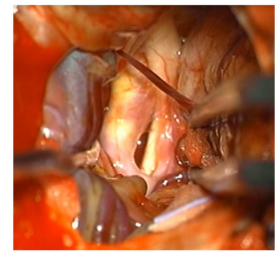


Difference of surgical view

Subfrontal

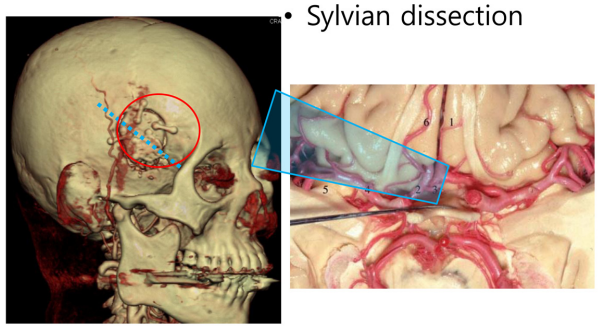


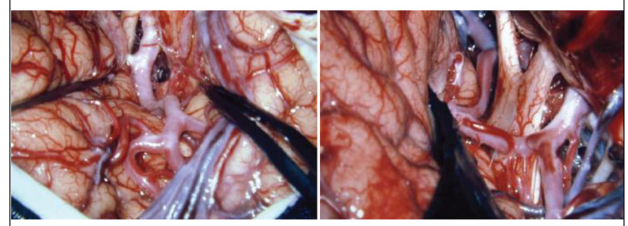
Trans-slyvian



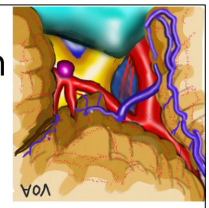
Trans-sylvian

- Sylvian dissection



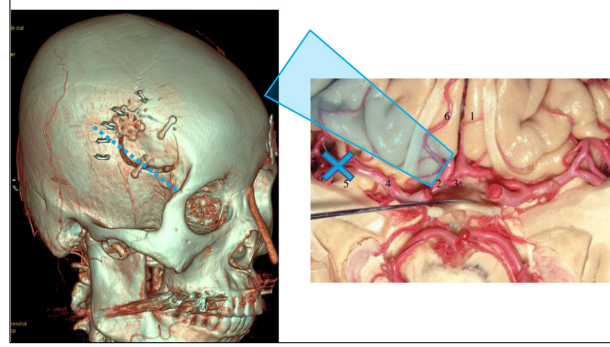


Trans-sylvian



- Advantages
  - Wider view
  - Proximal control: ICAB
  - Minimal olfactory nerve traction
- Disadvantages
  - Prominent deep or superficial sylvian vein
  - Sylvian cistern type

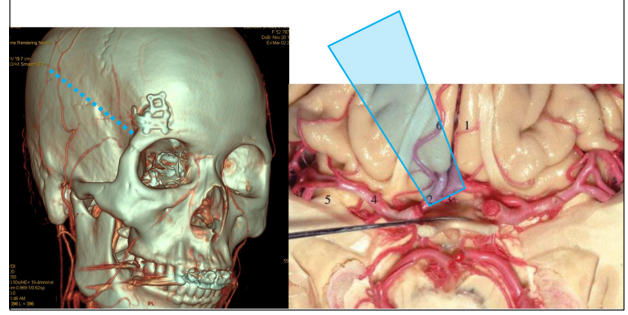
Lateral Supraorbital



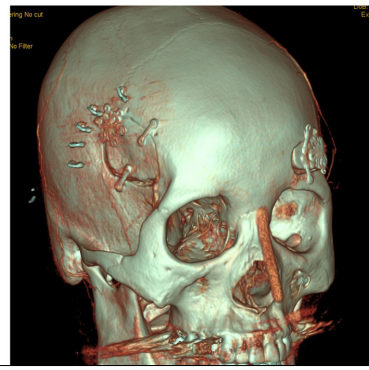
Lateral Supraorbital

- Advantage
  - Short cut to a-comm. a
  - Proximal control: ICAB – A1 proximal
  - Need not sylvian dissection
- Disadvantage
  - Olfactory nerve injury

Trans-Eyebrow Supraorbital



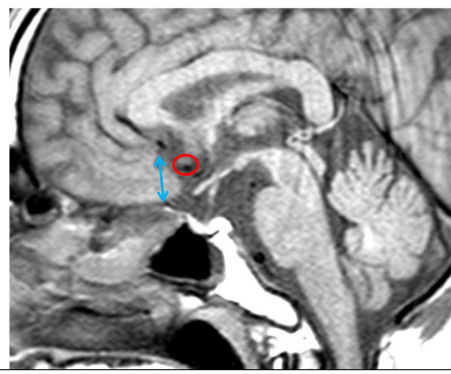
Lateral Vs Trans-ciliary

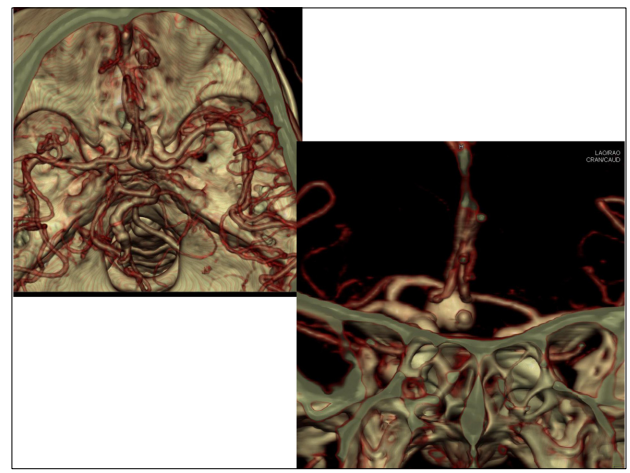


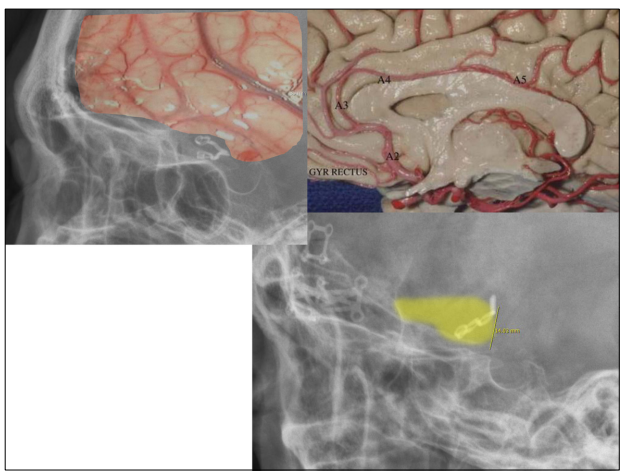
수술 전 확인사항

- 환자 임상 상태 : brain swelling정도
- Aneurysm configuration
  - Location : height from Planum Sphenoidale
  - Direction(projection) :ant, sup, inf, post
  - Parent vessel :dominancy
  - Shape, size
  - SAH distribution

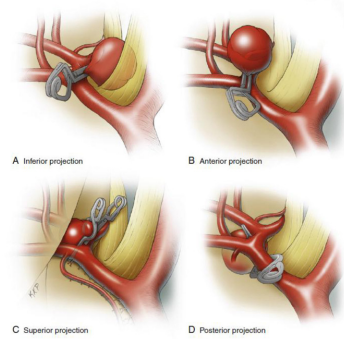
Aneurysm Location : Height



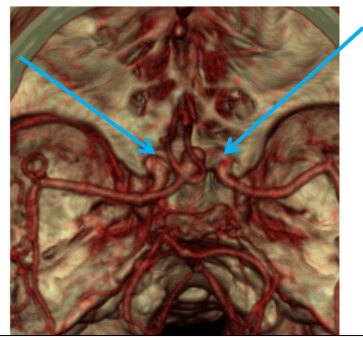


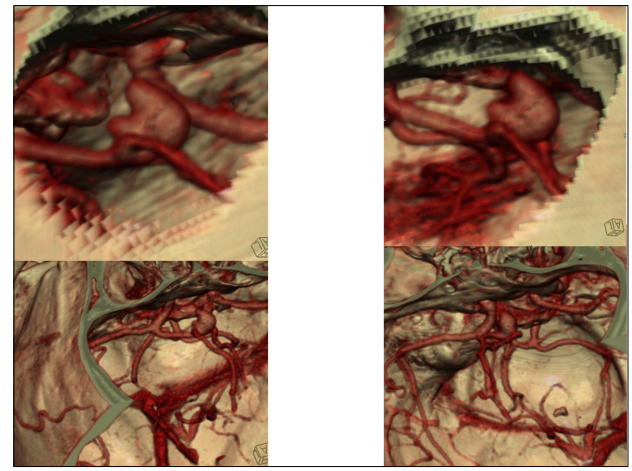


Aneurysm Projection



A1 Status- Approaching Site





Arachnoid dissection

- Carotid cistern
- Sylvian cistern
- Chiasmatic cistern
- Basal cistern
- Interhemispheric cistern

Proximal control

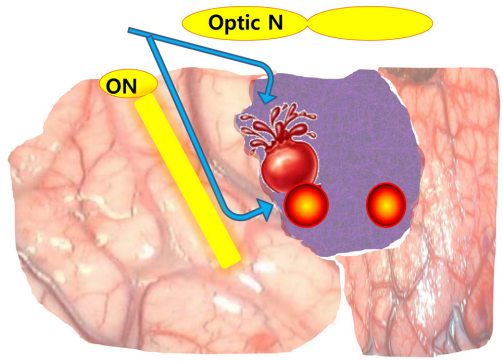
- ICA
- Ipsilateral A1
- Contralateral A1

Surgical view

- Brain relaxation
  - Cistern opening
  - Arachnoid dissection
  - Ventricle tapping
  - Laminar terminalis opening
- Gyrus rectus resection

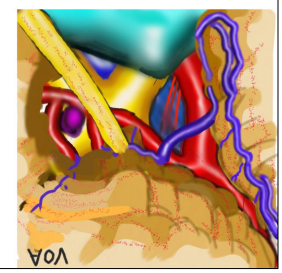
CSF drain - Laminar Terminalis Opening

Gyrus Rectus Resection:
- Working space
- Subpial approach



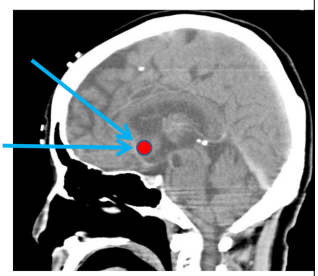
Specific consideration

- Unexpected rupture
- Temporary clipping
- Flow confirm
- Olfactory nerve injury



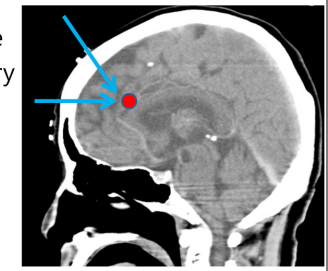
Interhemispheric approach

- For a-comm. Aneurysm:
  - High location
  - Approaching route



Interhemispheric approach

- For DACA Aneurysm:
  - Navigation guided
  - Approaching route
  - Avoid venous injury



Key Note

- Angio-architecture
  - Aneurysm projection
  - Aneurysm location
  - A1 dominancy
- Approaching route : sylvian vs subfrontal
- Step by step
  - Brain relaxation
  - Arachnoid dissection
  - Proximal control -Unexpected rupture
  - Olfactory nerve inspection
  - Gyrus rectus resection
  - Temporary clipping
  - Permanent clipping
  - Inspection
  - Flow confirm

How to coil assisted by STENT

김성림

가톨릭대 부천성모병원

How to Coil Assisted by STENT

- Workshop by Video for Beginner-

가톨릭대학교 부천성모병원 신경외과

김성림

Virchow's Triad

1. Blood flow
2. Endothelial thrombogenicity
3. Hematologic thrombogenicity

Anti-PLT agents

1. to modulate
   endothelial / hematologic thrombogenicity
2. Drug Resistance: aspirin, clopidogrel
3. Sufficient period before coil embolization

Stent: cell design

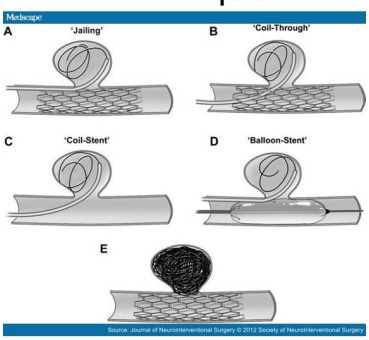
Open-cell

1. Recapturing 불가
2. 곡면에서 cell size가 일정하지 않다.

Closed-cell

1. Recapturing 가능
2. 비교적 일정한 cell size

technique



Technique: stent deployment

1. Unsheathing technique
2. Push & Pull-Back technique

Technical considerations of stent deployment

1. Incomplete stent apposition.
2. Landing zone of distal/proximal ends.

Configurations of stenting for bifurcation aneurysms

1. Single stent
2. Horizontal
3. Y-configuration
   i. kissing-Y
   ii. Crossing-Y
   iii. Non-overlapping Y
4. Waffle cone

How to Coil Assisted by Balloon

윤석만

순천향대 천안병원

뇌동맥류 코일색전술시 balloon은 매우 유용한 tool이다. 특히 wide necked aneurysm, aneurysm neck에서 branch가 기시하는 경우, unfavorable geometry(aspect ratio 〈2) aneurysm은 balloon을 사용하여 효과적으로 치료할 수 있다. Wide necked aneurysm치료에 stent를 점차 많이 사용하는 추세이나 스텐트는 항혈소판제전 처치가 되어 있어야 하고 평생동안 항혈소판제를 복용해야 하는 부담이 있다. 특히 파열동맥류에서는 스텐트사용으로 인한 혈전색전 합병증이 적지 않으므로 balloon이 보다 더 유용할 수 있다. Balloon remodeling technique(BRT)은 Jacques Moret 등이 1997년 처음으로 기술한 방법으로, hypercompliant 혹은 compliant balloon catheter를 aneurysm neck을 cross하여 위치시킨 후 미세도관으로 동맥류를 초선택하고 balloon inflation 상태에서 코일을 packing한다. Detach에 앞서 balloon deflation 하여 packing한 코일이 안정적인지 확인하고 안정적이면 balloon inflation 하에서 detach하는 것이다. 그 후 추가적인 코일 packing시에도 이러한 과정을 반복하는 것이다. Side wall aneurysm에는 주로 compliant balloon인 HyperGlide나 Scepter C가 사용되고 bifurcation aneurysm이나 aneurysm neck에서 branch가 기시하여 이를 보호해야 하는 동맥류의 경우에는 Supercompliant balloon인 HyperForm이나 Scepter XC가 주로 사용된다. Hypercompliant balloon을 조심스럽게 overinflation하면 aneurysm neck으로 herniation되면서 neck에서 기시하는 branch을 보호할 수 있어 p-com aneurysm에 효과적으로 사용된다. Fiorella등은 2009년 BRT의 변형으로 한번 balloon inflation한 후 여러 개의 코일을 연속적으로 packing하여 코일 mass을 안정화 시키는 conglomerate coil mass technique을 기술 하였다. 이는 original BRT에 비해 balloon inflation, deflation 반복을 최소화함으로써 vessel manipulation을 최소화 하고 빠른 속도로 코일을 시행할 수 있는 장점이 있다. Balloon으로 혈류를 차단할 경우 thromboembolic complication 위험이 높아지므로 balloon inflation에 앞서 반드시 heparin을 bolus로 injection하여 ACT를 2-3배 연장시키도록 해야 한다. 코일색전술시 balloon은 뇌동맥류 수술시 temporary clip과 마찬가지로 파열위험에 대처하기 위해 endovascular neurosurgeon이 반드시 갖추어야 할 필수 술기로 사료된다.

Balloon assisted coiling technique

① 사용에 앞서 Balloon catheter lumen을 70% 조영제로 irrigation하여 air를 완전히 제거한 후 microwire를 넣고 Y-connector에 three way를 달아 연결한다. Three way의 한쪽 끝에는 약 3cc정도의 조영제가 담긴 10cc syringe를 다른 쪽에는 1cc syringe를 연결하고 적절히 wire shaping을 한 후 test inflation을 시행하여 balloon상태를 확인하고 guiding catheter에 insertion한다. 초심자의 경우는 1cc rotating syringe를 사용하는 것이 더 안전할 수 있다.

② 6F Envoy guiding catheter에 balloon catheter와 코일용 microcatheter를 같이 넣을 경우 가능하면 balloon catheter를 aneurysm 근처까지 먼저 올린 후 microcatheter를 올리는 것이 좋다.

③ ICA aneurysm에 BRT시에는 balloon microwire를 MCA bifurcation을 지나 굵고 tortuous하지 않은 혈관에 위치시켜 만약에 발생할 수 있는 Ballooning시 sudden jumping으로 인한 혈관파열의 위험을 최소화해야 한다.

④ Balloon inflation에 앞서 balloon catheter를 gentle하게 withdraw하여 tension을 완전히 푼 후, inflation을 시작한다. Ballooning에 따라 혈류가 차단되기 시작하면 혈류 저항 때문에 balloon catheter가 distal로 딸려 올라가게 되므로 ballooning과 동시에 한 손으로는 balloon catheter를 서서히 당겨야 한다.

⑤ Balloon inflation은 대부분 코일 몇 loop를 deploy한 후 시작하는 것이 안전하며 roadmap하에서 full heparinization후 시행하게 된다. 코일이 안정적으로 말리고 완전히 다 들어가면 balloon을 풀어 코일 frame이 stable한지 확인 후 다시 inflation하고 detach 한다.

⑥ Balloon deflation은 10cc syringe로 aspiration하면 쉽고 빠르게 시행할 수 있다.

⑦ Branch를 보호하기 위한 목적으로 할 경우는 Hyper-compliant balloon을 gentle over-inflation 하여 balloon일부가 neck으로 intentionally herniation 되게 한다.

⑧ Syringe로 balloon inflation을 하였는데도 roadmap상 balloon이 보이지 않을 경우, 추가적으로 계속 balloon하지 말고 balloon catheter를 제거하여 다시 prep한 후 사용하여야 한다. Balloon microwire는 가급적 balloon catheter 안으로 들어가지 않도록 유지하여야 한다.

How to coil assisted by Multiple catheter

강현승
서울대병원

Scientific session III

좌장 : 나형균(가톨릭대), 고준석(경희대)

Update in the management of intracranial stenosis

1. Medical management and follow up — 이종영(한림대)
2. Endovascular treatment — 이재일(부산대)
3. Surgical treatment — 김정은(서울대)
4. Current recommendation and literature review — 정승영(을지대)

Medical Management of intracranial stenosis

Jong Young Lee
Hallym University Kangdong Sacred Heart Hospital

Medical management of intracranial stenosis

Dual Antiplatelet Therapy in Stroke patients : Pros vs Cons

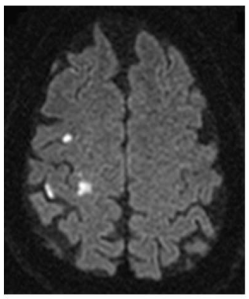
Jong Young Lee

Hallym University Kangdong Sacred Heart Hospital

AHA/ASA Guidelines for the Prevention of Stroke in Patients With Stroke and Transient Ischemic Attack

Intracranial atherosclerosis	For patients with recent stroke or TIA (within 30 days) attributable to severe stenosis (70%–99%) of a major intracranial artery, the addition of clopidogrel 75 mg/d to aspirin for 90 days might be reasonable *(Class IIb; Level of Evidence B)*.	New recommendation
	For patients with stroke or TIA attributable to 50% to 99% stenosis of a major intracranial artery, the data are insufficient to make a recommendation regarding the usefulness of clopidogrel alone, the combination of aspirin and dipyridamole, or cilostazol alone *(Class IIb; Level of Evidence C)*.	New recommendation
	For patients with a stroke or TIA attributable to 50% to 99% stenosis of a major intracranial artery, maintenance of systolic BP below 140 mm Hg and high-intensity statin therapy are recommended *(Class I; Level of Evidence B)*.	1. New cholesterol recommendation is consistent with 2013 ACC/AHA cholesterol guideline[16] 2. Class changed from IIb to I
	For patients with a stroke or TIA attributable to moderate stenosis (50%–69%) of a major intracranial artery, angioplasty or stenting is not recommended given the low rate of stroke on medical management and the inherent periprocedural risk of endovascular treatment *(Class III; Level of Evidence B)*.	New recommendation
	For patients with stroke or TIA attributable to severe stenosis (70%–99%) of a major intracranial artery, stenting with the Wingspan stent system is not recommended as an initial treatment, even for patients who were taking an antithrombotic agent at the time of the stroke or TIA *(Class III; Level of Evidence B)*.	New recommendation
	For patients with stroke or TIA attributable to severe stenosis (70%–99%) of a major intracranial artery, the usefulness of angioplasty alone or placement of stents other than the Wingspan stent is unknown and is considered investigational *(Class IIb; Level of Evidence C)*.	1. Change from 50% to 99% stenosis to 70% to 99% stenosis 2. Rewording to mention Wingspan device used in SAMMPRIS
	For patients with severe stenosis (70%–99%) of a major intracranial artery and recurrent TIA or stroke after institution of aspirin and clopidogrel therapy, achievement of systolic BP <140 mm Hg, and high-intensity statin therapy, the usefulness of angioplasty alone or placement of a Wingspan stent or other stents is unknown and is considered investigational *(Class IIb; Level of Evidence C)*.	New recommendation
	For patients with severe stenosis (70%–99%) of a major intracranial artery and actively progressing symptoms after institution of aspirin and clopidogrel therapy, the usefulness of angioplasty alone or placement of a Wingspan stent or other stents is unknown and is considered investigational *(Class IIb; Level of Evidence C)*.	New recommendation

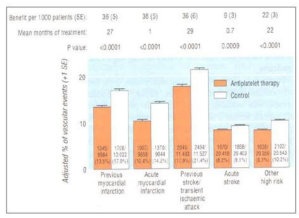
Stroke 2014;45:2016-2236




"Combined aspirin and clopidogrel therapy for high-risk patients with atherothrombotic stroke"

Meta-analysis of RCTs of anti-PLTs therapy Antithrombotic Trialists' Collaboration BMJ 2002

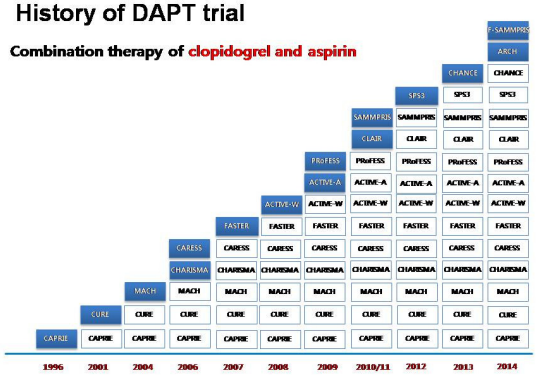
- Overall, **¼ reduction** of any serious vascular events
- ARR
  - 36 per 1000 treated for 2 years among those with previous stroke or TIA
  - 22 per 1000 treated for 3 weeks among those with acute stroke



- **Aspirin failure**
  - **Require more potent treatment**, such as new anti-PLTs agent or combination anti-PLTs therapy

History of DAPT trial

Combination therapy of clopidogrel and aspirin



CAPRIE, 1996

- **Design & Objective**
  - **RCT**
  - **To compare clopidogrel with aspirin**
- **Inclusion**
  - **19,185**
  - Patients with **recent ischemic stroke, recent MI, or symptomatic PAD**.
- **Primary outcome**
  - **Composite of ischemic stroke, MI, or vascular death**.

Clopidogrel is more effective and slightly safer than aspirin as secondary prevention.

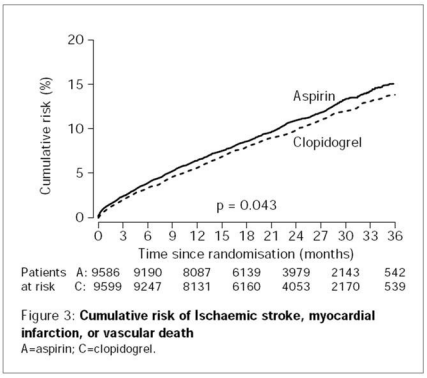


Figure 3: **Cumulative risk of Ischaemic stroke, myocardial infarction, or vascular death**
A=aspirin; C=clopidogrel.

History of DAPT trial in patients with ACS or after PCI

PROS

CURE, 2003

- **Design & Objective**
  - **RCT**
  - **To compare clopidogrel plus aspirin with aspirin monotherapy**
- **Inclusion**
  - **12,562**
  - Patients with **acute coronary syndromes** without ST-segment elevation
- **Primary outcome**
  - **Composite of cardiovascular death, nonfatal MI, or stroke** during one year

The **combination of clopidogrel plus aspirin is more beneficial than aspirin monotherapy** in patients with **acute coronary syndromes.**

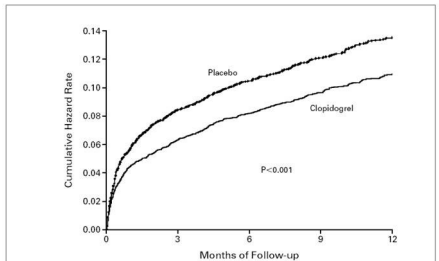


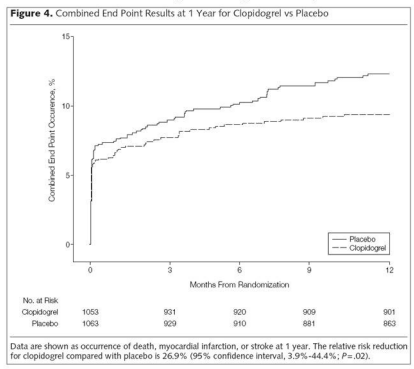
Figure 1. Cumulative Hazard Rates for the First Primary Outcome (Death from Cardiovascular Causes, Nonfatal Myocardial Infarction, or Stroke) during the 12 Months of the Study.
The results demonstrate the sustained effect of clopidogrel.

PROS

CREDO, 2002

- **Design & Objective**
  - RCT
  - **To compare clopidogrel plus aspirin with aspirin monotherapy**
- **Inclusion**
  - **2,116**
  - Patients who were referred for **PCI**, or thought to be at high likelihood for requiring PCI
- **Primary outcome**
  - **Composite of death, MI, or stroke** during one year

The combination of clopidogrel plus aspirin is beneficial in patients undergoing PCIs, with or without drug-eluting stent placement.



DAPT trials in patients with ACS or after PCI

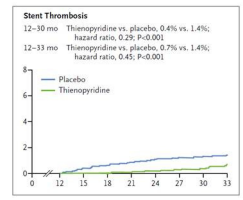
- **The combination of clopidogrel plus aspirin is more beneficial** than placebo plus aspirin
  - **in patients with acute coronary syndromes**
  - **in patients undergoing PCIs, with or without drug-eluting stent placement.**

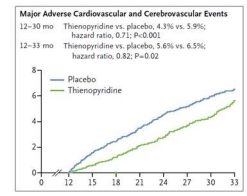
PROS

Optimal duration of DAPT in patients with ACS or after PCI

- DAPT beyond 1 year after stenting with DES **significantly reduced the risks of stent thrombosis** and major adverse cardiovascular and cerebrovascular events, **but was associated with an increased risk of bleeding.**

N Engl J Med 2014;371:2155-66.



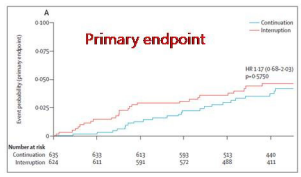


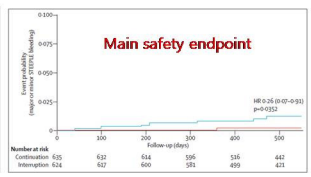
Optimal duration of DAPT in patients with ACS or after PCI

CONS

- **No apparent benefit but instead harm** with extension of DAPT beyond 1 year after stenting with DES **when no event has occurred within the first year after stenting**

Lancet 2014; 384: 1577–85





DAPT trials in patients with ACS or after PCI

- **The combination of clopidogrel plus aspirin is more beneficial** than placebo plus aspirin
  - **in patients with acute coronary syndromes**
  - **in patients undergoing PCIs, with or without drug-eluting stent placement.**
- **Duration < 1 year**

History of DAPT trials in patients with ischemic stroke

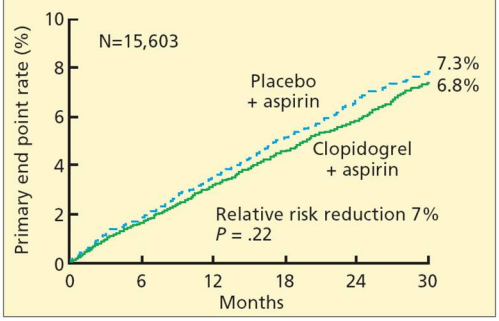
CHARISMA, 2006

CONS

- **Design**
  - RCT
  - To compare clopidogrel plus aspirin vs placebo plus aspirin
- **Inclusion**
  - 15,603
  - Patients at high risk of cardiovascular events.
- **Primary outcome**
  - Composite of MI, stroke, or cardiovascular death

CHARISMA: No benefit from dual antiplatelet therapy in the overall cohort of stable patients studied...

CONS



Outcomes in CHARISMA

END POINT	CLOPIDOGREL AND ASPIRIN (N = 7,802)	PLACEBO AND ASPIRIN (N = 7,801)	RELATIVE RISK WITH CLOPIDOGREL	P VALUE
Efficacy end points				
Primary efficacy end point[a]	6.8%	7.3%	0.93	.22
Death from any cause	4.8%	4.8%	0.99	.90
Death from cardiovascular causes	3.1%	2.9%	1.04	.68
Myocardial infarction (nonfatal)	1.9%	2.0%	0.94	.59
Ischemic stroke (nonfatal)	1.7%	2.1%	0.81	.07
Stroke (nonfatal)	1.9%	2.4%	0.79	.03
Secondary efficacy end point[b]	16.7%	17.9%	0.92	.04
Hospitalization for unstable angina, transient ischemic attack, or revascularization	11.1%	12.3%	0.90	.02
Safety end points				
Severe bleeding	1.7%	1.3%	1.25	.09
Fatal bleeding	0.3%	0.2%	1.53	.17
Primary intracranial hemorrhage	0.3%	0.3%	0.96	.89
Moderate bleeding	12.1%	1.3%	1.62	< .001

CONS

[a] Myocardial infarction, stroke, or death from cardiovascular causes
[b] Myocardial infarction, stroke, death from cardiovascular causes, or hospitalization for unstable angina, a transient ischemic attack, or revascularization procedure

Inclusion criteria in the CHARISMA study

MULTIPLE RISK FACTORS*

Major risk factors
Type 1 or 2 diabetes
Diabetic nephropathy
Ankle-brachial index < 0.9
Asymptomatic carotid stenosis (≥ 70% of luminal diamete
More than one carotid plaque (evidenced by intima-media thic

Minor risk factors
Systolic blood pressure ≥ 150 mm Hg (despite 3 months of th
Primary hypercholesterolemia
Current smoking (> 15 cigarettes/day)
Male sex and age ≥ 65 years, or female sex and age ≥ 70

ESTABLISHED CARDIOVASCULAR DISEASE

Documented coronary disease
Angina with documented multivessel coronary disease
History of multivessel percutaneous coronary intervention
History of multivessel coronary artery bypass grafting
Myocardial infarction

Documented cerebrovascular disease
Transient ischemic attack during prior 5 years
Ischemic stroke during prior 5 years

Documented symptomatic peripheral arterial disease
Current intermittent claudication and ankle-brachial index ≤
History of intermittent claudication and previous interventi (ie, amputation, peripheral bypass, or angioplasty)

Why (-) ?

Patients at high risk of cardiovascular events ??

2 major or
3 minor or
1 major and 2 minor risk factors

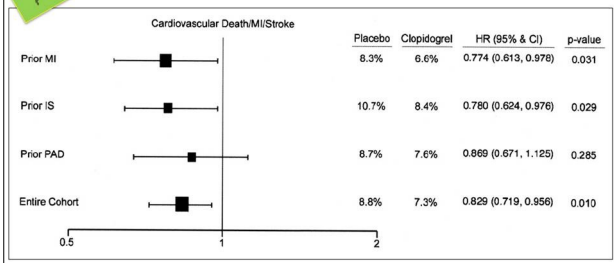
Or Established Cardiovascular Ds.

But, more stable patients cohort

	IS	MI
CHARISMA	≤ 5 yrs	No time limit
CAPRIE	1 wk – 6 mon	≤ 35 days
CURE/CREDO	-	acute

In patients with established cardiovascular disease (CAPRIE-like, but stable CHARISMA cohort)

PROS



PROS

Time from onset to randomization

Time of Ischemic Event Prior to Randomization	Clopidogrel + Aspirin	Placebo + Aspirin	HR (95% CI)
Within 30 days	8.2% (86/1,053)	10.5% (109/1,041)	0.773 (0.583–1.025)
Between 30 to 300 days	6.7% (68/1,014)	8.0% (83/1,036)	0.831 (0.603–1.146)
Between 300 days to 30 months	6.8% (68/997)	8.0% (81/1,018)	0.848 (0.614–1.171)
More than 30 months	6.6% (71/1,078)	7.2% (74/1,034)	0.918 (0.663–1.271)

Adapted from DL Bhartt et al , Journal of the ACC. 2007

Limitation of CHARISMA

Relatively low risk patients

- Include the patients for primary prevention
  - ~ 40%
- Include patients with established cardiovascular disease, but mostly chronic stage
  - ~89% : 30 days after index event
  - ~50% : 300 days after index event

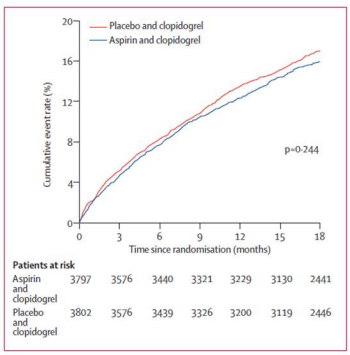
MATCH, 2004

CONS

- Design
  - RCT
  - To **compare clopidogrel plus aspirin *vs* clopidogrel plus placebo**
- Inclusion
  - Patients with **TIA or IS within 3 M** and **at least 1 additional vascular risk factor**
- Primary Outcome
  - **Composite of MI, stroke, vascular death, re-hospitalization**

MATCH, 2004

CONS



MATCH, 2004

CONS

	Number (%) with event		Difference (%) between aspirin and placebo (95% CI)	p*
	Aspirin and clopidogrel (n=3759)	Placebo and clopidogrel (n=3781)		
Life-threatening bleeding	96 (3%)	49 (1%)	1·26 (0·64 to 1·88)	<0·0001
Fatal bleeding	16 (<1%)	11 (<1%)	0·13 (−0·14 to 0·40)	
Non-fatal bleeding	81 (2%)	38 (1%)	1·15 (0·59 to 1·71)	
Symptomatic intracranial haemorrhage†	40 (1%)	25 (1%)	0·40 (−0·01 to 0·82)	
Primary intracranial haemorrhage	32 (1%)	17 (<1%)	0·40 (0·04 to 0·76)	
Major bleeding	73 (2%)	22 (1%)	1·36 (0·86 to 1·86)	<0·0001
Minor bleeding	120 (3%)	39 (1%)	2·16 (1·51 to 2·81)	<0·0001

*Pearson's χ^2 test. †All symptomatic (and thus primary) intracranial haemorrhages were life-threatening bleeds.

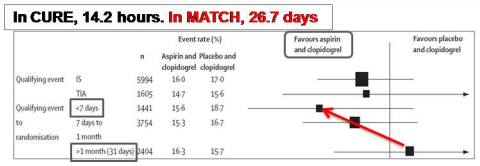
Table 4: Number (%) of patients with bleeding events

Why (-) ?

The difference between CURE and MATCH

1. The difference of time from onset to randomization

In CURE, 14.2 hours. In MATCH, 26.7 days



2. The difference of enrolled patients' type

In CURE, patients with acute coronary syndrome (**atherosclerosis**)
In MATCH, patients with ischemic stroke
- **Small vessel occlusion, 53 % of all patients**
- **Large artery disease (atherosclerosis), 34 % of all patients**

SPS3 (2012)

Secondary Prevention of Small Subcortical Strokes

CONS

- **Double-blind, randomized, multicenter**
- **Subject : lacunar stroke**
  Within 180 days symptom onset
- **Factorial design : ASA (325 mg/day) ± clopidogrel** (75 mg/day), and systolic BP control (<130 vs. 130 to 149 mmHg)
- **Outcome : Any recurrent stroke at 3 M**

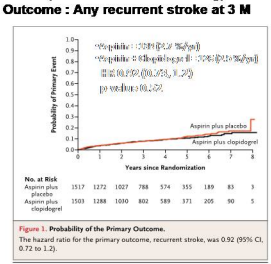
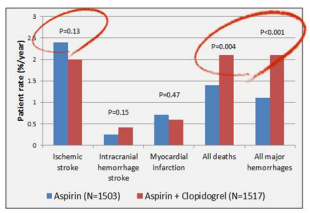


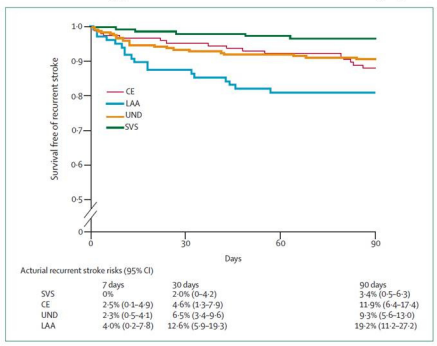
Figure 1. Probability of the Primary Outcome.
The hazard ratio for the primary outcome, recurrent stroke, was 0.92 (95% CI, 0.72 to 1.2).

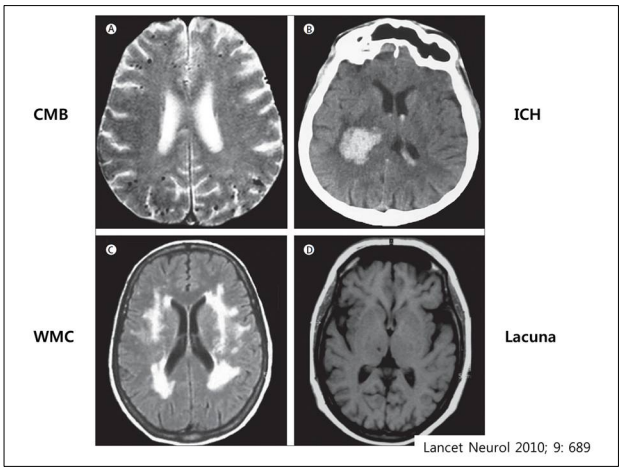


- **Combination do not reduce the risk of recurrent stroke among patients with recent lacunar infarction.**
- Annual rate of both major hemorrhage (2.1 versus 1.1 percent, HR 1.97, 95% CI 1.41-2.71)
- All-cause mortality (2.1 versus 1.4 percent, HR 1.52, 95% CI 1.14-2.04)

SPS3 Investigators, et al. N Engl J Med 2012;367:817-25.

Risk of Stroke Recurrence according to Stroke Subtypes





Lancet Neurol 2010; 9: 689

CHARISMA & MATCH

- Dual antiplatelets are not beneficial in non-selective patients.

Risk of Stroke Recurrence
after a minor stroke or TIA
= 10-20% within 90 days

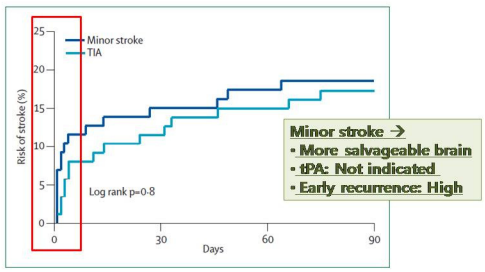


Figure 1: Cumulative risk of stroke following a transient ischaemic attack or minor stroke in the Oxford Vascular Study[21]

Question

- Benefit of dual antiPLT therapy (A+C)
  in selected patients with high risk of stroke recurrence?
  - In patients with atherothrombotic stroke
    (e.g. ≥ 50% significant symptomatic stenosis)
  - In patients with acute or recent ischemic stroke
    (e.g. start within 1 days)
  - In patients with TIA and minor stroke
    (e.g. TIA (ABCD2 ≥ 4) or ischemic stroke (NIHSS 0-3)

Recent | Atherothrombotic | Surrogate endpoint

PROS

CARESS, 2005

- **Design:** Randomized, double-blinded
- **Inclusion : 107 patients**
  - Symptomatic carotid stenosis > 50%;
    ipsilateral TIA or IS in the previous 3 months
- **Primary Outcome:**
  - % of MES-positive patients at Day 7

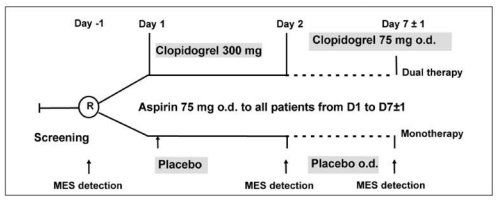


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TABLE 3. Summary of Primary and Secondary End Point Results for Both the ITT and Per Protocol Analyses

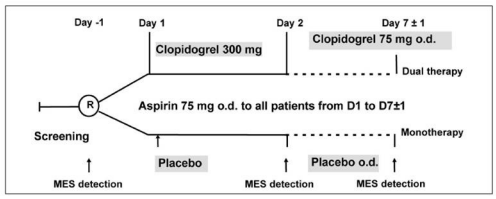
End Point	Treatment Group: Dual Thgerapy	Treatment Group: Monotherapy	Relative Risk Reduction or Embolization Rate Reduction, % (95% CI)	*P*
ITT analysis	n=51	n=56		
MES present at day 7, n (%)	21 (43.8)	40 (72.7)	39.8 (13.8, 58.0)	0.005
MES present at day 2, n (%)	28 (56.0)	40 (74.1)	24.4 (−1.2, 43.5)	0.065
MES frequency day 7, mean±SD	1.8±3.9	5.9±9.3	61.4 (31.6, 78.2)	0.001
MES frequency day 2, mean±SD	3.3±6.4	9.5±14.6	61.6 (34.9, 77.4)	<0.001

Acute | Atherothrombotic | Surrogate endpoint

PROS

CLAIR, 2010

- **Design**: Randomized, open-label, blinded-endpoint
- **Inclusion** : 100 patients
  - Symptomatic MCA or ICA > 50%; ipsilateral TIA or IS in the previous 7 days
- **Primary Outcome**:
  - % of MES-positive patients at Day 2

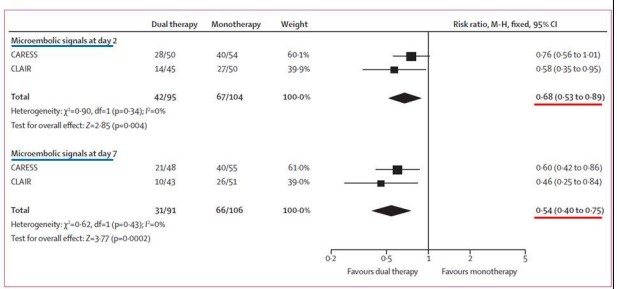


	Dual therapy	Monotherapy	Difference (95% CI)*	p
Modified intention to treat				
Baseline	n=46	n=52		
Mean (SD)	3·2 (5·7)	4·1 (6·1)	..	..
Median (range)	1·5 (0–31)	2 (0–29)	0 (–1 to 0)	0·292
Day 2	n=45	n=50		
Mean (SD)	0·5 (1·3)	2·2 (3·6)	..	..
Adjusted mean (SD)†	0·5 (0·1)	1·8 (0·2)	–1·3 (–1·7 to –0·9)	0·0001
Median (range)	0 (0–8)	1 (0–18)	0 (–1 to 0)	0·004
Day 7	n=43	n=51		
Mean (SD)	0·3 (0·7)	1·8 (2·7)	..	..
Adjusted mean (SD)†	0·3 (0·1)	1·6 (0·3)	–1·2 (–1·6 to –0·9)	0·0004
Median (range)	0 (0–3)	1 (0–11)	0 (–1 to 0)	0·002
Per protocol				
Baseline	n=25	n=31		
Mean (SD)	5·8 (6·7)	6·1 (6·7)	..	..
Median (range)	3 (1–31)	4 (1–29)	0 (–2 to 1)	0·815
Day 2	n=25	n=30		
Mean (SD)	0·8 (1·6)	3·2 (4·2)	..	..
Median (range)	0 (0–8)	1·5 (0–18)	–1 (–2 to 0)	0·002
Day 7	n=24	n=31		
Mean (SD)	0·5 (0·9)	2·2 (3·1)	..	..
Median (range)	0 (0–3)	1 (0–11)	–1 (–1 to 0)	0·014

Recent | Atherothrombotic | Surrogate endpoint

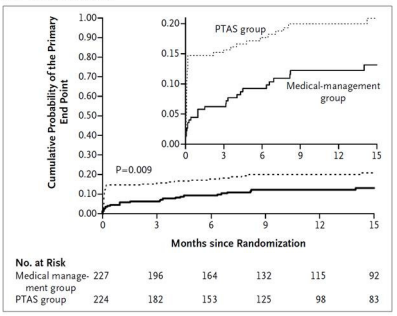
PROS

CARESS + CLAIR



SAMMPRIS, 2011

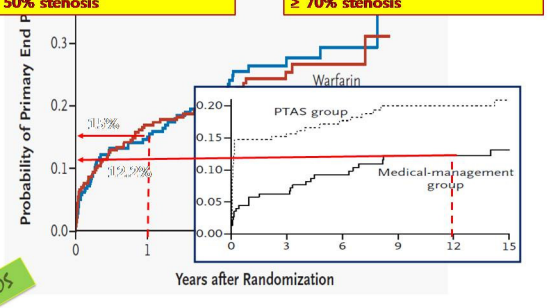
- Stenting *vs* Aggressive Medical Therapy for Intracranial Arterial Stenosis
- **Aggressive medical** management group:
  - A + C for 90 days



WASID (1995) and SAMMPRIS (2011)

TIA or nondisabling stroke **within 90 days** of enrollment and **≥ 50% stenosis**

TIA or nondisabling stroke **within 30 days** of enrollment and **≥ 70% stenosis**



PROS

Acute | Minor | Clinical endpoint

CONS

FASTER, 2007

Similar to CHANCE trial

- **Design**
  - RCT
  - To compare clopidogrel (300 loading, followed by 75) plus aspirin vs aspirin / simvastatin vs placebo
- **Inclusion**
  - Minor stroke (< NIHSS 4) or TIA (symptom including weakness or dysarthria, & duration > 5 min), within 24 hours of onset
- **Primary outcome**
  - Stroke (ischemic and hemorrhagic) within 90 days.
- *Stopped early due to low enrollment rate*
  - 392 patients from 18 centers over 30 months)

42

	Risk difference (95% CI)	Risk ratio (95% CI)	p
Primary efficacy outcomes			
Clopidogrel *vs* placebo			
At the margins	−3·8% (−9·4 to 1·9)	0·7 (0·3–1·2)	0·19
Inside the table	−4·4% (−11·7 to 3·0)	0·5 (0·2–1·5)	0·24
Simvastatin *vs* placebo			
At the margins	3·3% (−2·3 to 8·9)	1·5 (0·8–2·8)	0·25
Inside the table	2·6% (−6·1 to 11·4)	1·3 (0·6–2·9)	0·55

CONS

	n (%)		Risk difference (95% CI)	p*
	No clopidogrel (n=194)	Clopidogrel (n=198)		
Intracranial haemorrhage	0	2 (1·0%)	1% (−0·4 to 2·4)	0·5
Extracranial haemorrhage				
Severe	0	1 (0·5%)	0·5% (−0·5 to 1·5)	1·0
Moderate	0	2 (1·0%)	1% (−0·4 to 2·4)	0·5
Mild	0	1 (0·5%)	0·5% (−0·5 to 1·5)	1·0
Total symptomatic	0	6 (3·0%)	3·0% (0·6 to 5·4)	0·03
Total asymptomatic	27 (13·9%)	61 (30·8%)	16·9% (8·8 to 25·0)	0·0001

	Double placebo (n=95)	Simvastatin only (n=99)	Clopidogrel only (n=98)	Simvastatin and clopidogrel (n=100)
Cardioembolic	10 (10·8%)	7 (7·4%)	5 (5·2%)	4 (4·1%)
Lacunar	26 (28·0%)	24 (25·3%)	28 (28·9%)	35 (36·1%)
Large artery	27 (29·0%)	21 (22·1%)	25 (25·8%)	21 (21·2%)
Other	2 (2·2%)	1 (1·1%)	1 (1·0%)	1 (1·0%)
Unknown	28 (30·1%)	42 (44·2%)	38 (39·2%)	36 (37·1%)

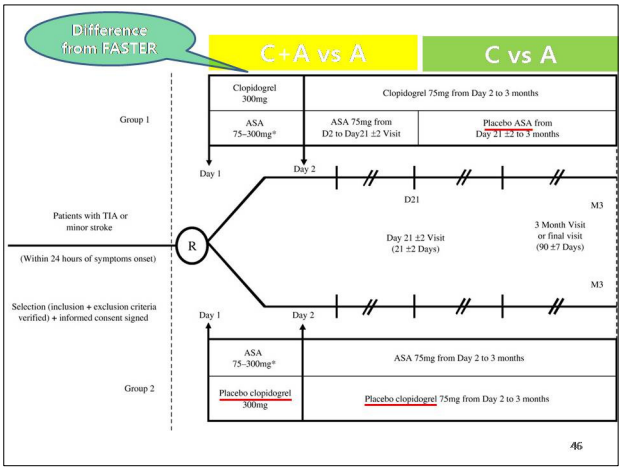
Only patients with an ischaemic cerebrovascular event are included in this table.

Table 4: Mechanism of event leading to randomisation by treatment allocated

Acute Minor Clinical endpoint

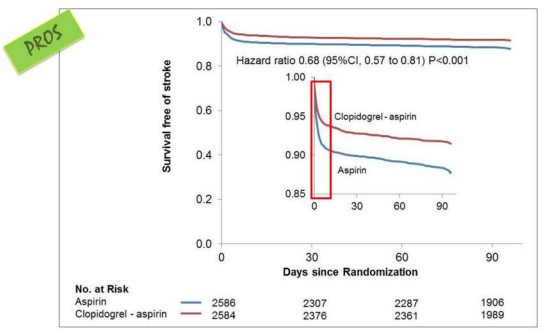
CHANCE, 2013

- Design & Objective
  - **RCT**
  - **To compare clopidogrel (300 loading and 75/day) + aspirin with aspirin for 21 days**
- Inclusion
  - **5,100**
  - **TIA (ABCD2 ≥ 4) or minor ischemic stroke (NIHSS 0-3) within 24 hours** from onset
  - **Exclude possible CE / previous ICH**
  - **Study drug administration within 24 hours** from onset
- Primary outcome
  - **New stroke (ischemic or hemorrhage) at 3 months**



Primary end point : any recurrent stroke (ischemic or hemorrhagic) at 90 days

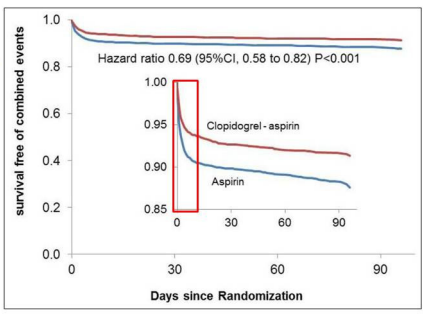
PROS



Wang Y et al CHANCE investigators ISC 2013 presentation

Secondary combined outcome: stroke, MI, death from cardiovascular causes

PROS



Wang Y et al CHANCE investigators ISC 2013 presentation

Safety outcomes

PROS

Outcomes	Aspirin (N=2586)		Clopidogrel-Aspirin (N=2584)		Hazard Ratio (95% CI)	P Value
	Event No.	Event Risk	Event No.	Event Risk		
Any Bleeding	41	1.6%	60	2.3%	1.41(0.95-2.10)	0.09
Severe Bleeding	4	0.2%	4	0.2%	0.94(0.24-3.79)	0.93
Moderate Bleeding	4	0.2%	3	0.1%	0.73(0.16-3.26)	0.68
Mild Bleeding	19	0.7%	30	1.2%	1.57(0.88-2.79)	0.13
Death from any cause	10	0.4%	10	0.4%	0.97(0.40-2.33)	0.94

Wang Y et al CHANCE investigators ISC 2013 presentation

However...

Is the CHANCE trial true savior of dual therapy ?

1. **Higher event rate:**
   8.2% (clopidogrel group) *vs* 11.7% (placebo)

   cf. In FASTER trial : 7.1% (clopidogrel group) *vs* 10.8% (placebo)
   In CRCS-5 (Korea): 3.1% (3 months), 4.8% (1 year)

2. **Poor control of risk factor**
   - Less than half were on any drug for hypertension during follow-up.

Anti-hypertension drug*	886(34.5%)	928(36.2%)	0.20
Anti-diabetes drug*	335(13.0%)	323(12.5%)	0.58
Lowering-lipid drug*	1076(41.9%)	1096(42.8%)	0.52

Acute Minor Clinical endpoint

POINT (ongoing, USA)

ClinicalTrials.gov
A service of the U.S. National Institutes of Health

Platelet-Oriented Inhibition in New TIA and Minor Ischemic Stroke (POINT) Trial (POINT)

This study is currently recruiting participants. (see Contacts and Locations)
Verified December 2015 by University of California, San Francisco

Sponsor:
University of California, San Francisco

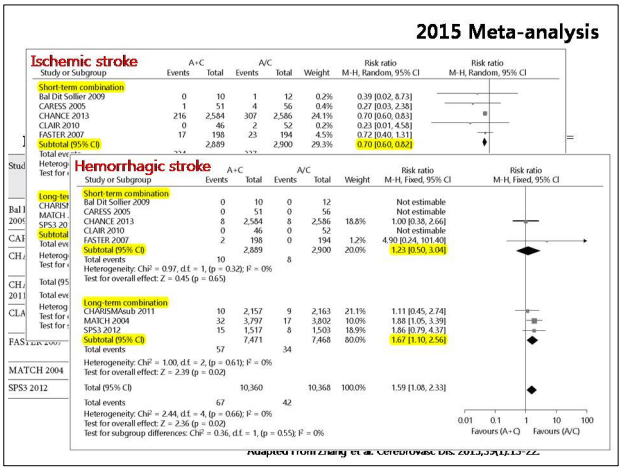
Collaborators:
Neurological Emergencies Treatment Trials Network (NETT)
Medical University of South Carolina
The EMMES Corporation

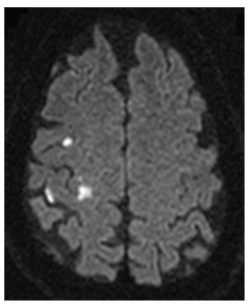
Information provided by (Responsible Party):
University of California, San Francisco

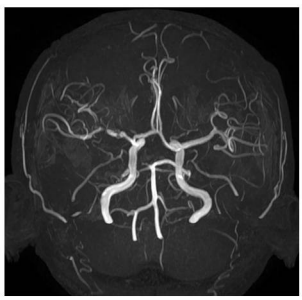
ClinicalTrials.gov Identifier:
NCT00991029

First received: October 6, 2009
Last updated: December 1, 2015
Last verified: December 2015
History of Changes

2015 Meta-analysis







Optimal duration ?

Thank you for your attention

Endovascular treatment

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Department of Neurosurgery Interventional Neuroraddiology School of Medicine, Pusan National University
Pusan National University Hospital Busan, Korea

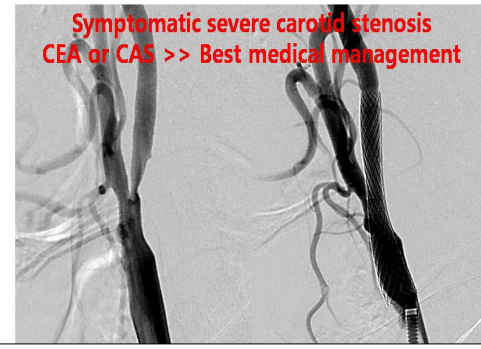
2016 KSCVS-SKEN 합동 연수강좌

Scientific session III

Update in the management of intracranial artery stenosis
: Endovascular treatment

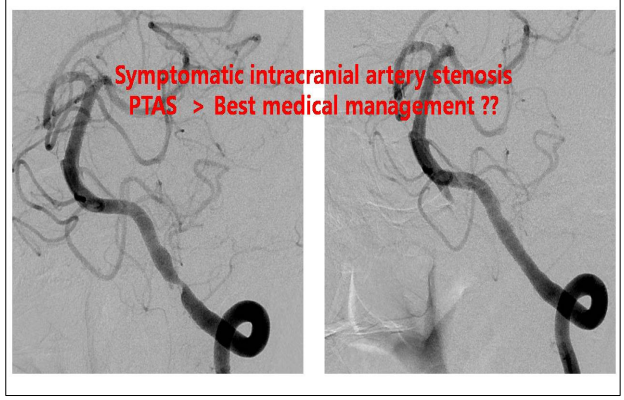
Lee Jae Il , M.D.
Department of Neurosurgery, Interventional Neuroradiology
School of Medicine, Pusan National University
Pusan National University Hospital
Busan, Korea

Update in the management of intracranial stenosis : Endovascular treatment



Characteristics of intracranial artery

- More tortuous than extracranial artery
- Small vessel size
- Tapering in diameter from proximal to distal
- Stroke due to thromboembolism
- No elastic external lamina -> Easy to rupture



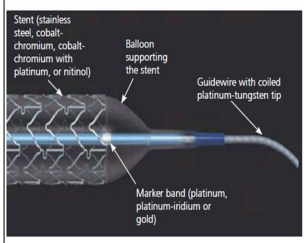
Intracranial endovascular revascularization

- Stent technology
- IER History (before and after SAMPPRIS trial)
- IER cases and complication cases
- My intracranial stenting for ICAD after SAMMPRIS
- My technical consideration of IER

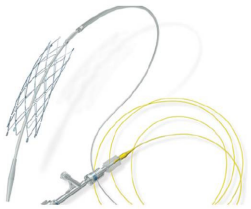
Current Stent technology

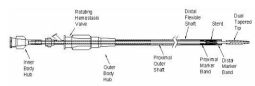
- Balloon mounted stents
  - Semi-compliant balloon for expansion
- Self expanding stents
  - Sheathed, low trauma approach
  - Gentle, radial force maintains lumen

Balloon mounted stent Self expanding stent



Jostent FlexMaster, Abbott, USA





Wingspan, Stryker, USA

Current Stent technology

	BMS (Balloon mounted stent)	SES (Self expanding stent)
Stiffness	Stiff, difficult to delivery	Flexible, easy to delivery
Predilatation	No	Often yes, Two steps
Stent sizing	Critical (over or undersize)	Easy (approximation good)
	Oversize : dissection or rupture	
	Undersize : poor wall apposition, TE	
Risk of vessel rupture	High (due to ballooning pr.)	Low
Restenosis	Passive support	Continuous radial force
	Inward crush resistance	Positive plaque remodeling

History of intracranial endovascular revascularization

Balloon angioplasty
- 1980's First report
- 1990's Many individual series of cases reports
  : >90% success rate, 0-20% complication rate

Balloon mounted stenting
- 2000's Many case series
  : >90% success rate, 0-15% complication rate

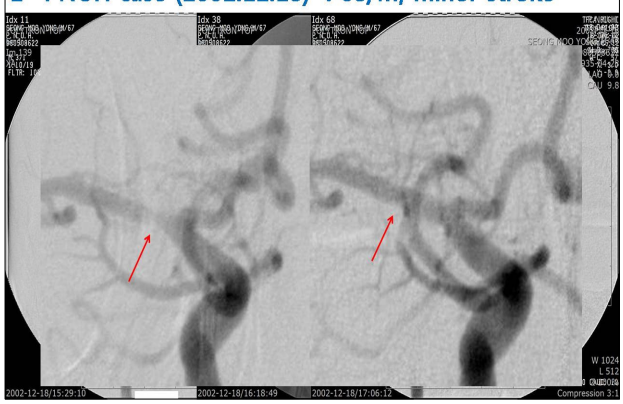
Drug eluting stenting
- Sirolimus-eluting stent and paclitaxel-eluting stent

Jun, 2004, Stroke

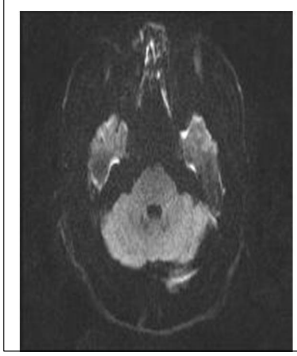
SSYLVIA trial (Stenting of Symptomatic atherosclerotic Lesions in the Vertebral or Intracranial Arteries)

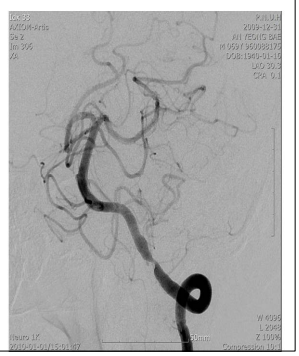
- Symptomatic, >50% stenosis, Neurolink stent (Guidant Corp, IN)
- Success rate 95%, 39% symptomatic restenosis after 6 months, 7.3% stroke after 30 days
- FDA granted a humanitarian device exemption to treat patients

1st PNUH case (2002.12.18) : 68/M, minor stroke

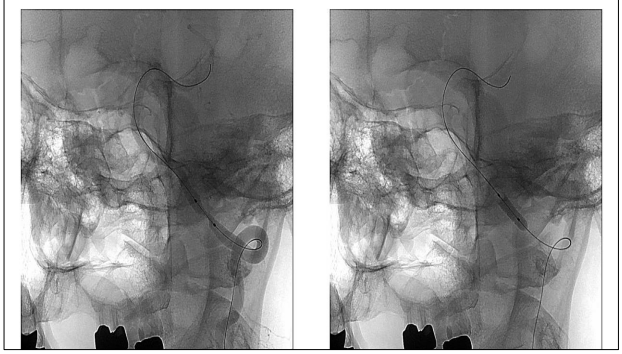


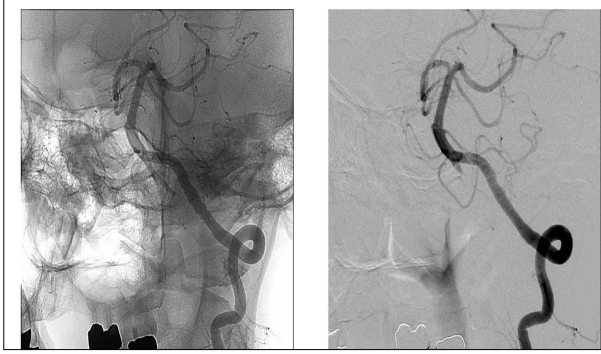
69/M, VBI Sx



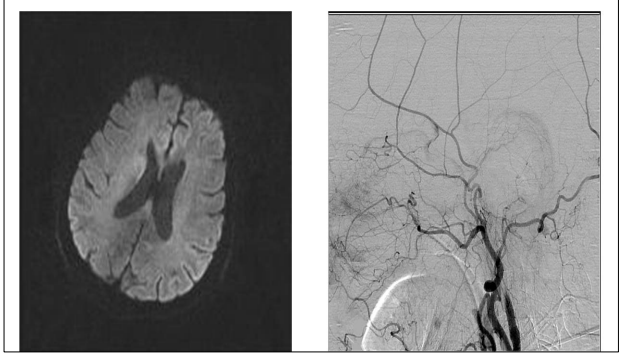


BMS (Jo stent 4/12mm)

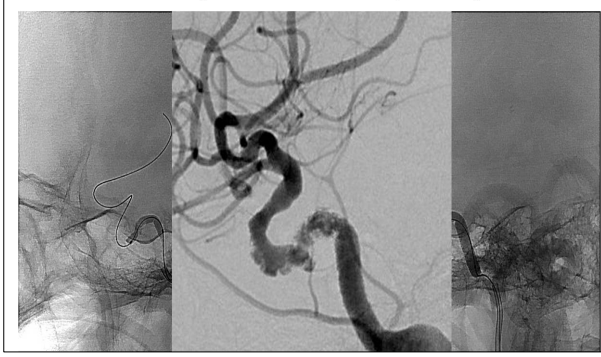




78/M, Acute minor stroke



BMS (Jo Flexmaster 4.5/26mm)



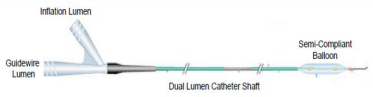
History of intracranial endovascular revascularization

Wingspan and
Gateway balloon system

Stenting planning

- Symptomatic intracranial stenosis more than 50%
- Pre-procedure
  - ASA 300mg or 325mg p.o. before 3 days or 300-650mg po on the day before the procedure
  - Clipidogrel 74mg p.o. before 3 days or 225mg po twice the day before the procedure
- Under G.A., ACT >250 sec.
- Post procedure
  - Heparin to maintain ACT 2 to 3 times or PTT 70 to 90 for 24 hrs
  - ASA 300 or 325mg daily
  - Clopidogrel 75mg daily or ticlopidine 250mg p.o. twice a day for 30 days

Gateway™ PTA Balloon Catheter

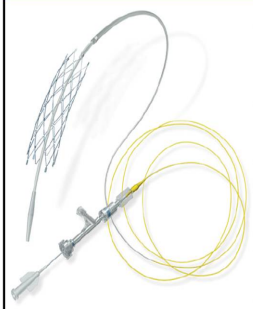


Shaft Configuration	Over-The-Wire (OTW) Dual Lumen Catheter: guidewire port, balloon inflation port
Balloon Diameters (mm)	1.5, 2.0, 2.25, 2.5, 2.75, 3.0, 3.25, 3.5, 3.75, 4.0
Balloon Lengths (mm)	9, 15, 20
Balloon Material	LEAP®/SoftLEAP® semi-compliant balloon material
Nominal Inflation Pressure	6 atm
Rated Burst Pressure	12 atm 14 atm - 2.25-3.25mm diameters only

Humanitarian Device: The Wingspan® Stent System with Gateway™ PTA Balloon Catheter is authorized by Federal Law for use in improving cerebral artery lumen diameter in patients with intracranial atherosclerotic disease, refractory to medical therapy, in intracranial vessels with ≥50% stenosis that are accessible to the system. The effectiveness of this device for this use has not been demonstrated.

NVUS1615

Wingspan® Stent System



Configuration	3.5 F Unified Over-The-Wire (OTW) Self-Expanding Stent System
Nominal Stent Diameters (mm)	2.5, 3.0, 3.5, 4.0, 4.5
Stent Lengths (mm)	9, 15, 20
Recommended Guidewire	.014" exchange length (300 cm)
Recommended Guide Catheter	6F (minimum .064" ID), 90cm length

Humanitarian Device: The Wingspan® Stent System with Gateway™ PTA Balloon Catheter is authorized by Federal Law for use in improving cerebral artery lumen diameter in patients with intracranial atherosclerotic disease, refractory to medical therapy, in intracranial vessels with ≥50% stenosis that are accessible to the system. The effectiveness of this device for this use has not been demonstrated.

NVUS1615

Stent technique

- **Balloon size**
  - Match the lesion length (9, 15, 20mm)
  - Balloon norminal diameter <80% of parent vessel diameter
- **Stent size :**

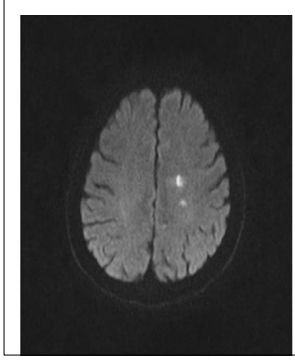
Stent Diameter

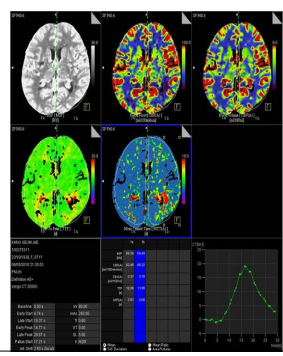
Labeled Stent Diameter	Self-Expanded Stent Diameter	Recommended Vessel Diameter
2.5 mm	2.8 mm	>2.0 and ≤ 2.5mm
3.0 mm	3.4 mm	>2.5 and ≤ 3.0mm
3.5 mm	3.9 mm	>3.0 and ≤ 3.5mm
4.0 mm	4.4 mm	>3.5 and ≤ 4.0mm
4.5 mm	4.9 mm	>4.0 and ≤ 4.5mm

Stent Length

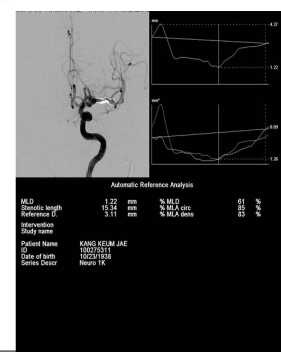
- The stent requires a minimum of **3mm proximal and distal** to the lesion.
- The stent length should be at **minimum 6mm longer** than the lesion length.

70/F, Acute minor stroke

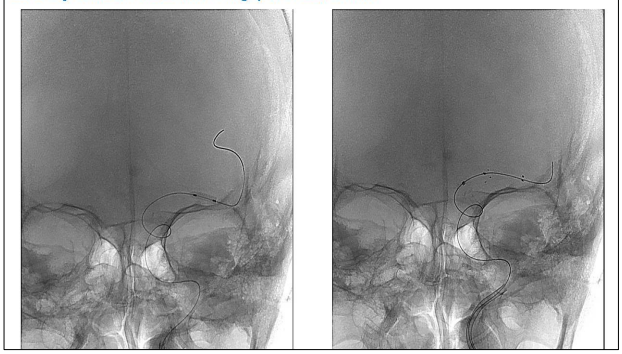


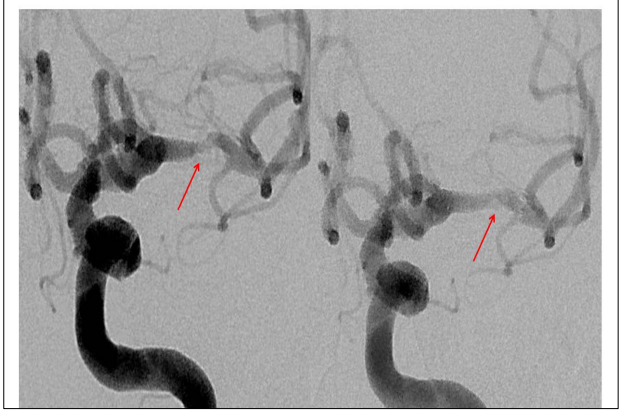


Stenotic degree : 83%



Reference M1 diameter : 3.1mm
Stenotic diameter : 0.5mm, 83% stenosis ((1-0.5/3.1)X100, WASID)
Stenotic length :10mm
Gateway balloon 2.5/9mm, Wingspan : 3.5/15mm





The NEW ENGLAND JOURNAL of MEDICINE

September 15, 2011

ORIGINAL ARTICLE

Stenting versus Aggressive Medical Therapy for Intracranial Arterial Stenosis

CONCLUSIONS

In patients with intracranial arterial stenosis, aggressive medical management was superior to PTAS with the use of the Wingspan stent system, both because the risk of early stroke after PTAS was high and because the risk of stroke with aggressive medical therapy alone was lower than expected. (Funded by the National Institute of Neurological Disorders and Stroke and others; SAMMPRIS ClinicalTrials.gov number, NCT00576693.)

non–stroke-related death, 0.4%) (P=0.002). Beyond 30 days, stroke in the same territory occurred in 13 patients in each group. Currently, the mean duration of follow-up, which is ongoing, is 11.9 months. The probability of the occurrence of a primary end-point event over time differed significantly between the two treatment groups (P=0.009), with 1-year rates of the primary end point of 20.0% in the PTAS group and 12.2% in the medical-management group.

- The **results of the SAMMPRIS** trial alarmed most experienced interventionists in Korea for two reasons
  - The high recur or complication rate in the stenting arm (**20%**, the first year) was higher than expected
  - The recurrent stroke rate in the aggressive medical treatment arm was lower than WASID trial (**12.2%, 1st year** vs. 22.5% WASID)
- Intracranial atherosclerotic disease (ICAD) accounts for **33–50% of all ischemic strokes** esp. in the Asian
- Important public health issue in Korea

- **WASID trial (2005, NEJM)**

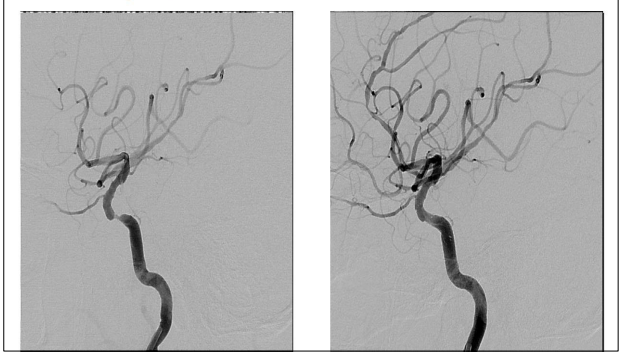
(wafarin-asprin symptomatic intracranial disease)

: Warfarin was associated with significantly higher rates of adverse events and provided no benefit over aspirin in this trial. **Aspirin should be used** in preference to warfarin for **patients with intracranial arterial stenosis**

Reasons

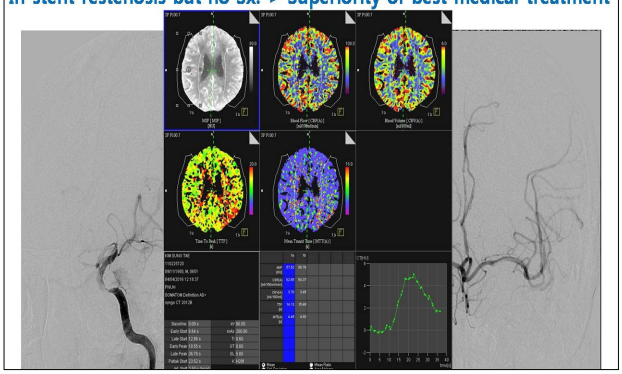
1. Subgroup analysis
   : Stenosis ≥70%, 1-year risk stroke 22.5%, TIA 14%
2. Aspirin monotherapy vs. dual antiplatelets
3. Intensive management of risk factors

60/M Acute minor stroke, Stent malposition



2 years follow up DSA (No Sx.)

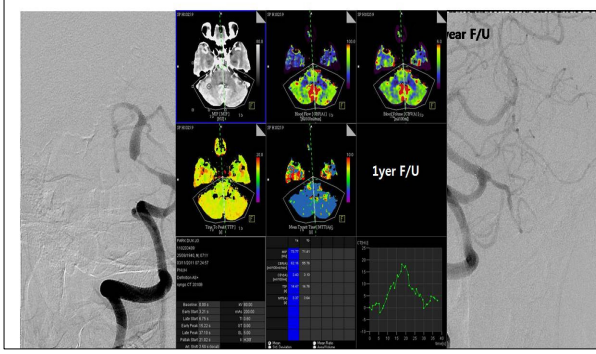
In-stent restenosis but no Sx.-> Superiority of best medical treatment



Limitation of SAMMPRIS or Wingspan stent

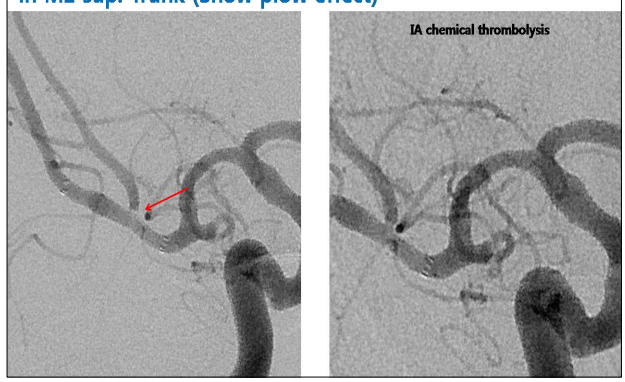
- Two steps technique of Wingspan stent
- Arterial dissection could develop during angioplasty
  - Rapid inflation of balloon -> dissection
- Lower radial force
- **Vessel characters (perforators) : BA, MCA vs. VA,ICA**

Proximal BA (Numerous Perforators), VBI

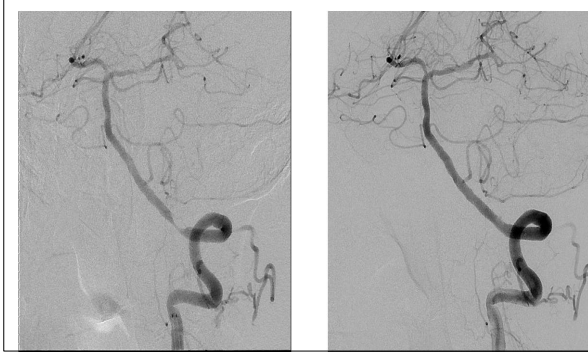


Rt distal M1 (Numerous Perforators), TIA

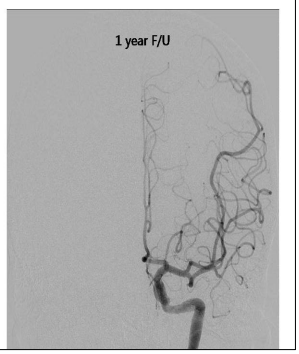
Acute in-stent thromboembolism in M2 sup. Trunk (Snow plow effect)



Lt Distal Vertebral artery (V4 segment)



Lt petrous ICA (intracranial extradural ICA)



Published in final edited form as:
Lancet. 2014 January 25; 383(9914): 333–341. doi:10.1016/S0140-6736(13)62038-3.

Aggressive medical treatment with or without stenting in high-risk patients with intracranial artery stenosis (SAMMPRIS): the final results of a randomised trial

Interpretation—The early benefit of aggressive medical management over stenting with the Wingspan stent for high-risk patients with intracranial stenosis persists over extended follow-up. Our findings lend support to the use of aggressive medical management rather than PTAS with the Wingspan system in high-risk patients with atherosclerotic intracranial arterial stenosis.

Original Investigation

2015, JAMA

Effect of a Balloon-Expandable Intracranial Stent vs Medical Therapy on Risk of Stroke in Patients With Symptomatic Intracranial Stenosis
The VISSIT Randomized Clinical Trial

Osama O. Zaidat, MD, MS; Brian-Fred Fitzsimmons, MD; Britton Keith Woodward, MD; Zhigang Wang, MD; Monika Killer-Oberpfalzer, MD; Ajay Wakhloo, MD, PhD; Rishi Gupta, MD, MBA; Howard Kirshner, MD; J. Thomas Megerian, MD, PhD; James Lesko, PhD; Pamela Pitzer; Jandira Ramos, MPH; Alicia C. Castonguay, PhD; Stanley Barnwell, MD; Wade S. Smith, MD; Daryl R. Gress, MD; for the VISSIT Trial Investigators

CONCLUSIONS AND RELEVANCE Among patients with symptomatic intracranial arterial stenosis, the use of a balloon-expandable stent compared with medical therapy resulted in an increased 12-month risk of added stroke or TIA in the same territory, and increased 30-day risk of any stroke or TIA. These findings do not support the use of a balloon-expandable stent for patients with symptomatic intracranial arterial stenosis.

2012, Stroke

Randomized Controlled Trial of Symptomatic Middle Cerebral Artery Stenosis
Endovascular Versus Medical Therapy in a Chinese population

Zhongrong Miao, MD, PhD*; Lidan Jiang, MD*; Hao Wu, MD, PhD; Yuhai Bao, MD, PhD; Liqun Jiao, MD, PhD; Shenmao Li, MD; Jian Wu, MD, PhD; Yang Hua, MD, PhD; Yan Li, MD; Junlei Zhu,MD; Fengshui Zhu, MD; Xuezong Liu, MD; Feng Ling, MD, PhD

Background and Purpose—To investigate the efficacy and safety of percutaneous transluminal angioplasty and stenting (PTAS) for symptomatic middle cerebral artery stenosis compared with standard medical treatment in a low-risk Chinese population.
Methods—A prospective, randomized, controlled, single-center clinical trial was conducted comparing PTAS with medical treatment for symptomatic middle cerebral artery stenosis (≥70%). Patients were enrolled according to 1:1 enroll ratio (PTAS: medical). The PTAS group received stenting or balloon angioplasty, whereas the medical treatment group received standard medical treatment (aspirin 100 mg plus clopidogrel 75 mg/d), and all the patients were under strict control of the risk factors. The end point events were any kind of ipsilateral stroke or transient ischemic attack, or death from any origin during 1-year follow-up.
Results—The enrollment was stopped after 70 patients were enrolled from August 2007 to December 2010, with a 30-day rate of end point events of 8.3% versus 5.9% (P=0.69) for PTAS and medical group, respectively, and 1-year rate of end point events of 19.4% versus 17.6% (P=0.85), respectively. There was no significant difference in baseline characteristics between the 2 groups. The mean follow-up time, which was ongoing, was 9.9±3.9 and 9.7±4.4 months, respectively. Among the risk factors, hypertension was the independent related to the outcome (P=0.015).
Conclusions—This study showed that endovascular treatment is as safe but not better than medical treatment for symptomatic middle cerebral artery stenosis in a low-risk Chinese population. History of hypertension increases the risk of recurrent ischemic events. (*Stroke*. 2012;43:3284–3290.)

Key Words: angioplasty and stenting ■ antiplatelet agents ■ middle cerebral artery ■ stenosis ■ stroke ■ transient ischemic attack

Intracranial stenting for ICAD before SAMMPRIS result

- Symptomatic (Stroke or TIA) intracrnial severe (>70%) stenosis
- Dual antiplatelets (asprin 100mg, clopigodrel 75mg) medication for 5 days before procedure
  - Coronary balloon mounted stent (Jo-flexmaster stent)
  - Wingspan stent system (Stryker, Kalamazoo, MI, USA)
    : available since 2005 in USA and available since 2010 in Korea
  - Balloon angioplasty only (Gateway balloon)

Intracranial stenting for ICAD after SAMMPRIS result

- **Patients selection**
  - **Two or more stroke despite aggressive medical management with 70-99% stenosis. (last stroke occurred more than 7 days ago)**
  - >40% decrease in **cerebral blood flow (CBF)** at the stenotic arterial territory compared to CBF at the reference area by CT or MRI perfusion
  - **No vascular reserve** on SPECT study with diamox

- Treatment planning
  - Antiplatlets agent (which one, how long and much)
  - Resistance test (VeryfyNow system, Accumetrics, USA, Turbidimetry)
    - Aspirin reaction Unit **(ARU)** : <550, 반응성, >550, 비반응성
    - P2Y12 reaction Unit **(PRU)** : <240, 반응 적절
      % Inhibition : 40-60% 적절, <40% 반응저하, <20% 내성
  - **GRAVITAS study** : Verify Now PRU 230 이상환자 및 표준환자에서 유지용량 150mg 과 75mg 사이의 심혈관질환의 사망, 심근경색증, 스텐트혈전증 발생비율 분석 -> 발생률 감소 못했고 (HT : 1.01) 중증 또는 중등도 출혈 또한 고용량군에서 유의하게 증가하지 않았다 (1.4% vs2.3%) 따라서 혈소판 반응검사로 혈소판 저항이 진단된다고 하더라도 클로피도그렐 고용량 요법으로 저항성을 극복하기 어렵다.
  - Resistance drug change
  - Triple antiplatelet therapy (aspirin, clopidogrel, cilostazole)

My Strategy for Intracranial artery stenosis

- **Recurrent symptomatic patients failed with best medical therapy, more than 70% intracranial stenosis**
  -> Intracranial Endovascular Revascularization consider
- **Asymptomatic or 1st stroke patient with severe stenosis**
  - Optimal medical therapy (aspirin 100mg + clopigodrel 75mg)
  - Antiplatelets resistance test -> drug modification
  - **Strong life-style modification**
    : **Stop smoking, HT : BP <140mmHg, HT with DM <130mmHg, Dyslipidemia : LDL<70, Regular exercise, Diet)**
- **Regular image follow up (6 month CTA or 1 year MRA)**

- **ICA intracranial-extradural segment** (Cavernous or petrous)
- **Vertebral artery V4 segment** (less perforators, straight)

-> Symptomatic severe (more than 70%) intracranial stenosis patient could be good candidate for primary scheduled stenting

- **BMS could be used in Mori type A intracranial arterial stenosis**
  - Ref. : Mori type A, short (5 mm or less in length), concentric or moderately eccentric, and less than totally occlusive

My technical consideration

- Primary stent and post ballooning
  - Undersize preballooning for stent delivery and post stenting same size ballooning
    - Minimize arterial dissection and maximize arterial dilatation
- Considering Mori classification, distal M1, mid basilar artery (numerous perforators or small vessel diameter) or small vessel diameter
  -> Balloon angioplasty alone

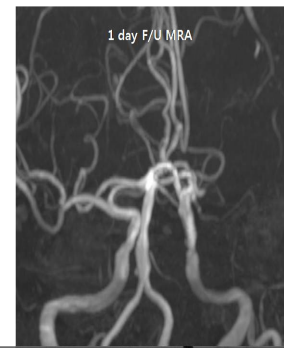
PNUH cases

	Acute stroke (remnant stenosis or occlusion)	Intracranial artery stenosis
Before Wingspan (-2009년)	8	40
After Wingspan (2010년-2012년) And before SAMMPRIS	193	21 (9.8%)
After SAMMPRIS (2013년-)	1	6

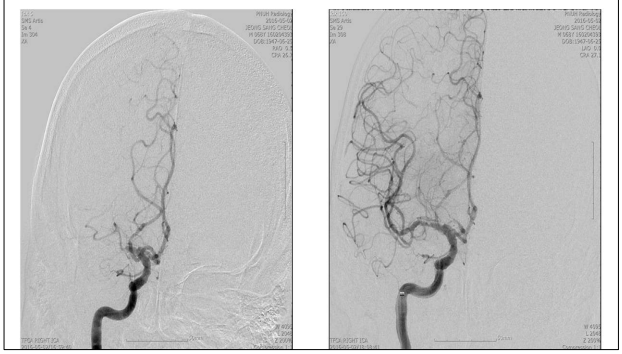
PNUYH cases

	Acute stroke (remnant stenosis or occlusion)	Intracranial artery stenosis
Before Wingspan (-2009년)	0	0
After Wingspan (2010년-2012년) And before SAMMPRIS	8	8
After SAMMPRIS (2013년-)	2	2

45/M, Lt MCA acute stroke (2016.5.)



68/M, Rt MCA acute stroke (2016.6.)



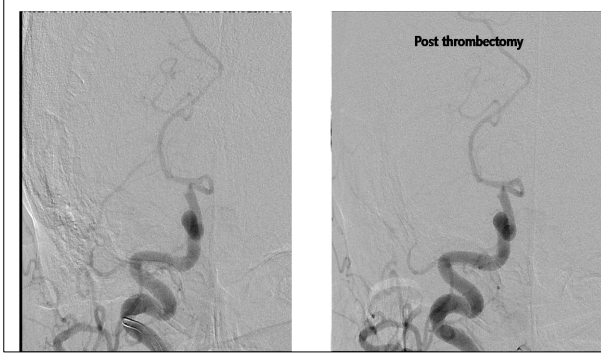
Remnant stenosis after revascularization (TICI >IIb)

2015년6월판 심평원 급여 기준

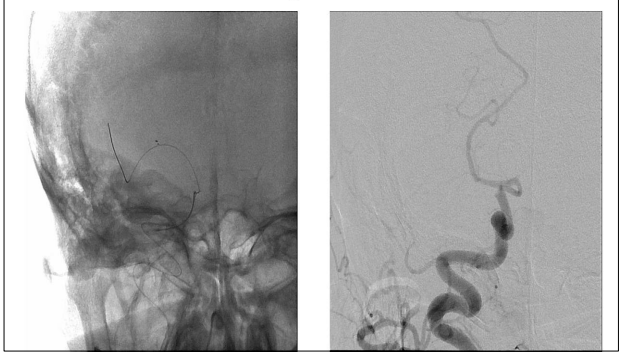
6. 뇌혈관내 수술료

연번	제 목	세부사항고시원문	심 계 불 여 쓰 기
49	경피적 두개장내 동맥스텐트 삽입술의 급여 인정범위 기준	두개장내 동맥(intracranial artery)스텐트 삽입술은 다음의 경우에 요양급여를 인정함. - 다 음 - 가.유증상의 70% 이상 두개장내 대혈관 협착 (내경동맥(Internal carotid artery), 중대뇌동맥(Middle cerebral artery), 척추동맥(Vertebral artery), 기저동맥(Basilar artery)) 나. 혈관내막박리가 있는 경우 (고시 제2014-168호, '14.10.1.시행)	두개장내 동맥(intracranial artery)스텐트 삽입술은 다음의 경우에 요양기관에서 비용을 청구할 수 있음. - 다 음 - 가. 유증상[1]의 70% 이상 두개장내 대혈관 협착 (내경동맥(Internal carotid artery), 중대뇌동맥(Middle cerebral artery), 척추동맥(Vertebral artery), 기저동맥(Basilar artery)) 나. 혈관내막박리가 있는 경우 <용어설명> 1) 유증상 : 뇌의 기능과 관련된 모든 증상(기멜케는 어지러움, 두통 부터 심하게는 사지마비, 안면마비, 이상 감각, 인지장애, 의식소실 등)이 있는 경우

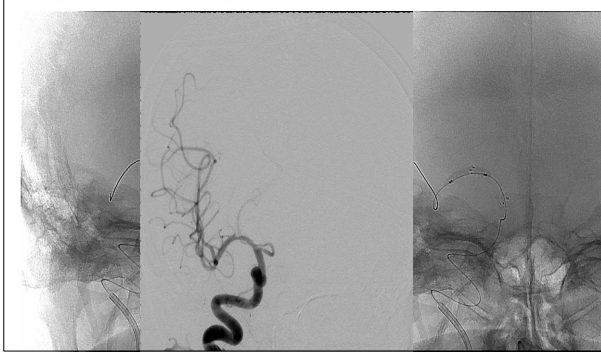
75/F, Rt MCA acute stroke



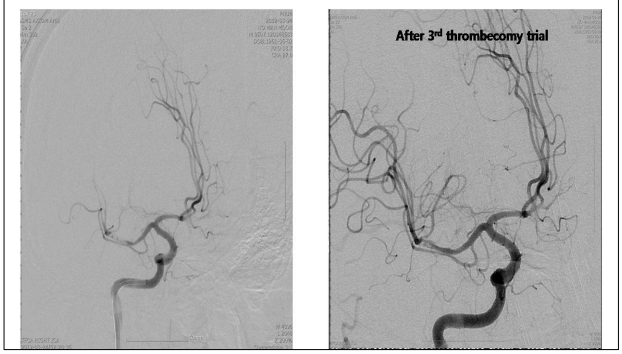
75/F, Solitiare thrombectomy after failed Penumbra



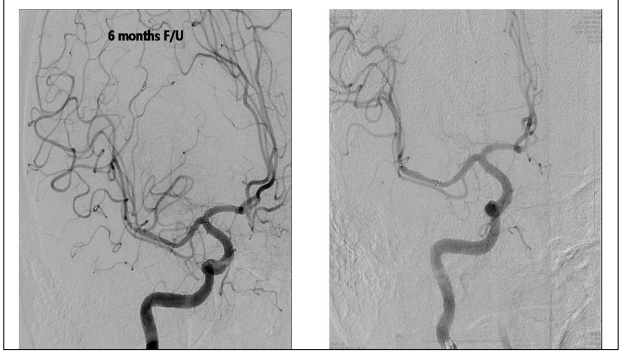
75/F, Wingspan stenting for recanalization



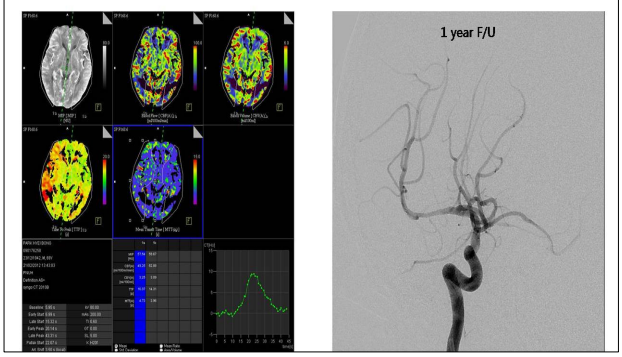
50/M, Rt MCA acute stroke



Remnant stenosis (thrombus) Stenting



Acute stroke, M1-2 occlusion, stent only



Thank you for your attention!

Surgical treatment

Jeong Eun Kim

Department of Neurosurgery, Seoul National University College of Medicine, Seoul National University Hospital

UPDATE 2016
KSCVS-SKEN

UPDATE IN THE MANAGEMENT OF INTRACRANIAL STENOSIS

- SURGICAL TREATMENT-

Jeong Eun Kim

Department of Neurosurgery
Seoul National University College of Medicine
Seoul National University Hospital

SNUH 서울대학교병원

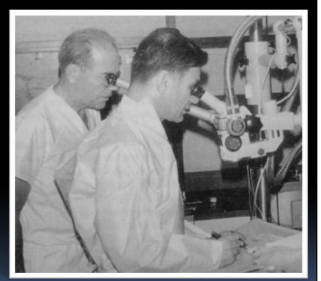
Historical Background

- 1963 Woringer & Kunlin
  - First described an EC-IC bypass procedure.
  - Proximal ICA occlusion
  - Saphenous vein graft
    - Anastomose entre la carotide primitive at la carotide intracranienne ou la sylvienne par greffon selon la technique de la suture suspendice.

Neurochirurgie 1963

Historical Background

- 1967 Donaghy & Yasargil
  - First STA-MCA bypass
    - Patch and bypass in microangional surgery. *Microvascular Surgery 1967*
    - Microneurosurgical arterial reconstruction. *Surgery 1970*



International Cooperative EC/IC Bypass Study 1977-1985

- Indication
  - TIA or TMB within 3 months before entry
  - Minor stroke in the carotid within 3 months before entry
  - At least 8 weeks after acute ischemic ND
  - Asymptomatic ICA or MCA occlusion [the largest subgroup]
  - Inaccessible atherosclerotic steno-occlusive ICA
  - Atherosclerotic stenosis or occlusion of the MCA trunk

International Cooperative EC/IC Bypass Study 1977-1985

- 1377 patients,
  - 714 randomized to best medical care
  - 663 randomized to STA-MCA bypass
- F/U duration
  - No patients were lost to follow-up
  - 56 months (28 to 90 months)
- Result
  - Bypass patency rate: 96%
  - Failure of extracranial-intracranial arterial bypass to reduce the risk of ischemic stroke.

N Eng J Med 1985

Critique of EC-IC Bypass Study

- Many patients operated outside the trial
  - Patients assigned to surgery: 663 patients
    - As many as 3,000 patients outside the trial
- Inclusion of patients with stenosis
  - MCA stenosis showed worse outcome with surgery!
    - Maybe initially embolic stroke
    - Increased thrombosis at stenosis after EIAB
      - Occlusion of stenotic lesion in 14%
- No evaluation of cerebral hemodynamics !
  - Inclusion criteria: symptom and angiography
    - No perfusion study, no CT or MRI
- Timing of surgery
  - At least 8 weeks after stroke (or TIA)
    - Most serious recurrence happens within 1 week
    - Very low incidence of recurrence after 6 weeks

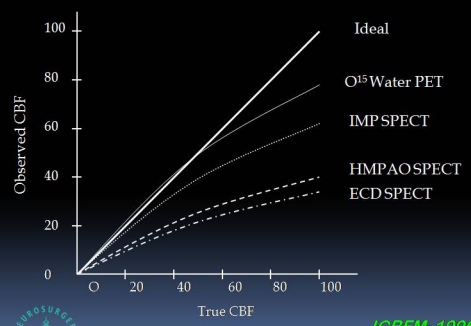
Assessment of Hemodynamic Compromise

- Decreased cerebrovascular reserve capacity
  - rCBF before & after vasodilatory stimulation
    - Hypercapnea or acetazolamide
- Increased rCBV or rCBV/rCBF (MTT)
- Increased OEF

Assessment of Hemodynamic Compromise

- PET: CBV, CBF, OEF, $CMRO_2$
  - Quantatative, OEF measurement
  - Good prediction of high risk group
  - Limited availability: esp. ^{15}O-labeled radiotracers
- SPECT: CBV, CBF
  - Good availability
  - Qualitative: normal hemispere as control
    - Hemispheric diaschisis
  - Some controversy over prediction value
- Xenon CT
- TCD

Tissue Perfusion Study Validation



JCBFM, 1996

Hemodynamic Impairment

Stage	CPP(%)	CBF	OEF	$CMRO_2$	CBV
Autoregulation	60-100	N	N	N	↑
Misery Perfusion	40-60	↓	↑	N	↑↑
Penumbra	20-40	↓↓	↑↑	↓	↑
Infarction	<20	↓↓↓	↓ ↑	↓↓	↓

Misery Perfusion vs. Stroke Risk - PET Study -

Ipsilateral Stroke	Normal OEF (n=42)	Increased OEF (n=39)
1 year	2.4 %	10.6 %
2 years	5.3 %	26.5 %

Grubb JAMA 1998

COSS (The Carotid Occlusion Surgery Study)

- Background
  - Based on PET OEF (STLCOS)
  - 2 yr ipsilat stroke: medical vs. surgical = 40% vs. 24%
- Design : July 24, 2002 – June 24, 2010
  - Ischemic stroke within 120 days (Barthel Index ≥ 12/20)
  - Angiographical occlusion
  - OEF ratio > 1.130
  - Screened 4967 > Enrolled for PET 705 > Randomized 195
    - Medical group 98 vs. Surgical group 97
- Primary end points
  - Ipsilateral ischemic stroke within 2 yrs
  - All stroke & 30 days after operation/randomization

COSS (The Carotid Occlusion Surgery Study)

- Results
  - 2-year ipsilateral stroke rate
    - 23% (Medical group) vs. 21% (Surgical group), p=0.7279
    - 15% strokes within 30 days in Surgical group
  - Surgical graft patency
    - 98% at 30 days vs. 96% at 2 yrs
  - Improvement in mean ipsilateral/contralateral OEF ratio
    - Improved from 1.258 to 1.109 for surgery group
- Conclusion
  - Because of improved non-surgical recurrence, there was no overall EC-IC bypass surgical benefit for 2-year stroke recurrence rate

Powers, JAMA 2011

Japanese EC-IC Bypass Trial (JET)

- From Nov. 1998 to Mar. 2004
- Minimum F/U: 2 years
- 28 centers in Japan
- Surgical indications
  - TIA or minor stroke within 3 months
  - ^{123}I-IMP (N-isopropyl-p-iodoamphetamine) SPECT
    - MCA territory
    - CBF < 80% of normal control
    - CVRC < 10%
      - Moderate group <10%
      - Severe group < 0%

JET study

- Interim report: published in Japanese journals
  - *Surg Cereb Stroke* 2002 P=0.0577 (n=128, primary end point)
  - *Surg Cereb Stroke* 2002 P=0.046 (n=196 , primary end point)
  - *Nihon Rinsho* 2006 P=0.046 (n=196 , primary end point)
- Ipsilateral stroke
  - Medical group: 11
  - Surgical group: 3
- Relative risk reduction: 74% !
  - P=0.042
- Critique: No surgical complications ?

Ogasawara, Nihon Rinsho 2006

JET 2nd Interim Analysis

Registration

	Moderate ischemia	Severe ischemia	Total
Medically-treated	52	46	98
Surgically-treated	52	46	98
Total	104	92	196

Primary end point

	Moderate ischemia	Severe ischemia	Total
Medically-treated	9 (17.3%)	5 (10.9%)	14 (14.3%)
Surgically-treated	3 (5.8%)	2 (4.3%)	5 (5.1%)
Total	12 (11.5%)	7 (7.6%)	19 (9.7%)

P=0.046

JET-2 study

- True threshold of CBF and CVR for subsequent ischemic stroke without bypass in symptomatic major cerebral arterial occlusive disease
- Comparison with medical artm of JET study including patients with CBF<80% and CVR<10% as a historical control
- Result
  - Incidence of ipsilateral stroke recurrence was significantly lower
- Conclusion
  - EC-IC bypass surgery is unlikely to benefit patients with CBF>80% or CVR>10%

Kataoka, Neurol Med Chir 2015

STA-MCA anastomosis: Results

	No.	Mortality	Morbidity	Patency	Subsequent ipsilat stroke
Sundt (1985)	415	1%	4%	99%	
Chater (1983)	400	2.5%	2%		0.9%/yr
EC/IC bypass study (1985)	663	0.6%	3% (major) 12% (incl. minor)	96%	

- Average results of STA-MCA anastomosis
  - Mortality : 1~2%
  - Major morbidity : 2~4%
  - Patency : 96~99%

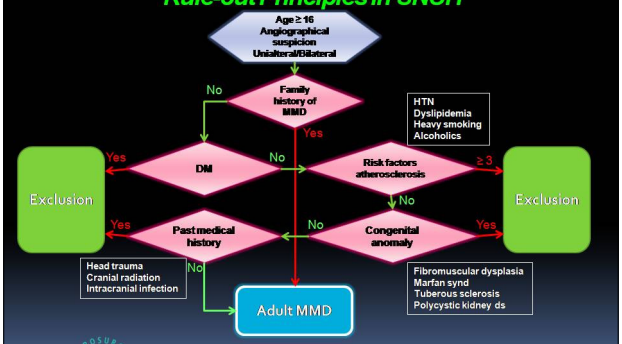
Practical Indications

- Occlusion or severe stenosis of ICA or MCA
- No evidence of embolic stroke
- Failure of best medical treatment
- SPECT: decreased reserve capacity

- Occlusive Pathology
  - Non-atherosclerotic >> atherosclerotic
  - Chronic progressive >> acute & abrupt
- Symptoms & hemodynamics
  - Progressive >> continual >> single episode

Diagnostic Criteria of Adult MMD

Rule-out Principles in SNUH

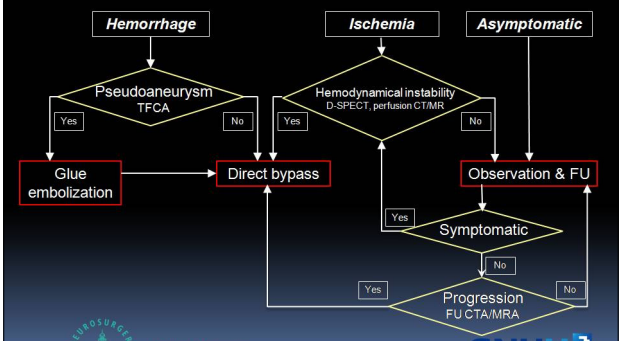


Surgical Indications *SNUH*

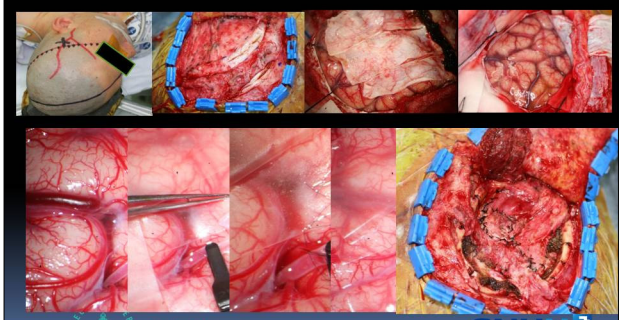
Moyamoya Disease
Atherosclerotic occlusion of carotid artery

- Symptomatic
  - Repeated hemorrhage
  - Asymptomatic but progression on MRA, CTA, TFCA
- Functionally independent: KPS ≥ 70
- No acute infarction/hemorrhage within 4 weeks
- Hemodynamically unstable
  - D-SPECT with perfusion CT or perfusion MR ASL

My Bypass Policy for Adult MMD *SNUH*

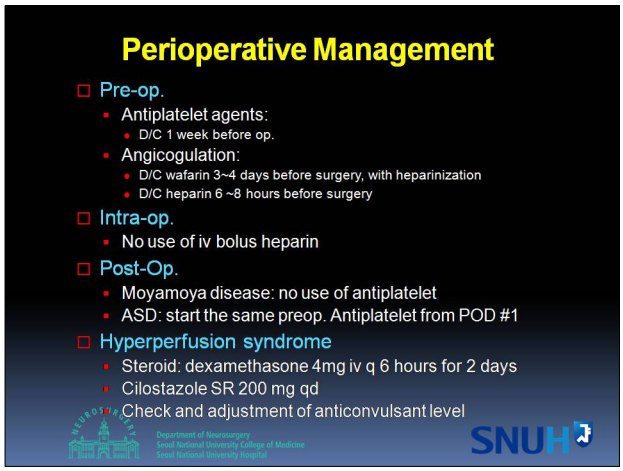


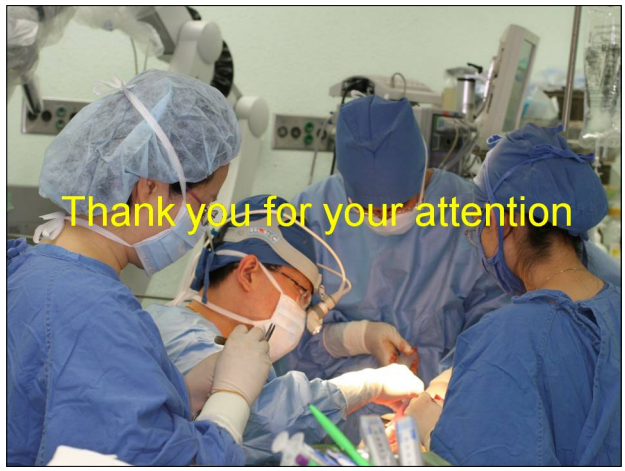
STA-MCA bypass, combined with indirect surgery of EDGS



Perioperative Management

- Intra-operatrive brain protection
  - PCO_2 > 40mmHg
  - Mild hypothermia: 33~34°C
  - BP : 20 – 30 mmHg higher than pre-op. BP
  - Penthothal 100mg IV bolus before MCA clamping
- Post-op management
  - BP : 20 – 30 mmHg higher than pre-op. BP
    Maximal SBP: less than 150 mmHg
  - Fluid & electrolyte balance


Perioperative Management
Pre-op.
Antiplatelet agents:
D/C 1 week before op.
Angicogulation:
D/C wafarin 3~4 days before surgery, with heparinization
D/C heparin 6 ~8 hours before surgery
Intra-op.
No use of iv bolus heparin
Post-Op.
Moyamoya disease: no use of antiplatelet
ASD: start the same preop. Antiplatelet from POD #1
Hyperperfusion syndrome
Steroid: dexamethasone 4mg iv q 6 hours for 2 days
Cilostazole SR 200 mg qd
Check and adjustment of anticonvulsant level
Department of Neurosurgery
Seoul National University College of Medicine
Seoul National University Hospital
SNUH


Thank you for your attention

Current recommendation and literature review

정승영
을지대학병원

Introduction

Intracranial atherosclerotic stenosis (ICAS) of a major intracranial artery is one of the most common causes of stroke worldwide and is associated with a high risk of recurrent stroke compared with other stroke subtypes. Recent clinical trials have improved understanding of risk factors associated with stroke recurrence, imaging characteristics that are associated with prognosis, and treatments that significantly reduce stroke recurrence in patients with ICAS. Although the results of these trials are changing the standard of care for patients with ICAS, they also emphasize the need for further research into identification of patients at highest risk of stroke from ICAS and development of new therapies to lower the risk of stroke in these patients. In this paper, we aim to define the optimal treatment strategies for this devastating disease, ICAS with literature review.

Methods

MEDLINE and PubMed searches of the English literature were performed with the following keywords: intracranial atherosclerosis, extracranial-intracranial bypass, intracranial stenting, Wingspan, drug-eluding stent, stroke, and medical therapy. The relevant literature was reviewed and was supplemented as necessary from the bibliography of selected articles, with a particular focus on articles which discussed therapeutic interventions for ICAS.

Management

Medical Management

Anticoagulation vs Antiplatelet Therapy

Anticoagulation was first reported as a treatment for symptomatic ICAS in 1955. Subsequently, data from a retrospective study suggested that warfarin was more effective than aspirin for stroke prevention in patients with symptomatic ICAS. However, the results of the Warfarin Aspirin Symptomatic Intracranial Disease (WASID) study not only demonstrated the role for medical therapy in ICAS, but also provided important information regarding the natural history. Based on the WASID data (a double-blinded, randomized trial comparing aspirin [1300 mg per day] with warfarin [target international normalized ratio (INR) 2–3]) showed no benefit of warfarin over aspirin for prevention of stroke and vascular death in patients with ICAS. Aspirin was also shown to be safer than warfarin, with a lower rate of death and major hemorrhage than warfarin. Although the WASID trial was not designed to study the importance of risk factor control, several important conclusions are reached from its substudies. Thus, while lowering blood pressure during follow up appears to reduce recurrence risk.

Choice of Antiplatelet Drug

The use of short-term dual antiplatelet therapy (aspirin and clopidogrel) could be particularly effective at lowering the early risk of stroke recurrence in patients with ICAS. In the Clopidogrel plus Aspirin for Infarction Reduction (CLAIR) study, patients with recently (≤7 days) symptomatic ICAS who were given clopidogrel (300 mg for the first day, then 75 mg per day) plus aspirin (75−160 mg per day) had significantly lower rates of microembolic signals detected by use of TCD on day 2 and day 7 after randomization than did those given aspirin (75−160 mg per day) alone. Additionally, when the recurrent stroke events in the CLAIR study were combined in a weighted analysis with the events from the similarly designed Clopidogrel and Aspirin for Reduction of Emboli in Symptomatic Carotid Stenosis (CARESS) trial (limited to patients with recently [within 3 months] symptomatic 〉50% extracranial carotid stenosis), patients given aspirin alone had significantly more recurrent stroke events than did those given aspirin and clopidogrel combined.

The antiplatelet agent cilostazol, a phosphodiesterase inhibitor, might decrease progression of atherosclerosis in patients with symptomatic middle cerebral and basilar artery stenosis. In the Trial of Cilostazol in Symptomatic Intracranial Arterial Stenosis (TOSS-2), a randomized, double-blind, multicenter clinical trial, combination antiplatelet therapies were compared for efficacy in preventing the progression of symptomatic ICAS amongst 457 acute ischemic stroke patients with symptomatic stenosis in the M1 segment of the MCA or in the basilar artery; the groups were aspirin 75−150 mg daily combined with either cilostazol 100 mg twice daily or clopidogrel 75 mg daily. New ischemic lesions or hemorrhagic events did not differ significantly between the cilostazol and clopidogrel groups. However, the overall cardiovascular event rate was significantly lower than in the WASID trial, perhaps due to the extensive use of statins and aggressive risk factor control. No data have been published for the superiority or equivalence of other antiplatelet regimens such as monotherapy with clopidigrel, cilostazol, or extended release dipyridamole, or the combination of dipyridamole and aspirin for stroke prevention in patients with symptomatic ICAS.

Risk factor modification

Results of secondary stroke prevention trials focusing on lowering of LDL concentrations or blood pressure showed significant reductions in recurrent stroke risk with a statin and angiotensin- onverting-enzyme (ACE) inhibitor. Data for the specific effect of risk factor control on risk of recurrent stroke in patients with ICAS are based on post-hoc analyses of the WASID and SAMMPRIS trials. The WASID trial also suggested that control of BP and LDL-C may reduce the risk of subsequent stroke. By contrast with the common practice of maintenance of slightly raised blood pressure in patients with ICAS to reduce the risk of stroke from distal hypoperfusion, post hoc analysis showed that patients with mean SBP ≥140 mm Hg had a significantly increased risk of recurrent stroke compared with patients with mean SBP 〈140 mm. Additionally, patients with a mean LDL-C ≥100 mg/dL had a significantly increased risk of recurrent stroke compared with patients with mean LDL-C 〈100 mg/dL. The recommended levels of LDL-C should be less than 70 mg/dL for a low rate of vascular events. Aggressive medical therapy in both arms consisted of aspirin 325 mg/d, clopidogrel 75 mg/d for 90 days after enrollment, intensive risk factor management that primarily targeted SBP 〈140 mm Hg (〈130 mm Hg in patients with DM) and LDL-C 〈70 mg/dL, and a lifestyle modification program.

Surgical Management

Endovascular treatment

From endovascular treatment emerged as a potential option for stroke prevention for ICAS in the 1980s, with rapid advances in endovascular technology, the use of endovascular therapy for patients with ICAS has become increasingly common. Options include angioplasty alone, balloon-expandable stents, and angioplasty followed by placement of self-expanding stents. However, all published studies examining the safety and utility of these endovascular treatments for patients with ICAS represent case series, often with limited data about long- term outcome and restenosis rates. Almost no randomized trials comparing these treatments against medical therapy have thus far been reported.

Primary Angioplasty

Angioplasty alone was typically used to treat severe ICAS in patients with recurrent ischemic events on medical therapy. In current practice, the technical success rate (defined as reduction of stenosis to 〈 50%) of angioplasty is more than 80%, and restenosis rates range from 0% to 30%. Retrospective single-center studies have reported a 30-day rate of stroke or death varying between 0% and 50%. Some of the variability in the outcome data is attributable to the heterogeneity of the patients treated. Generally, lower complication rates were reported in less acute cases whereas higher rates of stroke and mortality were recorded in patients with unstable symptoms. Device development and improvements in the technical aspects of the procedure, such as the application of undersized angioplasty balloons and a slow balloon inflation technique, have shown more promising results. Nevertheless, there are no prospective, multi-center, externally adjudicated studies on angioplasty alone to treat ICAS and no data comparing patients treated with angioplasty alone versus concurrent medically treated controls. Angioplasty alone is often associated with immediate elastic recoil of treated arteries, residual post-procedure stenosis in as many as 50% of treated patients, restenosis, and dissection.

Balloon-Expandable Stents

Because of these limitations of angioplasty and the success of stenting in the coronary circulation, stenting became the preferred endovascular treatment for ICAS for most interventionists. The initial studies of intracranial angioplasty and stent placement with balloon-mounted stents were retrospective case series in which high technical success rates (90%—98%) were reported. Initial experience with percutaneous angioplasty and stenting (PTAS) with coronary balloon expandable stents showed improved post-treatment luminal diameters compared with angioplasty alone; however, difficulty in navigation of the intracranial vessels, and trauma during balloon inflation and deployment of the stents, resulted in high morbidity and mortality rates. More recently, single-center studies have reported the initial experience with 2 new balloon-mounted stents specifically designed for intracranial use. One study evaluated the use of the Apollo stent (Micro-Port Medical) in 46 patients and demonstrated a technical success rate of 91.7%. However, delivery of the stent was limited in some cases by vessel tortuosity, and there was a relatively high rate of restenosis (28%). The other study used the Pharos intracranial stent (Micrus) in 21 patients. Seven of these patients received urgent intervention after acute stroke for hemodynamic instability and progressive worsening of stroke or after thrombolysis. The remaining 14 patients underwent elective treatment after a TIA or minor stroke. In these 14 patients, a technical success rate

of 85.7% and a procedure-related complication rate of 28.5% was observed.

Drug-eluting stents (DESs) were shown to greatly decrease the restenosis rates in coronary artery disease, and there have been attempts to duplicate this success in the treatment of ICAS. Initial work using DES in intracranial disease by Abou-Chebl et al. treating a small number of patients demonstrated a similarly promising decrease in short-term restenosis rates compared to bare metal stents. However, due to the known risk of delayed stent thrombosis, combined with the lack of long-term data, DES in the treatment of ICAS has largely fallen out of practice.

Self-Expanding Stents

In 2005, the FDA approved the self-expanding Wingspan stent (Stryker Neurovascular, Freemont, CA, USA) for use under the humanitarian device exception in medically refractory patients with transient ischemic attack or stroke secondary to 50—99% stenosis of a major intracranial artery. This approval was based on a European/Asian study of 45 patients. The main results of the study were that the stent was successfully delivered in 44 (98%) of 45 patients, the 30-day rate of stroke or death was 4.4%, and the 12-month rate of ipsilateral stroke or death was 9.3%. Only 3 (7.5%) of 40 patients had restenosis at 6 months, and none were symptomatic. Subsequently, the results of two multi-center registry studies in the USA (the National Institutes of Health [NIH]-sponsored Wingspan registry and the US Wingspan registry) suggested that intracranial PTAS with the Wingspan stent could be done with high technical success rates and with 30-day stroke rates of 6—9%.

These data compare favorably with the outcome in the WASID study and due to the initially promising and conflicting results of the Wingspan stent, the SAMMPRIS trial was designed. As noted earlier, the SAMMPRIS trial, which began enrollment in 2008, assessed high-risk patients with 70—99% ICAS who had had a stroke or transient ischemic attack within the preceding 30 days to establish whether aggressive medical management plus angioplasty and stenting with the Wingspan system was superior to aggressive medical management alone for stroke prevention. SAMMPRIS had enrolled 451 patients before enrolment was stopped in April, 2011, because of the high risk of periprocedural stroke and death in the PTAS group. The 30-day rate of stroke or death was 14 · 7% in the PTAS group and 5 · 8% in the medical group. The 1-year primary endpoint (30-day rate of stroke and death and ischemic stroke after 30 days) rates were 20 · 0% in the PTAS group and 12 · 2% in the medical group. The findings from SAMMPRIS showed that aggressive medical management was superior to PTAS in the treatment of patients with high-risk symptomatic ICAS. What has been released about this trial thus far implies that optimizing medical management remains the first treatment of choice for symptomatic intracranial atherosclerotic disease. Risk factors that were significantly associated with periprocedural ischemic events were non-smoking (possibly because smoking increases the conversion of clopidogrel to its active metabolite), basilar artery stenosis, diabetes, and older age, whereas risk factors associated with periprocedural intracranial hemorrhages included high percentage of stenosis and clopidogrel load associated with an activated clotting time above the target range. Possible explanations for the higher periprocedural events in SAMMPRIS than in the previous registries include the higher severity of stenosis needed for enrollment in SAMMPRIS and the earlier treatment in SAMMPRIS (within 30 days of the qualifying event), which might have increased the risk of PTAS. Additionally, SAMMPRIS had a more rigorous adjudication process, with local evaluation by study neurologists

(not required in the registries) followed by external blinded adjudication by a committee of expert neurologists. The SAMMPRIS trial did not address those patients who had failed optimal medical therapy. Endovascular treatment in these patients may still play an important role in optimizing clinical outcome.

Microsurgical treatment

Extracranial-Intracranial Bypass

Extracranial to intracranial (EC-IC) bypass surgery was the most commonly used and most thoroughly studied surgical technique for stroke prevention in patients with symptomatic ICAS. Flow augmentation in the setting of anterior circulation ischemia can be achieved surgically. Typically, the superficial temporal artery (STA) is anastomosed to the middle cerebral artery (MCA) provided sufficient flow is obtained via the STA. The EC-IC study published in 1985 quickly led to a sharp decline in the use of this intervention for anterior circulation ICAS, since it failed to demonstrate any reduction in strokes compared to best medical management. Briefly, 1377 patients were randomized to surgery plus medical management versus medical management alone. Long-term follow up at 55 months revealed no benefit with regards to stroke prevention. Upon closer examination, several shortcomings become apparent in this study. First and foremost, patients who had ICAS who were not amenable to carotid endarterectomy and who demonstrated symptoms were included in the study, with disregard toward hemodynamic compromise. Thus, patients who may have had disease due to embolic phenomenon and small vessel disease who would not have benefited from EC-IC were indiscriminately included in the study. Second, many patients who underwent surgery did so outside of the trial, potentially implicating that those who needed the surgery more urgently were omitted, thus diluting the beneficial effects of the procedure. Several single-institution case series examining the technical success and perioperative safety of direct EC-IC bypass for ischemic cerebrovascular disease have been published. In series that reported on EC-IC bypass for ischemic cerebrovascular disease including ICAS, the overall bypass patency, perioperative morbidity, and perioperative mortality rates vary from 87% to 99%, 0% to 6%, and 0% to 8%, respectively.
Instead of these criticisms, the Carotid Occlusion Surgery Study (COSS) and the Japanese EC-IC Bypass Trial (JET) were underway in the United Stated and Japan, respectively, to assess the potential for a newfound usefulness of this operation if the patients are selected based on a more sophisticated analysis of hemodynamic compromise. As recently announced premature stopping of the COSS suggested that among participants with recently symptomatic ICAS and hemodynamic cerebral ischemia, EC-IC bypass surgery plus medical therapy did not reduce the risk of recurrent ipsilateral ischemic stroke at 2 years, it is unlikely that direct EC-IC bypass will be proven effective for patients with ICAS-ven for those who have “failed” medical therapy and who have documented impaired cerebral hemodynamics. However, some groups have still suggested that assessment of cerebral hemodynamics with sophisticated imaging techniques may identify a subgroup of patients with ICAS who have hemodynamic impairment that would benefit from surgical revascularization and STA-MCA bypass surgery in carefully selected patients with symptomatic severe ICAS results in significant improvement in hemodynamic parameters and reduction in stroke recurrence.

Indirect Bypass

Others have begun to explore potentially less morbidity-causing indirect revascularization techniques to treat

patients with ICAD. Recently, Komotar et al. examined the role of indirect surgical bypass as a method of promoting angiogenesis and enhancing cerebral blood flow in patients with ICAD. In their series, 12 patients with ICAD and impaired cerebral hemodynamics were treated with indirect bypass: 11 underwent encephaloduroarteriosynangiosis, and 1 received bur holes with dural and arachnoid incisions. Perioperative morbidity was 27%; there were no perioperative deaths. Also, follow-up data showed that only 2 patients had increased perfusion in previously hypoperfused areas, and 5 patients suffered repeat ischemic infarction. In comparison with a meta-analysis of 4 studies of patients with symptomatic ICA occlusion and severe hemodynamic failure who were treated medically, it was observed that indirect surgical revascularization provided no protection against subsequent ischemic stroke. Based on this small retrospective case series, indirect surgical revascularization for patients with ICAD does not appear to be indicated and lacks therapeutic potential.

Treatment recommendations

On the basis of current data from randomized trials, we recommend the following treatment for patients with symptomatic ICAS. Patients with moderate stenosis (〈70%) or patients whose transient ischemic attack or stroke occurred more than 30 days ago (even if they have 〉70% stenosis) should be treated with aspirin (325 mg/day) and intensive risk factor management that primarily targeted SBP 〈140 mm Hg (〈130 mm Hg in patients with DM) and LDL-C 〈70 mg/dL. In WASID, the stroke rate would be even lower with intensive risk factor management. For patients with 70—99% stenosis and events within the past 30 days, a combination of clopidogrel (75 mg per day) with aspirin (325 mg per day) for 90 days seems warranted, on the basis of the results of SAMMPRIS and CLAIR, followed by aspirin (325 mg per day) alone plus intensive risk factor management. We do not recommend the use of clopidogrel in addition to aspirin for more than 90 days after initiation of treatment because of the risk of major haemorrhage from more prolonged use of dual antiplatelet therapy. However, the benefit of prolonged use of dual antiplatelet therapy for high-risk patients with intracranial stenosis might outweigh the risk of major hemorrhage, but this effect will need to be proven in future trials before the treatment can be recommended.

Conclusions

Symptomatic ICAS is a significant health burden, and often times, leads to recurrent, disabling strokes. The natural history of ICAS is poorly understood, as are optimal treatment strategies. The results of long-term outcome studies assessing the utility of both microsurgical and endovascular treatment options continue to support the fact that multifaceted medical management that incorporates short-term dual antiplatelet treatment (for 90 days) followed by aspirin monotherapy, coupled with intensive management of vascular risk factors is the treatment of choice for stroke prevention in these patients. Despite this aggressive medical management, a large subgroup of patients is still at high risk of recurrent stroke. As further research focus on identification and treatment of patients suffering from this devastating disease and refinements in both microsurgical and endovascular techniques continue, patients suffering from this devastating disease may have other alternatives.

Intracranial Atherosclerosis Recommendations of AHA 2014

1. For patients with a stroke or TIA caused by 50% to 99% stenosis of a major intracranial artery, aspirin 325 mg/d is recommended in preference to warfarin (*Class I; Level of Evidence B*). (Revised recommendation)
2. For patients with recent stroke or TIA (within 30 days) attributable to severe stenosis (70%–99%) of a major intracranial artery, the addition of clopidogrel 75 mg/d to aspirin for 90 days might be reasonable (*Class IIb; Level of Evidence B*). (New recommendation)
3. For patients with stroke or TIA attributable to 50% to 99% stenosis of a major intracranial artery, the data are insufficient to make a recommendation regarding the usefulness of clopidogrel alone, the combination of aspirin and dipyridamole, or cilostazol alone (*Class IIb; Level of Evidence C*). (New recommendation)
4. For patients with a stroke or TIA attributable to 50% to 99% stenosis of a major intracranial artery, maintenance of SBP below 140 mm Hg and high intensity statin therapy are recommended (*Class I;Level of Evidence B*). (Revised recommendation)
5. For patients with a stroke or TIA attributable to moderate stenosis (50%–69%) of a major intracranial artery, angioplasty or stenting is not recommended given the low rate of stroke with medical management and the inherent periprocedural risk of endovascular treatment (*Class III; Level of Evidence B*). (New Recommendations)
6. For patients with stroke or TIA attributable to severe stenosis (70%–99%) of a major intracranial artery, stenting with the Wingspan stent system is not recommended as an initial treatment, even for patients who were taking an antithrombotic agent at the time of the stroke or TIA (*Class III; Level of Evidence B*). (New recommendation)
7. For patients with stroke or TIA attributable to severe stenosis (70%–99%) of a major intracranial artery, the usefulness of angioplasty alone or placement of stents other than the Wingspan stent is unknown and is considered investigational (*Class IIb; Level of Evidence C*). (Revised recommendation)
8. For patients with severe stenosis (70%–99%) of a major intracranial artery and recurrent TIA or stroke after institution of aspirin and clopidogrel therapy, achievement of SBP 〈140 mm Hg, and high-intensity statin therapy, the usefulness of angioplasty alone or placement of a Wingspan stent or other stent is unknown and is considered investigational (*Class IIb; Level of Evidence C*). (New recommendation)
9. For patients with severe stenosis (70%–99%) of a major intracranial artery and actively progressing symptoms after institution of aspirin and clopidogrel therapy, the usefulness of angioplasty alone or placement of a Wingspan stent or other stents is unknown and is considered investigational (*Class IIb; Level of Evidence C*). (New recommendation)
10. For patients with stroke or TIA attributable to 50% to 99% stenosis of a major intracranial artery, EC/ IC bypass surgery is not recommended (*Class III; Level of Evidence B*).

Journal of Cerebrovascular and Endovascular Neurosurgery

JCEN 논문 투고규정

Instructions to Authors

Revised on April 2014 (4th Revision)

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