The Admitted Stroke Patient- Next Steps/Work-up

SANDEEP KUMAR, MD

DEPARTMENT OF NEUROLOGY/STROKE DIVISION

BETH ISRAEL DEACONESS MEDICAL CENTER

Disclosures

None Relevant

Outline

What can go wrong with the patient at this stage?

Early Neurological Deterioration

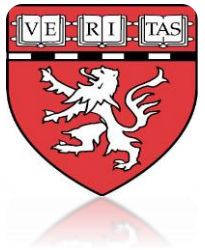
Neurological and Systemic Complications

Why did the patient have a stroke?

Investigations

Early preventive strategies

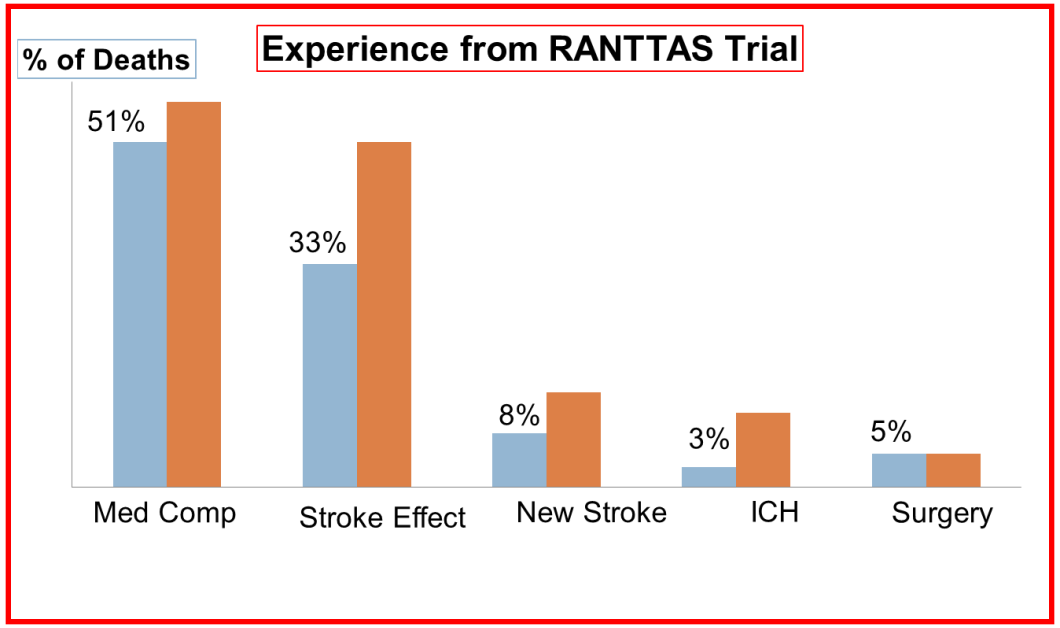
Organizing Care



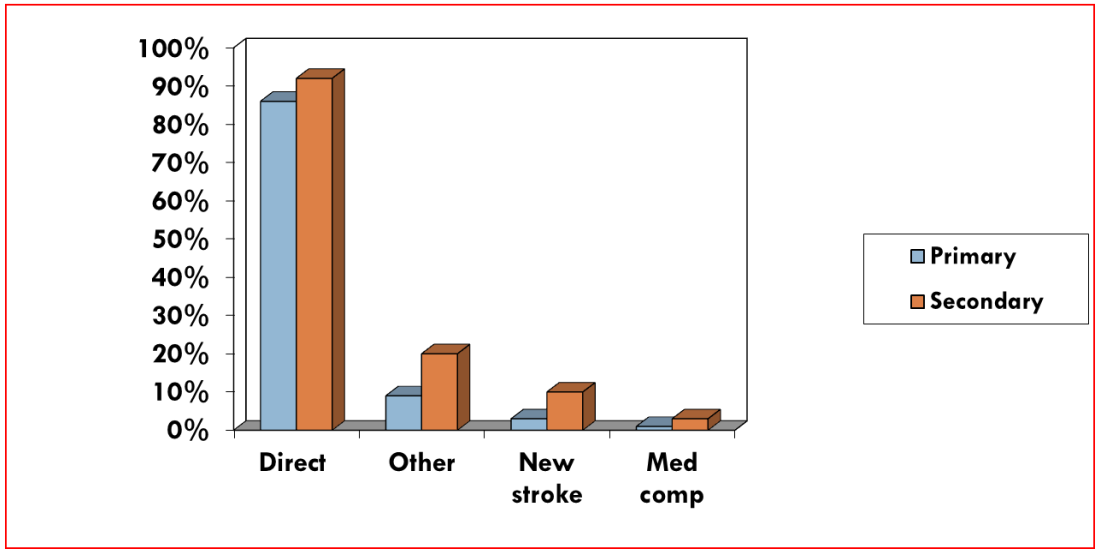
Complications

Post-Stroke Complications

CAUSES OF DEATH-AIS



CAUSES OF STROKE RELATED DISABILITY-PRIMARY AND SECONDARY CAUSES

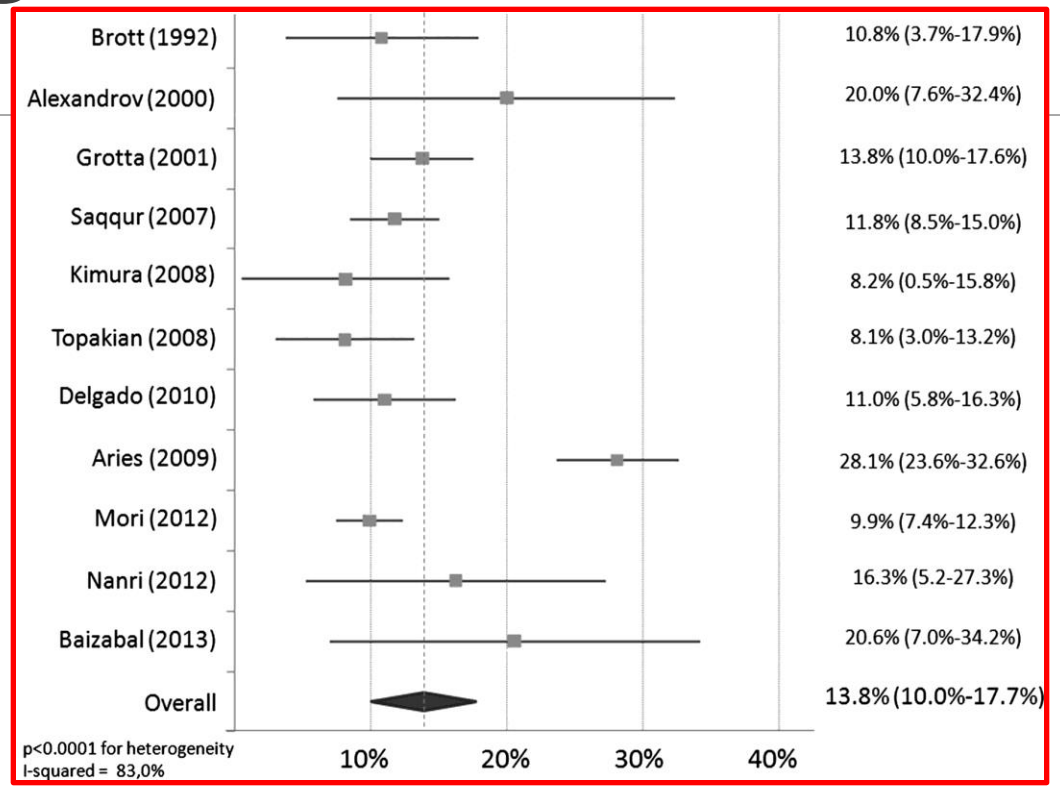


In multivariate analysis adjusted for NIHSS, age, DM ~ serious medical events associated with severe disability as determined by GOS (OR 4.4; 95% CI, 1.3-14.8)

Johnston et al., Stroke 1998

Early Neurological Deterioration

- A significant proportion of AIS patients deteriorate after a seemingly stable initial course
- Variable definitions (different scales, clinical thresholds, time cut-offs)
- Usually refers to deterioration ≤ 24 hours
- Almost half have no clear cause ("progressive stroke")
- Associated with increased risk of death and dependency

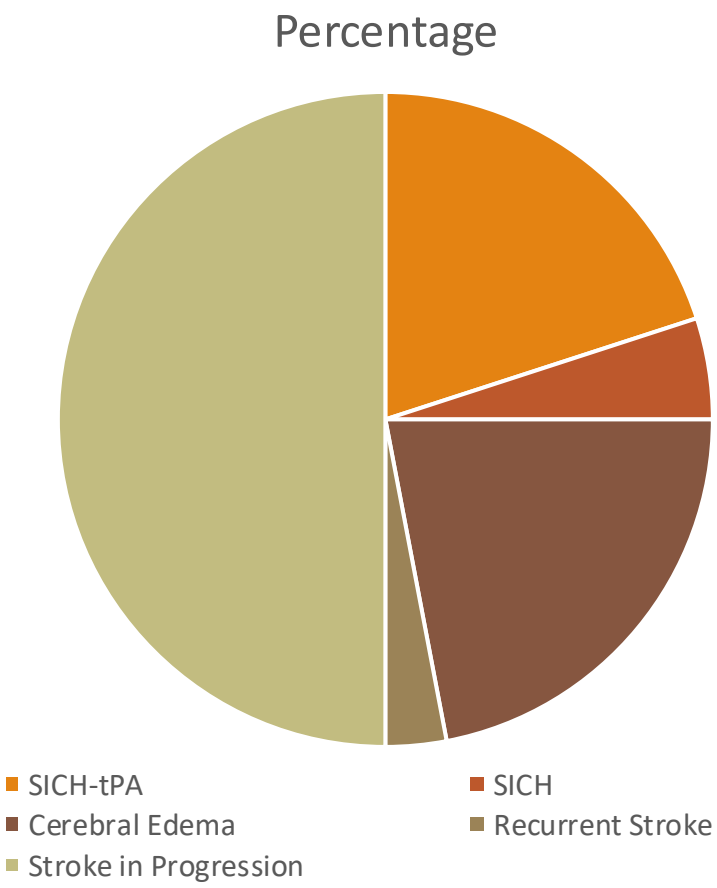


Pierre Seners et al., J Neurol Neurosurg Psych 2015

Table 2 Incidence of END_{24} in non-thrombolysed patients with AIS

Study	Inclusion criteria	N	Def. of END_{24}	Percentage of END_{24}	Percentage of END_{24} due to sICH
Dávalos *et al*[18]	AIS <8 h	98	CNS ≤1	31.6	NA
Camerlingo *et al*[20]*	MCA-AIS <5 h	45	CNS ≤1	13.3	16.7
Toni *et al*[21]	MCA-AIS <5 h	152	CNS ≤1	15.1	NA
Dávalos *et al*[23]†	AIS <6 h	305	SSS‡	36.8	7.1§
Alexandrov *et al*[25]	AIS <6 h, NIHSS <4	50	NIHSS ≥4	16.3	NA
Grotta *et al*[27]¶	AIS <3 h	312	NIHSS ≥4	17.6	3.6§

Potential Etiologies for END



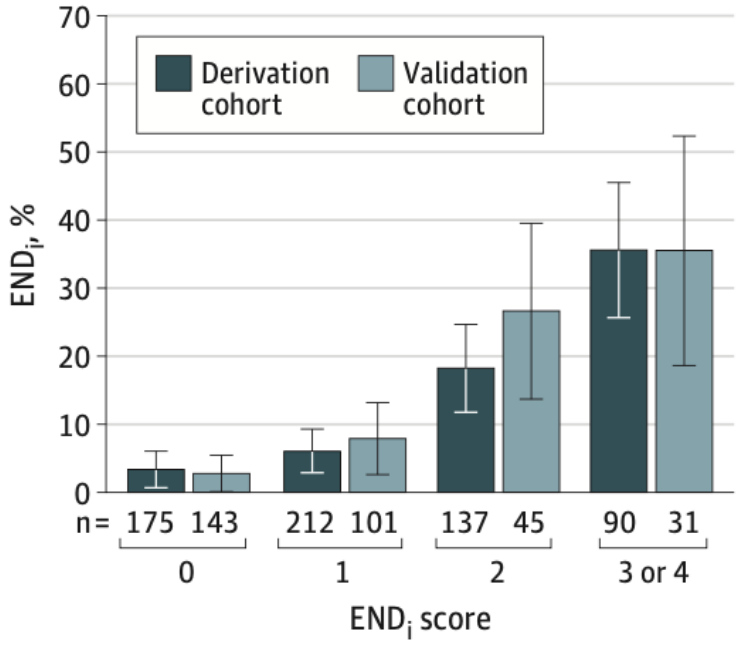
Risk Factors
High Stroke Severity
Arterial Stenosis or Occlusion
Blood Pressure-low/labile
Hyperglycemia
Treatment with Thrombolytics
Stroke Subtype: Large Vessel, Lacunar syndrome
Elderly

Predicting and Preventing END

A END_i risk prediction score

Category	Points
Thrombus length	
<9 mm	0
≥9 mm	1
Occlusion site	
M2	0
Distal M1	1
Proximal M1 or tandem or basilar	2
ICA-T/L	3

B Probability of END_i



ENDi Score for Prediction of Early Neurological Deterioration of Presumed Ischemic Origin in Patients With Minor Stroke Due to an LVO

- Monitor and treat hypotension (treatment of hypertension based on comorbid condition)
- Treat Hyperglycemia (target BS ~ 140-180 mg/dl)
- Treat Hypoglycemia (BS < 60 mg/dl)
- Treat Fever (temp > 38 F)
- Supplemental O2 for hypoxic patient

Seners et al., 2021

JAMA Neurology | Original Investigation

Argatroban in Patients With Acute Ischemic Stroke With Early Neurological Deterioration
A Randomized Clinical Trial

Multicenter, open-label, blinded endpoint assessment (28 Sites in China)

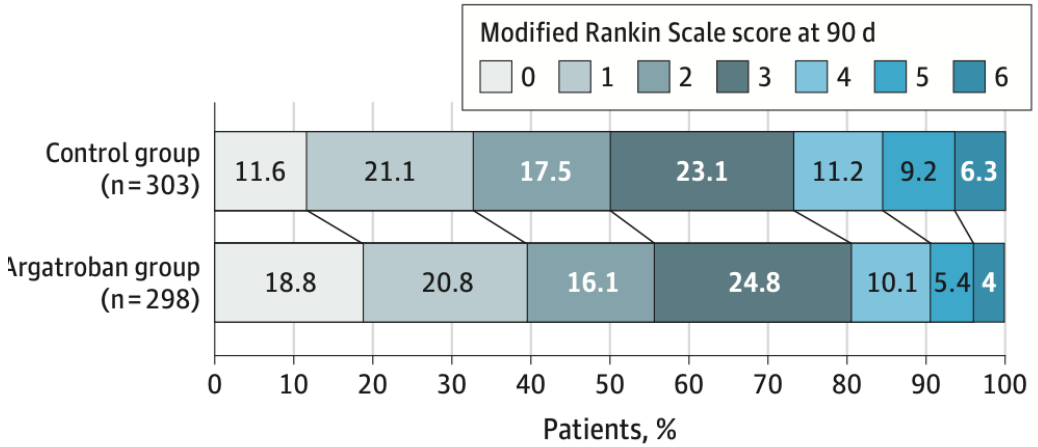
Inclusion Criteria:

- AIS ≤ 48 hours onset
- NIHSS ≥ 2 (END)
- On antiplatelet Rx (mono or DAPT)

Primary Outcome:

Good Outcome (mRS 0-3)

7.2% RD; 1.10 RR (p=0.04)



JAMA, 2024

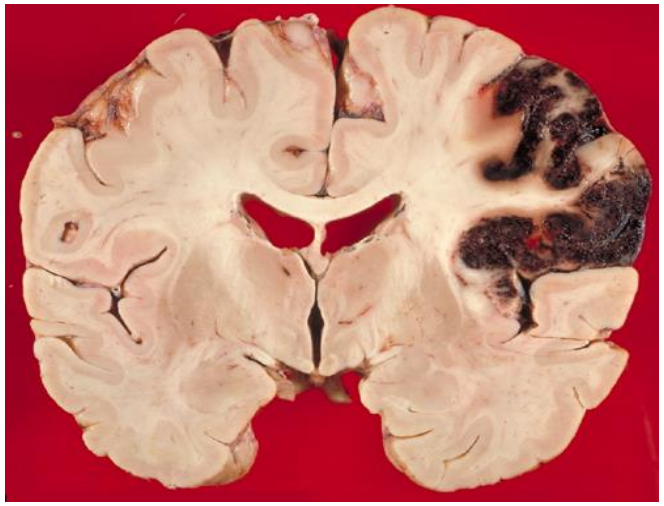
Hemorrhagic Infarction

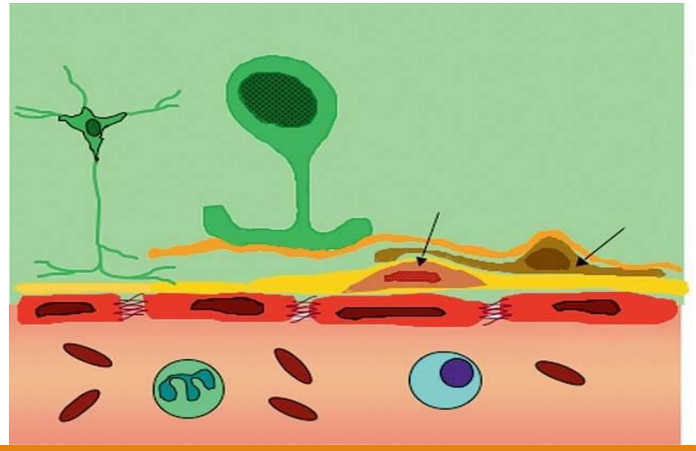
Blood staining of a pale infarct

Results from increased permeability of BBB/endothelial dysfunction from ischemia & reperfusion of ischemic tissues

Common after embolic infarcts

Mostly involves gray matter





Hemorrhagic Transformation

- Classified according to imaging characteristics or symptoms
- PH + relevant clinical deterioration is a predictor of long-term disability
- Clinical clues-reduction in alertness, new HA, abrupt increase in BP with persistently elevated levels
- Risk Factors: Age

  Infarct size

  Stroke subtype(embolic)

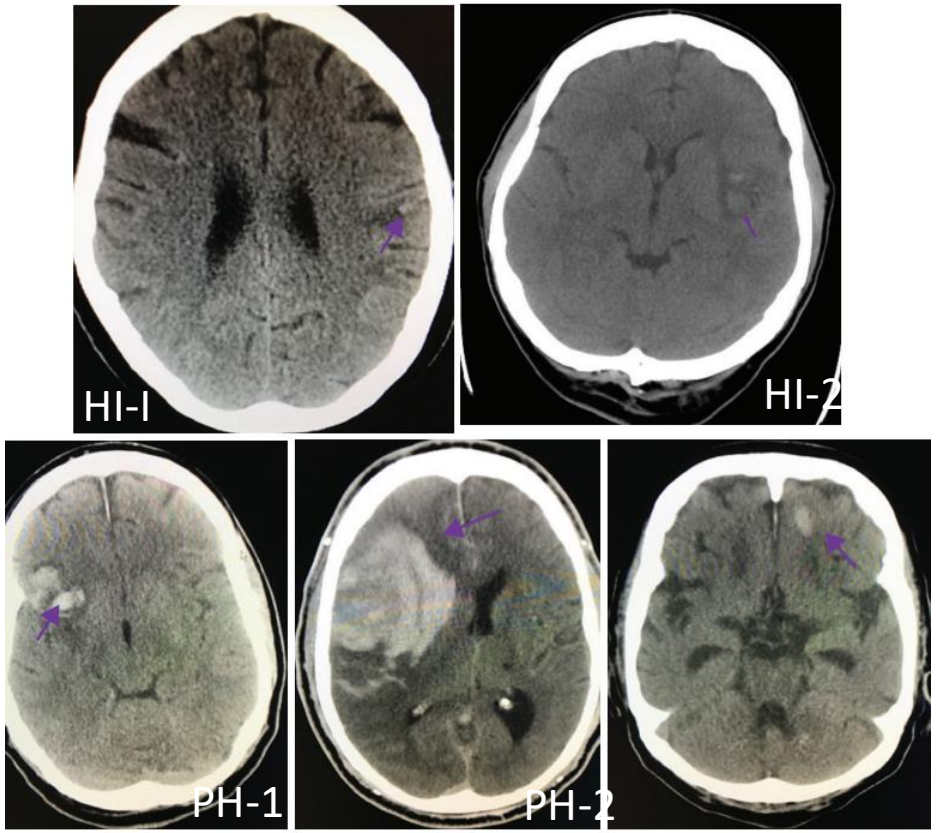
  Elevated blood sugar,

  Elevated SBP

  Pre-treatment/treatment with AC/APL

  Thrombolysis

  Revascularization Time

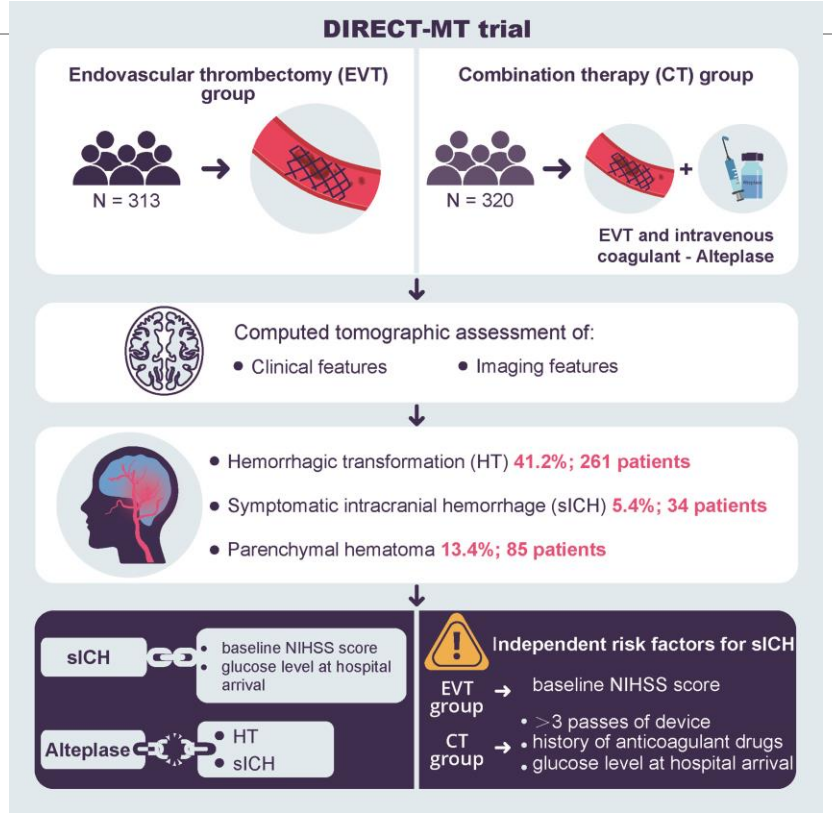


Yaghi et al., Stroke 2017

Risk of Hemorrhagic Transformation after iv tPA and EVT

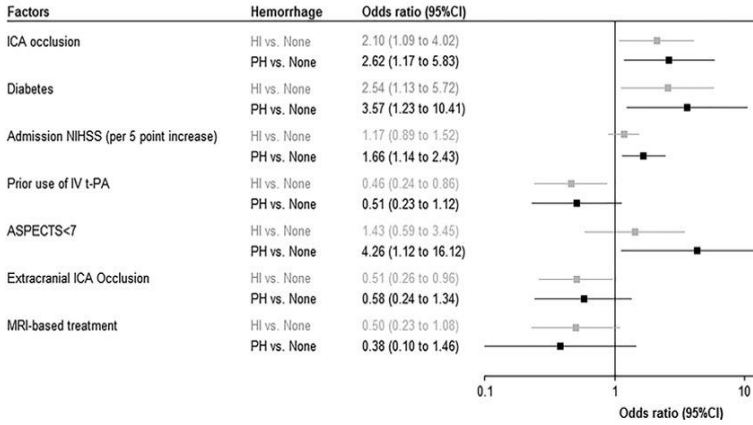
Score	Components	Receiver-Operating Characteristic Curve (C Statistics)
MSS[24]	Age, NIHSS score, glucose, platelets (0–4 points)	0.59–0.86
HAT[25]	NIHSS score, diabetes mellitus or glucose, early CT hypodensity (0–5 points)	0.59–0.79
SEDAN[26]	Age, NIHSS score, glucose, hyperdense middle cerebral artery sign, early CT hypodensity (0–5 points)	0.50–0.70
SITS-ICH[27]	Age, NIHSS score, glucose, weight, hypertension, antiplatelet therapy (none, aspirin, aspirin+clopidogrel), systolic blood pressure, onset-to-treatment time (0–12 points)	0.58–0.76
GRASPS GWTG[9]	Age, NIHSS score, glucose, systolic blood pressure, Asian vs non-Asian ethnicity, sex (0–101 points)	0.61–0.83
THRIVE[28]	Age, NIHSS score, hypertension, diabetes mellitus, atrial fibrillation (0–9 points)	0.6
SPAN-100[29]	Age, NIHSS score (0–1 points)	0.55–0.57

Yaghi et al., 2017



Tian et al., Stroke 2022

EVT-Tandem Lesion-TITAN



Zhu et al., Stroke; 2018

Management of Symptomatic ICH from IV tPA

Reversal Agent	Suggested Dose	Potential for Benefit	Adverse Effects
Cryoprecipitate	Consider sending a fibrinogen level immediately and empirically transfusing with 10 U cryoprecipitate, and anticipate giving more cryoprecipitate as needed to achieve a normal fibrinogen level of ≥150 mg/dL (10 U cryoprecipitate increases fibrinogen by nearly 50 mg/dL)	Potential for benefit in all sICH	Transfusion reaction and transfusion-related lung injury
Platelets	2 donors (8–10 U)	Potential for benefit is unclear except in patients with thrombocytopenia (platelets <100 000/μL), who may possibly benefit	Transfusion reaction, transfusion-related lung injury, volume overload
FFP	12 mL/kg	Potential for benefit is unclear except in patients on warfarin, in whom FFP may be considered	Transfusion reaction, transfusion-related lung injury, volume overload
PCC	25–50 U/kg (based on INR level)	Potential for benefit is unclear except in patients on warfarin, in whom PCC may be considered and is the preferred adjunctive treatment	Thrombotic complications
Vitamin K	10 mg intravenously	Potential for benefit is unclear except in patients on warfarin, in whom vitamin K may be used as an adjunctive treatment	Anaphylaxis
rFVIIa	20–160 μg/kg	Potential for benefit is unclear	Thrombotic complications
Antifibrinolytic agents	Aminocaproic acid: 4 g IV during first hour followed by 1 g/h for 8 h Tranexamic acid: 10 mg/kg 3–4 times/d (adjustment based on kidney function may be necessary)	Potential for benefit in all patients with sICH, particularly when blood products are contraindicated or declined by patient/family or if cryoprecipitate is not available	Thrombotic complications

AHA Scientific Statement, 2017

Table 6. Management of Symptomatic Intracranial Bleeding Occurring Within 24 Hours After Administration of IV Alteplase for Treatment of AIS

COR IIb	LOE C-EO
Stop alteplase infusion	
CBC, PT (INR), aPTT, fibrinogen level, and type and cross-match	
Emergent nonenhanced head CT	
Cryoprecipitate (includes factor VIII): 10 U infused over 10–30 min (onset in 1 h, peaks in 12 h); administer additional dose for fibrinogen level of <150 mg/dL	
Tranexamic acid 1000 mg IV infused over 10 min OR ε-aminocaproic acid 4–5 g over 1 h, followed by 1 g IV until bleeding is controlled (peak onset in 3 h) (Potential for benefit in all patients, but particularly when blood products are contraindicated or declined by patient/family or if cryoprecipitate is not available in a timely manner.)	
Hematology and neurosurgery consultations	
Supportive therapy, including BP management, ICP, CPP, MAP, temperature, and glucose control	

AHA AIS Guidelines, 2019

Medical Complications after Stroke

	Kalra et al[4]	Davenport et al[5]	Johnston et al[1]	Langhorne et al[6]	Roth et al[7]	Weimar et al[2]	Bae et al[9]	Hong et al[3]	Indredavik et al[8]
Design	Prospective (IS and HS), subacute	Retrospective (IS and HS), subacute	Prospective, RCT (IS), acute-subacute	Prospective (IS and HS), acute-subacute	Prospective (IS and HS), subacute	Prospective (IS), acute	Prospective (IS), acute	Prospective (IS), acute	Prospective, (IS and HS), acute-subacute
Participants	245	607	279	311	1029	3866	579	1254	489
Study setting	Single-centre	Single-centre	Multicentre	Multicentre	Single-centre	Multicentre	Single-centre	Multicentre	Single-centre
Complication rate (total)	60%	59%	95%	85%	75%	29·2%	27·6%	24·2%	64%
Chest infection	12%	12%	10%	22%	4%	7·4%	10·7%	12%	11·2%
Urinary tract infection	20·4%	16%	11%	23%	30·5%	6·3%	8·3%	6·9%	16%
Fever	NR	4%	16%	NR	NR	13·2%	1·2%	2%	24%
Pain	25·3%	NR	NR	43%	14·2%	NR	NR	NR	26%
Pressure sores	3·3%	18%	NR	21%	4·3%	NR	1·4%	3·3%	0·6%
Falls	NR	22%	NR	25%	10%	NR	NR	2·2%	8·4%
Depression	25·3%	5%	NR	16%	13%	NR	NR	NR	NR
Deep vein thrombosis	4%	3%	2%	2%	4%	0·2%	NR	NR	0·6%
Pulmonary embolism	1%	1%	1%	1%	1%	0·2%	NR	NR	0·6%
Myocardial infarction/angina	NR	NR	6%	NR	3%	0·5%	1·2%	1·9%	4·5%
Congestive heart failure	NR	NR	11%	NR	2%	2·9%	NR	NR	NR
Cardiac arrest/arrhythmia	NR	NR	2%	NR	3·2%	8·2%	NR	NR	NR
Gastrointestinal bleed	NR	NR	5%	NR	3·1%	NR	NR	NR	NR
Dysphagia	NR	NR	5%	NR	NR	NR	NR	NR	NR
Urinary incontinence	NR	NR	5%	NR	NR	NR	NR	NR	NR

HS=haemorrhagic stroke. IS=ischaemic stroke. NR=not reported. RCT=randomised controlled trial.

Kumar et al., 2010

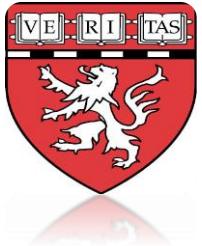
Systemic Stroke Complications in Hospitalized Patients

AHA SCIENTIFIC STATEMENT

Addressing Systemic Complications of Acute Stroke: A Scientific Statement From the American Heart Association

Sandeep Kumar, MD, Chair; Sherry H-Y Chou, MD, MSc, Vice Chair; Craig J. Smith, MD; Anusha Nallaparaju, MD; Osvaldo Jose Laurido-Soto, MD; Anne D. Leonard, MPH, BSN, RN, FAHA; Ajay K. Singla, MD; Ann Leonhardt-Caprio, DNP, RN, ANP-BC, SCRN, FAHA; Daniel Joseph Stein, MD, MPH; on behalf of the American Heart Association Stroke Council; Council on Cardiovascular and Stroke Nursing; and Council on Hypertension

Stroke; 2025



Investigations

Ischemic Stroke Sub-type-TOAST Classification

Large Artery Atherosclerosis

Extracranial or intracranial disease

Small Artery Occlusions

Cardio embolism

High and low risk lesions

Other Demonstrated Cause

Non-atherosclerotic vasculopathy

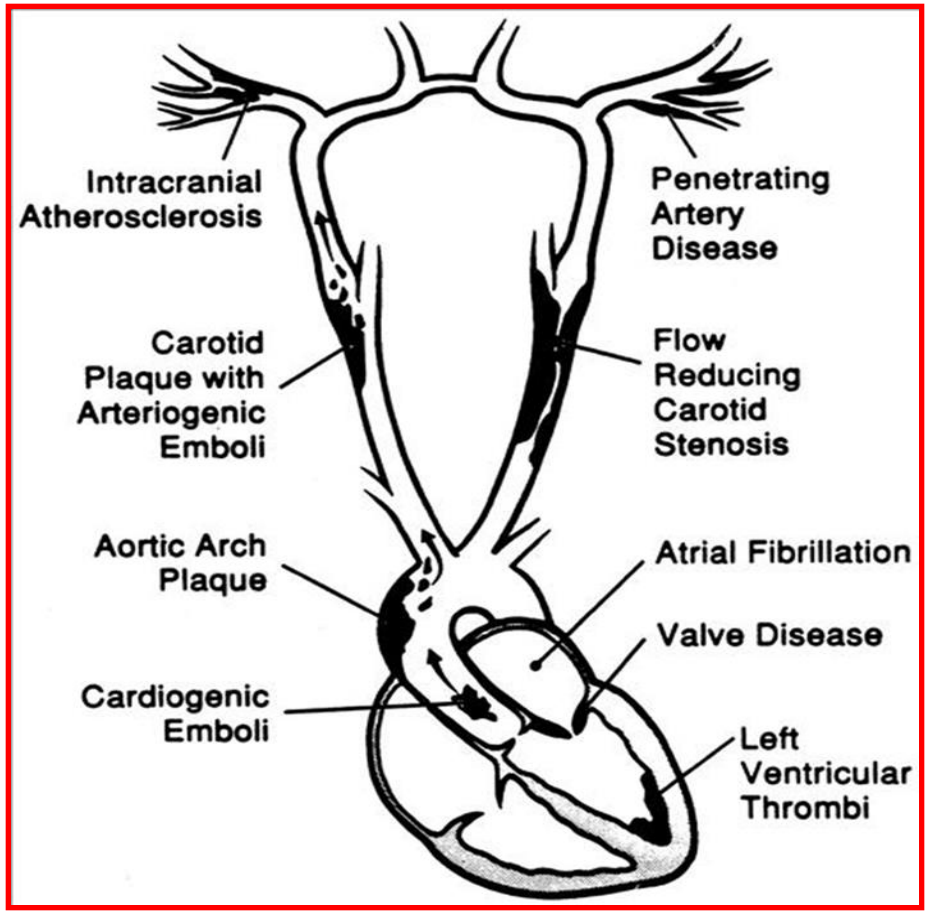
Prothrombotic state

Undetermined Cause

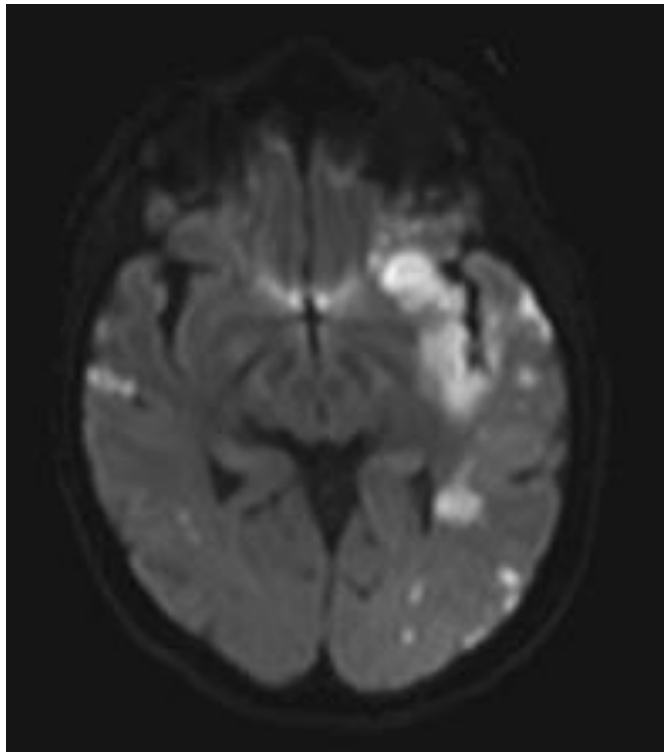
Incomplete Evaluation

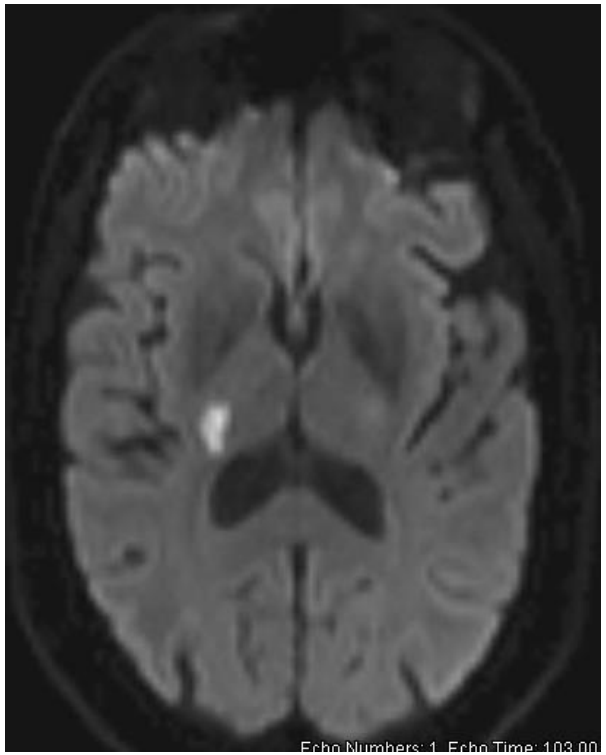
Diagnostic tests negative

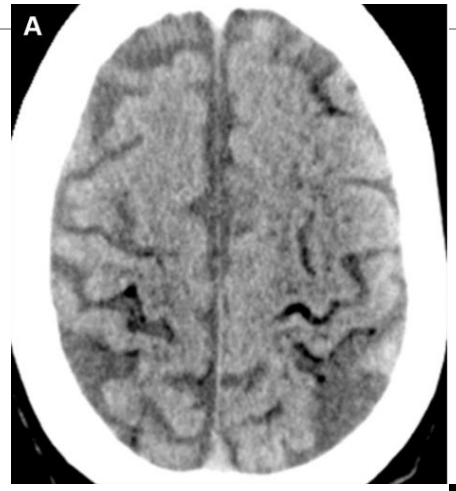
More than 2 competing causes

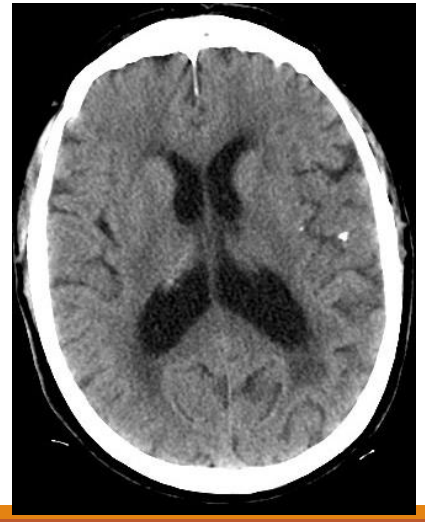


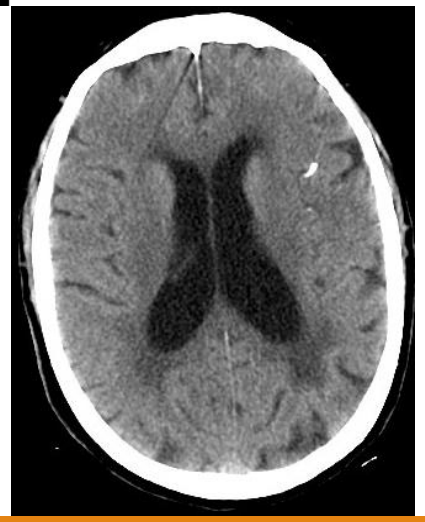
Brain Imaging



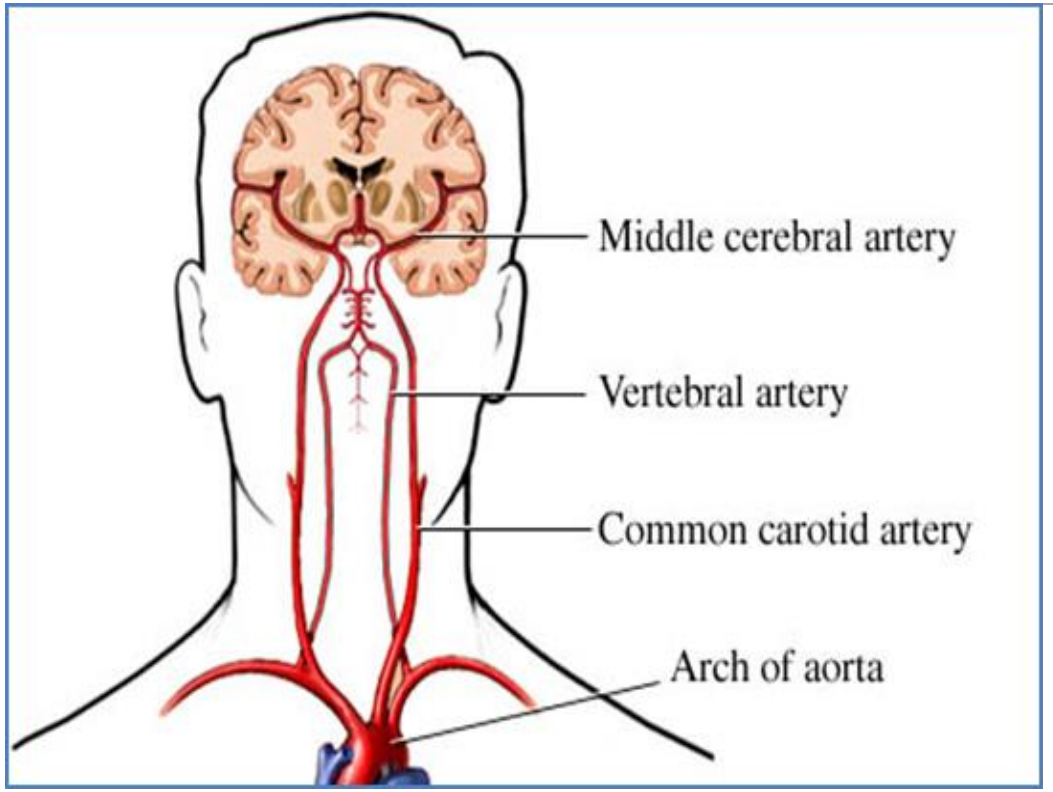








Arterial Pathologies



Atherosclerosis

Dissection

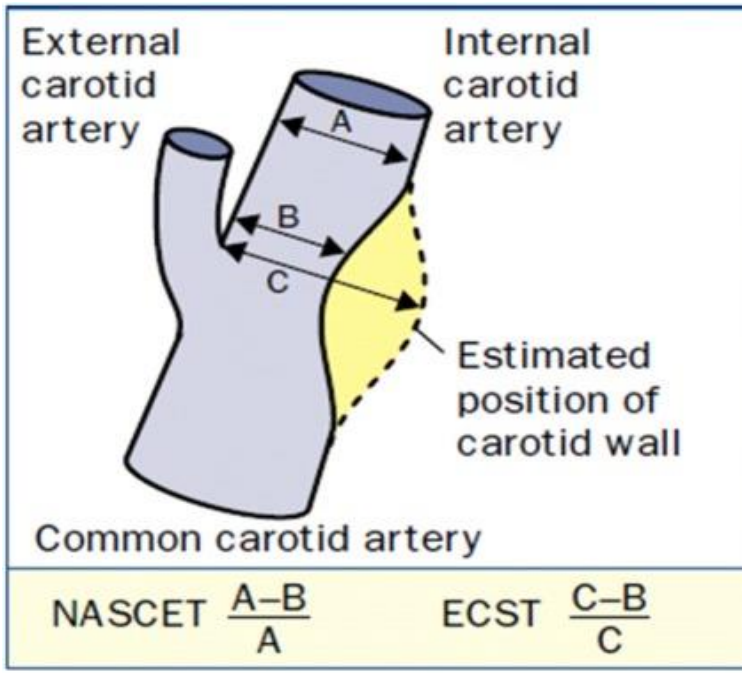
Fibromuscular Dysplasia

Carotid Web

Dolichoectasia

Arteritis

Vessel Imaging-Extracranial Carotid Stenosis



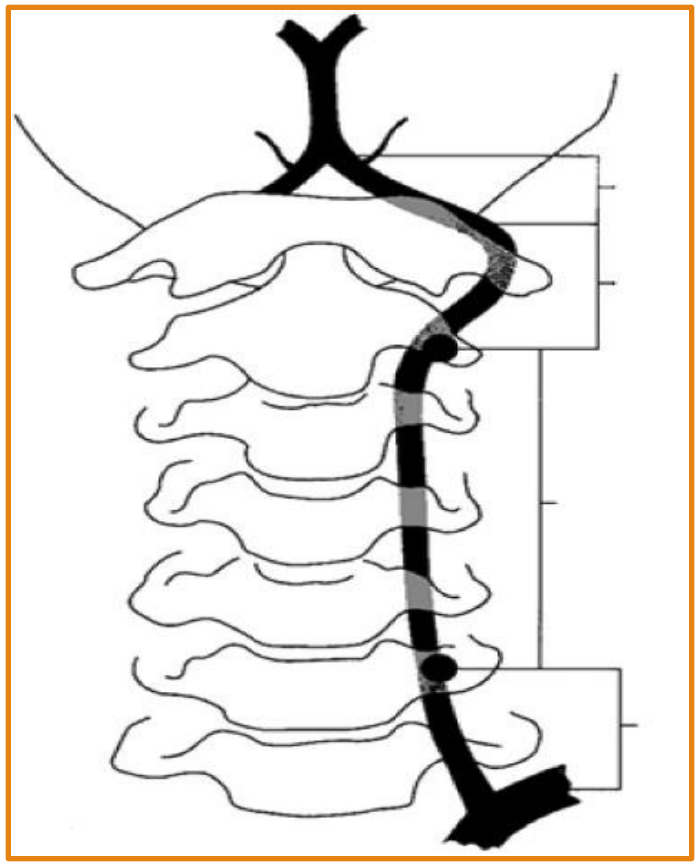
Modality (70-99% CS)	Sensitivity	Specificity
Carotid Duplex	0.89	0.84
MRA	0.92	0.76
MRA-CE	0.94	0.93
CTA	0.85	0.93

Saxena et al., 2019

50-69% stenosis	Carotid US	CTA	MRA
Sensitivity (95% CI)	0.36 (0.25-0.49)	0.67 (0.30-0.90)	0.37 (0.26-0.49)
Specificity (95% CI)	0.91 (0·87–0·94)	0.79 (0·63–0·89)	0.91 (0·78–0·97)

Wardlaw et al., Lancet 2006

Extracranial Vertebral Artery- Imaging



Modality	Sensitivity	Specificity
50-99% Stenosis		
Duplex	70.2	93.4
TOF MRA	71.4	95.1
CE-MRA	93.9	94.8
CTA	100	95.2

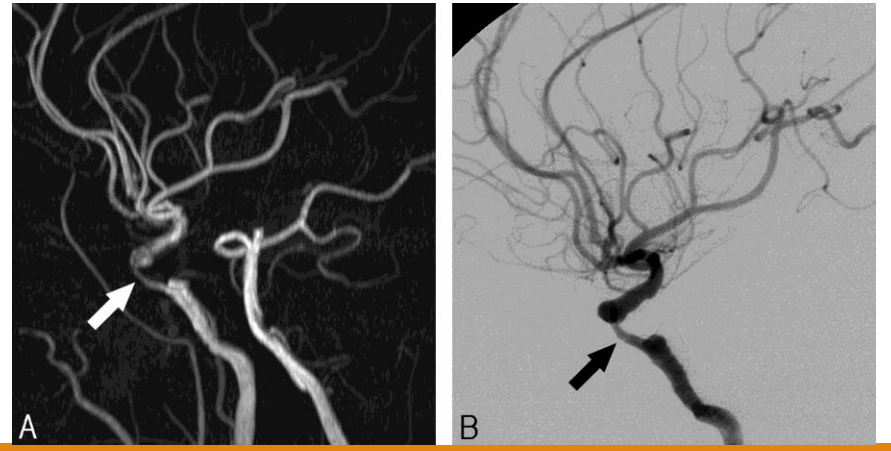
Khan et al., 2007

Intracranial Arterial Stenosis:

How good are the tests?

	PPV	NPV
TCD	55% (36, 74)	83% (79, 86)
MRA	66% (58, 73)	87% (85, 89)
	Adjusted test cutpoints*	
TCD	Initial (mean velocity)	Adjusted (mean velocity)
MCA	100 cm/s	240 cm/s
ICA	90 cm/s	120 cm/s
Vertebral	80 cm/s	110 cm/s
Basilar	80 cm/s	130 cm/s
MRA	≥ 50% stenosis or flow gap	≥ 80% stenosis or flow gap

	PPV	NPV
CTA 50-99%	46.7% (21.3-73.4)	73% (55.9-86.2)
70-99%	13.3% (1.7–40.5)	83.8% (68.0–93.8)



Feldmann et al., 2007; Liebeskind et al., 2014

Cardiac Sources of Embolism

Atrial

- AF, PAF, Aflutter
- Left Atrial Thrombus
- Left Atrial Myxoma
- PFO, ASD

Valvular

- Prosthetic Heart Valve
- Mitral Stenosis
- Endocarditis
- Fibroelastoma

Ventricular

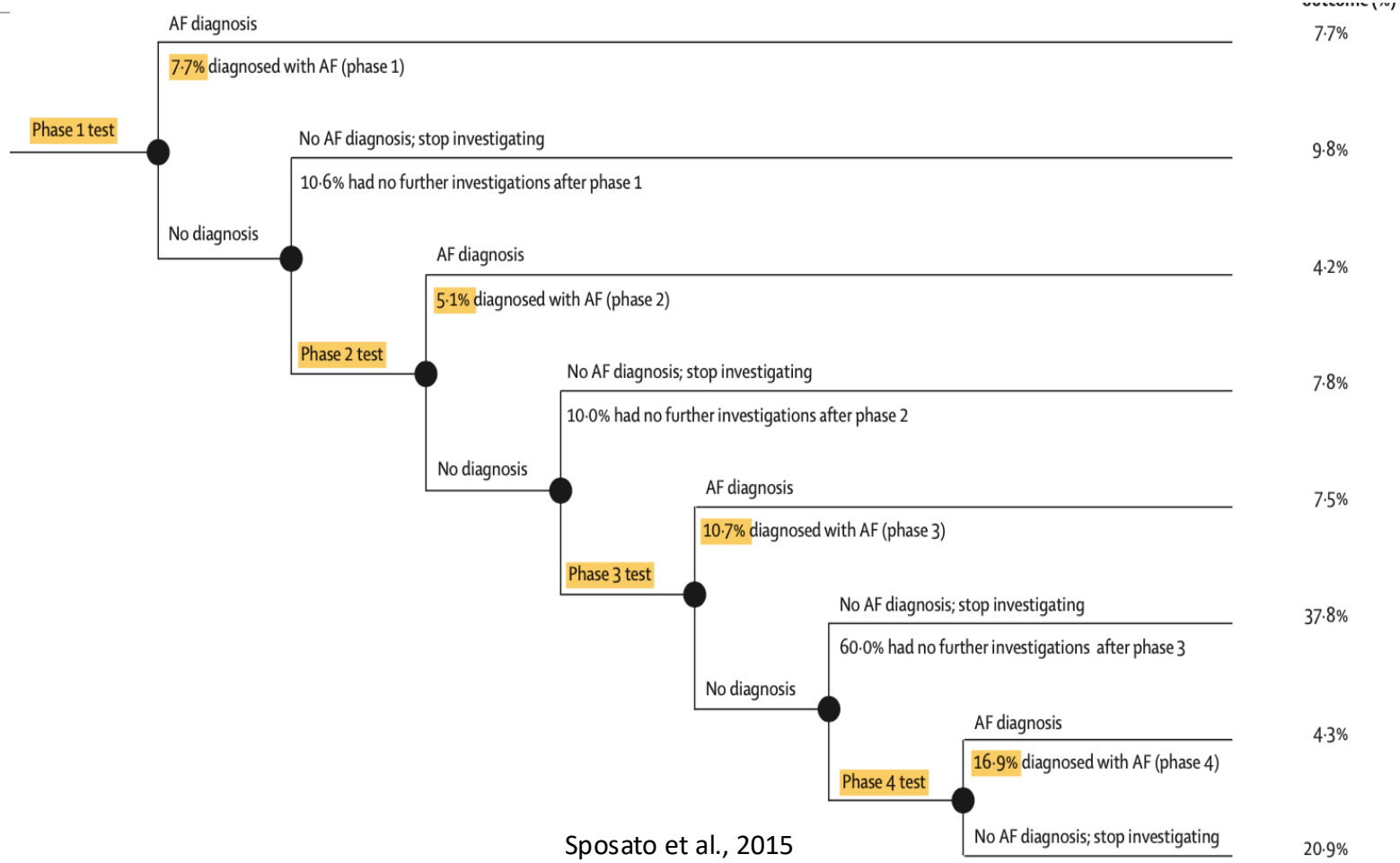
- LV thrombus
- Recent AMI
- DCM
- Non-impaction CMP

EKG and Cardiac Monitoring

Routine initial EKG- Post-stroke AF 7.7%

Concomitant MI in 3%

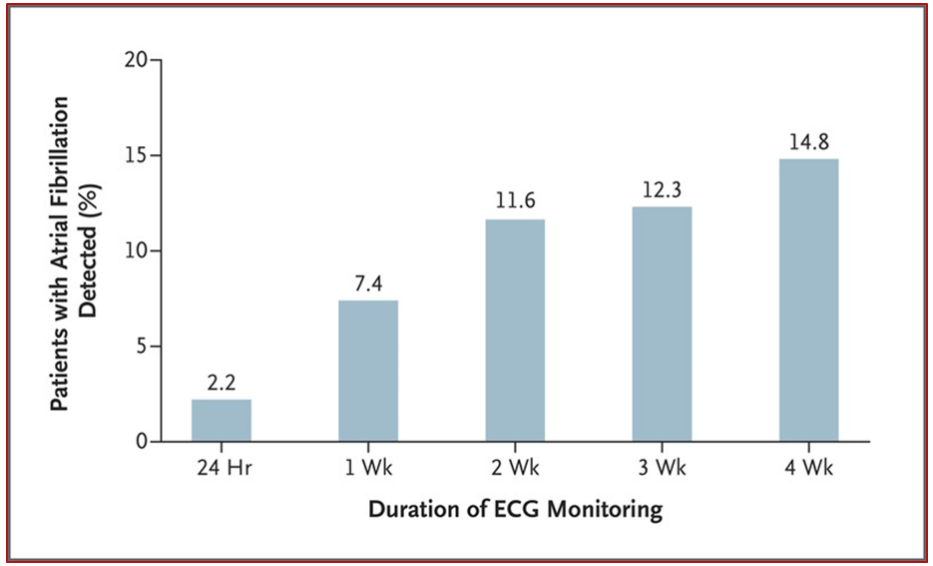
Inpatient cardiac monitoring (another 5.1% detected with AF)



Sposato et al., 2015

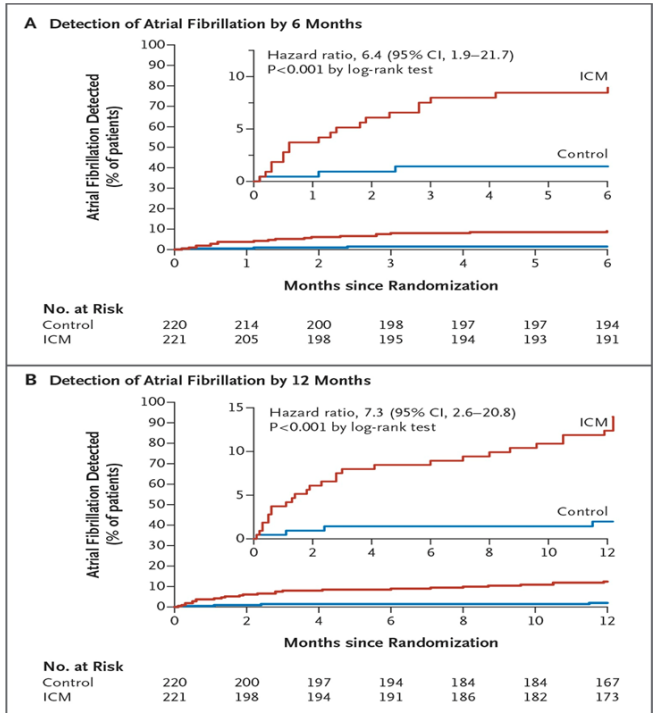
Ambulatory Cardiac Monitoring

EMBRACE TRIAL 30-DAY EVENT-TRIGGERED RECORDER VS 24-HOUR MONITOR



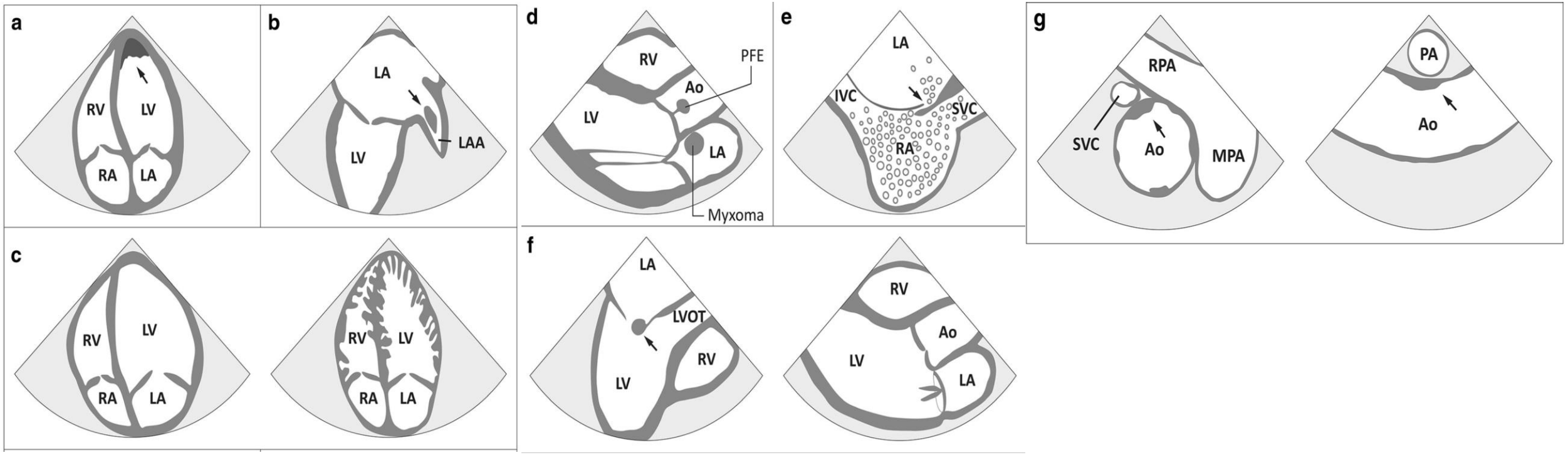
Gladstone et al., NEJM 2014

CRYSTAL-AF (ROUTINE EKG MONITORING VS ICM)



Sanna et al, NEJM, 2014

Cardiac Imaging



Camen et al., 2020

TEE vs TTE

	All patients $n = 485$	Cryptogenic etiology $n = 329$
Endocarditis, no (%)	3 (0.6%)	1 (0.3%)
SEC, no (%)	34 (7.0%)	7 (2.1%)
Vmax LAA ≤30cm/s, no (%)	19 (3.9%)	3 (0.9%)
LA/LAA-thrombus, no (%)	3 (0.6%)	0 (0.0%)
PFO, no (%)	44 (9.1%)	34 (10.3%)
ASA, no (%)	23 (4.7%)	17 (5.2%)
PFO plus ASA, no (%)	91 (18.8%)	64 (19.5%)
ASD, no (%)	6 (1.2%)	5 (1.5%)
Aortic plaque <4 mm, no (%)	316 (65.2%)	204 (62.0%)
Aortic Arch plaque ≥4 mm, no (%)	113 (23.1%)	72 (21.6%)
Aorta descendens plaque ≥4 mm, no (%)	197 (40.6%)	126 (38.1%)
Aortic thrombus, no (%)	16 (3.3%)	12 (3.6%)

Strecker et al., 2020

TABLE 1. Potential Cardiac Sources of Embolism in 231 TIA or Stroke Patients Assessed by TTE or TEE

Potential Cardiac Source	TTE	TEE
Major risk factor		
LA cavity thrombus	0	1 (1%)
LA appendage thrombus	1 (1%)	38 (16%)
LV thrombus	2 (1%)	*
Aortic thrombus	0	*
Dilated cardiomyopathy (LVEF<35%)	5 (2%)	*
Mitral valve stenosis	0	*
Minor risk factors		
Mitral valve prolapse	4 (2%)	*
Mitral annular calcification	4 (2%)	*
Calcified aortic stenosis	8 (3%)	*
Patent foramen ovale	3 (1%)	12 (5%)
Spontaneous echo contrast	2 (1%)	5 (2%)
Atrial septal aneurysm	5 (2%)	8 (3%)
LV aneurysm	1 (1%)	*
Aortic aneurysm	0	*
False tendon	0	*
Aortic plaques	1 (1%)	69 (30%)
Other	2 (1%)	*

De Bruijn et al., 2006

Identification of Risk Factors

HTN

DM: all patients should be screened (HbA1C-detected DM in 11.5% and prediabetes in 36%)

Hyperlipidemia: screened and in-hospital initiation of statin Rx

Smoking:

Substance Abuse

?Sleep Apnea

Organization of Care

Stroke Units

Systematic review of 28 RCT show that organized care in stroke units are superior to general wards with or without specialist input

Reduced OR death (0.87; 95% CI 0.69 to 0.94; P = 0.005)

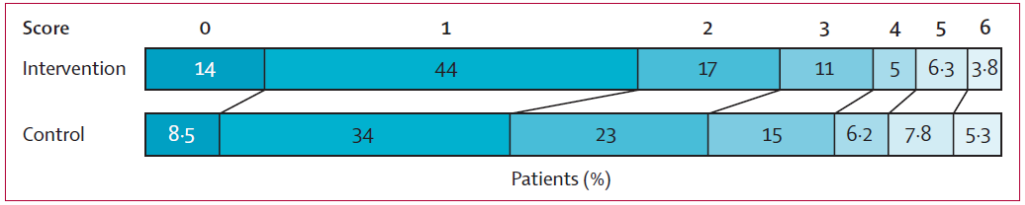
Reduced OR death or dependency (OR 0.79, 95% CI 0.68 to 0.90; P = 0.0007)

Reduced OR death or institutionalization (OR 0.78, 95% CI 0.68 to 0.89; P = 0.0003)

Stroke Unit Trialists' Collaboration; Cochrane Database of Systematic Reviews 2013.

Implementation of evidence-based treatment protocols to manage fever, hyperglycaemia, and swallowing dysfunction in acute stroke (QASC): a cluster randomised controlled trial

Implementation of multidisciplinary evidence-based protocols for the management of fever, hyperglycemia, and swallowing dysfunction delivers better patient outcomes after discharge from stroke units.



- 15·7% adjusted absolute difference in rates of 90-day death and dependency
- NNT 6.4

[*In comparison:*

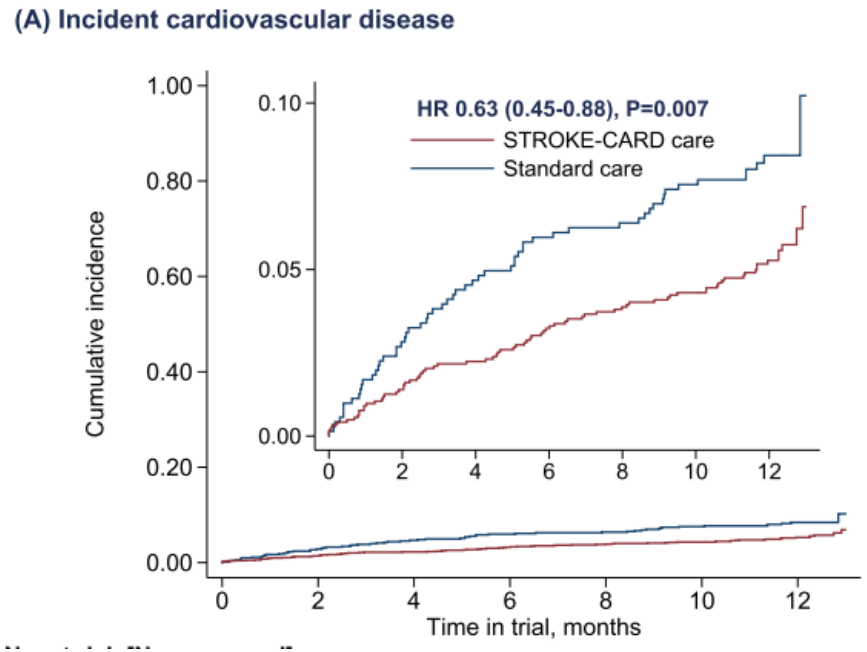
Aspirin 79

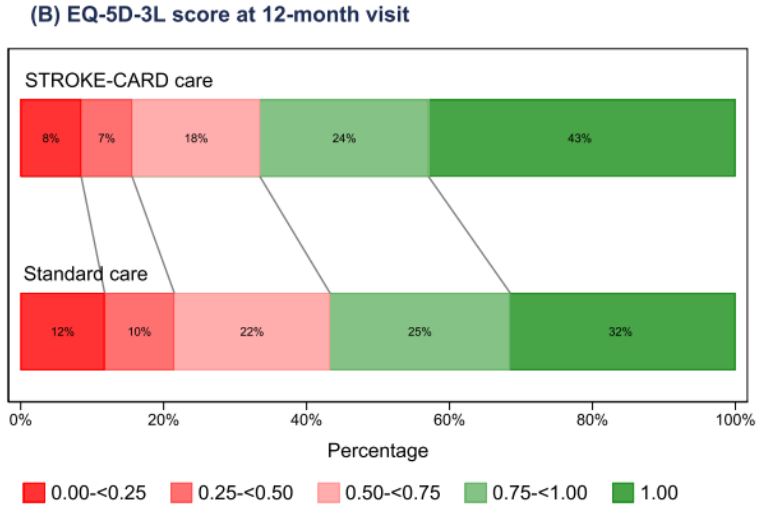
Thrombolysis 6-14]

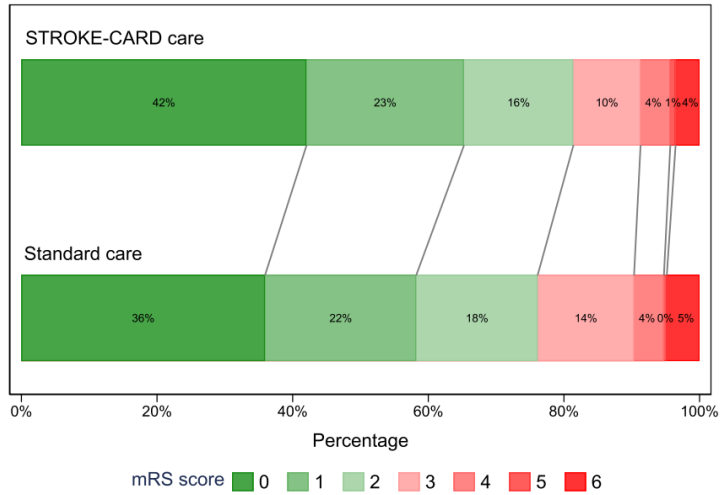
QASC Trialists Group; Lancet 2011

STROKE-CARD care to prevent cardiovascular events and improve quality of life after acute ischaemic stroke or TIA: A randomised clinical trial

Peter Willeit[a,b,*,1], Thomas Toell[a,1], Christian Boehme[a,1], Stefan Krebs[c], Lukas Mayer-Suess[a], Clemens Lang[c], Lisa Seekircher[a], Lena Tschiderer[a], Karin Willeit[a,d], Gerhard Rumpold[e], Gudrun Schoenherr[a], Andrea Griesmacher[f], Julia Ferrari[c], Michael Knoflach[a], Wilfried Lang[c,g,2], Stefan Kiechl[a,*,2], Johann Willeit[a,2], on behalf of the STROKE-CARD study group

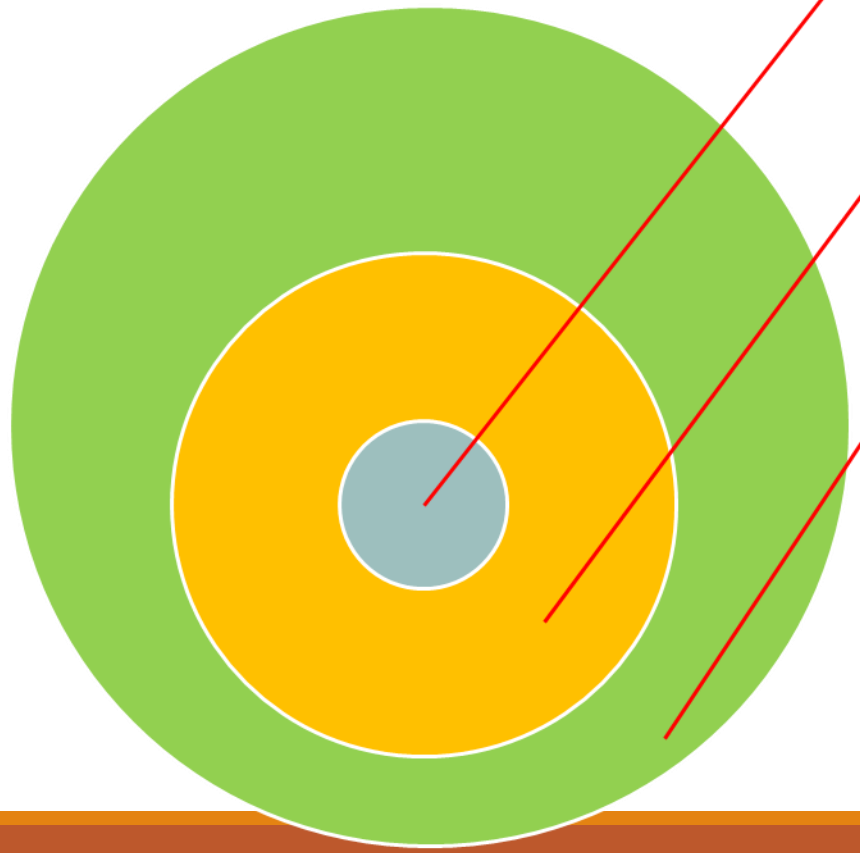






Willeit et al., 2020

Ultimately we need a community to ensure good care…

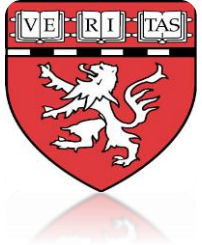


Patient

Core Team: *Neurologist/Physician, Nurse, PT/OT, SLP, Family, Social Worker*

Additional Members:

Discharge Planners, Palliative Care, Neuropsychologist, Vocational therapist, Peer support, Stroke Support Groups



Thank You!

Questions (skumar@bidmc.harvard.edu)