대한뇌혈관내수술학회 SKEN Society of Korean Endovascular Neurosurgeons

Korean Society of Cerebrovascular Surgeons 대한뇌혈관외과학회

대한뇌혈관내수술학회 대한뇌혈관외과학회

SKEN-KSCVS 합동 연수강좌

Theme : Leading the Way for Stroke Therapy

일 시 2015년 9월 4일 금요일 오전 9시

장 소 서울성모병원 본관 지하 1층 대강당

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주 관 대한신경외과학연구재단

평 점 6점

2015년도 대한뇌혈관내수술학회 임원

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김범태 | *순천향대 부천병원*

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성재훈 | *가톨릭대 성빈센트병원*

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신동성 | *순천향대학교 부천병원*

2015년도 대한뇌혈관외과학회 임원

회장 오창완 | *서 울 대*

부회장 박현선 | *인 하 대*

총무 안재성 | *울 산 대*

학술 김태선 | *전 남 대*

간행 김성림 | *가톨릭대*

기획홍보 정진환 | *한 양 대*

역사편찬 이재환 | *연 세 대*

정보통계 김대원 | *원 광 대*

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회원관리 고준석 | *경 희 대*

수련교육 이관성 | *가톨릭대*

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혈관내수술 성재훈 | *가톨릭대*

급성뇌경색 유도성 | *가톨릭대*

방사선수술 이선일 | *인 제 대*

감사 이상원 | *부 산 대*

감사 최석근 | *경 희 대*

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허필우 | *가톨릭대*

오창완 | *서 울 대*

박현선 | *인 하 대*

김범태 | *순천향대*

박인성 | *경 상 대*

정영균 | *인 제 대*

김태선 | *전 남 대*

김종수 | *성균관대*

고현송 | *충 남 대*

문창택 | *건 국 대*

임동준 | *고 려 대*

박익성 | *가톨릭대*

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나형균 | *가톨릭대*

홍승철 | *성균관대*

주진양 | *연 세 대*

강성돈 | *원 광 대*

INVITATION

대한뇌혈관내수술학회
회장 **김 범 태**

회원 여러분 안녕하십니까?

어려운 의료환경에서도 뇌혈관질환 연구와 진료를 선도하는 전문가 모임인 양 학회가 끊임없는 학문적 교류를 통해 서로의 발전을 이루어 나가는 성과에 찬사를 보냅니다.

뇌혈관내치료는 새로운 기구의 개발과 사용 경험을 통해 어렵기만 했던 뇌혈관 병소에 접근을 가능하게 했으며, 비침습적 한계는 뇌혈관외과로 해결함으로서 양대 치료가 상호 보완적으로 안전한 방법으로 발전해 오고 있습니다.

금년도 주제는 뇌혈관질환 치료의 새로운 길을 선도해 가자는 차원에서 "Leading the Way for Stroke Therapy"로 정했습니다.

고난이도 동맥류 접근, 술중 동맥류 파열에 대한 대처, 그리고 발전을 거듭하고 있는 급성뇌혈관폐색에 대한 최신 지견을 뇌혈관내치료와 뇌혈관외과 관점에서 접할 수 있습니다.

또한, 초청된 국내외 전문가들로부터 거대 동맥류의 혈관내치료, 새로운 뇌졸중 영상 진단법 그리고 경동맥협착증 치료의 경제성 평가에 대한 특강을 들을 수 있습니다.

아무쪼록 본 연수강좌가 회원님들의 학문적 발전과 함께 활발한 교류의 장이 되길 기대합니다.

감사합니다.

대한뇌혈관외과학회
회장 **오 창 완**

금년도 우리나라 의료관련 핵심어는 MERS가 될 것 같습니다. 이번 사태는 우리나라 의료의 현 상황 및 그 역할에 대하여 심각한 반성 및 논의의 기회를 제공할 것으로 예상됩니다. 이 사태를 바라보면서, 신경외과 분과 중 뇌혈관질환을 치료하는 저희 분야에서도 이러한 반성과 논의가 필요한 시점이 아닌가 생각하여 봅니다.

길게는 지난 20년 간, 좀 더 가깝게는 지난 10년 간 뇌혈관질환의 신경외과적 치료는 과히 '혁신적' 변혁을 이루었습니다. 그 특징은 증례수의 증가, 혈관내치료 비중의 증가 및 예방적 치료의 증가입니다. 특히 비파열 뇌동맥류 등 예방적 치료의 증가는 치료 합병증의 감소 등, 치료의 결과를 향상시켜야 되는 중요한 이유가 되고 있습니다. 이러한 치료 결과의 향상을 위해, 특히 개두술과 혈관내치료의 합리적 적용이 중요함은 모두 공감하고 있는 내용일 것입니다. 다행스럽게도 국내 뇌혈관질환 치료를 담당하고 있는 신경외과 전문의들은 이러한 치료 방법을, 경쟁적이 아닌 합리적 관계로 융합할 수 있는 위치에 있으며, 본 연수강좌 역시 이러한 의미에서 매우 중요한 기회로 생각됩니다.

이번 합동연수강좌는 우리가 진료현장에서 마주칠 수 있는 문제들 중, 결정이 망설여 질 수 있는 내용들을 모아서 구성하였습니다. 이러한 내용들에 대한 다양한 경험의 공유를 통하여, 본 합동 연수강좌가 참석자 모두에게 뇌혈관질환의 신경외과적 치료를 한 단계 향상시킬 수 있는 계기가 될 수 있기를 기원합니다.

감사합니다.

2015년 9월

대한뇌혈관내수술학회 회장 **김 범 태**

대한뇌혈관외과학회 회장 **오 창 완**

초청연자소개

Kenji Sugiu

Birth-date : February 27, 1963

Birth-place : 1345 Misu, Soja city, Okayama Prefecture, Japan

Permanent Address : 315 Monden, Soja city, Okayama Prefecture, Japan

Present Address : Department of Neurological Surgery, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences 2-5-1 Shikata-cho, Kita-ku, Okayama city, Okayama Prefecture, JAPAN 700-8558

Schools

Okayama Prefectural Soja High School from April 1978 to March 1981

Kurume University Medical School (premedical and medical) from April 1981 to March 1987.

Medical License

Doctor of Medical Science 307330-Japan, Received in May 1987

Japanese Board of Neurological Surgery

Passed in July 1994

Degree of Medical Science

Received in March 1996

Professional Training and Employment

Resident of Neurological Surgery at Okayama University Hospital from April 1987 to November 1987

Resident of Neurological Surgery at Himeji Central Hospital from December 1987 to December 1990

Research Fellow in the Laboratory of Neurological Surgery at Okayama University Medical School from January 1991 to August 1994

Medical Staff of Neurological Surgery at Saiseikai Okayama Hospital from August 1994 to

May 1995
Medical Staff of Neurological Surgery at Okayama University Hospital from June 1995 to March 1996
Medical Staff of Neurological Surgery at Kagawa Prefectural Central Hospital from April 1996 to March 1997
Research Fellow in the Laboratory of Neuroradiology at Geneva University Medical School from May 1997 to October 1999
Assistant Professor of Neurological Surgery at Okayama University Hospital from November 1999 to March 2003
Senior Assistant Professor of Neurological Surgery at Okayama University Hospital from April 2003 to July 2012
Associate Professor of Neurological Surgery, Vice President of IVR center at Okayama University Hospital from August 2012 to present

Rewards

Sunada Prize of Okayama University, June 1996
Special Prize of Neurovascular section of the Japan Neurosurgical Society, November 1996
Exhibit Award (Poster Prize) of Swiss Society of Radiology, 86. Annual Meeting, June 1999

초청연자소개

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Educational Background

Keimyung University College of Medicine, Daegu, Korea : M.D. (1988)
Chunbook National University Graduate School, Seoul, Korea : Ph.D. (2009)

Professional Background

1988-1989	Internship, Daegu Catholic university Hospital
1989-1992	Keimyung University Hospital, Department of Radiology, College of Medicine, Keimyung University
1992-1995	Military army hospital (205 MASH) (Military Service)
1995-1998	Clinical Fellow in Keimyung University Hospital
1998-2002	Assistant Professor, College of Medicine, Keimyung University Department of Radiology, Dongsan Medical Center
2003-2004	Fellow, Department of Radiology University of Calgary
2004-2008	Associate professor, College of Medicine, Keimyung University Department of Radiology, Dongsan Medical Center
2008-2015	Professor, Department of Radiology, Seoul National University College of Medicine

Licensure

Medical Doctor, Korea (no. 35369)

Membership

Korean Society Radiology
Korean Stroke Society
American Heart Association
ISMRM

초 청 연 자 소 개

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2005.03-2009.02 통계학 학사, 경북대학교 통계학과

초청연자소개

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2004.09-2006.09 연구원, 한양대학교 의과대학 예방의학교실

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2006-2010 보건학박사, 서울대학교 보건대학원(보건정책관리 전공)
2003-2005 보건학석사, 서울대학교 보건대학원(보건정책관리 전공)
1998-2002 행정학사, 인제대학교 보건행정학과

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2015-2017 한국보건의료기술평가학회 학술이사

CONTENTS

대한뇌혈관내수술학회-대한뇌혈관외과학회

합동 연수강좌

Symposium

좌장 : 오창완(서 울 대)

14:00~14:40 Carotid Artery Stenosis

Scientific Session III

좌장 : 권병덕(울 산 대), 조재훈(대구가톨릭대)

15:00~16:00 Video Session : How to Manage the Intraoperative Rupture of Aneurysms

Scientific Session IV

좌장 : 허필우(가톨릭대), 권오기(서 울 대)

16:00~17:20 Update in the Management of Acute Ischemic Stroke (AIS)

Scientific Session I

대한뇌혈관내수술학회 - 대한뇌혈관외과학회 춘동연수강좌

Para-ophthalmic Aneurysm

좌장 : 허승곤(연세대), 백민우(가톨릭대)

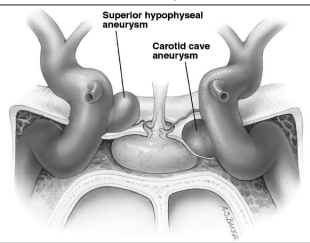
1. Surgical anatomy 주성필(전남대)
2. How to avoid visual complication during aneurysm clipping 안재성(울산대)
3. How to maintain microcatheter stability in the endovascular therapy 정진영(동의의료원)
4. New strategies upon the literature review 임동준(고려대)

Para-ophthalmic Aneurysm
- Surgical anatomy -

Sung-Pil Joo, Tae-Sun Kim
DEPARTMENT OF NEUROSURGERY, CHONNAM NATIONAL UNIVERSITY

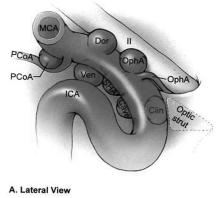
Classification of paraclinoid aneurysms

	Neck	Dome	Projection
Cavernous (C4) segment aneurysms			
Intracavernous aneurysms	Extradural	Extradural	Variable
Transitional cavernous aneurysms	Extradural	Intradural	Superior
Clinoid (C5) segment aneurysms			
Clinoid segment aneurysms	Extradural	Extradural	Variable
Ophthalmic artery aneurysms (infrequent)	Extradural	Extradural	Superior
Ophthalmic (C6) segment aneurysms			
Ophthalmic artery aneurysms	Intradural	Intradural	Superior
Superior hypophyseal aneurysms	Intradural	Intradural	Medial
Carotid cave aneurysms	Intradural	Intra- or extradural	Inferomedial
Posterior carotid wall aneurysms	Intradural	Intra- or extradural	Inferoposterior

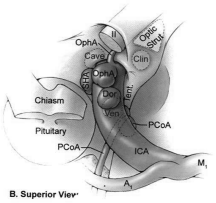


Kim JM. et al.: Neurosurgery, Vol. 46, No. 3, March 2000

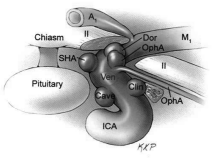
Paraclinoid An.



A. Lateral View



B. Superior View



C. Anterior View

- **OphA**
- **SHA**
- **Variant** – Dorsal carotid An
  - Carotid cave An.
  - Clinoid segment An
  - Ventral carotid An.

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Paraclinoid aneurysms

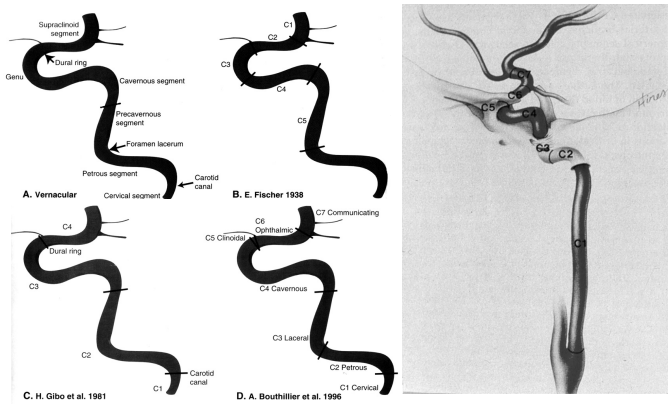
❑ **Arising from the ICA in close proximity to the ACP**

Broad concept	Narrow concept
• Intracavernous, • Clinoid, • Ophthalmic, • P-com ICA segment	• Clinoid segment • Ophthalmic segment

-The complex relationship of the vascular, neural, dural, and osseous structures surrounding the paraclinoid aneurysm often makes operative obliteration challenging

- Multiplicity

Segments of ICA



Classification

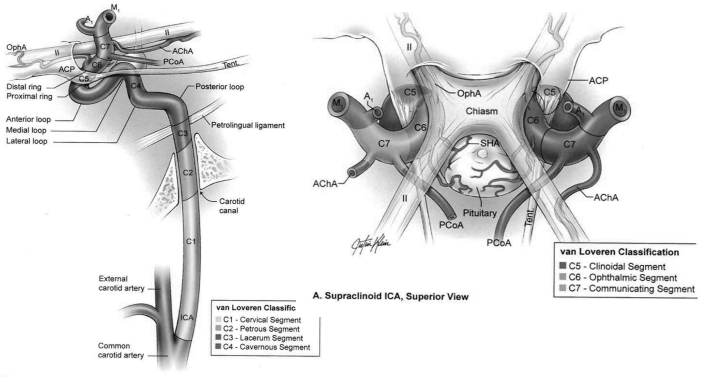
❑ **Rhoton**

- ✓ Cervical (C1)
- ✓ Petrous (C2)
- ✓ Cavernous (C3)
- ✓ Supraclinoid (C4)

❑ **Van Loveren**

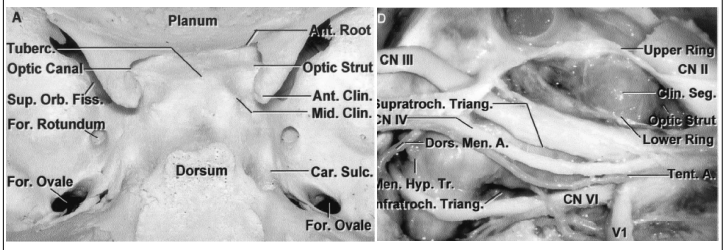
- ✓ Cervical (C1)
- ✓ Petrous (C2)
- ✓ Lacerum (C3)
- ✓ Cavernous (C4)
- ✓ Clinoid (C5)
- ✓ Ophthalmic (C6)
- ✓ Communicating (C7)

Arterial Anatomy



-- *Van Loveren classification*

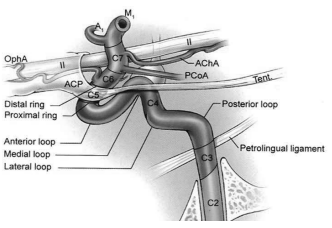
Gross Anatomy



Carvenous Segment

❑ **Petro lingual ligament ~ proximal dural ring**

- ✓ **Vertical portion, post. Bend, horizontal portion, ant. bend**
- ✓ **Various turtuosity**



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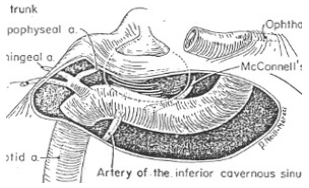
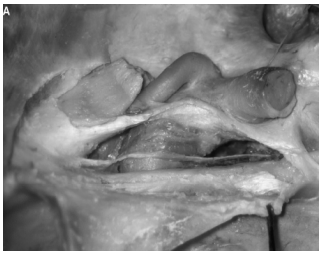
Branches of Carvenous Seg.

- ✓ **Meningohypophyseal trunk**
  - **tentorial a.(marginal & basal)**
  - **inf. hypophyseal a.**
  - **dorsal meningeal(lat. clival) a.**
- ✓ **Inferolateral trunk (vascular network of paracarvenous dura)**
  - **a. of foramen rotundum**
- ✓ **Capsular a. of McConell**



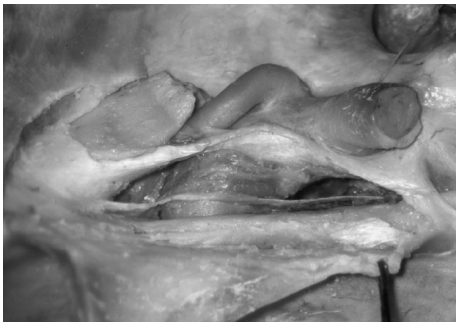
Clinoid Segment

- ❑ **Between proximal & distal dural rings**
- ✓ **Wedge shaped segment medial to ACP**
- ✓ **Difficult to define precise dural ring**
- ✓ **Generally no arterial branch, rarely SHA or Oph. A**
- ✓ **Great caution in decision making for aneurysm**



❖The incompetence of the proximal dural ring allows extension of the cavernous venus plexus around the C5 up to the distal dural ring **(clinoid venous plexus)** and there is great variability in the density of this plexus

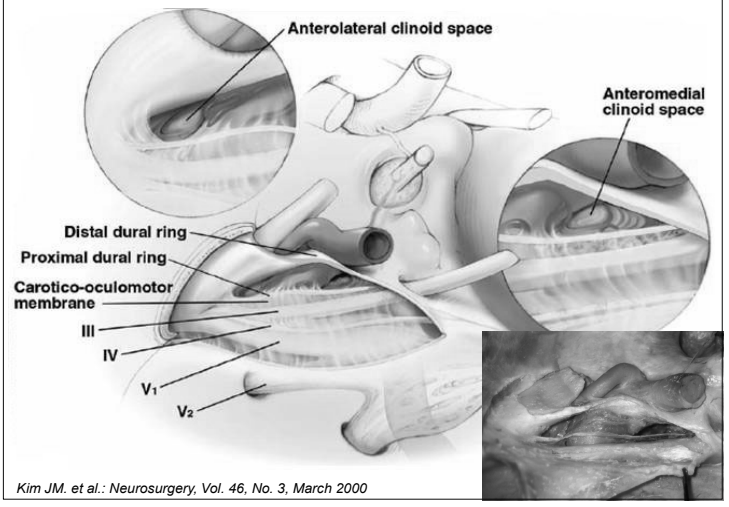
Clinoid space



- Surrounded by the thin inner dural layer of the cavernous sinus
- Wrapped in a “dural sleeve”,which named “carotid collar” formed by the inner dural layer
- Approximately 5 mm in length

Clinoid space

The space is bounded superiorly by the outer dural layer and inferiorly by the inner dural layer and represents an interdural, extracavernous, surgically created space



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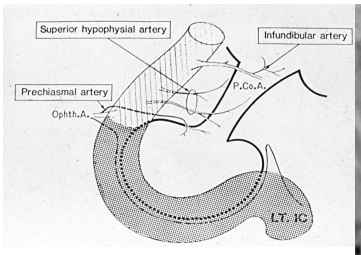
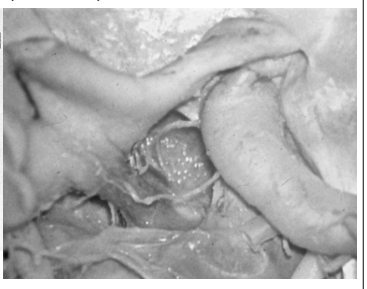
Superior hypophyseal artery

- ✓ **Number : average 2.3 per side (range: 1— 4)**
- ✓ **All originated from the medial or posterior aspect of the ICA**
- ✓ **Pituitary stalk &gland, optic nerve,& chiasm, floor of 3rd ventricle**





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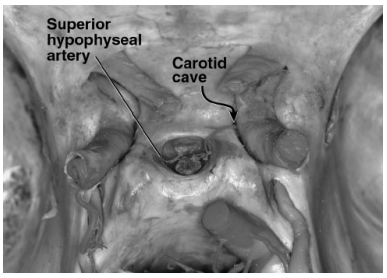
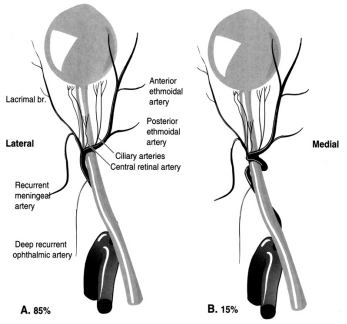
Ophthamic Segment

❑ Distal dural ring ~ origin of P-Com. a.
- ✓ Carotid cave ; intradutral & subarachnoid space
- ✓ Ophtalmic artery
- ✓ Superior hypophyseal artery

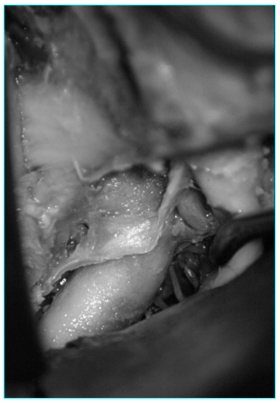


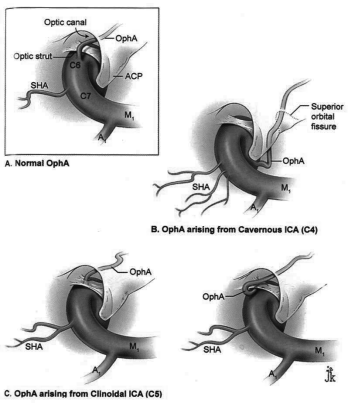
Ophthamic Artery

- ✓ Arises superior or superomedial side of ICA
- ✓ Intracranial
  :origin at just distal to distal dural ring (≥ 90%)
- ✓ Intracanalicular
- ✓ intraorbital
  - central retinal a.
  - RMA anastomoses with MMA
  - LB anastomoses with zygomatico-orbital br. of STA
  - Ethmoidal a. anastomoses with sphenopalatine a. of internal maxillary a.



Variation of OA





Ophthalmic artery

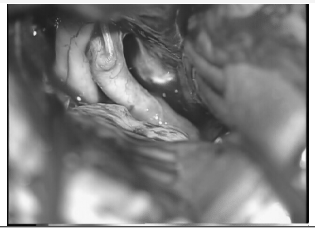
❖ The majority (91%) originated just distal to the distal dural ring (n=64)

★ Forty seven (67%) arose within 1 mm of the DDR

★ Seventeen (24%) between 1 — 5 mm of the DDR

❖ Four cases (6%) arose from the clinoid segment below the distal dural ring

❖ Two cases (3%) arose at the insertion of the distal dural ring with the ring attached to the ophthalmic artery itself



Communicating Segment

❑ **P-Com. a. origin ~ ICA bifurcation**

✓ **Posterior communicating artery**
- **arises posteromedial or posterior side of ICA**
- **infundibulum**
- **fetal type**

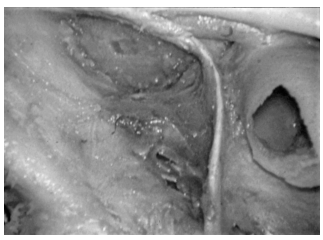
✓ **Anterior choroidal artery**
- **arises posteromedial , behind ICA**
- **two segments**
- **hemiparesis, hemisensory loss, hemianopsia**

Carotid collar

Seoane E et al. Neurosurgery 42: 869-886, 1998

✓ A membranous dural (periosteal) sleeve that surrounds the clinoid ICA

✓ Fibrous collar formed by the dura lining the medial surface of the ACP, the posterior surface of the optic strut, and the upper part of the carotid sulcus



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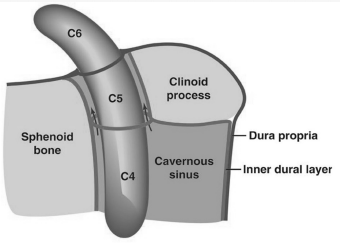
Carotid collar

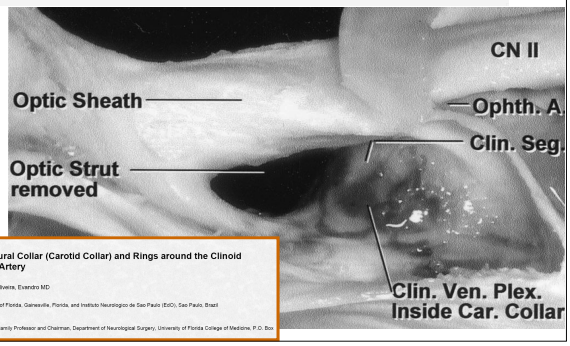
Kim JM. et al.: Neurosurgery, Vol. 46, No. 3, March 2000

- ✓ A small space exists between the inner dural layer and the clinoid ICA, which admits veins (clinoid venous plexus) from the cavernous sinus through the incompetent proximal dural ring
- ✓ The carotid collar separates the clinoid venous plexus from the clinoid space



Carotid venous plexus

❖ Venous channels communicating with the anterior part of the cavernous sinus through a narrow space between the dural collar and the clinoid segment wall



Neurosurgery: Volume 42(4) April 1998 pp 888-894
Microsurgical Anatomy of the Dural Collar (Carotid Collar) and Rings around the Clinoid Segment of the Internal Carotid Artery [Anatomic Report]
Sekane, Eduardo MD; Rhoton, Albert L. Jr. MD; de Oliveira, Evandro MD
Department of Neurological Surgery (ES, ALR), University of Florida, Gainesville, Florida, and Instituto Neurologico de Sao Paulo (EdO), Sao Paulo, Brasil
Received, April 29, 1997. Accepted, October 21, 1997.
Reprint requests: Albert L. Rhoton, Jr., M.D., R.D. Keene Family Professor and Chairman, Department of Neurological Surgery, University of Florida College of Medicine, P.O. Box 100265, Gainesville, FL 32610-0265

Proximal dural ring

- ✓ Inner dural layer of the roof of the cavernous sinus
- ✓ Does not fuse with the ICA adventitia, except posteromedial aspect
- ✓ Interclinoid ligament
- ✓ Incompetent
- ✓ Not true dural ring,

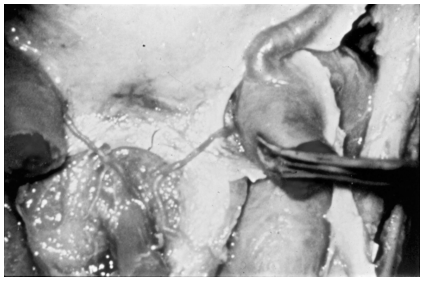
  but the surgical landmark

Distal dural ring

- ✓ Outer dural layer of the roof of the cavernous sinus
- ✓ With the exception of its medial aspect (carotid cave), tightly bounds to the ICA — not a true circle
- ✓ Anterior petroclinoid ligament
- ✓ Competent
- ✓ True dural ring

Carotid cave

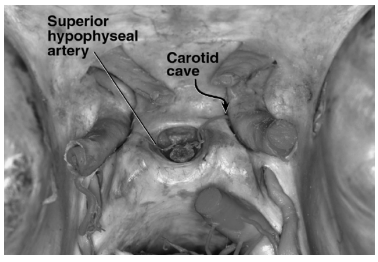
- ✓ A small dural recess of pouch (subarachnoid pouch) in the 1 to 6 O'clock position medial to the ICA
- ✓ Lies between the carotid artery and carotid sulcus of sphenoid bone



Kobayashi S et al.: J Neurosurg 70:216-221, 1989

Carotid cave (n=70)

- ❖ In the 54 specimens **(77%)** had a carotid cave
- ❖ Forty three (80%) had one or two superior hypophyseal arteries that arose from the ICA within the carotid cave
- ❖ The cave is **intradural** and contains subarachnoid space



Kim JM. et al.: Neurosurgery, Vol. 46, No. 3, March 2000

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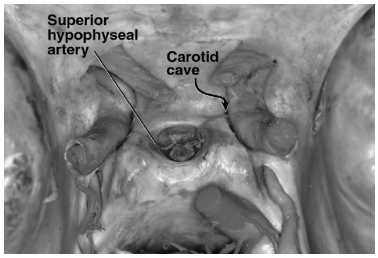
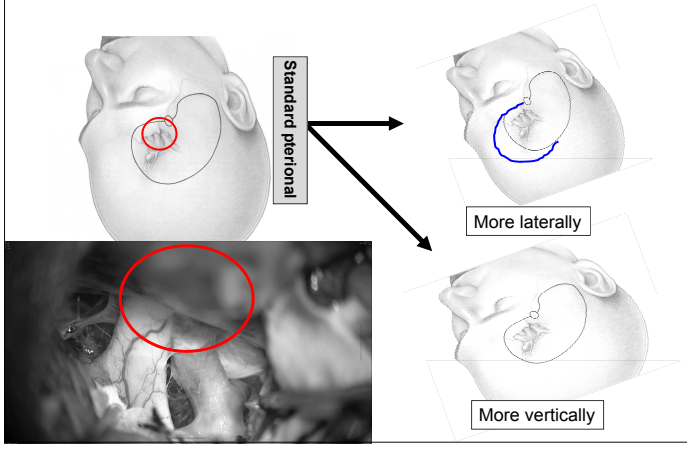


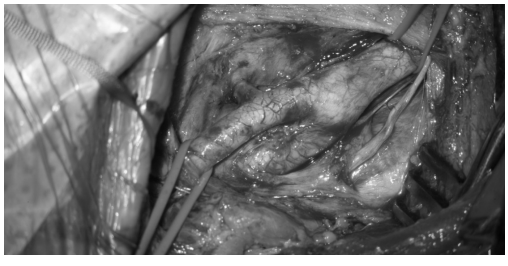
Kim JM. et al.: Neurosurgery, Vol. 46, No. 3, March 2000

Head positioning



Proximal vascular control

- **cervical ICA exposure (with retrograde suction decompression)**
- **petrous portion by drilling Glasscock's triangle**
- **temporary clip at clinoid ICA**
- **induced temporary cardiac arrest using adenosine**



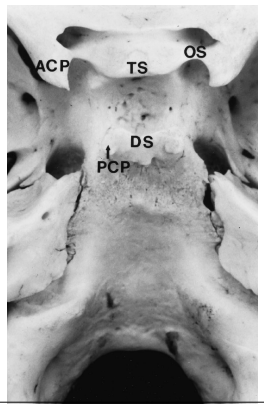
Anterior clinoidectomy

✓ **Paraclinoid and parasellar lesion**

- Enhanced visualization of the ophthalmic artery and the proximal neck
- Early decompression and mobilization of the optic nerve
- Improved surgical exposure
  - A twofold increase in the exposed length of the optic nerve
  - A three- to fourfold increase in the maximum width of the opticocarotid triangle

Evans JJ, et al.; Neurosurgery 46:1018–1023, 2000

Bony features of the sellar region

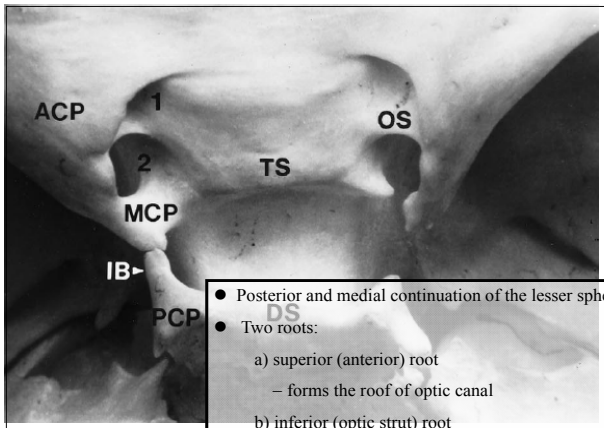


Sphenoid bone:
1) Lesser wings (orbitosphenoids)
2) Greater wings (alisphenoids)

A) Presphenoid portion :
planum sphenoidale
limbus sphenoidale
chiasmatic sulcus
tuberculum sellae

B) Basisphenoid bone :
hypophyseal fossa (sella turcica)
dorsum sellae – PCP

C) Basioccipital bone (clivus)



- Posterior and medial continuation of the lesser sphenoid wing
- Two roots:
  a) superior (anterior) root
  – forms the roof of optic canal
  b) inferior (optic strut) root
  – forms the lateral and ventral walls of optic canal
  connects the LSW with the basisphenoid
- length: 7.7 mm (3-8 mm), width: 5.6 mm (4-7.8 mm)

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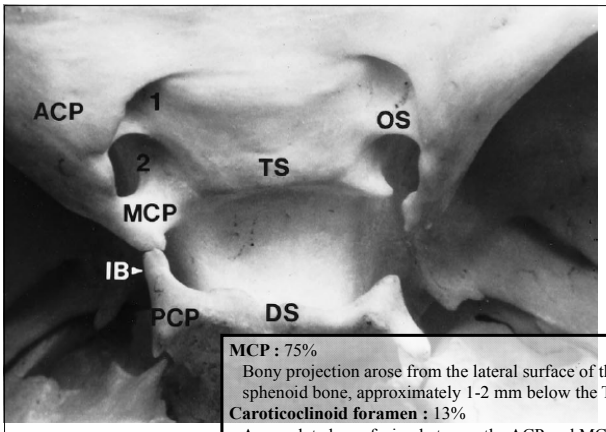
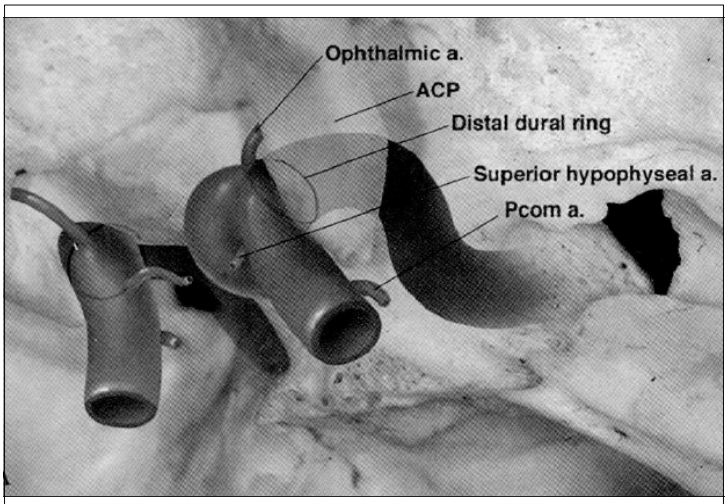


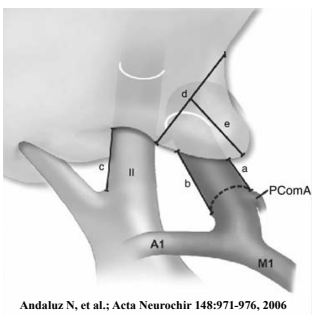
MCP : 75%
Bony projection arose from the lateral surface of the body of the sphenoid bone, approximately 1-2 mm below the TS
Caroticoclinoid foramen : 13%
A complete bony fusion between the ACP and MCP
incomplete fusion: 24%
Interclinoid osseous bridge : 6%
1) Bony connection between the ACP and PCP
2) Unilaterally or bilaterally

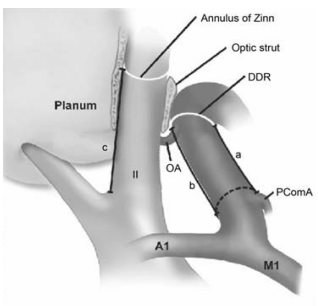


Kim JM. et al.: Neurosurgery, Vol. 46, No. 3, March 2000

Quantification of the exposure after anterior clinoidectomy

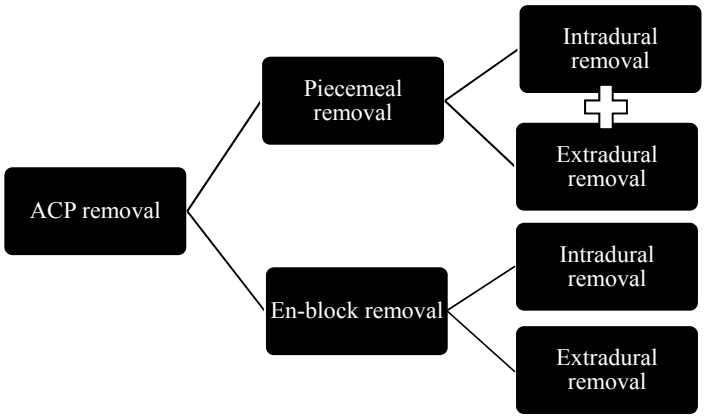
- ✓ Mean length of the **lateral C6 segment of the ICA increased 60%**
- ✓ Mean exposure of the **medial C6 segment of the ICA increased 113%**
- ✓ Exposure of the **optic nerve increased 150%**





Andaluz N, et al.; Acta Neurochir 148:971-976, 2006

Anterior Clinoidectomy

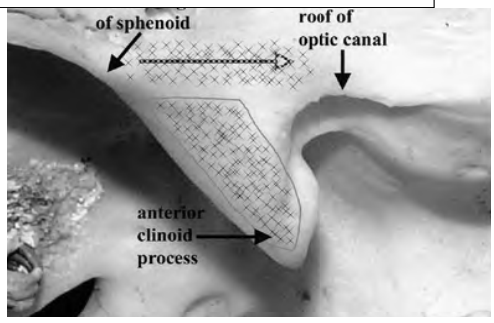


Extradural clinoidectomy

J Neurosurg 102:945–950, 2005

Disengage the ACP from its three supporting structures

1. **The lesser wing of the sphenoid bone**
2. **The roof of the optic canal**
3. **The optic strut**



Extradural clinoidectomy

Several advantages over extradural clinoidectomy.

- ✓ **Easy anatomical orientation**, therefore an extensive removal is possible.
- ✓ Dura mater acts as a **natural barrier** to protect neurovascular structures.
- ✓ Does **not** expose the subarachnoid space to bone debris
- ✓ Performed much **more quickly**.

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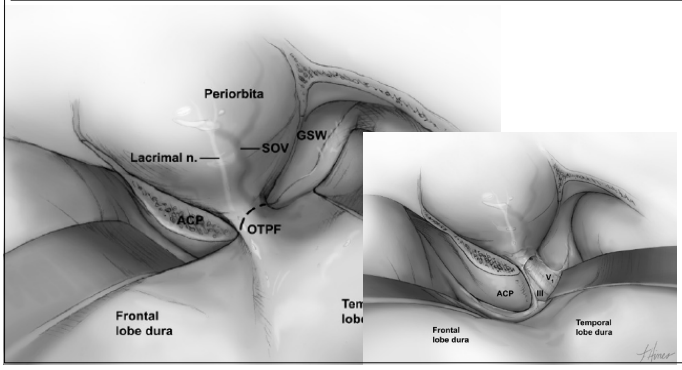
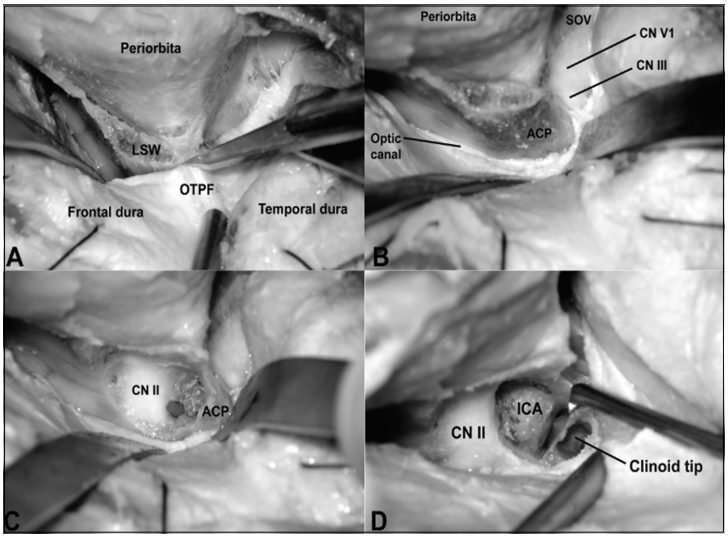
Anatomy of the orbitotemporal periosteal fold

- ✓ Sharp incision of the orbitotemporal periosteal fold (OTPF) to increase the extradural exposure of the ACP
- ✓ The level of the sphenoid ridge and restricted to the periosteal bridge

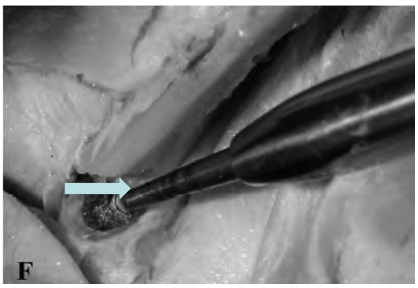




Extradural clinoidectomy step 1

1.The optic canal is unroofed from a lateral to medial direction(2-mm diamond burr)

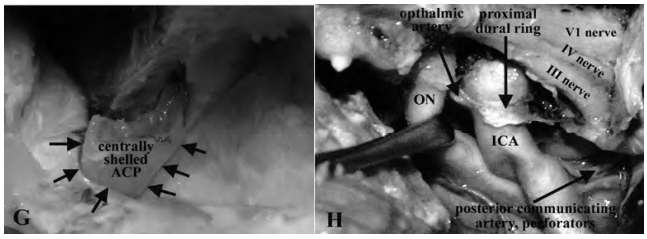
2.Constant-cooling irrigation to prevent thermal damage of surrounding neural structures



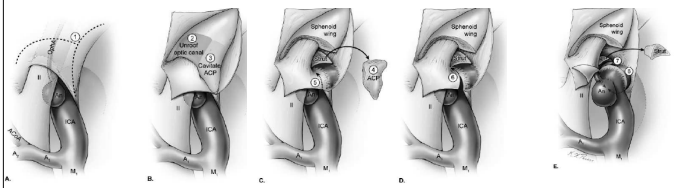
Extradural clinoidectomy step 2

1. Centrally hollowing out the dense cortical bone in the center of the ACP with the aid of a diamond burr and constant-cooling irrigation.

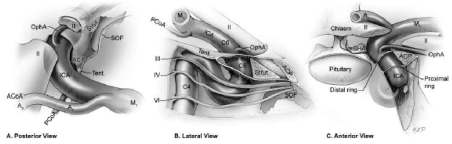
2. A circumferential dissection plane between the surrounding dural folds and the centrally shelled ACP is established



Intradural Anterior Clinoidectomy



Anterior Clinoidectomy



MEMO

How to avoid visual complications during aneurysm clipping ?

안 재 성
울산대학교 의과대학 서울아산병원 신경외과

MEMO

Intracranial Aneurysms with visual impairment
- rare entity of aneurysm-related visual impairment
- paraclinoid ICA aneurysm : most common

Possible mechanisms of visual impairment
- direct mass effects of the aneurysm on the anterior optic pathway
- compression of the optic nerve against the bony structure / dura
- compromised vascular supply

Treatment of symptomatic UIAs
- reduce mass effect & prevent rupture

- **microsurgical clipping**
  - cranial nerve decompression by reduction of mass effect
  - can cause additional injury to optic pathway

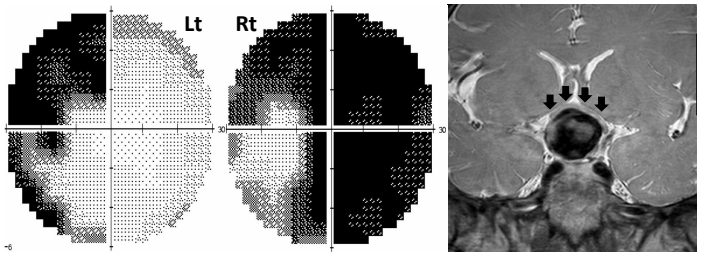
- **endovascular coiling**
  - NOT reducing of space-occupying effect,
  - BUT, reduce aneurysmal pulsation without direct injury
  - in case of recur,

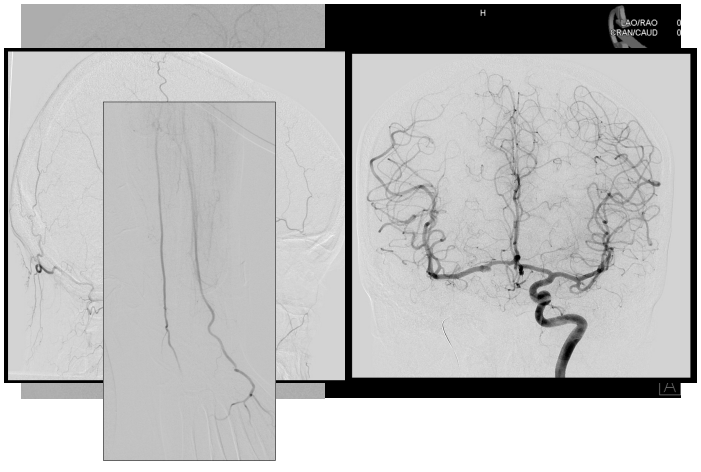
To minimize injury to optic pathway

- Minimal manipulation of optic pathway
  - 'no touch technique'
- Thermal injury during bone drilling
- Save perforators

- Surgical field
  - clean : proximal control
    proximal & distal ICA, ophthalmic a.
  - wide : optic nerve mobilization
    : decompression of the aneurysm sac
    : ICA mobilization

- Ophthalmology (Visual field examination)
- Compression on optic pathways confirmed by MRI
- Ballon test occlusion (cross filling) / TFCA, 3D





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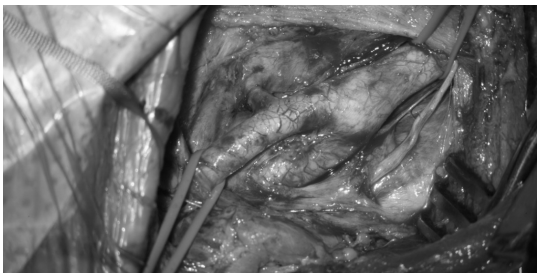
Surgical procedures

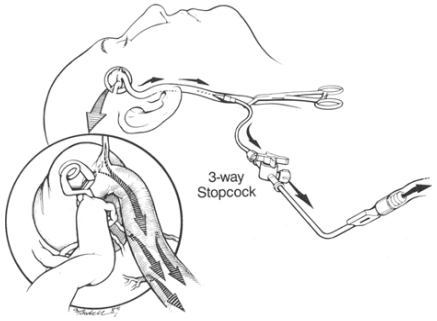
- Vascular proximal control (cervical ICA, ophthalmic a.)
- Removal of the anterior clinoid process (extra-/ intradural)
- Dural incision (falciform ligament, optic sheath)
- Dissection of the aneurysm
- Clipping of the aneurysm neck
- Repair of the dural incision

Vascular control

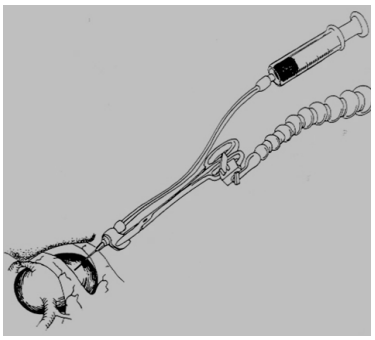
- cervical ICA exposure (with retrograde suction decompression)
- petrous portion by drilling Glasscock's triangle
- temporary clip at clinoid ICA
- induced temporary cardiac arrest using adenosine



- retrograde suction-decompression technique (JNS 1990)

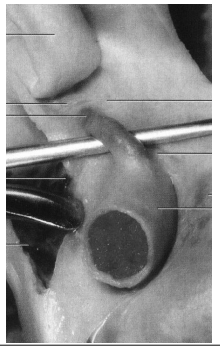


- suction-decompression technique

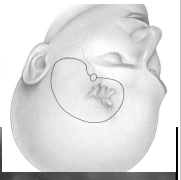


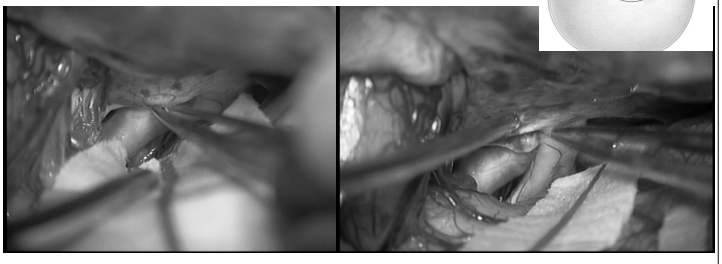
Anterior Clinoidectomy

- medial end of lesser wing of sphenoid
- mobilization of proximal supraclinoid ICA, optic n.
- exploration of cavernous sinus - initial step
- extradural / intradural removal
  - bone dust
  - dural protection
  - wider resection
- pneumatization
- carotid clinoid foramen - ICA
  middle clinoid process



Anterior clinoidectomy





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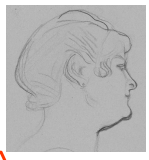
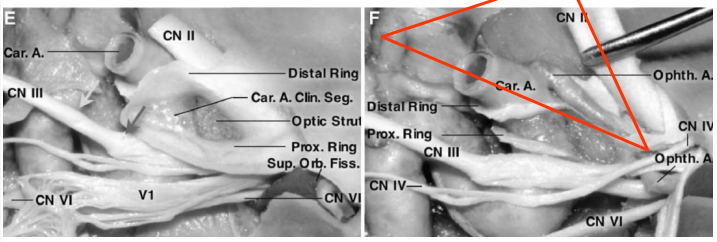
Dural Incision / Repair



- Relieve optic nerve
- Mobilize optic nerve
- Identification of the ophthalmic a.
- Easy repair



Dural Incision / Repair

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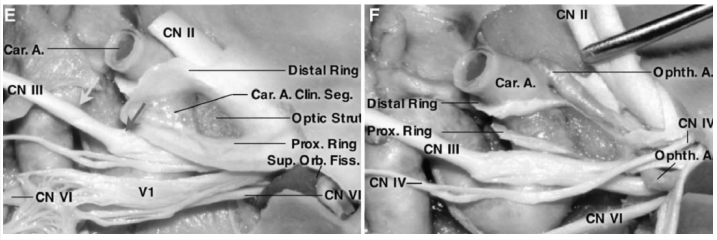
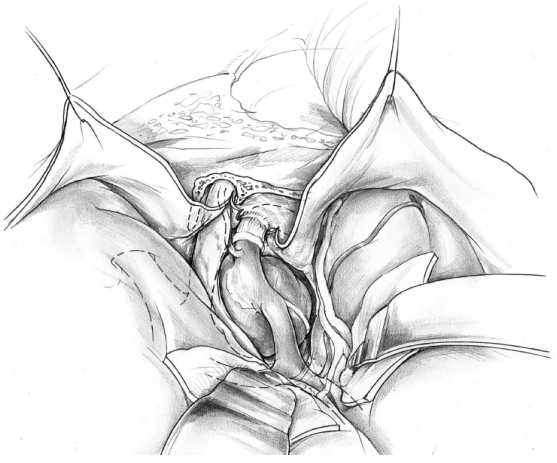
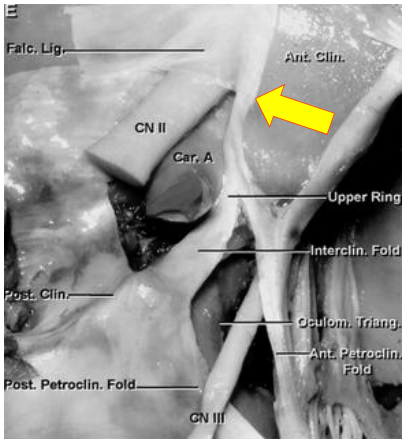
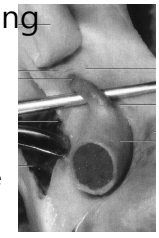




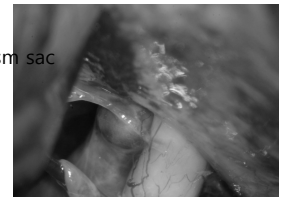


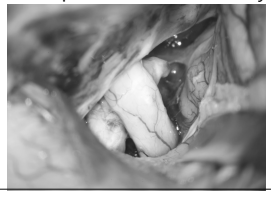
Aneurysm dissection / clipping



- Identify proximal end of the neck
- Identify ophthalmic a.
- Hidden aspect of the neck
- Distal dural ring
- Sphenoid bone as a obstacle advancing clip blade

- get the space to dissect
  - mobilize optic nerve
  - decompression of the aneurysm sac





JoS JOURNAL OF STROKE

ONLINE MANUSCRIPT SUBMISSION

Title:	Anterior Optic Pathway Compression due to Internal Carotid Artery Aneurysms: Neurosurgical Management and Outcomes
Type of Manuscript:	Original article
Running Title:	Visual symptoms caused by ICA aneurysm

Abstract

Paraclinoid aneurysms with visual symptoms

for aneurysms and visual deficits: surgery and endosaccular coiling. This study retrospectively analyzed and compared the resolution of visual deficits following surgery or endosaccular coiling. Methods: We reviewed data on 33 patients with unruptured ICA aneurysms who presented with visual field deficits caused by mass effects over the anterior optic pathway. Statistical analyses were performed to identify the variables associated with the recovery of visual symptoms. Results: Aneurysms were clipped (18 patients), bypass surgery with endovascular trapping was performed (3 patients), or endovascular trapping without bypass surgery was performed (2 patients) (group A). Ten patients received endosaccular coiling (group B). The visual outcomes included the following: in group A, 17 patients (73.9%) demonstrated improvement and 6 patients (26.1%) demonstrated no changes or worse outcomes; in group B, 2 patients (20.0%) demonstrated improvement and 8 patients (80.0%) demonstrated no changes or worse outcomes. Group A was associated with a higher rate of favorable outcome than group B (p=0.007). According to the multivariate analysis, treatment without endosaccular coiling (group A) was the only variable significantly associated with improvement of visual outcome (p = 0.005; OR = 28.523; 95% CI = 2.683-303.171). Conclusion: Treatment modality was the only predictor of improvement in visual deficits. Treatment without endosaccular coiling resulted in visual improvement more often in comparison with endosaccular coiling.

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- Jul 2009 - Dec 2012
- 26 patients (3 male and 23 female)
- age: mean 59.9 years (range 43 to 77 years)
- size of aneurysms: mean 19.8 mm (range 7.8 to 42 mm)
  23 aneurysms (88.5%); > 10 mm
  6 aneurysms (23.1%); > 25 mm
- Opthalmic segment (24/26), Cavernous segment (2/26)
- clinical follow-up duration:
  mean 20.6 months (range 6 to 45 months)
- visual field follow-up
  mean 11 months (range 3 to 45 months)

Treatment modalities (N=26)

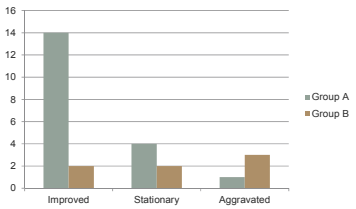
- 14 direct neck clipping with/without suction decompression
- 3 EC-IC bypass + endovascular trapping
- 2 endovascular trapping without saccular embolization
  → Group A (non saccular embolization)
- 7 saccular embolization with/without stent-assisted
  → Group B

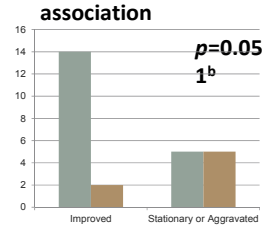
	Group A (N=19)	Group B (N=7)	*P-Value*
Sex (M:F)	3:16	0:7	0.540
Age (years ± SD)	58.0 ± 9.2	65.0 ± 8.4	0.089
Size of aneurysm (mm ± SD)	20.5 ± 9.8	17.8 ± 7.1	0.517
Sx duration (months ± SD)	6.0 ± 6.1	5.7 ± 3.3	0.179
Intra-aneurysmal thrombosis (n=4)	3/19 (15.8%)	1/7 (14.3%)	1.000
Involved Quadrant	3.47 ± 1.68	3.14 ± 1.68	0.660

Results of Treatment

	Group A (N=19)	Group B (N=7)	*P-Value*
Improved	14 (73.7%)	2 (28.6%)	0.014[a]
Stationary	4	2	
Aggravated	1	3	

[a] linear by linear association





[b] OR 7.0, 95% CI 1.01-48.3 (Fisher exact test)

Summary

- Get the space for aneurysm dissection
  release falciform ligament, optic sheath
  decompression of the aneurysm sac
- Remove mass effect on optic nerve
- Minimal manipulation on optic nerve
- No foreign body beneath optic nerve
- Early decision of Direct clipping / bypass & trapping

MEMO

Para-ophthalmic Aneurysms ; How to maintain microcatheter stability in the endovascular therapy

정 진 영
동의의료원 신경외과

Introduction

ICA paraclinoid segment 에 위치한 동맥류의 endovascular treatment 는 다양한 동맥류의 방향, carotid siphon의 tortuosity 에 의해 때로는 매우 치료가 어려운 상황을 만날 수 있으므로 이 위치의 동맥류를 치료하기 위한 기술적 이해가 필요하다.

Paraophthalmic 또는 paraclinoid aneurysm 의 endovascular treatment 시 balloon 또는 stent 등을 이용한 adjuvant technique 을 사용한다 하더라도 혈관의 해부학적 구조에 적합한 모양의 microcatheter를 이용하여야 시술이 진행되는 동안 안정적이고 안전한 coil packing 이 이루어 질 수 있으며 이것이 가장 선행되어야 할 중요한 부분이다.

1. Shapes of Microcatheters

일반적으로 국내에서 사용되는 aneurysm 용 microcatheters

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

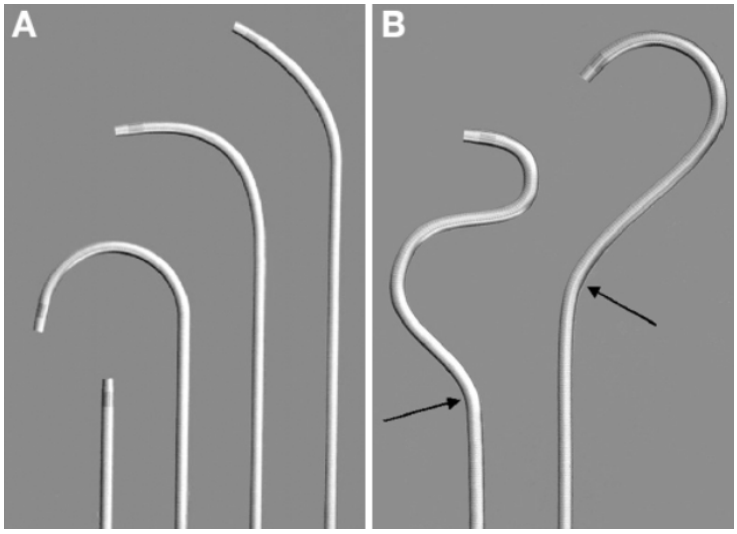


Fig. 1. Photographs of preshaped microcatheters: straight, J, 90, and 45(A), and S and C(B) presented in order. The S and C shapes have an additional small obtuse curve at the beginning of the shapes (arrows).

2. Steam shaping of microcatheters

제조 시부터 preshaped 된 제품을 쓰면 가장 안정적인 microcatheter stability 를 얻을 수 있겠지만 특히 paraclinoid/paraophthalmic aneurysm 의 치료 시에는 이 만으로는 불충분 한 경우가 많으므로 개별 혈관의 모양에 따른 tailored shape 의 microcatheter 를 steam 에 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)

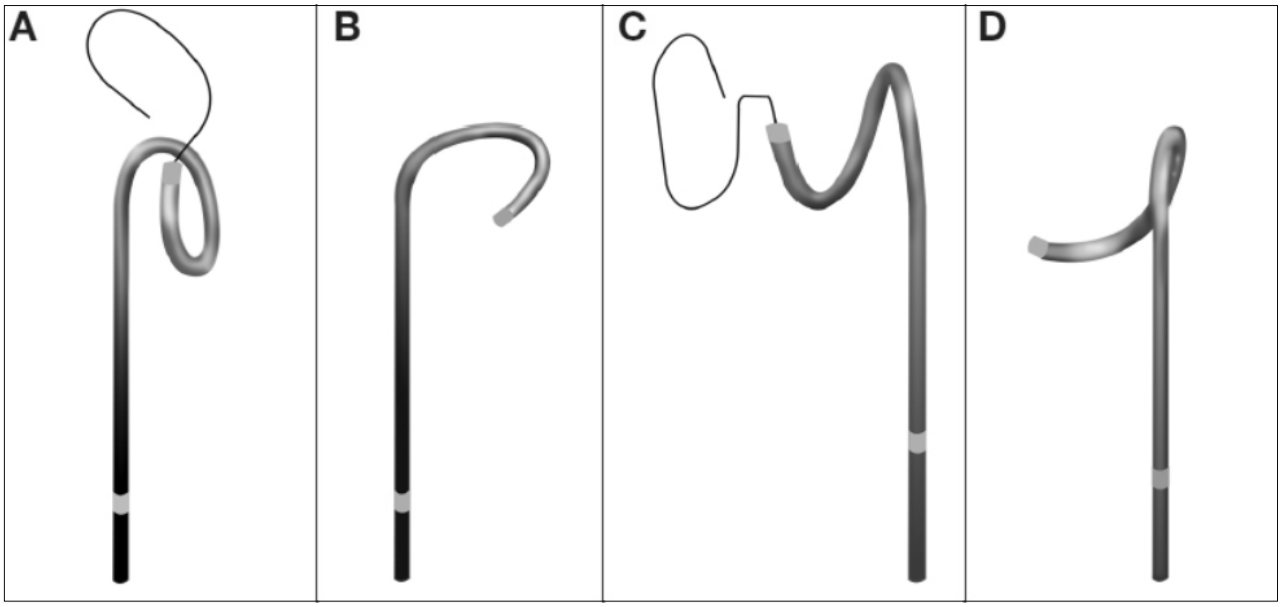


Fig. 2. *Diagram of "pigtail" shape before and after steaming. A, diagram of 2-dimensional "Pigtail-simple" shape shows curling at the portion with a shaper for steaming. Steaming usually takes 30 to 40 seconds and steamed micro-catheters are soaked in normal saline for 30 seconds or more. B, diagram 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 us right (not shown), is determined with the direction of the shaped tip to the main shaft of the microcatheter.*

Pig tail shape 을 만드는 방법

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

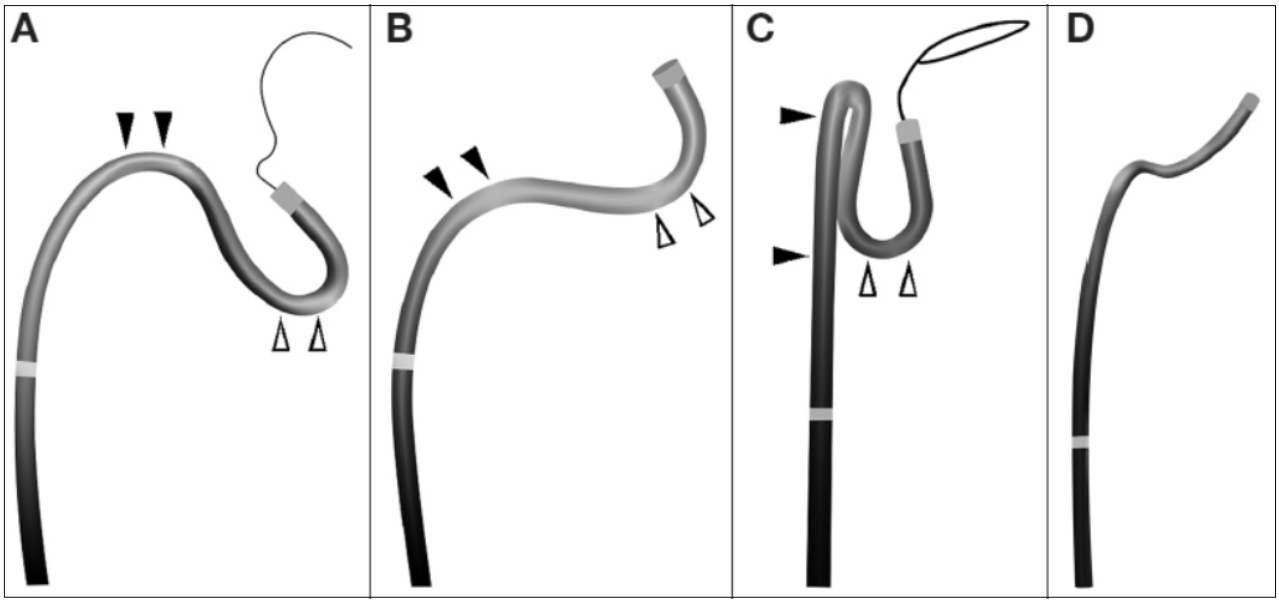


Fig. 3. *Diagram of "S" shape before and after steaming. Presteam (A) and poststeam (B) diagrams of 2-dimensional "S-simple" shape show the superior (open arrowheads) and inferior (black arrowheads) curves of the character "S" Varying the size and length of each curve provides the most appropriate "S" 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 arrow-heads) is perpendicular to the inferior curve and main shaft (black arrowheads) before steaming. The side, right us left (not shown), is determined with the relative direction of the superior curve to the main shaft of the microcatheter.*

S-shape shape 을 만드는 방법

mandrel 을 S shape 으로 만든 후 동일한 방법으로 steam shaping 하면 simple S-shape 을 얻을 수 있다. 이러면 proximal 과 distal part 에 superior, inferior 방향으로 두 개의 curve 가 만들어 지고 혈관의 모양에 맞추어서 이 curve 의 정도를 달리하면 좀 더 안정적인 microcatheter stability 를 유지할 수 있다. 이 기본 모양에 동맥류의 방향을 고려하여 distal end 부분을 오른쪽, 또는 왼쪽으로 shaping 을 하면 혈관과 동맥류의 방향을 모두 만족시키는 3차원 구조의 응용된 microcatheter shape 을 얻을 수 있다.

3. Navigating methods of Microcatheters

1) Shaping 된 microcatheter 자체 만을 microguide wire 의 도움 없이 advance 하거나 목표지점을 지난 후 withdrawal 하며 aneurysm 을 selection 하는 방법 (가장 안전하고 이상적인 microcatheter shape 이 이루어 졌을 때 가능).
2) Wire-steering method: shaping 된 microguide wire 를 microcatheter 의 distal end 부위에 위치시킨 후 aneurysm 입구에서 steering 하여 microcatheter 를 aneurysm 내로 navigation 하는 방법.
3) Looping method: 급격한 angle 의 방향을 가진 동맥류의 경우 microcatheter 를 looping 시킨 상태에서 aneurysm 을 지난 후 pulling 하면서 aneurysm 내로 navigation.
4) Coil 또는 microguide wire 를 이용하여 직접 aneurysm 내로 navigation.

4. To increase intra-aneurysmal stability of microcatheters during coiling

Paraclinoid aneurysm 의 성공적인 coiling을 위해서는 microcatheter 를 aneurysm 내로 positioning 시키는 것뿐만 아니라 indwelling 시킨 microcatheter 의 stability 를 유지하는 것이 매우 중요하다. Micro-guide wire 등을 이용하여 강제로 aneurysm 을 superselection하더라도 microcatheter 의 모양이 해부학적 구조와 일치하지 않으면 coiling 이 진행되는 동안 microcatheter 의 kick back 을 유발시키고 불완전한 치료나 치료관련 합병증으로 이어질 가능성을 높이게 된다. 그러므로 각각 동맥류의 방향 및 혈관 모양에 맞는 microcatheter 의 shaping 은 navigation 및 positioning 을 쉽게 해주고 coil 이 진행되는 동안 microcatheter stability 도 유지할 수 있게 해주는 중요한 요소이다.

Coil 이 진행되는 동안 microcatheter stability 를 좋게 유지하기 위해서는 **microcatheter 가 동맥류 반대쪽 ICA wall 에 지지할 수 있도록 모양을 만들어야 한다**. 대부분의 para-ophthalmic aneurysm 처럼 superior projection 의 aneurysm 의 경우, S-shape microcatheter 의 첫 번째 curve 와 두 번째 curve 사이 부분이 aneurysm 반대 쪽 ICA inferior wall 에 위치할 수 있도록 shaping을 하면 안정적인 coiling 을 하는데 큰 도움을 얻을 수 있다. Paraclinoid aneurysm 의 가장 흔한 형태인 medical projection 의 aneurysm 을 pig tail shape 의 proximal widening part 가 ICA lateral wall 을 지지할 수 있도록 디자인 되면 또한 안정적인 microcatheter support 을 유지할 수 있다.

5. Shapability and shape-retention of various catheters

Non-braided 또는 fiber-braided microcatheter 가 stainless-steel-braided microcatheters (ex, Excelsior SL-10) 보다 shapability 가 우월한 것으로 보고되고 있으며[2] 또 다른 test 에서는 steam- shaped Proweler 14 microcatheter (platinum, larger pitch-coiled design)가 Excelsior SL-10 microcatheter 보다 shapability 와 shape-retention 능력이 부족하나 preshaped Proweler 14 microcatheter 는 SL-10 microcatheter 와 동등한 결과를 보여준다[3].

6. Conclusion

Paraclinoid or paraophthalmic aneurysm 의 coiling 을 계획할 때 동맥류의 방향을 고려하여 steam shaping 된 microcatheter 를 이용하면 aneurysm 을 selection 하는데 있어서 불필요한 노력과 시간을 줄일 수 있고 coiling 이 진행되는 과정에서도 안정적인 packing 을 얻을 수 있다.

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New strategies upon the literature review

임 동 준
고려대 안산병원 신경외과

Special Lecture I

좌장 : 김범태(순천향대)

Endovascular Treatment of Large and Giant Aneurysms

Kenji Sugiu (Okayama University Medical School)

Endovascular Treatment of Large and Giant Aneurysms

Kenji Sugiu, Tomohito Hishikawa, Masafumi Hiramatsu, Jun Haruma,
Yuji Takasugi, Yukei Shinji, Shingo Nishihiro, Isao Date
Department of Neurological Surgery, Okayama University Graduate School of Medicine, Okayama, Japan

Introduction: Large and giant aneurysms pose difficulties for both microsurgical and endovascular treatment (EVT). Despite recent steep development of EVT, these aneurysms carry a high risk of morbidity and mortality. We would like to share our experience of EVT for such aneurysms.

Methods: We retrospectively evaluated our results of EVT for the large (?10mm) and giant (?25mm) between 2010 and 2014.

Results: 409 patients were treated by endovascular aneurysmal occlusion using detachable coils. There were 8 giant and 71 large aneurysms among them. Stent-assisted coiling was applied 75% in giant, 35% in large, and 2% in small aneurysms. Initial complete occlusion was obtained 25% in giant, 46% in large, and 53% in small aneurysms. Procedure related permanent complication occurred 25% in giant, 6% in large, and 2% in small aneurysms. Major recurrence was observed 25% in giant, 11% in large, and 3% in small aneurysms.

Discussion: Our recent data of endosaccular occlusion of the aneurysms showed relatively good result comparing to historical control. Stent usage may play an important role in the treatment of large and giant aneurysms. However, some giant aneurysms are still challenging for EVT. Flow diverter stent such as Pipeline Embolization Device is expected in the future for the treatment of such complex aneurysms.

Conclusion: Our small case series demonstrated relatively good clinical results of EVT for the treatment of large and giant aneurysms.

Key Words: coil, balloon, stent

Special Lecture II

좌장 : 이호국(한림대)

Advanced MRI Stroke Imaging 손철호(서울대 영상의학과)

Advanced MRI Stroke Imaging

Chul-Ho Sohn, MD, PhD
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Stroke is a major cause of mortality and morbidity. More than 80% of strokes stem from ischemic damage to the brain due to the acute reduction of the blood supply. It was calculated that 1.8 million neurons are lost every minute that appropriate treatment is not given ('time is brain'). For these reasons, 'stroke imaging' is crucial and has to be performed in a fast and efficient process.

1. Susceptibility-weighed imaging

Susceptibility-weighted imaging (SWI) usually contains magnitude and phase information of MR signal. The phase information was ignored and usually discarded before even reaching the viewing console. Phase images, however, contain a wealth of information about local susceptibility changes between tissues, which can be useful in measuring iron content. So SWI is more sensitive to magnetic susceptibility than conventional T2*-GRE. Wide concept SWI sequence includes conventional T2*-GRE and different type of gradient echo sequences

Susceptibility-weighted imaging (SWI or T2*-GRE) MRI sequences are extremely sensitive for detecting intracerebral hemorrhage and subarachnoid hemorrhage. SWI also detects micrbleeds easily.

T2 *-gradient-echo MR imaging, including the more sensitive SWI can detect acute thrombus as an MRI signal drop, the so-called 'artery susceptibility sign'.

SWI demonstrates additional vessel 'signs' (transmedullary vein sign, leptomeningeal vein sign). The increased oxygen extraction fraction (OEF) in the ischemic tissue leads to a local increase in deoxyhemoglobin, which in turn causes the so-called BOLD (blood oxygen level dependent) effect.

SWI is more sensitive in detecting cavernomas than is T2*-weighted imaging, and lesions that are presumed to be telangiectasias are detected only with this technique.

2. Perfusion imaging

1) Dynamic susceptibility contrast MR perfusion (DSC-MR perfusion)

DSC-MR perfusion technique is dynamic imaging technique (a time series of fast T2*-weighted images) necessitating the administration of intravenous contrast medium (gadolinium). As these high magnetic susceptibility agents traverse

through the brain capillary network, signal loss occurs due to the presence of magnetic field gradients between the vessels and the extravascular space, which is sampled using a fast MRI method using a repetition time on the order of 1-2 sec. Since the bolus passes through the brain parenchyma within several seconds, a complete PWI scan rarely lasts over a minute or two. The signal loss induced by the bolus can be related to the tissue concentration, which, coupled with a measurement of the arterial delivery of the agent (the arterial input function [AIF]), is used to estimate multiple hemodynamic parameters, including the relative cerebral blood volume (CBV), relative cerebral blood flow (CBF), mean transit time (MTT). Additionally, measurements of the delay of the agent arrival can be measured, either directly (the time-to-peak signal, or TTP) or via deconvolution with the AIF (Tmax).

The reduced CBF triggers energy-dependent autoregulatory mechanisms to keep the CBV normal or even slightly elevated accompanied by elevated MTT and TTP. These compensatory mechanisms fail in the infarcted area causing a CBV drop. Thus, CBV drop is a marker of infarction and correlates with the diffusion restriction only in hyperacute stroke.

The penumbra is traditionally defined on MRI as the area of DWI<PI mismatch. For PI, a Tmax with a delay of >6 s and >10 s has been used in large stroke trials, for instance, DEFUSE2, to define the thresholds for penumbra and infarct core lesion, respectively. TTP and MTT are also good alternatives to Tmax in determining the diffusion/perfusion mismatch.

[In CT, a mismatch between CBV (threshold at 2.0 ml/100 g for infarct core) and MTT (threshold at a relative MTT of 145% for the tissue at risk of infarction) defines the ischemic penumbra. Almost all cases with an anterior circulation stroke show mismatch within the first 3 hr. This declines to 75% within the first 6 hr and to 50% 12-18 hr after onset.]

The diffusion/perfusion mismatch concept is currently considered by several authors as inadequate for patient selection in ischemic stroke treatment trials. Several experts suggest that the indication for endovascular intervention is set in case of severe neurological deficit, presence of a large vessel occlusion and a small (<70 ml) infarct core. Thus, the necessity of perfusion imaging for therapeutic decision making has to be proven.

DSC-MR perfusion analyses are not standardized, and can lead to variation in perfusion lesions of 50% or more. In a recent study, academic programs outperformed commercial perfusion software.

2) Arterial spin labeling MR perfusion

Arterial spin labeling (ASL) perfusion imaging uses blood as an endogenous contrast agent by magnetically labeling it with radiofrequency pulses and does not require gadolinium-based contrast agents. The perfusion contrast is given by the difference in magnetization induced by the exchange of these labeled spins at the brain tissue level and a non-labeled control image. Limited by its low intrinsic signal-to-noise ratio, ASL perfusion measurements generally take several minutes for an accurate perfusion measurement.

There are several different ASL-MRI approaches that vary mainly on the basis of the technique that is used to label

the inflowing arterial blood. Three main labeling strategies can be distinguished: pulsed ASL (PASL), in which the blood within a large spatial volume is inverted by a relatively short inversion pulse (typically 10-20ms); continuous ASL (CASL), in which blood flowing through a specific plane is inverted for a labeling period of 1-3 s; and, pseudo-continuous ASL (pCASL), which recently has been introduced as a more efficient and easy way to achieve such a labeling plane by means of a long train of small radiofrequency pulses. An improved pCASL, however, has increased the signal-to-noise ratio because it has a higher labeling efficiency and enables the combined use of the body transmit coil with the multi-detector coils. By combining it with background suppression, the signal-to-noise ratio is increased further, by almost 2-fold, allowing for shorter imaging time and increased spatial resolution.

Potential advantages of ASL versus DSC perfusion imaging include relative insensitivity to blood-brain barrier permeability changes, which occur frequently in acute ischemic stroke. Perfusion quantification using ASL generally does not rely on the selection of arterial input function.

The main limitation of ASL is the short tracer half-life (blood T1 =1-2 seconds) resulting in limited sensitivity and potential underestimation of perfusion in the presence of prolonged transit delay resulting from arterial occlusion.

A. Acute stroke

ASL tends to overestimate the PWI time to maximum lesion volume in acute stroke patient.

ASL cerebral blood flow and DSC-MR perfusion maps provided largely consistent results in delineating hypoperfused brain regions in acute ischemic stroke. Hyperemic lesions, which also appeared frequently in the acute ischemic stroke cases studied, were more conspicuous on ASL cerebral blood flow than on DSC-MR perfusion CBF, MTT and Tmax of the tissue residual function maps.

Ischemic penumbra is of variable size, depending on the degree of collateral flow from unaffected territories and the length of time from stroke onset. The penumbra is generally accepted as the volume of brain showing a perfusion-DWI mismatch. ASL CBF maps show this area as a larger region of diminished signal intensity. ASL allows for the measurement of rCBF in the core and mismatch regions. Values in the mismatch were significantly higher than in the core, suggesting there is potential salvageable tissue.

The bright vessel appearance on ASL imaging can provide an important diagnostic clue for the detection and localization of arterial occlusion sites in patients with acute ischemic stroke.

B. Chronic Cerebrovascular Occlusive Disease

In patients with carotid or other proximal arterial stenosis, tissue at risk for subsequent ischemia and infarction can be identified with spin-tag perfusion, though a current limitation of most versions of ASL is the inability to assess CBV. However, transit time maps can be generated with ASL by imaging at additional inversion times. If CBF is relatively decreased with a compensatory increase in CBV, a side-to-side flow asymmetry can be appreciated representing at-risk

tissue that may benefit from stent placement, endarterectomy, or bypass. A focal decrease in signal intensity of compromised CBF can be seen most commonly in the anterior or posterior watershed zones. A common feature also seen is linear high signal intensity representing slow flow or collateral flow in cortical vessels. Because of its repeatability, ASL is particularly capable of assessing cerebrovascular reserve in these patients by obtaining CBF maps before and after an acetazolamide or hypercapnia challenge. Finally, serial assessment following revascularization or confirmation of the postendarterectomy hyperperfusion syndrome is feasible with ASL.

Scientific Session II

Cerebral Venous Thrombosis (CVT)

좌장 : 박현선(인하대), 고현송(충남대)

1. Etiology and pathogenesis / Diagnostic tools 김태곤(차의과대)
2. Endovascular treatment of CVT 신승훈(분당제생병원)
3. Current recommendation: Literature review 이형중(한양대)

Cerebral Venous Thrombosis
-Etiology and pathogenesis/Diagnostic tools-

Tae Gon Kim, M.D.
차의과대

Cerebral venous thrombosis (CVT) represents a pathologic process of a thrombosis in the cerebral venous sinuses, the deep venous system or the cortical veins, which can give rise to venous hypertension, brain hypoxia, neural ischemia and finally cerebral infarctions or cerebral hemorrhages. The underlying mechanisms of CVT are associated with alterations in the physical properties of the dural sinuses and veins (trauma), alterations in the chemical properties of blood (hypercoagulable state, coagulation system abnormalities, infection, oral contraceptives) and alterations in the hemodynamic properties of blood flow (trauma, dural AVF). However, the 40% of the cases is idiopathic. The exact incidence of CVT is unknown, but it is relatively rare. It affects all age groups and both sexes, but it shows a strong preponderance in women between 20 - 40 years of age and is associated with oral contraceptives and puerperium. CVT shows a variety of clinical manifestations such as headache, nausea, vomiting, papilledema, mental changes, focal neurological deficits, seizures and etc. These rarity and highly variable clinical manifestations of CVT result in difficulty to make a diagnosis and frequently in delayed diagnosis. Therefore it is necessary for clinicians to have a high level of suspicion to make a diagnosis. The diagnostic tools include computed tomography (CT), brain magnetic resonance imaging/angiography (MRI/MRA) and cerebral angiography. Brain CT is usually an initial diagnostic test. The cord sign (hyperdense cortical vein) and the dense triangle sign (or delta sign; hyperdense sinuses) can be noted in the non-contrast brain CT during the first 1-2 weeks after thrombosis. The contrast brain CT can show the empty delta sign (peripheral dural leaf enhancement along with a central nonopacified thrombus). Brain MRI/MRA is the best and most sensitive method for detecting CVT. The thrombus can be directly visualized and cortical lesions such as edema and hemorrhagic infarction can be detected in the brain MRI/MRA. Cerebral angiography is rarely used to make a diagnosis and now indicated in cases of uncertain diagnosis, documentation of the lesion extension, documentation of the collateral venous pathways and intervention. The typical finding of cerebral angiography is nonvisualization of veins or sinuses.

Endovascular Treatment of Cerebral Venous Thrombosis(CVT)

신 승 훈
분당제생병원

Thrombosis of the dural sinus and/or cerebral veins (CVT) is an uncommon form of stroke, usually affecting young individuals. Despite advances in the recognition of CVT in recent years, diagnosis, and management can difficult because of the diversity of underlying risk factors and the absence of a uniform treatment approach.

Current mainstay of treatment is anticoagulation therapy; to prevent thrombus growth, to facilitate recanalization, and to prevent DVT or PE. Controversy has ensued because cerebral infarction with hemorrhagic transformation or ICH is commonly present at the time of diagnosis of CVT, and it may also complicate treatment.

In special situation of a patient with major contraindication for anticoagulation (Such as recent major hemorrhage), the clinician must balance the risks and benefits of anticoagulation, depending on the clinical situation.

Limited data from randomized controlled clinical trials in combination with observational data on outcomes and bleeding complications of anticoagulation support a role for anticoagulation in treatment of CVT, regardless of the presence of pretreatment ICH.

In general, thrombolytic therapy and/or endovascular treatment are used if clinical deterioration continues despite anticoagulation or if a patient has elevated intracranial pressure that evolves despite other management approaches.

Many invasive therapeutic procedures have been reported to treat CVT. These include direct catheter chemical thrombolysis using urokinase and direct thrombectomy with or without thrombolysis. There are no randomized controlled trials to support these interventions compared with anticoagulation or with each other. Most evidence is based on small case series or anedoctal reports. Hera, I review the studied interventions.

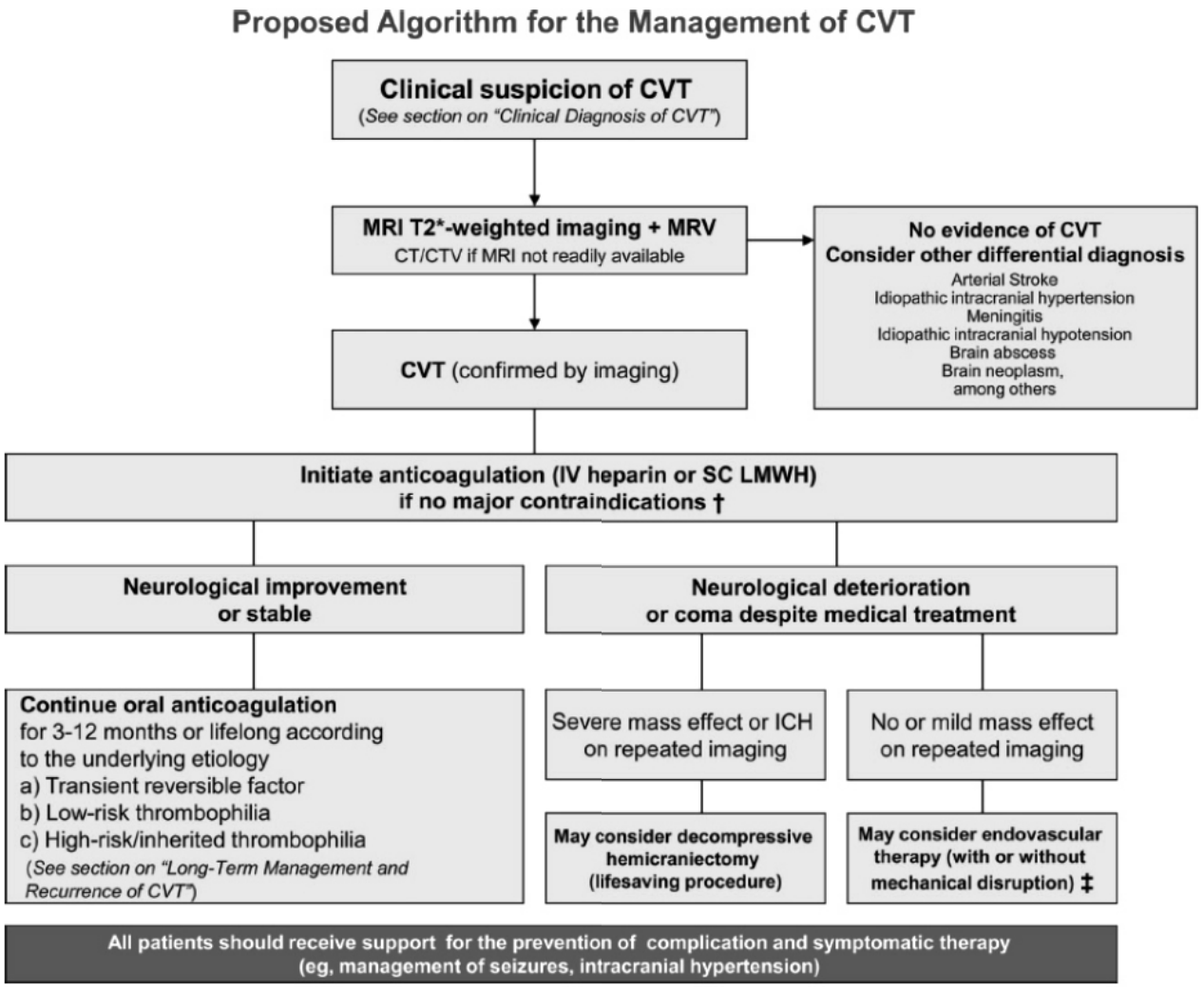

Proposed Algorithm for the Management of CVT
Clinical suspicion of CVT
(See section on "Clinical Diagnosis of CVT")
MRI T2*-weighted imaging + MRV
CT/CTV if MRI not readily available
No evidence of CVT
Consider other differential diagnosis
Arterial Stroke
Idiopathic intracranial hypertension
Meningitis
Idiopathic intracranial hypotension
Brain abscess
Brain neoplasm,
among others
CVT (confirmed by imaging)
Initiate anticoagulation (IV heparin or SC LMWH)
if no major contraindications †
Neurological improvement
or stable
Neurological deterioration
or coma despite medical treatment
Continue oral anticoagulation
for 3-12 months or lifelong according
to the underlying etiology
a) Transient reversible factor
b) Low-risk thrombophilia
c) High-risk/inherited thrombophilia
(See section on "Long-Term Management and
Recurrence of CVT")
Severe mass effect or ICH
on repeated imaging
No or mild mass effect
on repeated imaging
May consider decompressive
hemicraniectomy
(lifesaving procedure)
May consider endovascular
therapy (with or without
mechanical disruption) ‡
All patients should receive support for the prevention of complication and symptomatic therapy
(eg, management of seizures, intracranial hypertension)

Fig. 1.

Cerebral Venous Thrombosis (CVT) : Current recommendation - Literature review

Hyeong-Joong Yi, M.D.
Department of Neurosurgery, Hanyang University Hospital, Seoul

Introduction: Cerebral venous thrombosis (CVT) is a multifactorial cerebrovascular disease resulting from the interaction between many acquired and genetic risk factors that predispose to one of the individual components of the Virchow's triad, characterized by endothelial damage, venous stasis, and hypercoagulability. To enhance understanding this rare, but potentially lethal disease, about 60 English-written literatures regarding CVT within a recent decade were thoroughly reviewed.

Methods: With the key words of CVT, stroke, and guidelines, searching by web engine (pubmed, google, scopus) was undertaken. Of the 350 literatures approached, 60 ones were chosen for author's discretion. For these, a thematic review was made according to their categories; mainly by treatment and prognosis.

Results: Although its rarity, CVT has an important diagnostic consideration because of the differences in management from other common arterial stroke. Early anticoagulation is often considered as both treatment and early secondary prophylaxis for patients with CVT. Only 2 controlled data were available with superior results to the placebo group; dose-adjusted unfractionated heparin (pTT≥2.0) and nadoparin (90 anti-factor Xa U/kg bid). On the basis of Cochrane meta-analysis, the use of anticoagulation with heparin or LMWH acutely in the setting of CVT is recommended, regardless of the presence of hemorrhagic conversion. When thrombosis is persisted, or recanalization is incomplete, various endovascular (local) thrombolysis either chemical or mechanical, may be attempted to such a refractory case, however the efficacies were supported by anecdotal reports and small case series. With regard to the duration of anticoagulation, no RCT data exist. Patients with inherited thrombophilia are often treated for longer periods than those with a transient (reversible) risk factor such as oral contraceptive use. Antiplatelet therapy is often given indefinitely after discontinuation of warfarin, although there are no data to support this. Poor prognosis (death or dependency) at 6 month follow-up, has been reported more commonly when patients were older than 37 years, male sex, coma, and patients had mental status disorder, hemorrhage on admission imaging, thrombosis of the deep cerebral venous system, central nervous system infection, and cancer.

Conclusions: Anticoagulation os reasonable for patients with acute CVT, even in selected patients with intracranial hemorrhage. In CVT patients without a recognized thrombiphilia, it is reasonable to administer anticoagulation for ≥3 months, followed by antiplatelet therapy. The above high-risk patients may benefit from more aggressive therapeutic interventions.

Symposium

Carotid Artery Stenosis

좌장 : 오창완(서울대)

1. **국내 경동맥협착증 환자에서 경동맥 내막절제술과 스텐트삽입술의 임상적 효과비교**

이자연(한국보건의료연구원)

2. **국내 경동맥협착증 환자에서 경동맥내막절제술과 스텐트삽입술의 비용-효과성**

신상진 (한국보건의료연구원)

3. Which one is better, CEA, or CAS : Pannel discussion

1) CEA 김태선(전남대)

2) CAS 유승훈(강릉아산병원)

국내 경동맥 협착증 환자에서 경동맥 내막절제술과 스텐트삽입술의 임상적 효과비교

이 자 연
한국보건의료연구원

연구진행경과

- 연구주제 수요조사 (2012)
  - Comparative Effectiveness Research
- 연구주제 선정 (2013. 3)
  - 경동맥 협착증 치료는 뇌졸중 발생을 예방하는 측면에서 임상적 중요성이 큼
  - 현재 스텐트 삽입술과 내막절제술 모두 건강보험권에 포함되어 있음. 경동맥 스텐트 삽입술의 비용이 현저히 높음에도 불구하고 국내에서 경동맥 스텐트 삽입술의 사용이 월등히 선호되는 상황임
  - 치료관행의 개선을 위한 국내 근거자료 생성이 필요함
- 연구과제 수행 (2013. 4 ~ 2014. 6)

연구진 구성

원외연구진		원내연구진(NECA)	
박현선	인하대 의과대학	신상진	보건의료근거연구본부 연구위원
전 평	성균관대 의과대학	오성희	보건의료근거연구본부 주임연구원
조용필	울산의대 의과대학	유지혜	보건의료근거연구본부 연구원
김병문	연세대 의과대학	이자연	보건의료근거연구본부 연구원
김태선	전남대 의과대학	박지정	보건의료근거연구본부 연구원
서상현	연세대 의과대학		

MEMO

MEMO

연구목적

- 경동맥 협착증에서 스텐트 삽입술이 내막절제술의 대체 치료로 사용이 가능한 유증상 경동맥 협착(협착률 50% 이상)을 가진 환자를 대상으로 국내 상황에서 두 시술의 임상적 효과성(clinical effectiveness)를 비교평가함

연구방법 (1): 대상선정

환자자료 수집

- **연구참여기관**
  : 인하대병원, 삼성서울병원, 서울아산병원, 전남대병원, 신촌 세브란스병원

- **연구대상자**
  : 2008년 1월 1일 ~ 2011년 12월 31일 협착률 50%이상의 유증상 경동맥 협착증으로 내막 절제술 또는 스텐트 삽입술을 받은 환자

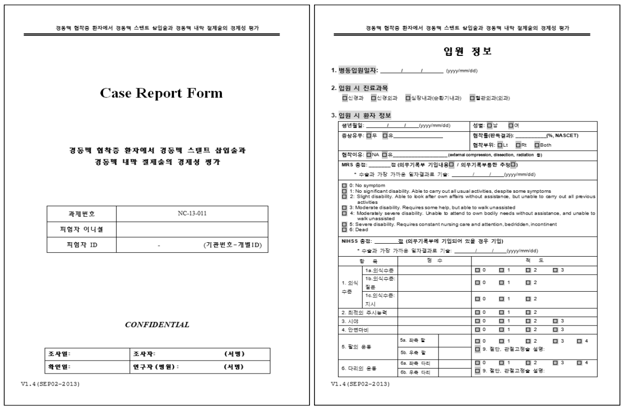
- **연구방법**
  - 문헌고찰 및 임상전문가 논의를 통해 비교 가능한 대상자 선정을 위한 포함/배제 기준 선정
  - 객관적으로 표준화된 정보 조사를 위하여 CRF개발 및 자료수집

연구방법 (2): 포함/배제기준

포함기준	배제기준
◆ 경동맥 협착률 50%이상의 유증상 환자(NASCET기준)	◆ 중증 뇌졸중(mRS>2 또는 NIHSS≥9 또는 임상적 판단)
◆ 유증상의 경동맥 협착으로 인한 스텐트 삽입술 또는 내막절제술(6개월 이내의 일과성 허혈성 발작 또는 경증 뇌졸중)	◆ 심근경색(30일 이전)
◆ 동측 경동맥 협착(Ipsilateral Carotid Stenosis, ICS)	◆ 만성 폐색(Chronic occlusion)
◆ 19세 이상	◆ 출혈 과거력(출혈 체질(hemorrhagic diathesis)또는 응고장애(coafulopathy))
◆ 기대여명 2년 이상	◆ 두개내 원인 협착(뇌동정맥기형(intracranial arteriovenous malformation, 동맥류(aneurysm), 폐쇄성질환(occlusive disease), 종괴병변(mass lesions), 모야모야병(moyamoya disease))
	◆ 심장계 원인 협착(만성심방세동(chronic atrial fibrillation), 부정맥(arrhythmia))
	◆ 외부압박(external compression), 박리(dissection), 방사선조사(radiation), 섬유근형성이상(fibromuscular dysplasia)로 인한 협착
	◆ 유증상 협착의 기왕력(재협착)
	◆ Planned simultaneous surgical procedures: 중증 다발병소(severe tandem lesions) 포함
	◆ 전환 (스텐트 삽입술→내막절제술 또는 내막절제술→스텐트 삽입술)
	◆ 내원 후 24시간내 응급 시술
	◆ 양쪽 시술
	◆ 시술 반대측 협착률 70% 이상
	◆ 기타: 환자 상태 (중증 치매, 경부경직(rigid neck), 탈원으로 인한 퇴원정보 누락)

MEMO

연구방법 (3): 환자증례기록지



경동맥 협착증 환자에서 경동맥 스텐트 삽입술과 경동맥 내막 절제술의 경제성 평가

Case Report Form

경동맥 협착증 환자에서 경동맥 스텐트 삽입술과
경동맥 내막 절제술의 경제성 평가

과제번호	NC-13-011
피험자 이니셜	
피험자 ID	- (기관번호-개별ID)

CONFIDENTIAL

조사일:	조사자: (서명)
확인일:	연구자(병원): (서명)

V1.4(SEP02-2013)

경동맥 협착증 환자에서 경동맥 스텐트 삽입술과 경동맥 내막 절제술의 경제성 평가

입원 정보

1. 병동입원일자: ___/___/___ (yyyy/mm/dd)

2. 입원 시 진료과목
☐신경과 ☐신경외과 ☐심장내과(순환기내과) ☐혈관외과(외과)

3. 입원 시 환자 정보

생년월일: ___/___/___(yyyy/mm/dd) 성별: ☐남 ☐여
증상유무: ☐무 ☐유___ 협착률(판독결과): ___(%, NASCET)
협착부위: ☐Lt ☐Rt ☐Both
협착이유: ☐NA ☐유___(external compression, dissection, radiation 등)
MRS 총점: ___점 (의무기록부 기입내용☐ / 의무기록부통한 추정☐)
* 수술과 가장 가까운 일자결과로 기술: ___/___/___(yyyy/mm/dd)

☐ 0: No symptom
☐ 1: No significant disability. Able to carry out all usual activities, despite some symptoms
☐ 2: Slight disability. Able to look after own affairs without assistance, but unable to carry out all previous activities
☐ 3: Moderate disability. Requires some help, but able to walk unassisted
☐ 4: Moderately severe disability. Unable to attend to own bodily needs without assistance, and unable to walk unassisted
☐ 5: Severe disability. Requires constant nursing care and attention, bedridden, incontinent
☐ 6: Dead

NIHSS 총점: ___점 (의무기록부에 기입되어 있을 경우 기입)
* 수술과 가장 가까운 일자결과로 기술: ___/___/___(yyyy/mm/dd)

항목		점수	척도
1. 의식수준	1a.의식수준		☐0 ☐1 ☐2 ☐3
	1b.의식수준: 질문		☐0 ☐1 ☐2
	1c.의식수준: 지시		☐0 ☐1 ☐2
2. 최적의 주시능력			☐0 ☐1 ☐2
3. 시야			☐0 ☐1 ☐2 ☐3
4. 안면마비			☐0 ☐1 ☐2 ☐3
5. 팔의 운동	5a. 좌측 팔		☐0 ☐1 ☐2 ☐3 ☐4 ☐9. 절단, 관절고정술 설명:
	5b. 우측 팔		
6. 다리의 운동	6a. 좌측 다리		☐0 ☐1 ☐2 ☐3 ☐4 ☐9. 절단, 관절고정술 설명:
	6b. 우측 다리		

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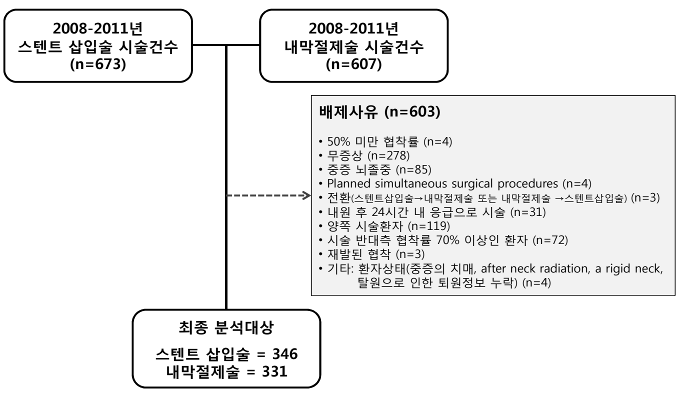
연구방법 (4): 최종 분석 대상자



연구방법 (5): 주요결과변수

1) 일차결과변수 (Primary outcome)		
단기결과 (Peri-procedure)	시술 후 30일 이내	사망/경증 뇌졸중/중증 뇌졸중/심근경색
장기결과 (Post-procedure)	시술 후 2년 이내	사망/경증 뇌졸중/중증 뇌졸중
2) 이차결과변수 (Secondary outcome)		
단기결과 (Peri-procedure)	시술 후 30일 이내	뇌신경마비/ 수술 중 감염/ 출혈관련 합병증
	시술 후 1년 이내	재시술

MEMO

연구방법 (5): 주요결과변수 정의

▶ 뇌졸중 척도에 따른 경증 뇌졸중, 중증 뇌졸중 정의

뇌졸중 척도	경증 뇌졸중	중증 뇌졸중
NIHSS	2점 이상~9점 미만	9점 이상
mRS	2점 이하	2점 초과

자료원: Alberts, 2001; Brott, 2010; 대한뇌졸중학회, 2009

▶ 뇌졸중 척도에 따른 경증 뇌졸중, 중증 뇌졸중 발생환자 정의

경증 뇌졸중 발생환자		중증 뇌졸중 발생환자	
신환	시술 전: 뇌졸중 아님→시술 후: 경증 뇌졸중	신환	시술 전: 뇌졸중 아님→시술 후: 중증 뇌졸중
악화	시술 전: 경증 뇌졸중→시술 후: 경증 뇌졸중 (점수상승)		시술 전: 경증 뇌졸중→시술 후: 중증 뇌졸중 (점수상승)

연구결과 (1): 인구학적 정보

	Total (N=677)		CAS (N=346)		CEA (N=331)		p-value
	n	(%)	n	(%)	n	(%)	
연령[1]							
Mean±SD	68.3±8.3		68.5±8.6		68.2±7.8		0.568
[min, max]	[24, 92]		[24, 92]		[42, 86]		
50세 미만	9 (1.3)		6 (1.7)		3 (0.9)		0.794
50-59세	96 (14.2)		48 (13.9)		48 (14.5)		
60-69세	235 (34.7)		116 (33.5)		119 (36)		
70-79세	298 (44)		154 (44.5)		144 (43.5)		
80세 이상	39 (5.8)		22 (6.4)		17 (5.1)		
70세 미만	340 (50.2)		170 (49.1)		170 (51.4)		0.563
70세 이상	337 (49.8)		176 (50.9)		161 (48.6)		
성별							
남성	570 (84.2)		295 (85.3)		275 (83.1)		0.437
여성	107 (15.8)		51 (14.7)		56 (16.9)		
평균 추적관찰기간[2]							
n	653		337		316		**0.048**
Mean±SD	499.9±246.8		518.4±237.0		480.1±255.8		
협착률							
70% 미만	115 (17.0)		34 (9.8)		81 (24.5)		**<.0001**
70% 이상	562 (83.0)		312 (90.2)		250 (75.5)		
EPD[3] **사용여부**							
유	335 (49.5)		335 (96.8)				
무	11 (1.6)		11 (3.2)				

1) 수술일 기준연령 2) 수술일 기준 마지막 추적관찰일 3) EPD: Embolic protection device

연구결과 (2): 주요결과변수

(단기결과: 30일 추적관찰)

	CAS (N=346)			CEA (N=331)			Absolute Difference for the CAS (95% CI)		P-value
	n	(%)	rate[%][1]	n	(%)	rate[%][1]			
일차결과									
사망	2	(0.58)	[0.59]	1	(0.30)	[0.31]	0.28	(-0.72 to 1.27)	1.000
모든 뇌졸중	17	(4.91)	[4.99]	6	(1.81)	[1.89]	3.10	(0.41 to 5.79)	**0.026**
중증 뇌졸중	7	(2.02)	[2.06]	1	(0.30)	[0.30]	1.72	(0.12 to 3.32)	0.069
경증 뇌졸중	10	(2.89)	[2.94]	5	(1.51)	[1.59]	1.38	(-0.82 to 3.58)	0.256
심근경색	1	(0.29)	[0.30]	0	(0.00)	[0.00]	0.29	(-0.28 to 0.85)	1.000
이차결과									
뇌신경마비	0	(0.00)	[0.00]	12	(3.63)	[3.64]	-3.63	(-5.64 to -1.61)	**<0.001**
일시적	0	(0.00)	[0.00]	10	(3.02)	[3.04]	-3.02	(-4.87 to -1.18)	
영구적	0	(0.00)	[0.00]	2	(0.60)	[0.61]	-0.60	(-1.44 to 0.23)	
재시술[2]									
CAS 또는 CEA	0	(0.00)	[0.00]	0	(0.00)	[0.00]			

1) Estimated by Kaplan-Meier method
2) 재협착으로 인하여 첫 시술부위와 동일한 쪽에 1년 이내 CAS 또는 CEA를 다시 시술받는 경우로 정의

연구결과 (2): 주요결과변수

(단기결과: 30일 추적관찰)

	CAS (N=346)		CEA (N=331)		P-value*
	n	(%)	n	(%)	
이차결과					
합병증[1]	2	(0.58)	4	(1.21)	0.442
수술 중 감염	2	(0.58)	3	(0.91)	
UTI	1	(0.29)	1	(0.30)	
폐렴	1	(0.29)	0	(0.00)	
wound 감염	0	(0.00)	2	(0.60)	
Bleeding events	0	(0.00)	2	(0.60)	
Blood transfusion	0	(0.00)	1	(0.30)	
출혈로 인한 기도폐쇄	0	(0.00)	1	(0.30)	

1) 수술 중 감염 또는 Bleeding events 중복응답 가능

연구결과 (2): 주요결과변수

(장기결과: 2년 추적관찰)

	CAS (N=346)			CEA (N=331)			Absolute Difference for the CAS (95% CI)		P-value
	n	(%)	rate[%][1]	n	(%)	rate[%][1]			
일차결과									
사망	5	(1.45)	[1.57]	1	(0.30)	[0.31]	1.14	(-0.25 to 2.53)	**0.217**
모든 뇌졸중	24	(6.94)	[7.27]	14	(4.23)	[5.05]	2.71	(-0.74 to 6.15)	0.126
증증 뇌졸중	14	(4.05)	[4.46]	6	(1.81)	[2.40]	2.23	(-0.29 to 4.76)	0.086
경증 뇌졸중	11	(3.18)	[3.25]	9	(2.72)	[3.00]	0.46	(-2.09 to 3.01)	0.743
심근경색	1	(0.29)	[0.30]	0	(0.00)	[0.00]	0.29	(-0.28 to 0.85)	1.000
이차결과									
뇌신경마비	0	(0.00)	[0.00]	12	(3.63)	[3.64]	-3.63	(-5.64 to -1.61)	**<.0001**
일시적	0	(0.00)	[0.00]	10	(3.02)	[3.04]	-3.02	(-4.87 to -1.18)	
영구적	0	(0.00)	[0.00]	2	(0.60)	[0.61]	-0.60	(-1.44 to 0.23)	
재시술[2]									
CAS	1	(0.29)	[0.35]	1	(0.30)	[0.44]	-0.01	(-0.83 to 0.81)	1.000
CEA	0	(0.00)	[0.00]	0	(0.00)	[0.00]			

1) Estimated by Kaplan-Meier method
2) 재협착으로 인하여 첫 시술부위와 동일한 쪽에 1년 이내 CAS 또는 CEA를 다시 시술받는 경우로 정의

연구결과 (3): 하위그룹분석

(협착률 70%미만, 단기결과:30일 추적관찰)

	CAS (N=34)			CEA (N=81)			Absolute Difference for the CAS (95% CI)		P-value
	n	(%)	rate[%][1]	n	(%)	rate[%][1]			
일차결과									
사망	0	(0.00)	[0.00]	0	(0.00)	[0.00]			
모든 뇌졸중	2	(5.88)	[5.88]	1	(1.23)	[1.30]	4.65	(-3.62 to 12.91)	0.208
증증 뇌졸중	0	(0.00)	[0.00]	0	(0.00)	[0.00]			
경증 뇌졸중	2	(5.88)	[5.88]	1	(1.23)	[1.30]	4.65	(-3.62 to 12.91)	0.208
심근경색	0	(0.00)	[0.00]	0	(0.00)	[0.00]			
이차결과									
뇌신경마비	0	(0.00)	[0.00]	0	(0.00)	[0.00]			
일시적	0	(0.00)	[0.00]	0	(0.00)	[0.00]			
영구적	0	(0.00)	[0.00]	0	(0.00)	[0.00]			
재시술[2]									
CAS 또는 CEA	0	(0.00)	[0.00]	0	(0.00)	[0.00]			

1) Estimated by Kaplan-Meier method
2) 재협착으로 인하여 첫 시술부위와 동일한 쪽에 1년 이내 CAS 또는 CEA를 다시 시술받는 경우로 정의

MEMO

MEMO

연구결과 (3): 하위그룹분석

(협착률 70%이상, 단기결과: 30일 추적관찰)

	CAS (N=312)			CEA (N=250)			Absolute Difference for the CAS (95% CI)		P-value
	n	(%)	rate[%][1]	n	(%)	rate[%][1]			
일차결과									
사망	2	(0.64)	[0.66]	1	(0.40)	[0.41]	0.24	(-0.94 to 1.42)	1.000
모든 뇌졸중	15	(4.81)	[4.89]	5	(2.00)	[2.08]	2.81	(-0.13 to 5.75)	0.074
중증 뇌졸중	7	(2.24)	[2.29]	1	(0.40)	[0.40]	1.84	(0.02 to 3.66)	0.082
경증 뇌졸중	8	(2.56)	[2.61]	4	(1.60)	[1.68]	0.96	(-1.38 to 3.31)	0.504
심근경색	1	(0.32)	[0.33]	0	(0.00)	[0.00]	0.32	(-0.31 to 0.95)	1.000
이차결과									
뇌신경마비	0	(0.00)	[0.00]	12	(4.80)	[4.82]	-4.80	(-7.45 to -2.15)	<0.001
일시적	0	(0.00)	[0.00]	10	(4.00)	[4.02]	-4.00	(-6.43 to -1.57)	
영구적	0	(0.00)	[0.00]	2	(0.80)	[0.80]	-0.80	(-1.9 to 0.3)	
재시술[2]									
CAS 또는 CEA	0	(0.00)	[0.00]	0	(0.00)	[0.00]			

1) Estimated by Kaplan-Meier method
2) 재협착으로 인하여 첫 시술부위와 동일한 쪽에 1년 이내 CAS 또는 CEA를 다시 시술받는 경우로 정의

연구결과 (3): 하위그룹분석

(협착률 70%미만, 장기결과: 2년 추적관찰)

	CAS (N=34)			CEA (N=81)			Absolute Difference for the CAS (95% CI)		P-value
	n	(%)	rate[%][1]	n	(%)	rate[%][1]			
일차결과									
사망	0	(0.00)	[0.00]	0	(0.00)	[0.00]			
모든 뇌졸중	2	(5.88)	[5.88]	5	(6.17)	[6.98]	-0.29	(-9.78 to 9.2)	1.000
중증 뇌졸중	0	(0.00)	[0.00]	3	(3.70)	[4.29]	-3.70	(-7.82 to 0.41)	0.554
경증 뇌졸중	2	(5.88)	[5.88]	3	(3.70)	[4.12]	2.18	(-6.74 to 11.09)	0.631
심근경색	0	(0.00)	[0.00]	0	(0.00)	[0.00]			
이차결과									
뇌신경마비	0	(0.00)	[0.00]	0	(0.00)	[0.00]			
일시적	0	(0.00)	[0.00]	0	(0.00)	[0.00]			
영구적	0	(0.00)	[0.00]	0	(0.00)	[0.00]			
재시술[2]									
CAS 또는 CEA	0	(0.00)	[0.00]	0	(0.00)	[0.00]			

1) Estimated by Kaplan-Meier method
2) 재협착으로 인하여 첫 시술부위와 동일한 쪽에 1년 이내 CAS 또는 CEA를 다시 시술받는 경우로 정의

연구결과 (3): 하위그룹분석

(협착률 70%이상, 장기결과: 2년 추적관찰)

	CAS (N=312)			CEA (N=250)			Absolute Difference for the CAS (95% CI)		P-value
	n	(%)	rate[%][1]	n	(%)	rate[%][1]			
일차결과									
사망	5	(1.60)	[1.75]	1	(0.40)	[0.41]	1.20	(-0.4 to 2.8)	0.233
모든 뇌졸중	22	(7.05)	[7.45]	9	(3.60)	[4.48]	3.45	(-0.21 to 7.11)	0.075
중증 뇌졸중	14	(4.49)	[4.99]	3	(1.20)	[1.84]	3.29	(0.62 to 5.95)	**0.024**
경증 뇌졸중	9	(2.88)	[2.96]	6	(2.40)	[2.63]	0.48	(-2.17 to 3.14)	0.781
심근경색	1	(0.32)	[0.33]	0	(0.00)	[0.00]	0.32	(-0.31 to 0.95)	1.000
이차결과									
뇌신경마비	0	(0.00)	[0.00]	12	(4.80)	[4.82]	-4.80	(-7.45 to -2.15)	**<0.001**
일시적	0	(0.00)	[0.00]	10	(4.00)	[4.02]	-4.00	(-6.43 to -1.57)	
영구적	0	(0.00)	[0.00]	2	(0.80)	[0.80]	-0.80	(-1.9 to 0.3)	
재시술[2]									
CAS	1	(0.32)	[0.40]	1	(0.40)	[0.59]	-0.08	(-1.08 to 0.92)	1.000
CEA	0	(0.00)	[0.00]	0	(0.00)	[0.00]			

1) Estimated by Kaplan-Meier method
2) 재협착으로 인하여 첫 시술부위와 동일한 쪽에 1년 이내 CAS 또는 CEA를 다시 시술받는 경우로 정의

연구결과 (4): 하위그룹분석

(연령 70세 미만, 단기결과: 30일 추적관찰)

	CAS (N=170)			CEA (N=170)			Absolute Difference for the CAS (95% CI)		P-value
	n	(%)	rate[%][1]	n	(%)	rate[%][1]			
일차결과									
사망	0	(0.00)	[0.00]	1	(0.59)	[0.61]	-0.59	(-1.74 to 0.56)	1.000
모든 뇌졸증	6	(3.53)	[3.56]	3	(1.76)	[1.85]	1.76	(-1.64 to 5.17)	0.502
중증 뇌졸중	1	(0.59)	[0.60]	0	(0.00)	[0.00]	0.59	(-0.56 to 1.74)	1.000
경증 뇌졸중	5	(2.94)	[2.97]	3	(1.76)	[1.85]	1.18	(-2.04 to 4.4)	0.723
심근경색	0	(0.00)	[0.00]	0	(0.00)	[0.00]			
이차결과									
뇌신경마비	0	(0.00)	[0.00]	6	(3.53)	[3.55]	-3.53	(-6.3 to -0.76)	**0.030**
일시적	0	(0.00)	[0.00]	5	(2.94)	[2.96]	-2.94	(-5.48 to -0.4)	
영구적	0	(0.00)	[0.00]	1	(0.59)	[0.59]	-0.59	(-1.74 to 0.56)	
재시술[2]									
CAS 또는 CEA	0	(0.00)	[0.00]	0	(0.00)	[0.00]			

1) Estimated by Kaplan-Meier method
2) 재협착으로 인하여 첫 시술부위와 동일한 쪽에 1년 이내 CAS 또는 CEA를 다시 시술받는 경우로 정의

연구결과 (4): 하위그룹분석

(연령 70세 이상, 단기결과: 30일 추적관찰)

	CAS (N=176)			CEA (N=161)			Absolute Difference for the CAS (95% CI)		P-value
	n	(%)	rate[%][1]	n	(%)	rate[%][1]			
일차결과									
사망	2	(1.14)	[1.17]	0	(0.00)	[0.00]	1.14	(-0.43 to 2.7)	0.500
모든 뇌졸증	11	(6.25)	[6.38]	3	(1.86)	[1.94]	4.39	(0.25 to 8.53)	**0.044**
중증 뇌졸중	6	(3.41)	[3.47]	1	(0.62)	[0.62]	2.79	(-0.15 to 5.73)	0.124
경증 뇌졸중	5	(2.84)	[2.92]	2	(1.24)	[1.32]	1.60	(-1.39 to 4.59)	0.506
심근경색	1	(0.57)	[0.60]	0	(0.00)	[0.00]	0.57	(-0.54 to 1.68)	1.000
이차결과									
뇌신경마비	0	(0.00)	[0.00]	6	(3.73)	[3.73]	-3.73	(-6.65 to -0.8)	**0.011**
일시적	0	(0.00)	[0.00]	5	(3.11)	[3.11]	-3.11	(-5.79 to -0.43)	
영구적	0	(0.00)	[0.00]	1	(0.62)	[0.62]	-0.62	(-1.83 to 0.59)	
재시술[2]									
CAS 또는 CEA	0	(0.00)	[0.00]	0	(0.00)	[0.00]			

1) Estimated by Kaplan-Meier method
2) 재협착으로 인하여 첫 시술부위와 동일한 쪽에 1년 이내 CAS 또는 CEA를 다시 시술받는 경우로 정의

연구결과 (4): 하위그룹분석

(연령 70세 미만, 장기결과: 2년 추적관찰)

	CAS (N=170)			CEA (N=170)			Absolute Difference for the CAS (95% CI)		P-value
	n	(%)	rate[%][1]	n	(%)	rate[%][1]			
일차결과									
사망	0	(0.00)	[0.00]	1	(0.59)	[0.61]	-0.59	(-1.74 to 0.56)	1.000
모든 뇌졸증	7	(4.12)	[4.18]	5	(2.94)	[3.25]	1.18	(-2.74 to 5.1)	0.557
중증 뇌졸중	2	(1.18)	[1.42]	1	(0.59)	[0.69]	0.59	(-1.4 to 2.58)	1.000
경증 뇌졸중	6	(3.53)	[3.58]	5	(2.94)	[3.25]	0.59	(-3.17 to 4.35)	0.759
심근경색	0	(0.00)	[0.00]	0	(0.00)	[0.00]			
이차결과									
뇌신경마비	0	(0.00)	[0.00]	6	(3.53)	[3.55]	-3.53	(-6.3 to -0.76)	**0.030**
일시적	0	(0.00)	[0.00]	5	(2.94)	[2.96]	-2.94	(-5.48 to -0.4)	
영구적	0	(0.00)	[0.00]	1	(0.59)	[0.59]	-0.59	(-1.74 to 0.56)	
재시술[2]									
CAS 또는 CEA	0	(0.00)	[0.00]	0	(0.00)	[0.00]			

1) Estimated by Kaplan-Meier method
2) 재협착으로 인하여 첫 시술부위와 동일한 쪽에 1년 이내 CAS 또는 CEA를 다시 시술받는 경우로 정의

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연구결과 (4): 하위그룹분석

(연령 70세 이상, 장기결과: 2년 추적관찰)

	CAS (N=176)			CEA (N=161)			Absolute Difference for the CAS (95% CI)		P-value
	n	(%)	rate[%][1]	n	(%)	rate[%][1]			
일차결과									
사망	5	(2.84)	[3.16]	0	(0.00)	[0.00]	2.84	(0.39 to 5.3)	0.062
모든 뇌졸중	17	(9.66)	[10.41]	9	(5.59)	[7.14]	4.07	(-1.56 to 9.69)	0.162
중증 뇌졸중	12	(6.82)	[7.51]	5	(3.11)	[4.35]	3.71	(-0.88 to 8.3)	0.120
경증 뇌졸중	5	(2.84)	[2.92]	4	(2.48)	[2.74]	0.36	(-3.08 to 3.79)	0.876
심근경색	1	(0.57)	[0.60]	0	(0.00)	[0.00]	0.57	(-0.54 to 1.68)	1.000
이차결과									
뇌신경마비	0	(0.00)	[0.00]	6	(3.73)	[3.73]	-3.73	(-6.65 to -0.8)	**0.011**
일시적	0	(0.00)	[0.00]	5	(3.11)	[3.11]	-3.11	(-5.79 to -0.43)	
영구적	0	(0.00)	[0.00]	1	(0.62)	[0.62]	-0.62	(-1.83 to 0.59)	
재시술[2]									
CAS	1	(0.57)	[0.74]	1	(0.62)	[0.93]	-0.05	(-1.7 to 1.59)	1.000
CEA	0	(0.00)	[0.00]	0	(0.00)	[0.00]			

1) Estimated by Kaplan-Meier method
2) 재협착으로 인하여 첫 시술부위와 동일한 쪽에 1년 이내 CAS 또는 CEA를 다시 시술받는 경우로 정의

임상적 효과 (1): 선행연구와 비교

F/U 기간	결과	체계적 문헌고찰						후향적 자료 수집			
		CAS			CEA			CAS (n=346)		CEA (n=331)	
		모집단	event	%	모집단	event	%	event	%	event	%
단기 F/U (~30일)	**사망자수**	1,943	26	1.34%	1,938	15	0.77%	2	0.58%	1	0.30%
	모든 뇌졸중	2,621	206	7.86%	2,598	120	4.62%	17	4.91%	6	1.81%
	중증 뇌졸중	2,611	83	3.18%	2,588	57	2.20%	7	2.02%	1	0.30%
	경증 뇌졸중							10	2.89%	5	1.51%
	심근경색	2,555	11	0.43%	2,539	25	0.98%	1	0.29%	0	0.00%
	수술 중 감염							2	0.58%	3	0.91%
	CNP							0	0.00%	12	3.63%
장기 F/U (30일~)	**사망자수**	1,545	142	9.19%	1,519	139	9.15%	3	0.87%	0	0.00%
	모든 뇌졸중	1,502	33	2.20%	1,475	36	2.44%	7	2.02%	8	2.42%
	중증 뇌졸중	615	14	2.28%	607	10	1.65%	6	1.73%	4	1.21%
	경증 뇌졸중							1	0.29%	4	1.21%
	재수술: 후향적 연구			3%			1%	1	0.29%	4	1.21%
	CREST			4%			6.10%				

임상적 효과 (2): 국내선행연구

	연구설계	환자수	주요결과지표	주요결과
함형용 (2011)[1]	후향적 조사 (1999-2010)	CEA: 168 CAS: 66	시술 30일 뇌졸중, 사망, 심근경색, 마비, 혈종	뇌졸중: CEA 1.79%, CAS 6.06% 사망: CEA 0%, CAS 1.52% 두 군간의 통계적 차이 없음
윤우성 (2011)[2]	후향적 조사 (2004-2009)	CEA: 69 CAS: 42	시술 30일 뇌졸중, 혈종, 마비 1년/3년 뇌졸중, 재협착	뇌졸중(30일): CEA 1.45%, CAS 9.52% -Major stroke: CEA 0%, CAS 2.4% 뇌졸중 관해율(3년): CEA 99%, CAS 84%

1) Korean J Cerebrovasc Surg. 2011;13(3):222-9
2) J Korean Surg Soc. 2011;80(4):283-8

고찰

- 내막절제술에서 사망, 뇌졸중의 발생빈도는 낮았고, 시술과 관련된 합병증의 발생빈도는 높게 나타남
- 선행연구들과 결과 발생 경향 유사
  - 선행연구: 스텐트 삽입술에서 사망, 뇌졸중↑, 내막절제술에서 심근경색↑
  - 본 연구: 스텐트 삽입술에서 사망, 뇌졸중, 심근경색↑
- 전반적인 발생률은 낮은 경향
  - 후향적 연구자료수집으로 인한 일부 정보 수집 제한과 왜곡의 가능성
  - 비교효과연구 목적달성을 위해 엄격한 연구대상 선정의 가능성
- 이러한 비교효과연구는 경동맥 내막절제술 및 스텐트 삽입술의 적절한 사용에 대한 근거를 제공할 수 있을 것으로 기대됨

MEMO

국내 경동맥 협착증 환자에서 경동맥 내막절제술과 스텐트삽입술의 비용-효과 분석

신 상 진
한국보건의료연구원

MEMO

연구진행경과

- 연구주제 수요조사(2012)
  - Comparative Effectiveness Research
- 연구주제 선정 (2013. 3)
- 연구과제 수행 (2013. 4 ~ 2014. 6)

연구진

원외연구진		원내연구진(NECA)	
박현선	인하대 의과대학	신상진	경제성평가연구팀 연구위원
전 평	성균관대 의과대학	오성희	경제성평가연구팀 주임연구원
조용필	울산의대 의과대학	유지혜	진료지침협력연구팀 연구원
김병문	연세대 의과대학	이자연	경제성평가연구팀 연구원
김태선	전남대 의과대학	박지정	신개발유망의료기술탐색연구팀 연구원
서상현	연세대 의과대학		

연구배경 (1)

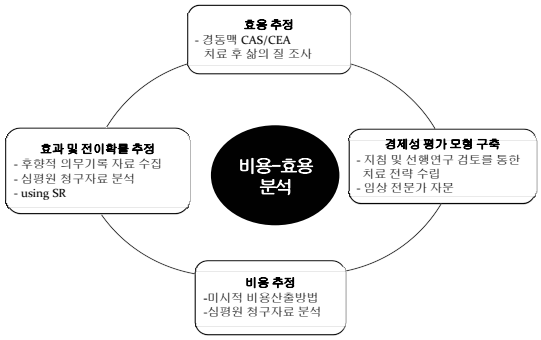
▶ 뇌졸중임상연구센터는 '보건복지부 임상연구센터 지원'으로 외국의 자료들을 정리한 후 국내의 의료환경을 고려하여 '뇌졸중 이차예방: 두개강외 경동맥 협착(개정본), 2011'을 발행함

구분	무증상			유증상	
협착률	50%-59%	60-99%	-50%	50-69%	70-99%
권고사항	금기사항이 없는 경우 **항혈소판제제** 처료권고 (근거수준 IIa, 권고수준 B)	수술관련 합병증 3% 미만 시 -CEA(근거수준 Ia, 권고수준 A) -CAS(근거수준 IIb, 권고수준 B)	**내과적 치료** 우선 권장 (근거수준 Ib, 권고수준 A)	환자의 연령, 성별, 동반질환, 증상의 정도를 고려한**CEA**권고 (근거수준Ib, 권고수준A)	**CEA** 권고 (근거수준 Ib, 권고수준 A) : 수술 전후 뇌졸중 발생률/사망률 6% 미만 의사시행
		수술 고위험군은 **CAS** 권고(근거수준 IIa, 권고수준 B)		**6% 미만의 뇌졸중 발생률/사망률 예측되는 경우 CAS가 CEA의 대체처료로 사용 (근거수준 Ib, 권고수준 A)**	

연구목적

- 경동맥 협착증에서 스텐트 삽입술이 내막절제술의 대체 치료로 사용이 가능한 유증상 경동맥 협착(협착률 50% 이상)을 가진 환자를 대상으로 국내 상황에서 두 시술의 비용-효과성(cost-effectiveness)을 평가함

연구방법 (1): 경제성 평가 수행 전략



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연구방법 (2): 경제성 평가 개요

비용-효용 분석(Cost-utility analysis)	
분석관점	보건의료체계 관점
분석대상	유증상 경동맥 협착증(협착률 50% 이상) 환자
비교대안	경동맥 스텐트 삽입술(CAS) vs. 경동맥 내막절제술(CEA)
분석모형	마콥 모형
분석기간	15년(평생)/ 분석주기 1년
효과지표	질 보정 수명(Quality Adjusted Life Years, QALYs)
할인율	5%

연구방법 (3): 경제성 평가 모형구축

- 마콥모형개발을 위한 치료전략 모식도

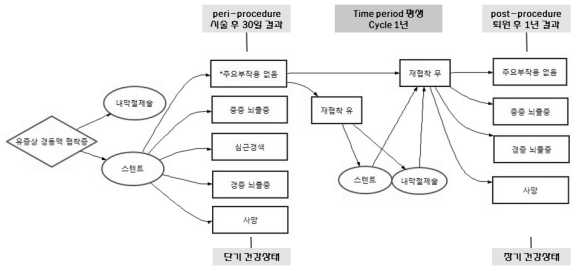

그림. 치료전략 및 주요 합병증 발생 경로 모식도

*자료원: 임상진료지침, RCT, 경제성평가 선행연구

연구방법 (3): 경제성 평가 모형구축

- 마콥모형: 건강상태 정의

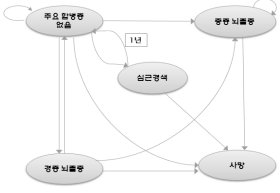

그림. Markov transition diagram

마콥 건강상태	세부정의
주요 합병증 없음 (No major adverse events)	뇌졸중, 심근경색이 아닌 생존 상태
심근경색(Myocardial infarction)	시술 후 30일 이내 심근경색이 발생한 상태
중증 뇌졸중 (Major stroke)	중증 뇌졸중이 발생한 상태 (NIHSS 9점 이상, 치명적 또는 회복 불가능한 뇌졸중(Fatal/disabling stroke), Modified Rankin scale 2점 초과)
경증 뇌졸중 (Minor stroke)	경증 뇌졸중이 악화 또는 발생한 상태 (NIHSS 2점 이상 9점 미만, 회복 가능한 뇌졸중 (Non-disabling stroke), Modified Rankin scale 2점 이하)
사망(Dead)	수술 및 주요합병증 또는 기타원인으로 인한 사망

연구결과 (1): 효과 및 전이확률 추정

- 자료원: 후향적 의무기록 조사(기본분석)

	내막절제술	스텐트 삽입술
30일 결과		
중증 뇌졸중 30일 발생률	0.30%	2.02%
경증 뇌졸중 30일 발생률	1.81%	3.18%
MI 30일 발생률	0.00%	0.29%
CNP 30일 발생률	0.60%	0.00%
30일 사망률	0.30%	0.58%
입원일수(일)	**13.6일**	**8.7일**
1년 결과		
중증 뇌졸중 1년 발생률	1.21%	1.73%
경증 뇌졸중 1년 발생률	1.21%	0.29%
Progress (경증 >중증 뇌졸중)	33.33%	36.36%
재시술률	0.30%	0.29%
MI 발생 후 1년 사망률(저명률)	15.4%	
중증 뇌졸중 발생 후 1년 사망률(저명률)	24.0%	
기타원인으로 인한 1년 일반사망률		
65 - 69세	1.33%	
70 - 74세	2.29%	
75 - 79세	4.05%	
80 - 84세	7.02%	
기타		
재시술시 중증 뇌졸중 위험 가중치	**1.15 (CREST)**	

연구결과 (2): 삶의 질 조사

- 건강상태별 효용값(Utility index)조사방법

✓ **시술 후 주요 합병증 없는 상태**
- 측정도구 : Time Trade Off, EQ-5D-3L
- 대상: 일반인 대상(N=400) 면접조사

✓ **심근경색이 발생한 상태**
- 측정도구 : EQ-5D-3L
- 제5기 국민건강영양조사(2012)

✓ **경증/중증 뇌졸중이 발생한 상태**
- 측정도구 : EQ-5D-3L
- 서울대병원 뇌졸중 레지스트리 등록 환자 대상 (N=465)

연구결과 (2): 삶의 질 조사

- 건강상태별 효용값 산출결과

건강상태	평균	표준편차	삶의 질 측정 도구
주요 합병증 없음			
초기시술 후	0.79	0.10	설문조사(TTO)
재시술 후	0.61	0.13	
심근경색	0.77	0.05	국건영(EQ-5D-3L)
경증 뇌졸중	0.79	0.06	병원자료(EQ-5D-3L)
중증 뇌졸중	0.41	0.48	

▪ 모형에 적용한 경동맥 협착증 환자의 시술 후 건강상태에 따른 효용값
주요 합병증 없음≥ 경증 뇌졸중> 심근경색> 재시술 후 주요 합병증 없음> 중증 뇌졸중

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연구결과 (3): 비용 추정

- **시술 관련 비용**
  - 항목: 시술 및 처치, 검사, 마취, 약제비, 입원비, 간병비
  - 방법: 미시적 비용 산출
  - 자료원: 건강보험요양급여비용수가, 치료재료 급여·비급여목록, 임상 전문가 자문
- **합병증으로 인한 비용**
  - 항목: 뇌졸중, 심근경색, 뇌신경마비
  - 방법: 포괄적 비용 산출
  - 자료원: 심평원 청구자료(원시자료), KDRG

연구결과 (3): 비용 추정

- **시술 후 건강상태 별 소요비용 (시술~2년)**

시술 관련 비용[1]				합병증으로 인한 비용[2]			
				건강상태	시술~30일	~1년 30일	~2년 30일
CEA	항목별		총	주요 합병증 없음	1,516,720	292,798	226,560
	초기 시술	3,667,827	4,478,110	심근경색	6,129,894	3,591,540	292,798
	재시술	3,375,597		경증 뇌졸중	3,010,052	292,798	226,560
	간병비용	810,283		중증 뇌졸중	4,006,551	9,994,058	7,593,266
CAS	항목별		총	주요 합병증 없음	1,180,574	292,798	226,560
	초기 시술	6,028,481	6,545,581	심근경색	6,129,894	3,591,540	292,798
	재시술	5,523,043		경증 뇌졸중	3,010,052	292,798	226,560
	간병비용	517,100		중증 뇌졸중	4,006,551	9,994,058	7,593,266

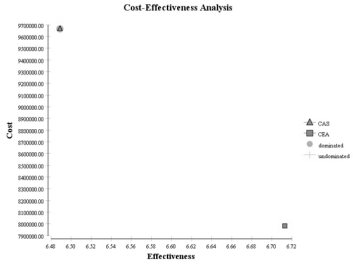
▪ **총 소요비용**
- **스텐트삽입술 > 내막절제술**
  >> **스텐트 삽입술과 내막절제술의 시술비가 약 240만원 차이**
- **시술 후 건강상태에 따라, 중증 뇌졸중 > 심근경색 > 경증뇌졸중 > 주요 합병증 없음**
- **초기 시술 > 재시술**

연구결과 (4): 비용-효용 분석

기본분석 (5개 병원 후향적 의무기록자료)

전략	비용	점증적 비용	QALYs	점증적 QALYs	ICER	순화폐가치	(CEA-CAS)NMB
CEA	7,982,934	-	6.71			196,785,870	
CAS	9,665,264	1,682,329	6.49	-0.22	dominated	188,268,652	-8,517,218

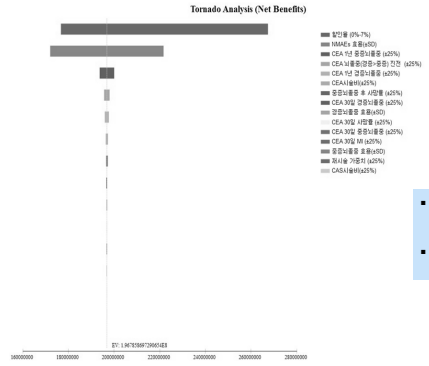
ICER: Incremental Cost Effectiveness Ratio



경동맥 내막절제술이 스텐트 삽입술보다 비용은 적게 들고 효과는 좋은 대안

연구결과 (5): 비용-효용 분석

- 일원민감도 분석

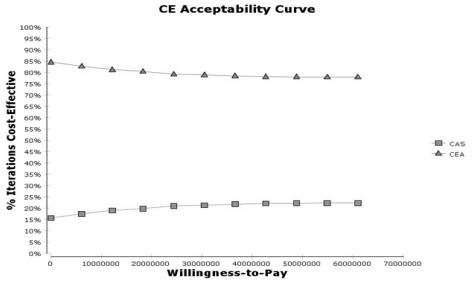


▪ 할인율(0-7%), 주요부작용이 없는 상태 효용값 등이 가장 민감하게 반응

▪ 기본분석 결과를 바꿀만한 영향을 주는 민감한 변수는 없음

연구결과 (6): 비용-효용 분석

- 확률적 민감도 분석



▪ 비용 효과성 판단기준(지불용의액)이 3,050만원(안정훈 등, 2013)일 때, 내막절제술이 비용효과적일 확률이 78.8%, 스텐트 삽입술이 비용효과적일 확률이 21.2%

연구결과 (7): 비용-효용 분석

- 다원민감도 분석

하위군	비교대안	비용 (원)	△비용 (원)	QALYs (년)	△QALYs (년)	ICER	NMB (원)	INMB (원)
체계적 문헌고찰	CEA	8,285,366		6.57			191,988,047	
	CAS	9,934,216	1,648,850	6.35	-0.22	dominated	183,681,018	-8,307,029
CREST	CEA	7,923,646		6.61			193,772,343	
	CAS	9,688,860	1,765,214	6.44	-0.17	dominated	186,875,102	-6,897,241

△: 스텐트 삽입술-내막절제술 ; QALYs=Quality Adjusted Life years; ICER=Incremental Cost Effectiveness Ratio (점증적 비용-효과비); NMB=Net Monetary Benefit (순화폐가치); INMB=Incremental Net Monetary Benefit (점증적 순화폐가치)

▪ 본 연구의 체계적 문헌고찰과 가장 대표적인 RCT인 CREST를 기반으로 한 분석 결과, 기본분석결과와 유사함. 단, CREST를 기반으로 분석한 결과, 두 시술의 비용-효과성 격차가 좀혀짐

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연구결과 (8): 비용-효용 분석

- 하위군 분석

하위군		비교대안	비용 (원)	△비용 (원)	QALYs (년)	▲QALYs (년)	ICER	NMB (원)	INMB (원)
연령	연령 70세 이상[1]	CEA	8,128,139		5.72			166,362,200	
		CAS	11,471,997	3,343,857	5.19	-0.53	dominated	146,737,162	-19,625,039
	연령 70세 미만[1]	CEA	6,872,148		6.90			203,648,317	
		CAS	6,422,374	-449,774	7.17	0.27	dominant	212,244,075	8,595,758
경동맥 협착증 중증도	협착률 70% 이상	CEA	6,785,726		6.90			203,822,401	
		CAS	10,055,295	3,269,569	6.40	-0.50	dominated	185,299,741	-18,522,660
	협착률 70% 미만[2]	CEA	11,841,962		6.01			171,590,860	
		CAS	6,521,852	-5,320,110	7.15	1.14	dominant	211,582,776	39,991,916
시술자 숙련도	시술자의 숙련도 높은 군[3]	CEA	7,983,453		6.71			196,785,327	
		CAS	9,885,900	1,902,447	6.47	-0.24	dominated	187,590,881	-9,194,446

1) 연령에 따른 분석시, 기대여명에 따라 분석기간 변경(70세 이상 분석기간 13년)하였으며, 임상적 효과 및 효용 변경, 2) CAS 34건, CEA 81건, 3) 시술자의 숙련도가 낮은 1개 병원 제외; △: 스텐트 삽입술-내막절제술 ; QALYs=Quality Adjusted Life years; ICER=Incremental Cost Effectiveness Ratio (점증적 비용-효과비); NMB=Net Monetary Benefit (순화폐가치); INMB=Incremental Net Monetary Benefit (점증적 순화폐가치)

연구결과 (8): 비용-효용 분석

▪ 70세 미만

➢ CREST, SPACE 등의 임상연구에 따르면, 70세를 기준으로 젊을수록 스텐트 삽입술의 효과가 좋고, 나이가 많을수록 내막절제술의 임상적 효과가 좋게 나타남(Mantese 등, 2010; Voeks 등, 2011)

➢ 연령이 70세 미만인 유증상 경동맥 협착증 환자를 대상으로 경제성 평가를 수행한 결과, **스텐트 삽입술**의 비용이 내막절제술에 비해 약 45만원 적게 소요되었으며, 효과(QALYs)는 0.27만큼 더 좋은 **우등(dominant) 대안**으로 분석됨

▪ 협착률 70% 미만

➢ 국내외 지침에 따르면 중증 경동맥 협착증 환자는 협착률 70%를 기준으로 구분

➢ 협착률이 70% 미만인 군에서도 경동맥 스텐트 삽입술이 비용은 적게 들고 효과는 좋게 나타났음. 단, **분석 대상자 수가 적다는 제한점**이 있음

경제성 평가: 선행연구

참고문헌	대상 및 비교군	방법 및 결과	자료원
Janssen (2008)	**•협착률 70% 이상 유증상 경동맥 협착증** •CAS vs. CEA	•비용효용분석 /분석기간: 10년 **•스텐트 삽입술이 비용은 높고 효과는 낮아서 dominated**	ECST, 코크란 SR
Young (2010)	**• 70세 이상 유증상 경동맥 협착증** •CAS vs. CEA	•비용효용분석 /분석기간: 평생 **•스텐트 삽입술이 비용은 높고 효과는 낮아서 dominated**	CREST, SAPPHIRE, EVA-3S 및 SR
Mahoney (2011)	**• 수술 고위험군** 중 **유증상 경동맥 협착증** •CAS(EPD) vs. CEA	•비용효용분석 /분석기간: 평생 •무증상 경동맥 협착증에서는 스텐트 삽입술이 비용효과적 (ICER=$6,555)임 **•스텐트 삽입술은 비용이 높으며, 효과도 높음(0.03 QALYs) >비용효과적이지 않음 (ICER= $204,229)**	SAPPHIRE
Vilain (2012)	**•유.무증상 경동맥 협착증** •CAS vs. CEA	•비용효용분석 /분석기간: 10년 **•내막절제술보다 스텐트 삽입술이 평균 환자 당 $524 더 많이 지출되며, QALYs는 0.008만큼 낮아서 dominated**	CREST

고찰

- 국내외 진료지침에서 50% 이상 유증상 경동맥 협착증에서 스텐트 삽입술이 내막절제술의 대체치료가 될 수 있다고 권고하고 있으나,
- 국외 유증상 경동맥 협착증 환자에서 스텐트 삽입술과 내막 절제술을 비교한 다수의 경제성 평가연구에서 스텐트 삽입술은 비용-효과적이지 않거나 오히려 비용이 높은데 효과는 낮은 것으로 나타남
- 국내 현황을 반영한 본 경제성 평가에서도 유증상 경동맥 협착(50% 이상)을 가진 환자에서 내막 절제술과 스텐트 삽입술이 효과는 유사한 반면 내막 절제술이 비용이 낮은 더 경제적인 대안이라는 일관된 결과를 보임

MEMO

Which one is better: CEA

김 태 선
전남대 병원 신경외과

MEMO

High surgical risk for CEA

- **SAPPHIRE (Stenting and Agnioplasty with Protection in Patients at High Risk for Endarterectomy) trial**
- **Youman 5th text-book**
- **2010년 CREST (Carotid Revascularization Endarterectomy versus Stenting Trial)**
- **2010년 ICSS (International Carotid Stenting Study)**

1. SAPPHIRE (Stenting and Agnioplasty with Protection in Patients at High Risk for Endarterectomy) trial

Clinically significant cardiac disease
(CHF, abnormal stress test, need for open heart surgery)
Severe pulmonary disease
Contralateral CA occlusion
Contralateral laryngeal nerve palsy
Previous radical neck dissection or radiotherapy of the neck
Recurrent stenosis after CEA
Age > 80 years

TABLE 351-4 -- High-risk Features for Carotid Endarterectomy (Youman 6th edition)

Anatomic	Comorbid Conditions
Restenosis after endarterectomy	Unstable angina
Bilateral stenosis	Left ventricular ejection fraction <30%
Contralateral carotid occlusion or laryngeal nerve palsy	Congestive heart failure
Previous radiation therapy or surgery on the neck	Planned coronary artery bypass or valve replacement
Lesion inaccessible by surgery	Renal failure
Neck immobility	Chronic obstructive pulmonary disease
Tracheostomy or tracheostoma	Coronary artery disease with ≥70% stenosis
Severe intracranial stenosis	Planned peripheral vascular surgery
	Myocardial infarction within 6 weeks of the procedure
	Age older than 80 years

ICSS (International Carotid Stenting Study)

Lancet. 2010 Mar 20;375(9719):985-97

Patients with **recently symptomatic** carotid artery stenosis

	120 –day rate of stroke, death or procedural MI (p=0.006)	Risk of any stroke	All-case death	Procedural MI	Cranial nerve palsy	Hematoma
CAS (n=855)	8.5%	65	19	3 (all fatal)	1	31
CEA (n=858)	5.2%	35	7	4 (non-fatal)	45	50

Conclusion : Carotid endarterectomy should remain the treatment of choice for patients suitable for surgery.

CREST (Carotid Revascularization Endarterectomy versus Stenting Trial)

Stroke. 2010 Oct;41(10 Suppl):

Symptomatic and asymptomatic patients

Primary end point: any stroke, myocardial infarction, or death during the peri-procedural period and ipsilateral stroke thereafter, up to 4 years.

	Primary end point (p=0.51)	Stroke (p=0.02)	MI (p=0.032)	Age
CAS	7.2%	4.1%	1.1%	< 70 years
CEA	6.8%	2.3%	2.3%	> 70 years

Conclusion : CAS and CEA had similar short- and longer-term outcomes. During the peri-procedural period, there was higher risk of stroke with CAS and higher risk of myocardial infarction with CEA

MEMO

MEMO

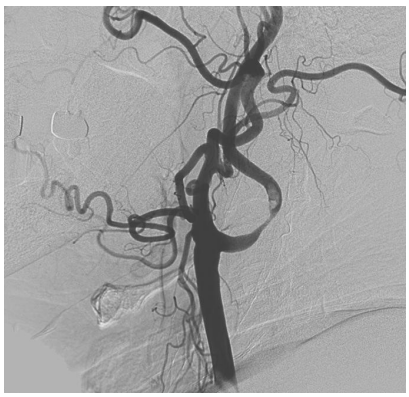
◆ Age and Sex limitation ?

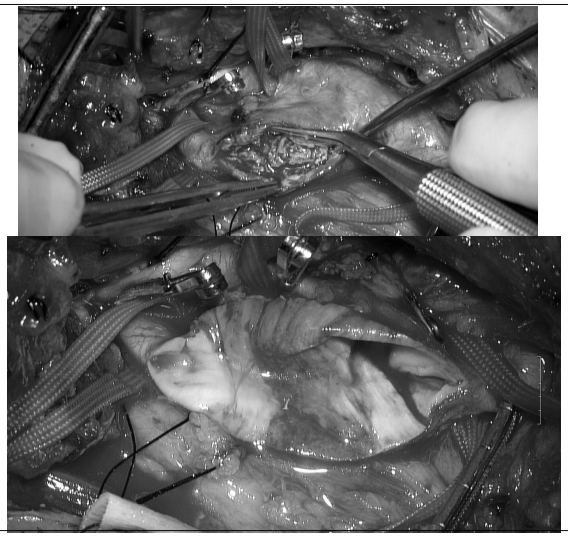
Surgical indication (Youman 6th edition)

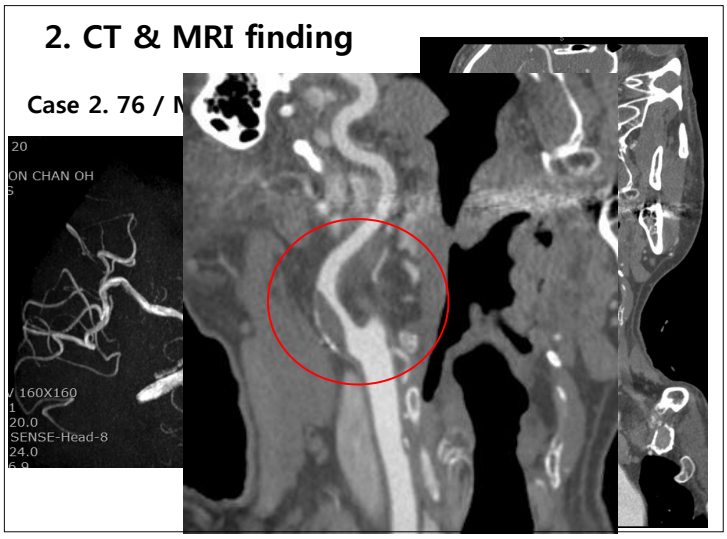
- **Symptomatic carotid stenosis (2 weeks of the last symptom)**
  70% to 99% in patients with **a life expectancy of at least 5 years**
  + **perioperative risk is expected to be less than 6%**
- **Symptomatic carotid stenosis**
  50% to 69% with the **same caveats as above**
  women : no benefit from CEA and should probably be managed medically
- **Asymptomatic patients**
  between the ages of **40 and 79 years with greater than 60% stenosis**
  : no significant comorbid conditions that might increase their perioperative risk or result in a **life expectancy of less than 5 years**
  The overall perioperative risk should be less than 3%
  The benefit **to women is controversial**

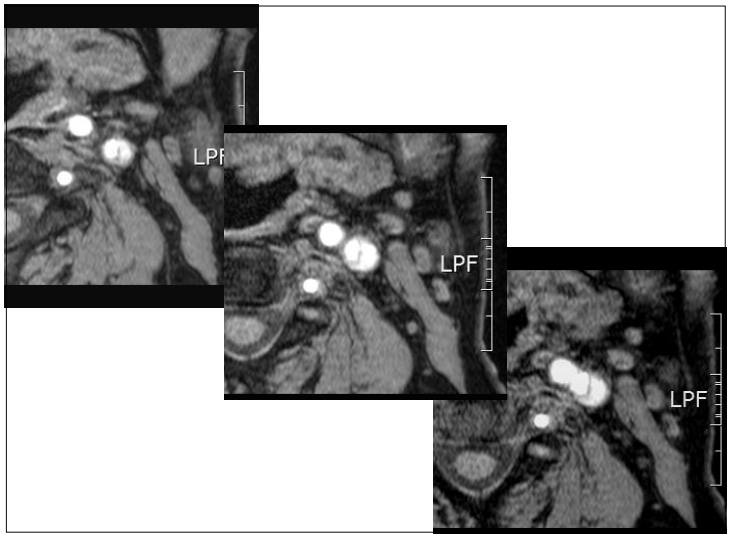
Better Indications for CEA

1. Acute thrombus or severe calcification






2. CT & MRI finding
Case 2. 76 / M
20
ON CHAN OH
160X160
20.0
SENSE-Head-8
24.0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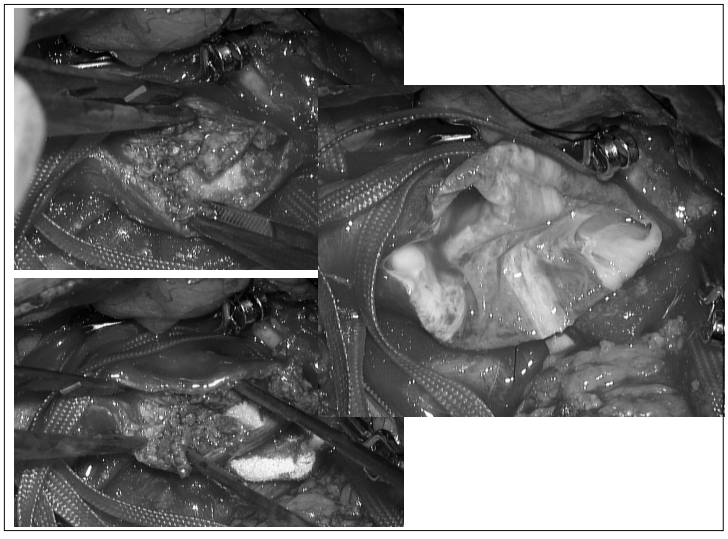
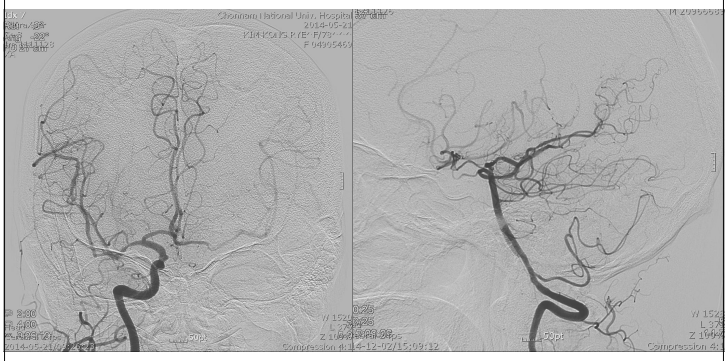


MEMO

MEMO

Better Indications for CEA

3. No angiographic risk



Better Indications for CEA

- No medical complication
- Difficult to guide ICA
- Hyper-perfusion (?)

◆ **Clinical results : Postoperative complications within 30 days after CEA (1998 – 2014)**

	No of patients (N=421)	
Good recovery	417 (99.04%)	
Severe disabled	2 (0.48%)	1 : Pos-CEA major cerebral infarction 1 : Hyper-perfusion
Death	2 (0.48%)	Wound hematoma
Any stroke	11 (2.5%)	

1. How to prevent and treat wound hematoma

- **Change the pattern of suture**
  : Inter-locking suture
  : Muscle을 suture 위에 놓고 한번 더 tie
  → 시간적으로 3-5분 정도 더 소요되지만
  : 타코콤 (TachoComb)
- **Postoperative BP control and check the PT and APTT**
- **Aggressive treatment of wound hematoma**

2. How to prevent Post-CEA cerebral infarction

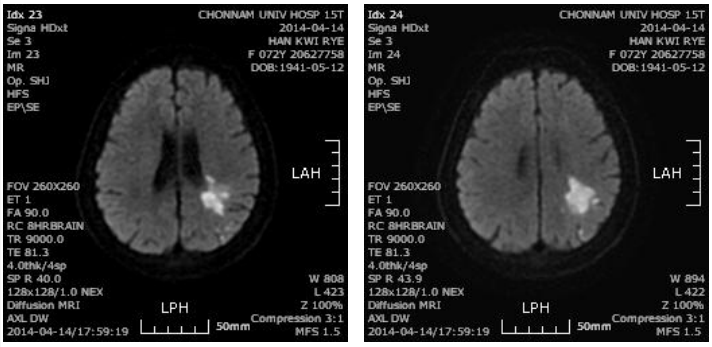
1. **Internal Shunt**
2. **Trapping of ICA**
3. **Contra-lateral ICA occlusion**
   → STENT

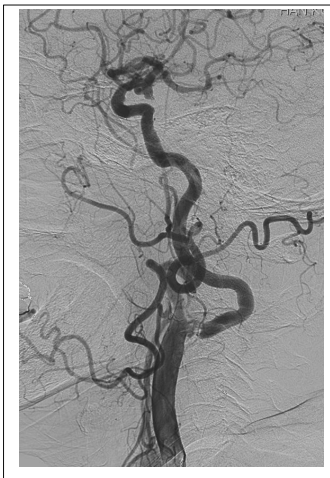
3. Hyper-perfusion syndrome

MEMO

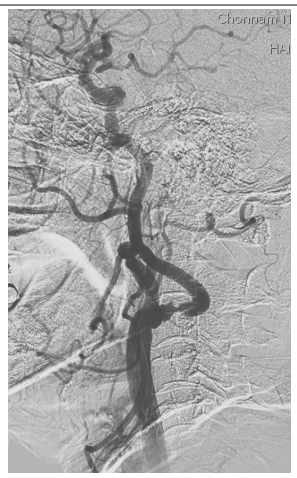
MEMO

73/F, left side infarction, both ICA stenosis



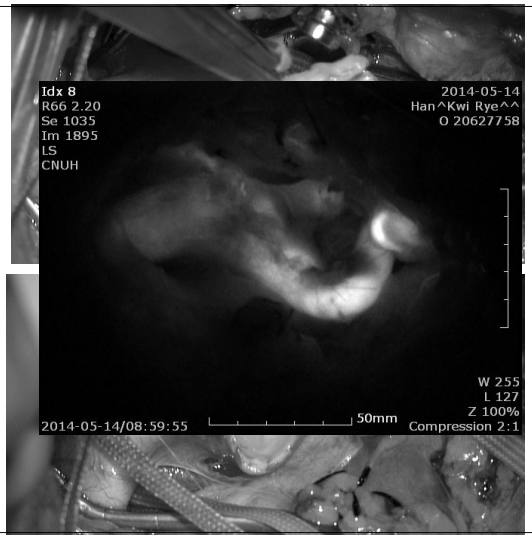


Right ICA

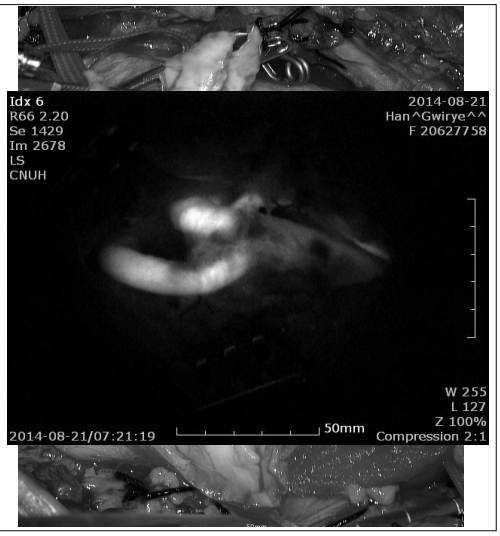


Left ICA

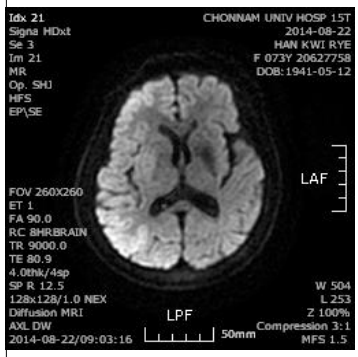
Symptomatic Left CEA : 2014-05-14

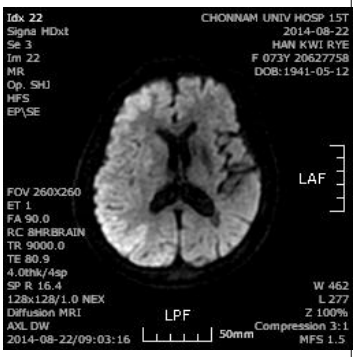


Asymptomatic Right CEA : 2014-08-21

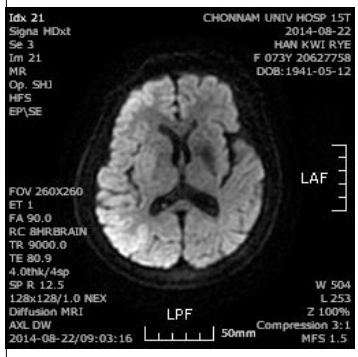


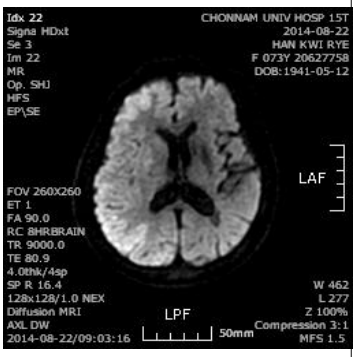
Left hemiparesis / Stuporous M/S





Left hemiparesis / Stuporous M/S





MEMO

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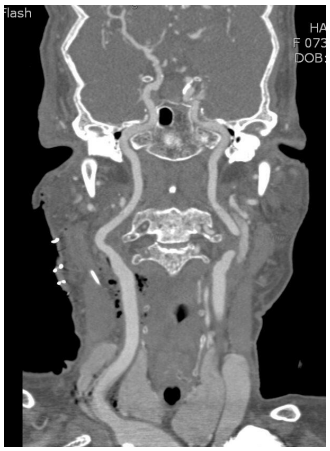
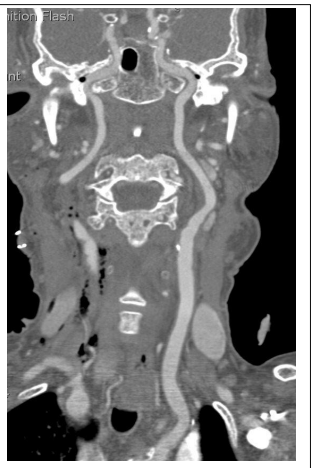
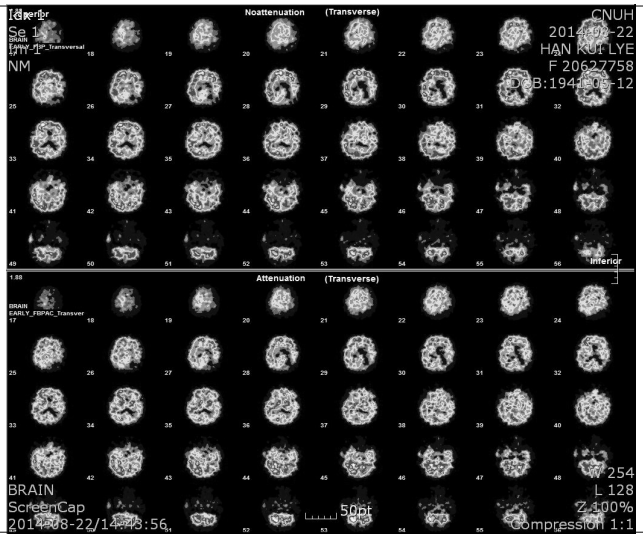
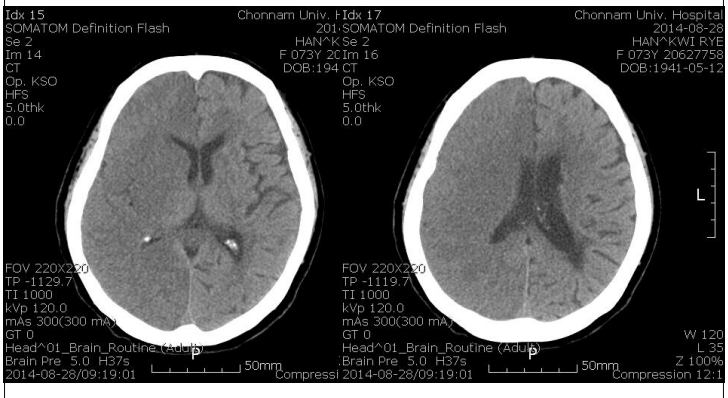


Right

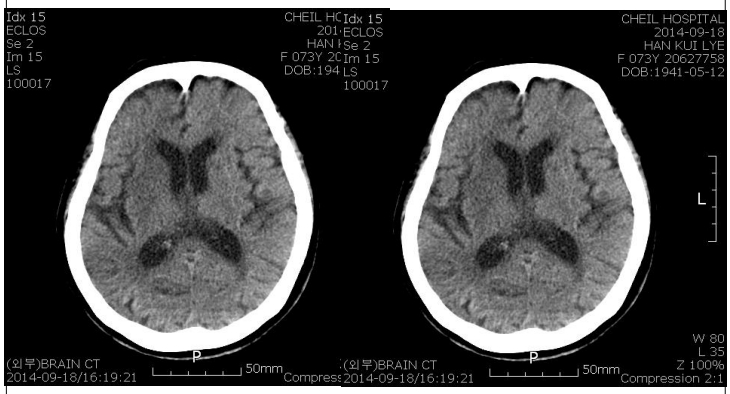


Left





One week later



One month later

◆ **Clinical results : Postoperative complications within 30 days after CEA (1998 – 2014)**

	No of patients (N=421)	
Good recovery	417 (99.04%)	**0 % !!!**
Severe disabled	2 (0.48%)	1 : Pos-CEA major infarction 1 : Hyper-perfusion
Death	2 (0.48%)	Wound hematoma
Any stroke	11 (2.5%)	

MEMO

Near perfect protection of distal thromboembolism is possible with the proximal balloon occlusion embolic protection system for CAS without consideration of intolerance

Seung-Hoon You, M.D.
Department of Neurosurgery, Gangneung Asan Hospital, College of Medicine, Ulsan University, Gangneung, Korea

Purpose: The purpose of this study is to assess the factors which influence intolerance in the use of proximal balloon occlusion embolic protection device for carotid artery stenting (CAS).

Materials and Methods: From sep. 2012 to Aug. 2015, 81 consecutive patients (mean age: 69.5±7.1 years) with proximal internal cerebral artery (pICA) stenosis were treated with proximal balloon occlusion embolic protection system. Only except the first case, all of them were treated with IV injection of pentobarbital (100mg ~ 250mg) before the CCA ballooning. Forty-five patients presented with acute infarction and the other 36 patients with transient ischemic attacks (TIAs). Mean stenosis rate was 83.7±8.2% (70.0~99.0%). Thirty-two patients had the lesion at the left side (39.5%). Contralateral ICA occlusion or severe stenosis was observed in 30 patients (37.0%). Clinical data, angiographic findings, occlusion time, and procedure-related complications were analyzed according to the presence or absence of intolerance.

Results: All cases were treated successfully and no peri-procedural untoward events such as thromboembolic infarction occurred. All 3 steps i.e. prestent ballooning, stenting, and poststent ballooning were done in 77 of 81patients (95.1%) and, in the other 4 patients, only stenting and poststent ballooning were done. Mean occlusion time is 6 minutes and 1 second (3′ 40″~10′ 30″). Intolerance was observed only in 6 patients (7.4%) at the end of the procedure, and the mean duration of intolerance is 21.7±20.4 seconds (10~60 seconds). There was no statistically significant difference between two dividing groups according to the presence or absence of intolerance in the comparison of clinical and angiographic factors including age, sex, presenting symptoms, stenosis rate, lesion side, and the presence of contralateral occlusion or flow compromising stenosis. However, occlusion time is longer in the group of intolerance than the other (7′32″±1′32″ vs. 5′54″±1′38″, p=0.021), and all of them were in the early stage of learning curve.

Conclusion: The proximal balloon occlusion embolic protection system seems to be useful in CAS, and the intolerance does not appeared to be necessary restrictive consideration even when the patient does not have eligible collateral systems in conventional terms.

Scientific Session III

Video Session : How to Manage the Intraoperative Rupture of Aneurysms

좌장 : 권병덕(울산대), 조재훈(대구가톨릭대)

1. During the clipping 김종수(성균관대), 정영균(인제대)

2. During the endovascular treatment 장철훈(영남대), 강현승(서울대)

During clipping

Jong Soo Kim
Samsung Medical Center Sungkyunkwan University School of medicine

Intraoperative rupture

- **Incidence**
  - 5-20 %
- **Timing of Premature rupture**
  - Dissection
  - Clip application
  - Induction or initial exposure (rare)

MEMO

Risk factors of intraoperative rupture

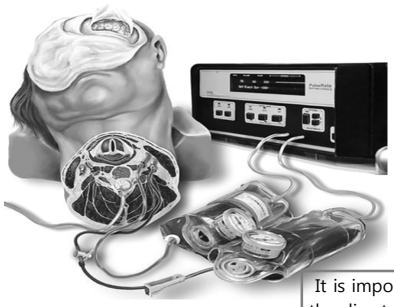
- **Ruptured Aneurysm**
  - **Lower initial Hunt and Hess grade**
- **Location and morphology of aneurysm**
  - **PICA, A-com P-com** *Neurosurgery Mar 2005*
- **Surgical technique and experience**
  - **Blunt dissection**
  - **Early attempted aneurysm occlusion**
    - **Before adequate neck exposure**

MEMO

Intraoperative rupture

- Outcome of intraoperative rupture
  - Jeopardize a patient's outcome
    - Increasing poor outcome around 2 fold
      Stroke 39:1501-1506, 2008
  - Could improved by increased experience
- Decreased exposure of trainee
  - Trend toward minimal or non-invasive treatment
  - Inadequate exposure
    - Could Increase the risk of rupture
    - Could decrease outcome of intraoperative rupture

Live cadavers for training



It is important to increase
the direct or indirect experience

J Neurosurg July 3, 2015

How to manage?

- Should not!
  - Blind clip placement
- Visualization !
  - Large Frazier suction
  - Temporary clipping : either afferent and efferent
    - Burst surpression with thiopental or propopol :
    - With prolonged temporary clipping
      - » Should not exceed 20 min
  - Adenosine : temporary cardiac standstill
  - Attempt bleeding control
    - Bipolar coagulation.
    - Local pressure with cottonoid (could be dangerous)

Intraoperative cerebral aneurysm Rupture (IAR)

정 영 균
인제대학교 부산백병원 신경외과

MEMO

Intraoperative Misadventures: Complication Avoidance and Management in Aneurysm Surgery

Daniel L. Barrow, MD

There are no secrets to success. It is the result of preparation, hard work, and learning from failure.
Colin Powell

- Adequate exposure, sharp dissection, proximal control, and use of temporary clips
- Avoiding intraoperative rupture
- The bleeing was controlled with large-bore suctions and a small piece of cotton placed gently over the aneurysm for absorbency
- Adenosine
- If the tear at the neck of the aneurysm
  - Microsuturing the defect
  - Placing a Sundt clip graft
  - Trapping the aneurysm with or without a bypass

A small piece of cotton to tamponade and bolster the Repair of a tear at the neck of an aneurysm.

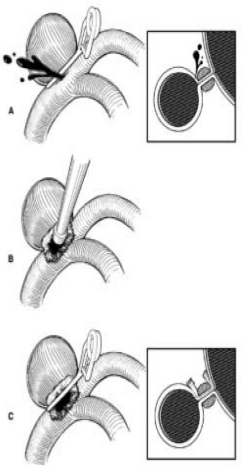
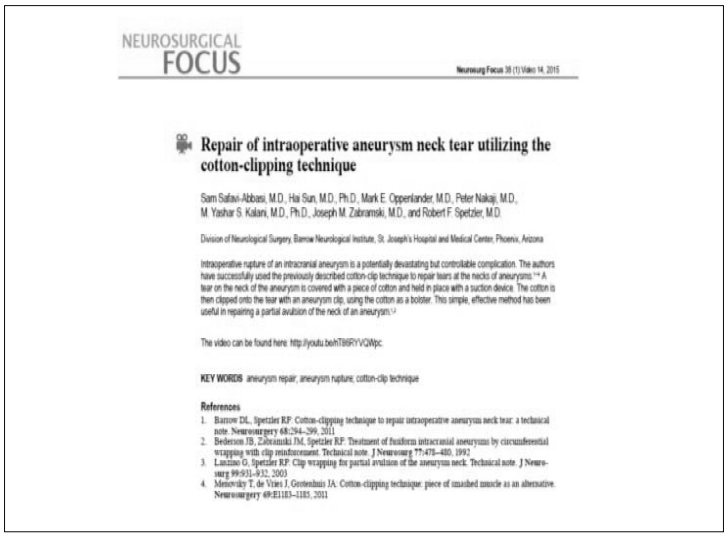


FIGURE 21. Artist's illustration of technique for repairing a tear at the neck of an aneurysm. A, a tear at the neck cannot be clipped without compromising the parent artery. B, a small piece of free cotton is placed over the tear to halt the bleeding. C, the clip is placed just above the tear, clipping the cotton as a bolster to tamponade the tear. From Barrow and Spetzler.[8]

MEMO



NEUROSURGICAL FOCUS

Neurosurg Focus 38 (1):Video 14, 2015

Repair of intraoperative aneurysm neck tear utilizing the cotton-clipping technique

Sam Safavi-Abbasi, M.D., Hai Sun, M.D., Ph.D., Mark E. Oppenlander, M.D., Peter Nakaji, M.D., M. Yashar S. Kalani, M.D., Ph.D., Joseph M. Zabramski, M.D., and Robert F. Spetzler, M.D.

Division of Neurological Surgery, Barrow Neurological Institute, St. Joseph's Hospital and Medical Center, Phoenix, Arizona

Intraoperative rupture of an intracranial aneurysm is a potentially devastating but controllable complication. The authors have successfully used the previously described cotton-clip technique to repair tears at the necks of aneurysms.[1-4] A tear on the neck of the aneurysm is covered with a piece of cotton and held in place with a suction device. The cotton is then clipped onto the tear with an aneurysm clip, using the cotton as a bolster. This simple, effective method has been useful in repairing a partial avulsion of the neck of an aneurysm.[1,2]

The video can be found here: http://youtu.be/hTB6RYVQWpc.

KEY WORDS aneurysm repair; aneurysm rupture; cotton-clip technique

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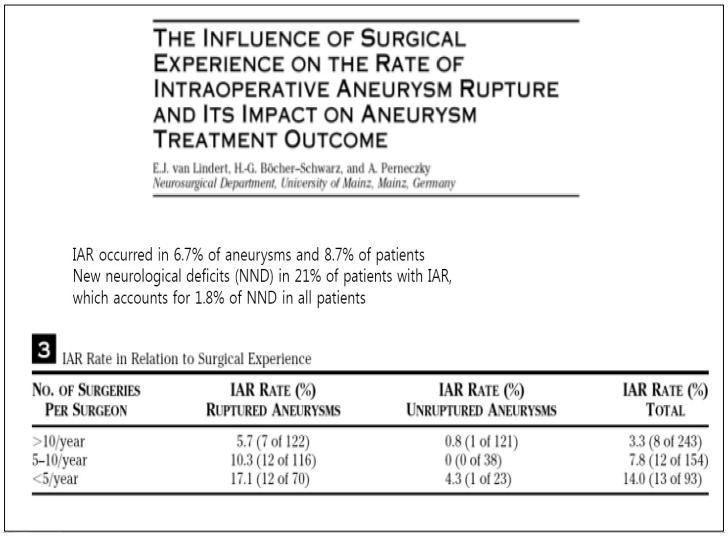
4. Menovsky T, de Vries J, Grotenhuis JA: Cotton-clipping technique: piece of smashed muscle as an alternative. Neurosurgery 69:E1183–1185, 2011



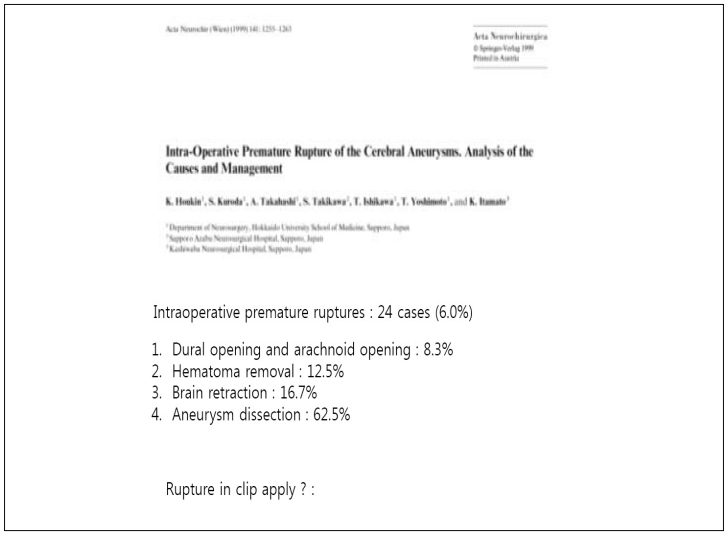
THE INFLUENCE OF SURGICAL EXPERIENCE ON THE RATE OF INTRAOPERATIVE ANEURYSM RUPTURE AND ITS IMPACT ON ANEURYSM TREATMENT OUTCOME

E.J. van Lindert, H.-G. Böcher-Schwarz, and A. Perneczky
Neurosurgical Department, University of Mainz, Mainz, Germany

IAR occurred in 6.7% of aneurysms and 8.7% of patients
New neurological deficits (NND) in 21% of patients with IAR,
which accounts for 1.8% of NND in all patients

3 IAR Rate in Relation to Surgical Experience

No. of Surgeries Per Surgeon	IAR Rate (%) Ruptured Aneurysms	IAR Rate (%) Unruptured Aneurysms	IAR Rate (%) Total
>10/year	5.7 (7 of 122)	0.8 (1 of 121)	3.3 (8 of 243)
5–10/year	10.3 (12 of 116)	0 (0 of 38)	7.8 (12 of 154)
<5/year	17.1 (12 of 70)	4.3 (1 of 23)	14.0 (13 of 93)



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Intra-Operative Premature Rupture of the Cerebral Aneurysms. Analysis of the Causes and Management

K. Houkin[1], S. Kuroda[1], A. Takahashi[1], S. Takikawa[2], T. Ishikawa[3], T. Yoshimoto[1], and K. Itamato[1]

[1] Department of Neurosurgery, Hokkaido University School of Medicine, Sapporo, Japan
[2] Sapporo Azabu Neurosurgical Hospital, Sapporo, Japan
[3] Kushiwaba Neurosurgical Hospital, Sapporo, Japan

Intraoperative premature ruptures : 24 cases (6.0%)

1. Dural opening and arachnoid opening : 8.3%
2. Hematoma removal : 12.5%
3. Brain retraction : 16.7%
4. Aneurysm dissection : 62.5%

Rupture in clip apply ? :

Predictors and Outcomes of Intraprocedural Rupture in Patients Treated for Ruptured Intracranial Aneurysms

The CARAT Study

Lucas Elijovich, MD; Randall T. Higashida, MD; Michael T. Lawton, MD; Gary Duckwiler, MD; Steven Giannotta, MD; S. Claiborne Johnston, MD, PhD; for The Cerebral Aneurysm Rerupture After Treatment (CARAT) Investigators*

2008 Stroke

IPR intraprocedural rupture

Data from International Subarachnoid Hemorrhage Trial
: Coiling : 5.4%
Clipping : 19%

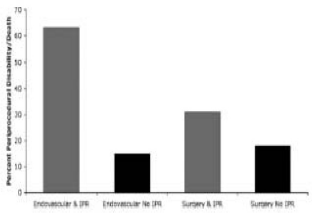
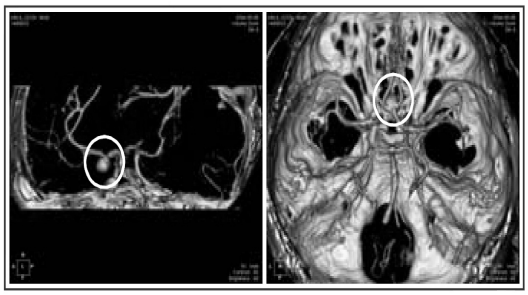
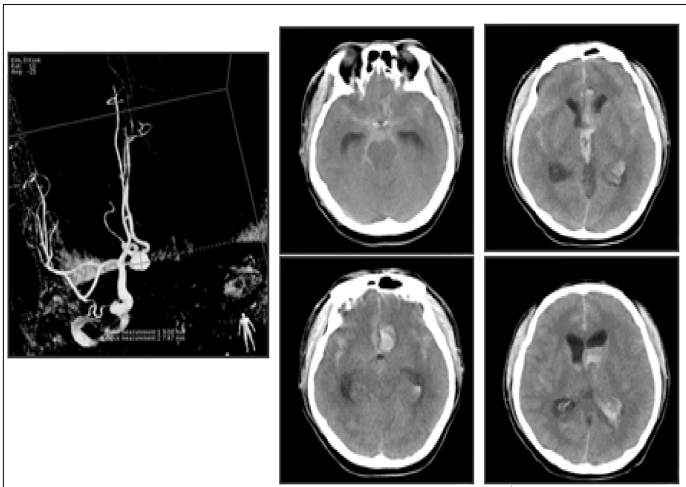


Figure 1. Risk of periprocedural death/disability by occurrence of IPR and by treatment type. The risk of periprocedural disability/death in the endovascular group with and without IPR (63% versus 15%, $P<0.001$). Risk of periprocedural disability/death in the surgical group with and without IPR (31% versus 18%, $P=0.001$).

- Kim 0 0
- 40 years male
- Op. at 4hrs after 2nd attack
- Intraop. premature 3rd rupture after dural opening
- Rt. A-com Aneurysm

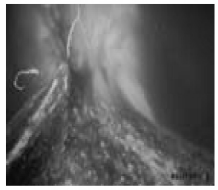




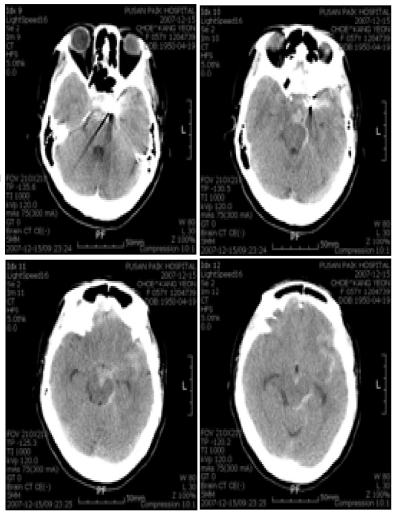
Brain CT after 2nd attack

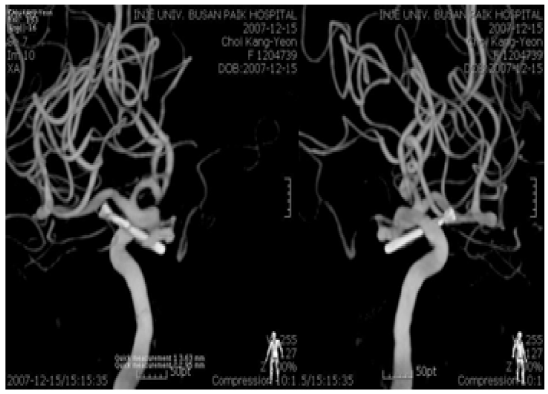
MEMO

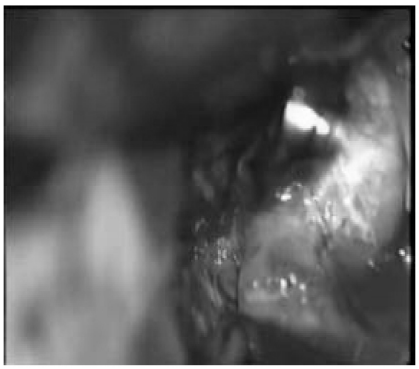
MEMO

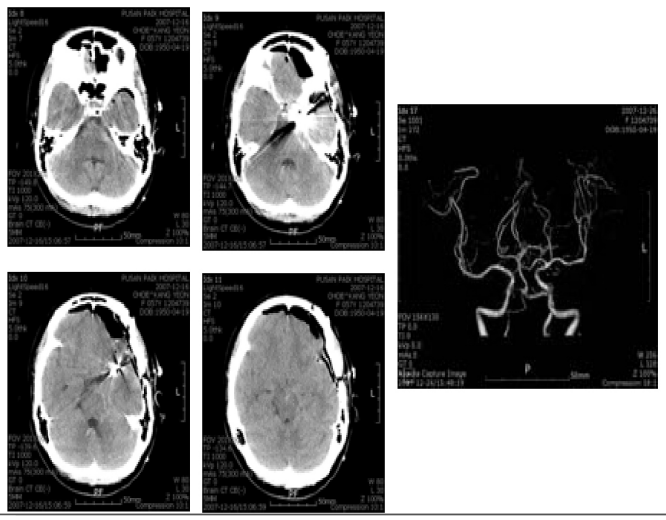


Case
57 year-old age woman
Headache
13 years ago, a ruptured P-com Artery aneurysm op.
Hunt-Hess grade II
Fisher grade II









Conclusions

- Avoid !
- My own strategy ! Inferior directed A-com, lateral projected P-com aneurysm etc
- No retraction, sharp dissection after temporay clip in perianeurysmal dissection
- Clip selection
- 2 large bore suckers with small cottons
- Temporary proximal control < Temporary trapping
- Endure and face to fear
- Think perforators

MEMO

During the Endovascular Treatment

장 철 훈, 김 종 훈
영남의대 신경외과

MEMO

Incidence and Risk factors

Frequency

- A meta-analysis of 17 reports found a significant difference in the frequency of perforations
  - Ruptured : 4.1%
  - Unruptured : 0.5% ($p < 0.001$)
- Occur in 2% to 8% of patients

Risk factors

- Small aneurysm
- Ruptured aneurysm
- Blebs or Pseudoaneurysm
- Balloons or Stents
- Local anesthesia
- Operator experience

Avoidance of IOR

- Extra caution when treating smaller aneurysm
- Minimize anterograde force on the microcatheter & microwire
- Tighten the rotatory hemostatic valve around the microcatheter when doing guide catheter angiograms
- Avoid excessive(?) packing

Management of IOR

- The first sign of recognition
  : An abrupt rise in blood pressure
- ***Calm down !!***
- Resist the impulse to pull back on the perforating device
- Reverse heparin with protamine
- Continous deployment of coils till no hemorrhage

Management of IOR

- If the microcatheter has perforated the aneurysm wall, a coil can be partially deployed into the subarachnoid space first, then the microcatheter can be pulled back slightly until the tip of microcatheter is inside the aneurysm again, and the remaining portion of the coil can be deployed within the aneurysm

Management of IOR

- 2nd(double) microcatheter technique or Balloon catheter
- Occasionally, the tear in the aneurysm may extend into the parent vessel.
  In this situation, coil-occlusion of the parent vessel may be the only way to stop the hemorrhage
- Once the aneurysm is secured, EVD may be necessary

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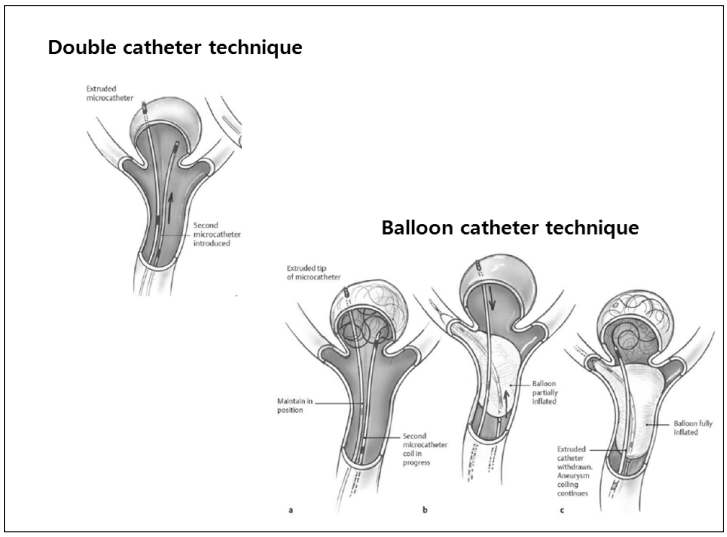

Conclusion

- Early & Adequate recognition
- Calm down & Trust your technique
- Never pull back the perforating devices
- Double microcatheter or balloon assisted technique
- Fix it at angioroom

During the endovascular treatment

강 현 승
서울대

During the period between September 1988 to July 2015, there were 81(2.0%) procedural bleeding among 4451 endovascular treatment sessions (3512 patients with 4144 aneurysms) in a single institution.

Among the 81 aneurysms, there were 40 unruptured aneurysms (including 2 aneurysms presenting with cranial nerve palsies), 2 previously ruptured aneurysms, and 39 acutely ruptured aneurysms (Hunt-Hess grade I to III in 31, grade IV to V in 8).

Glasgow outcome scale scores were 1 (death) in 3 (4%), 3 (severe disability) in 6 (7%), 4 (moderate disability) in 4 (5%), and 5 (good recovery) in 64 (79%); no outcome data in the other 4 patients.

Technical details related to causes of procedural bleeding and management will be presented.

Scientific Session IV

대한뇌혈관내수술학회 - 대한뇌혈관외과학회 합동연수강좌

Update in the Management of Acute Ischemic Stroke (AIS)

좌장 : 허필우(가톨릭대), 권오기(서울대)

1. What is right? What is wrong? BP management- AIS and hemorrhagic transformation
장인복(한 림 대)
2. Current role of antiplatelet therapy in secondary prevention of stroke
조준성(단 국 대)
3. Current status of mechanical thrombectomy 임용철(아 주 대)
4. Role of embolectomy/bypass surgery in AIS 박익성(가톨릭대)

What is right? What is wrong? BP management- AIS and hemorrhagic transformation

CHANG IN BOK
Department of Neurosurgery Institute of Neuroscience Hallym University Medical Center

Blood pressure in AIS

- BP levels are commonly elevated during the first 24 hours after the onset of stroke symptoms
  - 80% : SBP>160 mm Hg and DBP> 90 mm Hg
- Fall spontaneously in the subsequent 10 to 14 days.
- Cerebral autoregulation is impaired after an acute stroke
- Cerebral blood flow is believed to be very sensitive to changes in systemic BP.
- Debate :
  - elevation of BP after acute stroke may be of benefit in terms of increasing cerebral blood flow in the ischemic areas of brain.
  - elevated BP can increase the risk of cerebral edema and hemorrhagic transformation of the infarct.

Blood pressure in AIS

- A total of 60–80% of patients present with hypertension on admission for acute stroke.
- Both hypertension and hypotension during the acute phase of ischemic stroke are associated with death and disability.
- Current guidelines recommend treating
  - SBP>greater than 220
  - SBP> 185 in candidates for thrombolysis in AIS
  - SBP>180 in acute hemorrhagic stroke.
- There are little data to guide the choice of antihypertensive agent in acute stroke, but agents that are short acting and titratable are preferred.

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Lowering BP is dangerous

- Hypertension and its treatment in the NINDS rt-PA stroke trial

  (stoke 29:1504-1509, 1998)
  - postrandomization antihypertensive therapy was associated with less favorable

    outcomes for the tPA patients who were hypertensive
- Blood pressure and clinical outcomes in the international Stroke trial

  (Stroke 33:1315-1320, 2002)
  - early death increased by 17.9% for every 10 mm Hg below 150 mm Hg (P<0.0001)
  - U-shaped curve

Blood Pressure and Clinical Outcomes in the International Stroke Trial

Jo Leonardi-Bee, MSc; Philip M.W. Bath, FRCP; Stephen J. Phillips, FRCPC; Peter A.G. Sandercock, FRCP; for the IST Collaborative Group

Background and Purpose—Among patients with acute stroke, high blood pressure is often associated with poor outcome, although the reason is unclear. We analyzed data from the International Stroke Trial (IST) to explore the relationship between systolic blood pressure (SBP), subsequent clinical events over the next 2 weeks, and functional outcome at 6 months in patients with acute stroke.

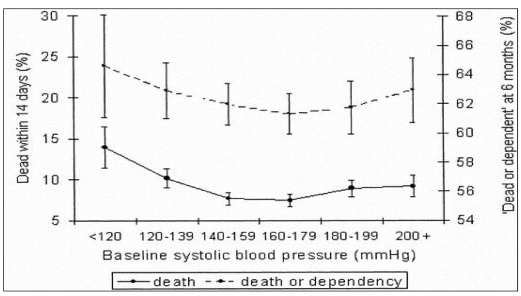
Methods—We included in the analysis 17 398 patients from IST with confirmed ischemic stroke. A single measurement of SBP was made immediately before randomization. Clinical events within 14 days of randomization were recorded: recurrent ischemic stroke, symptomatic intracranial hemorrhage, death resulting from presumed cerebral edema, fatal coronary heart disease, and death. Survival and dependency were assessed at 6 months. Outcomes were adjusted for age, sex, clinical stroke syndrome, time to randomization, consciousness level, atrial fibrillation, and treatment allocation (aspirin, unfractionated heparin, both, or neither).

Results—A U-shaped relationship was found between baseline SBP and both early death and late death or dependency: early death increased by 17.9% for every 10 mm Hg below 150 mm Hg ($P<0.0001$) and by 3.8% for every 10 mm Hg above 150 mm Hg ($P=0.016$). The rate of recurrent ischemic stroke within 14 days increased by 4.2% for every 10–mm Hg increase in SBP ($P=0.023$); this association was present in both fatal and nonfatal recurrence. Death resulting from presumed cerebral edema was independently associated with high SBP ($P=0.004$). No relationship between symptomatic intracranial hemorrhage and SBP was seen. Low SBP was associated with a severe clinical stroke (total anterior circulation syndrome) and an excess of deaths from coronary heart disease ($P=0.002$).

Conclusions—Both high blood pressure and low blood pressure were independent prognostic factors for poor outcome, relationships that appear to be mediated in part by increased rates of early recurrence and death resulting from presumed cerebral edema in patients with high blood pressure and increased coronary heart disease events in those with low blood pressure. The occurrence of symptomatic intracranial hemorrhage within 14 days was independent of SBP. (***Stroke.*** **2002;33:1315-1320.)**

Key Words: blood pressure ■ brain edema ■ hemorrhage ■ recurrence ■ stroke, ischemic

U shaped curve



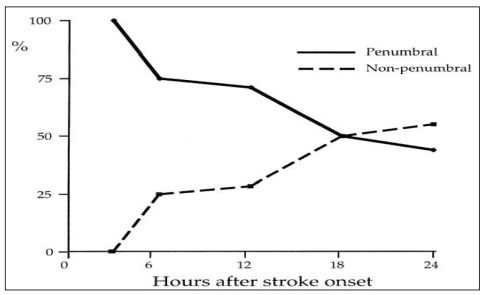
- Every 10mmHg ↑in SBP above 150, death at 14 days increased by 3.8%,
- Every 10mmHg ↓below 150, death at 14 days and disability at 6 months increased by 17.9 and 3.6%, respectively

(Stroke 33:1315-1320, 2002)

Lowering BP is dangerous

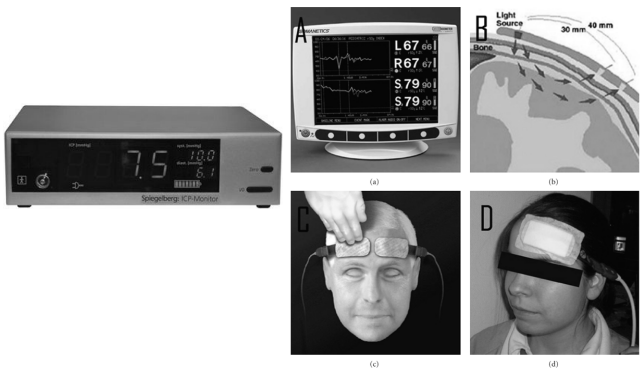
- Detrimental effect of blood pressure reduction in the first 24 hours of acute stroke onset (Neurology 61:1047- ,2003)
  - degree of systolic blood pressure reduction in the first 24 hours (OR = 1.89 per 10% decrease; 95% CI = 1.02 to 3.52; p = 0.047)
- Should hypertension be treated after acute stroke? A randomized controlled trial using SPECT (Arch Neurol 50:855 ,1993)
  - BP dropped >16% of the baseline value on any 24 hours in the first 3 days -> impairs cerebral perfusion regardless of drug used
  - Hypertensive ischemic stroke patients with a moderate elevation of BP in the first few days may not require antihypertensive therapy

What's the limit for infarction



Salvageable tissue at risk even out to 12 – 24 hours
Not easy to measure it in the individual patients
(Stroke 33:1315-1320, 2002)

Invasive tissue monitoring



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LOWERING BP IS NOT DANGEROUS

Effect of Blood Pressure During the Acute Period of Ischemic Stroke on Stroke Outcome

A Tertiary Analysis of the GAIN International Trial

Stella Aslanyan, MD; Franz Fazekas, MD; Christopher J. Weir, PhD; Susanna Horner, MD; Kennedy R. Lees, MD, FRCP; for the GAIN International Steering Committee and Investigators

Background and Purpose—The effects of blood pressure (BP) and its fluctuations during the acute phase on the clinical course of ischemic stroke are incompletely understood. We tested the hypotheses that baseline mean arterial BP [MAP=(2×diastolic BP+systolic BP)/3], weighted average MAP, and an increase or decrease of >30% from baseline MAP are independently associated with stroke outcome.

Methods—We studied the 1455 patients with ischemic stroke in the Glycine Antagonist (Gavestinel) in Neuroprotection (GAIN) International Trial. BP management was at the discretion of investigators and was measured at 0, 0.5, 4, 12, 12.25, 60, and 60.25 hours. Outcome was assessed by mortality, Barthel Index (dead or 0 to 55 versus 60 to 90 versus ≥95), National Institutes of Health Stroke Scale (NIHSS) score (dead or ≥2), and Rankin Scale (dead or ≥2). Cox proportional-hazards and stepwise logistic regression modeling corrected for demography, medical history, stroke severity, and clinical subtype.

Results—Elevated weighted average MAP was associated with poor outcome assessed by mortality at 3 months (hazard ratio, 1.16; 1.06 to 1.27 per 10 mm Hg), NIHSS score (odds ratio [OR] 1.14; 95% confidence interval [CI], 1.01 to 1.28), and Barthel Index at 1 month (OR, 1.12; 95% CI, 1.03 to 1.23). A 30% increase from baseline MAP was associated with poor outcome assessed by NIHSS score and Barthel Index at 1 and 3 months and by Rankin score at 1 month (OR, 2.01; 95% CI, 1.16 to 3.49 to OR, 3.03; 95% CI, 1.30 to 7.02).

Conclusions—Baseline MAP was not associated with poor ischemic stroke outcome. However, variables describing the course of BP over the first 2.5 days have a marked and independent relationship with 1- and 3-month outcome. **(*Stroke*. 2003;34:2420-2425.)**

Key Words: blood pressure ■ outcome ■ stroke, ischemic

- 1445 Pts
- Baseline MAP was not associated with poor ischemic stroke outcome.

Acute BP change in AIS

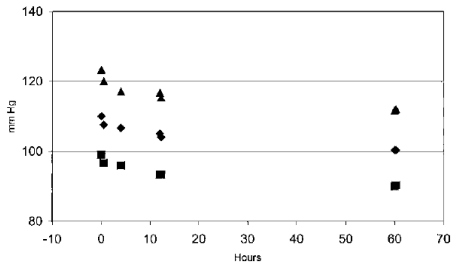


Figure 1. Quartiles of MAP over time. ■, Lower quartile; ◆, median; ▲, upper quartile.

(*Stroke* 2003;34:2420-2425.)

BP and outcome in AIS

TABLE 2. Statistically Significant Associations Between Primary Outcomes and BP Variables

		30% Increase From Baseline MAP		Weighted Average MAP	
Outcome	Time	OR (95% CI)	*P*	OR (95% CI)*	*P*
Mortality, HR	3 mo		>0.05	1.16 (1.06–1.27)	>0.01
Barthel Index (dead or 0–55 vs	7 d		>0.05		>0.05
60–90 vs ≥95)	1 mo	2.01 (1.16–3.49)	0.01	1.12 (1.03–1.23)	0.01
	3 mo	2.39 (1.42–4.03)	>0.01		>0.05
NIHSS score (dead or ≥2)	7 d		>0.05		>0.05
	1 mo	2.74 (1.11–6.73)	0.03	1.14 (1.01–1.28)	0.03
	3 mo	2.87 (1.33–6.20)	0.01		>0.05
Rankin Scale score (dead or ≥2)	1 mo	3.03 (1.30–7.02)	0.01		>0.05
	3 mo		>0.05		>0.05

*Per additional 10 mm Hg.

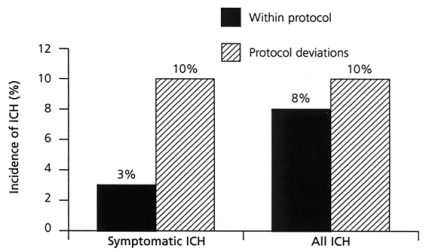
Table 4. Minor Protocol Deviation Frequency and Adverse Event Rates in the Connecticut Cohort*

Deviations	Frequency	In-Hospital Mortality	Serious Extracranial Hemorrhage	Intracranial Hemorrhage
Blood pressure not monitored per recommendations	50 (79)	14/50 (28)	6/50 (12)	8/50 (16)
Stroke diagnosis not made by stroke expert	13 (21)	5/13 (38)	2/13 (15)	2/13 (15)
Edema, shift, or herniation on admission brain CT image	6 (10)	1/6 (17)	0	2/6 (33)
Antithrombotic, anticoagulant, or antiplatelet aggregating medication within 24 h of tPA dose	6 (10)	2/6 (33)	1/6 (17)	0
Head CT image not read by radiologist or neurologist	5 (8)	0	0	0
Improving symptom course	3 (5)	1/3 (33)	1/3 (33)	0
Major surgery within preceding 14 d	1 (2)	1/1 (100)	0	0
Streptokinase as thrombolytic agent	0	...	...	...
Minor neurological deficit	0	...	...	...
Blood glucose level, <50 mg/dL or >400 mg/dL†	0	...	...	...
Gastrointestinal or urinary tract bleeding within preceding 21 d	0	...	...	...
Recent myocardial infarction	0	...	...	...
Facility not capable of treating bleeding complications and blood pressure management	0	...	...	...

*Data are given as number (percentage) of events. Cohort and abbreviations are explained in the first footnote to Table 1.
†To convert to millimoles per liter, multiply by 0.0555.

Arch Intern Med. 2002;162(17):1994-2001

Community Hospital Use of t-PA and Incidence of ICH



Am Fam Physician. 1999 May 15;59(10):2828-2834.

MEMO

MEMO

The ACCESS Study

Evaluation of Acute Candesartan Cilexetil Therapy in Stroke Survivors

Joachim Schrader, MD; Stephan Lüders, MD; Anke Kulschewski, MD; Jürgen Berger, PhD; Walter Zidek, MD; Johannes Treib, MD; Karl Einhäupl, MD; Hans Christoph Diener, MD; Peter Dominiak, MD; on behalf of the ACCESS Study Group

Background and Purpose—The Acute Candesartan Cilexetil Therapy in Stroke Survivors (ACCESS) study was designed to assess the safety of modest blood pressure reduction by candesartan cilexetil in the early treatment of stroke. The study was also designed to provide an estimate of the number of cases required to perform a larger phase III efficacy study.

Methods—Five hundred patients were recruited in a prospective, double-blind, placebo-controlled, randomized, multicenter phase II study.

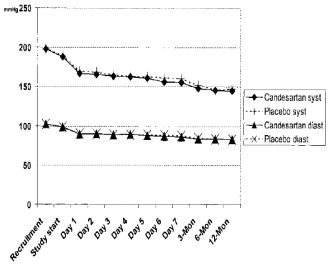
Results—This safety trial was stopped prematurely when 342 patients (339 valid) had been randomized because of an imbalance in end points. Demographic data, cardiovascular risk factors, and blood pressure on admission, on study onset, and within the whole study period were not significantly different between the 2 groups. However, the cumulative 12-month mortality and the number of vascular events differed significantly in favor of the candesartan cilexetil group (odds ratio, 0.475; 95% CI, 0.252 to 0.895). There were no significant differences in concomitant medication and in number or type of side effects.

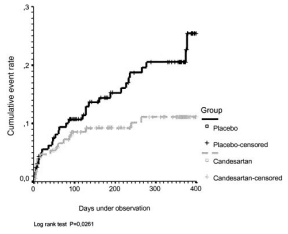
Conclusions—Although the mechanisms by which angiotensin type 1 (AT_1) receptor blockade affects cardiovascular morbidity and mortality are still unresolved, the present study shows that early neurohumoral inhibition has similar beneficial effects in cerebral and in myocardial ischemia. The fact that no cardiovascular or cerebrovascular event occurred as a result of hypotension is of significant clinical importance. When there is need for or no contraindication against early antihypertensive therapy, candesartan cilexetil is a safe therapeutic option according to the ACCESS results. **(*Stroke*. 2003;34:1699-1703.)**

Key Words: antihypertensive therapy ■ benzimidazoles ■ blood pressure ■ stroke, acute

- 342 Pts with AIS
- Candesartan (AT1 recepter blockade) 4-16mg
- Early stopped due to overwhelming efficacy

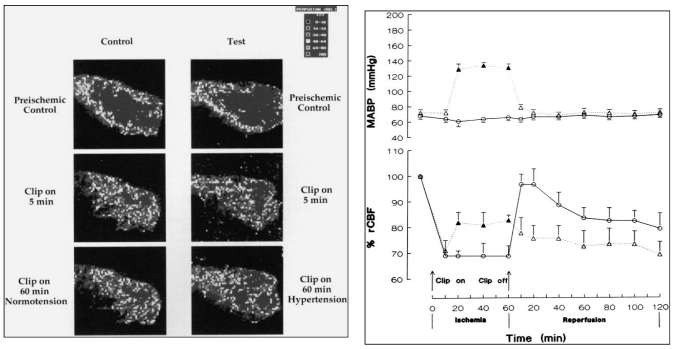
BP & Cumulative event rate in ACCESS





BENEFIT OF RAISING BP IN AIS

Effect on rCBF by induced hypertension



Neurosurgery. 1998;42(3):617-24;

Effects of Induced Hypertension on Intracranial Pressure and Flow Velocities of the Middle Cerebral Arteries in Patients With Large Hemispheric Stroke

Stefan Schwarz, MD; Dimitrios Georgiadis, MD; Alfred Aschoff, MD; Stefan Schwab, MD

Background and Purpose—Our aim was to prospectively evaluate the effects of induced arterial hypertension in patients with large ischemic stroke.

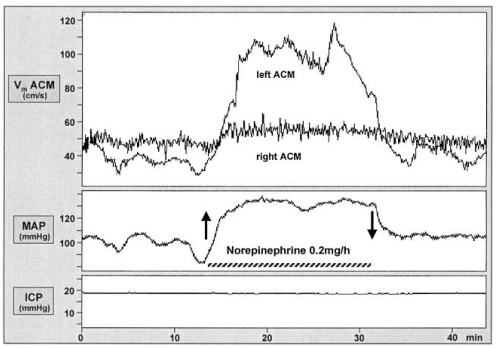
Methods—A total of 47 monitoring sessions in 19 patients with acute, complete, or subtotal middle cerebral artery (MCA) territory stroke were performed. Intracranial pressure (ICP) was monitored using a parenchymal catheter. Mean arterial blood pressure (MAP), ICP, and peak mean flow velocity of the middle cerebral arteries (V_mMCA) were continuously recorded. Patients with acute ICP crises were excluded. After obtaining baseline values, MAP was raised by an infusion of norepinephrine to reach an MAP increase of at least 10 mm Hg. After MAP had reached a peak plateau level, the norepinephrine infusion was stopped.

Results—Baseline MAP was 83.6±1.6 mm Hg and rose to 108.9±2.0 mm Hg after infusion of norepinephrine. ICP slightly increased from 11.6±0.9 mm Hg to 11.8±0.9 mm Hg (P<0.05). Cerebral perfusion pressure rose from baseline 72.2±2 mm Hg to 97±1 mm Hg (P<0.0001). V_mMCA was already higher on the affected side during baseline measurements. At maximum MAP levels, V_mMCA rose by 25.5±5.5 cm/s on the affected side and by 8.6±1.6cm/s on the contralateral side.

Conclusions—In patients with large hemispheric stroke without an acute ICP crisis, induced hypertension enhances cerebral perfusion pressure and augments the V_mMCA(s), more so on the affected side. The ICP slightly increases; however, this is probably not clinically significant. **(*Stroke*. 2002;33:998-1004.)**

Key Words: blood flow velocity ■ cerebral perfusion pressure ■ hypertension ■ intracranial pressure ■ norepinephrine ■ stroke

ICP, MAP & VmMCA in AIS
(Lt MCA infarction)



(*Stroke. 2002;33:998-1004.*)

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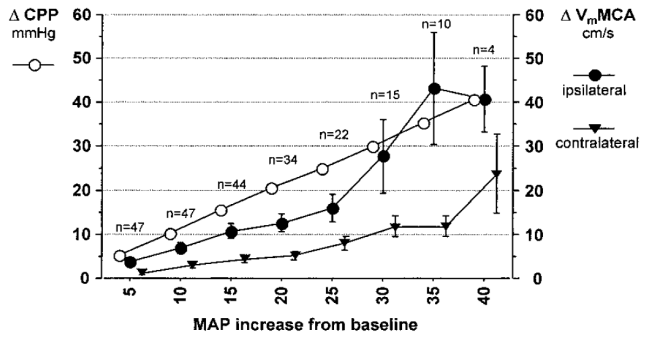
Chang in CPP & VmMCA from baseline



(*Stroke. 2002;33:998-1004.*)

Induced hypertension in AIS

A pilot study of drug-induced hypertension for treatment of acute stroke

Article abstract—The aim of this pilot study was to determine whether the use of induced hypertension in acute stroke is feasible and associated with neurologic improvement. Phenylephrine was used to raise the systolic blood pressure in patients with acute stroke by 20%, not to exceed 200 mmHg. Of 13 patients treated, 7 improved by 2 points on the NIH Stroke Scale. No systemic or neurologic complications were seen. The authors conclude that induced hypertension in acute stroke is feasible and likely safe and can improve the neurologic examination in some patients.

NEUROLOGY 2001;56:1210–1213

G. Rordorf, MD; W.J. Koroshetz, MD; M.A. Ezzeddine, MD; A.Z. Segal, MD; and F.S. Buonanno, MD

Feasible and likely safe
NIHSS improved by 2

Blood Pressure Decrease During the Acute Phase of Ischemic Stroke Is Associated With Brain Injury and Poor Stroke Outcome

José Castillo, MD, PhD; Rogelio Leira, MD, PhD; María M. García, MD, PhD; Joaquín Serena, MD, PhD; Miguel Blanco, MD, PhD; Antoni Dávalos, MD, PhD

Background and Purpose—Studies on the relation between blood pressure (BP) and stroke outcome have shown contradictory results. We explored the association of systolic (SBP) and diastolic (DBP) BP during acute stroke with early neurological deterioration, infarct volume, neurological outcome, and mortality at 3 months.

Methods—We included 304 patients with acute ischemic stroke. SBP and DBP on admission and on the first day were the average values of all readings obtained in the emergency department and during a 24-hour period after patient allocation in the stroke unit.

Results—A U-shaped effect was observed: for every 10 mm Hg ≤180 mm Hg of SBP, the risk of early neurological deterioration, poor outcome, and mortality increased by 6%, 25%, and 7%, respectively, whereas for every 10 mm Hg >180 mm Hg, the risk of early neurological deterioration increased by 40% and the risk of poor outcome increased by 23%, with no effect on mortality. Mean infarct volume increased 7.3 and 5.5 cm^3 for every 10 mm Hg ≤180 and >180 mm Hg. A similar pattern was found in patients with DBP ≤100 or >100 mm Hg. These effects disappeared after adjustment for the use of antihypertensive drugs and BP drop >20 mm Hg within the first day, with the latter being the more important prognostic factor of poor outcome.

Conclusions—High and low SBP and DBP, as well as a relevant drop in BP, are associated with poor prognosis in patients with ischemic stroke. **(*Stroke.* 2004;35:520-527.)**

Key Words: blood pressure ■ cerebral infarction ■ hypertension ■ prognosis ■ stroke

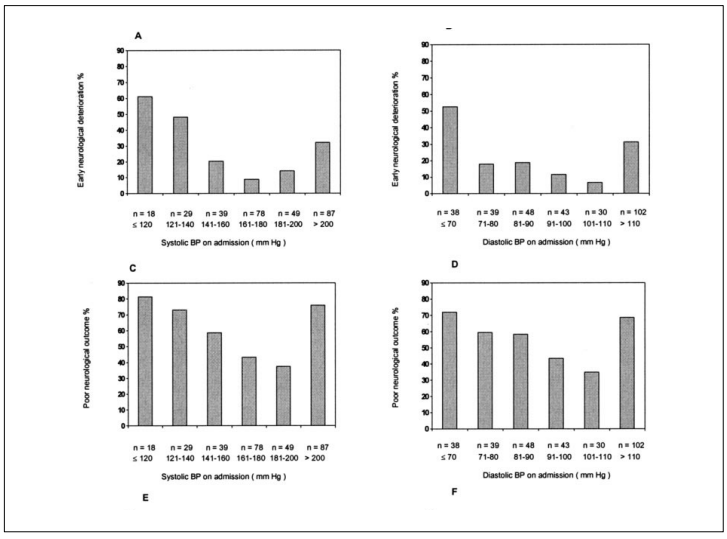


TABLE 4. Adjusted Increase in Mean (95% CI) Infarct Volume for SBP on Admission, Use of Antihypertensive Drugs, and Differences in SBP During the First Day

	SBP ≤180 mm Hg (n=161)	R^2	SBP >180 mm Hg (n=135)	R^2
Model 1				
SBP, by 10 mm Hg	7.3 (4.0, 10.6)	0.89	5.5 (1.6, 9.4)	0.87
Model 2				
SBP, by 10 mm Hg	...		1.4 (−3.8, 6.7)	0.88
Hypotensive drugs	...		23.1 (28, 43.4)	
Model 3				
SBP, by 10 mm Hg	6.0 (2.5, 9.6)	0.89	−1.6 (−7.1, 3.7)	0.89
Hypotensive drugs	...		11.1 (−9.9, 32.1)	
Difference in SBP:				
Decrease 0–20 mm Hg	0		0	
Decrease >20 mm Hg	61 (13.3, 109.6)		32.2 (12.1, 52.3)	
Any increase in SBP	12.1 (−2.3, 26.6)		...	

Mean volumes for SBP on admission are expressed by 10 mm Hg difference under or above 180 mm Hg. All models were adjusted for stroke subtype (lacunar vs nonlacunar), time from onset to inclusion, CSS, body temperature (<37.5°C vs ≥37.5°C), and serum glucose on admission. Values are in milliliters.

AHA Recommendations

(General Supportive Care and Treatment of Acute Complications)

2. For treatment with intravenous rtPA

- their SBP<185 mm Hg and their DBP<110 mm Hg *before* fibrinolytic therapy is initiated*(Class I; Level of Evidence B)* .

- before beginning treatment with intravenous rtPA and maintained below 180/105 mm Hg for at least the first 24 hours after intravenous rtPA treatment.

7. Who do not receive fibrinolysis

- reasonable goal is to lower blood pressure by 15% during the first 24 hours after onset of stroke.

- should be withheld unless the SBP>220 mm Hg or the DBP>120 mm Hg *(Class I; Level of Evidence C). (Revised from the previous* guideline13)

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AHA Recommendations

(General Supportive Care and Treatment of Acute Complications

13.

- **The management of arterial hypertension in patients not undergoing reperfusion strategies remains challenging.**
- **Data to guide recommendations for treatment are inconclusive or conflicting.**
- **Many patients have spontaneous declines in blood pressure during the first 24 hours after onset of stroke.**
- **Until more definitive data are available, the benefit of treating arterial hypertension in the setting of acute ischemic stroke is not well established *(Class IIb; Level of Evidence C).***
- ***Patients who have malignant hypertension* or other medical indications for aggressive treatment of blood pressure should be treated accordingly.** (Revised from the previous guideline13)

Table 9. Potential Approaches to Arterial Hypertension in Acute Ischemic Stroke Patients Who Are Candidates for Acute Reperfusion Therapy

Patient otherwise eligible for acute reperfusion therapy except that BP is >185/110 mm Hg:
Labetalol 10–20 mg IV over 1–2 minutes, may repeat 1 time; or
Nicardipine 5 mg/h IV, titrate up by 2.5 mg/h every 5–15 minutes, maximum 15 mg/h; when desired BP reached, adjust to maintain proper BP limits; or
Other agents (hydralazine, enalaprilat, etc) may be considered when appropriate
If BP is not maintained at or below 185/110 mm Hg, do not administer rtPA
Management of BP during and after rtPA or other acute reperfusion therapy to maintain BP at or below 180/105 mm Hg:
Monitor BP every 15 minutes for 2 hours from the start of rtPA therapy, then every 30 minutes for 6 hours, and then every hour for 16 hours
If systolic BP >180–230 mm Hg or diastolic BP >105–120 mm Hg:
Labetalol 10 mg IV followed by continuous IV infusion 2–8 mg/min; or
Nicardipine 5 mg/h IV, titrate up to desired effect by 2.5 mg/h every 5–15 minutes, maximum 15 mg/h
If BP not controlled or diastolic BP >140 mm Hg, consider IV sodium nitroprusside

BP indicates blood pressure; IV, intravenously; and rtPA, recombinant tissue-type plasminogen activator.

Table 12. Treatment of Acute Ischemic Stroke: Intravenous Administration of rtPA

Infuse 0.9 mg/kg (maximum dose 90 mg) over 60 minutes, with 10% of the dose given as a bolus over 1 minute.
Admit the patient to an intensive care or stroke unit for monitoring.
If the patient develops severe headache, acute hypertension, nausea, or vomiting or has a worsening neurological examination, discontinue the infusion (if IV rtPA is being administered) and obtain emergent CT scan.
Measure blood pressure and perform neurological assessments every 15 minutes during and after IV rtPA infusion for 2 hours, then every 30 minutes for 6 hours, then hourly until 24 hours after IV rtPA treatment.
Increase the frequency of blood pressure measurements if systolic blood pressure is >180 mm Hg or if diastolic blood pressure is >105 mm Hg; administer antihypertensive medications to maintain blood pressure at or below these levels (Table 8).
Delay placement of nasogastric tubes, indwelling bladder catheters, or intra-arterial pressure catheters if the patient can be safely managed without them.
Obtain a follow-up CT or MRI scan at 24 hours after IV rtPA before starting anticoagulants or antiplatelet agents.

CT indicates computed tomography; IV, intravenous; MRI, magnetic resonance imaging; and rtPA, recombinant tissue plasminogen activator.

AHA Recommendations

(Volume Expansion, Vasodilators, and Induced Hypertension)

1. In exceptional cases with systemic hypotension producing neurological sequelae, a physician may prescribe vasopressors to improve cerebral blood flow.

If drug-induced hypertension is used, close neurological and cardiac monitoring is recommended *(Class I; Level of Evidence C). (Revised from the previous* guideline13)

4. The usefulness of drug-induced hypertension in patients with acute ischemic stroke is not well established *(Class IIb; Level of Evidence B). (Revised from* the previous guideline13)

Induced hypertension should be performed in the setting of clinical trials.

Alpha & Beta blocker

- Labetalol
  - control BP in pts with either acute hemorrhage or AIS
  - cheap & long acting
  - CHHIPS study (*Lancet Neurol 2009; 8: 48–56) :* reduce mortality and potential disability

Vasodilators

- Nitroprusside
  - rarely used in AIS
  - ICP (14 mmHg↑), MAP (33%↓)(JNS 48:329-31. 1978)
- Nitroglycerin
  - less effective than nitrprusside
  - effect on CBF/ICP unclear
  - bad coronary disease (MI)

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Calcium channel blocker

- Nicardipine
  - few side effects: cerebral, cardiac, pulmonary
  - no increase in ICP
  - neuroprotective effect

ACE-I & ARB

- Angiotensin Converting Enzyme Inhibitor
  - captopril, lisinipril,perindopril
  - orolingual angioedema
- Angiotensin receptor antagonist
  - candesratan (ACCESS, 2003)
  - telmisartan (PRoFESS, 2007)

Symptomatic ICH after Thrombolysis

- Symptomatic hemorrhage occurs in 5% to 6% of patients after use of intravenous rtPA and intra-arterial recanalization strategies and anticoagulant use.
- Most sICHs occur within the first 24 hours after intravenous rtPA; the vast majority of fatal hemorrhages occur within the first 12 hours.
- A standardized guideline for managing fibrinolytic-associated hemorrhages does not exist.

Risk factors for sICH after thrombolysis

Table 1. Risk Factors for SICH After Thrombolysis.[8,15,33]

CT hypodensity (early ischemic changes >1/3 of MCA territory)
Elevated serum glucose or history of diabetes mellitus
Symptom severity
Time to treatment
High systolic blood pressure
Low platelets
Advanced age

Abbreviations: CT, computed tomography; MCA, middle cerebral artery; SICH, symptomatic intracerebral hemorrhage.

Neurohospitalist 5(3):133-41, 2015

Managements of sICH after thrombolysis

Table 2. Protocol for Management of Postthrombolysis Intracerebral Hemorrhage.[1,48-50]

Suspect ICH (new headache, nausea, vomiting, etc)
- ☐ Discontinue r-tPA infusion
- ☐ STAT blood draw: PT, PTT, platelet count, fibrinogen, type & cross
- ☐ STAT noncontrast CT head

Hemorrhage confirmed?
- ☐ Administer 6-8 units of cryoprecipitate, followed by 6-8 units platelets
- ☐ Consult neurosurgeon & alert to ICH
- ☐ Consult hematologist & alert to current coagulation status
- ☐ Administer ε-aminocaproic acid 4-5 gm IV over 1 hour, followed by 1 gm PO or IV hourly until bleeding is controlled
- ☐ Fibrinogen levels should be rechecked every Q 4 hours & cryoprecipitate transfused PRN to maintain fibrinogen levels > 150 mg/dL
- ☐ Blood pressure monitoring Q 15 minutes
- ☐ Periodic blood work (CBC, PT/PTT) to re-assess coagulation status & need for blood transfusion
- ☐ Consider repeat CT head to assess for ICH growth
- ☐ Consensus decision regarding surgical and/or medical therapy

Abbreviations: ICH, intracerebral hemorrhage; r-tPA, recombinant tissue-type plasminogen activator; STAT, at once; PT, prothrombin time; PTT, partial thromboplastin time; IV, intravenous; PO, orally; Q, every; PRN, as needed; CBC, complete blood count.

Neurohospitalist 5(3):133-41, 2015

Table 3. Suggested Management of Elevated Blood Pressure in Postthrombolysis ICH.[a]

If SBP > 200 mm Hg or MAP > 150 mm Hg, consider aggressive reduction in BP with continuous IV infusion
If SBP > 180 mm Hg or MAP > 130 mm Hg and there is concern for elevated ICP, then initiate ICP monitoring and reduce BP using intermittent or continuous IV antihypertensives, while cautiously maintaining CPP above 60 mm Hg
If SBP > 180 mm Hg or MAP > 130 mm Hg, but there is no indication of increased ICP, then a modest reduction in BP may be considered (eg, MAP of 110 mm Hg or target BP of 160/90 mm Hg) as long as BP is monitored every 15 minutes

Abbreviations: SBP, systolic blood pressure; MAP, mean arterial pressure; BP, blood pressure; ICP, intracerebral pressure; CPP, cerebral perfusion pressure.
[a]Adapted from Morgenstern et al.[60]

Neurohospitalist 5(3):133-41, 2015

MEMO

Current role of antiplatelet therapy in secondary prevention of stroke

조 준 성
단국대

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Antiplatelet therapy for noncardioembolic stroke or TIA

• Aspirin

- Non-cardioembolic ischemic stroke or TIA, antiplatelet agents rather than oral anticoagulation are recommended
(ASA: Class I, Level of Evidence A, EUSI: Level I)

- Low or medium-dose aspirin (50-325mg) should be given as first choice agent to reduce stroke recurrence
(ASA: Class IIa, Level of Evidence A, EUSI: Level I)

Antiplatelet therapy for noncardioembolic stroke or TIA

• Aspirin

- CAPRIE (Clopidogrel versus aspirin in patients at risk of ischemic events)
- ESPIRIT (Aspirin plus dipyridamole versus aspirin alone after cerebral ischemia of arterial origin)

- 하루300mg 이하의 용량과 비교해 그 효과의 우수성이 확실히 밝혀지지 않았다. 또한 하루300mg 이상의 아스피린을 복용할 때 오히려 위장관 출혈발생의 가능성이 높아 사용을 피하는 것이 좋다

Antiplatelet therapy for noncardioembolic stroke or TIA

• Aspirin

- 심장탓 뇌색전증을 제외한 뇌경색과 일과성 허혈발작 환자들은 허혈증상 재발 방지를 위해 하루 50-300mg 사이의 아스피린을 사용할수있다.(근거수준Ia, 권고수준A)

Antiplatelet therapy for noncardioembolic stroke or TIA (Thienopyridine)

• Ticlopidine, clopidogrel

- 1. All patients with ischemic stroke or TIA who are not on anticoagulation should be taking an antiplatelet agent, ie aspirin (50-300mg), daily or clopidogrel, or a combination of low-dose aspirin and dipyridamole modified release (MR) (RCP: Grade of Recommendation A)

- 2. Clopidogrel is slightly more effective than aspirin in the prevention of further vascular events (EUSI: Level of Evidence I, AHA/ASA: Class IIb, Level of Evidence B)

- 3. Where patients are aspirin intolerant, an alternative antiplatelet agent (eg clopidogrel 75mg daily or dipyridamole MR 200mg twice daily) should be used (RCP: Grade of Recommendation A, AHA/ASA: Class IIa, Level of Evidence B).

Antiplatelet therapy for noncardioembolic stroke or TIA (Thienopyridine)

• Ticlopidine, clopidogrel

- 뇌졸중, 심근경색, 말초혈관질환을 가진 환자를 대상으로 Clopidogrel75mg과 aspirin 325mg을 투여한 후 3년간 뇌경색, 심근경색, 혈관질환으로 인한 사망률을 비교한 CAPRIE연구에서, Clopidogrel이 aspirin보다 혈관질환의 발생을 감소시켰다. (상대위험률감소, 8.7%)

- 뇌졸중 환자만을 대상으로 분석 하였을 때는 의미있는 결과를 보여주지 못했다. 이 연구의 사후검정에서 뇌경색의 과거력 또는 뇌허혈의 증상이 있었던 관상동맥질환, 당뇨병환자에서는 Clopidogrel이 aspirin에 비해 이차예방 효과가 우수하였다

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Antiplatelet therapy for noncardioembolic stroke or TIA (Thienopyridine)

• Ticlopidine, clopidogrel

-1. Clopidogrel단독투여는aspirin단독투여, 또는 aspirin과 dipyridamole의 복합투여와 함께 비심장탓 허혈 뇌졸중 환자의 일차 선택약제로 사용할수 있다. (근거수준Ib, 권고수준A)

-2. aspirin에 과민증이 있는 환자에게는 Clopidogrel등 다른 항혈소판제가권장 (근거수준Ib, 권고수준A)

-3. Ticlopidine은 aspirin과 비교하였을 때 뇌졸중의 이차적 예방에 도움을줄 수 있다. (근거수준1b,권고수준A). 하지만 호중구감소증 등의 위험성이 있으므로 투약시 주의가 필요하다.(근거수준Ib, 권고수준A)

Antiplatelet therapy for noncardioembolic stroke or TIA; Triflusal, Dipyridamole, Cilostazol

- 1. Compared with aspirin alone, the combination of aspirin and extended-release dipyridamole is safe and an acceptable option for initial therapy for secondary stroke prevention (AHA/ASA: Class IIa, Level of Evidence A, EUSI: Level of Evidence I)

- 2. Patients who do not tolerate either aspirin or clopidogrel may be treated with dipyridamole 200 mg twice daily (EUSI: Level of Evidence II)

Antiplatelet therapy for noncardioembolic stroke or TIA; Triflusal, Dipyridamole, Cilostazol

-1. 저용량의 aspirin과 dipyridamole을 함께 사용하는 것은 뇌졸중의 이차예방을 위한 초기치료로 사용할 수 있다. (근거수준Ib, 권고수준A)

-2. trifusal과 cilostazol은 aspirin이나 clopidogrel을 사용하기 어려운 경우에 뇌졸중의 이차예방 목적으로 고려될 수 있다. (근거수준II, 권고수준B)

-3. 뇌출혈을 포함한 심각한 출혈의 위험이 있는 환자에게 항혈소판제 치료가 필요할 때, triflusal은뇌졸중의 이차예방을 위해서 추천될 수 있다. (근거수준Ib, 권고수준A)

Antiplatelet therapy for noncardioembolic stroke or TIA; Triflusal, Dipyridamole, Cilostazol

Cilostazol for prevention of secondary stroke (CSPS 2): an aspirin-controlled, double-blind, randomised non-inferiority trial

*Yukito Shinohara, Yasuo Katayama, Shinichiro Uchiyama, Takenori Yamaguchi, Shunnosuke Handa, Kempei Matsuoka, Yasuo Ohashi, Norio Tanahashi, Hiroko Yamamoto, Chokoh Genka, Yasuhisa Kitagawa, Hideo Kusuoka, Katsuya Nishimaru, Motoo Tsushima, Yukihiro Koretsune, Tohru Sawada, Chikuma Hamada, for the CSPS 2 group**

Lancet Neurol. 2010;9:959–968

Interpretation **Cilostazol seems to be non-inferior, and might be superior, to aspirin for prevention of stroke after an ischaemic stroke, and was associated with fewer haemorrhagic events. Therefore, cilostazol could be used for prevention of stroke in patients with non-cardioembolic stroke.**

Antiplatelet therapy for noncardioembolic stroke or TIA; Triflusal, Dipyridamole, Cilostazol

Cilostazol as an alternative to aspirin after ischaemic stroke: a randomised, double-blind, pilot study

Yining Huang, Yan Cheng, Jiang Wu, Yansheng Li, En Xu, Zhen Hong, Zhengyi Li, Weiwei Zhang, Meiping Ding, Xuguang Gao, Dongsheng Fan, Jinsheng Zeng, Kasing Wong, Chuanzhen Lu, Jiangxi Xiao, Chen Yao, on behalf of the cilostazol versus aspirin for secondary ischaemic stroke prevention (CASISP) cooperation investigators

Lancet Neurol. 2008;7:494–499

Interpretation **The results of this pilot study showed no significant difference in the rate of recurrence of stroke between patients with ischaemic stroke who were randomly assigned to take either cilostazol or aspirin. The lower rates of ischaemic and haemorrhagic stroke in the cilostazol group suggest that cilostazol might be a more effective and safer alternative to aspirin for Chinese patients with ischaemic stroke; however, a larger phase III trial is required to confirm this.**

Antiplatelet therapy for noncardioembolic stroke or TIA; Triflusal, Dipyridamole, Cilostazol

ELSEVIER

Journal of the Neurological Sciences 143 (1996) 1–13

JOURNAL OF THE NEUROLOGICAL SCIENCES

Dipyridamole i

Abstract

In 1988, we undertook a randomized, placebo-controlled, double-blind trial to investigate the safety and efficacy of low-dose acetylsalicylic acid (ASA), modified-release dipyridamole, and the two agents in combination for secondary prevention of ischemic stroke. Patients with prior stroke or transient ischemic attack (TIA) were randomized to treatment with ASA alone (50 mg daily), modified-release dipyridamole alone (400 mg daily), the two agents in a combined formulation, or placebo. Primary endpoints were stroke, death, and stroke or death together. TIA and other vascular events were secondary endpoints. Patients were followed on treatment for two years. Data from 6,602 patients were analysed. Factorial analysis demonstrated a highly significant effect for ASA and for dipyridamole in reducing the risk of stroke ($p \leq 0.001$) and stroke or death combined ($p < 0.01$). In pairwise comparisons, stroke risk in comparison to placebo was reduced by 18% with ASA alone ($p = 0.013$); 16% with dipyridamole alone ($p = 0.039$); and 37% with combination therapy ($p < 0.001$). Risk of stroke or death was reduced by 13% with ASA alone ($p = 0.016$); 15% with dipyridamole alone ($p = 0.015$); and 24% with the combination ($p < 0.001$). The treatment had no statistically significant effect on the death rate alone. Factorial analysis also demonstrated a highly significant effect of ASA ($p < 0.001$) and dipyridamole ($p < 0.01$) for preventing TIA. The risk reduction for the combination was 36% ($p < 0.001$) in comparison with placebo. Headache was the most common adverse event, occurring more frequently in dipyridamole-treated patients. All-site bleeding and gastrointestinal bleeding were significantly more common in patients who received ASA in comparison to placebo or dipyridamole. We conclude that (1) ASA 25 mg twice daily and dipyridamole, in a modified-release form, at a dose of 200 mg twice daily have each been shown to be equally effective for the secondary prevention of ischemic stroke and TIA; (2) when co-prescribed the protective effects are additive, the combination being significantly more effective than either agent prescribed singly; (3) low-dose ASA does not eliminate the propensity for induced bleeding.

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Antiplatelet therapy for noncardioembolic stroke or TIA; Triflusal, Dipyridamole, Cilostazol

Aspirin plus dipyridamole versus aspirin alone after cerebral ischaemia of arterial origin (ESPRIT): randomised controlled trial

*The ESPRIT Study Group**

Lancet 2006; 367: 1665–73

Interpretation **The ESPRIT results, combined with the results of previous trials, provide sufficient evidence to prefer the combination regimen of aspirin plus dipyridamole over aspirin alone as antithrombotic therapy after cerebral ischaemia of arterial origin.**

Antiplatelet therapy for noncardioembolic stroke or TIA; Triflusal, Dipyridamole, Cilostazol

- Triflusal vs aspirin for the prevention of infarction: a randomized stroke study (TAPIRSS)
  431명의 환자를 trifusal 600mg군과 aspirin 325mg 군으로 무작위 배정하여 평균586일을 투여하였다.
  TAPIRSS연구 에서도 역시 triflusal과 aspirin은 뇌졸중의 이차 예방 면에서 동등한 효과를 보였으나, 주요 혹은 경미한 출혈의 발생률이 triflusal군에서 유의하게 낮았다

Antiplatelet therapy for noncardioembolic stroke or TIA; Triflusal, Dipyridamole, Cilostazol

-1. cilostazol 단독치료는 비심인성 뇌졸중환자, 특히 열공성 뇌경색환자에서 뇌졸중의 이차예방에 사용할 수 있다. (근거수준Ia, 권고수준A)-new

-2. 저용량의 aspirin과 dipyridamole을 함께 사용하는 것은 뇌졸중의 이차예방을 위한 초기치료로 사용할 수 있다. (근거수준Ib, 권고수준A)

-3. triflusal은 aspirin이나 clopidogrel을 사용하기 어려운 경우에 뇌졸중의 이차예방 목적으로 고려될 수 있다. (근거수준Ib, 권고수준A)-수정

-4. 뇌출혈을 포함한 심각한 출혈의 위험이 있는 환자에게 항혈소판제 치료가 필요할 때, cilostazol 또는triflusal은 뇌졸중의 이차예방을 위해서 추천될 수 있다. (근거수준Ib, 권고수준A)-수정

Antiplatelet therapy for noncardioembolic stroke or TIA; combination therapy

- 1. Aspirin (50 to 325mg/d), the combination of aspirin and extended release dipyridamole, and clopidogrel are all acceptable options for initial therapy (AHA/ASA: Class IIa, Level of Evidence A, EUSI: Level of Evidence I,RCP: Grade of Recommendation A)
- 2. The combination of aspirin and extended-release dipyridamole is suggested instead of aspirin alone (AHA/ASA: Class IIa Level of Evidence A, RCP: Grade of Recommendation A, EUSI: Level of Evidence I).
- 3. The addition of aspirin to clopidogrel increases the risk of hemorrhage and is not routinely recommended for ischemic stroke or TIA patients (AHA/ASA: Class III, Level of Evidence A).
- 4. Patients with TIA or ischemic stroke and unstable angina or non-Q-wave MI should be treated with a combination of clopidogrel 75mg and aspirin 75mg (EUSI: Level of Evidence III).

Antiplatelet combination therapy

Aspirin and clopidogrel compared with clopidogrel alone after recent ischaemic stroke or transient ischaemic attack in high-risk patients (MATCH): randomised, double-blind, placebo-controlled trial

*Hans-Christoph Diener, Julien Bogousslavsky, Lawrence M Brass, Claudio Cimminiello, Laszlo Csiba, Markku Kaste, Didier Leys, Jordi Matias-Guiu, Hans-Jürgen Rupprecht, on behalf of the MATCH investigators**

Lancet 2004; 364: 331–37

Interpretation **Adding aspirin to clopidogrel in high-risk patients with recent ischaemic stroke or transient ischaemic attack is associated with a non-significant difference in reducing major vascular events. However, the risk of life-threatening or major bleeding is increased by the addition of aspirin.**

Antiplatelet combination therapy

Clopidogrel added to aspirin versus aspirin alone in secondary prevention and high-risk primary prevention: Rationale and design of the Clopidogrel for High Atherothrombotic Risk and Ischemic Stabilization, Management, and Avoidance (CHARISMA) trial

Deepak L. Bhatt, MD, and Eric J. Topol, MD, on behalf of the CHARISMA Executive Committee* *Cleveland, Ohio*

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Antiplatelet combination therapy

Effects of *Cilostazol* on Angiographic Restenosis After Coronary Stent Placement

Seong-Wook Park, MD, PhD, Cheol Whan Lee, MD, Hyun-Sook Kim, MD, Nae-Hee Lee, MD, Deuk Young Nah, MD, Myeong-Ki Hong, MD, Jae-Joong Kim, MD, PhD, and Seung-Jung Park, MD, PhD

Am J Cardiol. 2000;86:499–503

In conclusion, aspirin plus cilostazol seems to be an effective antithrombotic regimen with comparable results to aspirin plus ticlopidine, but it does not reduce the overall angiographic restenosis rate after elective coronary stenting

Antiplatelet combination therapy

Coronary Stent Restenosis in Patients Treated With Cilostazol

John S. Douglas, Jr, MD; David R. Holmes, Jr, MD; Dean J. Kereiakes, MD; Cindy L. Grines, MD; Elizabeth Block, BS; Ziyad M.B. Ghazzal, MD; Douglas C. Morris, MD; Henry Liberman, MD; Karen Parker, BS; Claudine Jurkovitz, MD; Nancy Murrah, BSN; Jovonne Foster, MS; Pamela Hyde, BSN; G.B. John Mancini, MD; William S. Weintraub, MD; for the Cilostazol for Restenosis Trial (CREST) Investigators*

Conclusions—Treatment with the drug cilostazol resulted in a significantly larger minimal luminal diameter and a significantly lower binary restenosis rate compared with placebo-treated patients. These favorable effects were apparent in patients at high risk for restenosis. (***Circulation*. 2005;112:2826-2832.**)

Antiplatelet combination therapy

Cilostazol Prevents the Progression of the Symptomatic Intracranial Arterial Stenosis

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

Sun U. Kwon, MD, PhD; Yong-Jin Cho, MD, PhD; Ja-Seong Koo, MD; Hee-Joon Bae, MD, PhD; Yong-Seok Lee, MD; Keun-Sik Hong, MD, PhD; Jun Hong Lee, MD; Jong S. Kim, MD, PhD

Background and Purpose—Cilostazol, a phosphodiesterase inhibitor, has been reported to reduce restenosis rate a

Conclusion—Our study suggests that symptomatic IAS is a dynamic lesion and cilostazol may prevent its progression. (***Stroke*. 2005;36:782-786.**)

Antiplatelet therapy for noncardioembolic stroke or TIA; combination therapy

-1. 심장탓 뇌색전증을 제외한 허혈뇌졸중 이나 일과성 허혈발작의 재발을 막기 위해 aspirin과 dipyridamole의 복합투여는 aspirin단독투여에 비해 효과적 일 수 있다. (근거수준Ia, 권고수준A)

-2. 뇌졸중의 이차예방을 위해서 clopidogrel 과aspirin의 복합투여는 관상동맥질환(unstable angina, non Q-wave MI)을 동반한 일부 환자에게는 효과적 일 수 있으나, 두개내 출혈의 위험성이 있으므로 이를 고려하여 사용 하여야 한다. (근거수준Ia, 권고수준A)

-3. cilostalzol은 유증상 두개강내 동맥 협착 환자에게 고려될 수 있다. (근거수준III, 권고수준B)

Anticoagulation

-1. For patients with noncardioembolic ischemic stroke or TIA, antiplatelet agents rather than oral anticoagulation are recommended to reduce the risk of recurrent stroke and other cardiovascular events (AHA/ASA: Class I, Level of Evidence A). Anticoagulants should not be used for patients in sinus rhythm (RCP: Grade of Recommendation A), unless there is a major source of cardiac embolism (RCP: Grade of Recommendation D)

-2. Anticoagulation should not be used after non-cardioembolic ischemic stroke, except in some specific situations, such as aortic atheroma, fusiform aneurysms of the basilar artery or cervical artery dissection (EUSI: Level of Evidence IV)

조1
조2
조3

Anticoagulation

- SPIRIT (The Stroke Prevention in Reversible Ischemia Trial)
  : 고용량의 경구용 항응고제(INR, 3.0-4.5) vs Aspirin
- WARSS (The Wafarin Aspirin Recurrent Stroke Study)
- WASID (Warfarin-Aspirin Symptomatic Intracranial Disease)
- ESPRIT (European/Australasian Stroke Prevention in Reversible Ischaemia Trial)

-1. 심장탓뇌색전증을 제외한 허혈뇌졸중이나 일과성 허혈발작의 재발을 막기 위해서는 경구용 항응고제 보다는 항혈소판제 사용이 권고된다. (근거수준Ia, 권고수준A)

MEMO

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Specific consideration of antiplatelet agents

• Ischemic stroke while taking antiplatelet agent

–1. For patients who have an ischemic stroke while taking aspirin, there is no evidence that increasing the dose of aspirin provides additional benefit. Although alternative antiplatelet agents are often considered for noncardioembolic patients, no single agent or combination has been studied in patients who have hand an event while receiving aspirin (AHA/ASA).

Specific consideration of antiplatelet agents

• Ischemic stroke while taking antiplatelet agent

- 1. 아스피린을 복용하고 있는 허혈 뇌졸중환자에서 허혈 뇌졸중이 재발 했을때 아스피린의 용량을 증가시키는 것이 뇌졸중의 추가 재발방지에 도움이 된다는 근거는 없다. 또한 기존에 아스피린을 복용하고 있는 비심장탓 허혈 뇌졸중환자에서 허혈 뇌졸중이 재발 하였을때 단일 항혈소판제나 복합제재를 투여하는 것이 도움이 된다는 유용한 연구 결과도 없다. 따라서 아스피린을 복용하고 있는 환자에서 허혈 뇌졸중이 재발했을 때 이후 약제의 선택은 환자 개개인의 특성과 약제의 위험을 고려하여 처방이 이루어져야 한다. (근거수준IV, 권고수준C)

- 2. 기존에 아스피린을 복용하고 있는 비심장탓 허혈뇌졸중 환자에서 허혈뇌졸중이 재발하였을 때 담당의사의 판단과 환자의 개별적인 특성을 고려해서 서방형 디피리다몰과 아스피린의 복합제를 투여할 수 있다. 만일 서방형 디피리다몰 투여가 적절하지 않는 경우에는 clopidogrel을 단일제제로 변경투여 할 수 있다. 그 외의 약제의 선택에 대해서는 아직까지 유용한 연구결과가 미흡한 실정이다. (근거수준IV, 권고수준C)

- 3. 아스피린 이외의 항혈소판제를 복용하고 있던 비심장탓 허혈뇌졸중 환자에서 허혈뇌졸중이 재발했을때 이후에 처방 되어야하는 적절한약제에대한유용한연구결과는아직까지없다. (근거수준IV, 권고수준C)

Specific consideration of antiplatelet agents

• Ischemic stroke mixed with hemorrhage

-뇌출혈을 동반한 환자에게 항혈전제(antithrombotic agent)를 투여할때 안전성과 효과에 대해서는 아직까지 명확한 기준이 정립되지 않았다. 그러나 과거 뇌출혈 병력을 가진 환자에서 뇌경색이 발생할 수 있으며, 혈전용해술 이후에도 이와관련된 뇌출혈이 발생할 수 있으므로 이에대한 실질적인 연구가필요하다. 엽상출혈(lobar hemorrhage)이나 심부출혈(deep hemorrhage)을 동반한 심방세동을 가진 환자에서 항응고제를 투여하는 경우 출혈의 재발과 허혈질환의 발생에 따른 환자의 삶의질이라는 측면에서 고려되어야 할 것이다. 또한, 뇌출혈의 발생후 항혈소판제의투약은 재출혈의가능성이 낮은 환자에게 고려되어야한다.

-뇌영상검사기법이 발전하여 뇌미세출혈(cerebral microbleeding)이 경사에코(Gradient-echo) MRI에서 저신호 강도소견으로 흔히 관찰되는데, 이는 임상적으로 대부분 무증상의 소혈관 출혈을 의미한다. 뇌미세출혈은 아시아인과 비아시아인 사이에서 다양한 유병률차이를 보이며 고령에서나 고혈압을 가진 경우 뇌미세출혈의 출현이 증가 된다고 보고되었다.그러나, 뇌미세출혈과 항혈전제치료의 관련성에 관해서는 여전히 논란이 있으므로 이에 대한 전향적인 연구가 필요하다.

Specific consideration of antiplatelet agents

• ischemic stroke mixed with hemorrhage

-1. The decision to restart antithrombotic therapy after ICH related to antithrombotic therapy depends on the risk of subsequent arterial or venous thromboembolism, the risk of recurrent ICH, and the overall state of the patient. For patients with a comparatively lower risk of cerebral infarction (eg, AF without prior ischemic stroke) and a higher risk of amyloid angiopathy (eg, elderly patients with lobar ICH) or with very poor overall neurological function, an antiplatelet agent may be an overall better choice for prevention of ischemic stroke than warfarin. In patients with a very high risk of thromboembolism in whom restarting warfarin is considered, warfarin therapy may be restarted at 7 to 10 days after onset of the original ICH (AHA/ASA: Class IIb, Level of Evidence B)

-2. After having re-checked the indication for anticoagulation (following the EUSI recommendation on ischaemeic stroke) oral anticoagulation treatment may be continued after 10-14 days, depending on the perceived risk of thromboembolic occlusion and ICH recurrence (EUSI: Level of Evidence IV)

Specific consideration of antiplatelet agents

• ischemic stroke mixed with hemorrhage

-1. 뇌출혈이 발생한 환자에서 항혈전제 투약을 다시 시작해야 할지를 결정할때 혈전의 발생위험성, 뇌출혈의 재발 위험성 및 환자의 전반적인 위험인자등 상태를 고려해서 결정 되어야 한다 (근거수준IV, 권고수준C)

-2. 항응고제 복용 이후 뇌출혈이 발생한 환자에서 뇌색전증의 재발 가능성이 낮은경우나 출혈의 위험성이 높은 경우에는 항응고제 대신 항혈소판제가 투여될 수도 있지만, 뇌색전증의 발생 위험이 매우 높은 환자에서는 항응고제가 다시 투여되어야한다. 재투여를 시작하는 시기는 이전 뇌출혈 발생 후 7-10일 이후가 될수있다. (근거수준III, 권고수준B)

-3. 뇌미세출혈과 항혈전제의 연관성에 대한 유용한 전향적인 연구가 발표되지 않았으므로, 뇌미세출혈을 가진 환자에서 항혈전제의 투약을 제한할 필요는 없을것으로 고려된다. (근거수준IV, 권고수준C)

Antithrombotic therapy of cardioembolic stroke or TIA (Anticoagulation)

• 1. Patients with proven cardio-embolic stroke should be anticoagulated, if the risk of recurrence is high, with a target INR between 2.0 and 3.0 (EUSI: level of Evidence III)

1. 색전증의 위험이 높은 심장질환을 동반한 뇌졸중 또는 일과성 허혈 발작환자는 심장탓 색전성뇌졸중 또는 일과성허혈발작의 재발 가능성이 높으므로 특별한 금기가 없는한 INR 2.0-3.0 목표의 와파린치료가권장된다. (근거수준III, 권고수준C, GPP)

MEMO

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Antithrombotic therapy of cardioembolic stroke or TIA (Anticoagulation)

• Antiplatelet therapy or combination therapy

–1. Oral anticoagulation (INR 2.0–3.0) is indicated after ischemic stroke associated with atrial fibrillation (EUSI: level I). Oral anticoagulation is not advisable in patients with comorbid conditions such as falls, epilepsy, severe dementia, or gastro-intestinal bleedings

• 1. 항응고제 치료를 할 수 없는 심장탓 색전 으로 인한 허혈 뇌졸중 또는 일과성 허혈발작 환자의 이차예방을 위해서 아스피린 투여를 고려할 수 있다. (권고수준GPP)

Antithrombotic therapy of cardioembolic stroke or TIA (specific conditions)

• Atrial fibrillation

–1. 지속 또는 발작 심방세동을 가진 허혈뇌졸중 또는 일과성 허혈발작 환자에서, 특별한 금기가 없는한 INR 2.0–3.0 목표의 와파린 치료가 권장된다.(근거수준Ia, 권고수준A)

–2.항응고제를 투여할 수 없다면, 아스피린을 투여할 수 있다. (근거수준Ia, 권고수준A)

–3. 적절한 아스피린 용량으로는 하루325mg가 권장되나, 우리나라에서는 실제 처방 가능한 용량인 하루300mg을 고려할 수 있다.(근거수준IV, 권고수준GPP)

–4. 적절한 항응고제 치료를 받던 심방세동환자에서 허혈뇌졸중 또는 일과성 허혈 발작이 재발한 경우,INR 2.5–3.5로 치료목표를 높이거나 항혈소판제 병용투여를고려할수있다.(근거수준IV, 권고수준C)

Antithrombotic therapy of cardioembolic stroke or TIA (specific conditions)

• Atrial fibrillation

–이번 권고안에서 가장 새로운 부분은 지속 또는 발작 비판막성 심방세동을 동반한 허혈뇌졸중 또는일과성 허혈 발작 환자에서 특별한 금기가 없는한 뇌졸중의 이차 예방목적으로 와파린 또는 새로운 경구항응고제인 dabigatran, rivaroxaban, apixaban을 사용할수있다는문구를근거수준Ia, 권고수준A로 제시한 것 이다

Antithrombotic therapy of cardioembolic stroke or TIA (specific condtions)

- 와파린 사용중 뇌졸중이 재발하는 환자에 대한 항혈전제 치료에 대한 임상시험은 없으나 임상진료에서 자주 접하는 문제
  >> 기존지침에서INR 상향조정을 근거수준IV, 권고수준C로 제시
- 비판막성심방세동을 동반한 허혈뇌졸중 또는 일과성허혈발작 환자에서 출혈뇌졸중을 경험했거나 출혈뇌졸중의 위험이 높지만 항응고제 치료가 필요한 경우 새로운 경구항 응고제를 고려할수있다는내용을 근거수준III, 권고수준B로제안

Antithrombotic therapy of cardioembolic stroke or TIA (specific conditions)

- 비판막성 심방세동을 동반한 허혈 뇌졸중 또는 일과성 허혈 발작환자에서 항응고제를 투여할 수 없는 경우에 대한 지침도 수정 하였다. 개정 전 진료지침은 항응고제를 사용할 수 없는 심방세동 환자에서 아스피린 사용을 근거수준Ia, 권고수준A로 권고하였는데 메타연구에서위약과 비교하여 항혈소판제의 예방효과가 입증 되었으므로 아스피린을 항혈소판제로 변경하였다
- 따라서 항혈소판제는 아스피린 단독투여 또는 아스피린과 클로피도그렐 병용요법 을사용할 수 있으며, 출혈 위험성과 허혈성 혈관질환의 감소 효과간의 균형을 고려하여 개별적으로 결정 되어야 할 것 이다 라는 내용을 근거수준Ib, 권고수준A로제안

Antithrombotic therapy of cardioembolic stroke or TIA (Anticoagulation)

- 지속 또는 발작 비판막성 심방세동에서 특별한 금기가 없는 한 뇌졸중의 이차예방 목적으로 와파린또는새로운 경구항응고제인 다비가트란, 리바록사반, 아픽사반을사용할수있다.(근거수준Ia, 권고수준A) 약물의선택은환자의임상적특성또는약물상호작용에따라판단한다.(GPP) (신규권고안)
- 와파린 사용시에는 INR 2.0-3.0 목표로 약물 농도조절이 권장된다.(근거수준Ia, 권고수준A) (수정권고안)
- 새로운 경구항응고제 사용을 고려할때 신기능을평가해야한다. 항응고치료가 필요한 비판막성 심방세동환자에서 중증의신기능저하가있는경우 다비가트란, 리바록사반 및 아픽사반 사용은 권장되지않는다.(근거수준III, 권고수준B) (신규권고안)
- 와파린 치료를 받던 심방세동환자에서 심인성허혈뇌졸중또는일과성허혈발작이재발한경우, INR 치료목표를 높이거나, 항혈소판제를 추가, 혹은 새로운 경구항 응고제 사용을 고려할 수있다.(근거수준IV, 권고수준C) (수정권고안)
- 비판막성 심방세동을 동반한 환자에서두개강내 출혈을 경험했거나 두개강내출혈의 위험이 높은경우 이차예방으로 새로운경구 항응고제를고려할수있다.(근거수준III, 권고수준B) (신규권고안)
- 비판막성 심방세동을 동반한 허혈뇌졸중 또는 일과성 허혈발작환자에서 항응고제를 투여할수없다면, 항혈소판제치료가 고려되어야 한다.(근거수준Ia, 권고수준A) 항혈소판제는 아스피린 단독투여또는 아스피린과 클로피도그렐 병용요법을사용할수있으며, 출혈위험성과 허혈성혈관질환의 감소효과간의 균형을 고려하여 개별적으로결정되어야할것이다.(근거수준Ib, 권고수준A) (수정권고안)

MEMO

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Antithrombotic therapy of cardioembolic stroke or TIA (specific conditions)

• Congestive heart failure

-For patients with ischemic stroke or TIA who have dilated cardiomyopathy, either warfarin (INR, 2.0 to 3.0) or antiplatelet therapy may be considered for prevention of recurrent events (ASA; Class IIb, Level of Evidence C)

-낮은 좌심실박출계수를 보이는 심장근육병증의 뇌졸중이차예방을 위해서 와파린또는항혈소판제 사용을 고려해 볼 수 있다 (권고수준GPP)

Antithrombotic therapy of cardioembolic stroke or TIA (specific conditions)

• Acute myocardial infarction

-1. For patients with an ischemic stroke or TIA caused by an acute
MI in whom LV mural thrombus is identified by echocardiography or another form of cardiac imaging, oral anticoagulation is reasonable, aiming for an INR of 2.0 to 3.0 for at least 3 months and up to 1 year (ASA: Class IIa, Level of Evidence B).

-2. Aspirin should be used concurrently for ischemic coronary artery disease during oral anticoagulant therapy in doses up to 162 mg/d (ASA: Class IIa, Level of Evidence A).

Antithrombotic therapy of cardioembolic stroke or TIA (specific conditions)

• Acute myocardial infarction

-1. 좌심실혈전을 동반한 급성심근경색에 의한 허혈 뇌졸중 또는 일과성 허혈 발작환자에서, 항응고 치료의 특별한 금기가없는 한INR 2.0-3.0으로 최소3개월에서1년 동안 와파린 치료를 하는 것이 바람직하다. (근거수준IIa, 권고수준B)

-2. 항응고제 투여기간 동안에도 아스피린을 병용투여해야한다. (근거수준Ia, 권고수준A)

Antithrombotic therapy of cardioembolic stroke or TIA (specific conditions)

• Valvular heart disease

-1. For patients with ischemic stroke or TIA who have rheumatic mitral valve disease, whether or not AF is present, long-term warfarin therapy is reasonable, with a target INR between 2.0 and 3.0 (ASA: Class IIa, Level of Evidence C).
-2. For patients with rheumatic mitral valve disease, whether or not AF is present, who have a recurrent embolism while receiving warfarin, adding low dose aspirin is suggested (ASA: Class IIa, Level of Evidence C).
-3. For patients with ischemic stroke or TIA who have mechanical prosthetic heart valves, oral anticoagulants are recommended, with a target INR between 2.5 and 3.5 (ASA: Class I, Level of Evidence B, EUSI: level II).
-4. For patients with mechanical prosthetic heart valves, whether or not AF is present, who have a recurrent embolism while receiving warfarin, adding low-dose aspirin is reasonable (ASA: Class IIa, Level of Evidence B).
-5. For patients with ischemic stroke or TIA who have bioprosthetic heart valves with no other source of thromboembolism, anticoagulation with warfarin (INR 2.0 to 3.0) may be considered (ASA: Class IIb, Level of Evidence C).

• Valvular heart disease

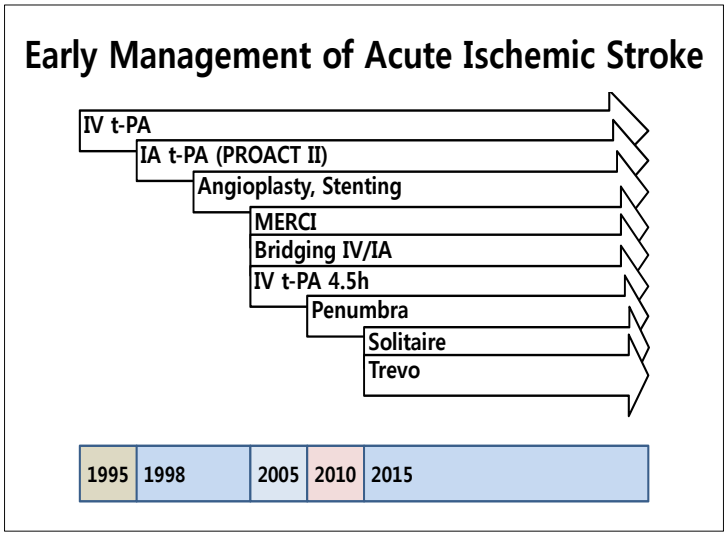
1. 류마티스 승모판막 질환이 동반된 허혈뇌졸중또는 일과성 허혈발작 환자에서 심방세동 유무와 관계없이 특별한 금기가 없는한 INR 2.0-3.0 목표의 와파린치료가추천된다. (근거수준III, 권고수준B)
2. 류마티스 승모판막 질환이 동반된 허혈 뇌졸중 또는 일과성 허혈발작환자에서 적절한 항응고제투여에도 불구하고 색전증이재발한경우, 저용량(하루100mg)의아스피린 병용투여를 고려할 수 있다. (근거수준IV, 권고수준C)
3. 기계적 인공판막 치환술 후 발생한 허혈뇌졸중 또는 일과성허혈발작 환자에서 특별한 금기가 없는 한, INR 2.5-3.5 목표의 와파린 치료가 추천된다. (근거수준IIb, 권고수준B)
4. 기계적 인공판막 치환술후 적절한 항응고제 투여에도 불구하고 색전증이 재발한경우, 저용량 100mg의 아스피린 병용투여가 추천된다. (근거수준IIa, 권고수준B)
5. 생체 인공판막 치환술후 발생한 허혈뇌졸중 또는 일과성 허혈 발작환자에서 다른 혈전 색전증의 원인이 없다면, INR 2.0-3.0 목표의 와파린치료를 고려할수있다. (근거수준IV, 권고수준C)

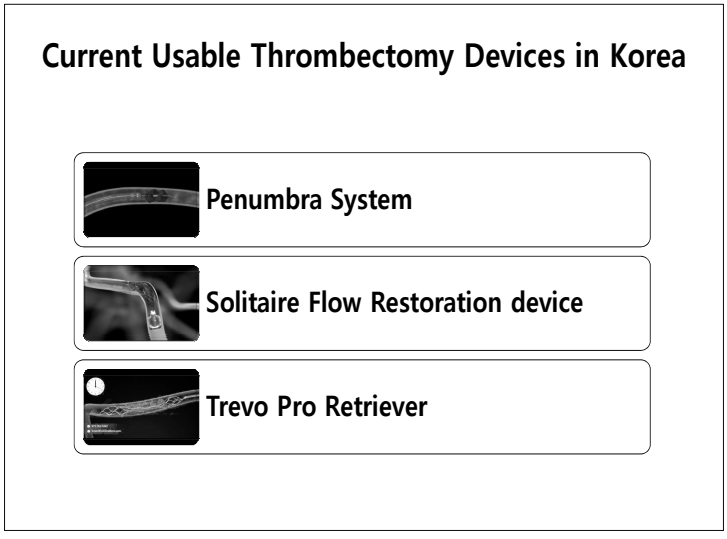
MEMO

Current status of Mechanical Thrombectomy

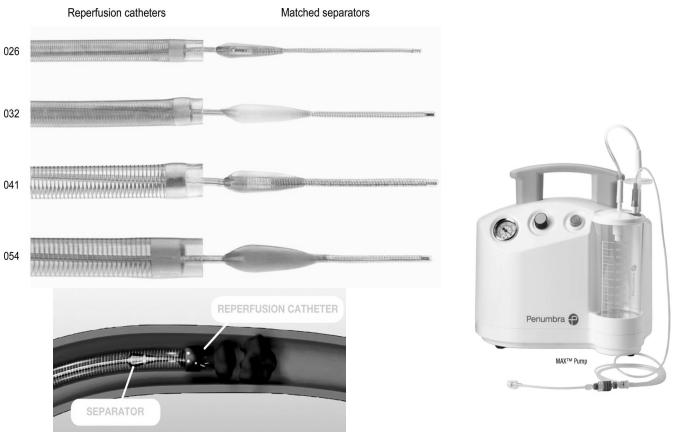
Yong-Cheol Lim
Ajou University School of Medicine Department of Neurosurgery

MEMO

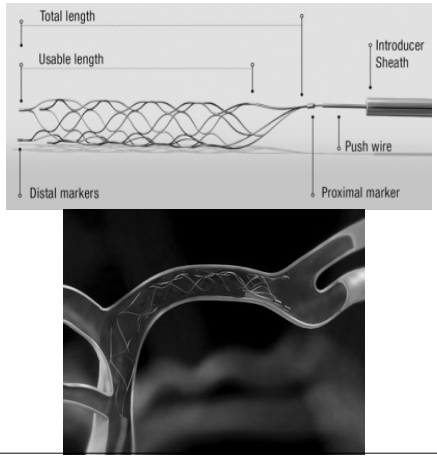




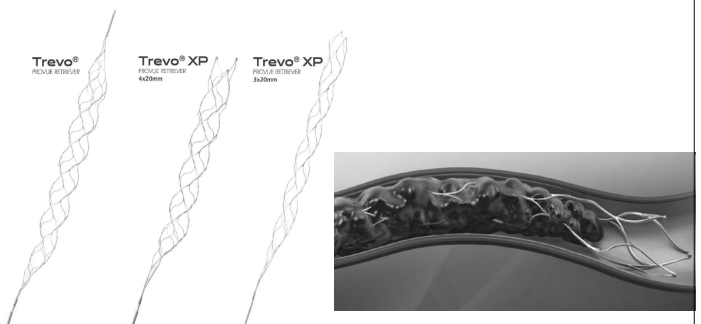
Penumbra System



Solitaire Flow Restoration device



Trevo Pro Retriever



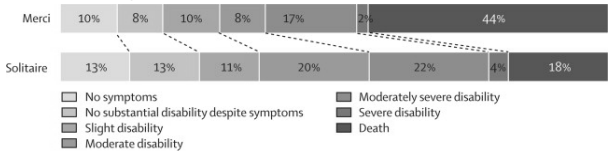
MEMO

MEMO

Lancet 2012;380:1241-1249

Solitaire flow restoration device versus the Merci Retriever in patients with acute ischaemic stroke (SWIFT)

- 18 center
- 58 Solitaire, 55 Merci

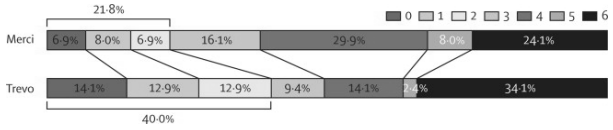


The Solitaire Flow Restoration Device achieved substantially better angiographic, safety, and clinical outcomes than did the Merci Retrieval System. The Solitaire device might be a future treatment of choice for endovascular recanalisation in acute ischaemic stroke.

Lancet 2012;380:1231-1240

Trevo versus Merci retrievers for thrombectomy revascularisation of large vessel occlusions in acute ischaemic stroke (TREVO 2): a randomised trial

- 26 center, 18-85 years, NIHSS 8-29, within 8h of Sx onset
- 88 Trevo, 90 Merci



Patients who have had large vessel occlusion strokes but are ineligible for (or refractory to) intravenous tissue plasminogen activator should be treated with the Trevo Retriever in preference to the Merci Retriever.

Early multi-center trials

(First-Generation Mechanical Thrombectomy Devices)

SYNTHESIS Expansion

Ciccone A et al. N Engl J Med 2013;368:904-913

IMS-III

Broderick JP et al. N Engl J Med 2013;368:893-903

MR RESCUE

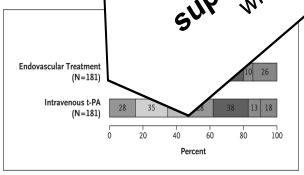
Kidwell CS et al. N Engl J Med 2013;368:914-923

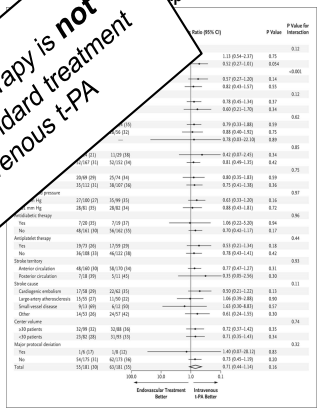
N Engl J Med 2013;368:904-913

SYNTHESIS Expansion

- **Treatment Group**
  - Active: IA drug / any device / both
  - Control: IV rtPA
- **Eligibility**
  - IV rtPA eligible: required
  - Time: 6hrs to IAT
  - Territory: any
  - NIHSS: ≤ 25
  - Prestroke function: mRS
  - ASPECT: no
  - Vascular imaging
  - other imaging
- **Primary En**
- **up**

endovascular therapy is **not** **superior** to standard treatment with intravenous t-PA

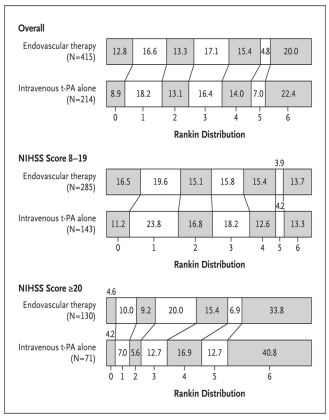




N Engl J Med 2013;368:893-903

IMS-III

- **Treatment Group**
  - Active: 2/3 standard dose IV rtPA + IA drug / any device / both
  - Control: IV rtPA
- **Eligibility**
  - IV rtPA eligible: required, ≤ 3hrs
  - Time: 5hrs to IAT
  - Territory: any
  - NIHSS: ≥ 10 or 8-9 with occlusion
  - Prestroke function: mRS 0-2
  - ASPECT: < 4
  - Vascular imaging: no
  - other imaging: > 1/3 MCA excluded
- **Primary Endpoint (mRS 0-1 at 3mos)**

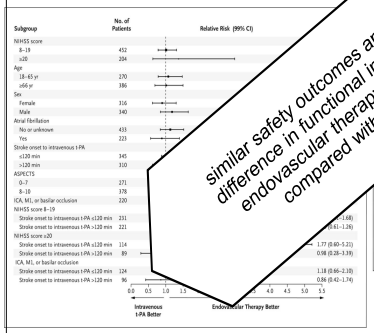


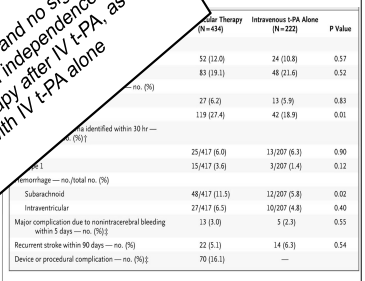
N Engl J Med 2013;368:893-903

IMS-III

- **Adjusted Relative Risk for Predefined Subgroups, mRS 0-2 at 90 Days**
- **ry Safety End Points**

similar safety outcomes and no significant difference in functional independence with endovascular therapy after IV t-PA, as compared with IV t-PA alone





MEMO

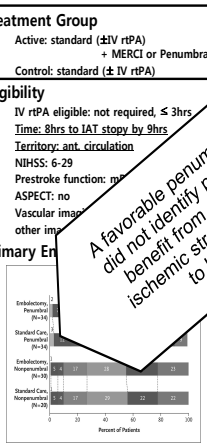
MEMO

N Engl J Med 2013;368:914-923

MR RESCUE

- **Treatment Group**
  - Active: standard (±IV rtPA) + MERCI or Penumbra
  - Control: standard (± IV rtPA)
- **Eligibility**
  - IV rtPA eligible: not required, ≤ 3hrs
  - Time: 8hrs to IAT stopy by 9hrs
  - Territory: ant. circulation
  - NIHSS: 6-29
  - Prestroke function: mr
  - ASPECT: no
  - Vascular imag
  - other im
- **Primary En**

A favorable penumbral pattern on neuroimaging did not identify patients who would differentially benefit from endovascular therapy for acute ischemic stroke, nor was embolectomy shown to be superior to standard care



Outcome	Study Group			P Value‡
	Embolectomy, Penumbral (N=34)	Standard Care, Penumbral (N=17)	Embolectomy, Nonpenumbral (N=19)	Standard Care, Nonpenumbral (N=20)	
					0.23
			4.0	4.4	
			4.0	4.0	
		2.8 to 4.0	3.4 to 4.6	3.6 to 5.2	
					0.30
		3.4	4.3	4.2	
		3.0	4.0	4.0	
	3.2 to 4.4	2.9 to 3.9	3.8 to 4.7	3.7 to 4.8	
	7 (21)	9 (26)	5 (17)	2 (10)	0.48
	14	23	9	10	0.39
	6 (18)	7 (21)	6 (20)	6 (30)	0.75
(%)					
matic	3 (9)	2 (6)	0	0	0.24
mptomatic	19 (56)	14 (41)	23 (77)	12 (60)	0.04
tal infarct volume					
No. of patients evaluated	32	32	30	19	
Median (interquartile range) — ml	58.1 (34.5 to 138.2)	37.3 (24.9 to 78.3)	172.6 (84.6 to 273.8)	217.1 (144.3 to 282.8)	<0.001¶
Absolute infarct growth					
No. of patients evaluated	32	32	30	19	
Median (interquartile range) — ml	27.1 (−0.5 to 89.1)	6.7 (−8.3 to 52.0)	55.1 (−33.2 to 104.8)	83.8 (24.1 to 137.5)	0.009‖
Reperfusion — no./total no. (%)**	16/28 (57)	14/27 (52)	7/19 (37)	6/12 (50)	0.59
Partial or complete revascularization — no./total no. (%)††	20/30 (67)	25/27 (93)	20/26 (77)	14/18 (78)	0.13

Latest multi-center trials

MR CLEAN	Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands
ESCAPE	Endovascular Treatment for Small Core and Anterior Circulation Proximal Occlusion with Emphasis on Minimizing CT to Recanalization Times
EXTEND-IA	Extending the Time for Thrombolysis in Emergency Neurological Deficits — Intra-Arterial
SWIFT PRIME	Solitaire with the Intention for Thrombectomy as Primary Endovascular Treatment
REVASCAT	Randomized Trial of Revascularization with Solitaire FR Device versus Best Medical Therapy in the Treatment of Acute Stroke Due to Anterior Circulation Large Vessel Occlusion Presenting within Eight Hours of Symptom Onset
THERAPY	The Randomized, Concurrent Controlled Trial to Assess the Penumbra System's Safety and Effectiveness in the Treatment of Acute Stroke
THRACE	The Contribution of Intra-arterial Thrombectomy in Acute Ischemic Stroke in Patients Treated With Intravenous Thrombolysis

N Engl J Med 2015;372:11-20

MR CLEAN

- **Treatment Group**
  - Active: standard (± IV rtPA) + IA UK, rtPA, device
  - Control: standard (±dose IV rtPA)
- **Eligibility**
  - IV rtPA eligible: not required
  - Time: 6hrs to IAT
  - Territory: ant. circulation
  - NIHSS: >2
  - Prestroke function: non
  - ASPECT: no
  - Vascular imaging: CTA, MRA, DSA
- **82% retrievable stents**

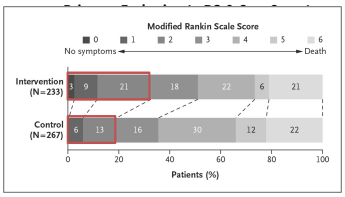


Table 2. Primary and Secondary Outcomes and Treatment Effects.*

Outcome	Intervention (N=233)	Control (N=267)	Effect Variable	Unadjusted Value (95% CI)	Adjusted Value (95% CI)†
Primary outcome: modified Rankin scale score at 90 days — median (interquartile range)	3 (2 to 5)	4 (3 to 5)	Common odds ratio	1.66 (1.21 to 2.28)	1.67 (1.21 to 2.30)
Secondary outcomes					
Clinical outcomes					
Modified Rankin score of 0 or 1 at 90 days — no. (%)	27 (11.6)	16 (6.0)	Odds ratio	2.06 (1.08 to 3.92)	2.07 (1.07 to 4.02)
Modified Rankin score of 0–2 at 90 days — no. (%)	76 (32.6)	51 (19.1)	Odds ratio	2.05 (1.36 to 3.09)	2.16 (1.39 to 3.38)
Modified Rankin score of 0–3 at 90 days — no. (%)	119 (51.1)	95 (35.6)	Odds ratio	1.89 (1.32 to 2.71)	2.03 (1.36 to 3.03)
NIHSS score after 24 hr — median (interquartile range)‡	13 (6 to 20)	16 (12 to 21)	Beta	2.6 (1.2 to 4.1)	2.3 (1.0 to 3.5)
NIHSS score at 5–7 days or discharge — median (interquartile range)§	8 (2 to 17)	14 (7 to 18)	Beta	3.2 (1.7 to 4.7)	2.9 (1.5 to 4.3)
Barthel index of 19 or 20 at 90 days — no./total no. (%)¶	99/215 (46.0)	73/245 (29.8)	Odds ratio	2.0 (1.3 to 2.9)	2.1 (1.4 to 3.2)
EQ-5D score at 90 days — median (interquartile range)‖	0.69 (0.33 to 0.85)	0.66 (0.30 to 0.81)	Beta	0.08 (0.00 to 0.15)	0.06 (−0.01 to 0.13)
Imaging outcomes					
No intracranial occlusion on follow-up CT angiography — no./total no. (%)**	141/187 (75.4)	68/207 (32.9)	Odds ratio	6.27 (4.03 to 9.74)	6.88 (4.34 to 10.94)
Final infarct volume on CT††					
Patients evaluated — no. (%)	138 (59.2)	160 (59.9)			
Median (interquartile range) — ml	49 (22 to 96)	79 (34 to 125)	Beta	20 (3 to 36)	19 (3 to 34)

- **proximal intracranial occlusion of the anterior circulation, IA treatment administered within 6 hours after stroke onset was effective and safe.**

N Engl J Med 2015; 372:1019-1030

ESCAPE

- **Treatment Group**
  - Active: standard (±IV rtPA) + stent retriever
  - Control: standard (± IV rtPA)
- **Eligibility**
  - IV rtPA eligible: not required
  - Time: 12hrs to IAT
  - Territory: ICA, MCA
  - NIHSS: >5
  - Prestroke function: Barthel ≥ 90
  - ASPECT: ≥6
  - Vascular imaging: CTA
  - other imaging: multiphase CTA/CTP for core size collateral
- **Primary Endpoint (mRS 0-2 at 3mos)**

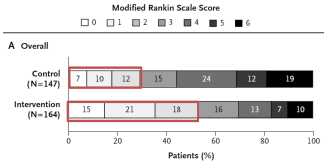


Table 2. Primary and Secondary Efficacy Outcomes.

Outcome	Intervention (N=165)	Control (N=159)	Difference (95% CI)*	Effect Variable	Unadjusted Value (95% CI)	Adjusted Value (95% CI)†
Primary outcome: modified Rankin score at 90 days‡				Common odds ratio	2.6 (1.7–3.8)	3.1 (2.0–4.7)
Modified Rankin score of 0–2 at 90 days — no./total no. (%)§	87/164 (53.0)	43/147 (29.3)	23.8 (13.2–34.4)	Rate ratio	1.8 (1.4–2.4)	1.7 (1.3–2.2)
NIHSS score of 0–2 at 90 days — no./total no. (%)	79/153 (51.6)	31/134 (23.1)	28.4 (17.8–39.2)	Rate ratio	2.2 (1.6–3.2)	2.1 (1.5–3.0)
Barthel Index score of 95–100 at 90 days — no./total no. (%)¶	94/163 (57.7)	49/146 (33.6)	24.1 (13.3–34.9)	Rate ratio	1.7 (1.3–2.2)	1.7 (1.3–2.2)
TICI score of 2b or 3 at final angiogram — no./total no. (%)‖	113/156 (72.4)					
Modified AOL score of 2 or 3 — no./total no. (%)**		43/138 (31.2)				
NIHSS score at 24 hours — median (interquartile range)††	6 (3–14)	13 (6–18)		Beta coefficient	4.0 (2.2–5.8)	4.1 (2.6–5.6)
NIHSS score at 90 days — median (interquartile range)††	2 (1–8)	8 (3–19)		Beta coefficient	6.5 (3.2–9.8)	6.5 (3.5–9.6)
EQ-5D visual-analogue scale score at 90 days — median (interquartile range)‡‡‡	80 (60–90)	65 (50–80)		Beta coefficient	9.4 (3.5–15.2)	9.9 (3.8–16.0)

- proximal vessel occlusion, a small infarct core, and moderate-to-good collateral circulation, rapid endovascular treatment improved functional outcomes and reduced mortality.

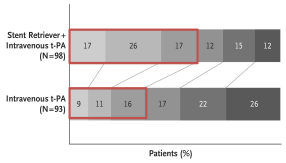
N Engl J Med 2015;372:2285-2295

SWIFT PRIME

- **Treatment Group**
  - Active: standard (±IV rtPA) + stent retriever
  - Control: standard (±IV rtPA)
- **Eligibility**
  - IV rtPA eligible: required
  - Time: 6hrs to groin
  - Territory: ICA, M1
  - NIHSS: 8-29
  - Prestroke function: mRS 0-1
  - ASPECT: ≥6
  - Vascular imaging: CTA, MRA
  - other imaging: CT/MRI mismatch
- **Primary Endpoint (mRS 0-2 at 3mos)**

Table 2. Primary and Secondary Outcomes.*

Outcome	Intravenous t-PA Alone (N=98)	Stent Retriever plus Intravenous t-PA (N=98)	Risk Ratio (95% CI)	P Value
Primary outcome: score on modified Rankin scale at 90 days†				<0.001
No. of patients with data	93	98		
Median score	3	2		
Interquartile range	2–5	1–4		
Secondary outcomes				
Clinical efficacy outcome				
Functional independence at 90 days — no./total no. (%)‡	33/93 (35)	59/98 (60)	1.70 (1.23–2.33)	<0.001
Change in NIHSS score at 27 hr				
No. of patients with data	92	97		
Mean change	−3.9±6.2	−8.5±7.1		<0.001
Death at 90 days — no./total no. (%)§	12/97 (12)	9/98 (9)	0.74 (0.33–1.68)	0.50
Revascularization outcome¶				
Substantial reperfusion immediately after thrombectomy — no./total no. (%)	NA	73/83 (88)	NA	NA
Successful reperfusion at 27 hr — no./total no. (%)	21/52 (40)	53/64 (83)	2.05 (1.45–2.91)	<0.001

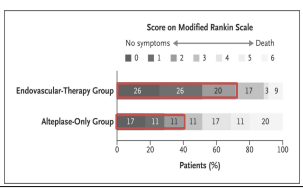


- In patients receiving IV t-PA for AIS d/t occlusions in the proximal anterior intracranial circulation, thrombectomy with a stent retriever within 6 hours after onset improved functional outcomes at 90 days.

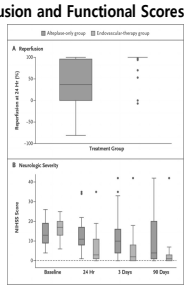
N Engl J Med 2015;372:1009-1018

EXTEND-IA

- **Treatment Group**
  - Active: standard (±IV rtPA) + stent retriever
  - Control: standard (± IV rtPA)
- **Eligibility**
  - IV rtPA eligible: required
  - Time: 6hrs to groin, complete in 8
  - Territory: ant. circulation
  - NIHSS: non
  - Prestroke function: mRS 0-1
  - ASPECT: no
  - Vascular imaging: CTA, MRA
  - other imaging: CT/MRI mismatch
- **mRS 0-2 at 3mos**



- **Reperfusion and Functional Scores**



- proximal cerebral arterial occlusion and salvageable tissue on CT perfusion imaging, early thrombectomy with the Solitaire FR stent retriever, as compared with alteplase alone, improved reperfusion, early neurologic recovery, and functional outcome.

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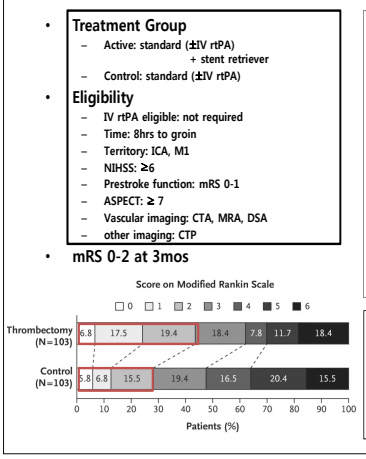
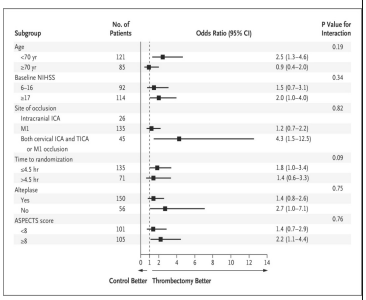
N Engl J Med 2015;372:2296-2306

REVASCAT

- **Treatment Group**
  - Active: standard (±IV rtPA) + stent retriever
  - Control: standard (±IV rtPA)
- **Eligibility**
  - IV rtPA eligible: not required
  - Time: 8hrs to groin
  - Territory: ICA, M1
  - NIHSS: ≥6
  - Prestroke function: mRS 0-1
  - ASPECT: ≥ 7
  - Vascular imaging: CTA, MRA, DSA
  - other imaging: CTP
- **mRS 0-2 at 3mos**





- **Among patients with anterior circulation stroke who could be treated within 8 hours after symptom onset, stent retriever thrombectomy reduced the severity of post-stroke disability and increased the rate of functional independence**

Recommendations (AHA 2015) EVT with a stent retriever

- **Patients should receive *(Class I; Level of Evidence A)***
  : EVT with stent retrievers is recommended over IA fibrinolysis as first-line therapy *(Class I; Level of Evidence E)*
- **Indication**
  - **Prestroke mRS score: 0 - 1**
  - **AIS receiving IV r-tPA within 4.5 hours of onset according to guidelines from professional medical societies**
  - **ICA or proximal MCA (M1) occlusion**
  - **age ≥18 years**
  - **NIHSS score: ≥6**
  - **ASPECTS: ≥6**
  - **groin puncture within 6 hours of symptom onset**
- **Reperfusion**
  : **TICI grade 2b/3** should be achieved as early as possible and **within 6 hours** of stroke onset *(Class I; Level of Evidence B-R)*
- **>6 hours from symptom onset + ICA or M1 occlusion**
  : the effectiveness is **uncertain** *(Class IIb; Level of Evidence C).*
- **anterior circulation + contraindications to IV r-tPA + within 6hr**
  : reasonable *(Class IIa; Level of Evidence C).*

Recommendations (AHA 2015) EVT with a stent retriever

- There are inadequate data available at this time to determine the clinical efficacy of EVT with stent retrievers for those patients whose contraindications are time-based or non-time based (eg, prior stroke, serious head trauma, hemorrhagic coagulopathy, or receiving anticoagulant medications). (New recommendation)
- **M2, M3, ACA, VA, BA, PCA occlusion + within 6hr**
  : the benefits are uncertain but reasonable *(Class IIb; Level of Evidence C)*
- **<18 years + large vessel occlusion + within 6hr**
  : may be reasonable *(Class IIb; Level of Evidence C)*
- **prestroke mRS score of >1, ASPECTS <6, or NIHSS score <6 + ICA, M1 occlusion**
  : the benefits are uncertain, but resonable within 6 hours *(Class IIb; Level of Evidence B-R)*
- **Observing patients after IV r-tPA**
  : **not required** and is not recommended. *(Class III; Level of Evidence B-R)*
- Use of stent retrievers is indicated in **preference to the MERCI device**. *(Class I; Level of Evidence A).*
- The use of mechanical thrombectomy devices other than stent retrievers may be reasonable in some circumstances *(Class IIb, Level B-NR).*

Recommendations (AHA 2015)

- The use of **proximal balloon guide catheter** or a **large bore distal access catheter** rather than a cervical guide catheter alone in conjunction with stent retrievers may be beneficial *(Class IIa; Level of Evidence C).*
- **Angioplasty and stenting** of proximal cervical atherosclerotic stenosis or complete occlusion at the time of thrombectomy
  : considerable, but the usefulness is unknown *(Class IIb; Level of Evidence C).*

Recommendations (AHA 2015) IA fibrinolysis

- Use of **salvage technical** adjuncts **including IA fibrinolysis**
  - may be reasonable, if completed within 6 hours of symptom onset
    (Class IIb; Level of Evidence B-R)
- **Initial treatment with IA fibrinolysis** is **beneficial** for carefully selected patients with major ischemic strokes of **<6 hours**' duration caused by **occlusions of the MCA** *(Class I; Level of Evidence B-R).*
- A clinically beneficial **dose of IA r-tPA is not established**, and r-tPA does not have FDA approval for IA use**.**
- IA fibrinolysis initiated within 6 hours of stroke onset in carefully selected patients who have contraindications to the use of IV r-tPA might be considered, but the consequences are unknown *(Class IIb; Level of Evidence C).*

Recommendations (AHA 2015) Images

- Emergency imaging of the brain is recommended before initiating any specific treatment for acute stroke *(Class I; Level of Evidence A).*
- If endovascular therapy is contemplated, a noninvasive intracranial vascular study is strongly recommended during the initial imaging evaluation
  : should not delay intravenous r-tPA
- The benefits of additional imaging beyond CT and CTA or MR and MRA, such as CT perfusion or diffusion- and perfusion-weighted imaging, for selecting patients for endovascular therapy are unknown *(Class IIb; Level of Evidence C).*
  : measures of infarct core, collateral flow status, and penumbra, are beneficial for selecting patients for acute reperfusion therapy who are within 6 hours of symptom onset and have an ASPECTS <6.
  : beyond 6 hours from symptom onset - controlled trials should be done

MEMO

Role of Surgical Embolectomy / Bypass Surgery in Acute Ischemic Stroke

박 익 성
가톨릭대학교 부천성모병원 신경외과

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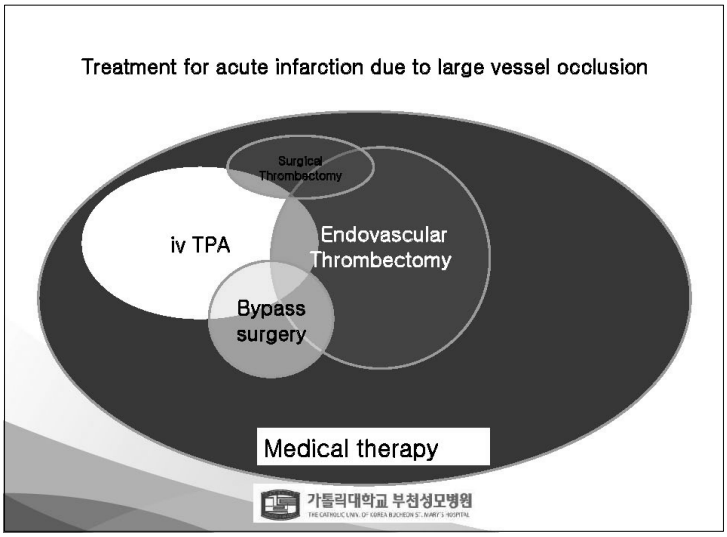

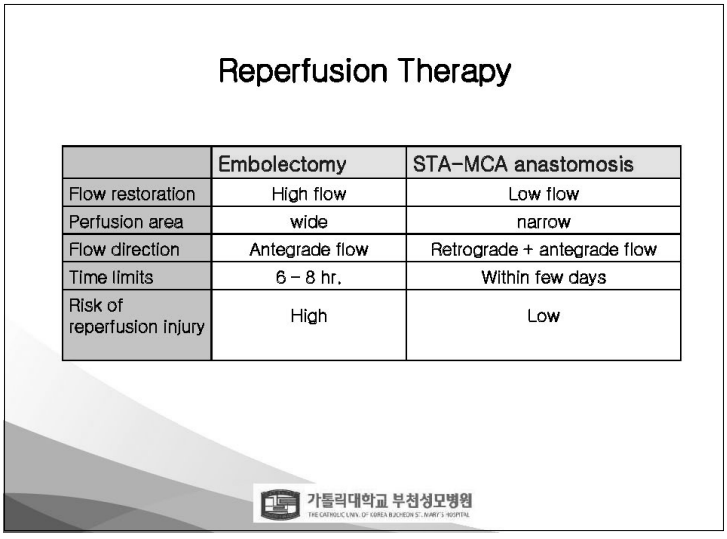

	Embolectomy	STA-MCA anastomosis
Flow restoration	High flow	Low flow
Perfusion area	wide	narrow
Flow direction	Antegrade flow	Retrograde + antegrade flow
Time limits	6 – 8 hr.	Within few days
Risk of reperfusion injury	High	Low

Surgical Thrombectomy Reports

- Excision of occlusive lesions of the middle cerebral artery. Welch K J Neurosurg 1956

Author	Year	Study type	No. of patients	Occluded vessel(s)	Mean occlusion time (min)	Outcome
Garrido [4]	1976	Case report	1	MCA right	360–420	Favourable
Gagliardi [3]	1983	Retrospective	4	MCA (4 left)	345	50% favourable, 50% poor
Chalif [2]	1983	Case report	1	ICA left	150	Favourable
Meyer [5]	1985	Retrospective	20	MCA (17 left, 3 right)	570–594	70% Favourable, 30% poor
Swann [8]	1986	Case report	1	MCA right	180	Favourable
Linksey [6]	1992	Case report	1	MCA left	270–300	Favourable
Linskey [7]	1993	Retrospective	2	MCA (2 left)	270–300	100% Favourable
Vazguez-Barquero [9]	1994	Case report	1	MCA left	240	Favourable
Kakinuma [10]	1999	Retrospective	10	MCA (5 left, 5 right)	441	40% Favourable, 60% poor
Sakai [11]	2008	Retrospective	14	2 ICA (2 right)	338	78% Favourable, 22% poor
Horiuchi [12]	2009	Retrospective	30	MCA (20 left, 10 right)	375	53% Favourable, 47% poor
Park [13]	2009	Retrospective	3	2 MCA (1 left, 1 right)	488	75% Favourable, 25% poor

Surgical Thrombectomy Reports

- Surgical embolectomy for large vessel occlusion of anterior circulation **Tomohiro Inoue** *British Journal of Neurosurgery* ***2013***
  - 23 case retrospective analysis
- Surgical embolectomy for internal carotid artery terminus occlusion **Tomohiro Inoue** *Neurosurg Rev* ***2015***
  - 25 case review
- Recent surgical embolectomy reports in endovascular era
- Neurosurgical service that can perform microsurgery but cannot perform endovascular surgery on a 24-h basis

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Surgical Thrombectomy Reports Summery

- Favorable factor : similar with EVT
  - Time window : within 6 hr. – 8 hr.
  - Type of embolus : red > white
  - Location : M2 > M1 > ICA + MCA
  - Good collaterals

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Considering Surgical Thrombectomy

- Unavailable / Failed EVT
- Origin of embolus
- Time limit
- Radiologic findings

- Highly effective
- Technique : Common vascular surgery
- Concept and skill – trainable

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Surgical Thrombectomy Indication

- Origin : cardioembolic, artery to artery
  - Contraindication : atherosclerotic occlusion
- Time window : same as endovascular thrombectomy – reperfusion injury
- Radiologic findings : reperfusion injury
  - infarction volume, location
  - Diffusion / Perfusion mismatching

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Approaching Route

- Pterional craniotomy
  - Anatomically familiar
  - Plan B : STA-MCA anastomosis
  - Wide exposure
- Transcilliary craniotomy
  - Shorter reperfusion time
  - Needs experience

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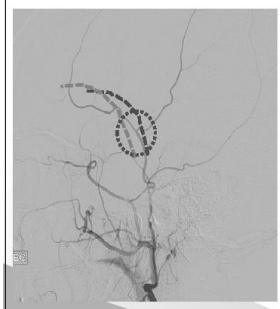
Pterional Craniotomy



- Needs not pin fixation
- Hair shaving – operation site
- STA identification: inspection or doppler
- Flap design : which vessel to be preserved
- Drape : wide as possible
- Incision : curvilinear around STA, need not flap preparation
- Muscle dissection : sub periosteal, short

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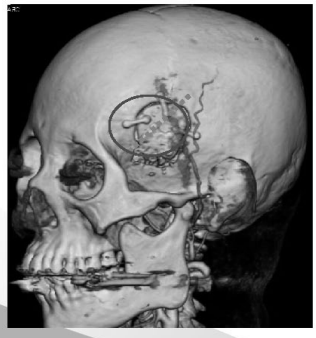
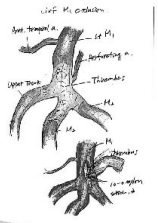
Pterional Craniotomy



- Craniotomy extent : including distal sylvian area – Chatter's point
- Sylvian dissection : lateral to medial
- Exposure : ICA, A1 proximal, MCA



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Arteriotomy Direction

- **Transverse incision**
- Multiple
- Atherosclerotic vessel
- Incisional injury
- Narrow orifice

- **Longitudinal incision**
- Wide opening
- Various closure technique
- Dissection

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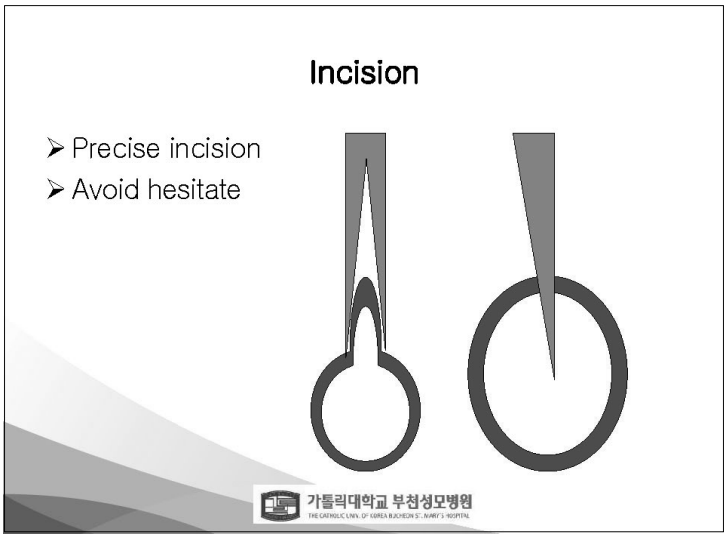
Incision
➢ Precise incision
➢ Avoid hesitate
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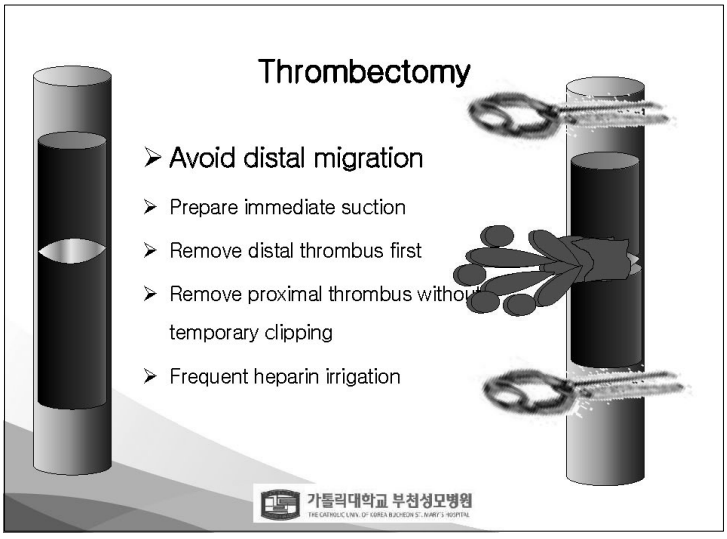
Thrombectomy
➢ Avoid distal migration
➢ Prepare immediate suction
➢ Remove distal thrombus first
➢ Remove proximal thrombus without
temporary clipping
➢ Frequent heparin irrigation
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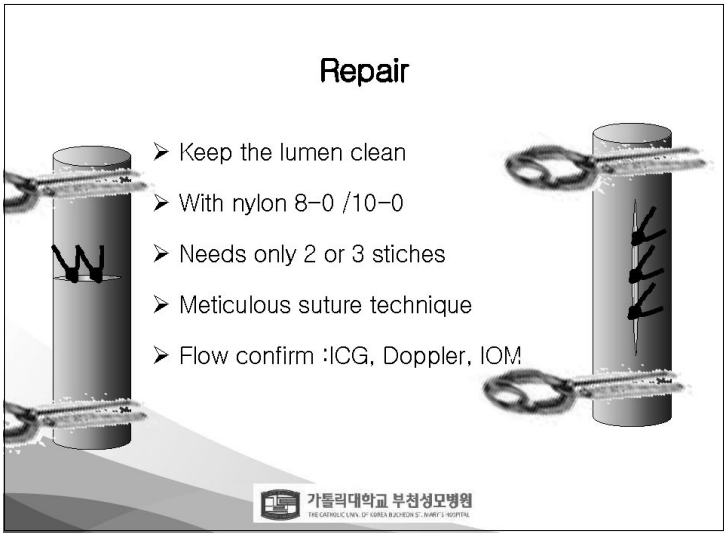
Repair
➢ Keep the lumen clean
➢ With nylon 8-0 /10-0
➢ Needs only 2 or 3 stiches
➢ Meticulous suture technique
➢ Flow confirm :ICG, Doppler, IOM
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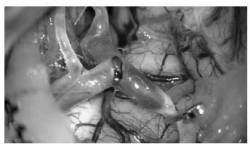
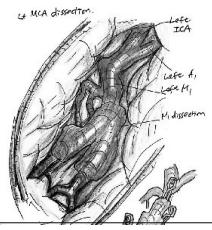
Unexpected Condition

- Waive thrombectomy
  - In-situ atherosclerotic occlusion
  - Dissection
- Long segment occlusion
  - Fogarty's balloon catheter
- Rethrombosis –reopen
  - Distal vessel occlusion – reperfusion
  - Suture site problem
- Additional bypass
  - In-situ
  - STA-MCA bypass



from Tomohiro Inoue *Neurosurg Rev* **2015**



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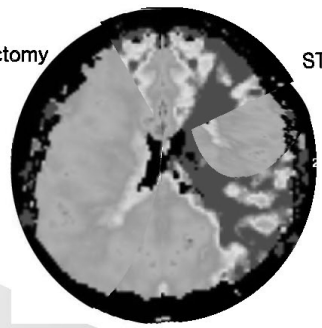
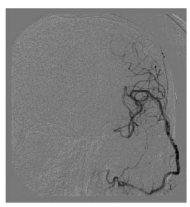
Reperfusion Amount

Surgical embolectomy



STA-MCA bypass



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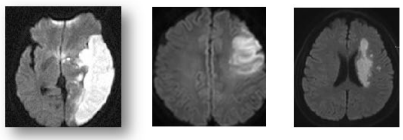
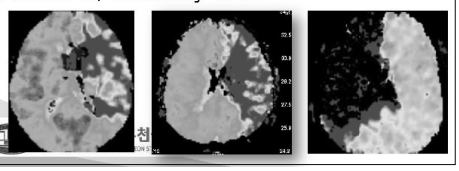
Factors for Reperfusion Injury

- Infarction volume/ location in DWI



- Perfusion defect volume/ severity in PI



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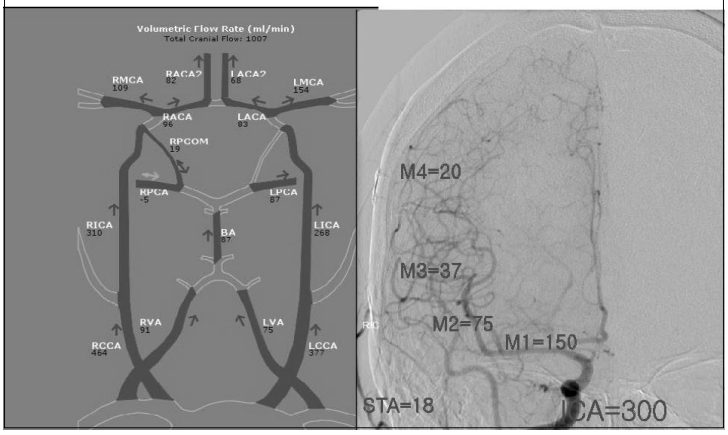
Cerebral Blood Flow Estimation



STA-MCA Bypass

- Low flow bypass
- Donor vessel diameter : 1 – 2mm
- Flow amount : 10 – 25 ml/min (40 ~ 80)
- Flap bypass
- Practical use
  - Ischemic disease
  - Aneurysm surgery
  - Tumor surgery

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Ischemic Cerebrovascular Disease

- Moyamoya disease
  - Ischemic presentation
  - Adult hemorrhagic presentation
- Atherosclerotic steno-occlusive disease
  - Chronic ischemic state – hemodynamic impairment ?
  - Acute infarction

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Surgical Role of STA-MCA Anastomosis In Secondary Stroke Prevention

- On June 24, 2010, the Carotid Occlusion Surgery Study (COSS) was stopped early by the US National Institutes of Health.
- JET 1 & JET 2 in Japan : controversial
- Fail to confirm the benefit of surgery in chronic state
  - Change of stroke incidence due to best medical therapy
  - Rate of surgery related complication

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Timing of STA-MCA Anastomosis

- 급성기는 피하자
  - 수술의 목적 : secondary prevention of stroke, 현 증상의 개선 ?
  - Reperfusion injury를 최소화 하기 위해
  - BBB stabilization시기를 지나자
- 뇌경색 발병 후 4-6주
  - 증상이 진행하고 고정된 환자는 제외됨

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Change The Strategy

- STA-MCA anastomosis on acute stage of infarction
  - Primary treatment – revascularization
  - Reperfusion injury – not higher than expected
  - Accumulated surgical experience in chronic state

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Bypass Surgery in Acute Ischemic Stroke

- Purpose of surgery – regional revascularization
  - Augmentation of collateral circulation by STA flow (15–60 ml/min)
  - Keeping adequate perfusion pressure on the distal part of occlusion
    - Reducing ischemic penumbra area – tissue saving
    - Prevention of core zone enlargement
  - Enhancing autolysis of thrombus
  - Improving functional outcome
- Considering
  - Diffusion volume : Reperfusion injury
  - Perfusion defect volume : ischemic penumbra – collateral circulation

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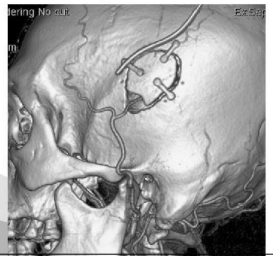
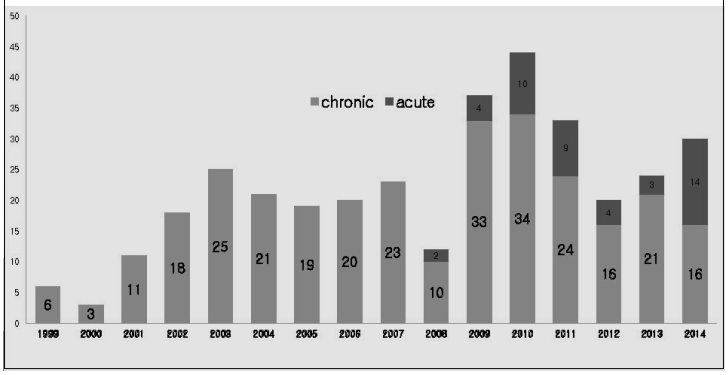
STA-MCA Anastomosis in Bucheon St. Mary's Hospital (BSMH)

- Presurgical selection of recipient site with radiologic study
- Small craniotomy with simplified procedure
- Keeping antiplatelet agent with cautious hemostasis



STA-MCA Anastomosis, Atherosclerotic Dis.

- Total 346 (300 +46) cases at Bucheon St. Mary's Hosp.



Surgery Related Complication
– Atherosclerotic Occlusion, Chronic State

- Hyper perfusion syndrome : 8 (2.6%)
- ICH : 3 (1%)
- Acute – SDH :2 (0.6%)
- Chronic – SDH :3 (1%)
- Subdural hygroma :6(2%)
- Wound infection: 1 (0.3%)

➢ Total 23 (7.7%) => 6 (2%)

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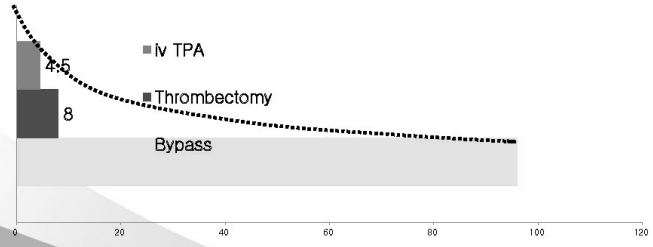
Advantage of Emergency STA-MCA Anastomosis

➢ Low incidence of reperfusion injury

➢ Wide time window



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Candidates of Surgery: BSMH
Neurologic Consideration

➢ Significant neurologic deficit
- NIHSS : ≥ 4
- Motor weakness : ≤ G III
- Language dysfunction

➢ Progressive infarction
- Initial good grade : NIHSS : < 4
- Symptom aggravation : NIHSS ≥ 2

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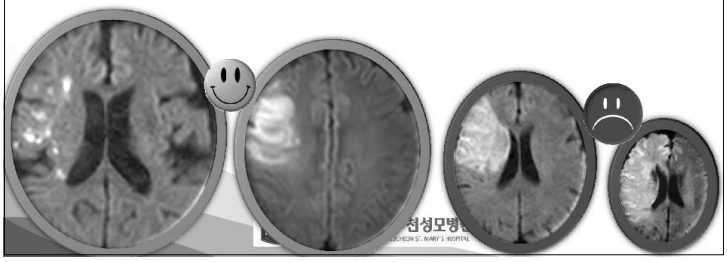
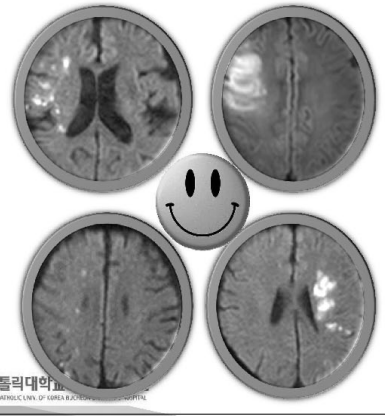
Candidates of Surgery: BSMH Radiologic Consideration

- Infarction volume : extent of cell damage
  - Correlation with clinical status severity
  - Correlation with outcome
  - Correlation reperfusion injury



Candidates of Surgery: BSMH Radiologic Consideration

- Infarction type :
  - Scattered subcortical
  - Small territorial
  - Watershed area
  - Perforator territory
  - Large territorial
  - Combined



Candidates of Surgery: BSMH Radiologic Consideration

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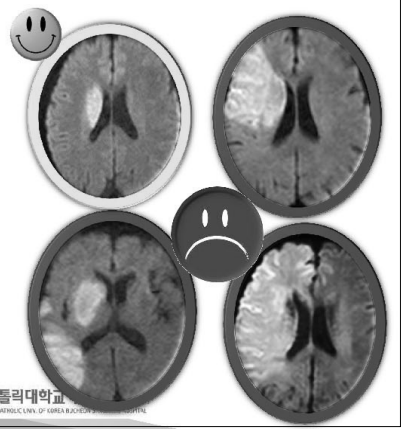
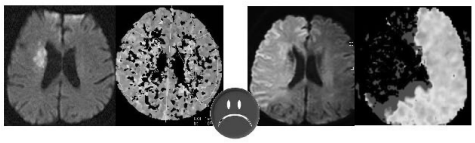
  - Large territorial
  - Combined

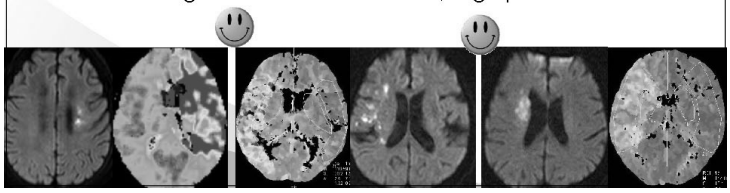


Candidates of Surgery: BSMH Radiologic Consideration

- Diffusion Perfusion consideration
  - Matching



  - Mismatching- small diffusion volume/large penumbra



Emergency STA-MCA Anastomosis :BSMH

- Total : 45 cases
- Progression : 22, Static : 23
- t-PA : 5
- IA - thrombectomy : 5
- Occlusion-reperfusion interval
  - Within 24 hr:13
  - 24 - 48 hr. : 13
  - Day 2-8: 21

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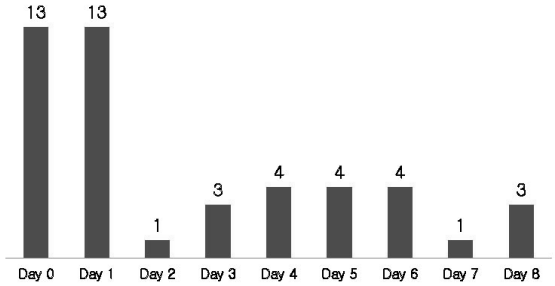
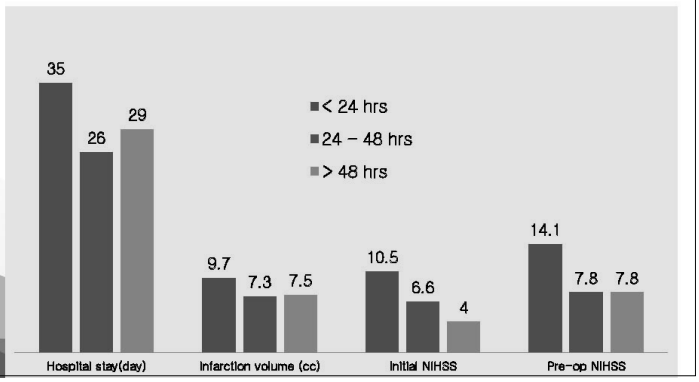
Distribution According Reperfusion Time



MEMO

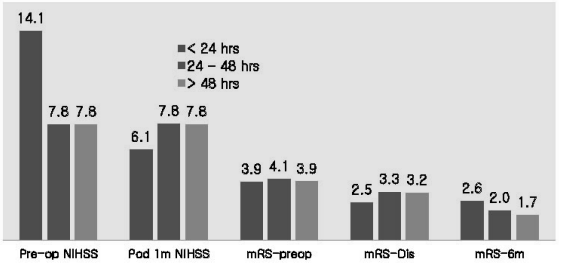
MEMO

Distribution According Reperfusion Time



Clinical Status Change

- NIHSS score : decrease at 24hr group
- Motor power : little change
- mRS : improved in all group



Emergency STA-MCA Anastomosis

- Total : 47 cases
- Progression : 24, Completed : 23
- t-PA : 5
- IA – thrombectomy : 5
- Occlusion-reperfusion interval
  - Within 24 hr:13
  - 24 – 48 hr. : 13
  - Day 2-8: 21

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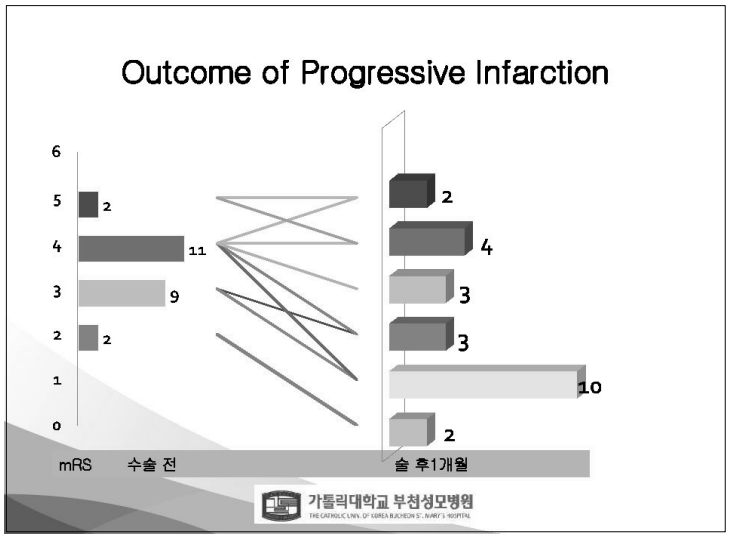

Prevention of Fatal Outcome ?

- Non – surgical group
  - Incidence of progression : 10 – 35 % of major infarction
  - Our series : 8/8 patients remained mRS 5 or 6 at last
- Surgical group
  - 24 of progressive infraction patients underwent emergency bypass surgery : mRS 0 – 5

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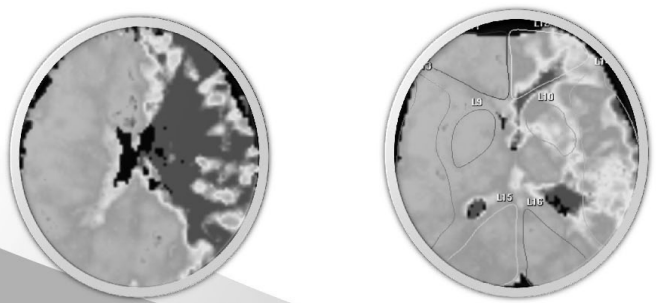
Flow Restoration

- Pre op

post op 1 week



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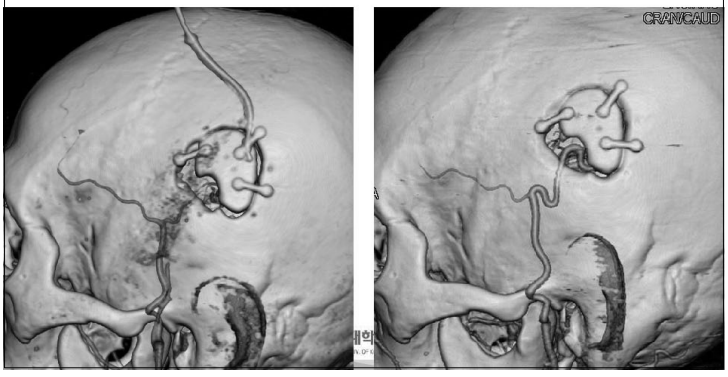
STA Size Change During 2 Weeks



Post Op Consideration

- Surgery related complication
  - Op site SDH, EDH : no revision, small craniotomy
  - Wound infection : 0
  - Reperfusion injury : 0
- Early rehabilitation
  - H/V removal : pod # 1 day
  - Open dressing : pod # 3 day

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Conclusion

- Surgical embolectomy : Like Army Training
- Surgical role of bypass in AIS : Primary treatment rather than prevention
- Evaluation of Hemodynamics :multimodal study
- Case selection : Favorable findings
- Time window << Radiologic window
- Reperfusion risk << Benefit
- Emergency or acute stage STA-MCA anastomosis is a good option for selected case of major vessel occlusion

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Journal of Cerebrovascular and Endovascular Neurosurgery

JCEN 논문 투고규정

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- Accepted file format for figure submissions: .jpg
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- Typeface: Times/Times New Roman or similar serif typeface.
- Body Text Size: 11pt
- Page Size: A4
- Margin: 3 cm on each side of the text
- Do not include author names or their institutions in headers or footers.
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- STROBE: Observational studies in epidemiology
- QUOROM: Systematic reviews
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- **Original Work**: Clinical and laboratory research articles on cerebrovascular disease.
- **Case Reports:** Clinical cases (individual or a series) should be unique and preferably be a first-time report/ a novel finding.
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This section not only presents any major findings of the study but also clearly and concisely details their significance. *Discussion* is a reiteration of the *Methods* and *Results* sections, but offers original insights and significance about the specific findings in the study. The authors may wish to use subheadings for organization and readability.

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Authored Book

Jefferson G. The Invasive Adenomas of the Anterior Pituitary. Springfield, IL. Charles C Thomas, 1995, p. 56-60.

Article or Chapter in an Edited Book

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