Fundació La Marató 3

23rd SOCIAL RETURN OF THE RESEARCH
Strokes and traumatic spinal cord and brain injury

COMPUTERISED TOMOGRAPHY OF PERFUSION CHARACTERISED BY LACK OF CLINICAL IMPROVEMENT AFTER RECHANNELLING IN PATIENTS WITH ACUTE ISCHAEMIC STROKE (CTP_AFT_REC)

Dr Marta Aurora Rubiera del Fueyo

Institut de Recerca Hospital Universitari Vall d'Hebron - VHIR

1. Project summary

HYPOTHESIS: Perfusion computed tomography performed immediately after endovascular reperfusion treatment (CTPpost) would be able to discriminate between futile recanalization, lack of reperfusion, hyperperfusion, and “stunned brain” in patients treated with thrombectomy who achieved complete recanalization.

MAIN OBJECTIVE: To identify and standardize CTPpost parameters after endovascular treatment that better reflect the phenomenon of lack of clinical improvement after successful recanalization.
Secondary objectives:
- determine CTPpost parameters to identify "stunned brain" or delayed enhancement;
- identify different patterns of CTPpost based on the pathophysiology of the lack of reperfusion after recanalization
- identify the presence of reperfusion damage and its frequency and determine baseline characteristics that can predict the evolution of the different phenomena.

PROCEDURES: Consecutive patients with an intracranial M1 or ICA occlusion treated with cerebral thrombectomy who achieved complete recanalization (TICI 2b-3) received CTPpost and non-contrast CT within 30 minutes of recanalization. Specialized software was used to analyze the different post-CTP patterns and the baseline clinical and radiological characteristics that can predict the different recanalization phenomena without a good functional outcome.

A control CT scan of 24+/- 6 hours was performed. Clinical stroke severity was assessed by NIHSS score at baseline, immediately before and after endovascular reperfusion therapy, at 24+/- 6 hours from symptom onset, and at discharge. The functional evaluation was determined by the mRS at 3 months in the outpatient follow-up visit. An mRS <3 was considered as a good functional outcome. Patients reported outcomes (PROMs) were also recorded.

2. Results

We have shown that more than 50% of patients present a perfusion defect after mechanical thrombectomy, despite recanalization of the initially occluded artery. Although there is a relationship between the degree of recanalization measured by the TICI scale and hypoperfusion in the CTPpost measured by the volume of Tmax delayed >6 seconds (Tmax6), almost 40% of patients with a TICI 3 have perfusion defects. CTPpost is a better predictor of early neurological evolution and functional prognosis at 3 months than the final TICI scale. With the volume of hypoperfusion in CTPpost we can discriminate with moderate precision patients with poor functional outcome (futile recanalization or recanalization without reperfusion) and those with "stunned brain" (late clinical improvement). Hyperperfusion, at least according to our definition, does not seem to be comparable to reperfusion injury, and it is not related to clinical results or hemorrhagic transformation.

On the other hand, the analysis by machine-learning processing of the different maps and thresholds of the CTPpost allows predicting, within 30 minutes after thrombectomy, the neurological deficit at discharge by the NIHSS scale, with an accuracy of 35.1%, which increases to 38.9% by adding clinical data to the model. Regarding PROMs, patients with perfusion defect in the CTPpost measured by Tmax6 had a significantly worse score on the Hospital Anxiety and Depression Scale (HADS) in the anxiety domain at 3 months (rho -0.31, p=0.05), and a trend towards a worse PROMIS-10 score one week after discharge in its physical domain (rho -0.22, p=0.06). The PROMS data is limited by the low percentage of collection of PROMs that was achieved, which is a classic problem of outcome measurement in value-based medicine.

3. Relevance and possible future implications

We consider that CTPpost could be a selection tool for patients who, after endovascular reperfusion treatment, have a poor functional prognosis due to cerebral hypoperfusion, despite arterial recanalization. At present, there is no additional treatment approved after thrombectomy, but there are multiple candidate substances that could improve cerebral hypoperfusion (e.g. fibrinolytics or intra-arterial antiplatelets). In addition,

some neuroprotective drugs could have a beneficial effect in patients after thrombectomy but their effectiveness would be diluted in those patients who will improve late ("stunned brain"). The CTPpost is an easy and early acquisition tool, which could also help in the selection of these patients, and increase the chances of demonstrating the effectiveness of new neuroprotective treatments. We are currently working on these lines of research.

In addition, until now we have used automated software designed to study patients with stroke prior to thrombectomy, simplifying the analysis by determining a single parameter, Tmax6. Thanks to machine-learning analysis, we have detected that our predictive capacity improves by combining different thresholds and perfusion maps. We plan to test new combinations of maps and thresholds to try to improve patient selection in future clinical trials. These combinations should be automated so that therapeutic decisions immediately after thrombectomy can be adopted early, given that their efficacy, similar to other treatments in acute stroke, will probably be time-dependent. We plan to design automated software that is capable of giving recommendations within a few minutes after CTPpost acquisition, allowing early selection of patients for adjuvant treatment and/or clinical trials after cerebral thrombectomy.

4. Scientific bibliography

- Poster Presentation in European Stroke Organization Congress 2019:
Garcia-Tornel, M. Ribo Jacobi, N. Rodriguez, D. Rodriguez-Luna, J. Pagola, J. Juega, S. Boned, M. Muchada, D. Anguizola, M. Requena, M. Olive, A. Tomasello, D. Hernandez, C.A. Molina and M. Rubiera. AS10-051. HYPOPERFUSION VOLUME AFTER RECANALIZATION: ACCURATE PREDICTOR OF CLINICAL AND FUNCTIONAL OUTCOME AND CORRELATION WITH DEGREE OF RECANALIZATION. European Stroke Journal 2019, Vol. 4(1S) 150–778

- Poster Presentation in International Stroke Conference 2020:
Garcia-Tornel, M. Olive-Gadea, M. Ribo, D. Rodriguez-Luna, J. Pagola, M. Muchada, M. Requena, M. Deck, S. Boned, J. Juega, N. Rodriguez-Villatoro, C. Piñana, D. Hernandez, A. Tomasello, C.A. Molina and M. Rubiera. Abstract WMP17: Computerized

Tomography Perfusion to Characterize Lack of Clinical Improvement After Recanalization in Acute Ischemic Stroke. Stroke 2020, Vol 51 (S AWMP17)

- Publication in a scientific journal: https://doi.org/10.1161/STROKEAHA.120.029212