

Stroke Systems and Cryptogenic Stroke

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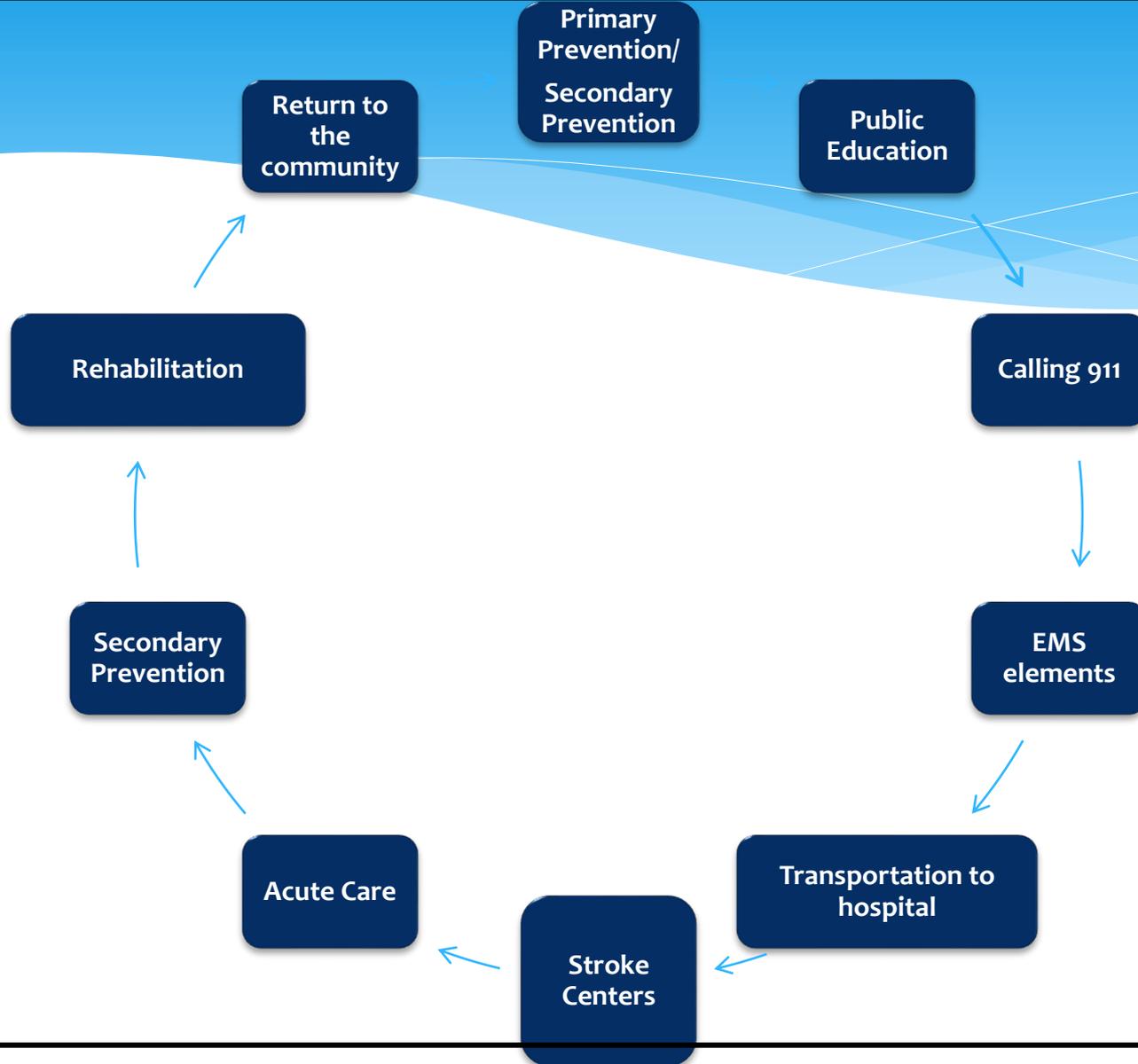
Disclosures

- * I am a speaker and/or consultant to any company that has made, is making, or will make a NOAC
- * I am a consultant for Medtronic

What is a Stroke System of Care?

- * **A comprehensive, diverse, longitudinal system that addresses all aspects of stroke care in an organized and coordinated manner**
- * **Spans the spectrum of stroke care from primary prevention, calling 9-1-1, acute care, secondary prevention, rehabilitation, return to the community**
- * **As with any system, it is only as strong as its weakest link**
- * **This talk will focus the roles of different types of stroke centers and Emergency Medical Services**

Pictorial Stroke System of Care



Characteristics of Different Stroke Centers

Comprehensive Stroke Center

**Academic Medical Center
Tertiary Care facility**

Primary Stroke Center

**Wide range of hospitals;
standard stroke care; stroke unit;
use TPA**

Acute Stroke Ready Hospital

**Rural hospitals; basic care;
drip and ship;
use tele-technologies**

Numbers of Types of Stroke Centers in the US

> 5000 total acute care hospitals in the U.S.

Comprehensive Stroke Center

**About 95 now
150-200 total**

Primary Stroke Center

**About 1070 now
1200-1500 total**

Acute Stroke Ready Hospital

**Very few now
500-700 total**

The Comprehensive Stroke Center

- * Provides complete care to patients with the worst, most severe, most complex strokes
 - * Large ischemic strokes (might need ICP interventions, surgery, etc.)
 - * ICH
 - * SAH
 - * Multi-system disease
 - * Cryptogenic strokes
- * Might require surgical or endovascular therapy
- * Might require NICU level care
- * Has all services available 24/7, 365 days/year

Why did we specifically highlight cryptogenic stroke for CSCs??

- * By definition they are the most challenging to Dx and Rx
- * They require specialists in many different areas
 - * Vascular neurology, vascular neurosurgery, neuroradiology, cardiology, hematology, etc.
- * Often require extensive testing
- * Often affect younger patients with high life expectancy

“Common” Causes of “Cryptogenic” Stroke

- * **Cardiac etiologies:**
 - * Paroxysmal Afib, SBE with negative Cx, papillary fibroelastoma
- * Subtle arterial dissections, CNS vasculitis (isolated)
- * Hypercoagulable state in setting of cancer (see this often)
- * Metabolic disorders: Hyper-homocysteine, Fabry’s disease
- * Plaque in aortic arch
- * HIV (often not tested for), CNS infection
- * Drug abuse (often not tested for)
- * Genetic etiologies (CADASIL, CARASIL, MELAS, etc.)
- * Hemoglobinopathies

Risk of Recurrent Stroke After Cryptogenic Stroke

Younger patients = 1-3% per year

Older patients = 5-10% per year

**This is similar to recurrent stroke risk in
typical stroke populations**

Risk of Recurrent Stroke in Cryptogenic Stroke Patients

- * **Very few specific focused studies**
- * **Best surrogate likely PFO Studies**
 - * Fairly large number of enrolled patients
 - * Reasonable work-up and follow-up
- * **Standard therapy—usually ASA**
- * **Major limitation is young patient age**
 - * 20-40 years

Biomarkers in Cryptogenic Stroke

Table 2. Comparison of Aspirin and Warfarin in Preventing the Primary Outcome of Recurrent Ischemic Stroke and Death Over 2 Years Among Patients Whose NT-ProBNP Was ≤ 750 pg/mL or > 750 pg/mL

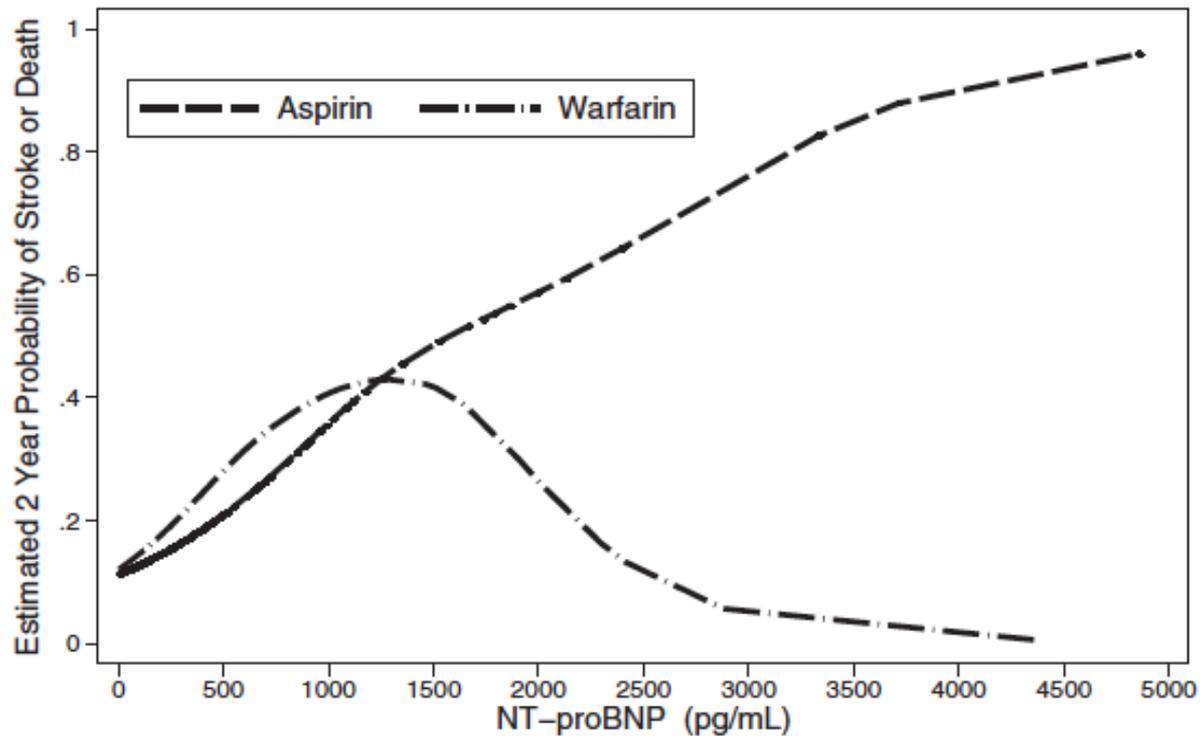
Treatment by NT-ProBNP	Number at Risk (Number of Events†)	Rate Per 100 Person-Years	Hazard Ratio*	95% Confidence Interval	P-Value
≤ 750 pg/mL					
Aspirin	477 (49, 13)	6.8	1.0		
Warfarin	502 (63, 17)	8.5	1.21	0.87, 1.69	0.24
> 750 pg/mL					
Aspirin	28 (7, 9)	45.9	1.0		
Warfarin	21 (4, 2)	16.6	0.30	0.12, 0.84	0.02

NT-proBNP indicates amino terminal pro-B-type natriuretic peptide.

*Adjusted for age, sex, and natural logarithm of NT-proBNP level as a continuous variable.

†Stroke, death.

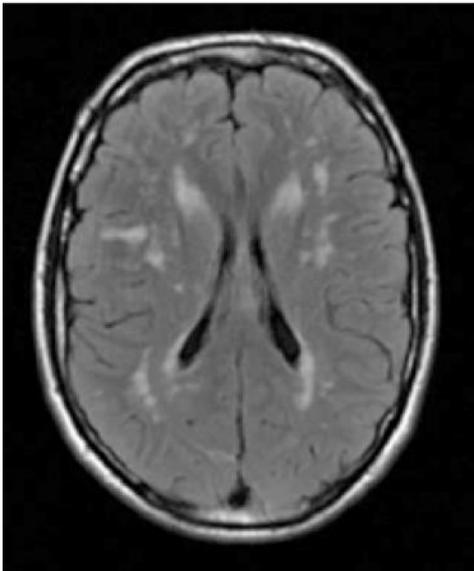
Biomarkers and Recurrent Stroke Risk with Therapy



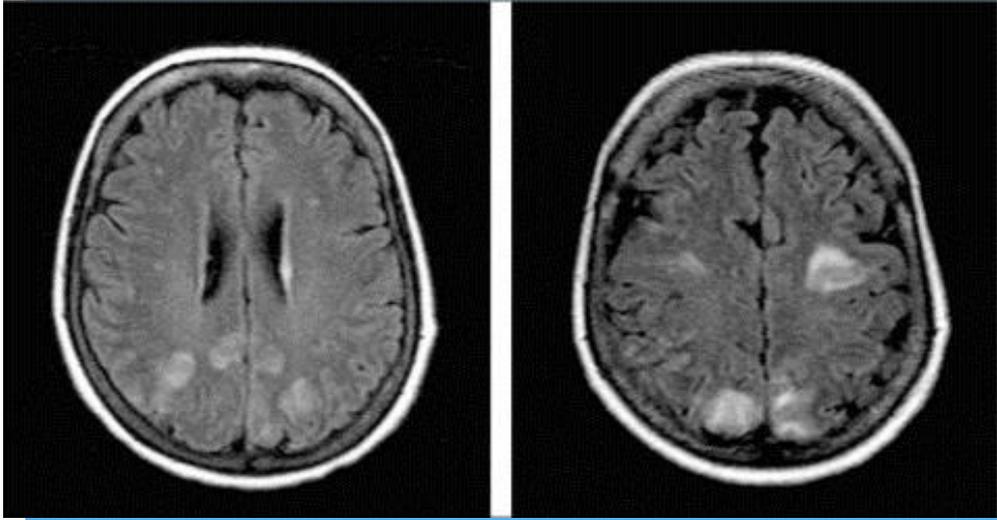
Longstreth et al., Stroke, 2013

The ESUS Paradigm

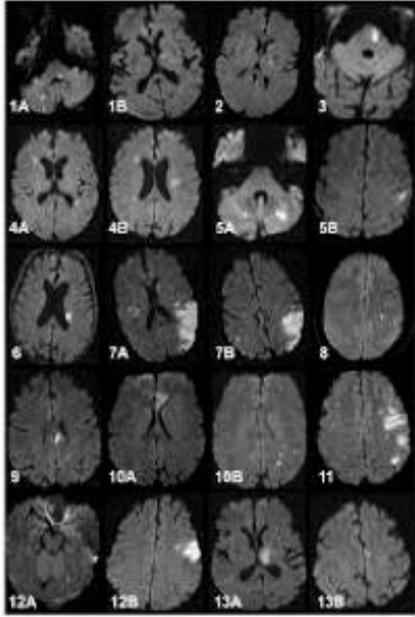
- * Embolic Strokes of Uncertain Source.....
- * Really???
- How do you know they are embolic strokes??



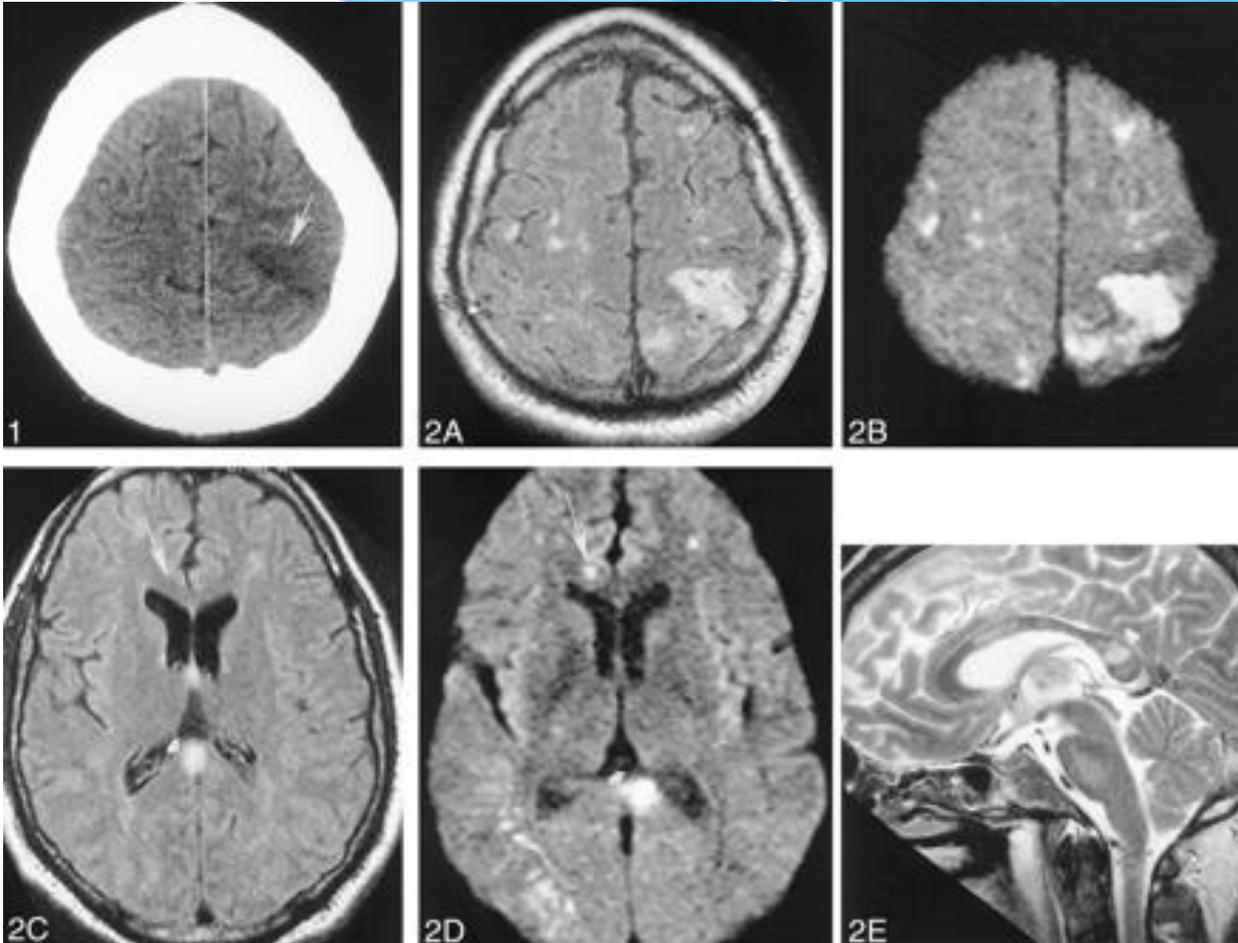
When does ESUS become just SUS???



ESUS or just SUS???



ESUS or just SUS??



Risks of ESUS Treatment Paradigm

- * **Assumption #1**

- * A significant % of these strokes are due to either:
 - * 1. Afib, or.....
 - * 2. Another mechanism that is responsive to anticoagulation therapy

- * **Assumption #2**

- * Treatment with an anticoagulant will be effective and safe for these other etiologies

- * **Assumption #3**

- * The rate of recurrent events will be high enough to show a treatment benefit, and.....
- * Enough patients will survive long enough to show overall benefit

Cryptogenic Stroke Treatment Options

- * Preferred therapy = single antiplatelet agent...UNLESS:
 - * Monitoring shows Afib.....NOAC
 - * TTE with large LA or LAA.....NOAC/Anticoagulation
 - * Elevated BNP.....NOAC?? Limited data.....
 - * Body scan shows cancer.....SQ Lovenox
 - * PFO.....antiplatelet therapy, ? closure
 - * Failure of 2 antiplatelet agents.....consider NOAC

Implications

- * **The treatment of patients with cryptogenic stroke is always a challenge**
 - * **Selection of the proper medication is = educated guess**
- * **Other paths forward**
 - * **Risk stratification**
 - * **Use of biomarkers**
- * **Due to the complexity of the work-up, most of these patients probably benefit from the resources of a CSC**

Conclusions

- * By their very nature, patients with a cryptogenic stroke are probably best evaluated and treated at a CSC
- * The thoroughness of the work-up (and the accuracy of the diagnosis) may vary greatly if the patient is not evaluated at a CSC
- * Although up to 30% of these patients may have paroxysmal Afib, what about the other 70%??
- * While we all agree that the best way to treat a stroke is to prevent the stroke, this is a greater challenge without a clear etiology