

# TIME IS BRAIN

In patients experiencing a typical large vessel acute ischemic stroke

each minute **1.9 million** neurone

**14 billion** synapse

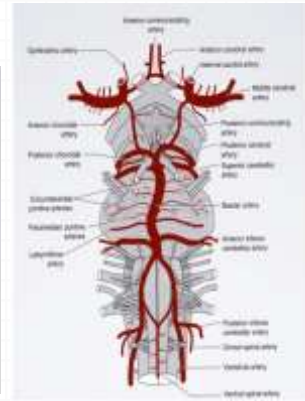
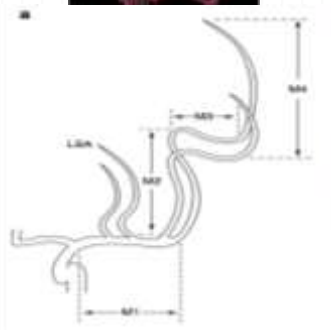
**12 Km** of myelinated fiber

**are destroyed!!!**



Saver J. stroke. 2006

## Our cerebral “coronaries”

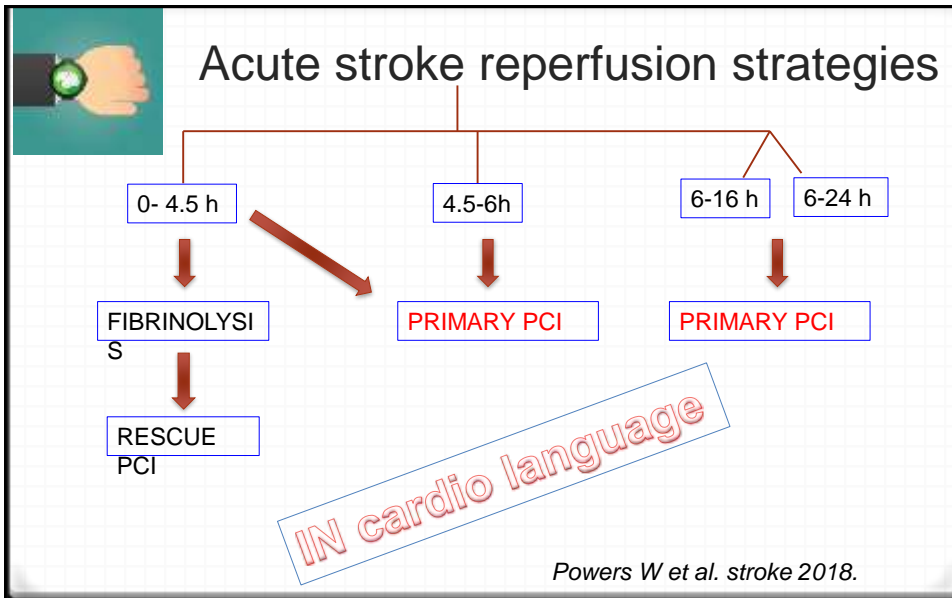


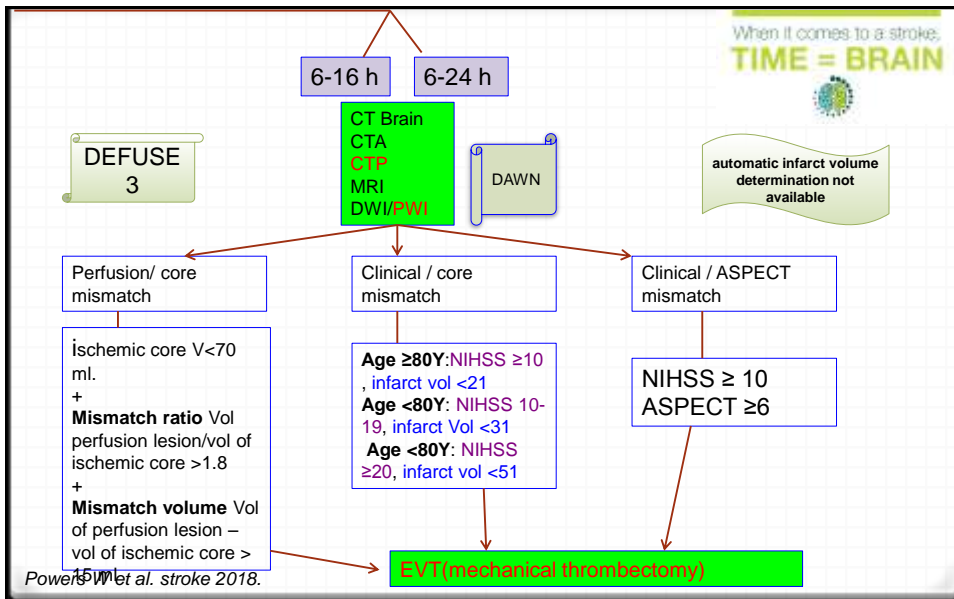
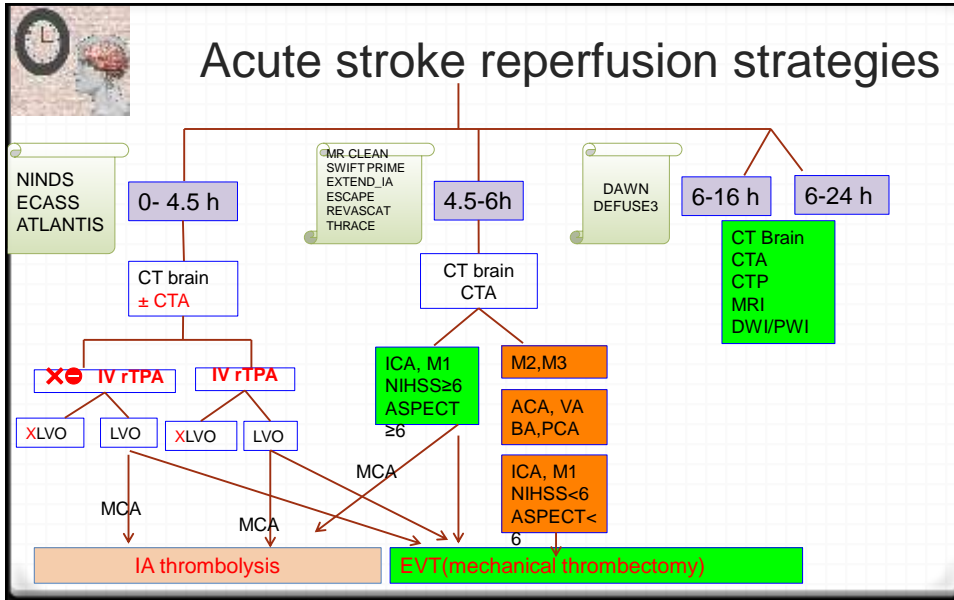
## Strength of recommendation & level of evidence in guidelines

**Table 3. Applying ACC/AHA Class of Recommendation and Level of Evidence to Clinical Strategies, Interventions, Treatments, or Diagnostic Testing in Patient Care\*** (Updated August 2015)

CLASS (STRENGTH) OF RECOMMENDATION	LEVEL (QUALITY) OF EVIDENCE
<b>CLASS I (STRONG)</b> Suggested practice for setting recommendations: <ul style="list-style-type: none"> <li>Is necessary</li> <li>Is evidence-based/efficacious/beneficial</li> <li>Should be performed/avoided/preferred</li> <li>Operational effectiveness/feasible</li> <li>Resource/utility A to unacceptable/undesired or prohibitive in treatment B</li> <li>Benefit A should far exceed harm B</li> </ul>	<b>LEVEL A</b> <ul style="list-style-type: none"> <li>High quality evidence showing that more than 50% of patients benefit</li> <li>Level 1 evidence of high quality RCTs</li> <li>Meta-analysis of multiple high quality RCTs</li> </ul>
<b>CLASS IIa (MODERATE)</b> Suggested practice for setting recommendations: <ul style="list-style-type: none"> <li>Is necessary</li> <li>Can be useful/efficacious/beneficial</li> <li>Considerable evidence/feasible</li> <li>Resource/utility A to probably unacceptable/undesired or prohibitive in treatment B</li> <li>Is recommended for routine treatment B</li> <li>Level 1 evidence B</li> </ul>	<b>LEVEL IIa</b> (Moderate) <ul style="list-style-type: none"> <li>Randomized clinical trial showing that 50% of cases benefit</li> <li>Level 2 evidence of moderate quality RCTs</li> </ul>
<b>CLASS IIb (WEAK)</b> Suggested practice for setting recommendations: <ul style="list-style-type: none"> <li>May/might be necessary</li> <li>May/might be useful</li> <li>Beneficial/efficacious in patients/setting/condition or in some populations</li> </ul>	<b>LEVEL IIb</b> (Moderate-Low) <ul style="list-style-type: none"> <li>Randomized clinical trial showing that 50% of cases may benefit</li> <li>Level 2 evidence (observational or expert opinion, observational studies, or registry studies)</li> <li>Level 3 evidence of such studies</li> </ul>
<b>CLASS III (NO RECOMMENDATION)</b> Suggested practice for setting recommendations: <ul style="list-style-type: none"> <li>Is not necessary/needed</li> <li>Is not necessary/needed/efficacious/beneficial</li> <li>Should not be performed/avoided/preferred, either</li> </ul>	<b>LEVEL III (Low)</b> <ul style="list-style-type: none"> <li>Observational or retrospective observational or registry studies with limitations of design or execution</li> <li>Meta-analysis of such studies</li> <li>Expert opinion or consensus opinion in patient care</li> </ul>
<b>CLASS IIIa (Weak)</b> Suggested practice for setting recommendations: <ul style="list-style-type: none"> <li>Probably harmful</li> <li>Probably not</li> <li>Unclear</li> <li>Unclear with known or unknown harms</li> <li>Should not be performed/avoided/preferred, either</li> </ul>	<b>LEVEL III (Low)</b> <ul style="list-style-type: none"> <li>Consensus of expert opinion based on clinical judgment</li> </ul>

CCM and LGE are abbreviated interventions from CCM used for patient with one LGE. A recommendation with LGE 2 does not mean that the recommendation is weak. Many patients with aortic atherosclerosis undergo CABG to prevent the risk from developing in other sites. Although CABG was considered, there may be a very clear clinical rationale that a coronary stent or bypass is better in certain cases.  
\* The outcome in favor of the intervention should be specified (as opposed to overall benefit or treatment superiority) unless an important adverse effect is present.  
† For observational effectiveness recommendations (level I and the LGE 2 and 3), studies that assess the role of treatment with a control group are preferred at all times, unless in settings being studied.  
‡ The overall of evidence used to establish the position of observational study level 2 and guideline writing groups (level 3) and the overall of evidence for the treatment of an aortic disease is low.  
Level evidence class of recommendation: III, expert opinion; III, expert opinion; LGE, level of evidence; III, observational, R, randomized, and RCT, randomized clinical trial.





Exclusion criteria for the use of IV rTPA	
Absolute exclusion criteria:	
Historical	<p>Previous intracranial hemorrhage            Intracranial or GIT neoplasm, AVM, or aneurysm            In the previous 3 months:                significant stroke or head trauma.                intracranial or intraspinal surgery            In the previous 7 days:                arterial puncture at non compressible site</p>
Clinical	<p>Symptoms suggestive of SAH or infective endocarditis            Persistent BP elevation:                SBP <math>\geq 185</math> mmhg or                DBP <math>\geq 110</math> mmhg.            Serum glucose <math>&lt; 50</math> mg/dl.            Active internal bleeding.            Acute bleeding diathesis.</p>
Hematological	<p>Platelet: <math>&lt; 100,000/\text{mm}^3</math>            Current anticoagulant use with INR <math>&gt; 1.7</math> or PT <math>&gt; 15</math> sec            Heparin use within 24 hours or abnormal aPTT <math>&gt; 40</math> sec            Current use of DTI or DFTI (within 48 h)</p>
Radiological	<p>Evidence of hemorrhage.            Hypodensity more than 1/3 of the hemisphere            ASPECT <math>\leq 6</math></p>

Exclusion criteria for the use of IV rTPA	
Relative exclusion criteria:	
<p>Careful consideration and weighting of risk to benefit.            May receive despite of 1 or more relative contraindications.</p>	<p>In the <b>previous 3 months</b> MI            In the <b>previous 3 weeks</b>: GIT or Urinary tract bleeding            In the <b>previous 2 weeks</b>: major surgery or serious trauma.            Seizure at onset.            Pregnancy.            Rapidly improving or minor symptoms (non disabling)</p>
<p>Extended window relative exclusion</p>	<p>Patients <math>&gt; 80</math> years            taking OAC irrespective of INR            NIHSS <math>&gt; 25</math>            both previous stroke and DM</p>

<h1>Similarities</h1>		
	AMI	AIS
Pathophysiology	Arterial occlusion/ischemic necrosis	Arterial occlusion/ischemic necrosis
Clinical picture	Acute onset	Acute onset
Prognosis	High mortality (if untreated)	High mortality (if untreated)
Effective treatment	Reperfusion therapy	Reperfusion therapy
Thrombolytic treatment	Early reperfusion achieved in <50% of treated patients	Early reperfusion achieved in <50% of treated patients
Catheter-based thrombectomy	Clearly established as the most effective therapy.	Clearly established as the most effective therapy.

*Widimsky et al. European Heart journal 2014*

Differences	AMI	AIS
<b>Etiology</b>	Uniform: plaque rupture or thrombosis in situ in 90–95% patients, other causes are rare	Multiple: cardioembolic, arterioembolic, thrombosis in situ, lacunar, cryptogenic.
<b>Death of cells after ischemia</b>	begins after 20-40 min (myocyte)	begins after 5 min (neurone)
<b>Arterial occlusive thrombus feasible for catheter-based thrombectomy</b>	Found in 95% of acute coronary angiograms.	Found only in cca 35% of acute CT-angiograms.
<b>Time window symptom onset—intervention start (to offer benefit and not harm)</b>	24 h (48 h in some patients)	6 hours (24 h in some)
<b>Reperfusion damage</b>	Only theoretical, clinically always reperfusion benefit.	Reperfusion damage (bleeding) is a real clinical problem
<b>Clinical picture</b>	Pain alerts the patient to call early for help	Neurologic dysfunction plus absence of pain causes late medical contacts in most pts.
<b>Diagnostic method before reperfusion therapy indication</b>	ECG (fast, simple, cheap, can be done in any facility)	CT (takes more time, expensive, in-hospital)
<b>Laboratory diagnostic marker</b>	Troponin	None yet available
<b>Contraindications for catheter-based thrombectomy</b>	None	intracranial bleeding or advanced ischemia on CT
<b>% of hospitalized patients who undergo reperfusion therapy</b>	>90%	<10%

