

## Supplementary Material

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**Supplementary Table 1: Definitions of severe stroke, large infarction, malignant brain edema, and critically severe stroke.**

Concepts	Definition	Other terms reported
<b>Severe stroke</b>		
Severe stroke	NIHSS $\geq 8^{[1]}$ ; $\geq 10^{[2]}$ ; $\geq 11^{[3-5]}$ ; $\geq 15^{[6-17]}$ ; $\geq 16^{[18-20]}$ ; $\geq 17^{[21]}$ ; $\geq 18^{[22]}$ ; $\geq 20^{[13, 23, 24]}$ ; $\geq 21^{[25, 26]}$ ; $> 25^{[8, 15]}$ GCS $\leq 12^{[5, 27]}$ , GCS $\leq 8^{[21, 22]}$	
<b>Large cerebral/cerebellar infarction</b>		
Large hemispheric infarction	Infarction $>$ total or subtotal ( $>2/3$ ) MCA territory <sup>[28, 29]</sup>	Large MCA infarction [30] Massive MCA infarction [31] Massive

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cerebral  
infarction  
[32]

Infarction >both the anterior and posterior divisions of MCA territory<sup>[33]</sup>

Large  
MCA  
infarction  
[34]

Infarction >1/2 MCA territory<sup>[35, 36]</sup>

Large  
MCA  
infarction  
[37-40]

Malignant  
MCA  
infarction  
[41]

Infarction >82 cm<sup>3</sup> on DWI <10 h<sup>[42]</sup>

Infarction >1/2 MCA territory or >82 cm<sup>3</sup> on DWI <24 h<sup>[43]</sup>

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Large MCA infarction    Infarction >145 cm<sup>3</sup> on DWI<sup>[22]</sup> <14 h<sup>[44]</sup>  
infarction    Infarction >1/2 MCA territory or >145 cm<sup>3</sup> on DWI <48 h<sup>[45]</sup>

Large cerebral infarction    Infarction ≥one division of MCA territory<sup>[46]</sup>

Large cerebral infarct    Infarction ≥1/2 MCA, ACA, or PCA territory<sup>[47]</sup>

Space-occupying cerebral infarction    Infarction >2/3 MCA territory and space-occupying edema<sup>[48, 49]</sup>

Large space-occupying MCA infarction<sup>[49]</sup>

Infarction >1/2 MCA territory and local brain swelling<sup>[50]</sup>

Malignant brain edema<sup>[51]</sup>

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Massive cerebellar infarction

Cerebellar infarction with mass effect<sup>[52]</sup>

Large cerebellar infarction

Infarction >3 cm<sup>[53]</sup>

### **Malignant brain edema**

#### **Clinical signs**

Malignant MCA infarction

A severe hemispheric stroke syndrome including hemiplegia, forced eye and head deviation, and progressive deterioration of consciousness, leading to herniation and death<sup>[54]</sup>

Fatal midbrain herniation<sup>[55]</sup>

#### **Imaging evidence**

Complete MCA infarction<sup>[54]</sup>

MCA infarction with mass effect<sup>[55]</sup>

Space-occupying MCA infarction

[55]

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Raised intracranial pressure, and brain herniation and brain death <sup>[56]</sup>	Mass effect with midline shift <sup>[56]</sup>	Malignant hemispheric infarction <sup>[56]</sup>
Deterioration of neurological and consciousness status with clinical signs of uncal herniation <sup>[44]</sup> Clinical signs of herniation <sup>[37, 57]</sup>	Mass effect leading to early death or hemicraniectomy <sup>[44]</sup> Space-occupying brain edema with a midline shift >2 mm at the level of the septum pellucidum on CT corresponds to >5.54 mm <i>in situ</i> <sup>[37, 57]</sup>	
Signs of clinical deterioration (deteriorating level of consciousness, anisocoria) <sup>[58]</sup>	Large (total or subtotal) MCA with progressive brain swelling <sup>[58]</sup>	
Neurological deterioration (decrease in the level of consciousness to somnolence or stupor) <sup>[31]</sup>	Infarction >2/3 MCA territory with midline shift and basal cisterns compression <sup>[31]</sup>	
Signs of herniation (unilateral fixed and dilated pupils) <sup>[38, 59]</sup>	Space-occupying brain edema with a midline shift >5 mm at the level of septum pellucidum <sup>[38, 59]</sup>	

Decreased arousal, pupillary changes, and a rapid decline in neurological status <sup>[60]</sup>	Space-occupying brain edema with a midline shift >5 mm <sup>[60]</sup>	Malignant infarction <sup>[60]</sup>
Clinical signs of uncal herniation <sup>[61]</sup>	Infarction >1/2 MCA territory with a midline shift >5 mm ( <i>in situ</i> ) at the level of the septum pellucidum <sup>[61]</sup>	
Decrease of consciousness to NIHSS 1a ≥1 or clinical deterioration of NIHSS ≥4; anisocoria or death attributable to herniation <sup>[62]</sup>	Midline shift >5 mm ( <i>in situ</i> ) at the level of the septum pellucidum <sup>[62]</sup>	
Severe MCA syndrome (dense hemiplegia, head and eye deviation, hemi-neglect and aphasia, impaired and progressively deteriorating consciousness) <sup>[63]</sup>	Infarction >2/3 MCA territory <sup>[63]</sup>	
NIHSS >15 (or >20) <sup>[64]</sup>	Infarction >2/3 of MCA territory, without perfusion–diffusion mismatch <sup>[64]</sup>	Malignant supratentorial/brain

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n/cerebra  
1  
infarction  
[64]

NIHSS  $\geq 15$  with NIHSS 1a  $\geq 1$ <sup>[65]</sup>

Infarction  $>2/3$  MCA territory, with ventricle compression or midline shift<sup>[65]</sup>

NIHSS score  $\geq 16$  with NIHSS 1a  $\geq 1$ <sup>[66, 67]</sup>

Infarction  $>1/2$  MCA territory, or, infarction  $>145$  cm<sup>3</sup><sup>[66, 67]</sup>

NIHSS  $>18$  (or  $>20$ ) with NIHSS 1a  $\geq 1$ <sup>[68]</sup>

Infarction  $>2/3$  MCA territory, including basal ganglia<sup>[68]</sup>

NIHSS  $>18$  with NIHSS 1a  $\geq 1$ <sup>[49]</sup>

Infarction  $>2/3$  MCA territory, with ventricle compression or midline shift<sup>[49]</sup>

NIHSS 1a  $\geq 1$ <sup>[69]</sup>

Infarction  $>2/3$  MCA territory, with ventricle compression or midline shift<sup>[69]</sup>

NIHSS  $\geq 20$  with NIHSS 1a  $\geq 1$ <sup>[70]</sup>

Infarction  $>145$  cm<sup>3</sup> or midline shift/mass effect<sup>[70]</sup>

Malignant  
brain edema      Neurological deterioration (NIHSS increase by  $>2$ ) and decrease in the level of consciousness (NIHSS 1a  $\geq 1$ )<sup>[71]</sup>

Complete MCA infarction ( $>1/2$  MCA territory with brain swelling of sulcal effacement and compression of the lateral ventricle), and midline shift  $>5$  mm

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Clinical signs of herniation (decrease in consciousness and/or anisocoria) <sup>[72]</sup>	with obliteration of basal cisterns <sup>[71]</sup>	Potentially lethal malignant edema <sup>[75, 78]</sup>
Syndrome of clinical worsening, or death, or requirement for DHC <sup>[73, 74]</sup>	Brain swelling (midline shift of brain structure or effacement of basal cisterns) <sup>[72]</sup>	
Decompressive craniectomy, discharge in coma, or in-hospital death attributed to symptomatic brain swelling (neurological deterioration, increase in NIHSS $\geq 2$ ) <sup>[47]</sup>	Brain swelling <sup>[73, 74]</sup>	
Clinical signs of herniation (decrease in consciousness and/or anisocoria) <sup>[40, 75]</sup>	Compression of lateral ventricle, midline shift, or compression of basal cistern <sup>[47]</sup>	
Need for DHC and/or death <sup>[76, 77]</sup>	Midline shift $\geq 5$ mm <sup>[40, 75]</sup>	
Edema requiring hemicraniectomy or osmotic drug therapy,	Midline shift $\geq 5$ mm <sup>[76, 77]</sup>	
	Midline shift $\geq 5$ mm <sup>[79]</sup>	



	with death or decline in GCS $\geq 2$ <sup>[79]</sup>	
	Decreased consciousness, unilateral dilated pupil, and severe neurological deficit, need for decompressive surgery or death <sup>[80]</sup>	Midline shift $\geq 5$ mm <sup>[80]</sup>
Severe brain edema	Clinical signs of uncal herniation or rapid deterioration of neurological and consciousness status, clinical symptoms of increased intracranial pressure (nausea or vomiting) <sup>[81]</sup>	Mass effect leading to hemicraniectomy <sup>[81]</sup>
Life-threatening edema	Decrease in consciousness <sup>[82]</sup>	Infarction $>2/3$ MCA territory with space-occupying edema <sup>[82]</sup>
	Decrease of consciousness to NIHSS 1a $\geq 1$ or clinical deterioration of NIHSS $\geq 4$ <sup>[83]</sup>	Midline shift $\geq 5$ mm <sup>[83]</sup>
Fatal brain swelling	Death caused by brain herniation with documented evidence of brain stem compression (enlarged pupil, coma, or loss of other brain stem reflexes) <sup>[33]</sup>	Infarction $>$ both anterior and posterior divisions of MCA territory <sup>[33]</sup>
	Progressive neurological deterioration leading to coma and death <sup>[84]</sup>	Anterior circulation strokes <sup>[84]</sup>
<b>Critically severe stroke</b>		

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Critical cerebral infarction	A critical condition after cerebral infarction accompanied with malignant brain edema, or other conditions that require neurocritical care including the need for intubation and/or mechanical ventilation due to decreased level of consciousness or respiratory failure, persistent unstable blood pressure, or severe dysfunction in other vital organs such as renal failure or cardiac dysfunction <sup>[85]</sup>
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Local brain swelling (also known as space-occupying brain edema or mass effect) refers to the imaging signs of effacement of cortical sulci, compression of ventricles, shift of midline structure, and effacement of basal cisterns.

ACA: Anterior cerebral artery; DHC: Decompressive hemicraniectomy; DWI: Diffusion-weighted imaging; GCS: Glasgow coma score; ICA: Internal carotid artery; MCA: Middle cerebral artery; NHSS: National Institutes of Health Stroke Scale score; PCA: Posterior cerebral artery.

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