Stroke

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Case-Based Learning: Stroke

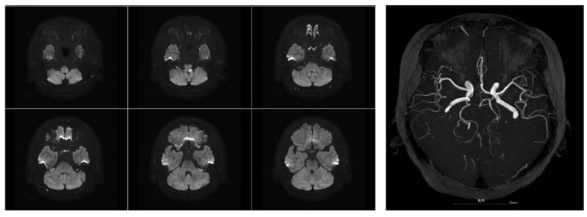
- **Case #1**
  - **Evaluation and treatment of embolic stroke with undetermined source**
- **Case #2**
  - Evaluation and treatment for patients with antiphospholipid antibody syndrome
- **Case #3**
  - Perfusion Imaging based thrombolysis and mechanical thrombectomy

Case Presentation #1

- 53세 여자 환자
- 갑자기 발생한 어지럼증으로 타원 내원함.
- 입원 치료 5일 째 갑자기 발생한 언어 장애, 우측 근력 저하로 전원.
- She had no history of hypertension, diabetes, or cancer
- N/E
  - Right hemiparesis Grade II
  - Global aphasia
  - Right facial palsy
  - ➢ NIHSS score 17

Case Presentation #1

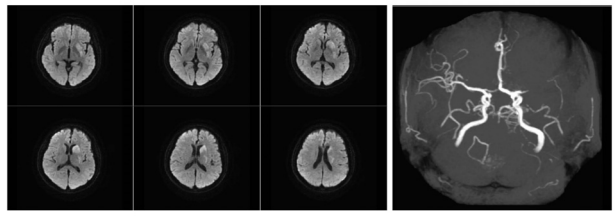
- Brain MRI/A (initial)



- Acute infarction in left lateral medullary.
- No significant steno-occlusive lesion or aneurysm.

Case Presentation #1

- Brain MRI/A (HD #5)



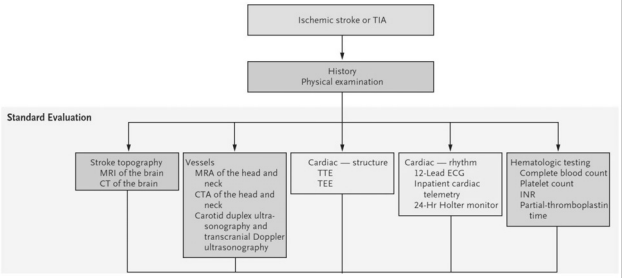
- Newly seen, acute infarction in left basal ganglia.
- Occlusion of mid-M1 segment of left MCA.

Case Presentation #1

- Mechanical thrombectomy

  - Mechanical thrombectomy with Trevo device was done, resulting in successful recanalization.
  - Recanalization of proximal M1 segment of left MCA.
  - NIHSS score 17 -> 1

Evaluation for Cryptogenic Stroke



NEJM 2016

Case Presentation #1

- Evaluation for embolic sources
  - EKG

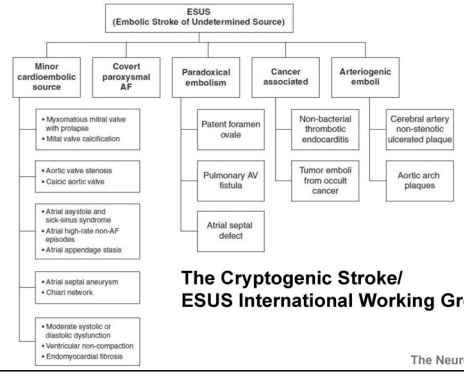
  - 24hr holter monitoring: Some PACs, isolated
  - TTE: Diastolic dysfunction, Gr 1

ESUS International Working Group

- **Necessary diagnostic assessment**
  - Embolic stroke of undetermined source (ESUS)
    - Brain CT or MRI showing non-lacunar infarct
    - Precordial echocardiography
    - ECG and cardiac monitoring for ≥24 h
    - Imaging of the extracranial and intracranial arteries supplying the area of the brain infarct
  - Cryptogenic ischemic stroke
    - Not specified

Lancet 2014
Med Clin 2018

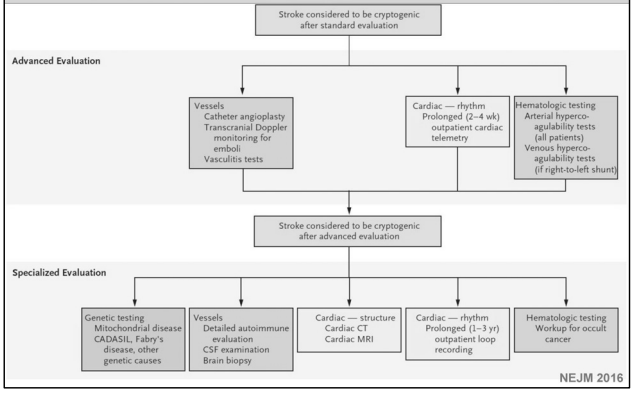
Potential causes of ESUS/Cryptogenic Stroke



The Cryptogenic Stroke/ ESUS International Working Group

Lancet 2014
The Neurologist 2017

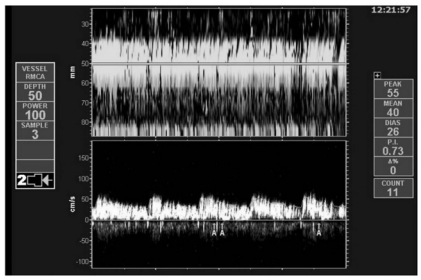
Evaluation for Cryptogenic Stroke



NEJM 2016

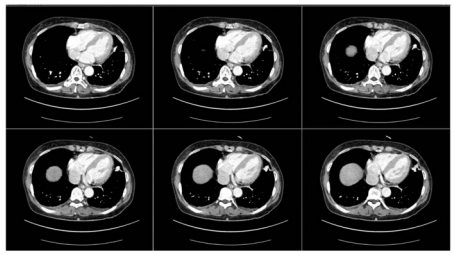
Case Presentation #1

- Evaluation for embolic sources
  - FDP 27.1 ug/ml, D-dimer 9.28 mg/L
  - TCD bubble test: positive HITs



Case Presentation #1

- Evaluation for embolic sources
  - TEE: No definite evidence of PFO or atrial septal aneurysm
  - Leg CTA: No definite evidence of DVT in this study
  - Chest CTA: No evidence of PTE

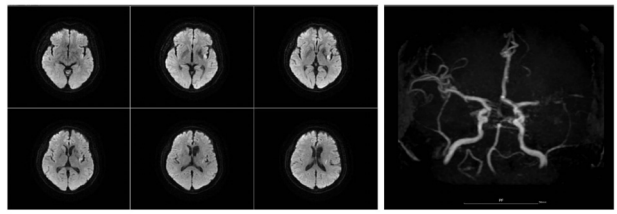


Case Presentation #1

- 55세 여자 환자
- 2시간 전 갑자기 발생한 언어 장애, 우측 근력 저하로 응급실 내원.
- 복용 중인 약물
  - Aspirin, Clopidogrel, Statin
- N/E
  - Right hemiparesis Grade II
  - Global aphasia
  - Right facial palsy
  - NIHSS score 12

Case Presentation #1

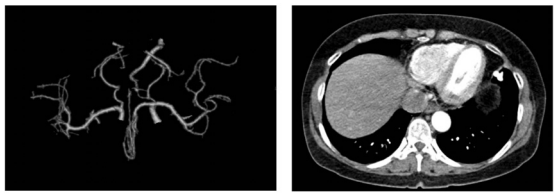
- Brain MRI/A



- Acute infarction in left posterolateral basal ganglia and insular lobe.
- Occlusion of mid-M1 segment of left MCA.

Case Presentation #1

- Intravenous thrombolysis



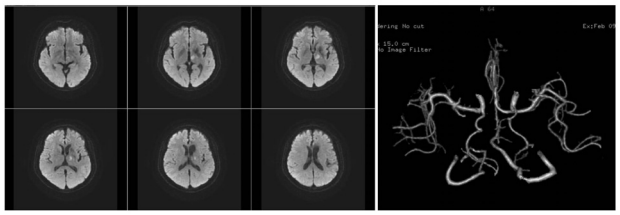
- Recanalization of proximal M1 segment of left MCA.
- NIHSS score 12 -> 0
- No remarkable change of pulmonary AVM.
- TEE: No PFO / Leg CTA: No DVT / Chest CTA: No PTE / 24hr holter: No AF

Case Presentation #1

- 56세 여자 환자
- 내원 1시간 전 갑자기 발생한 우측 감각 이상으로 내원.
- 복용 중인 약물
  - Aspirin, Cilostazol, Statin
- N/E
  - Right hypesthesia
  - Right hemiparesis Grade IV

Case Presentation #1

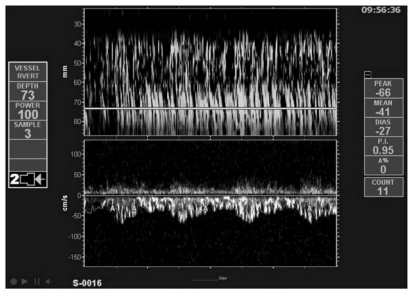
- Brain MRI



- Acute infarction in left thalamus.
- No evidence of aneurysm or significant steno-occlusive lesion.

Case Presentation #1

- TCD bubble test
  - Multiple HITs, Grade V

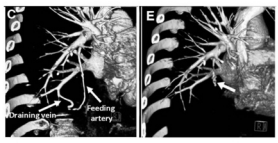


Case Presentation #1

- Treatment plan
  - Coil embolization of pulmonary AVM

without remnant nidus, mRS 0

vs



Computed tomography imaging confirming complete closure of the anomaly by the vascular plug (arrow).

JACC: Cardiovascular Intervention 2013

  - Antiplatelet vs Anticoagulant
    - In general, coils are associated with a 20% recanalization rate and 5% for vascular plugs.

The International Journal of Cardiovascular Imaging 2019

Case Presentation #1

- Anticoagulants *vs.* Antiplatelets
  - The majority of ischaemic strokes in patients with PAVM are treated with antiplatelet agents, which are generally tolerated well.
  - Antiplatelet agents are currently used selectively based on symptoms and previous history of TIA or ischaemic stroke.
  - Anticoagulants are rarely required for prevention of strokes due to PAVMs but may be required if there is concurrent atrial fibrillation or VTE.

Thorax 2017

- Medical treatment *vs.* Embolization
  - Endovascular embolization of the feeding artery can prevent the complications associated with PAVMs.
  - The procedure is minimally invasive, associated with minimum morbidity and high success rates.
  - With the advancements in the development of newer techniques and embolization materials, recanalization rates of PAVMs are expected to decrease.

The International Journal of Cardiovascular Imaging 2019

Case-Based Learning: Stroke

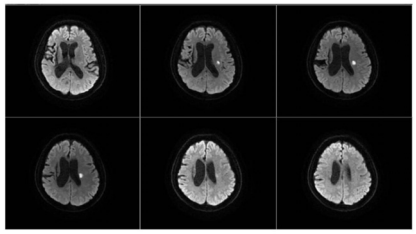
- **Case #1**
  - Evaluation and treatment of embolic stroke with undetermined source
- **Case #2**
  - **Evaluation and treatment for patients with antiphospholipid antibody syndrome**
- **Case #3**
  - Perfusion Imaging based thrombolysis and mechanical thrombectomy

Case Presentation #2

- 54세 남자 환자
- 1시간 반 전 갑자기 발생한 오른쪽 근력 저하로 내원함
- 과거력: 고혈압 (+), S-ICH (7년 전), 당뇨 (-), 고지혈증 (-), 종양 (-)
- N/E
  - Right hemiparesis Grade IV
  - Dysarthria
  - Right facial palsy
  - ➢ NIHSS score 4
- Acute treatment
  - Contraindication for rTPA

Case Presentation #2

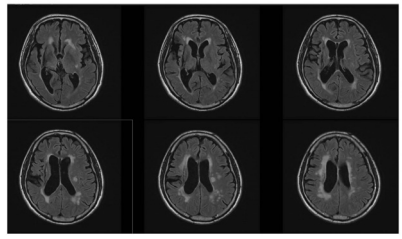
- Brain MRI



- Acute infarction in left corona radiata.
- Chronic hemorrhagic cavity in right basal ganglia.

Case Presentation #2

- Brain MRI



- Acute infarction in left corona radiata.
- Chronic hemorrhagic cavity in right basal ganglia.

Case Presentation #2

- Evaluation for risk factors
  - Anti cardiolipin Ab: Positive(47.7) GPL-U/mL
  - Anti Phospholipid Ab: Positive(41.6) GPL-IU/mL
  - B2-glycoprotein-1 IgG: Positive(43.2) U/mL
  - Hb A1c 8.6 %
- Follow up after 12 weeks
  - Anti cardiolipin Ab: Positive(44.2) GPL-U/mL
  - Anti Phospholipid Ab: Positive(43.7) GPL-IU/mL
  - B2-glycoprotein-1 IgG: Positive(42.5) U/mL

Case Presentation #2

- Treatment plan?
  - Anticoagulants *vs.* Antiplatelets
- Current AHA guideline
  - For patients with ischemic stroke or TIA who have an antiphospholipid antibody but who do not fulfill the criteria for antiphospholipid antibody syndrome, antiplatelet therapy is recommended (Class I; Level of Evidence B).
  - For patients with ischemic stroke or TIA who meet the criteria for the antiphospholipid antibody syndrome but in whom anticoagulation is not begun, antiplatelet therapy is indicated (Class I; Level of Evidence A).
  - For patients with ischemic stroke or TIA who meet the criteria for the APS, anticoagulant therapy might be considered depending on the perception of risk for recurrent thrombotic events and bleeding (Class IIb; Level of Evidence C).

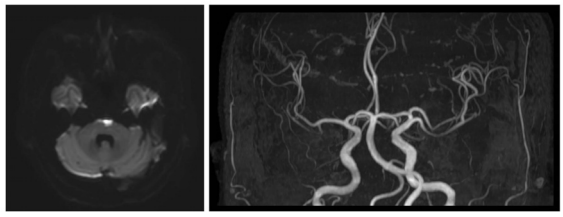
Stroke 2014

Case Presentation #2

- 57세 남자 환자
- 1시간 반 전 갑자기 악화된 오른쪽 근력 저하로 내원함
- 과거력: 고혈압 (+), S-ICH (8년 전), 당뇨 (+), 뇌경색 (3년 전)
- N/E
  - Right hemiparesis Grade III
  - Dysarthria
  - Right facial palsy
  - ➢ NIHSS score 2 → 6
- Acute treatment
  - Contraindication for rTPA

Case Presentation #2

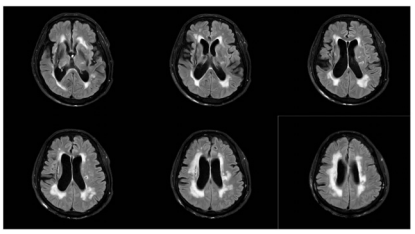
- Brain MRI/A



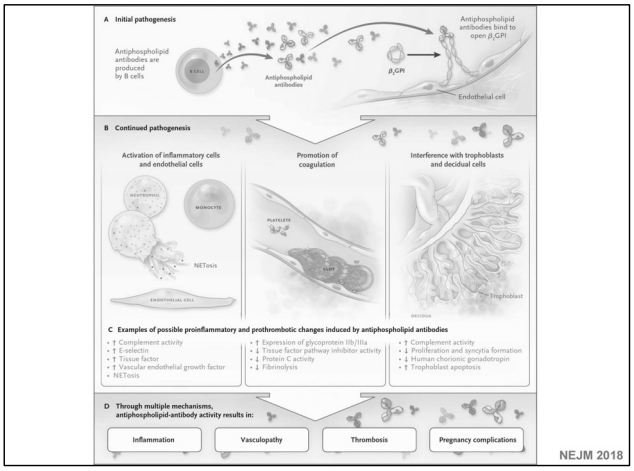
- Acute infarction in left ventral pons.
- No significant steno-occlusive lesion or aneurysm.

Case Presentation #2

- Brain MRI



- Acute infarction in left ventral pons.
- Diffuse brain atrophy with mild ventriculomegaly.
- Chronic small vessel ischemic disease.



NEJM 2018

Case Presentation #2

Table 2. Major Clinical Manifestations of the Antiphospholipid Syndrome That Are Not Included in the Revised Sapporo Classification Criteria.

Hematologic
Thrombocytopenia
More common: mild (platelet count, 50,000–150,000 per mm³), asymptomatic
Less common: severe (platelet count, <20,000 per mm³), with or without thrombotic microangiopathy
Hemolytic anemia
Without schistocytes, suggesting immune-mediated hemolytic anemia
With schistocytes, suggesting thrombotic microangiopathy
Renal
Acute thrombotic microangiopathy
Chronic vaso-occlusive lesions (cortical ischemia or infarction with arteriosclerosis, arteriolosclerosis, arterial fibrous intimal hyperplasia, glomerular ischemia, interstitial fibrosis, tubular thyroidization, tubular atrophy, organized thrombi with or without recanalization, or a combination of such lesions)
Cardiac
Valve vegetations or thickening (valve thickness >3 mm, thickening of the proximal or middle portion of the leaflet, or irregular nodules on the atrial face of the edge of the mitral valve, the vascular face of the aortic valve, or both)
Dermatologic
Livedo reticularis or racemosa
Livedoid vasculopathy (recurrent, painful skin ulcerations)
Neurologic
Cognitive dysfunction (in the absence of stroke)
Subcortical white-matter changes

NEJM 2018

Table 1. Key Concepts for Clinicians Evaluating the Results of Antiphospholipid-Antibody Testing.*

Key Concepts	Comments
Step 1: Understanding the basics	Antiphospholipid antibodies (aPL) are not only a diagnostic marker for APS but also a risk factor for thrombosis and pregnancy complications, which are commonly multifactorial. Thus, consideration of non-aPL thrombotic risk factors is critical in evaluating patients who are positive for aPL. Transient aPL positivity is common during infections.
Step 2: Assessing individual aPL tests	Not every positive aPL test is clinically significant.
LA testing	LA testing is a three-step functional coagulation assay to detect aPL.[19] The LA test correlates better with clinical events than do aCL and anti-β_2GPI tests.[20] False positive LA results may occur in patients treated with warfarin, heparin, or direct oral anticoagulants; thus the LA test should not be ordered for such patients (or should be interpreted with caution if performed). Given the lack of accuracy in LA determination and nonstandardized reporting of the results, the LA test report should be discussed with an experienced laboratory specialist or a clinician when the interpretation is difficult.
ELISA	The aCL and anti-β_2GPI antibodies (IgG, IgM, or IgA) are most commonly detected by ELISA; they should be tested by experienced laboratory specialists, given the relatively high variability among commercially available assays.[20] Moderate to high titers (40 GPL or MPL or 99th percentile) of aCL or anti-β_2GPI IgG or IgM (99th percentile) correlate better with aPL-related clinical events than do lower titers; IgG is more strongly associated with clinical events than is IgM.[21] Isolated moderate-to-high-titer aCL or anti-β_2GPI IgA is rare and of unknown clinical significance.
Step 3: Assessing the aPL profile	Assessment of the aPL profile has diagnostic implications and helps risk-stratify patients who are persistently positive for aPL. "Persistent" is defined as tested "on two or more occasions at least 12 weeks apart" based on the revised Sapporo classification criteria[1]; a high-risk aPL profile is more likely to remain positive when repeated, independent of the timing. For diagnostic purposes, both high- and moderate-risk aPL profiles are important; a high-risk profile provides more confidence in the diagnosis.
High risk†	A high-risk profile is defined as a positive LA test with or without a moderate-to-high-titer‡ of aCL or anti-β_2GPI IgG or IgM.
Moderate risk	A moderate-risk profile is defined as a negative LA test with a moderate-to-high titer‡ of aCL or anti-β_2GPI IgG or IgM.
Low risk	A low-risk profile is defined as a negative LA test with a low titer‡ of aCL or anti-β_2GPI IgG or IgM.
Clinical judgment	Clinical judgment is important if the LA test is performed on an anticoagulated patient, if the aPL profile is low-risk, if the aPL result for only a single time point is available, or if aCL or anti-β_2GPI IgA is the only positive aPL test.
Step 4: Understanding the future	Although LA, aCL, and anti-β_2GPI tests are the mainstay of APS diagnosis, several additional aPL tests have been developed recently; the clinical significance of other proposed aPL tests must be established with additional outcome-based studies.

NEJM 2018

Treatment for antiphospholipid antibody syndrome

- NEJM review
  - Low-dose aspirin (<100 mg per day)
    - Primary thrombosis prevention, if indicated, based on guidelines for cardiovascular disease prevention in the general population; secondary arterial thrombosis prevention, if patient has other risk factors for cardiovascular disease; prevention of pregnancy complications in pregnant patients with obstetrical or thrombotic APS or both; potential add-on treatment for recurrent thrombosis despite therapeutic-dose anticoagulant therapy
  - Warfarin
    - Secondary thrombosis prevention (INR, 2–3); target INR of 3–4 is a possible strategy for recurrent thrombosis despite therapeutic dose anticoagulant therapy
  - Statins
    - Potential add-on treatment for recurrent thrombosis despite therapeutic-dose anticoagulant therapy

NEJM 2018

Case-Based Learning: Stroke

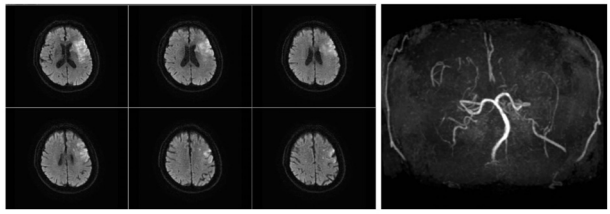
- **Case #1**
  - Evaluation and treatment of embolic stroke with undetermined source
- **Case #2**
  - Evaluation and treatment for patients with antiphospholipid antibody syndrome
- **Case #3**
  - **<u>Perfusion Imaging based thrombolysis and mechanical thrombectomy</u>**

Case Presentation #3

- 71세 남자 환자
- 8시간 전 갑자기 발생한 오른쪽 근력 저하 및 언어 장애로 내원함
- 과거력: 고혈압 (+), 당뇨 (+), 고지혈증 (-), 종양 (-)
- N/E
  - Right hemiparesis Grade III
  - Global aphasia
  - Right facial palsy
  - ➢ NIHSS score 12
- Acute treatment
  - Contraindication for rTPA

Case Presentation #3

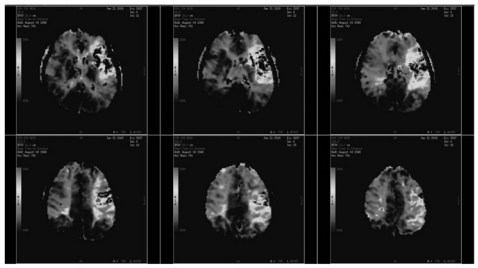
- Brain MRI/A



- Acute left superior divisional MCA territorial infarction
- No visible flow-related enhancement in both ICAs, both MCAs and both proximal ACAs.

Case Presentation #3

- Perfusion MRI



- Delayed MTT in both MCA territories (left>right), and perfusion defect in left fontal and insular lobes.

Case Presentation #3

- Treatment plan?
  - Conservative management vs Endovascular treatment

3.7. Mechanical Thrombectomy (Continued)	COR	LOE	New, Revised, or Unchanged
7. In selected patients with AIS within 6 to 16 hours of last known normal who have LVO in the anterior circulation and meet other DAWN or DEFUSE 3 eligibility criteria, mechanical thrombectomy is recommended.	I	A	New recommendation.
8. In selected patients with AIS within 16 to 24 hours of last known normal who have LVO in the anterior circulation and meet other DAWN eligibility criteria, mechanical thrombectomy is reasonable.	IIa	B-R	New recommendation.
The DAWN trial used clinical imaging mismatch (a combination of NIHSS score and imaging findings on CTP or DW-MRI) as eligibility criteria to select patients with large anterior circulation vessel occlusion for treatment with mechanical thrombectomy between 6 and 24 hours from last known normal. This trial demonstrated an overall benefit in function outcome at 90 days in the treatment group (mRS score 0–2, 49% versus 13%; adjusted difference, 33%; 95% CI, 21–44; posterior probability of superiority >0.999).[168] In DAWN, there were few strokes with witnessed onset (12%).The DEFUSE 3 trial used perfusion-core mismatch and maximum core size as imaging criteria to select patients with large anterior circulation occlusion 6 to 16 hours from last seen well for mechanical thrombectomy. This trial showed a benefit in functional outcome at 90 days in the treated group (mRS score 0–2, 44.6% versus 16.7%; RR, 2.67; 95% CI, 1.60–4.48; *P*<0.0001).[169] Benefit was independently demonstrated for the subgroup of patients who met DAWN eligibility criteria and for the subgroup who did not. DAWN and DEFUSE 3 are the only RCTs showing benefit of mechanical thrombectomy >6 hours from onset. Therefore, only the eligibility criteria from one or the other of these trials should be used for patient selection. Although future RCTs may demonstrate that additional eligibility criteria can be used to select patients who benefit from mechanical thrombectomy, at this time, the DAWN or DEFUSE-3 eligibility should be strictly adhered to in clinical practice.			See Table XXIII in online Data Supplement 1.

Stroke 2018

Case Presentation #3

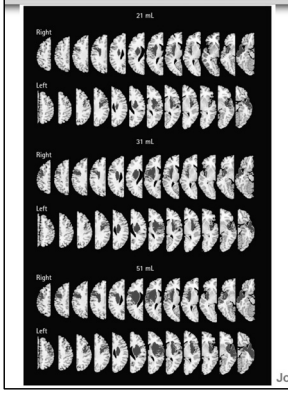
- DAWN Trial (6~24 hours)
  - Group A were 80 years of age or older, had a score of 10 or higher on the NIHSS, and had an infarct volume of less than 21 ml;
  - Group B were younger than 80 years of age, had a score of 10 or higher on the NIHSS, and had an infarct volume of less than 31 ml;
  - Group C were younger than 80 years of age, had a score of 20 or higher on the NIHSS, and had an infarct volume of 31 to less than 51 ml.

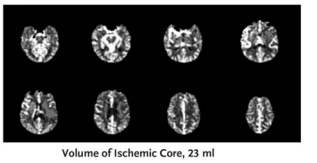
NEJM 2017

- DEFUSE 3 Trial (6~16 hours)
  - Patients were eligible if they had an initial infarct volume (ischemic core) of less than 70 ml, a ratio of volume of ischemic tissue to initial infarct volume of 1.8 or more, and an absolute volume of potentially reversible ischemia (penumbra) of 15 ml or more.

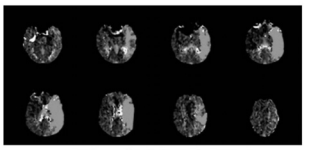
NEJM 2018

Case Presentation #3





Volume of Ischemic Core, 23 ml



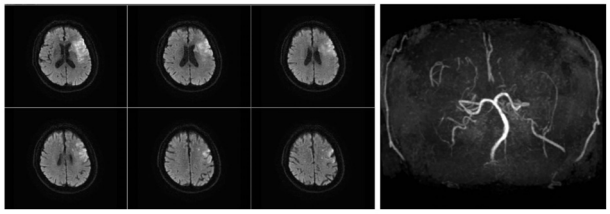
Volume of Perfusion Lesion, 128 ml

JoS 2019

NEJM 2018

Case Presentation #3

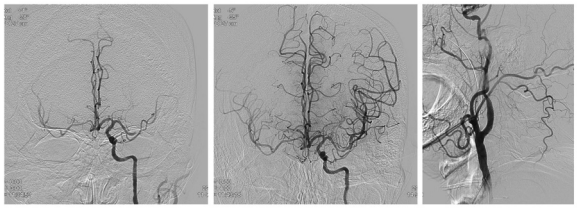
- Brain MRI/A



- Acute left superior divisional MCA territorial infarction
- No visible flow-related enhancement in both ICAs, both MCAs and both proximal ACAs.

Case Presentation #3

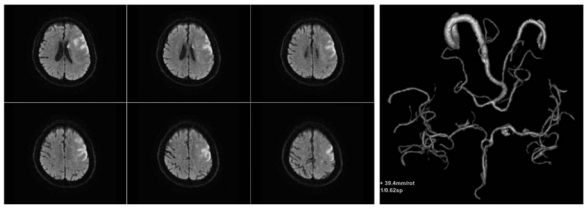
- Endovascular treatment



- Mechanical thrombectomy was done for intracranial occlusion at distal M1 segment of left MCA, resulting in successful intracranial recanalization.
- Balloon angioplasty and stent implantation were done for occlusion in proximal cervical segment of left ICA, resulting in successful recanalization.

Case Presentation #3

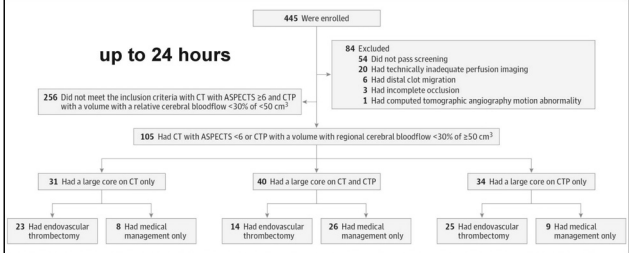
- f/u Brain MRI & CTA (HD #5)



- Right hemiparesis Grade III, Global aphasia (NIHSS score 12, mRS 4)
  - ➢ 퇴원시 Right hemiparesis Grade IV, Aphasia (-) (NIHSS score 4, mRS 2)
  - ➢ 3개월 째: Right hemiparesis Grade IV+ (NIHSS score 2, mRS 1)

EVT in Patients With Large Ischemic Cores

Figure 1. Flowchart of Patients Enrolled in the Optimizing Patient's Selection for Endovascular Treatment in Acute Ischemic Stroke (SELECT) Study, Patients With Large Cores, and Distribution Based on Treatment and Imaging Profile



The number enrolled refers only to the 445 individuals who were eligible after screening and consented to participate. ASPECTS indicates Alberta Stroke Program Early CT Score; CT, computed tomography; and CTP, computed tomographic perfusion (imaging).

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EVT in Patients With Large Ischemic Cores

Figure 2. Ninety-Day Modified Rankin Scale Score Distribution in Patients Treated With Endovascular Thrombectomy vs Medical Management Only

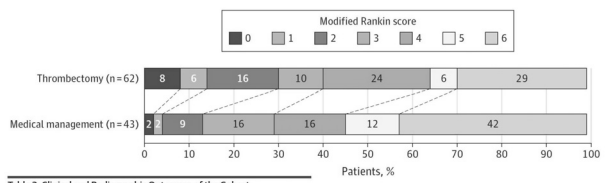

Table 2. Clinical and Radiographic Outcomes of the Cohort Based on Treatment Received

Characteristic	Patients, No. (%) Endovascular Thrombectomy (n = 62)	Medical Management Only (n = 43)	P Value
Final infarct volume, median (IQR), cm³	97 (43-189)	190 (127-252)	.001[f]
Infarct growth, median (IQR), cm³	44 (1-108)	98 (63-149)	.006[f]

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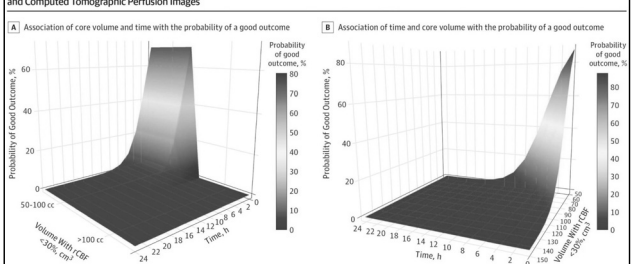
Figure 3. Association of Time and Stroke Size With Thrombectomy Outcomes in Patients With Large Core on Computed Tomographic and Computed Tomographic Perfusion Images



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Thrombolysis Guided by Perfusion Imaging up to 9 Hours after Onset of Stroke

- Patients were eligible for inclusion
  - Perfusion lesion–ischemic core mismatch was defined as a ratio greater than 1.2 between the volume of hypoperfusion and the volume of the ischemic core, an absolute difference in volume greater than 10 ml, and an ischemic-core volume of less than 70 ml.

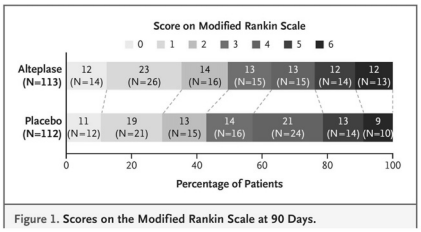

Figure 1. **Scores on the Modified Rankin Scale at 90 Days.**

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Thank you for your attention.