

Back to the Future

Current and Upcoming Promising Stroke Research

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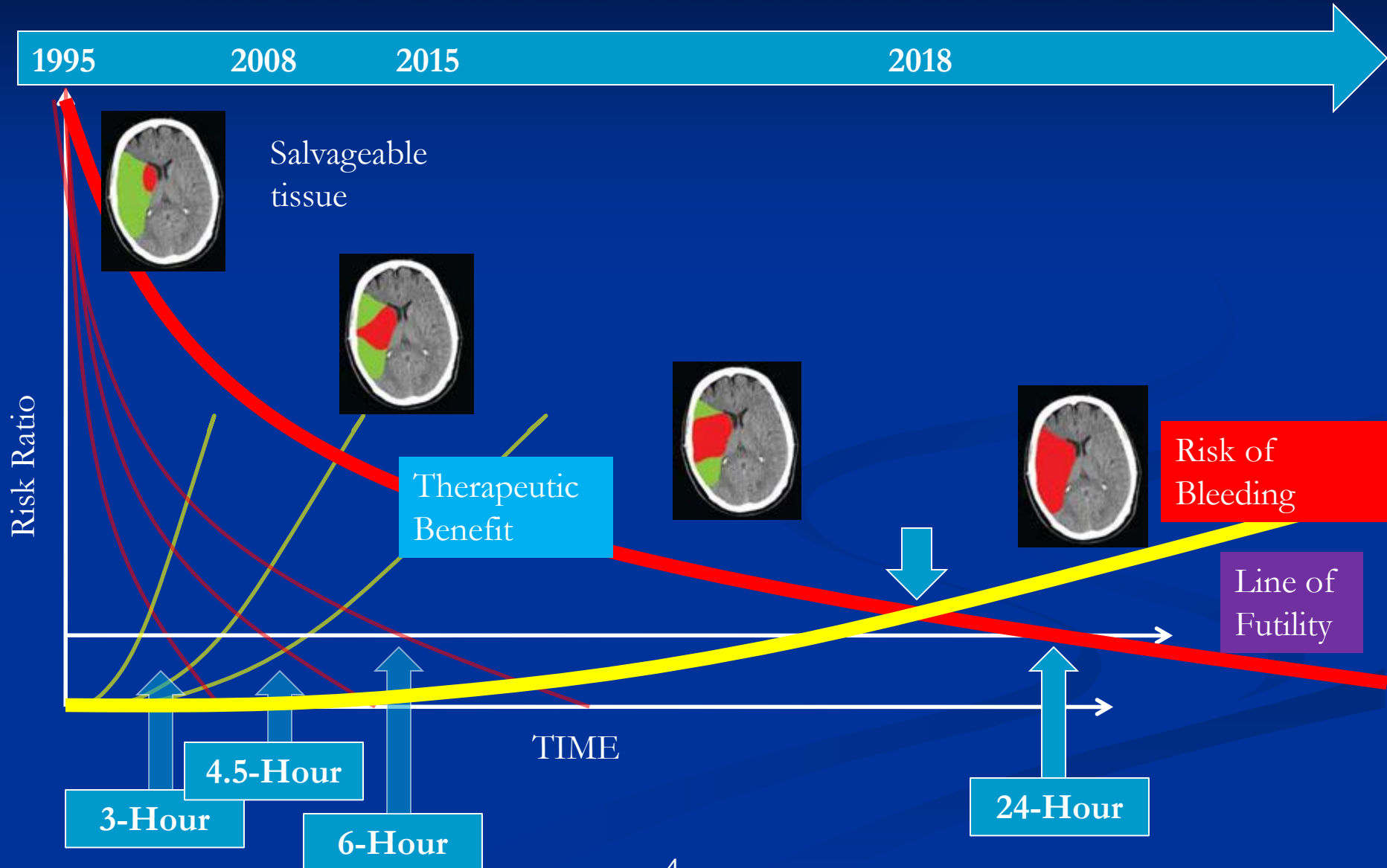
Disclosure

■ none

Educational Objectives:

1. Review evolution of stroke therapies over the decades
2. Discuss current stroke trials being done
3. Learn about upcoming stroke research and how they would impact the future of stroke care

Acute Stroke Treatment Evolution



Current Stroke Trials

■ Ischemic Stroke

- MOST trial: 0-3 hr (188/1200)
 - Argatroban or Eptifibatide in addition to TPA or TPA/MER
- ACTIVIS trial: 0-4.5 hr completed July 2021
 - Glanzocimab in addition to TPA or TPA/MER
- TIMELESS trial: 4.5-24 hr
 - TNK plus MER
- CHARM trial: 0-10 hr
 - (IV Glibenclamide to prevent cerebral edema)

■ Hemorrhagic

- FASTEST trial: 0-2 hrs
 - recombinant Factor VIIa for Acute Hemorrhagic Stroke

Current Stroke Trials

■ Prevention Trials

- Ischemic Stroke primary prevention
 - CREST-2
- Ischemic Stroke secondary prevention
 - ARCADIA
 - Sleep SMART
- Hemorrhagic stroke primary prevention
 - none
- Hemorrhagic stroke secondary prevention
 - ASPIRE
 - SATURN

Current Stroke Trials

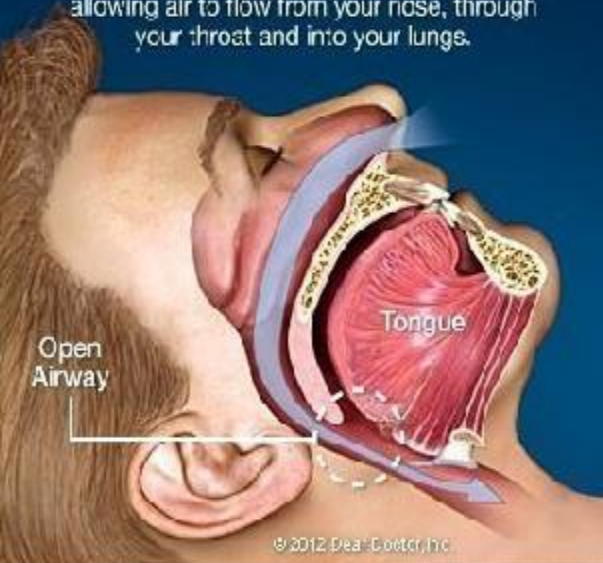
■ Prevention Trials

Sleep SMART (534/3062)

does treatment of sleep apnea after ischemic stroke reduces recurrent stroke?

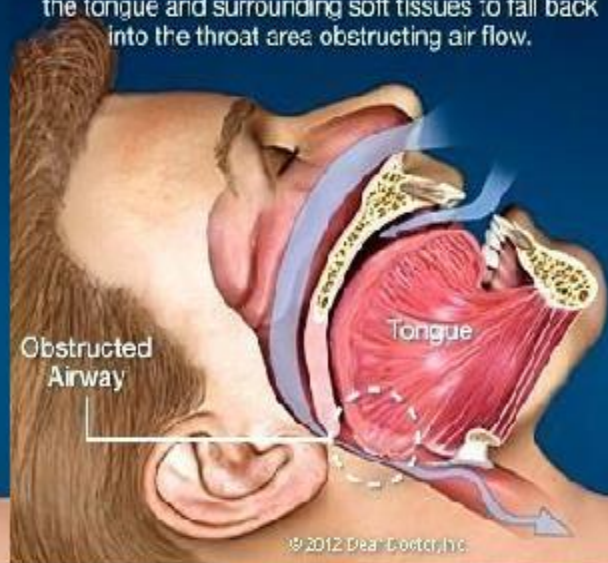
Normal Anatomy & Function

Your upper airway is open and unobstructed allowing air to flow from your nose, through your throat and into your lungs.



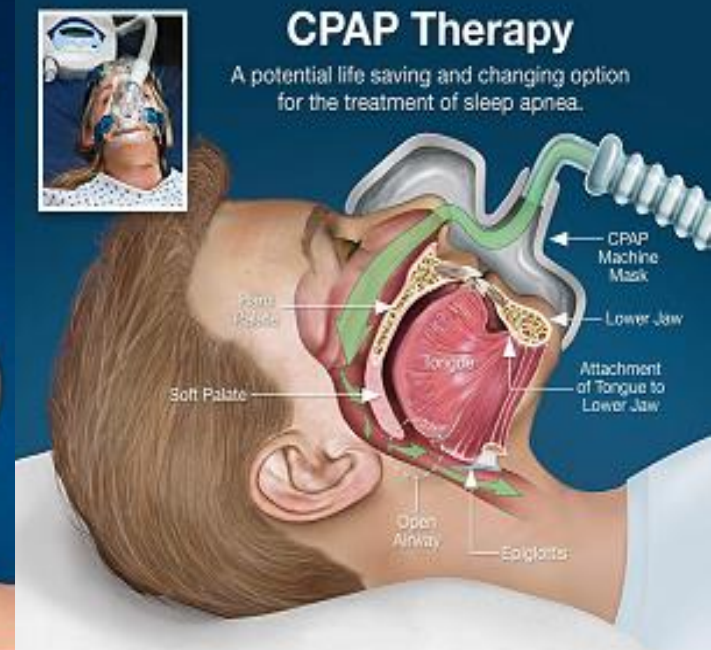
Obstructive Sleep Apnea

During sleep, gravity and muscle relaxation allows the tongue and surrounding soft tissues to fall back into the throat area obstructing air flow.



CPAP Therapy

A potential life saving and changing option for the treatment of sleep apnea.



Current Stroke Trials

■ Prevention Trials

ASPIRE (28/700)

Apixaban vs Aspirin in patients with AFib, after ICH

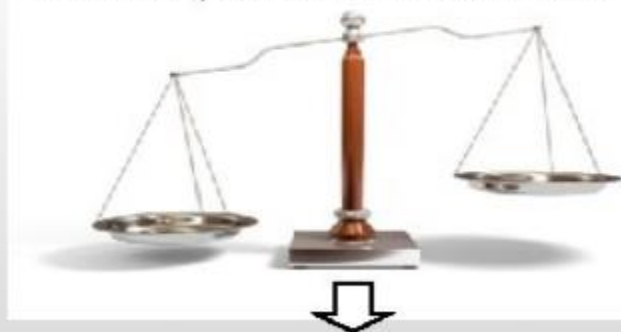
■ Ischemic Stroke secondary prevention

**Resumption of oral anticoagulation is
a major clinical dilemma in ICH care**

Currently available evidence:

Thrombosis Risk

- CNS: ischemic stroke
- Systemic Thromboembolism



Hemorrhage Risk

- CNS: recurrent ICH
- Systemic Bleeding

Mortality

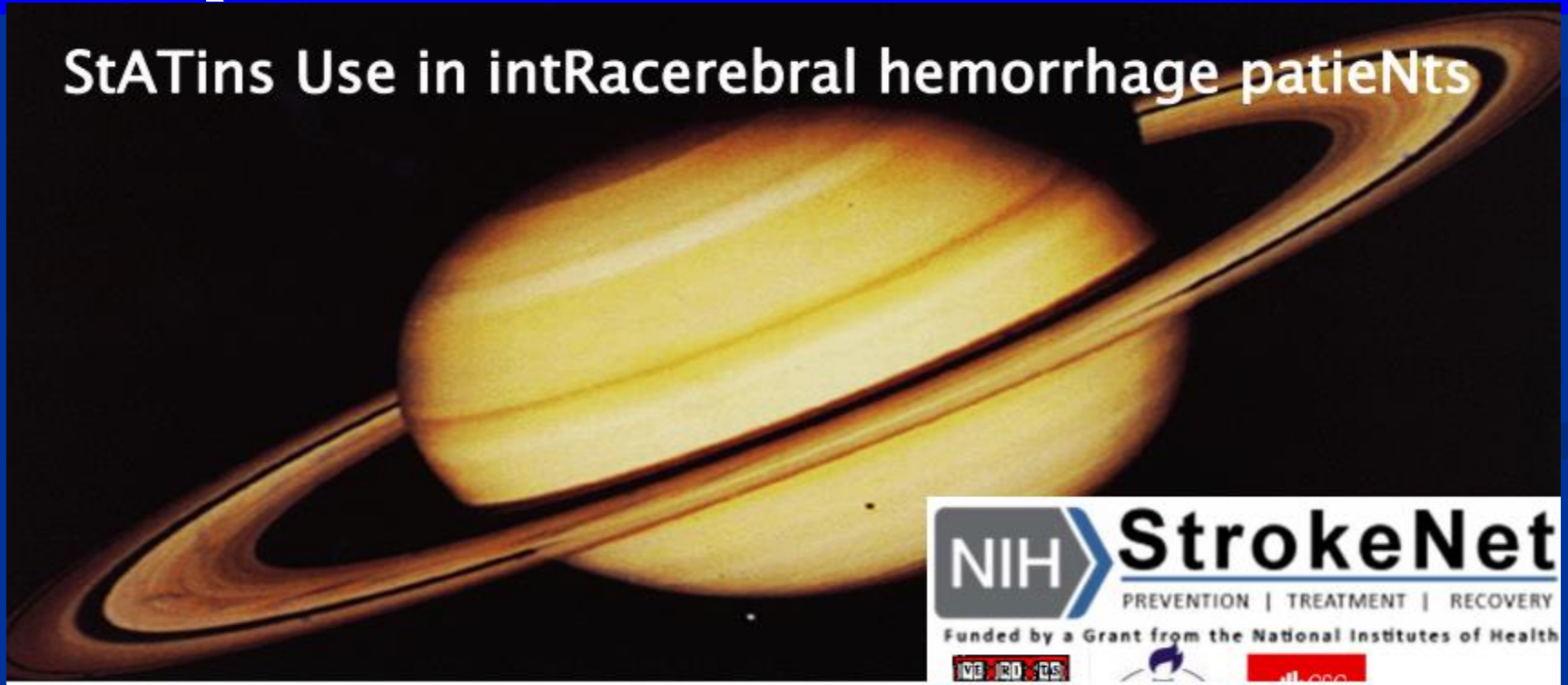
Current Stroke Trials

■ Prevention Trials

SATURN (101/456)

Resumption vs Discontinuation of Statin after ICH

StATins Use in intRacerebral hemorrhage patieNts



Stroke Trials at Upstate

STUDY	Target Patient	Intervention	Principal Investigator	Status
Sleep-SMART	Acute stroke Px with sleep apnea within 14 d	Auto-CPAP vs standard care	Latorre 39 subjects	Recruiting
CHARM	Large Ischemic stroke within 10 hours	IV Glibenclamide vs placebo	Latorre 3 subjects	Recruiting
MOST	Acute stroke receiving IVTPA within 3 hrs	Integrillin or Argatroban or Placebo	Latorre 4 subjects	Recruiting
PassPORT	Acute stroke or TIA within 30 hours	Personalized antiplatelet therapy based on genetics	Albright 76 subjects	Recruiting
ASPIRE	ICH patients with AF	Apixaban vs ASA	Albright 0 subjects	Recruiting
SATURN	ICH patients on statin	Resume vs Discont statin	Schmidt 3 subjects	Recruiting

Therapeutic GAP

Last Known Well	Large Vessel Occlusion (LVO)	Medium Vessel Occlusion	Small Vessels
0-4.5 hours 30-40%	EVT + TPA	TPA	TPA
4.5-9 hours 10-15%	EVT	TPA?	TPA?
9-24 hours 20-30%	EVT	???	???
Wake up Stroke (15-20%)	?EVT	???	???

Promising Stroke Trials

Last Known Well	Large Vessel Occlusion (LVO)	Medium Vessel Occlusion	Small Vessels
0-4.5 hours 30-40%	EVT + TPA	TPA	TPA
4.5-9 hours 10-15%	EVT	TPA?	TPA?
9-24 hours 20-30%	EVT	SISTER trial	
Wake up Stroke (15-20%)	?EVT		

TS23 – a novel inactivating antibody of a2AP (alpha-2 antiplasmin)
- Allows plasmin generated locally on fibrin surface to safely dissolve thrombus without toxicity

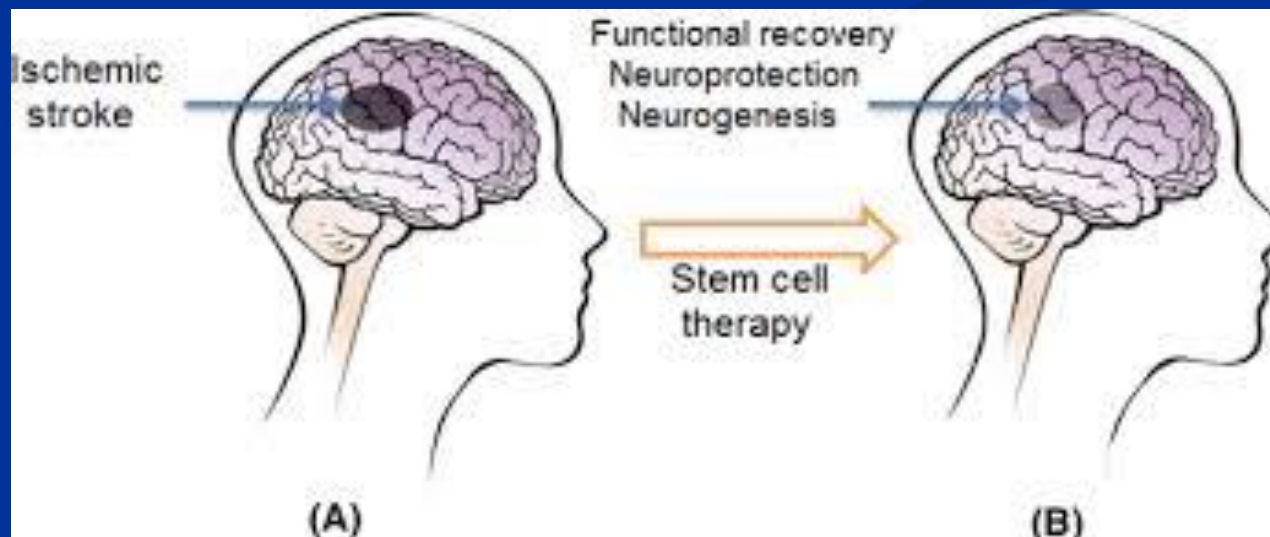
Advantages of TS23 (a2AP-I) vs. TPA

Outcome	TPA	TS23 (a2AP-I)
Effect on brain after prolonged ischemia	Harmful	Protective
Brain hemorrhage	Significant; fatal	Protective, prevents
Systemic Bleeding	Significantly increases	No effect
Coagulation	Impairs	No effect
Microvascular thrombosis	Activates clotting and microvascular thrombosis	Prevents microvascular thrombosis
MMP-9, BBB breakdown	Increases, deleterious	Decreases, protective
Time window for benefit	Limited	10-fold longer
Mortality Benefit	Equivocal	Prolongs life
Dosing	Complex (bolus(es) followed by infusions)	Simple (single bolus)

Promising Stroke Trial

Last Known Well	Large Vessel Occlusion (LVO)	Medium Vessel Occlusion	Small Vessels
0-4.5 hours 30-40%	EVT + TPA	TPA	TPA
4.5-9 hours 10-15%	EVT	TPA?	TPA?
9-24 hours 20-30%	EVT	TREASURE trial	
Wake up Stroke (15-20%)	TPA?		

TREASURE trial – use of multipotent stem cells (Multistem) 24-36 hours from stroke onset



THANK YOU



THIS ISN'T FUNNY

I'm having a stroke

Current Stroke Trials

■ Rehab and Recovery Trials

■ I-ACQUIRE (60/240)

- Perinatal arterial Stroke, study of intensive infant rehabilitation (usual care vs 3 hour/day vs 6 hr/day therapy)

■ TRANSPORT2 (40/129)

- Use of transcranial direct current stimulation for post stroke motor recovery

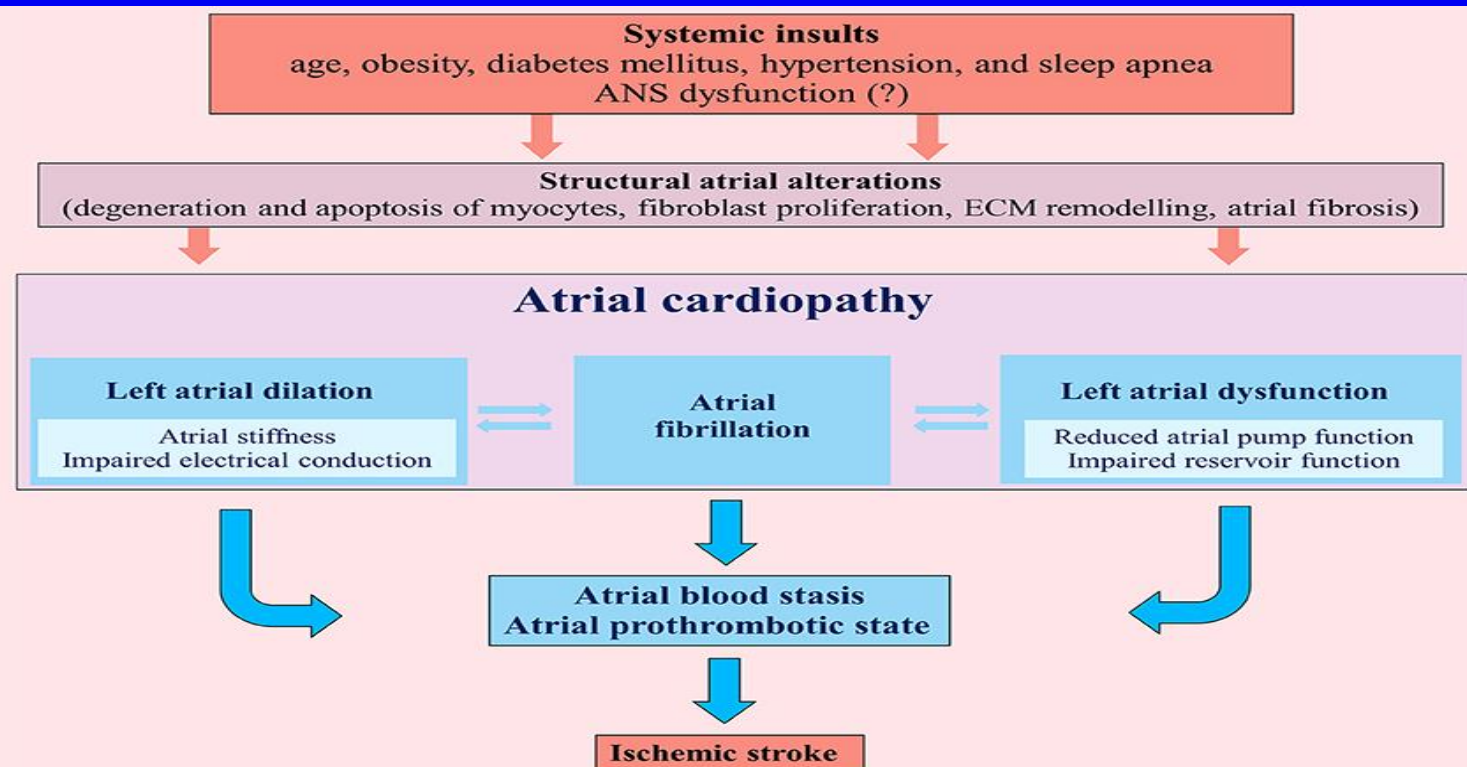


Current Stroke Trials

■ Prevention Trials

ARCADIA (662/1100)

apixaban vs aspirin in cryptogenic stroke with



Current Stroke Trials

■ Prevention Trials

CREST2 (1861/2480)

Carotid stenting vs Carotid Endarterectomy in patients with Asymptomatic Carotid Stenosis 70% or greater

