Imaging Selection in Endovascular Stroke Trials

REVASCAT: Randomized Trial Of Revascularization With Solitaire FR® Device Versus Best Medical Therapy In The Treatment Of Acute Stroke Due To Anterior Circulation Large Vessel Occlusion Presenting Within 8 Hours Of Symptom Onset

(clinicalTrials.gov, NCT01692379)

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Baseline Imaging

Modality	Required or Optional	No. obtained (%)
CT non-contrast	REQUIRED	206 (100%)
CT perfusion	OPTIONAL	64 (31.1%)
CT angiography	REQUIRED *	195 (94.7%)
MR diffusion	OPTIONIAL	11 (5.3%)
MR perfusion	OPTIONAL	5 (2.4%)
MR angiography	REQUIRED*	11 (5.3%)

* EITHER CT ANGIOGRAPHY OR MR ANGIOGRAPHY WERE REQUIRED

Time to Treatment

	Mean (SD)	Median (IQR)
Multimodal CT acquisition time, min	N/A	N/A
CTP post-processing time, min	N/A	N/A
Multimodal MR acquisition time, min	N/A	N/A
PWI/DWI post-processing time, min	N/A	N/A
"Door-to-Groin" time, min		
for entire cohort (n=103)	125.1 (55.6)	109.0 (85.0,163.0)
for patients selected based on NCCT alone	N/A	N/A
for patients selected based on NCCT/CTA (n=97)	124.6 (55.7)	108.0 (85.0,163.0)
for patients selected based on NCCT/CTA/CTP (n=31)	107.2 (36.9)	103.0 (76.0,136.0)
for patients treated with t-PA (n= 150)	127.2 (55.7)	110.5 (85, 171)
for patients not treated with t-PA (n=56)	120.5 (56)	108(83, 136)

Time to Treatment

	Mean (SD)	Median (IQR)
Multimodal CT acquisition time, min	N/A	N/A
CTP post-processing time, min	N/A	N/A
Multimodal MR acquisition time, min	N/A	N/A
PWI/DWI post-processing time, min	N/A	N/A
"Door-to-randomization" time, min		
for entire cohort (n=206)	88.0 (46.5)	78.0 (53.0,115.0)
for patients selected based on NCCT alone	N/A	N/A
for patients selected based on NCCT/CTA (n=195)	88.3 (46.7)	78.0 (53.0,115.0)
for patients selected based on NCCT/CTA/CTP (n=64)	83.5 (42.2)	70.0 (53.0,104.5)
for patients selected based on MRI (n=11)	82.2 (44.4)	78.0 (52.0,100.0)
for patients treated with t-PA (n= 150)	89.9 (47.4)	80 (54, 123)
for patients not treated with t-PA (n=56)	82.8 (44.2)	72.5 (52, 103.5)

OUTCOMES BY CTP/MRI vs NO CTP/MRI

1 mRS by CTP or MRI

		CTP or MRI		Not CTP and MRI	
		Intervention	**Control**	**Intervention**	**Control**
mRS					
Total no-missing	n	31	33	72	70
0-2	n (%)	14 (45.2%)	10 (30.3%)	31 (43.1%)	19 (27.1%)
3-6	n (%)	17 (54.8%)	23 (69.7%)	41 (56.9%)	51 (72.9%)
Missing	n	0	0	0	0

Logistic Regression mRS 0-2 (OR 95%) / CMH

	OR (95% CI) for mRS 0-2	OR IC 95% for mRS 0-2 CMH	OR (95% CI) shift analysis
Variables			
Treatment (Exp vs Med)	1.985 (1.111 – 3.546)	1.985 (1.112 -3.546)	1.685 (1.032 – 2.751)
CTP or MRI (No vs Yes)	0.889 (0.487 – 1.654)		1.158 (0.684 - 1.963)

Selection Criteria

Criteria for	Description
Vessel Occlusion	M1, intracranial ICA ; Tandem cervical ICA/ intracranial ICA or cervical ICA/M1 allowed
Small Core	ASPECTS > 6 ON CT ** OR ASPECTS > 5 ON DWI MRI
Mismatch	CLINICAL/CORE MISMATCH (NIHSS >5) (NO IMAGING PROOF OF MISMATCH REQUIRED)
Collaterals	NOT REQUIRED

** investigators were encouraged to use CTA source imaging or CTP for ASPECTS score interpretation

Biases and Limitations

- *Selection Criteria were followed and adherence monitored in a concomitant parallel registry throughout the entire study*
- *Selection criteria changed during the study to include patients aged 81-85 with ASPECTS > 8 (AGE ADJUSTED CORE BASED SELECTION)*
- *Could certain patient groups have been excluded even though they met inclusion criteria (ie were there "unwritten" exclusion criteria) ? Unlikely. Only 8/206 (4%) patients who met eligibility criteria at participating centers were excluded.*

Baseline Imaging Characteristics

Characteristic	Medical Treatment (n=103)	Endovascular Treatment (n=103)
Site of vessel occlusion – no. (%)		
ICA (only -not included terminus ICA with involvement of M1)	1 (1.1%)	
MCA-M1	65 (64.4%)	66 (64.4%)
MCA-M2	8 (7.9%)	10 (9.8%)
Any ICA (with or without M1 or M2)		
Extracranial ICA (± TICA or M1)	13 (12.6%)	19 (18.4%)
Intracranial ICA (+ M1)	27 (26.21%)	26(25.24%)
Ischemic core volume - ml	N/A	N/A
Mean (SD)	N/A	N/A
Median (IQR)	N/A	N/A
ASPECTS		
Mean (SD)	7.2 (2.1)	7.4 (2.0)
Median (IQR)	8.0 (6.0,9.0)	7.0 (6.0,9.0)
Perfusion volume - ml	N/A	N/A
Mean (SD)	N/A	N/A
Median (IQR)	N/A	N/A
Other variables (eg collateral status)	N/A	N/A

Subgroup Analysis
According to Baseline Imaging Characteristics

Example Criteria	Endovascular Tx		Medical Tx		OR (95% CI) for mRS 0-2	OR (95% CI) for CMH	OR (95% CI) shift analysis
	mRS 0-2	Total	mRS 0-2	Total			
Core	n	N	n	N			
<25 ml	N/A	N/A	N/A	N/A			
25-50 ml	N/A	N/A	N/A	N/A			
ASPECT (CORE LAB)	N=45 (43.7%)	N= 103	N=29 (28.2%)	N=103		1.993 (1.113,3.566)	
8-10	25 (50%)	50	16 (29%)	55 (53.4%)	1.919 (0.640,5.755)		2.173 (0.899,5.251)
5-7	17 (38%)	44	11 (29%)	37 (35.9%)	1.502 (0.488,4.623)		1.756 (0.713,4.327)
0-4	3 (33%)	9 (8.7%)	2 (18%)	11 (10.7%)	1		1
Treatment (SOLITAIRE vs CONTROL)					2.001 (1.116,3.587)		1.698 (1.038,2.778)
Other criteria (eg collateral or mismatch status)							

Subgroup Analysis

According to Baseline Imaging Characteristics

Example Criteria	Endovascular Tx		Medical Tx		OR (95% CI) for mRS 0-2	OR (95% CI) for CMH	OR (95% CI) shift analysis
	mRS 0-2	Total	mRS 0-2	Total			
ASPECT **(CRD investigator)**	N=45	N=103	N=29	N=103		1.922 (1.072,3.446)	
8-10	38 (48.%)	79	22 (30%)	72	1.851 (0.922,3.715)		1.710 (0.976,2.998)
6-7	7 (15.6%)	24	7 (22.%)	31	1		1
0-5	0 (0.0%)	0	0 (0.0%)	0 (0.0%)	--		
Treatment (SOLITAIRE VS CONTROL:)					1.922 (1.071,3.447)		1.652 (1.011,2.702)

Key Imaging Finding

- *Requirement to perform CTA 30 min after iv t-PA administration led to enrichment of study with t-PA non-responders (only 5/103 (4.8%) patients with TICI 3 or TICI2b on baseline angiography and high rates of ICA occlusion) but likely resulted in treatment delays*
- *Significant discrepancies between core lab ASPECTS and Investigator ASPECTS*
- *Significant discrepancies between M1 vs. M2 between CORE LAB and INVESTIGATORS*
- *Clear benefit in patients with ASPECTS score 5-10 by CORE LAB and 7-10 by INVESTIGATORS*
- *Some benefit with lower ASPECTS SCORES (0-4 by CORE LAB) cannot be entirely excluded. No signals of harm with lower ASPECTS scores*
- *Results (showing robust treatment effect - NNT of 6, despite selection based on ASPECTS alone) support ASPECTS based patient selection*
- *Even though no apparent delays could be demonstrated with advanced imaging (CTP/MRI) the added value of these studies in REVASCAT is unclear*
- *The possibility that patients who were excluded based on imaging criteria would have benefitted from IA therapy is not ruled out*

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