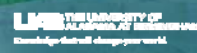




**Endovascular Treatment of Stroke:
An Update**

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Disclosures

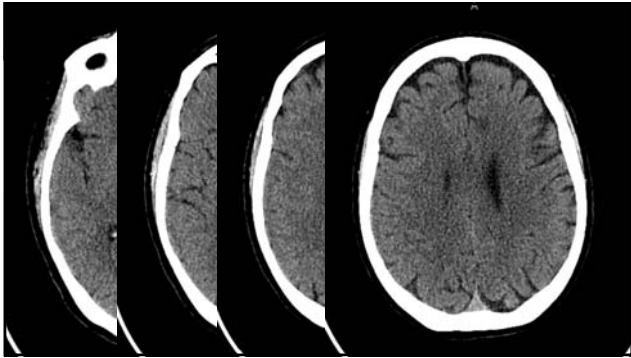
- No financial disclosures

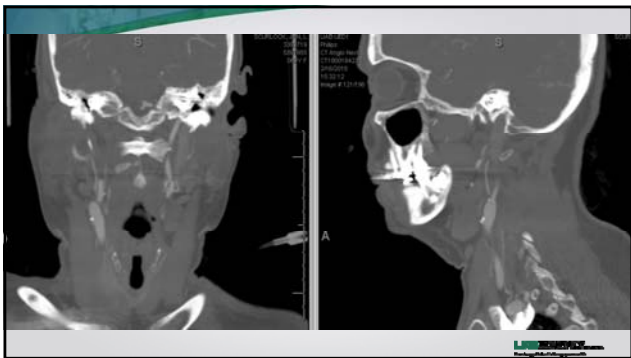


IA Stroke Therapy

- 62 y/o F w/ h/o HTN, HLD, tobacco use presents with L hemiparesis
- LKN 2:30AM, went to OSH, then transferred to UAB at 3PM
- CT scan – no hemorrhage
- Exam: Left hemiparesis, gaze preference

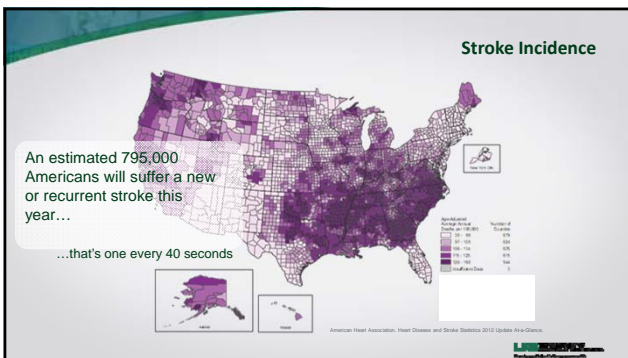


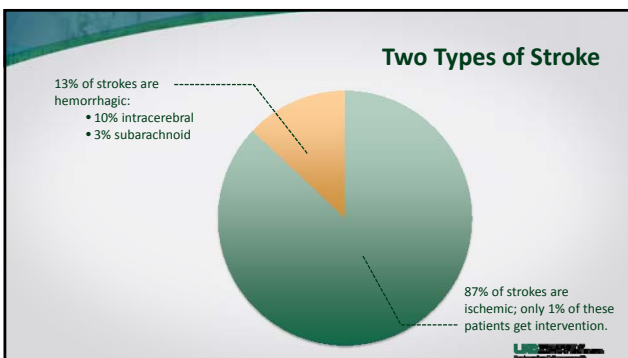












Physiological Impact of Stroke

Estimated Pace of Neural Circuitry Lost in a Typical Large Vessel Acute Ischemic Stroke

| Time | Neurons Lost | Synapses Lost | Myelinated Fibers Lost | Accelerated Aging |
|-------------|--------------|---------------|------------------------|-------------------|
| 1 second | 32,000 | 230 million | 218 yards | 8.7 hours |
| 1 minute | 1.9 million | 14 billion | 7.5 miles | 3.1 weeks |
| 1 hour | 120 million | 830 billion | 447 miles | 3.6 years |
| Avg. stroke | 1.2 billion | 8.3 trillion | 4470 miles | 36 years |

Source: Jeffrey, Time in Brain - Quantified Stroke 2006, 17, 203-206.

IV t-PA (alteplase)

- Currently the only FDA-approved medical treatment for acute ischemic stroke
- ≤ 3 hours since symptom onset
- Long list of exclusionary criteria
- Ineffective against large clots

Impact of Clot Burden on Success Rate of IV tPA

35-40% of Ischemic Strokes are Considered "Large Vessel"

- This subset of ischemic stroke comprises blockages in the:
 - Internal Carotid Artery (ICA)
 - Middle Cerebral Artery (MCA)
 - Vertebral / Basilar Artery
- If left untreated, patient prognosis with these types of stroke is poor

| Vessel | Mortality Rate |
|----------------|---------------------|
| ICA | 53% ¹ |
| MCA | 27% ² |
| Basilar Artery | 89-90% ³ |

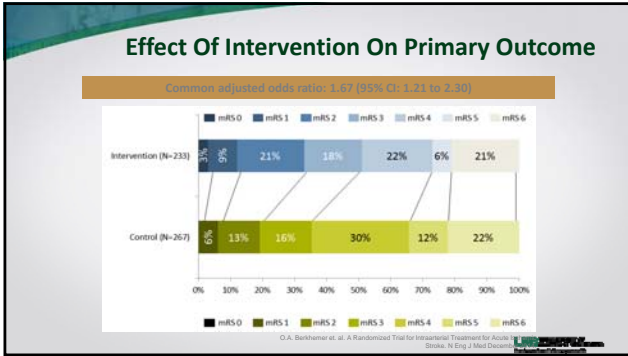
1. Jensen O, et al.
2. Fahren A, et al. (2002) J Stroke
3. Brottman E, et al.

A Multicenter Randomized Clinical trial of Endovascular treatment for Acute ischemic stroke in the Netherlands

Design

- RCT from Netherlands (16 centers) comparing endovascular treatment of acute ischemic stroke vs. best medical therapy:
 - Masked, web-based, 1:1 random treatment allocation
- Inclusion Criteria
 - Acute ischemic stroke, Age ≥18, NIHSS ≥2
 - Intracranial anterior circulation occlusion (confirmed by CTA)
 - Initiation of IA treatment within 6 hours from onset

O.A. Benkhamer et al. A Randomized Trial for Intracranial Treatment for Acute Stroke. N Engl J Med October 2015



MR CLEAN Study Conclusion

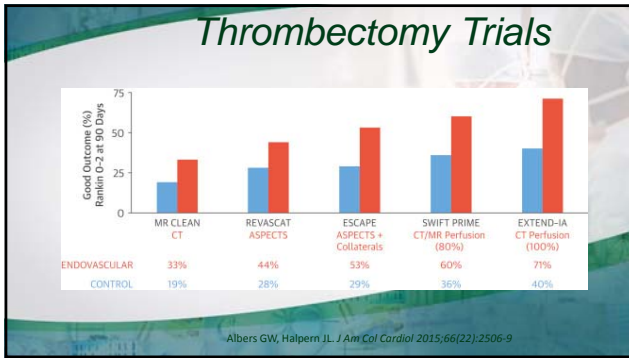
- In patients with acute ischemic stroke caused by a proximal intracranial arterial occlusion of the anterior circulation, intraarterial treatment administered within 6 hours after stroke onset was effective and safe
- This treatment leads to a clinically significant increase in the functional independence in daily life by 3 months, without an increase in mortality

O.A. Berkhemer et al. A Randomized Trial for Intraarterial Treatment for Acute Stroke. N Engl J Med. December 2015

2015: Important Clinical Trials

- MR CLEAN
- SYNTHESIS
- SWIFT PRIME
- EXTEND-IA
- REVASCAT

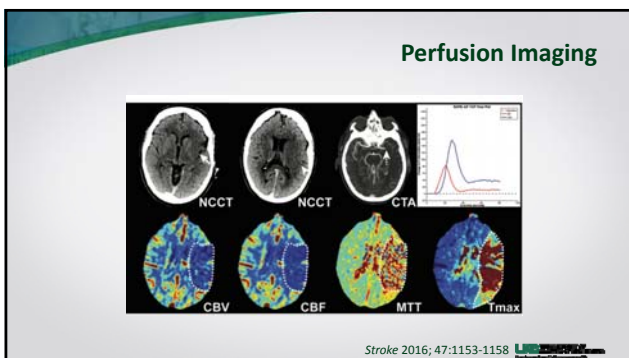
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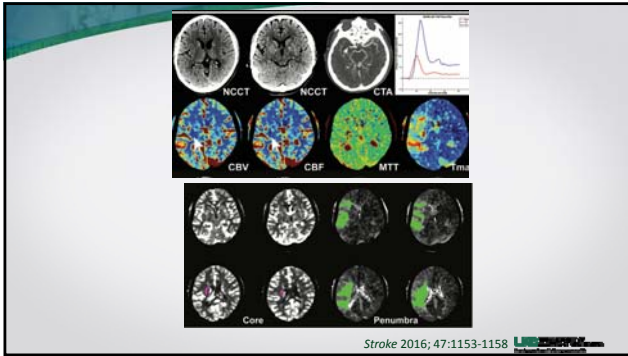


2015 AHA/ASA *Focused Update* of the 2013 Guidelines for the Early Management of Patients With Acute Ischemic Stroke

- “Patients **SHOULD** receive endovascular therapy with a stent retriever if they meet all of the following criteria:
 - Prestroke mRS score 0 to 1
 - Acute ischemic stroke receiving intravenous t-TPA with 4.5 hour of onset
 - Causative occlusion of the internal carotid artery
 - Age ≥ 18 years
 - ASPECTS of ≥ 6 and
 - Treatment can be initiated within 6 hours of symptom onset
- Etc etc...”


Stroke 2015; 46:000-000






DAWN

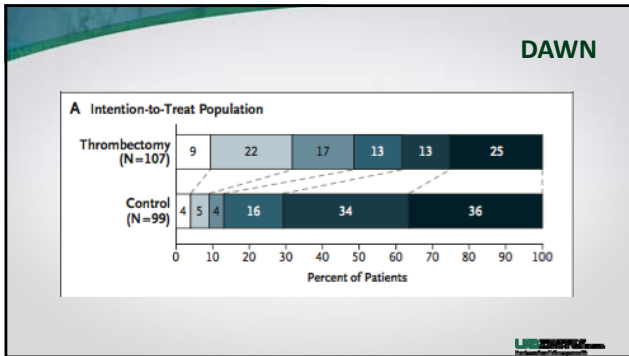
- DAWN = DWI or CTP Assessment with Clinical Mismatch in the Triage of Wake-Up and Late Presenting Strokes Undergoing Neurointervention
- RCT of ischemic stroke from LVO treated 6-24 hours after onset using perfusion imaging (CT or MRI)
- Inclusion:
 - Baseline NIHSS score ≥ 10
 - ICA or MCA-M1 occlusion
- Primary endpoint: 90 day mRS



DAWN

- Planned enrollment of 500 patients
 - Recently stopped early after 206 patients given significant benefit
- Primary endpoint met in 48.6% IA vs 13.1% BMT
- Relative reduction in disability of 73%
- NNT = 2.8





DAWN

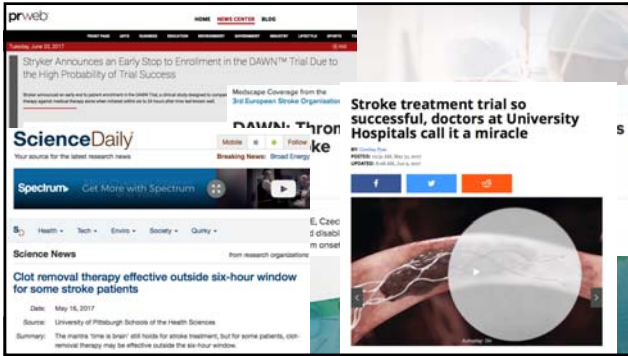
Table 2. Efficacy Outcomes.*

| 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 |

DAWN


Table 3. Safety Outcomes.*

| Outcome | Thrombectomy Group (N=107) | Control Group (N=99) | Absolute Difference (95% CI) | Risk Ratio (95% CI) |
|---|----------------------------|----------------------|------------------------------|---------------------|
| no. (%) | | | | |
| Stroke-related death at 90 days | 17 (16) | 18 (18) | -2 (-13 to 8) | 1 (1 to 2) |
| Death from any cause at 90 days | 20 (19) | 18 (18) | 1 (-10 to 11) | 1 (1 to 2) |
| Symptomatic intracranial hemorrhage at 24 hr‡ | 6 (6) | 3 (3) | 3 (-3 to 8) | 2 (1 to 7) |
| Neurologic deterioration at 24 hr‡ | 15 (14) | 26 (26) | -12 (-23 to -1) | 1 (0 to 1) |
| percentage points | | | | |
| Procedure-related complications | 7 (7) | NA | | |
| Distal embolization in a different territory | 4 (4) | NA | | |
| Intramural arterial dissection | 2 (2) | NA | | |
| Arterial perforation | 0 | NA | | |
| Access-site complications leading to intervention | 1 (1) | NA | | |




DEFUSE

- "Endovascular Therapy Following Imaging Evaluation for Ischemic Stroke 3"
- NIH funded through StrokeNet
- Inclusion:
 - 6-16hrs
 - Infarct volume < 70cc
 - Penumbra of > 15cc
- Secondary endpoint: functional independence at 90days
- Enrollment
 - 38 centers
 - 182 patients – terminated early for efficacy




DEFUSE: Details

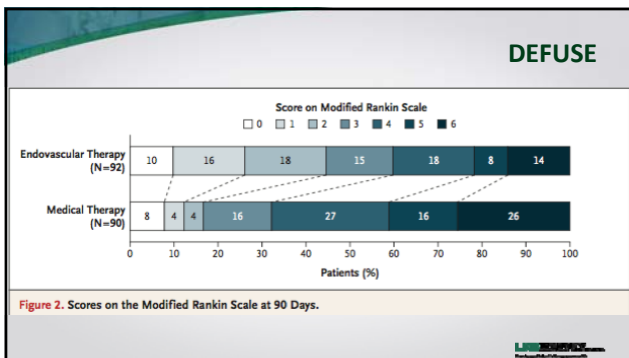
- IMAGING:
 - CT Perfusion
 - RAPID Software – uses an algorithm to automatically calculate penumbral tissue and infarct based of arrival time of contrast exceeding 5 seconds from normal
 - MRI Diffusion and Perfusion
 - Patients were imaged upon arrival and then again at 24hrs for imaging outcome measures
- Technique:
 - Any approved thrombectomy device
 - No IA tPA



DEFUSE: Results


- Patients were nearly 3x more likely to be functional at 90 days after IA + BMT than with BMT alone
 - mRS 0-2 = 45% with IA, 17% BMT → OR 2.7
- 90 day mortality 14% IA, 26% BMT
- Symptomatic ICH not statistically significant
 - 7% IA group vs 4% BMT group
- Infarct volume growth at 24hrs higher with BMT
 - 23ml increase in IA, 33ml increase in BMT
- Median time to imaging was 10.5hrs





DAWN vs DEFUSE

- DAWN:
 - 0-24 hrs
 - 26 centers
 - Industry sponsored
 - Smaller ischemic core infarcts
 - Core <21, <31
 - (3 groups based off age and core)
 - Median 7.6/8.9 (IA/BMT)
 - NIHSS 10+
- DEFUSE
 - 0-16 hrs
 - 38 centers
 - NIH sponsored
 - Larger core infarcts
 - Core < 70cc
 - Median infarct 9.4/10.1 (IA/BMT)
 - NIHSS 6+
 - Able to enroll a broader patient population
 - about 40% of the DEFUSE 3 patients would not meet the DAWN selection criteria

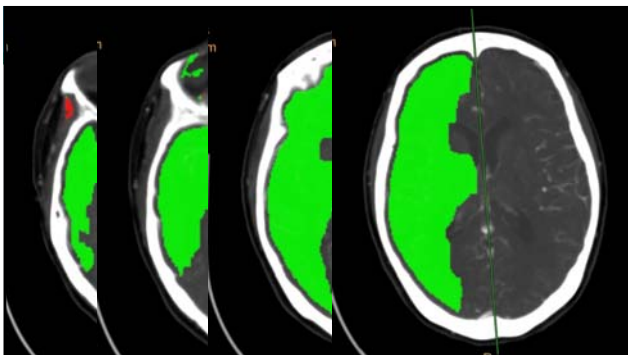


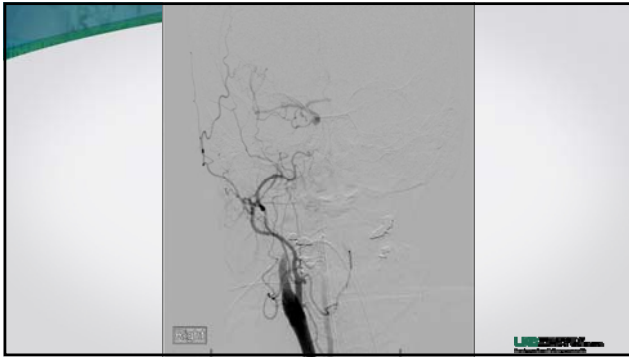
AHA Updates: 2018

- Endovascular thrombectomy up to 16hrs from LKN is **standard of care**
- Endovascular thrombectomy **should be considered** up to 24 hrs from LKN
 - Advanced imaging not necessary for IA care within 6hrs
- tPA up to 3-4.5hrs with more focus on clinical judgment
- For minor stroke DAPT should be considered for 21 days
- Aspirin can be given within 24hrs in select cases after tPA

Back to our original case.....

- What to do next?
- Functional imaging....









- Improvement in Left hemiparesis immediately
- Discharged on POD2 on DAPT
- 1 week clinic return with NIHSS 0

- CONCLUSIONS**
- Acute stroke care has gone from experimental to standard of care within 6 hours of LKN as of 2015
 - When perfusion imaging is favorable, standard of care based of 2018 AHA updated guidelines, is for thrombectomy up to 16hrs from LKN (considered up to 24hrs)
 - UAB Strategy: IA therapy should be considered based off the tissue clock, not the time clock
 - “You miss all the shots you don’t take” - Wayne Gretzky

