급성기 및 아급성기 뇌졸중 치료

서 우 근
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- Anti-thrombotics
- Blood pressure management
- Prevention and Management of complication
- Early rehabilitation
- Intercommunication with patients/care givers

Contents

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- Prevention and Management of complication
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- Anti-thrombotics
- Early rehabilitation
- Intercommunication with patients/care givers

Category	Recommendation	Class	LOE
Stroke unit	Comprehensive specialized stroke care (stroke unit)	I	A
Standardized order	The use of standardized stroke care order sets	I	A
Arterial hypertension	Anti-HTN should be withheld unless SBP>220mmHg or DBP>120mmHg. BP reduction 15% during the first 24 hours	I	C
Cardiac monitoring	Cardiac monitoring should be performed at least the first 24 hours	I	B
Cardiac output	Reducing cardiac output (hypovolemia, arrhythmia) should be corrected.		
Respiratory care	Airway support or ventilatory assistance for stroke with decreased consciousness or bulbar dysfunction	I	C
Supplementary oxygen	Maintain oxygen saturation > 94%	I	C
Swallowing test	Assessment of swallowing before the patients begins eating	I	B
Anti-thrombotics	Oral Administration of ASA within 24-48 hours	I	B
Nutrition	NG, nasoduodenal, or PEG tube feeding for patients who cannot take orally	I	B
Pneumonia or UTI	Appropriate antibiotics	I	A
DVP prevention	Subcu. Anticoagulation for immobilized patients	I	A
Brain edema and ICP	Measure the risk of edema and close monitoring of neurological worsening during the first days after stroke	I	A
Decompression	Decompressive surgical evacuation space-occupying cerebellar infarction	I	B
Decompression	Decompressive surgery for malignant edema of cerebral hemisphere	I	B
Recurrent seizure	Recurrent seizures after stroke treatment, antiepileptic selection by specific patient characteristics	I	B

Stroke Unit and Cardio/Neurological Monitoring

- The use of comprehensive specialized stroke care (stroke units) that incorporates rehabilitation is recommended (Class I; LOE A).
- 뇌졸중 환자는 뇌졸중 전문치료실 혹은 뇌졸중 센터(일차 혹은 포괄적)에서 치료하는 것이 권장된다. (근거수준Ia, 권고수준A)

- Regular communication, coordinated care
- Standardized stroke order/integrated stroke pathways
- Reduce mortality/diability, increase thrombolysis

Table 3. Mortality at Designated Stroke Centers and Nondesignated Hospitals

	No. (%)			
	Designated Stroke Center (n = 15 297)	Nondesignated Hospital (n = 15 650)	Adjusted Mortality Difference (95% CI)[a]	*P* Value
1 d	90 (0.6)	134 (0.9)	−0.3 (−0.6 to −0.0)	.04
7 d	665 (4.3)	842 (5.4)	−1.3 (−2.1 to −0.6)	.001
30 d	1543 (10.1)	1951 (12.5)	−2.5 (−3.6 to −1.4)	<.001
1 y	3412 (22.3)	4067 (26.0)	−3.0 (−4.4 to −1.5)	<.001

Abbreviation: CI, confidence interval.
[a]Negative values indicate lower mortality at designated stroke center vs nondesignated hospital. Adjusted for age, sex, race, health insurance status, rural status, 13 Charlson comorbid conditions, atrial fibrillation, hospital teaching status, and total number of hospital beds by using the instrumental variable analysis.

JAMA 2011;305:373-380

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Major Elements of Primary Stroke Center

Primary Care Area	Supportive services
Acute stroke teams	Commitment and support of medical organization: a stroke center director
Written care protocols	Neuroimaging services
Emergency medical services	Laboratory services
Stroke unit	Outcome and quality improvement activities
Neurosurgical services	Continuing medical education

JAMA 2000;283:3102-3109

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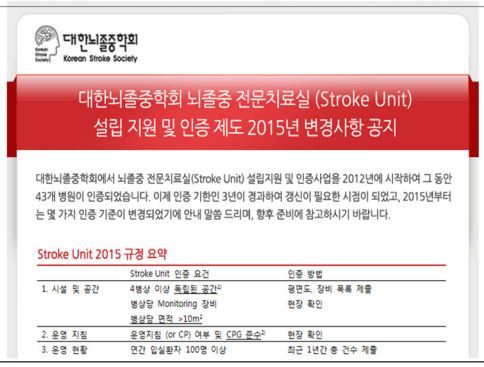

대한뇌졸중학회
Korean Stroke Society

대한뇌졸중학회 뇌졸중 전문치료실 (Stroke Unit)
설립 지원 및 인증 제도 2015년 변경사항 공지

대한뇌졸중학회에서 뇌졸중 전문치료실(Stroke Unit) 설립지원 및 인증사업을 2012년에 시작하여 그 동안 43개 병원이 인증되었습니다. 이제 인증 기한인 3년이 경과하여 갱신이 필요한 시점이 되었고, 2015년부터는 몇 가지 인증 기준이 변경되었기에 안내 말씀 드리며, 향후 준비에 참고하시기 바랍니다.

Stroke Unit 2015 규정 요약

	Stroke Unit 인증 요건	인증 방법
1. 시설 및 공간	4병상 이상 독립된 공간[1] 병상당 Monitoring 장비 병상당 면적 >10m²	평면도, 장비 목록 제출 현장 확인
2. 운영 지침	운영지침 (or CP) 여부 및 CPG 준수[2]	현장 확인
3. 운영 현황	연간 입실환자 100명 이상	최근 1년간 총 건수 제출

Stroke Unit and Cardio/Neurological Monitoring

- Airway support and ventilatory assistance are recommended for the treatment of patients with acute stroke who have decreased consciousness or who have bulbar dysfunction that causes compromise of the airway (Class I, LOE C)
- Supplemental oxygen should be provided to maintain oxygen saturation > 94% (Class I, LOE C).
- Supplemental oxygen is not recommended in nonhypoxic patients with acute ischemic stroke (Class III; LOE B)

- 의식저하 또는 호흡기 계통의 장애를 보이는 환자에서는 기관내 삽관 및 필요한 경우 기계호흡을 시행하는 것이 권장되며, 연수마비로 인한 호흡장애가 우려되는 환자에서도 기관내 삽관이 도움이 될 수 있다 (근거수준 IV, 권고수준 C).
- 저산소증이 없는 뇌경색 환자에의 추가적 산소공급은 권장되지 않는다 (근거수준 III, 권고수준 B)

Stroke Unit and Cardio/Neurological Monitoring

- Cardiac monitoring is recommended to screen for AF and other potentially serious cardiac arrhythmias that would necessitate emergency cardiac interventions. Cardiac monitoring should be performed for at least the first 24 hours (Class I; LOE B).

- 뇌경색 급성기 동안 심장리듬의 모니터링이 고려된다(근거수준 IV, 권고수준 C).

ECG Characteristics of AF (2014 ACC guideline)

- Irregular R-R interval
- Absence of distinct repeating P waves,
- Irregular atrial activity

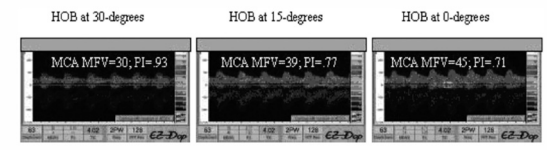
Classification of Atrial Fibrillation

Term	Definition
Paroxysmal AF	AF that terminates spontaneously or with intervention within 7 d of onset Episodes may recur with variable frequency
Persistent AF	Continuous AF that is sustained > 7d
Longstanding persistent AF	Continuous AF of >12mo duration
Permanent AF	• Permanent AF is used when there has been a joint decision by the patients and clinician to cease further attempt to restore and/or maintain sinus rhythm. • Acceptance of AF represents a therapeutic attitude on the part of the patient and clinician rather than an inherent pathophysiological attribute of the AF. • Acceptance of AF may change as symptoms, the efficacy of therapeutic interventions, and patient and clinician preference evolve.
Nonvalvular AF	AF in the absence of rheumatic mitral stenosis, a mechanical or bioprosthetic heart valve, or mitral valve repair

Patients position

Patients' position?

- Data indicate patients positioning can influence oxygen saturation, CPP, MCA mFV, and ICP.
- In ischemic stroke patients, the supine or side position has minimal effect on oxygen saturation.
- Thus, in nonhypoxic patients able to tolerate lying flat, a supine position is recommended.
- Consideration is needed for cardiopulmonary condition, sore, and airway obstruction.



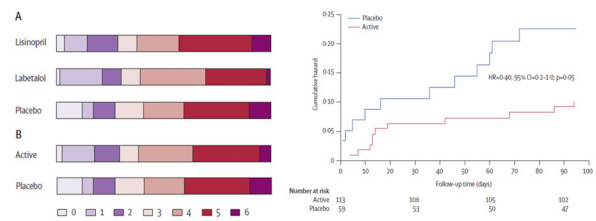
Neurology. 2005;64(8):1354-7

Blood Pressure & Hemodynamic Consideration

- In patients with markedly elevated blood pressure who do not receive fibrinolysis, a reasonable goal is to lower blood pressure by 15% during the first 24 hours after onset of stroke. The level of blood pressure that would mandate such treatment is not known, but consensus exists that medications should be withheld unless the systolic blood pressure is >220mmHg or the diastolic blood pressure is > 120mmHg (Class I, LOE C).
- The management of arterial hypertension ins patients not undergoing reperfusion strategies remains challenging …….Patients who have malignant hypertension or other medical indications for aggressive treatment of blood pressure should be treated accordingly. (Class IIb; LOE C)
- 급성기 허혈성 뇌경색 환자에서 SBP 220mmHg 또는 DBP 120mmHg 이하의 경우에는 적극적인 강압제의 사용을 유보하는 것이 권장된다. (근거수준 IV, 권고수준 C).
- 급성기 허혈성 뇌졸중 환자에서 일률적인 혈압 강하는 추천되지 않지만, 고혈압으로 인한 합병증 발생이 우려되는 상황에서는 적절한 혈압 강하가 필요하다. 고혈압성 뇌병증, 신동맥이 침범된 대동맥 파리 (근거수준 Ia, 권고수준 A), 심장기능부전, 대동맥 박리, 급성심근경색, 급성신장기능부전, 정맥내 혜파린정주 (근거수준 IV, 권고수준 C).

CHHIPS (Controlling Hypertension and hypotension immediately post-stroke)

- Effects of Immediate Blood Pressure Reduction on outcome in acute stroke (149 ischemic, 25 PICH)
- Intervention:
  - Active: Labetalol or lisinopril vs placebo
- End-points: Death or dependency at 2 wks



Lancet Neurol 2009;8:48-56

Acute BP trials in ischemic stroke: Candesartan

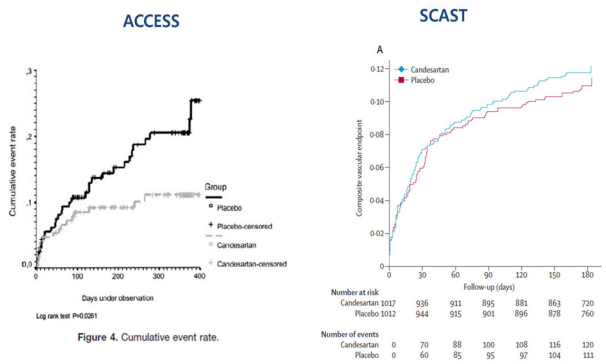
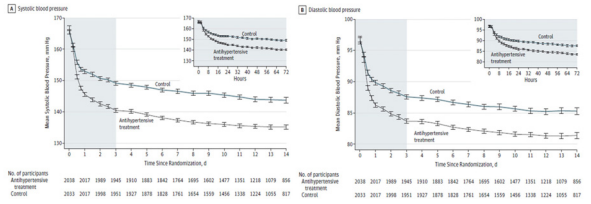


Figure 4. Cumulative event rate.

Lancet 2011;377:741-750, *Stroke* 2003;34:1699-1703

CATIS (the Chinese Antihypertensive Trial in Acute Ischemic Stroke)

- Effects of Immediate Blood Pressure Reduction on outcome in acute ischemic stroke
- Subjects: 4071 Chinese acute ischemic stroke, SBP 140 ~ 220mmHg
- Intervention:
  - Intensive: Lowering BP by 10~25% (first 24h; target 140/90mmHg)
  - Control: not receiving antihypertensives
- End-points: Death or major disability at 14 ds



JAMA 2014;311:479-489

CATIS (the Chinese Antihypertensive Trial in Acute Ischemic Stroke)

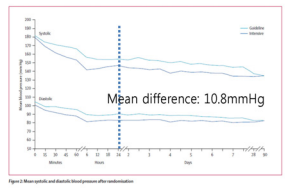
Table 2. Blood Pressure Reduction and Primary and Secondary Outcomes at 14 Days or Hospital Discharge

Variable	Antihypertensive Treatment (n = 2038)	Control (n = 2033)	Blood Pressure Difference or OR (95% CI)	P Value
Blood pressure reduction				
Blood pressure at 24 h after randomization, mean (SD), mm Hg				
Systolic	144.7 (15.0)	152.9 (15.9)	−8.1 (−9.1 to −7.2)	<.001
Diastolic	85.9 (8.9)	89.6 (9.6)	−3.8 (−4.3 to −3.2)	<.001
Absolute blood pressure changes from baseline to 24 h after randomization, mean (SD), mm Hg				
Systolic	−21.8 (15.9)	−12.7 (17.3)	−9.1 (−10.2 to −8.1)	<.001
Diastolic	−11.0 (10.5)	−6.9 (11.0)	−4.1 (−4.7 to −3.4)	<.001
Proportional blood pressure changes from baseline to 24 h after randomization, mean (SD), %				
Systolic	−12.7 (8.7)	−7.2 (9.8)	−5.5 (−4.9 to −6.1)	<.001
Diastolic	−10.7 (10.1)	−6.4 (11.1)	−4.3 (−3.6 to −4.9)	<.001
Blood pressure at day 7 after randomization, mean (SD), mm Hg				
Systolic	137.3 (11.8)	146.5 (13.6)	−9.3 (−10.1 to −8.4)	<.001
Diastolic	82.4 (7.2)	86.4 (8.1)	−4.0 (−4.5 to −3.5)	<.001
Blood pressure at day 14 after randomization, mean (SD), mm Hg				
Systolic	135.2 (10.4)	143.7 (14.0)	−8.6 (−9.7 to −7.4)	<.001
Diastolic	81.4 (7.4)	85.3 (8.3)	−3.9 (−4.6 to −3.1)	<.001
Primary outcome				
Death or major disability, No. (%)[a]	683 (33.6)	681 (33.6)	1.00 (0.88 to 1.14)	.98
Secondary outcomes				
Score on modified Rankin scale[b], median (IQR)	2.0 (1.0 to 3.0)	2.0 (1.0 to 3.0)		.70
Participants, No. (%)				
0 (no symptoms)	204 (10.0)	154 (7.6)	0.98 (0.88 to 1.09)[c]	.70
1 (no significant disability despite symptoms)	653 (32.2)	701 (34.6)		
2 (slight disability)	491 (24.2)	491 (24.2)		
3 (moderate disability)	292 (14.4)	297 (14.7)		
4 (moderately severe disability)	258 (12.7)	285 (14.1)		
5 (severe disability)	108 (5.3)	77 (3.8)		
6 (dead)	25 (1.2)	25 (1.2)		
Death, No. (%)	25 (1.2)	25 (1.2)	1.00 (0.57 to 1.74)	.99
Duration of initial hospitalization, median (IQR), d	13.0 (9.0 to 14.0)	13.0 (9.0 to 14.0)		.28

JAMA 2014;311:479-489

INTERACT

- CT-diagnosed acute spontaneous ICH (<6h)
- Intensive BP lowering (target 140) vs guideline-based management (target 180) Primary End point: proportional change of hematoma volume at 24 h
- No difference of functional outcome (mRS, Barthel I)

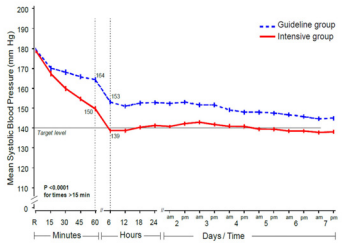


	Guideline (n=172)	Intensive (n=124)	Difference (95% CI)*	p
Haematoma				
Mean baseline volume (mL)	12·7 (11·6)	14·2 (14·5)	..	..
Mean volume at 24 h (mL)	15·4 (14·7)	15·2 (17·5)	..	..
Proportional increase (%)				
Mean (95% CI)	36·3% (15·8 to 56·8%)	13·7% (5·9 to 21·5%)	22·6% (0·6 to 44·5%)	0·04
Adjusted median (95% CI)†	16·2% (8·8 to 24·1%)	6·2% (−0·7 to 13·4%)	10·0% (0·0 to 20·5%)	0·06
Absolute increase (mL)				
Mean (95% CI)	2·7 (1·4 to 4·0)	0·9 (−0·9 to 2·7)	1·7 (−0·5 to 4·0)	0·12
Adjusted mean (95% CI)	2·6 (1·1 to 4·2)	0·9 (−0·6 to 2·5)	1·7 (−0·5 to 3·9)	0·13
Substantial growth‡	40 (23%)	26 (15%)	8% (−1·0 to 17·0%)§	0·05

Lancet Neurol 2008;7:391-99

INTERACT2

- CT-diagnosed acute spontaneous ICH (<6h) with BP 150~220mmHg, in 2838 patients
- Intensive BP lowering (target 140) vs guideline-based management (target 180) within 1 hour from randomization for 7 days
- Primary End point: death or major disability (mRS 3-6) at 90 ds
- Well balanced baseline characteristics



NEJM 2013;368:2355-2365

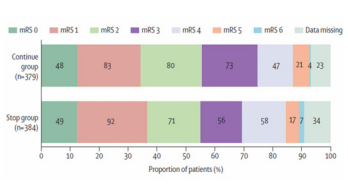
INTERACT2

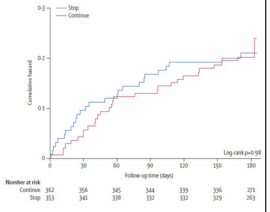
Variable	Intensive Blood-Pressure Lowering (N=1399)	Guideline-Recommended Blood-Pressure Lowering (N=1430)	Odds Ratio (95% CI)	P Value
Primary outcome: death or major disability — no./total no. (%)†	719/1382 (52.0)	785/1412 (55.6)	0.87 (0.75–1.01)	0.06
Secondary outcomes				
Score on the modified Rankin scale — no./total no. (%)‡			0.87 (0.77–1.00)	0.04
0: No symptoms at all	112/1382 (8.1)	107/1412 (7.6)		
1: No substantive disability despite symptoms	292/1382 (21.1)	254/1412 (18.0)		
2: Slight disability	259/1382 (18.7)	266/1412 (18.8)		
3: Moderate disability requiring some help	220/1382 (15.9)	234/1412 (16.6)		
4: Moderate–severe disability requiring assistance with daily living	250/1382 (18.1)	268/1412 (19.0)		
5: Severe disability, bed-bound and incontinent	83/1382 (6.0)	113/1412 (8.0)		
6: Death by 90 days	166/1382 (12.0)	170/1412 (12.0)		
Death — no./total no. (%)	166/1394 (11.9)	170/1421 (12.0)	0.99 (0.79–1.25)	0.96
Health-related quality of life§				
Problems with mobility — no./total no. (%)	767/1203 (63.8)	821/1231 (66.7)	0.88 (0.74–1.04)	0.13
Problems with self-care — no./total no. (%)	563/1202 (46.8)	635/1230 (51.6)	0.83 (0.70–0.97)	0.02
Problems with usual activities — no./total no. (%)	731/1203 (60.8)	814/1231 (66.1)	0.79 (0.67–0.94)	0.006
Problems with pain or discomfort — no./total no. (%)	477/1197 (39.8)	552/1227 (45.0)	0.81 (0.69–0.95)	0.01
Problems with anxiety or depression — no./total no. (%)	406/1192 (34.1)	463/1220 (38.0)	0.84 (0.72–1.00)	0.05
Overall health utility score	0.60±0.39	0.55±0.40		0.002
Living in residential care facility — no./total no. (%)	108/1222 (8.8)	114/1248 (9.1)	0.96 (0.73–1.27)	0.80
Duration of initial hospitalization — days				0.43
Median	20	19		
Interquartile range	12–35	11–33		

NEJM 2013;368:2355-2365

COSSACS (The Continue or Stop Post-Stroke Antihypertensives Collaborative Study)

- Acute stroke within 48 hours from antihypertensive medication (n=763, ischemic or hemorrhagic)
- Continue or stop BP med
- Death or dependency at 2 wks





	Continue (n=379)	Stop (n=384)	Difference (95% CI)	p
Systolic blood pressure (mm Hg)	140 (138 to 142)	153 (151 to 156)	13 (10 to 17)	<0·0001
Diastolic blood pressure (mm Hg)	76 (75 to 76)	84 (83 to 86)	8 (6 to 10)	<0·0001
National Institutes of Health stroke scale score	3·8 (3·2 to 4·3)	3·5 (2·9 to 4·0)	0·3 (−0·5 to 1·1)	0·46
Barthel index score	15·6 (15·0 to 16·2)	16·0 (15·4 to 16·6)	−0·5 (−1·3 to 0·4)	0·30

Data are mean (95% CI).

Table 2: Early secondary clinical outcomes

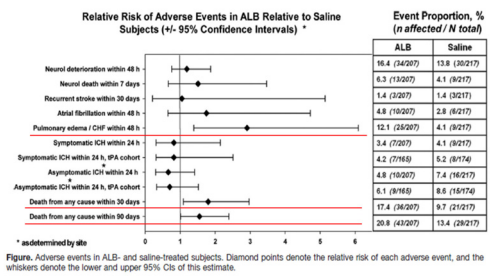
NEJM 2013;368:2355-2365

Induced Hypertension

- 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; LOE C).
- The usefulness of drug-induced hypertension in patients with acute ischemic stroke is not well established. Induced hypertension should be performed in the setting of clinical trials.
- The administration of high-dose albumin is not well established as a treatment for most patients with acute ischemic stroke until further definitive evidence regarding efficacy becomes available (Class IIb; LOE B).

ALIAS

- Potential benefit of Albumin in acute stroke: improving perfusion, decreasing edema, normalized ADC, reversed stagnation in post-ischemic cortical venules, improved microcirculation
- ALIAS: early termination by DSMB



Event Proportion, % (*n affected / N total*)	ALB	Saline
Neurol deterioration within 48 h	16.4 (34/207)	13.8 (30/217)
Neurol death within 7 days	6.3 (13/207)	4.1 (9/217)
Recurrent stroke within 30 days	1.4 (3/207)	1.4 (3/217)
Atrial fibrillation within 48 h	4.8 (10/207)	2.8 (6/217)
Pulmonary edema / CHF within 48 h	12.1 (25/207)	4.1 (9/217)
Symptomatic ICH within 24 h	3.4 (7/207)	4.1 (9/217)
Symptomatic ICH within 24 h, tPA cohort	4.2 (7/165)	5.2 (8/174)
Asymptomatic ICH within 24 h	4.8 (10/207)	7.4 (16/217)
Asymptomatic ICH within 24 h, tPA cohort	6.1 (9/165)	8.6 (15/174)
Death from any cause within 30 days	17.4 (36/207)	9.7 (21/217)
Death from any cause within 90 days	20.8 (43/207)	13.4 (29/217)

Figure. Adverse events in ALB- and saline-treated subjects. Diamond points denote the relative risk of each adverse event, and the whiskers denote the lower and upper 95% CIs of this estimate.

Stroke 2011;42:119-127

ALIAS part 2

- Inclusion: Acute ischemic stroke (18-83yrs), NIHSS 6 or more, Start albumin within 5hrs and 90min of the start of thrombolysis; Exclusion: numerous
- Intervention: 500ml of 25% albumin for 2 hours, IV fluid limits 4200mL during the first 48 hours, diuretics mandated
- Primary-end point: favorable outcome at 90 d (nRS 0-1 or NIHSS 0 or 1)
- 841 patients (albumin 422 vs saline 419)
- Increased risk of shortening of breath and ICH

	Albumin (n=422)	Saline (n=419)	RR (99% CI) or p value
Primary outcome			
NIHSS or mRS 0–1 (or both) at 90 (±30) days	186 (44%)	185 (44%)	0·96 (0·84–1·10*)
Composite outcome at 90 (±30) days			
mRS 0–1, NIHSS 0–1, or decrease in NIHSS from baseline by 10 or more points	227 (54%)	241 (58%)	0·93 (0·80–1·09)
NIHSS 0–1 at 24 h	65 (15%)	62 (15%)	0·99 (0·66–1·49)
NIHSS 0–1 at 90 days	150 (36%)	164 (39%)	0·88 (0·71–1·10)
mRS 0–1 at 90 days	155 (37%)	145 (35%)	1·03 (0·82–1·28)
mRS 0–2 at 90 days	227 (54%)	221 (53%)	0·99 (0·85–1·13)

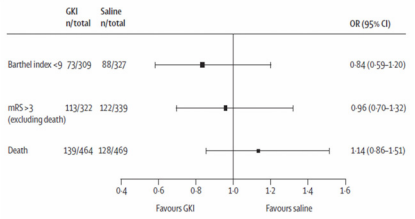
Lancet Neurology, 2012;11:397-404

Hyperglycemia and Hypoglycemia

- Hypoglycemia (BS < 60mg/dl) should be treated in patients with acute ischemic stroke (Class I; LOE C). The goal is to achieve normoglycemia.
- Evidence indicates that persistent in-hospital hyperglycemia during the first 24 hours after stroke is associated with worse outcomes than normoglycemia, and thus, it is reasonable to treat hyperglycemia to achieve BS level in a range of 140 to 180 mg/dL (Class IIa; LOE C).

- 급성기 뇌경색에서 고혈당은 교정되어야 한다 (근거수준 IV, 권고수준 C).
- 저혈당이 발생한 경우 포도당용액을 투여하여 교정하여야 한다(근거수준 IV, 권고수준 C).
- 특별한 이유가 없는 한, 급성기 뇌졸중에서 포도당용액의 투여는 권장되지 않는다 (근거수준 IV, 권고수준 C).

UK-GIST trial (n = 933)



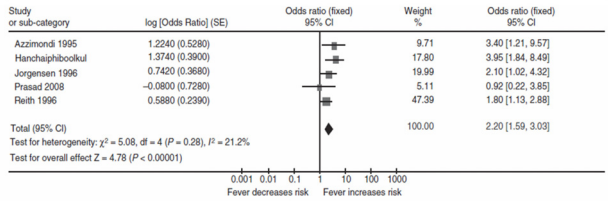
Lancet Neurol 2007;6:397-406

Hypothermia vs Hyperthermia

- Sources of hyperthermia (temperature > 38°C) should be identified and treated, and antipyretic medications should be administered to lower temperature in hyperthermic patients with stroke (Class I; LOE C).

- 급성 뇌경색환자의 체온은 가급적 정상 범위내로 유지되도록 한다 (근거수준 II, 권고수준 B).
- 발열이 있는 경우, 적절한 항생제 치료를 위하여 감염 부위 및 원인 병원체를 찾아 보아야 한다 (근거수준 IV, 권고수준 C).
- 열이 있을 경우, 체온을 낮추는 것이 도움이 될 수 있으며 (근거수준 IV, 권고수준 C), 해열제를 사용 할 수 있다 (근거수준 IIa, 권고수준 B).

Meta-analysis: fever and mortality in acute stroke



Acta Neurol Scand 2010;122:404-408

Hypothermia vs Hyperthermia

- The utility of induced hypothermia for the treatment of patients with ischemic stroke is not well established, and further trials are recommended (Class IIb; LOE B).

	Subjects	Methods	Outcome
COOL AID[1]	Anterior circulation infarction 18 hypothermia, 22 control	Endovascular cooling	No difference in terms of infarction growth or clinical outcome
ICTuS-L[2]	Acute stroke with t-PA within 6 hours (28 hypothermia, 30 control)	Endovascular cooling	No difference in neurological outcome, frequent pneumonia in hypothermia
COOLAID Oresund[3]	Acute stroke < 24 hrs (17 hypothermia, 14 control)	Endovascular and surface cooling	No difference in neurological outcome

[1]Neurology 2004;63:312-317, [2]Stroke 2010;41:2265-2270, [3]Acta Neurol Scand 2013;127:399-405

Prevention of Complication: Infection

- Patients with suspected pneumonia or UTIs should be treated with appropriate antibiotics (Class I; LOE A).
- Routine use of prophylactic antibiotics has not been shown to be beneficial (Class III; LOE B)

- 뇌졸중 환자가 발열이 있으면 흡인성 폐렴의 여부를 먼저 확인하고 치료여부를 결정하는 것이 필요하다.
- 비뇨기계 감염이 확인되면 적절한 항생제 치료가 필요하다.
- 비뇨기계 감염을 방지하기 위한 목적의 예방적 항생제 요법은 추천되지 않는다.
- 방광내 배뇨관 거치술은 꼭 필요한 경우에 가능한 한 짧은 기간 동안 시행을 추천한다. (권고사항 C, 근거사항 M)

- Ventilation in a semirecombent position, positioning of the airway, suctioning, early mobility, and shortened use of intubation
- Treat nausea/vomiting
- Exercise and deep breaths
- Indwelling catheters should be avoided if possible.
- External catheters, incontinence pants, intermittent catheterization are alternatives to an indwelling catheter.

Prevention of Complication: Nutrition

- Assessment of swallowing before the patient begins eating, drinking, or receiving oral medication is recommended (Class I; LOE B).
- The patients who cannot take solid foot and liquids orally should receive NG, nasoduodenal, or PEG tube feeding to maintain hydration and nutrition white undergoing efforts to restore swallowing (Class I; LOE B)
- Routine use of nutritional supplements has not been shown to be beneficial (Class III; LOE B)

- 급성 뇌졸중 환자들에게 연하곤란 여부에 대한 평가와 기본 영양상태에 대한 평가가 입원후 가능한 빠른 시기에 이루어져야 한다 (권고수준 IIb, 근거수준 B).
- 경구 섭취가 불충분한 환자는 비위관 삽입을 통해 영양공급과 약물투여를 시행하도록 하며, 연하 곤란에 대한 치료를 지속하면서 일정한 간격으로 연하곤란에 대한 재평가를 통해 비위관 유지의 필요성을 검토하도록 노력한다 (근거수준 IIb; 권고수준 B).
- 영양실조가 있는 환자에서는 영양균형을 찾기 위해 노력하여야 하나, 모든 뇌졸중 환자에서 일률적으로 영양제를 추가할 필요는 없다 (근거수준 IIb, 권고수준 A)

Prevention of Complication: Bed sore

- 뇌졸중 환자에서 욕창이 동반되었는지의 여부는 자주 확인하는 것이 좋다.
- 욕창의 예방에 조기거동이 도움이 될 수 있다 (권고사항 C, 근거사항 M)
- 조기거동이 불가능할 경우, 침상에서 자주 체위를 변경해 주거나, 공기 매트리스 (air mattress)의 사용을 고려해 볼 수 있다 (권고사항 B, 근거사항 IIb)

Prevention of Complication: DVT and PE

- Subcutaneous administration of anticoagulation is recommended for treatment of immobilized patients to prevent DVT (Class I; LOE A).
- The use of aspirin is reasonable for treatment of patients who cannot receive anticoagulation for DVT prophylasix (Class IIa, LOE A).
- The use of intermittent external compression devices is reasonable for treatment of patients who cannot receive anticoagulation (Class IIa; LOE B)

- 급성기 뇌졸중 환자에서 깊은정맥혈전증을 예방하기 위해 조기재활이 도움이 될 수 있다 (근거수준 III, 권고수준 C).
- 깊은 정맥혈전증의 발생위험이 높은 환자군은 예방을 위해 헤파린 피하주사를 사용할 수 있으나 출혈의 위험이 증가되는 것을 고려해야 한다 (근거수준 Ia, 권고수준 A). 헤파린 피하주사 대신에 저분자량 헤파린을 사용할 수 있다 (근거수준 Ia, 권고수준 A).
- 항혈수판제제의 투여로도 어느 정도는 깊은정맥혈전증을 예방하는 데에 효과가 있으므로, 급성기 뇌경색 환자에서 항혈소판제제는 투여되어야 한다 (근거수준 Ia, 권고수준 A).
- 깊은 정맥혈전증의 예방을 위해 compression stocking이나 pneumatic compression machine 단독 요법의 효과는 뚜렷하지 않으나, 과응고상태가 의심되는 경우 또는 마비된 상/하지에서 다른 치료방법의 보조요법으로 사용을 고려할 수 있다 (근거수준 IIb; 권고수준 B)

- External compression: potential for skin damage is a concern.

Antiplatelet agents

- Oral administration of aspirin (initial dose is 325mg) within 24 to 48 hours after stroke onset is recommended for treatment of most patients (Class I; LOE A)
- The usefulness of clopidogrel for the treatment of acute ischemic stroke is not well established (Class IIb; LOE C).

- 뇌출혈의 가능성이 배제된 허혈성 뇌졸중 환자에서는 아스피린을 뇌경색 발생 24-48시간 이내에 경구투여 (초기용량 160-300mg)해야 한다 (근거수준 Ia; 권고수준 A).
- 아스피린이 정맥내 혈전용해술을 포함한 급성 중재치료를 대체하지 못한다 (근거수준 Ia; 권고수준 A).

IST (International Stroke Trial)

- *ASA, heparin and control in acute stroke (n = 19,435)*
- *Outcome within 14 days*
  - Aspirin-allocated patients: ↓ recurrent strokes within 14 days (2·8% *vs* 3·9%, 2*p*<0·001)
  - ↓ death or any non-fatal recurrent stroke (11·3% *vs* 12·4%, 2*p*=0·02)
  - ↑ Fatal hemorrhage(1·1% *vs* 0·6%, 2*p*=0·0004).
- *Outcome at 6 months*
  - ↓ alive but dependent

Outcome	Heparin vs no heparin			Aspirin vs no aspirin		
	Heparin	No heparin	Events prevented per 1000 (SD)	Aspirin	No aspirin	Events prevented per 1000 (SD)
No randomised	9717	9718		9720	9715	
No with 14 day data	9716 (99·99%)	9717 (99·99%)		9719 (99·99%)	9714 (99·99%)	
Fatal and non-fatal events						
Recurrent ischaemic stroke	283 (2·9%)	370 (3·8%)	9 (3)**	275 (2·8%)	378 (3·9%)	11 (3)***
Haemorrhagic stroke (HS)	120 (1·2%)	41 (0·4%)	−8 (1)****	87 (0·9%)	74 (0·8%)	−1 (1)
Recurrent ischaemic stroke or HS	396 (4·1%)	411 (4·2%)	2 (3)	361 (3·7%)	446 (4·6%)	9 (3)**
Death or non-fatal stroke	1136 (11·7%)	1171 (12·0%)	4 (5)	1099 (11·3%)	1208 (12·4%)	11 (5)*
Pulmonary embolism	53 (0·5%)	81 (0·8%)	3 (1)*	57 (0·6%)	77 (0·8%)	2 (1)
Transfused or fatal extracranial haemorrhage	129 (1·3%)	37 (0·4%)	−9 (1)****	109 (1·1%)	57 (0·6%)	−5 (1)•••

HS=haemorrhagic stroke (ie, symptomatic intracranial haemorrhage or symptomatic haemorrhagic transformation or infarct) confirmed by CT scan, MRI, or necropsy. Negative numbers indicate that more events of this type occurred in patients allocated to receive active treatment. SD=standard deviation.
*2p<0·05. **2p<0·01. ***2p<0·001. ****2p<0·00001. Selected exact *p* values given in text.

Table 2: **Main outcome events within 14 days**

Lancet 1997;349:1569-1581

CAST (Chinese Stroke Trial)

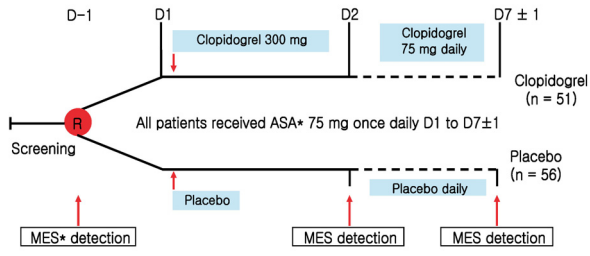
- Large, randomized, placebo-controlled trial
- Total 21106 patients from 403 hospitals in China
- CT scan before randomization was mandatory only for patients who were comatose.

	Number (%)		Absolute benefit with aspirin per 1000	2p
	Aspirin (n=10,335)	Placebo (n=10,320)		
Death				
All Deaths	343(3.3%)	398(3.9%)	5.4(2.6)	0.04
Due to initial stroke	144(1.4%)	175(1.7%)	3.0(1.7)	0.08
Recurrent stroke				
All	335(3.2%)	351(3.4%)	1.6(2.5)	>0.1
Ischemic	167(1.6%)	215(2.1%)	4.7(1.9)	0.01
Hemorrhagic	115(1.1%)	93(0.9%)	-2.1(1.4)	>0.1
Death or non-fatal stroke	545(5.3%)	614(5.0%)	6.8(3.2)	0.03
Transfused or extracranial bleed	86(0.6%)	58(0.6%)	-2.7(1.2)	0.02

Lancet 1997;349:1569-1581

CARESS (the Clopidogrel and Aspirin for Reduction of Emboli in Symptomatic Carotid Stenosis trial)

- 50% carotid stenosis with ipsilateral carotid territory TIA/stroke within the last 3 mo.
- ASA(75mg)/Placebo vs ASA(75mg)/Clopidogrel(300-> 75mg)
- Primary End point: MES



Circulation 2005;111(17):2233-40

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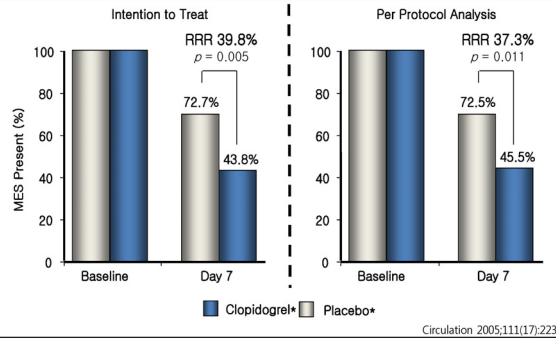
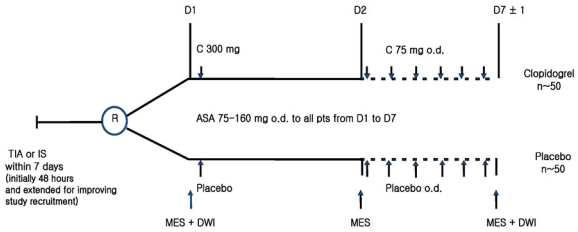


Circulation 2005;111(17):2233-40

CLAIR (Clopidogrel plus aspirin versus aspirin alone for reducingembolisation in patients with acute symptomatic cerebralor carotid artery stenosis)

- 50% carotid stenosis with ipsilateral carotid territory TIA/stroke within the last 3 mo.
- ASA(75mg)/Placebo vs ASA(75mg)/Clopidogrel(300-> 75mg)
- Primary End point: MES



Lancet Neurol. 2010 May;9(5):489-97

CLAIR (Clopidogrel plus aspirin versus aspirin alone for reducingembolisation in patients with acute symptomatic cerebralor carotid artery stenosis)

	Dual therapy	Monotherapy	Relative risk reduction, % (95% CI)	p
Modified intention to treat	n=46	n=52		
Baseline	26/46 (57%)	35/52 (67%)	16·0% (-15·2 to 38·8)	0·272
Day 2	14/45 (31%)	27/50 (54%)	42·4% (4·6 to 65·2)	0·025
Day 7	10/43 (23%)	26/51 (51%)	54·4% (16·4 to 75·1)	0·006
Per protocol	n=25	n=31		
Baseline	25/25 (100%)	31/31 (100%)	..	..
Day 2	10/25 (40%)	22/30 (73%)	45·5% (7·7 to 67·8)	0·013
Day 7	8/24 (33%)	20/31 (65%)	48·3% (3·7 to 72·3)	0·022

Table 2: Number of patients with at least one microembolic signal on transcranial doppler

Lancet Neurol. 2010 May;9(5):489-97

CARESS & CLAIR

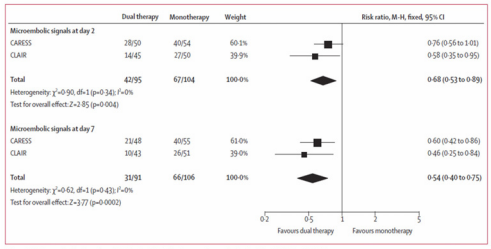


Figure 2: Meta-analysis of number of patients with at least one microembolic signal in CARESS and CLAIR
M-H=Mantel-Haenszel.

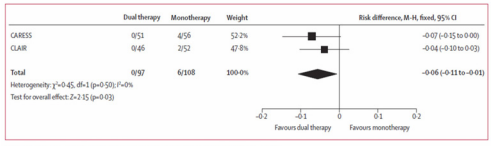
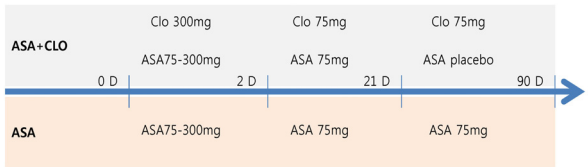


Figure 3: Meta-analysis of number of patients with recurrent stroke in CARESS and CLAIR
M-H=Mantel-Haenszel.

Lancet Neurol. 2010 May;9(5):489-97

CHANCE (Clopidogrel with aspirin in acute minor stroke or transient ischemic attack.)

- Randomized, double blind, placebo-controlled study
- clopidogrel + aspirin vs aspirin alone for 3m, in acute high-risk TIA or minor ischemic stroke
- Population: *acute (24h) minor stroke (NIHSS ≤3)or TIA (ABCD2 ≥4)*
- 5170 subjects, (2584 ASA+clo vs 2586 ASA)
- Primary efficacy outcome event: new stroke event at 90 ds
- Primary safety outcome event: moderate to severe bleeding event (GUSTO definition)



NEJM 2013;369:11-19

CHANCE (Clopidogrel with aspirin in acute minor stroke or transient ischemic attack.)

Table 2. Efficacy and Safety Outcomes.

Outcome	Aspirin (N=2586) Patients with Event no.	Aspirin (N=2586) Event Rate %	Clopidogrel and Aspirin (N=2584) Patients with Event no.	Clopidogrel and Aspirin (N=2584) Event Rate %	Hazard Ratio (95% CI)	P Value
Primary outcome						
Stroke	303	11.7	212	8.2	0.68 (0.57–0.81)	<0.001
Secondary outcomes						
Stroke, myocardial infarction, or death from cardiovascular causes	307	11.9	216	8.4	0.69 (0.58–0.82)	<0.001
Ischemic stroke	295	11.4	204	7.9	0.67 (0.56–0.81)	<0.001
Hemorrhagic stroke	8	0.3	8	0.3	1.01 (0.38–2.70)	0.98
Myocardial infarction	2	0.1	3	0.1	1.44 (0.24–8.63)	0.69
Death from cardiovascular causes	5	0.2	6	0.2	1.16 (0.35–3.79)	0.81
Death from any cause	10	0.4	10	0.4	0.97 (0.40–2.33)	0.94
Transient ischemic attack	47	1.8	39	1.5	0.82 (0.53–1.26)	0.36
Safety outcomes						
Bleeding*						
Severe	4	0.2	4	0.2	0.94 (0.24–3.79)	0.94
Moderate	4	0.2	3	0.1	0.73 (0.16–3.26)	0.68
Mild	19	0.7	30	1.2	1.57 (0.88–2.79)	0.12
Any bleeding	41	1.6	60	2.3	1.41 (0.95–2.10)	0.09

NEJM 2013;369:11-19

CHANCE (Clopidogrel with aspirin in acute minor stroke or transient ischemic attack.)

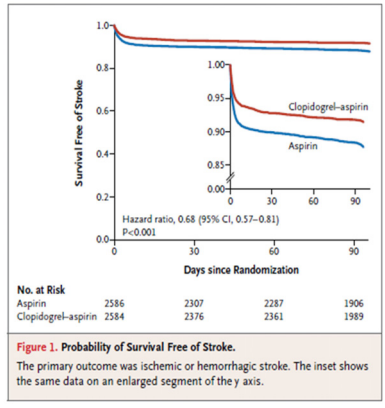


Figure 1. Probability of Survival Free of Stroke.
The primary outcome was ischemic or hemorrhagic stroke. The inset shows the same data on an enlarged segment of the y axis.

NEJM 2013;369:11-19

Anticoagulation

- At present, the usefulness of argatroban or other thrombin inhibitors for treatment of patients with acute ischemic stroke is not well established *(Class IIb; Level of Evidence B)*. These agents should be used in the setting of clinical trials. (New recommendation)
- The usefulness of urgent anticoagulation in patients with severe stenosis of an internal carotid artery ipsilateral to an ischemic stroke is not well established *(Class IIb; Level of Evidence B)*. (New recommendation)
- Urgent anticoagulation, with the goal of preventing early recurrent stroke, halting neurological worsening, or improving outcomes after acute ischemic stroke, is not recommended for treatment of patients with acute ischemic stroke *(Class III; Level of Evidence A)*. (Unchanged from the previous guideline13)
- Urgent anticoagulation for the management of noncerebrovascular conditions is not recommended for patients with moderate-to-severe strokes because of an increased risk of serious intracranial hemorrhagic complications *(Class III; Level of Evidence A)*. (Unchanged from the previous guideline13)
- Initiation of anticoagulant therapy within 24 hours of treatment with intravenous rtPA is not recommended *(Class III; Level of Evidence B)*.

Early Rehabilitation

- The use of comprehensive specialized stroke care (stroke units) that incorporates rehabilitation is recommended *(Class I; LOE A)*.
- 급성기 뇌졸중 환자의 재활치료는 내과적으로 안정이 되면 가능한 한 빠른 시간 내에 시작해야 한다 (근거수준 Ia, 권고수준 A)
- 뇌졸중 환자는 적응할 수 있는 범위내에서 기능 회복에 필요한 충분한 재활 치료를 받는 것이 권장 된다 (근거수준 Ia, 권고수준 A).
- 재활 치료로 얻어진 기술은 환자의 일상생활에서 지속적이고 반복적으로 사용하도록 권장된다 (근거수준 Ia, 권고수준 A).

- (재활의학과 권고사항)
- 급성기 뇌졸중 환자의 재활치료는 내과적으로 안정이 되면 가능한 한 빠른 시간내에 시작하는 것이 강력히 권고된다 (권고수준 A, 근거수준 1++).
- 급성기 뇌졸중 환자는 뇌졸중 후 72시간 이내에 재활치료를 시작해야 한다 (권고수준 B, 근거수준 1+).

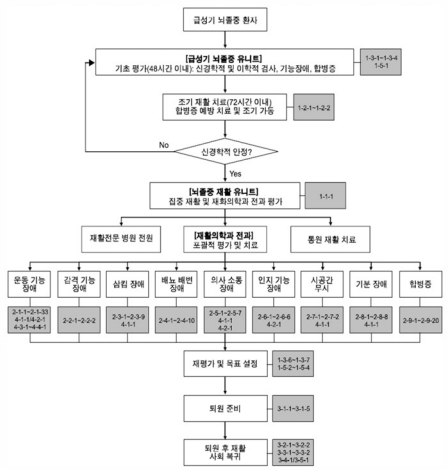
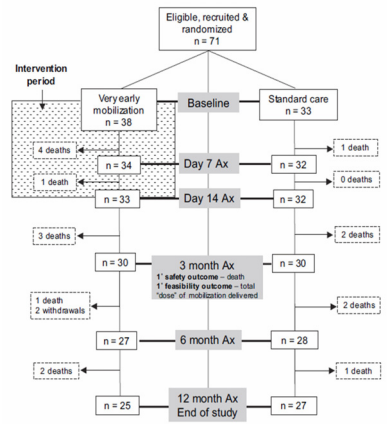


Fig. 1. Algorithm of stroke rehabilitation.

AVERT (A Very Early Rehabilitation Trial for Stroke)



Stroke 2008;39:390-396

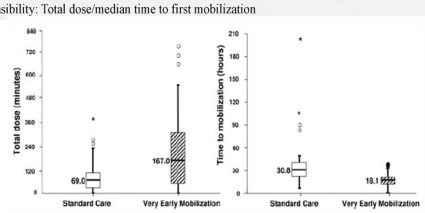
AVERT (A Very Early Rehabilitation Trial for Stroke)

Table 2. Good Outcome (mRS score 0–2) at 3, 6, and 12 Months After Stroke

				Multivariable Analysis*	
Good Outcome (mRS 0–2)	SC, n/N (%)	VEM, n/N (%)	Univariable *P*	OR (95% CI)	*P*
3 months	10/33 (30.3)	15/38 (39.5)	0.46	4.10 (0.99–16.88)	0.05
6 months	11/32 (34.4)	15/36 (41.7)	0.62	4.17 (0.87–20.07)	0.08
12 months	8/33 (24.2)	14/36 (38.9)	0.21	8.15 (1.61–41.21)	0.01

OR indicates odds ratio.
*Adjusted for age, baseline NIHSS score, and premorbid mRS score.

Primary End-point
- Safety: Mortality Very Early Mobilization(8/38) >Standard care (3/33), p = 0.20
- Feasibility: Total dose/median time to first mobilization



Stroke 2008;39:390-396

Table 1. Completed Trials of Early and Very Early Mobilization After Stroke

Publication (Trial Name)	Randomized Sample	Intervention Protocol	Time (Hours) Between Stroke and Mobilization Outcome*
Bernhardt et al 2008[7] (AVERT)	71	• Recruited within 24 h of stroke, goal to start mobilization within 24 h of stroke • Emphasis on patient being upright and out of bed (sitting or standing) • At least twice a day for first 14 days or until discharge	Intervention (n=38): Median=18.1, IQR=12.8–21.5 Control (n=33): Median=30.8, IQR=23.0–39.9
Langhorne et al 2010[8] (VERITAS)	32	• Recruited within 24 h of admission, with goal to start mobilization within 24 h of stroke • Goal for patient to be sitting, standing or walking (adjusted to patient needs) • Continued at least four times a day, during the inpatient stay, or for one week after recruitment	Intervention (n=16): Mean=27.3 Range=26–29 Control (n=16): Mean=32.0 Range=22.5–47.3
Diserens et al 2011[10] (Lausanne trial)	50 (42 included in analysis)	• Recruited within 12 h of admission, with protocol started 24 h after stroke • Patient's head of the bed kept at 0° for first 24 h poststroke, followed by 45° for 24 h, then 90° for 4 h • At 52 h poststroke, patients were moved out of the bed to either sitting or standing	Intervention (n=25): Not reported Control (n=17): Not reported
Sundseth et al 2012[9] (AKEMIS)	65 (56 included in analysis)	• Recruited if admitted to hospital within 24 h of stroke, with mobilization out of bed within 24 h of admission • No predefined mobilization protocol. Mobilization, defined as any out of bed activity, followed the stroke unit's standard routine for mobilization, adjusted to patients' needs • Mobilization occurred several times per day	Intervention (n=27): Median=13.1 IQR=8.5–25.6 Control (n=29): Median=33.3 IQR=26.0–39.0

Early Rehabilitation

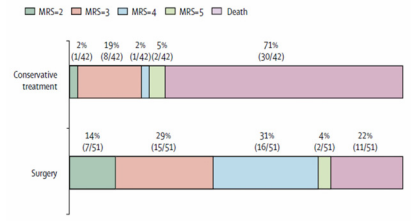
Table 2. Ongoing Trials of Early and Very Early Mobilization After Stroke

	Estimated Enrollment	Interventions	Recruitment Time Frame	Primary Outcome
AVERT Phase III (Florey Institute of Neuroscience and Mental Health) NCT01846247 Active, not recruiting	2104	Intervention: usual care + very early mobilization Patient will receive standard stroke unit care with earlier and additional physiotherapy and nursing sessions as per an intervention protocol Comparator: usual care	Recruited <24 h of onset of stroke symptoms	mRS at 3 months after stroke
SEVEL Trial (Nates University Hospital) NCT01573299 Terminated*	400	Intervention group 1: early vertical positioning The patient can sit outside of the bed, the day after stroke onset Intervention group 2: progressive vertical positioning The patient is progressively verticalized and is allowed to sit outside of the bed on the third day after the stroke onset	No time frame specified	mRS at 3 months after stroke

Source: http://www.clinicaltrials.gov (December 4, 2014). mRS indicates modified Rankin Scale.
*Trial stopped because of slow enrollment rate (Fanny Herisson, personal communication, 2014).

Management of Brain Swelling

- Decompressive surgical evacuation of a space-occupying cerebellar infarction is effective in preventing and treating herniation and brain stem compression *(Class I; LOE B)*. (Revised from the previous guideline)
- Decompressive surgery for malignant edema of the cerebral hemisphere is effective and potentially lifesaving (*Class I; LOE B*). Advanced patient age and patient/family valuations of achievable outcome states may affect decisions regarding surgery. (Revised from the previous guideline)



Lancet Neurol 2007;6:215-22

Management of Brain Swelling

- Placement of the patients in a semi-sitting position with elevated head.
- Avoidance of noxious stimuli
- Pain relief
- A low normal body temperature (36-37°C)
- Maintain CPP
- Osmotherapy with 10% glycerol, 15% mannitol, or hypertonic saline
- Avoid hypotonic saline or glucose solutions
- Short-term barbiturate – transient ICP, MAP, CPP drop

Communication

Communication

How do I communicate with a heart attack or heart surgery patient?

- Expect emotional ups and downs, crying for no reason, nightmares and fears of death.
- Give yourselves time to adjust and freely express your emotions to one another.
- Encourage your loved one to start making the necessary changes to prevent further events or complications.
- Accept the fact that your roles may be reversed, at least for now.
- Encourage your loved one to get back into life and make plans together for the future.
- Even though he or she is sick, remember that you still deserve to be treated with respect.
- Be a good listener. Your loved one may need to openly express how he or she is feeling.
- Use "I" messages rather than "you" messages.
- When you feel angry or frustrated, say "I feel angry," instead of "You make me angry" to express your feeling without blaming others.

How do I communicate with a stroke survivor?

- Remember that many stroke survivors may have damage that makes it difficult for them to communicate well.
- Accept whatever communication form they have, even if it's just making signs with their hands.
- Learn everything you can about their condition so you can be more understanding and helpful.
- Join support groups and learn how others have managed to break down communication barriers.
- With aphasia, it's not necessary to talk louder, just more slowly. Avoid talking down to your loved one, and be a good and patient listener.

(continued)