KANSAS INITIATIVE FOR STROKE SURVIVAL

A PROJECT BY AND FOR KANSANS

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Extended Time Window for Acute Stroke Intervention

"First Tuesdays" Lecture Series

Introduction and Goal of “First Tuesdays”

- Sabreena Slavin MD – Vascular Neurologist and Neurohospitalist at KU School of Medicine
- Didactic lecture series as part of the Kansas Initiative for Stroke Survival
- Updates in Practice and FAQ’s on Acute Stroke Care
- 20 minute didactic, 10 minutes for questions/discussion.

Review of Acute Stroke Interventions

- IV alteplase (tPA) for all patients who have **disabling symptoms** of acute stroke
- Mechanical thrombectomy: **only for large vessel occlusions (LVO).** Only hospitals with capabilities (eg: comprehensive stroke center) can perform thrombectomy.
  - A higher NIHSS (10 or more) can be indicative of a large vessel occlusion.
  - Diagnosed with CTA head/neck

Extended Time Window

- Time limit for IV tPA: 4.5 hours from last known normal. This is unchanged.
- Time limit for mechanical thrombectomy: Previously was up to 6 hours from last known normal. **Now can take up to 24 hours from last known normal. This is a new change in recommendation based on recent studies.**

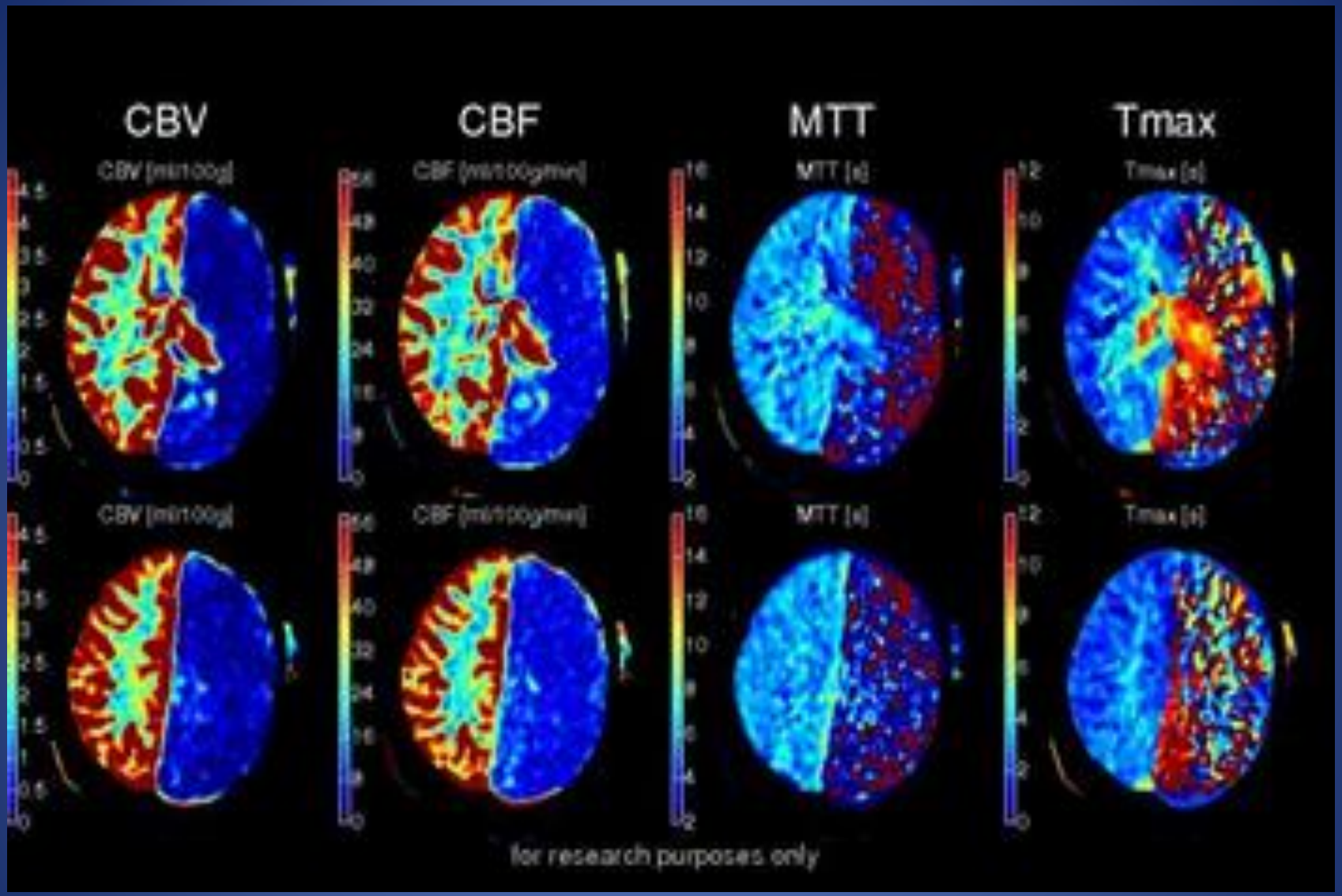
From the 2018 Guidelines for Management of Acute Ischemic Stroke

- New recommendations, class I, level A:
  - "In selected patients with AIS within **6 to 24 hours of last known normal** who have **LVO** in the anterior circulation, obtaining **CTP, DW-MRI, or MRI perfusion** is recommended to aid in patient selection for **mechanical thrombectomy**, but only when imaging and other eligibility criteria from RCTs showing benefit are being strictly applied in selecting patients for mechanical thrombectomy."

Based on DAWN and DEFUSE 3 trials
Powers et al, *Stroke,* 2018

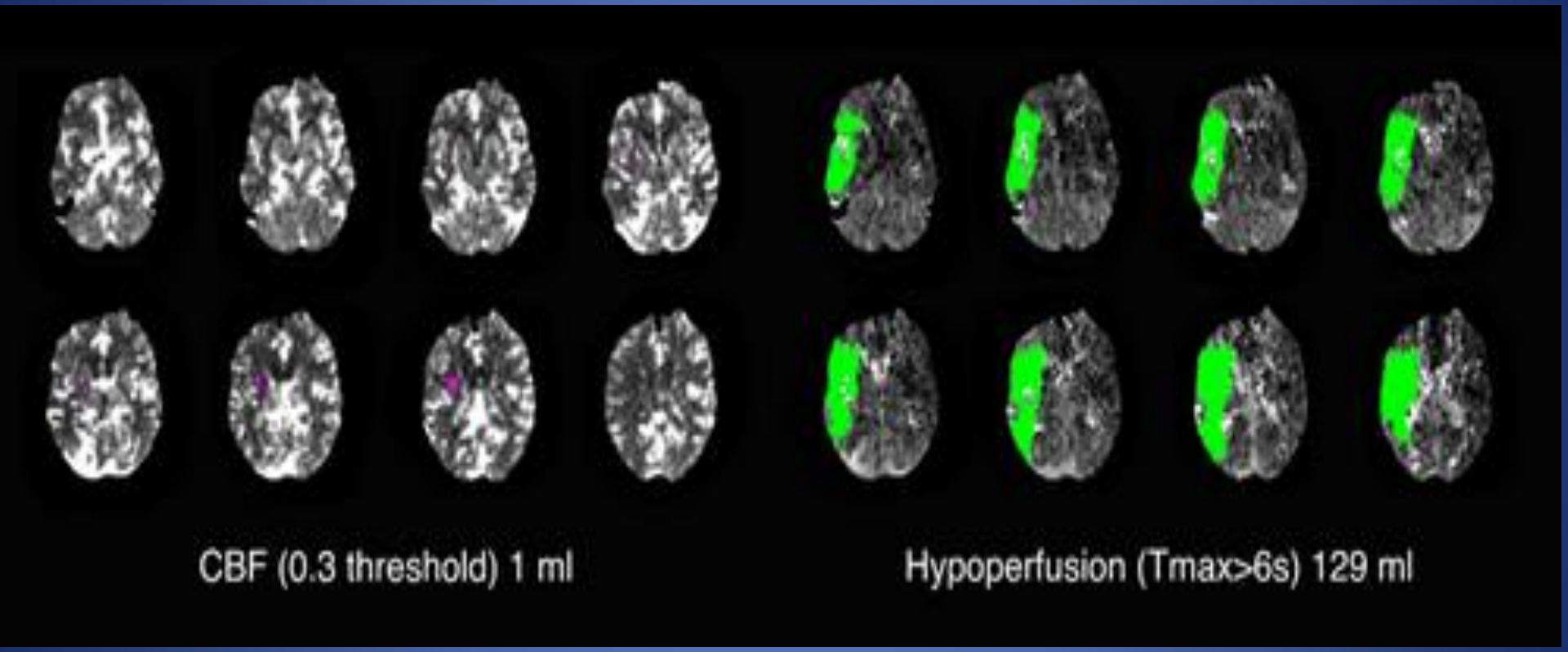
Perfusion Imaging

- CT perfusion and MR perfusion imaging is used to find a **mismatch** between ischemic core (area already damaged) and ischemic penumbra (area at risk of damage).
- Measures of core: cerebral blood volume, cerebral blood flow
- Measures of penumbra: mean transit time (ratio cerebral blood flow/cerebral blood volume), time to peak, time to drain, and T_{max} (measures of contrast arrival time to tissue).



Radiopedia, https://radiopaedia.org/articles/ct-perfusion-in-ischaemic-stroke

RAPID software to analyze core and penumbra:



iSchemaView RAPID: www.irapid.com

DAWN Trial

- Enrolled patients 6 to 24 hours after last known well with prestroke mRS 0-1 and with ICA or M1 occlusion.
- Imaging inclusion criteria: *clinical-core mismatch*
- If greater than 80, needed NIHSS ≥ 10 and core volume ≤ 20 mL
- If less than 80 and NIHSS ≥ 10, needed core volume ≤ 30 mL
- If less than 80 and NIHSS ≥ 20, needed core volume 31 to 50 mL.
- Max core volume should be 50 mL.
- Randomized 1:1 to thrombectomy vs standard medical care.

Nogueira et al, *NEJM,* 2018

Results of DAWN Trial

Outcome	Thrombectomy Group (N=107)	Control Group (N=99)	Absolute Difference (95% CI)†	Adjusted Difference (95% Credible Interval)‡	Posterior Probability of Superiority
Primary end points					
Score on utility-weighted modified Rankin scale at 90 days§	5.5±3.8	3.4±3.1	2.1 (1.2–3.1)	2.0 (1.1–3.0)	>0.999
Functional independence at 90 days — no. (%)¶	52 (49)	13 (13)	36 (24–47)	33 (21–44)	>0.999
				Risk Ratio (95% CI)	P Value
Secondary end points					
Early response — no. (%)‖	51 (48)	19 (19)	29 (16–41)	3 (2–4)	<0.001**
Recanalization at 24 hr — no. (%)††	82 (77)	39 (39)	40 (27–52)	2 (2–4)	<0.001**
Change from baseline in infarct volume at 24 hr — ml††					0.003‡‡
Median	1	13			
Interquartile range	0–28	0–42			
Infarct volume at 24 hour — ml††					<0.001‡‡
Median	8	22			
Interquartile range	0–48	8–68			
Grade of 2b or 3 on mTICI scale — no. (%)§§	90 (84)	NA			

Nogueira et al, *NEJM,* 2018

DEFUSE 3 Trial

- Enrolled patients **6 to 16 hours** post last known well with prestroke **mRS 0-2** and with ICA or M1 occlusion. **Max age 85, NIHSS ≥ 6.** This included a broader population than DAWN.
- Imaging inclusion criteria: *perfusion-core mismatch.*
- **Core < 70 mL, mismatch ratio > 1.8 and mismatch volume ≥ 15 mL**
- Randomized 1:1 to thrombectomy vs standard medical care.

Albers et al, *NEJM,* 2018

DEFUSE 3 Trial Results

Outcome	Endovascular Therapy (N=92)*	Medical Therapy (N=90)	Odds Ratio or Risk Ratio (95% CI)†	P Value
Primary efficacy outcome: median score on modified Rankin scale at 90 days (IQR)‡	3 (1–4)	4 (3–6)	2.77 (1.63–4.70)§	<0.001
Secondary efficacy outcome: functional independence at 90 days — no. (%)¶	41 (45)	15 (17)	2.67 (1.60–4.48)	<0.001
Safety outcomes — no. (%)				
Death at 90 days	13 (14)	23 (26)	0.55 (0.30–1.02)	0.05
Symptomatic intracranial hemorrhage‖	6 (7)	4 (4)	1.47 (0.40–6.55)	0.75
Early neurologic deterioration	8 (9)	11 (12)	0.71 (0.30–1.69)	0.44
Parenchymal hematoma type 2	8 (9)	3 (3)	2.61 (0.73–14.69)	0.21
Imaging outcomes**				
Median infarct volume at 24 hr (IQR) — ml	35 (18–82)	41 (25–106)	—	0.19
Median infarct growth at 24 hr (IQR) — ml	23 (10–75)	33 (18–75)	—	0.08
Reperfusion >90% at 24 hr — no./total no. (%)	59/75 (79)	12/67 (18)	4.39 (2.60–7.43)	<0.001
Complete recanalization at 24 hr — no./total no. (%)	65/83 (78)	14/77 (18)	4.31 (2.65–7.01)	<0.001
TICI score of 2b or 3 — no./total no. (%)	69/91 (76)	—	—	

Albers et al, *NEJM,* 2018

How this translates

- EMS:
  - Use prehospital triage scales for LVO, including FAST-ED, for all patients with suspected stroke within 24 hours. Communicate with ED prior to arrival.
  - If suspecting an LVO, stay near ED to facilitate further transport if necessary for fast door-out time.
- Community ED:
  - If higher NIHSS, please obtain ASPECTS from CT scan. Consider CTA/CTP imaging if resource available.
  - Call endovascular-capable center early if suspecting LVO to facilitate transport.

Bottom Line

- There is now evidence that mechanical thrombectomy can provide benefit for patients up to 24 hours after last seen at baseline if they fit imaging criteria.
- Both DAWN and DEFUSE 3 used strict criteria – in actual clinical practice, can consider extended window thrombectomy on patients that may not strictly fit study criteria (eg: M2 occlusion, greater core volume than 70 mL, older age, etc) on case by case basis.
- Still give IV tPA if able! Do not delay IV tPA to get advanced imaging.
- Consider all ways to obtain thrombectomy asap: prehospital scales, communication between EMS, community ED, and stroke center.

Questions?

- Call for help anytime!
- http://www.kissnetwork.us/
- KU BAT phone: 913-588-3727