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Comparison of computed tomography and magnetic resonance imaging in acute ischemic stroke

Choosing a hyperacute stroke imaging protocol for proper patient selection and time efficient reperfusive treatment

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1. Abstract

Acute ischemic stroke (AIS) is a clinical syndrome of rapid onset of focal cerebral deficit, lasting 24 hours or leading to death. The rationale behind intervention in hyperacute stroke is based on a three-compartment model of brain parenchyma following vascular occlusion. The infarct *core* represents non-viable brain that cannot be salvaged even with very prompt treatment (non-viable tissue, NVT). The ischemic *penumbra* is defined as functionally impaired yet still viable tissue surrounding the ischemic core. The penumbra includes ischemic areas that recover spontaneously (*benign oligemia*) and areas that progress to irreversible changes, unless effective treatment is used (referred to as tissue at risk, TAR). The penumbra is the most clinically relevant target for treatment by intravenous thrombolysis with intravenous tissue plasminogen activator (IVT rt-PA) and mechanical thrombectomy (MT). The goal of perfusion imaging is not only the diagnosis of ischemia, but also the detection of the penumbra. In order to quantify and more precisely detect brain perfusion, several standard flow parameters are calculated.

The objective of the present study is to assess the utility of computed tomography perfusion (CTP) and/or magnetic resonance imaging (MRI) protocols for selection of patients affected by AIS for reperfusive treatments and to better characterize the reliability of the two methods in predicting follow-up infarction.

We retrospectively reviewed consecutive AIS patients evaluated for the selection for reperfusive treatments at two comprehensive stroke centers (CSC), using two different hyperacute stroke imaging protocols (HSIP) for proper patient selection. The two CSC employ a FAST MRI based HSIP, including ASL and DWI sequences, and a multimodal CT based HSIP, including mCTA and CTP, respectively.

We enrolled 158 consecutive patients admitted for AIS, undergoing mCT-based hyperacute stroke imaging. CTP presented a prognostic accuracy (ACC) of 75.9%. In patients with perfusion deficit in anterior circulation territory, CTP-Tmax > 16s proved relatively reliable to identify the NVT, with an overestimation in patients with favorable clinical-instrumental outcomes. Similarly, CTP-Tmax > 9.5s proved reliable to identify the area of total hypoperfusion, overestimating TAR in the vast majority of patients untreated or with reperfusion treatment failure. On the other hand, we recruited 349 consecutive patients admitted for AIS, undergoing FAST-MRI based hyperacute stroke imaging. MRI with DWI and pcASL presented ACC of 97.4%, decreasing to 83.9%, when only hypoperfusion on pcASL was considered. In patients with perfusion deficit in anterior circulation territory, DWI confirmed the high reliability to identify the NVT in patients with favorable clinical-instrumental outcomes. Similarly, pcASL identified the area of total hypoperfusion, with an overestimation of TAR in patients with unfavorable outcome, but also a higher proportion of complete overlap with the final infarct.

In conclusion, our study showed that CTP-Tmax maps for the detection of AIS achieved a sufficiently reliable ACC, but this was not optimal. In patients with perfusion deficit in anterior circulation territory, CTP-Tmax > 16s proved relatively reliable to identify the ischemic core area, with a tendency, however, to overestimate NVT compared to FIA, in patients with favorable clinical-instrumental outcomes and, in particular, in patients undergoing early recanalization. Similarly, CTP-Tmax > 9.5s proved reliable to identify the area of total hypoperfusion, but the degree of correlation with FIA was in favor of an overestimation of TAR in the vast majority of patients untreated or with reperfusion treatment failure.

On the other hand, our study showed that DWI-pcASL for the detection of AIS achieved a highly reliable ACC. In patients with perfusion deficit in anterior circulation territory, DWI confirmed the high reliability to identify the NVT predicting FIA, in patients with favorable clinical-instrumental outcomes and, in particular, in patients undergoing early recanalization. Similarly, rCBF on pcASL proved reliable to identify the area of total hypoperfusion, with a higher proportion of cases showing a complete overlapping with the FIA, in the vast majority of patients untreated or with reperfusion treatment failure. However, the degree of correlation with FIA was in favor of an overestimation of TAR in many cases.

2. Research project theme and relevance

Acute ischemic stroke (AIS) is a clinical syndrome of rapid onset of focal cerebral deficit, lasting 24 hours or leading to death.

A cerebral blood flow (CBF) reduction below certain values is a critical event leading to a series of functional, biochemical and structural changes culminating into irreversible neuronal death.

The rationale behind intervention in hyperacute stroke is based on a three-compartment model of brain parenchyma following vascular occlusion. The infarct *core* represents non-viable tissue (NVT) of the brain that cannot be salvaged even with very prompt treatment. The ischemic *penumbra* is defined as functionally impaired yet still viable tissue surrounding the ischemic core. The penumbra includes ischemic areas that recover spontaneously (*benign oligemia*) and areas that progress to irreversible changes, unless effective treatment is used (referred to as tissue at risk - TAR) (1).

The penumbra is the most clinically relevant target for treatment by intravenous thrombolysis with intravenous tissue plasminogen activator (IVT rt-PA) and mechanical thrombectomy (MT). The outer zone represents brain that is likely to survive without such treatment. Rate of progression to infarction depends on the degree of collateral arterial circulation, duration of insult, and functional and metabolic cellular state (2).

Computerized tomography (CT) is the first-line imaging modality used in neurologic emergencies owing to its speed, accurate depiction of acute intracranial disease, and availability. At primary stroke centers, *nonenhanced CT (NECT)* should be performed rapidly in patients with signs and symptoms of acute stroke and is essential in the decision-making process by helping rule out intracranial hemorrhage (ICH) and identify large (ie, >100 mL or more than one-third of a brain territory at risk) well-established infarcts. Awareness of the typical findings, pearls, and pitfalls of CT image interpretation is therefore critical for radiologists, stroke neurologists, and emergency department providers to make accurate and timely decisions regarding both (a) immediate treatment with IVT rt-PA up to 4.5 hours after a stroke at primary stroke centers and (b) transfer of patients with large-vessel occlusion (LVO) at CT angiography to comprehensive stroke centers for endovascular thrombectomy (EVT) up to 24 hours after a stroke (3).

Early signs of proximal middle cerebral artery (MCA) large-vessel occlusive infarction seen at NECT include loss of gray-white matter differentiation at the insula, basal ganglia, and caudate head as well as sulcal effacement (4).

However, the revised 2018 American Heart Association/American Stroke Association(AHA-ASA) guidelines state that the extent or severity of the hypoattenuation seen at CT should not be used as a criterion for withholding rt-PA owing to insufficient evidence (5).

Since the DAWN (6) and DEFUSE 3 (7) trials showed the efficacy of endovascular thrombectomy (EVT) up to 24 hours after the onset of stroke, CT angiography has become the operational standard for rapid accurate identification of intracranial large-vessel occlusion (LVO).

CT angiography (CTA) helps identify proximal LVOs in patients with acute MCA or intracranial internal carotid artery (ICA) syndromes, aiding in the decision of whether to transfer a patient to a comprehensive stroke center accredited to perform EVT.

However, some measure of core infarct volume is required before proceeding with EVT to determine both ICH risk and the likelihood of treatment benefit. Small cores (<50–70 mL or in a symmetric collateral pattern) are considered favorable for EVT treatment, and large cores (>100 mL or in a collateral pattern typical of malignancy) are considered unfavorable to treat. Core volume can be estimated from cross-sectional images (ie, diffusion-weighted images, CT angiography source images as [length 3 width 3 height]/2) (8).

Perfusion CT (CTP) or multiphase CT angiography (mCTA) with collateral and source image assessment are emerging as important tools for treating stroke in eligible patients, especially those with delayed presentation (>6 hours from symptom onset) or stroke of unknown onset (from time last seen well) (5).

Dynamic or first-pass CTP is performed by sequentially imaging a defined section of tissue after a single high-flow bolus of contrast material is administered. The same section is imaged multiple times in cine mode as the bolus passes to track the degree of attenuation at both the tissue and arterial levels as a function of time. Modern scanners with helical capability and broader z-direction detectors can perform whole-brain CTP. (3).

Automated or semiautomated postprocessing of the CTP data generates multiple perfusion maps. Because attenuation change is linearly associated with the concentration of iodinated contrast material in a region, absolute values of perfusion parameters can be calculated.

The goal of perfusion imaging is not only the diagnosis of ischemia, but also the detection of the penumbra. In order to quantify and more precisely detect brain perfusion, several standard flow parameters are calculated.

Mean transit time (MTT, s) represents the mean time required for a volume to clear the capillaries, while the time-to-peak (TTP, s) reflects the time required for a volume to reach peak concentration. Both MTT and TTP are very sensitive to local perfusion disturbances, but less specific to ischemia or infarction. Cerebral blood volume (CBV, ml/100 g brain) represents the volume of blood in a volume of tissue, and reflects autoregulation. As perfusion pressure decreases, autoregulatory mechanisms are activated, locally resulting in vasodilatation and recruitment of supporting capillary networks to increase perfusion of the ischemic region. The results of these changes are increased CBV, MTT and TTP. Within the ischemic core there is a failure of autoregulation, and CBV is ominously decreased in this region. Cerebral blood flow (CBF, ml/100 g brain/min) represents the delivery of blood to tissue per unit time and is calculated by dividing the CBV by MTT. CBF is decreased in all hypoperfused regions, including both the penumbra and ischemic core. On CTP, CBV has been shown to correlate with infarct volume, and the subtraction of CBF and CBV is the usual way to detect the penumbra (9). CBF and time to maximum (Tmax) enhancement are among the most accurate values for use in acute stroke evaluation (10).

Parameters demonstrated on these maps include CBF, Tmax of the tissue residue function, CBV, and mean transit time. Only CBF and Tmax have been widely studied in recent randomized clinical trials. For example, in the CT arms of the DAWN and DEFUSE 3 trials, automated perfusion CT software estimated core infarct volume on the basis of a less than 30% threshold for CBF reduction and penumbral volume on the basis of a threshold greater than 6 seconds for prolongation of Tmax (6,7).

Different papers have been published on perfusional imaging in order to establish optimal threshold for predicting both penumbral tissue and infarct core in AIS.

According to data literature, the optimal approach to define the infarct and the penumbra is a combined approach using 2 CTP parameters. Three methods have been considered to assess the ischemic core/penumbra mismatch in CTP:

1) relative MTT (with an optimal threshold of 145% of mean contralateral MTT) and absolute CBV (with an optimal threshold at 2.0 ml x 100 g^{-1}) (11–14). The MTT is prolonged, and the CBF is reduced in both the core infarction and penumbra because of occlusion of a proximal artery that results in slowed passage of blood through the affected brain (total hypoperfusion = rMTT > 145 %). The CBV differs between the core and the penumbra and may be used to distinguish these regions of ischemia. The penumbra remains viable by inducing compensatory vasodilatation of collateral vessels that result in an increased CBV. By contrast, these compensatory mechanisms fail in the irreversibly injured core infarction, which results in a decreased CBV (infarct core = CBV < 2 ml/100gr). MTT - CBV

mismatch is able to identify favorable outcome in patients treated with IVT rt-PA and/or EVT < 12 hours (12,15–17). Nevertheless, clinical trials failed since patients with and without MTT - CBV mismatch had similar outcome after IVT rt-PA ≤ 9 hours from onset and EVT ≤ 8 hours from onset (18,19). Indeed, hyperemia occurring in penumbra region can mask infarct core, causing underestimation of CBV lesion (20). On the other hand, MTT lesion includes hypoperfused regions of benign oligoemia, causing overestimation of penumbra extent (21).

2) Tmax (with an optimal threshold of 6 seconds) and relative CBF (with an optimal threshold of 30% of mean contralateral CBF) (22,23). A Tmax threshold >4 seconds, 3 to 6 hours after stroke onset, provides the most accurate estimate of final infarct volumes in patients who do not reperfuse. Furthermore, the correlation between infarct growth and penumbra salvage volume is significantly better for perfusional alterations defined by Tmax >6 seconds and a threshold of >4 to 6 seconds is optimal for estimating the ischemic penumbra (total hypoperfusion = Tmax > 6 sec). Ischaemic core is estimated by CTP as relative CBF less than 30% of normal brain blood flow (infarct core = rCBF < 30%). Target mismatch slightly differs across the studies (24).

Tmax with optimal threshold of 9,5 and 16 seconds (25). A CTP derived Tmax threshold of around >16 s on average, in both grey matter (GM) and white matter (WM), has the highest sensitivity/specificity for brain tissue that is infarcted (infarct core = Tmax > 16 sec) even when reperfused early (within 90 min from CTP imaging). Further, progressively lower Tmax thresholds of ≈>12.5 and >9.5 s are associated with GM and WM infarction if reperfusion is achieved between 90 to 180 min from CTP and in the acute nonreperfusers, respectively (total hypoperfusion = Tmax > 9.5 sec). No data are currently available on Tmax - Tmax mismatch ability in predicting outcome.

The accuracy of CTP to distinguish large (>100 mL) from small (<50–70 mL) core infarct volumes in EVT selection has been studied in comparison with a *diffusion-weighted imaging (DWI)-MRI* reference standard (26).

CTP is grouped with **magnetic resonance imaging (MRI)** in the updated 2018 AHA-ASA guidelines for early management of patients with AIS, which states, “in selected patients with AIS within 6 to 24 hours of last known normal who have LVO in the anterior circulation, obtaining CTP, DWI-MRI, or MRI perfusion is recommended to aid in patient selection for MT, but only when imaging and other eligibility criteria from RCTs [randomized controlled trials] showing benefit are being strictly applied in selecting patients for MT” (5).

However, in the recent Hermes meta-analysis of early-window EVT trials and in a subgroup analysis of the DEFUSE 3 late-window trial that were presented at the 2018 AHA-ASA International Stroke Conference, DWI was found to be more efficient than perfusion CT when used to help select candidates for EVT. DWI was found to have higher odds ratios for selecting patients more likely to experience clinical improvement and functional independence (24). DWI remains the unequivocal reference standard used to assess core infarct volume (27). DWI-MRI has been considered the gold standard for ischemic core estimation, even if it does not accurately differentiate irreversibly damaged ischemic tissue from salvageable tissue. Depending on the speed and quality of reperfusion, regions affected by cytotoxic edema can evolve to full infarction, partial infarction, or normal tissue outcome, particularly if reperfusion occurs early on (28).

Additionally, recent trials have suggested that advanced CT and MRI can be used to extend the time window for intravenous rt-PA administration (29,30). The recent EXTEND, ECASS4-EXTEND, and EPITHET trials results have shown that patients benefit from treatment with intravenous tPA at 9 hours or after a wake-up stroke when they are selected using CTP or perfusion MRI (30).

Potential pitfalls of CTP include motion artifact, poor signal-to-noise ratio from a suboptimal contrast material bolus, faulty arterial and venous input functions, and truncation of the tissue and vascular time-

attenuation flow curves from a shortened acquisition time. Moreover, thresholds for determining core and penumbra can vary between vendors and between postprocessing platforms. Thresholds for determining irreversible ischemia likely vary with time after stroke, quality of collateral flow, and ischemic preconditioning. CTP thresholds can also be unreliable in the presence of old infarcts, partial reperfusion, or hyperemia associated with compensatory vasodilatation (3).

The acquisition time for NECT with multidetector CT is about 1 to 2 minutes. The addition of CTA and dynamic CTP to NECT increases the duration of the exam until 10 minutes. This fact does not extend the time of IVT rt-PA administration, since it can be done after the completion of NECT (31).

Advantages of MRI for brain parenchymal characterization in comparison with CT in patients with acute ischemic stroke, include its higher sensitivity for detecting symptomatic ischemic lesions within minutes of stroke onset, even if small and located in the posterior fossa, and, the ability to distinguish them from chronic ischemic lesions. Moreover, MRI provides reliable information about the size of the infarct, which is used for decision making, because patients with extended infarcts have an increased risk of symptomatic ICH, and is able to detect subclinical satellite ischemic lesions that provide information on stroke mechanism, and chronic ischemic changes and microbleeds that are considered to be markers of hemorrhage-prone small vessel disease, and have been linked to occurrence of future ICH. Despite all these advantages, MRI is usually not considered the imaging modality of choice in the process for selecting patients for thrombolytic therapy. This can mainly explained by the limited availability of MRI in many stroke centres (commonly MRI is not available 24 hours a day, 7 days a week), the relatively long duration of the exam that increases the risk of suboptimal studies due to motion artefacts (approximately 10% of patients are unable to remain motionless resulting in poor quality MRI scans, the need to exclude patients with absolute contraindications to this examination such as the presence of certain types of cardiac pacemakers, or with severe claustrophobia, and the difficulty of monitoring these patients within the MRI suite. Finally, MRI has been used in only a minority of patients in a few of the recent clinical trials, and therefore, evidence for the use of MRI in the acute endovascular stroke workflow is only modest (32).

One of the major arguments against routine use of MRI is the time required to perform a complete protocol, and although some centers have developed abbreviated protocols lasting 5-7 minutes making it competitive against CT, the real time required from when the exam is ordered until all data are post-processed and ready to be interpreted can exceed 30 minutes (33). This fact has limited use of MRI as the routine first-line method of neuroimaging to a very few centers around the world to screen AIS patients for IVT rt-PA or MT eligibility.

MRI protocol for selecting AIS patients for reperfusion therapies aims to provide reliable information on three key components of stroke physiology: 1) the presence and location of an intravascular thrombus that can be treated with thrombolysis or thrombectomy; 2) the presence and size of a core of irreversibly infarcted tissue; and 3) the presence and extension of hypoperfused tissue at risk for subsequent infarction unless adequate perfusion is restored (salvageable brain tissue). All these information, required to extend the therapeutic window, improve treatment outcome, minimize the risk of ICH, and can be obtained by using a multimodal MRI protocol that includes the following sequences: intracranial time-of-flight magnetic resonance angiography (MRA); diffusion-weighted imaging (DWI), T2-weigted fluid-attenuated inversion recovery (T2-FLAIR), and perfusion-weighted imaging (PWI) provided by Dynamic Susceptibility Contrast (DSC) (32). PWI is useful to reveal ischemic regions of the brain. In constrast, DWI reveals evidence of ischemic injury. The mismatch between the PWI lesion and the DWI lesion (PWI/DWI mismatch) refers to evidence of a larger area of ischemia on PWI (ie, territory with critically low perfusion) relative to a smaller area od irreversible ischemic injury (ie, infarct core) on DWI suggesting the presence of salvageable area (ie, the ischemic penumbra). In the DEFUSE 3 trial, either CT or MR perfusion imaging was used to select patients for MT. The study demonstrated a benefit of EVT regardless of whether CT or MRI was used for patient selection, but the

benefit was greater for patients selected using MR perfusion compared with patiens selected using CT perfusion (7).

With MRI, DWI is considered to correlate with infarct volume, and subtraction between CBF and DWI is used to demonstrate the penumbra. Aside from gadolinium contrast bolus perfusion imaging, another method of MRI perfusion imaging is *arterial spin labeling (ASL)*. ASL magnetically labels the blood entering the brain and within 24 hours of stroke symptoms onset can depict perfusion defects and diffusion-perfusion mismatches without the administration of a contrast agent (34). This technique, which enables the quantitative measurement of CBF, is based on magnetic labeling of blood prior to flowing into a volume of interest, typically in the neck (i.e., in the common carotid arteries). Labeling can be either continuous (CASL) or pulsed (PASL). In CASL, blood is labeled even during the readout phase. This approach requires a special labeling coil and has a higher signal-to-noise ratio (SNR) with a penalty of higher specific absorption rate (SAR). Therefore, PASL is more commonly used at 1.5 T and 3 T. With this approach, a saturation pulse is followed by a short delay, and then an echo-planar image of an area of interest is acquired. PASL benefits from higher SNR and T1 prolongation at 3 T. To limit the duration of the application of the radiofrequencypulse, the CASL may be approached by the use of several RF pulses, using the body coil. This method called ‘‘pseudo-continuous ASL’’ (PCASL) has the combined advantages of CASL and PASL The drawbacks of ASL are longer acquisition times and measurement of CBF only, as with ASL it is currently not possible to calculate MTT, TTP or CBV. The main advantage is the ability to perform imaging without the use of contrast, which can be crucial in subjects with known allergy, high risk of nephrogenic systemic fibrosis or in longitudinal studies (9).

In this observational study, we retrospectively analyzed patients with AIS referred to the comprehensive stroke center (CSC) of the Polyclinic University Hospital of Messina, that serves an area encompassing the whole of Sicily. Contextually, we compared these data with the CSC of Maggiore Hospital, that serves the area in the province of Bologna. The past few years have seen increasing trends towards centralized system for acute stroke care. Specifically, there has been a significant increase in the proportion of acute ischemic stroke patients receiving EVT and registered in the The Italian Registry of Endovascular Treatment in Acute Stroke (IRETAS) from 2014 to present, considering both Messina (32 in 2014, 67 in 2015, 104 in 2016, 141 in 2017, 164 in 2018, 190 in 2019, 187 in 2020, and 167 in 2021) and Bologna (14 in 2014, 20 in 2015, 24 in 2016, 57 in 2017, 127 in 2018, 164 in 2019, 190 in 2020, and 218 in 2021) CSC (35).

3. Aims of the study

The objective of the present study is to assess the utility of CTP and/or MRI protocols for selection of patients affected by AIS for reperfusive treatments and to better characterize the reliability of the two methods in predicting follow-up infarction. We estimated to enroll about a complexively 400 patients undergoing CT/MR HSIP, from each registry, during observation period.

Specific aims of our study are:

1) To assess the sensitivity and specifity of CTP for the detection of AIS and its reliability to identify the volume of the total hypoperfusion area and ischemic core/penumbra ratio using Tmax/Tmax mismatch.
2) To assess the sensitivity and specifity of MRI for the detection of AIS and its reliability to identify the volume of the total hypoperfusion area and ischemic core/penumbra ratio using DWI/ASL mismatch.

Moreover, secondary endpoint was the possibility to differentiate the portion of true TAR from false TAR (benign oligoemia) within penumbra.

In addition, we aimed to assess the prognostic accuracy (ACC) of CTP summary maps in predicting the FIA in patient with AIS. We hypotized that the best correlation between ischemic core and FIA should be found in early and fully recanalized patients with mTICI 2b-3 and/or in FCR patients. On the other hand, the hypoperfusion volume should better correlate with FIA in not treated patients and in EVT failure (TICI 0). In conjuction with this assessment, we evaluated the reliability of FAST MRI HSIP in predicting hypoperfusion volume. We expect the precision of MRI DWI may remain superior in accurately identifying infarct core, in early and fully recanalized patients with mTICI 2b-3 and/or in FCR patients. On the other hand, we expect to assess the ACC of rCBF ASL maps in predicting the FIA in patient with AIS, in not treated patients and in EVT failure (TICI 0) .

4. Materials and Methods

Study population and patient selection

We retrospectively reviewed consecutive AIS patients evaluated for the selection for reperfusive treatments at two comprehensive stroke centers (CSC), using two different hyperacute stroke imaging protocols (HSIP) for proper patient selection. Subjects have been enrolled from the cohort of the stroke registry of Stroke Unit of the Division of Neurology, Azienda Ospedaliera Universitaria Policlinico "G.Martino", Messina, between the 1st January 2019 and the 31st December 2020. Data have been compared to AIS patients from the cohort of the stroke registry of the UOC Neurologia e Rete Stroke metropolitana, IRCCS (Istituto di Scienze Neurologiche), Ospedale Maggiore, Bologna, between the 1st January 2019 and the 30th June 2020. The two CSC employ a FAST MRI based HSIP, including ASL and DWI sequences, and a multimodal CT based HSIP, including mCTA and CTP, respectively.

All patients were initially evaluated by neurologist in the emergency setting with initiation of an institutional stroke protocol facilitating expedited triage, imaging, interpretation and treatment when appropriate. The inclusion criteria were (1) suspected AIS; (2a) mCT scan dataset including NECT, supra-aortic CTA and CTP performed on admission OR (2b) FAST MRI based HSIP, including pcASL, DWI, FLAIR, and TOF sequences; (3) CT scan performed <24 hours after symptom onset.

Exclusion criteria were (1) nondiagnostic image quality, (2) evidence of another cause of neurological deficits, (3) incomplete coverage by the CTP slab of Alberta Stroke Program Early CT Score (ASPECTS) regions and (4) missing follow-up CT or MRI.

Patient characteristics and clinical information, including baseline NIHSS (National Institutes of Health Stroke Scale), and imaging data were recorded prospectively. Affected circulation territory was presumed using Oxford Community Stroke Project (OCSP) classification (36), and confirmed with radiological assessment, if possible. Operator assessed Thrombolysis in Cerebral Ischemia (TICI) reperfusion grade(37,38), evidence of hemorrhagic transformation and predischarge NIHSS were collected.

Patients were grouped in four population, depending on reperfusive treatment performed in the acute setting (untreated, treated with IVT, treated with EVT, and treated with IVT plus EVT).

Untreated population considered only patients with AIS excluded from reperfusive procedures, while the patients in which AIS was excluded after clinical and diagnostic assessment (stroke mimics) were omitted from database.

The primary outcome was the detection of ischemic lesion on imaging assessment (see the sections below), in order to define sensitivity, specificity and ACC of CTP and pcASL, respectively, for the detection of perfusion deficit in the AIS setting.

In the second part of the study, we performed a subanalysis in order to determine the ACC of the CTP summary maps in the forecast of the final infarct area (FIA). Considering controversial role of CTP for posterior stroke (39), only patients with anterior circulation stroke and perfusion deficit were analyzed. Therefore, we considered the same criteria, in order to perform this subanalysis for FAST MRI based HSIP too. We applied the very same criteria for selecting patient also in this latter group, because it has been reported a hemodynamic differences between the carotid and vertebrobasilar arteries, and this could be misinterpreted as true hypoperfusion (40). In fact, both posterior cerebral artery territories can demonstrate pseudo-hypoperfusion relative to the anterior circulation territories (41).

The eventual reperfusion status was used to group patients into separate cohorts depending on successful vs unsuccessful reperfusion. The primary end-point for the reperfusive procedures are successful recanalization (TICI 2b-3), acquired from angiograms control at the end of EVT, and favorable clinical

response (FCR) in patients treated with IVT rt-PA. An FCR is defined as an NIHSS of 0 to 1 or ≥ 8 points of improvement between baseline and hospital discharge (22).

Our assumption was that the CTP ischemic core might better predict FIA in cases of early and complete recanalization (TICI 2b-3) or in cases of FCR (subgroup with favorable outcome). Similarly, we evaluated the reliability of FAST MRI HSIP in predicting hypoperfusion volume, assuming that the precision of MRI DWI should have remained superior in accurately identifying infarct core, in early and fully recanalized patients with mTICI 2b-3 and/or in FCR patients.

On the other hand, the hypoperfusion volume should better predict FIA in EVT failure (TICI 0) or in untreated individuals (subgroup with unfavorable outcome). In this latter population, the assumption was that FIA should be specifically related to true TAR, within the total penumbra area. We likewise assessed the ACC of CBF ASL maps in predicting the FIA in patient with AIS, in not treated patients and in EVT failure (TICI 0).

Imaging assessment

Included are AIS patients in which CTP maps, for mCT based HSIP, and ASL maps, for FAST MRI based HSIP, respectively.

a) mCT based HSIP

Patients underwent an institutional stroke imaging protocol including NCCT, CTA and CTP at admission. CT protocol was conducted on a 64-detector row clinical system (Revolution Evo 128, GE Healthcare, Milwaukee, Wisconsin). NECT helical scans were performed from the skull base to the vertex (120 kV, 400 mA, 5 mm section thickness with 2.5 mm reconstructions). CTAs were conducted from the aortic arch to the vertex for arterial phase, and then with two following scans from C2 to vertex for venous and delayed phases (120 kV; 320–400 mA; section thickness 0.625 mm), after intravenous administration of 50-60 mL iodinated contrast medium injected at 4 mL/s and followed by 50 mL saline flush, using bolus tracking up to threshold level (80 HU) of a region of interest (ROI) placed at the level of the distal aortic arch (delay of 4s). CTP scans (80 kV, 300 mA) consisted of a continuous acquisition, with a total duration of about 154s and a scanning volume of 8cm, that started after administration of 50mL of iodinated contrast medium injected into an antecubital vein at 4mL/s and followed by 50mL saline flush.

b) FAST-MRI based HSIP

The radiological examination included a preliminar CT scan performed with a multidetector scanner Somatom Definition AS 64, Siemens Healthcare, Germany), for patient admitted with primary transfer, in order to exclude intracranial bleeding. CT scans were acquired using contiguous axial images, acquired on standard orbitomeatal plane from foramen magnum to vertex (1 mm3 isotropic voxel; kVp = 120, mAs = 360). Images were evaluated by two experts neuroradiologists in consensus to establish CT-ASPECT scores. (window width and level were centered at approximately 35–45 HU width and 35–45 HU level).
Then, brain MRI was performed according to the protocol for ischemia. All patients were examined on Ingenia (Philips Healthcare, Best, Netherlands) MR scanners with the field strength of 1.5 T, using a 15-minute ischemia protocol. This protocol included 5 sequences in the axial planes with standardized parameters:

- DWI (TR/TE 2946/86 ms; b values 0 and 1000 s/mm2; 5.0 mm section thickness with no intersection gap; voxel size 1.5 × 2.2 × 5 mm; ADC map; sequence duration 60 s);
- Fluid-attenuated inversion recovery (FLAIR) (TR/TE 11,000/130 ms; TI 2800 ms: 5.0 mm section thickness with no intersection gap; voxel size 0.9 × 1.12 × 5 mm; sequence duration 154 s);
- Non-contrast three-dimensional time-of-flight angiography (3D TOF-MRA) (TR/TE 23/6.9 ms; flip angle 23°; 144 sections; voxel size 0.62/0.82/0.8 mm; sequence duration 209 s);

- Suscepbility-weighted imaging (SWI fast) (TR/TE 52/11.9 msec; 4.0 mm section thickness with no intersection gap; matrix 200x164, flip angle 20º; and FOV = 230mm. voxel size AP 1.2 × 1.2 RL × 4 FH mm; sequence duration 185 s);
- Fast three-dimensional pseudocontinuous (3D PCASL) ASL technique was used with following parameters: axial, 15 images, TR/TE 4500/25 ms, NEX (NSA) 1, BW 818 Hz; post-label delay: 1600 ms, voxel resolution 3.6*3.53*6 mm, slice: 1 mm, matrix: 68x65, scantime: 279 s.

The entire MRI protocol lasts 14 min and 47 s.

Patients eligible for EVT were treated immediately after MR imaging.

With the goal of comparing CTP and MRI for evaluation of acute stroke patients, a new metric called "stroke imaging time" (SIT) has been used to evaluate the amount of time the patient spends undergoing imaging prior to intervention (42). SIT begins when the screening NECT is available to the radiologist for viewing and ends when the radiologist provides the results of the follow-up confirmatory study to the ordering provider (FAST MRI or mCT HSIP). A comparison between SIT for patients who underwent MRI and patients who underwent CTP is hypothesized to assess the real HSIP time and improve the time to iniziate reperfusive treatments.

Post-processing

a) mCT based HSIP

CTP data were processed by a commercially available delay-insensitive deconvolution software [CT Perfusion 4D (CTP4D), GE Healthcare, Waukesha, Milwaukee, Wisconsin]. After automatic vessel selection (arteries and veins), parametric color-coded maps were computed based on evaluation of CBV, CBF, MTT and Tmax. Additionally parametric color maps for Tmax were produced, with the purpose of calculating the total hypoperfusion area and the ischemic core with optimal threshold of 9.5 and 16 seconds, respectively. These maps were superimposed on the NECT to help locate the area of altered perfusion. These fusion images (Tmax map and NECT) were then automatically co-registered to the follow-up NECT to allow a qualitative evaluation of the correlation between hypoperfused areas on Tmax maps and FIA regions on the follow-up NECT. A quantitative evaluation was also performed by means of the automatic software calculation of Tmax volumes for both 9,5s and 16s thresholds using the vendor prespecified standard settings. The automatic tool might include non-stroke related areas, as ventricular structures and choroid plexus. Unfortunately, the software did not allow segmenting and isolating stroke-related lesions from non-stroke-related areas. In order to minimize this technique bias, we adjusted the function filtering to exclude the non-stroke-related areas. This process did not succeed in defining a reliable volumetric assessment of ischemic volume for all examined patients.

b) FAST-MRI based HSIP

The pCASL sequence was post-processed, corrected to reduce vascular artefacts, and CBF maps were calculated using the vendor's provided workstation (extended MR Workspace 2.6.3.5, Philips Medical Systems Nederland B.V.) to transfer the DICOM picture. The irrigation area and sides of the affected territory were localized by a visual approach using well known anatomical frames. Subtraction of alternating tag and control image pairs, motion correction, and development of an ASL grayscale and colored map were the steps used in the post-processing of arterial spin-tagging data. The relative values of CBF (rCBF) on the ASL perfusion sequence were performed by placing the axis through the anteroposterior plane and manually placing the region of interest (ROI) on the lesion, within the high signal area on the ASL grayscale map. The values on the unaffected contralateral side were obtained by automatic selection of a software function for the symmetrical measurement of equal surfaces. Relative CBF values were obtained by determining the ratio of the measured variables, and are shown as a percentage. The territorial involvement of the ischemic core

on DWI sequence was determined using the ASPECT score (DWI-ASPECTS) involving a ten-point topographic scoring system (43).

Follow-up imaging evaluation

Standard follow-up imaging consisted in NECT for all patients, which was used to determine the presence of an infarct, defined as parenchymal hypodensity with loss of grey–white matter differentiation, sulcal effacement and/or mass effect. Concerning the mCT based HSIP, the initial NECT and CTP data was then compared with the follow-up NECT data. About the FAST-MRI based HSIP, the DWI and ASL data was likewise compared with respective follow-up NECT data. The follow-up NECT has been evaluated with respect to infarct size. Patients with ICH have been excluded from study if the blod clot(s) within the infarct area causes space-occupying effect (44).

Follow-up brain NECT, performed at a median of two days (IQR: 1–7 days) after hospital admission, was used to define FIA. We differentiated between early (within 48 hours) and late (after 48 hours) CT scan controls. Hence, the presence of ischemic lesion could be detected at early and/or late radiologic assessment. Window/level settings were adjusted to maximize the contrast between the normal and the infarcted tissue.

If clinically indicated, MRI was performed either soon after CTP at the admission or later as follow-up control. MRI exams were performed on a 1.5T scanner (Philips Achieva Ingenia 1.5T, Philips Medical System, Best, Netherlands), and included DWI, apparent diffusion coefficient (ADC) maps and fluid-attenuated inversion recovery (FLAIR) sequences. We only used follow-up MRI data, if available, in order to confirm ischemic lesion. On follow-up MRI, an infarct was defined as DWI/ADC restricted tissue that was also hyperintense on T2 weighted images and/or FLAIR sequences with or without mass effect.

Neuroimaging data was independently reviewed by two board-certified neuroradiologists (with 15 and 2 years of experience in mCT imaging interpretation) blinded to patient clinical information using the institutional Picture archiving and communication system (PACS) of Maggiore Hospital in Bologna. They independently evaluated neuroimaging data with pre-structured charts. Final definition of FIA and CTP area was reached through consensus, and any discrepancies were resolved through a consensus discussion in a separate session.

To perform the quantitative analyses of FIA, we used a semi-automated software tool included in the institutional PACS; the operators manually outlined the area deemed to be lesioned on a ‘slice-by-slice’ basis using an axial view of the CT image, allowing infarct volume estimation.

Similar neurimaging data evaluation has been performed by two board-certified neuroradiologist (with 5 years of experience in MRI interpretation) blinded to patient clinical information using the institutional PACS of Universital Hospital in Messina.

Statistical analyses

All data sets will be checked for normality before analysis with the appropriate parametric or nonparametric tests.

Descriptive statistics is reported as median and IQR for quantitative values, and count and percentage for categorial ones.

Kruskal-Wallis test and chi-square test ($\chi 2$) were used whenever appropriate, with Bonferroni correction for the former or Yates correction for the latter, if indicated (45).

Correlation coefficients and linear regression analysis were used to compare ischemic cores and FIA in patients with FCR and/or TICI 2b-3, as well as the correlation between hypoperfusion and FIA in patients with TICI 0 or untreated.

Concerning patients treated with EVT, we calculated medians and interquartile ranges (IQR) instead of mean and standard deviations (standard deviation, SD), due to non-normal distribution of data. Time intervals between CTP and the end of the EVT procedure were divided according to median and IQR into: very early (≤109.5 minutes), early (≤127.5 minutes) and late (>127.5 minutes) timing. Time intervals between pcASL and the end of the EVT procedure were divided likewise, excluding patient in which the administration of IVT rt-PA preceeded MRI study.

For all analysis, two-tailed $P<0.05$ was considered significant. R software was used for analytical purpose [The R Project for Statistical Computing (https://www.r-project.org/)].

5. Results

A. mCT based HSIP (46)

1- Prognostic accuracy of CTP for the detection of AIS.

We retrospectively reviewed 302 consecutive patients admitted for AIS, undergoing mCT-based hyperacute stroke imaging. During the observation period, we recruited 158 patients (F=77; M=81). The average age of the examined sample was 74.09 (range 32-99) years.

Overall, 73 patients were untreated (46.2%), 39 received IVT (24.7%), 17 EVT (10.8%), and 29 IVT+EVT (18.4%).

Among these patients, 114 had a circulatory disorder in the anterior territory, 10 in the posterior territory, while it was not possible to determine the affected circulatory territory with instrumental examinations for 34 patients, of which 33 were untreated patient and one received IVT only. Using the Oxford Community Stroke Project (OCSP) classification 22, 29 patients had a presumed anterior circulation infarction and 5 had a presumed posterior circulation infarction. However, OCSP classification does not permit accurate discrimination between lacunar and small-volume cortical infarcts 24, thus we considered the group without radiological confirmation of circulation territory as undetermined.

For each intervention group, we assessed the association with the quantitative and categorical variables (Table Ia-b). NIHSS assessed on admission had a significant lower median in group a) and b). CTP-to-control imaging time was longer for untreated patients. At early radiological control, the ischemic area compatible with AIS was more easily found in groups c) and d) with high statistical significance. The same finding was most frequently detected at late radiological control in groups b), c) and d). Ischemic penumbra was detected in 81 patients, while 13 patients had an area of hypoperfusion without ischemic core; no perfusion defect was detected at the presentation in 64 patients. In patients undergoing EVT, a favourable recanalization rate (TICI 2b-3) was obtained in 60.87%.

According to the presence of perfusion deficit on CTP and ischemic lesion at post-treatment radiological assessment (Table II), we subdivided patients for the definition of sensitivity, specificity and ACC of CTP using Tmax-Tmax thresholds.

Comparing follow-up imaging and CTP data, the ischemic area identified at follow-up radiological assessment was outside the hypoperfused area in three patients. Two of these patients had exclusively TAR at CTP, in the absence of NVT. Twenty out of 64 patients without perfusion defects on CTP showed the presence of an AIS-compatible ischemic area at the control; among these, three patients had only MRI available. All these false negatives had a small-sized FIA (<20mm), mainly subcortical lacunar infarcts. In 15 out of 81 patients with perfusion deficiency including NVT, no ischemic lesion was found at the radiological control; however, among these patients, only nine performed late CT control that did not detect ischemic area compatible with AIS.

CTP for the detection of AIS in this population presented a sensitivity of 76.7% and a specificity of 74.6%, with a positive predictive value (PPV) of 81.5% and negative predictive value (NPV) of 68.8%. ACC stood at 75.9%. Considering global deficit on CTP, with or without inclusion of the NVT, PPV, specificity and ACC decreased. On the other hand, sensitivity slightly increased if TAR only defects were included (Figure 1; data categorized for circulation territory have been reported in Table III).

Study flowchart has been reported in Supplementary Figures as Figure I.

2- Reliability of CTP to identify total hypoperfusion area and ischemic core/penumbra ratio using Tmax/Tmax mismatch.

From the population of 158 patients, we selected a sample of 55 patients with AIS in anterior circulation territory and with perfusion deficiency detected at the initial CTP. In this subgroup, we evaluated the ACC of Tmax maps in predicting FIA, using qualitative assessment. These maps were superimposed on the NECT to help locate the area of altered perfusion. We only used MRI data, if available, in order to confirm ischemic lesion. This sample was divided into two subgroups according to the clinical and instrumental outcome:

a) Patients promptly and completely recanalized (TICI 2b-3) and/or patients with FCR: favorable, n. 34

b) Untreated patients or patients with EVT failure (TICI 0): unfavorable, n. 21

c) Patients who did not have these characteristics (TICI 1-2a and/or absence of FCR) were excluded from the test sample. Patients who had TAR only and did not presented NVT on CTP were excluded from the test sample, too, in order to avoid potential interpretation bias due to the conflicting imaging results (inclusion/exclusion criteria have been reported in Table IV).

Study flowchart for analysis n. 2 has been reported in Supplementary Figures as Figure II.

The association with age has been evaluated in the two subgroups. An older age is associated with an unfavorable outcome (p=0.026). As for the categorical variables, no statistically significant differences were found between the outcome subgroups concerning sex (χ^2=0.891; p=0.345). Concerning treatments and time between CTP and first NECT control for the determination of FIA, categorical data analysis has been reported in Table V.

Concerning the inclusion of the final infarction within the hypoperfused area detected at CTP, the presence of lesion was not confirmed in two (9.5%) patients belonging to group b). In the first case, the hypoperfusive deficit was located along the A2 section of the left anterior cerebral artery and there was a positive spontaneous evolution from the purely clinical point of view (NIHSS at admission 1, at discharge 0), although no treatment was performed; in the second case, the perfusion impairment was located in the left MCA M2 tract and the clinical evolution was spontaneously favourable in this case, too (NIHSS at admission 19, at discharge 2), despite a failure of the EVT (TICI 0). In the group a), ischemic lesion at follow-up controls was not detected in 11 patients (32.4%). CT ≤48 h alone was available in four of these patients; in one case (2.9%) the lesion area was located outside NVT detected at CTP.

Among the patients in which ischemic lesion confirmed NVT identified on CTP, FIA was smaller than NVT in 23 cases (41.8%), FIA and NVT matched in 8 patients (14.5%), FIA exceeded NVT in 10 (18.2%). Among patients with favorable clinical/instrumental outcomes, 15 (44.1%) had FIA smaller than NVT, while two (5.9%) had FIA corresponding to NVT; in five patients (14.7%) FIA was larger than NVT (Figure 2A).

As for the degree of inclusion of ischemic lesion in TAR identified on CTP, FIA was smaller than TAR in 34 cases (61.8%), FIA and TAR matched in seven patients (12.7%); FIA did not exceed TAR under any circumstances (0%). Among patients with unfavorable clinical/instrumental outcomes, 13 (61.9%) had FIA smaller than TAR, while six (28.6%) had FIA corresponding to TAR (Figure 2B).

Illustrative examples have been reported as figures 3-5 and online figure III.

In patients undergoing EVT, with or without bridging, three patients had TICI 0; two of these patients had a favourable clinical outcome despite the failure of recanalization and late conclusion of the procedure, so that the presence of infarct area was not confirmed at instrumental follow-up checks in one of these patients, while the other one had FIA smaller than NVT identified on CTP; in the third case considered, the procedure was interrupted early due to anatomical difficulties to access the occlusion site, and the ischemic area on

follow-up CT had dimensions ranging between NVT and TAR. About patients with TICI 2b-3 or FCR after EVT, qualitative data analysis for the inclusion of FIA on CTP has been reported in Table VI.

As prior stated in Material and Method section, the volumetric analysis was not performed in all patients.

Thus, the sample size decreased and quantitative assessment could not reach a statistically significant result. Nevertheless, volumetric assessment was substantially in agreement with qualitative results, namely that CTP overestimated NVT, in the vast majority of patients with favorable clinical-instrumental outcomes, and similarly tended to overestimate TAR, in patients untreated or with reperfusion treatment failure.

Volumetric analysis data are summarized in online Table VII. Correlation coefficients and linear regression analysis are showed in online Figure IV.

B. FAST-MRI based HSIP

1- Prognostic accuracy of DWI-pcASL protocol for the detection of AIS.

We retrospectively reviewed 627 consecutive patients admitted for AIS, undergoing FAST-MRI based hyperacute stroke imaging. During the observation period, we recruited 349 patients (F=188; M=161). The average age of the examined sample was 73 (range 30-99) years.

Overall, 86 patients were untreated (24.6%), 32 received IVT (9.2%), 183 EVT (52.4%), and 48 IVT+EVT (13.8%).

Among these patients, 321 had a circulatory disorder in the anterior territory, 24 in the posterior territory, while the affected circulatory territory involved both anterior and posterior circulation in four patients, one for each intervention group. The circulation territory was determined with radiological confirmation in the whole sample.

For each intervention group, we assessed the association with the quantitative and categorical variables (see Appendix part 1). NIHSS assessed on discharge had a significantly higher mean in group a), while the difference between NIHSS at admission and at discharge was lower, compared to the other groups. As expected, the 3-month mRS was significantly higher in untreated patient, as well. MRI-to-control imaging time was longer for untreated patients, similarly to the CTP-to-control imaging time. Considering that the most patients performed an ealry radiological control (<48 hours), we did not distinguish between early and late assessment. In regards to laboratory testing, there was a significant difference in red blood count (RBC) and hematocrit (Hct) count comparing the group c) and the groups a) and b), and in hemoglobinemia between the groups c) and d) and the group a) and b), due to the fact the patient undergoing endovascular procedures had an lower hematological count at admission. Considering white blood count (WBC), we found that neuthrophils and lymphocytes percentage were significanlty different considering variability between group using parametric and non-parametric tests. However, significance values have been adjusted by the Bonferroni correction for multiple tests and the p-value was not significant anymore (see Appendix part 1.1). LDL-cholesterol was significantly higher in patient in group b) compared to group c). Blood glucose was higher in untreated patients with a significant difference when compared to group d). Both sistolic and diastolic pressure were higher in untreated patients, in comparison with group c). Concerning qualitative variants, perfusion defects on pcASL were absent with statistically significance in untreated patient, whereas the group c) and d) had the larger proportion of hypoperfusion with salvageable penumbra, when compared to both groups a) and b). The TAR detected on pcASL was larger than the FIA in the groups undergone endovascular procedures, while there was a significant correspondence between TAR and FIA in both group a) and b). Nevertheless, we found a significantly higher correspondence between NVT on DWI and FIA in patient treated with IVT rt-PA alone when compared to group b), and conversely there was a significanlty higher proportion of EVT alone patient in which the FIA exceed the NVT detected on DWI. The stroke cause was classified as undetermined for the presence of multiple causes in untreated patients, with a significant

difference in comparison with group c). Smoking habit was higher in group a) and lower in group c), with a significant difference between this two groups. Atrial fibrillation was known at the baseline in the groups in which IVT rt-PA was not administered, and anticoagulant treatment was assumed in bridging group patient with significantly lower rate than EVT group. On the other hand, group b) had lower proportion of carotid stenosis >50% when compared to group c).

According to the presence of perfusion deficit on pcASL-MRI and ischemic lesion at post-treatment radiological assessment (Appendix part 2), we subdivided patients for the definition of sensitivity, specificity and ACC of rCBF using pcASL.

Comparing follow-up imaging and MRI data, the ischemic area identified at follow-up radiological assessment was outside the hypoperfused area in three patients. Two of these patients underwent EVT, one for MCA occlusion and the other one for VA occlusion. The remaining patient was not treated. All of them had a FIA smaller than the NVT detected with DWI, whereas the pcASL failed to predict the ischemic lesion in the hypoperfusion area detected. Twelve out of thirteen patients without perfusion defects on pcASL showed the presence of an AIS-compatible ischemic area at the control; among these, four patients had a NVT on DWI larger than te FIA, whereas the was a complete correspondence between DWI and CT control FIA in 6 cases; finally, two cases presented a FIA larger than the NVT detected with DWI. In four cases between these false negatives, the ischemic lesion involved the posterior circulation; the remaining nine patients had a small-sized FIA (<20mm), mainly subcortical lacunar infarcts. In ten out of 336 patients with perfusion deficiency (nine including NVT on DWI; one without core detection on DWI), no ischemic lesion was found at the radiological control; however, among these patients, only four performed late CT control that did not detect ischemic area compatible with AIS. Two patient had a hyperperfusion on pcASL corresponding to the NVT detected on DWI, one involving the posterior circulation and the other MCA territory: in both cases the FIA corresponded to the very same area involved at MRI.

MRI with DWI and pcASL for the detection of AIS in this population presented a sensitivity of 100% and a specificity of 10%, with a positive predictive value (PPV) of 97.4% and negative predictive value (NPV) of 7.7%. ACC stood at 97.4%. Considering the hypoperfusion on pcASL only, in patient with TAR, there was a decreasing in sensitivity (95.9%), PPV (95.9%), and ACC (83.9%). On the other hand, sensitivity (96.4%), PPV (96.4%), and ACC (93.1%) slightly increased if patient without NVT-TAR mismatch were included (Figure 6; data categorized for circulation territory have been reported in Table VIII).

Study flowchart has been reported in Supplementary material as Figure V.

2- Reliability of FAST MRI HSIP to identify total hypoperfusion area and ischemic core/penumbra ratio using DWI/pcASL mismatch.

From the population of 349 patients, we selected a sample of 272 patients with AIS in anterior circulation territory and with perfusion deficiency detected on the MRI at admission. In this subgroup, we evaluated the ACC of pcASL maps in predicting FIA, using qualitative assessment, as well as described in previous paragragraph regarding mCTP based HSIP. Similarly, the sample was divided into two subgroups according to the clinical and instrumental outcome:

a) Patients promptly and completely recanalized (TICI 2b-3) and/or patients with FCR: favorable, n. 148.

b) Untreated patients or patients with EVT failure (TICI 0): unfavorable, n. 96

c) Patients who did not have these characteristics (TICI 1-2a and/or absence of FCR) were excluded from the test sample. For 28 patients, the interventional-clinical outcome was not consistent (TICI 2b-3 and Delta-NIHSS <0), and therefore they were not considered in the post-hoc tests for multiple comparison, in order to avoid potential interpretation bias due to the conflicting imaging results (inclusion/exclusion criteria have been reported in Supplementary material, Table IX).

Study flowchart for analysis n. 2 has been reported in Supplementary material as Figure VI.

The association with age has been evaluated, without statistically significant differences between the outcome subgroups. The time from onset to the FAST MRI HSIP was significally higher in group a) ($p=0.042$), as well as the time between pcASL and first NECT control for the determination of FIA ($p<0.001$). Categorical data analysis has been reported in Appendix part 2.

Concerning the inclusion of the final infarction within the hypoperfused area detected at MRI, the presence of lesion was not confirmed in one (1.0%) untreated patient and in six patients (4.1%) with favorable clinical/instrumental outcomes. In the first case, the hyperintense DWI lesion and the hypoperfusive deficit were located along the M2 section of the left middle cerebral artery and there was a positive spontaneous evolution from the purely clinical point of view (NIHSS at admission 1, at discharge 0), although no treatment was performed; between the six patient with favourable outcome, a patient presented TAR without NVT on DWI. Considering the group with unfavorable outcome, in two cases (2.1%) the lesion area was located outside the hypoperfused area, but corresponded to the NVT detected on DWI. In 12 patient of the favorable outcome group and 11 of the unfavorable outcome group, the pcASL could not be assessed for the visual analysis.

Among the patients in which ischemic lesion confirmed NVT identified on DWI, FIA was smaller than NVT in 15 cases (5.5%), FIA and NVT matched in 168 patients (61.8%), FIA exceeded NVT in 82 (30.1%). Among patients with favorable clinical/instrumental outcomes, 10 (6.8%) had FIA smaller than NVT, while 99 (66.9%) had FIA corresponding to NVT; in 33 patients (22.3%) FIA was larger than NVT (Figure 7A).

As for the degree of inclusion of ischemic lesion in TAR identified on pcASL, FIA was smaller than TAR in 163 cases (65.7%), FIA and TAR matched in 73 patients (29.4%), and FIA exceeded TAR in four cases (1.6%). Among patients with unfavorable clinical/instrumental outcomes, 31 (36.9%) had FIA smaller than TAR, while 47 (56.0%) had FIA corresponding to TAR and in three cases (3.6%) FIA exceeded the TAR (Figure 7B).

Illustrative examples have been reported as figures 8-10.

Between patients undergoing EVT, with or without bridging, a patient of the group c) had TICI 0, but had a favourable clinical outcome despite the failure of recanalization, so that the FIA was smaller than NVT identified on DWI. About patients with TICI 2b-3 or FCR after EVT, qualitative data analysis for the inclusion of FIA in NVT/TAR detected on MRI has been reported in Table X.

The volumetric analysis was not performed in this patients, due to technical software limits.

6. Discussion

The TAR is critically hypoperfused tissue that can be salvaged from infarction by early reperfusion after acute ischemia. If early reperfusion or a successful neuroprotective intervention does not occur, the NVT will expand and the penumbra will be incorporated into the FIA. Successful interventions can lead to penumbra salvage. Penumbra salvage integrates the effects of early reperfusion with other critical factors that influence the fate of hypoperfused tissue, such as the time elapsed since the onset of ischemia, the severity of cerebral blood flow reduction, and the presence of collateral blood flow (22,23).

The purpose of stroke imaging is to help select patients for reperfusion therapy, relying on individual vascular and physiologic information rather than on rigid time windows (5,47). To date, NECT, CTA, and CTP comprise the ‘‘state-of-the-art-advanced imaging’’ protocol of many stroke centers to assess for vessel occlusion, core/penumbra ratio, and degree of collaterals (48). CT-based imaging has been preferred for use in AIS, because of its distinctive advantages over MRI, such as its widespread availability, cost effectiveness, and rapid acquisition time. However, two recent trials (THRACE and GOLIATH) compared the efficacy of CT- and

MR-based protocols for patient selection and concluded that the MR-based imaging protocol was not inferior to the CT-based protocol (49,50). The inclusion of DWI, GRE, FLAIR, MRA, and PWI using DSC is ideal for establishing a standard protocol. For the total acquisition time, a reasonable maximum time that is not inferior to the CT-based protocol is approximately 10 min (50,51). On the other hand, the FAST-MRI based HSIP with pcASL has been used in few centres and its reliability for the patient selection has not been widely analysed. Most of the published studies have shown CBF values indicating the existence of TAR, but no cutoff CBF values based on the ASL sequence indicating outcome prediction after AIS have been published in literature to date (52).

A. mCT based HSIP (46)

For the decision-making process, both over- and underestimation of NVT and TAR volumes may have important clinical consequences in the management of acute stroke. Patient selection remains a problem quite hard to solve, as only 15-20% of AIS patients are eligible for rt-PA IVT. In addition, many of these patients (25-50%) do not achieve a good clinical outcome despite an effective recanalization (futile recanalization) and an increase in infarct area was found in 35% of cases, even after a full recanalization (53,54). It is to outline that even areas in the so-called benign oligoemia, can evolve towards infarction, in 10% of patients with AIS (55).

Patients with AIS might be excluded from effective EVT because of a malignant profile; this applies in particular for patients in an early time window (56). Volume differences between prognosis and final infarct volume are crucially dependent on the degree of recanalization ultimately achieved, the time needed for recanalization, additional reperfusion injuries due to recanalization, edema, or temporary dysregulation of the systemic blood pressure due to additional medical treatment (57). In patients undergoing EVT, with or without bridging, three patients had TICI 0; two of these patients had a favourable clinical outcome despite the failure of recanalization and late conclusion of the procedure, so that the presence of infarct area was not confirmed at instrumental follow-up checks in one of these patients, while the other one had FIA smaller than NVT identified on CTP; in the third case considered, the procedure was interrupted early due to anatomical difficulties to access the occlusion site, and the ischemic area on follow-up CT had dimensions ranging between NVT and TAR (56).

CTP thresholds have been shown to be time-dependent, since the infarct tissue increases with time elapsed between the CTP study and the recanalization of the occluded vessel; since it is not possible to predict this time interval after the CT-based protocol at admission, CTP thresholds are difficult to identify beforehand (25,58). It is at present believed that the prognosis of patients with AIS depends on CT-to-recanalization time, assuming in < 90 minutes the time better related with a favorable outcome (59,60). The model according to which the CTP thresholds for NVT change with time has been confirmed in several recent studies (61–63). On the other hand, the penumbral salvage and the favorable outcome would not depend on time of onset, but from the extent of TAR and collaterals; these findings could explain why in the most recent trials the treatment effect is larger in late than in early time windows (late time window paradox) (64,65).

As mentioned before, Tmax of the residue function has been suggested as a very promising parameter, although its physiological meaning and sensitivity to experimental conditions are not well-understood (66). The optimal Tmax thresholds associated with follow-up infarction might depend on different times of reperfusion (22,25), although it has recently been proposed that also Tmax thresholds might vary with the onset-to-imaging-time (67) or onset-to-reperfusion-time (63).

The vast majority of the patients recruited from the cohort investigated had a circulatory disorder in the anterior territory (5,68–70). We found statistically significant differences between treatment groups only with regard to NIHSS at admission, which was higher in patients undergoing EVT (as expected in patients with AIS due to LVO (70)), and time elapsed between CTP and first radiological assessment, delayed in untreated

patients. The latter difference may depend on the low rate of hemorrhagic transformation in patients who did not undergo reperfusion therapy (5,68,70). In fact, this delay is explained by the higher necessity of an early radiological assessment after 24 hours in patients with AIS undergoing reperfusive procedure, both for the possible onset of haemorrhagic complication and for the therapeutic management after treatment in the acute phase. Patients undergoing EVT, with or without bridging, were more likely to have an ischemic area compatible with AIS at early radiological control, and these findings were likely due to the larger size of the area affected by the injury, already visible at the first CT check in patients with LVO. The final infarct was detected in late controls even in patients treated only with rt-PA IVT. The difference in these cases was statistically significant between the untreated group and all groups of patients undergoing reperfusive procedures. The latter data can be explained by the potential presence of smaller lesions, not detected in CT and for which in-depth diagnostic search with MRI was skipped during hospitalization in the comprehensive stroke center. With regards to untreated patients, it should be considered that early CT control and follow-up radiological control of >48 h were not available for 30.1% and 43.8%, respectively: in the first case, an explanation can be found in the fact that untreated patients, after the mCT study, were sent to the primary stroke center of the area of territorial pertinence; in the second case, untreated patients, after the hyperacute phase of AIS management (<72 hours), continued the diagnostic-therapeutic process at another hospital.

As a result of our analysis, CTP based on the use of Tmax maps for the detection of AIS showed a moderate ACC, which was slightly lower when the study included perfusion defects with TAR only on CTP. The ACC, sensitivity, and specificity for infarct detection is similar to reported values from the CTP literature and the current CTP paradigm available at the authors' institution (25,63,67,71). Considering the limitation that NECT is less sensitive than MRI in detecting infarcted brain on follow-up, the ischemic area was detected at MRI only in 12/158 (7.59%) patients. However, all the false negatives (31.25%) had small-sized infarcts, mainly subcortical lesions, as expected from previous results (25,63,67,71). In addition, among the false positives (18.52%), only 60% performed a late CT control.

In the sample of patients with anterior circulation AIS and perfusion deficit detected at the initial CTP, we highlighted the presence of an older age in patients with unfavourable clinical-instrumental outcomes, in line with the data in the literature.

To evaluate the prognostic accuracy of the CTP summary maps in predicting FIA, we assumed that the best correlation between ischemic core and FIA should be found in early and fully recanalized patients with TICI 2b-3 and/or in patients with FCR: within this sub-group, NVT was larger than FIA in the vast majority of patients (44.1%), with a high percentage of patients in which a infarction area was not confirmed (32.4%). Previous studies reported that CTP based on CBV and rCBF < 30% may overestimate NVT on admission and consequently include ghost infarct core in a definitive lesional area, especially in patients imaged in the very early time window and with fast complete reperfusion (72–74). According to our results, Tmax >16s could overestimate NVT similarly, but we could not calculate reperfusion time for all patients in our sample, as reported in previous studies (25,58). Considering data for patients undergoing EVT, with or without bridging, with very early recanalization, NVT identified with Tmax threshold of 16 seconds almost entirely overestimated the lesion found at the follow-up control, although the intervention times were not within the so-called "golden hour" (<45 minutes from CTP) (58). Even in patients with early recanalization, NVT overestimated FIA in most cases, indicating in a longer time interval the correspondence of the ischemic core with the 16-second threshold of the Tmax maps (Supplementary material–Online Figure III).

On the other hand, the hypoperfusion volume should better correlate with FIA in not treated patients and in EVT failure (TICI 0): even concerning this evaluation, we found a tendency of CTP to overestimate TAR with Tmax thresholds of 9.5 seconds. According to previous studies, Tmax>9.5s should be better than Tmax > 6 sec in delineating total hypoperfusion area (25). Nevertheless, the complete matching of TAR with FIA was

found only in 28.6% of patients with unfavorable clinical-instrumental outcomes and in a patient undergoing complete but late recanalization. FIA did not exceed the size of TAR in any of the cases considered, thus excluding infarction of 'non-core–non-penumbral' tissue after stroke (55). From this analysis, we can deduce that the portion of tissue considered at risk with the threshold of 9.5 seconds could actually include a substantial portion of benign oligoemia. There were no case with underestimation of TAR, so we can affirm a tendency to incorporate the benign oligoemia with the use of the threshold of 9.5 seconds in Tmax maps.

B. FAST-MRI based HSIP

ASL has been applied in most of the neuroscience fields, on healthy subjects and patients, thanks to its non-invasive nature and the access to a reproducible and validated quantification of the CBF with respect to other cerebral perfusion techniques. The value of ASL has been demonstrated in acute and chronic neurovascular diseases where the perfusion anomalies revealed concord with other techniques, sometimes with an overestimate when compared with perfusion MRI(75–78). The absence of irradiation or the exogenous injection of acontrast medium, as well as the access to a reproducible quantification of perfusion parameters, make ASL an especially interesting technique in the study of tissue perfusion. The main disadvantage is the low SNR related to the subtraction between ''labeled'' images and ''control'' images. This requires a minimum acquisition of 3 min and a spatial resolution that is inferior that of the other techniques (MRI or CT-scan) (79).

In practice, using MRI to triage stroke patients for EVT is fraught with many obstacles that cause SIT to be delayed. The MRI takes considerably more time to obtain as compared to a CTP examination, which only takes about two minutes to complete and can potentially be done while the patient is already in the CT scanner for prerequisite NECT and CTA. In addition to moving the patient to a different machine to undergo MRI, there are checklists that must be completed by the MRI technologist to ensure that MRI is not contraindicated in the patient due to incompatible devices and so on. Completing these checklists and lying still for an MRI may be difficult for a patient with multiple neurologic defects demonstrated by an average NIH stroke scale of 12-14 in this study (42). Using ASL should decrease the SIT, minimizing the delay between the two HSIP evaluated. Bivard et al. (80) demonstrated the ACC of ASL in the detection of an ischemic lesion by making a comparison with contrast CT and MR perfusion, and they found rCBF values of the affected side<40% as threshold for the detection of TAR. In addition to the rCBF, ASL may detect the absolute CBF, without the need for complex post-processing using external softwares (52). ASL-DWI mismatch showed similar results to PWI-DWI mismatch provided by DSC (40,81).

The vast majority of the patients recruited from the cohort investigated had a circulatory disorder in the anterior territory, similarly to the CTP cohort. NIHSS at discharge and 3-month mRS had a significantly higher mean in untreated patient, with a lower Delta-NIHSS, as expected. MRI-to-control imaging time was longer for untreated patients, similarly to the CTP-to-control imaging time. The delay is explained by the higher necessity of an early radiological assessment after 24 hours in patients with AIS undergoing reperfusive procedure, as discussed before about the very same difference that we found in CTP population.

For the decision-making process, the use of DWI reduced the risk of over- and underestimation of NVT, as the result of our analysis confirmed. However, a complete FAST MRI HSIP was not performed for every patient admitted for suspected AIS, thus the selection bias could not be avoided. Therefore, we evaluated the use of pcASL for the detection of AIS, which showed a high ACC. The low specifity and NPV may be addressed to the above-mentioned selection bias. The ACC was slightly lower when the study included perfusion defects with NVT-TAR mismatch. The ACC, sensitivity, and PPV for infarct detection is similar to reported values from the ASL literature and the current pcASL paradigm available at the authors' institution (52,80,82). Considering the limitation that NECT is less sensitive than MRI in detecting infarcted brain on

follow-up, the ischemic area was detected at MRI only in 3/339 (0.88%) patients. However, all the false negatives at pcASL assessment (3.43%) had small-sized infarcts, mainly subcortical or infratentorial lesions, as assumed from previous results (34). In addition, among the false positives (3.43%), only three patients performed a late CT control.

As previously discussed, TAR volumes may have important clinical consequences in the management of acute stroke, and therefore the identification of the true penumbra volume in our main aim in the analysis about FAST MRI HSIP. Hence, in our study, CBF values differed in patients with AIS primarily due to the smaller or larger presence of collateral circulation maintaining the tissue functional, to the size of the NVT and an initial neurological deficit, affecting the final stroke outcome. Therefore, a decreased CBF is one of the first of many sequential events eventually resulting in brain damage, occurring after that the autoregulation mechanisms maintaining the tissue viable become exhausted over time. When the CBF drop reaches a certain threshold, the tissue becomes irreversibly injured, thus causing a poorer functional outcome. Consequently, patients with a smaller deficit, higher DWI-ASPECTS, milder initial NIHSS score, and higher CBF values have a good prognosis as a consequence of the development of collateral circulation. In these patients, the extent of parenchymal damage is insufficient for causing irreversible damage (52,83). We found 27 cases with TICI 0 between the patients undergoing EVT, with or without bridging; four of these patients had a favourable clinical outcome despite the failure of recanalization and late conclusion of the procedure, so that the infarct area on follow-up CT was smaller than the TAR identified on pcASL in three of these patient (DWI-ASPECTS ≥7), while the other one had FIA equal to the TAR (DWI-ASPECTS=5, but complete reperfusion assessed with Careggi Collateral Score(84)); between this four cases, the only patient undergone bridging tratment had the ischemic area smaller than NVT identified on DWI (DW-ASPECTS=8) (75,85). On the other hand, the large blood vessel occlusion and the absence of collateral circulation development result in the progression towards irreversible tissue damage. Therefore, we had 96 patient achieving a satisfying endovascular result (TICI 2b-3), without a FCR, but only 27 patient had a negative Delta-NIHSS. In all of the 96 patients, the FIA never exceeded TAR detected on pcASL, as expected.

The absence of perfusion defects on pcASL in untreated patient, and the larger proportion of hypoperfusion with salvageable penumbra in patient undergone endovascular treatment were widely expected, as well as the higher proportion of TAR>FIA in the latter population. On the other hand, we found a significantly higher correspondence between NVT on DWI and FIA in patient treated with IVT rt-PA alone when compared to group treated with EVT alone, with a significanlty higher proportion of EVT alone patient in which the FIA exceed the NVT detected on DWI. This finding could not be related to the higher onset-to-imaging time in EVT group, while it more likely relied on the significantly higher imaging-to-reperfusion time in the EVT group.

As mentioned before, pcASL has been suggested as a very promising technique, although its physiological meaning and sensitivity to experimental conditions are not well-understood (75). Perfusion value are dependent on age, sex, hematocrit, and exogenous factors such as nicotine or sedation, therefore considerable physiological variability exists in CBF (86). On the other hand, the influence of the cardiac cycle on pCASL-signal stability is small and should not have practical implications to improve stability (87). There is currently no consensus on the level of restriction of these exogenous perfusion modifiers before performing ASL, but should be taken into account when the results are unclear (40). In regards to laboratory testing, there was a higher proportion of patient with reduced RBC, Hct, and Hb in patients undergone EVT alone, and this could be a selection bias affecting the absolute CBF assessed with pcASL. However the rCBF should not be affected by the reduced hematocrit values (86). In fact, pcASL resulted in better matching of CBF estimates in anemic subjects, compared to phase contrast PWI-MRI (88). Blood glucose was higher in untreated patients with a significant difference when compared to patient undergone bridging; this might be a selection bias for the decision to treat patient with rt-PA IVT (68). The finding of higher arterial blood pressure in untreated patients, in comparison with EVT group, could represent a selection bias likewise (70). LDL-cholesterol was significantly higher in patient treated with IVT alone compared to EVT group, and this

could be due to the differences in TOAST classification, but we did not achieve statically significance in this matter. On the other hand, the stroke cause was classified as undetermined for the presence of multiple causes in untreated patients, with a significant difference in comparison with EVT group. According with this finding, mRS at admission was significantly higher in untreated patient. It is not surprising that the presence of multiple risk factors for stroke and previous vascular accident reducing functional indipendence excluded these patients from acute treatments. Smoking habit was higher in untreated patients and lower in EVT alone group, and this could be related to the higher proportion of patients with small vessel disease in the former group. In addition, the IVT only patients had lower proportion of carotid stenosis >50% when compared to EVT group, probably because of relative lower proportion of atherosclerosis and higher rate of small vessel disease as stroke etiology. Atrial fibrillation was known at the baseline in the groups in which IVT rt-PA was not administered, probably because of the anticoagulant treatment (68). This could also explain the lower proportion of anticoagulant in the bridging group patient compared to EVT group.

With regard to the proximal occlusion, evaluation of patients with tandem occlusions requires special caution in interpreting the findings, to avoid underestimation of the perfusion values. In fact, Hendrikse et al showed that the labeled blood flow transit time increase to the brain tissue may be expanded by the collateral blood flow in severe obstructive ICA patients, and a delay in collateral flow leads to decreased ASL signal intensity, resulting in erroneous indication of reduced CBF while transit time effects are the primary cause of the signal decrease(52,89). In our population, however, the fraction of proximal and tandem occlusions population was rather low (18.62%) and only in two cases the FIA was larger than TAR detected with FIA.

In the sample of patients with anterior circulation AIS and perfusion deficit detected at the initial pcASL, we did not find statistical differences concerning the age in patients with unfavourable clinical-instrumental outcomes, differently from the data of the analysis in CTP sample. This could be related to the reduced difference in treatment group, considering that the mean in untreated patient (74.47) was only slightly superior to the mean in the treated patients. In fact, we performed reperfusion treatments despite the age (maximum values for each group were respectively: 96 years in untreated, 90 in IVT alone, 95 in EVT alone, and 99 in bridging treatment), accordingly with recent observations (90–92).

To evaluate the prognostic accuracy of the FAST MRI HSIP in predicting FIA, we assumed that the best correlation between ischemic core and FIA should be found in early and fully recanalized patients with TICI 2b-3 and/or in patients with FCR: within this sub-group, NVT correlates to FIA in the vast majority of patients (66.9%), according with literature (93–95). However, we also found a relatively high percentage of patient with FIA larger than NVT (22.3%). This data could be related to previous studies, revealing that an infarct growth has been found in 35% of AIS patients after full recanalization (54,96). The lower rate of infarct growth in this subgroup could be due both to the exclusion of futile recanalization (97) and the selection of patient using MRI (98). Finally the rate of patient with NVT larger than FIA and the percentage of patients in which a infarction area was not confirmed was 14.9% overall, confirming that increased signal intensity on DWI can be partially reversible, particularly in the early time window(28). Considering data for patients undergoing EVT, with or without bridging, with very early recanalization, NVT identified with DWI almost entirely correspond to the lesion found at the follow-up control, although the intervention times were not within the "golden hour" (58). Even in patients with early recanalization, NVT correlates with FIA in most cases, comfirming the high predictive value of DWI (Supplementary figure – Figure VII).

On the other hand, the hypoperfusion volume should better correlate with FIA in not treated patients and in EVT failure (TICI 0): even concerning this evaluation, we found a complete matching of TAR with FIA using pcASL in most cases (56%), but we found an overestimation of TAR in 40.5% overall. FIA exceeded the size of TAR in 3.6% of this group, considering that in 10% of AIS patients oligoemic areas could evolve into infarct (55). From this analysis, we can deduce that the portion of tissue considered at risk with the rCBF calculated on pcASL could actually include a substantial portion of benign oligoemia. There were few cases with

underestimation of TAR, so we can affirm a lower tendency to incorporate the benign oligoemia, compared to the corresponding analysis with the use of Tmax 9.5s on CTP.

7. Limitations

The study is based on two single center experience, which makes difficult to avoid possible biases. While CTP was exclusively performed in the mCT based HSIP of one CSC (Bologna), DW/ASL MR was included in the FAST MRI HSIP used only in the other CSC (Messina), and therefore the two techniques were not performed in both centers. The retrospective design of the investigation is a clear limitation, too. In this context, one major limitation of this study is that the exact time of recanalization could not be determined for patients undergoing IVT rT-PA alone. Assessment of recanalization after reperfusive treatments is not routinely performed with CT/MR angiography. This limitation could not be avoided given the retrospective study design. As referred in "Methods" section, we considered FCR as criterion more important than TICI score for selection of group A, when successfully recanalization was not detectable/achieved. Hence, we included in the group A also FCR patients undergoing bridging therapy, who did not achieve TICI 2b-3 at the end of EVT, in order to include eventual delayed beneficial effect of IVT rT-PA. On the other hand, we did not include patient with unconsistent interventional-clinical outcome in the post-hoc tests for multiple comparison, in order to avoid potential interpretation bias due to the conflicting imaging results. Furthermore, if complete recanalization took place at an early time, especially with regard to bridging procedures, final lesion size may be smaller than predicted by NVT on CTP/MRI images in group with favourable outcome. This is one possible explanation for NVT lesions being slightly larger than FIA in many cases. This study had several other limitations. First, we assessed CTP/MRI ACC for the detection of AIS, and considered both CT and MRI data. The detection of ischemic lesion at follow-up radiological assessment was detected on MRI alone in 7.59% (Table II) and 0.88% of patients, respectively. However, MRI was not systematically performed during hospitalization in the CSC, and the potential presence of smaller lesions, not detected in CT and for which in-depth diagnostic search with MRI was skipped, could not be excluded. To reduce a possible bias that may be caused by using two different imaging modalities as a reference standard in this study, future studies should use only one reference standard. Second, to identify the infarct core and penumbra, the part of the study about CTP relies on Tmax mismatch. However, the remaining above-mentioned two (MTT-CBV mismatch and Tmax-CBF mismatch) will be the subject of a different work and further analysis. Otherwise, we will not be able to assess the analysis on different mismatch concerning the FAST MRI HSIP, because CBF is the only parameter that could be evaluated on pcASL. Concerning the latter assessment, we have already mentioned that a complete FAST MRI HSIP was not performed for every patient admitted for suspected AIS, and therefore the selection bias could not be avoided resulting in low specifity and NPV. For this reason, we could not compare the ACC between the two different HSIP.

Another limitation of this study is the relatively small sample size. Nevertheless, formal sample size analysis demonstrated that the sample size of this study is sufficient for stratified analysis, with a hypothesized correlation greater than 0.66, alpha set at 0.05 and beta set at 0.20. However, further studies with larger sample sizes are desirable.

Additionally, we proposed a qualitative assessment of the main sectional area of the ischemic lesion based on neuroimaging data evaluation with pre-structured charts. Due to technical software limits, quantitative volumetric analysis could not be performed for all the patients, resulting in a decreased sample size that could not reach a statistically significant difference with regard to discrepancy between FIA, NVT, and TAR. Furthermore, we could not assess a volumetric analysis for the MRI analysis, because of the differene in scanning volume between the MR-pcASL at admission and the CT control scan, as performed in the most patients.

Finally, a scanning volume of 8cm for CTP may be considered a limitation. In future studies, limited coverage could be addressed by using state-of-the-art CT systems that allow whole-brain perfusion. In regard to the MRI analysis, the use of 1.5T only could be a limitation too, comparing to similar analysis performed with 3T MR.

8. Conclusions

In conclusion, our study (46) showed that CTP-Tmax maps for the detection of AIS achieved a sufficiently reliable ACC, but this was not optimal. In patients with perfusion deficit in anterior circulation territory, CTP-Tmax > 16s proved relatively reliable to identify the ischemic core area, with a tendency, however, to overestimate NVT compared to FIA, in patients with favorable clinical-instrumental outcomes and, in particular, in patients undergoing early recanalization.

Similarly, CTP-Tmax > 9.5s proved reliable to identify the area of total hypoperfusion, but the degree of correlation with FIA was in favor of an overestimation of TAR in the vast majority of patients untreated or with reperfusion treatment failure.

In our experience, the Tmax threshold considered to detect TAR did not give satisfactory results in differentiating true penumbra and benign oligoemia, as full correspondence between the hypoperfuse area and FIA was found only in a very limited number of cases. There were no case with underestimation of TAR, so we can affirm a tendency to incorporate the benign oligoemia with the use of the threshold of 9.5 seconds in Tmax maps. In particular, the overestimation of NVT could have serious consequences in not selecting potential candidates for a reperfusion treatment. For this reason, according to our results, particular attention is needed in the use of the Tmax-Tmax mismatch.

On the other hand, our study showed that DWI-pcASL for the detection of AIS achieved a highly reliable ACC, considering the above-mentioned limitations. In patients with perfusion deficit in anterior circulation territory, DWI confirmed the high reliability to identify the NVT predicting FIA, in patients with favorable clinical-instrumental outcomes and, in particular, in patients undergoing early recanalization.

Similarly, rCBF on pcASL proved reliable to identify the area of total hypoperfusion, with a higher proportion of cases showing a complete overlapping with the FIA, in the vast majority of patients untreated or with reperfusion treatment failure. However, the degree of correlation with FIA was in favor of an overestimation of TAR in many cases. Therefore, the differentiation between true penumbra and benign oligoemia was not completely satisfactory, with a tendency to incorporate the benign oligoemia, although it was lower in comparison to the rate we found using Tmax maps.

Hence, the overestimation of TAR in many cases could still be a problem with the use of FAST MRI HSIP, but data concerning clinical outcome should reassure in the preference of including patients rather than excluding them from reperfusive treatment. Further analyses concerning outcome measures as well as intracranial or systemic bleeding and other complications are ongoing. In addition, we aim to increase the sample size, in order to clarify laboratory data that could affect absolute CBF results, especially with regards to hematocrit count and inflammatory index.

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10. Figures

Figure 1.

Prognostic accuracy of CTP for the detection of AIS. Perfusion deficit parameters. Sensitivity, specificity, positive predictive value, negative predictive value (NPV), and diagnostic accuracy (ACC) for CTP in detecting AIS. PPV, specificity and ACC decreased, but sensitivity slightly increased, if global deficit on CTP was considered, with or without inclusion of non-viable tissue (NVT).

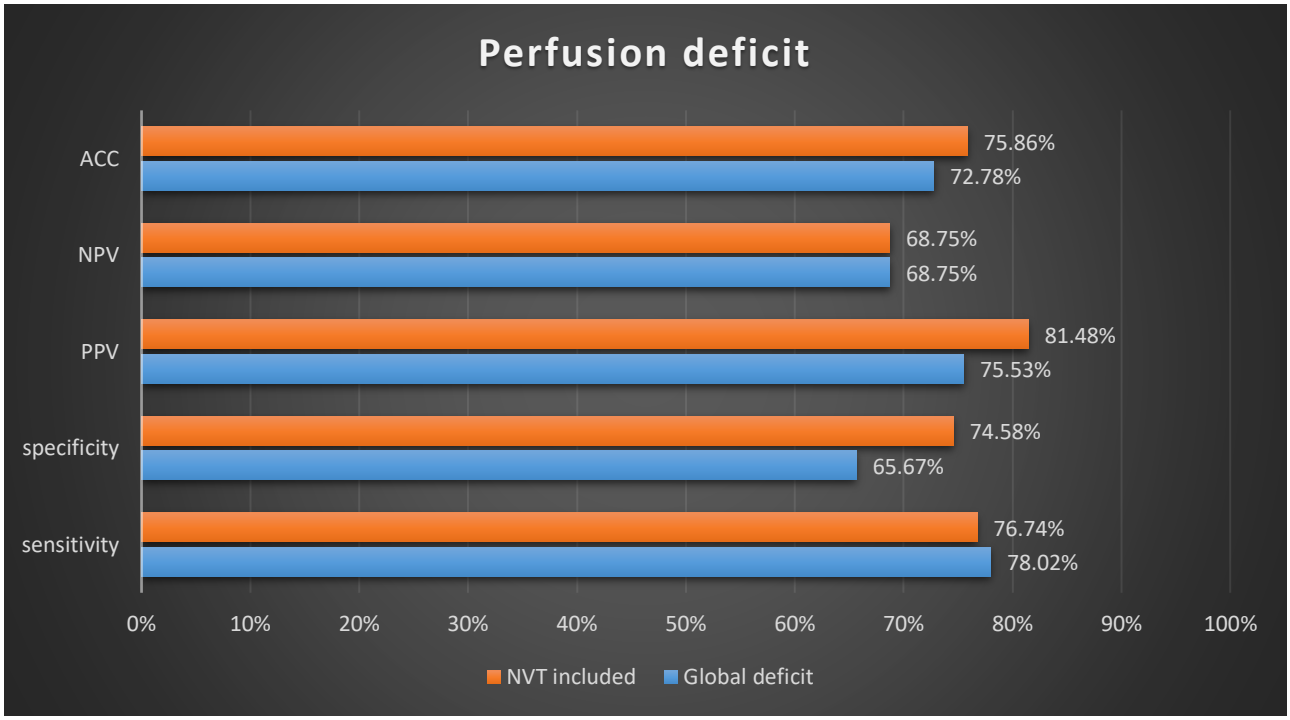
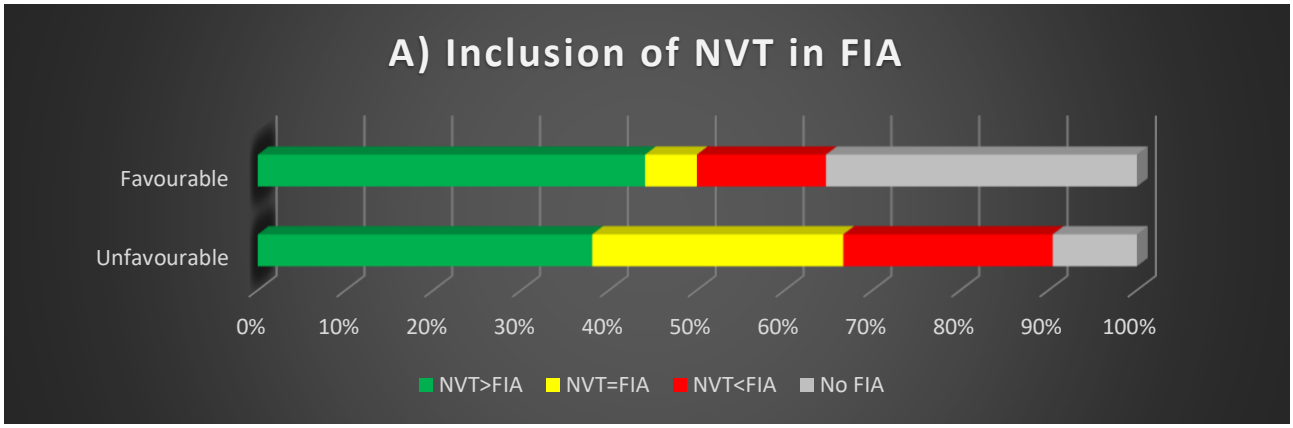


Figure 2.

Reliability of CTP to identify total hypoperfusion area and ischemic core/penumbra ratio using Tmax/Tmax mismatch. Correlation between CTP and final infarct area (FIA) detected on follow-up non-enhanced computed tomography (NECT). A) Degree of Inclusion of NVT in FIA. B) Degree of inclusion of TAR in FIA.



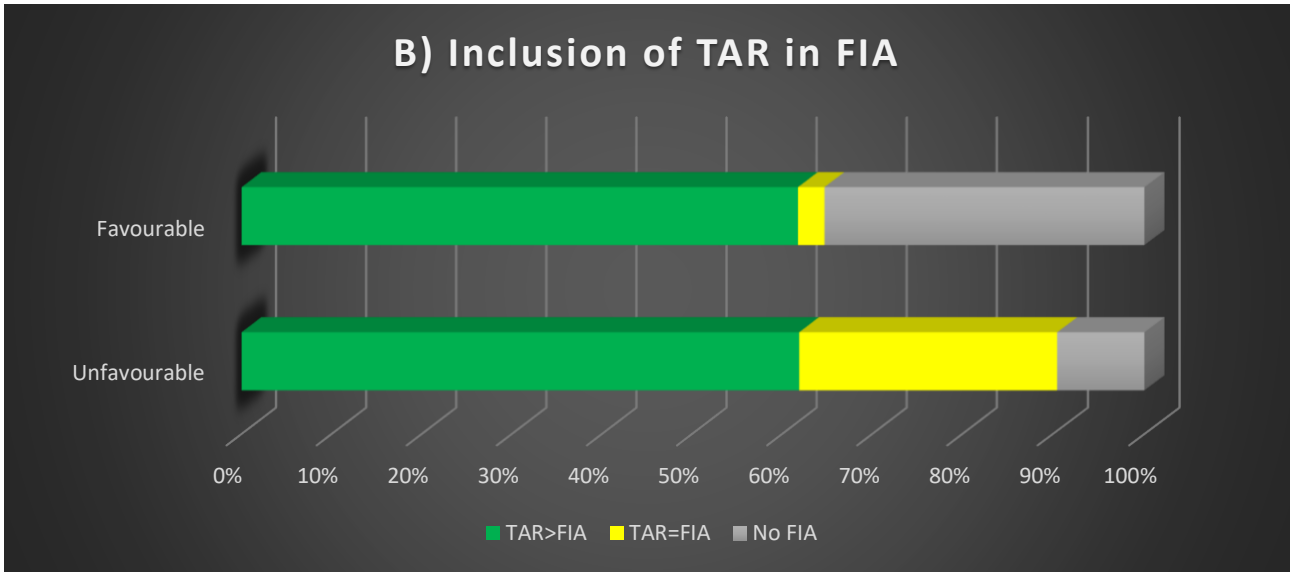


Figure 3.

Perfusion maps and follow-up CT of two patients. On the superior raw, perfusion maps with a threshold of Tmax>16s shows an automatically outlined area of critically hypoperfused tissue in the left insula (A), whose areas is substantially overlapping with the infarct lesions on follow up NECT (B). On the inferior raw, perfusion maps with a threshold of Tmax>9,5s shows an automatically outlined area of globally hypoperfused tissue in right parietal lobe (C), whose areas is substantially overlapping with the infarct lesions on follow up NECT (D).

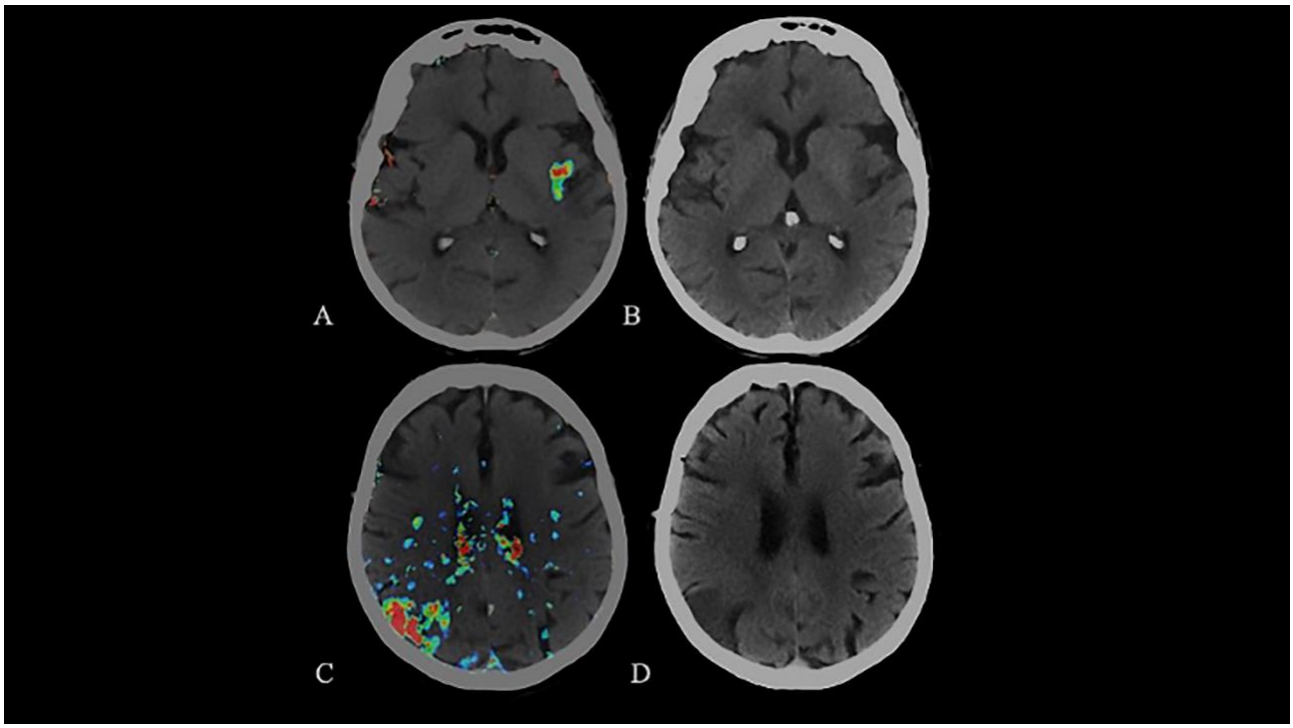


Figure 4.

Perfusion maps and follow-up CT of one patient. Perfusion maps with a threshold of Tmax>16s and of Tmax>9.5s show the automatically outlined areas of critically hypoperfused tissue and of globally hypoperfused tissue in right fronto-temporal region (A and B, respectively). The follow up CT shows a final infarct area, which appears wider than the hypoperfused area on Tmax>16s map and overlapping with the

hypoperfused area seen on Tmax>9.5s map (C). Volumetric assessment is depicted in panel D, with numeric value included in the light blue box.

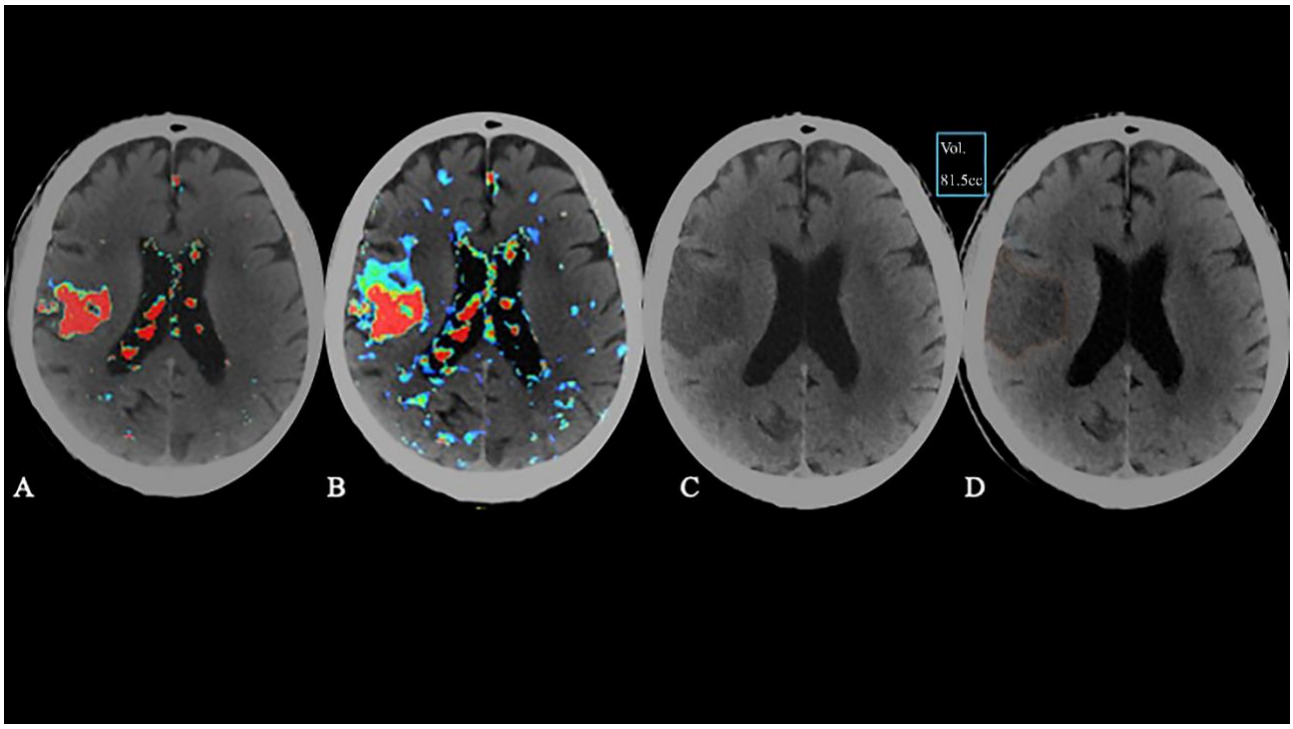


Figure 5.

Perfusion maps and follow-up CT of one patient. Perfusion maps with a threshold of Tmax>16s and of Tmax>9.5s show the automatically outlined areas of critically hypoperfused tissue and of globally hypoperfused tissue in left temporal and insular region (A and B, respectively). The follow up CT shows a final infarct area, which appears greater than the hypoperfused area on Tmax>16s map but smaller than the hypoperfused area seen on Tmax>9.5s map (C). Volumetric assessment is depicted in panel D, with numeric value included in the light blue box.

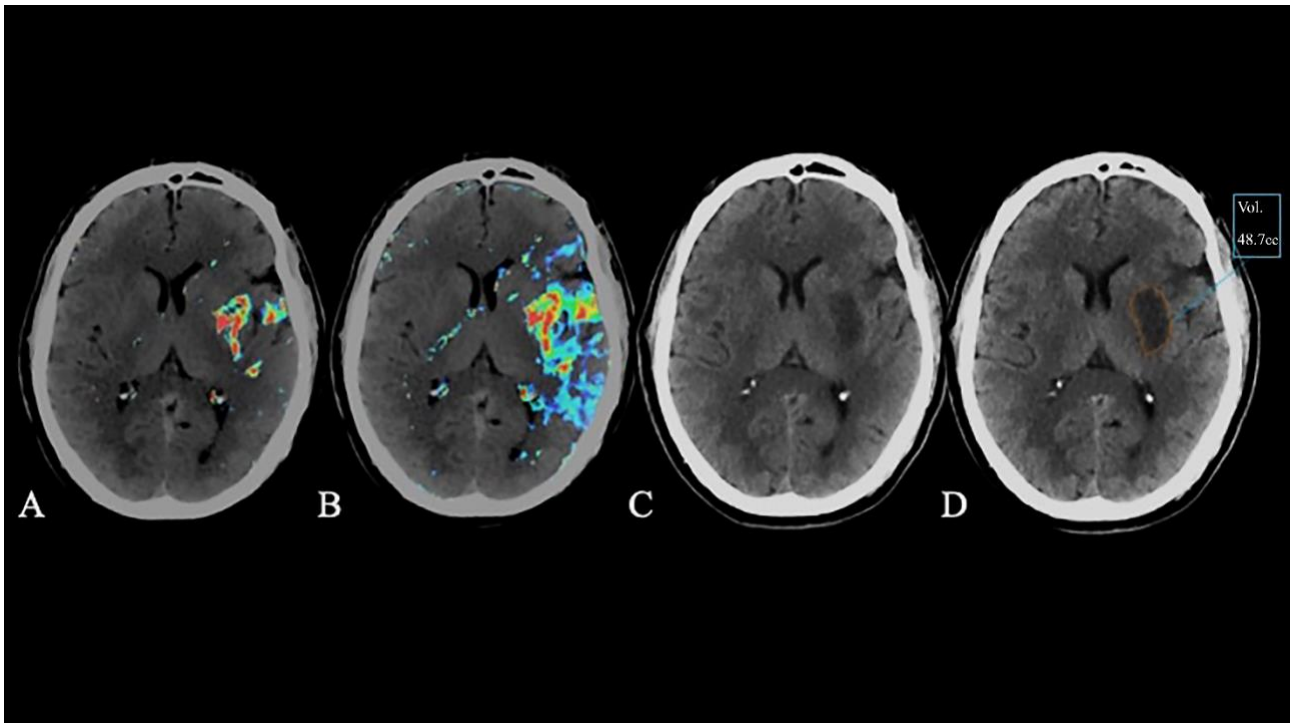


Figure 6.

Prognostic accuracy of DWI-pcASL protocol for the detection of AIS. Perfusion deficit parameters. Sensitivity, specificity, positive predictive value, negative predictive value (NPV), and diagnostic accuracy (ACC) for DWI-pcASL protocol in detecting AIS. Considering the hypoperfusion on pcASL only, in patient with TAR, there was a decreasing in sensitivity, PPV, and ACC. On the other hand, sensitivity, PPV, and ACC slightly increased if patient without NVT-TAR mismatch were included.

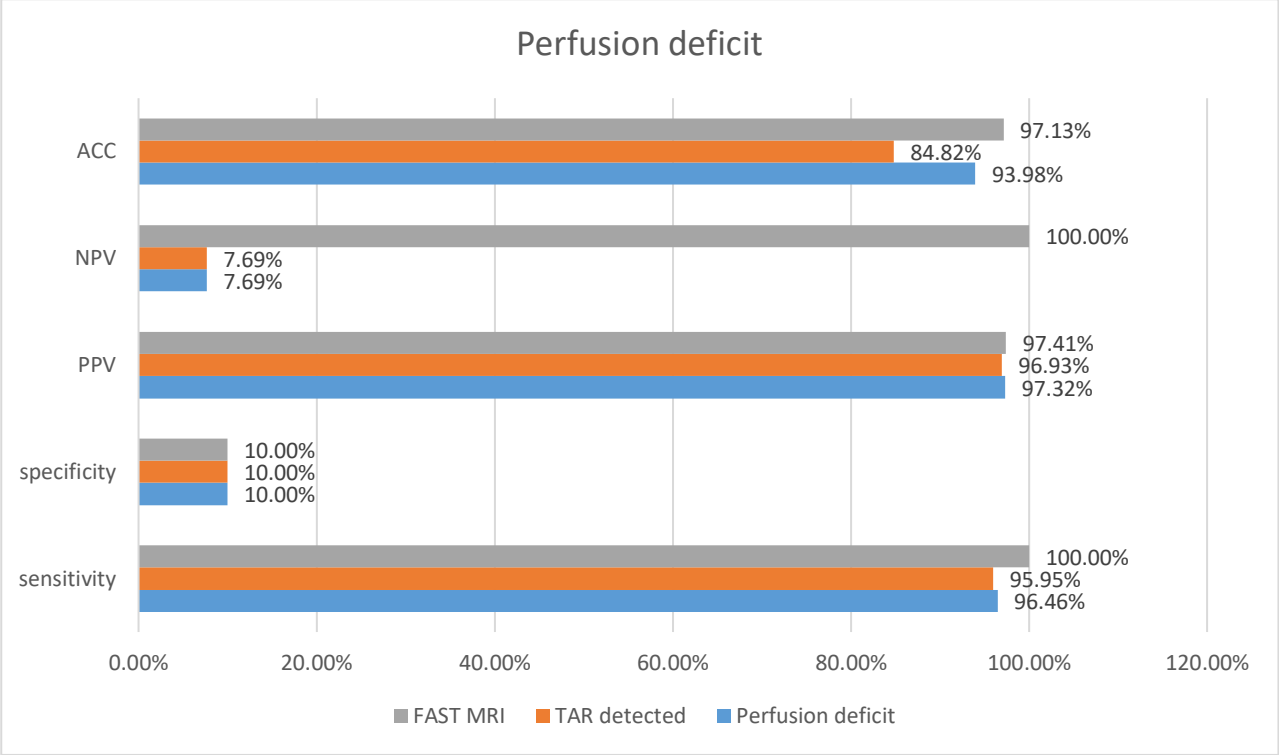
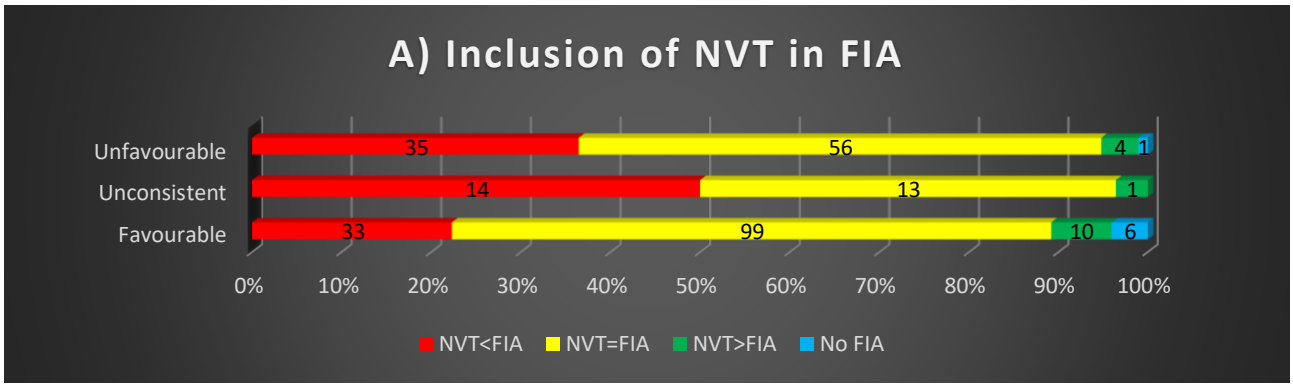


Figure 7.

Reliability of FAST MRI HSIP to identify total hypoperfusion area and ischemic core/penumbra ratio using DWI/pcASL mismatch. Correlation between DWI-pcASL and final infarct area (FIA) detected on follow-up non-enhanced computed tomography (NECT). A) Degree of Inclusion of NVT in FIA. B) Degree of inclusion of TAR in FIA.



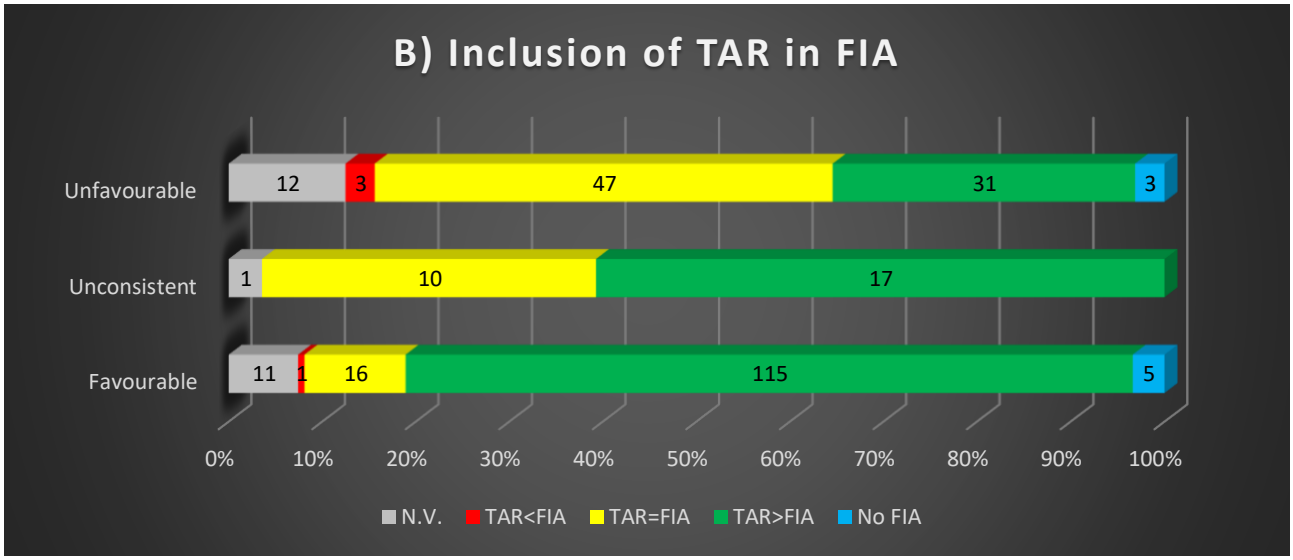


Figure 8.

Admission MRI and follow-up CT of one patient. Perfusion rCBF map with pcASL shows an area of critically hypoperfused tissue in the left pre-rolandic area (A), whose areas is substantially overlapping with the ischemic core identified on DWI (B). Both tissue at risk and non-viable tissue are substantially overlapping with the infarct lesion on follow up NECT (C).

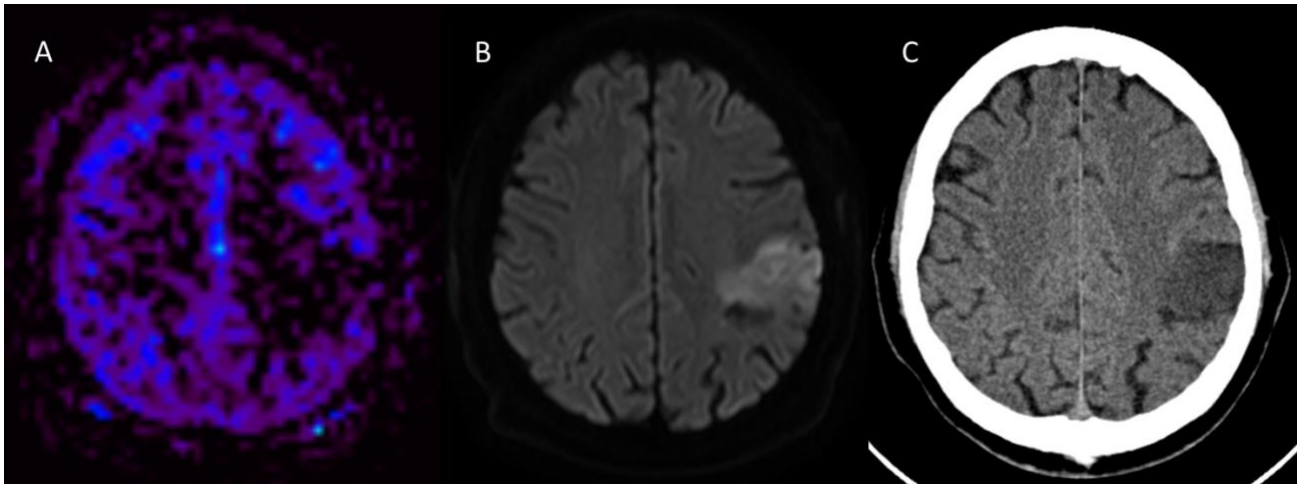


Figure 9.

Admission MRI and follow-up CT of one patient. PcASL shows the areas of globally hypoperfused tissue with leptomeningeal collaterals in the right fronto-parietal region (A), while the ischemic core on DWI involve only the right frontal operculum (B). The follow up CT shows a final infarct area, which appears less wide than the hypoperfused area on rCBF map and overlapping with the non-viable tissue seen on DWI (C).

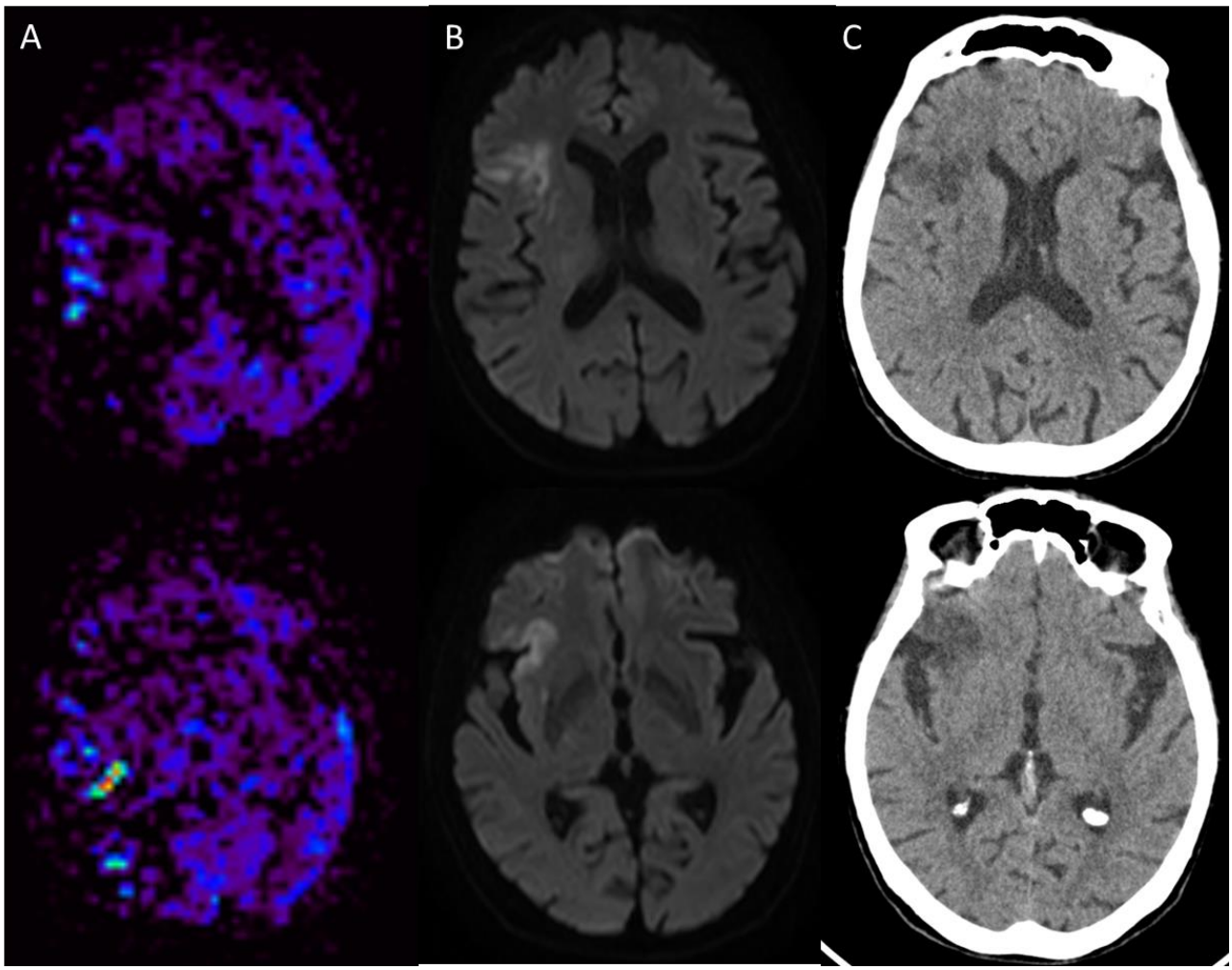
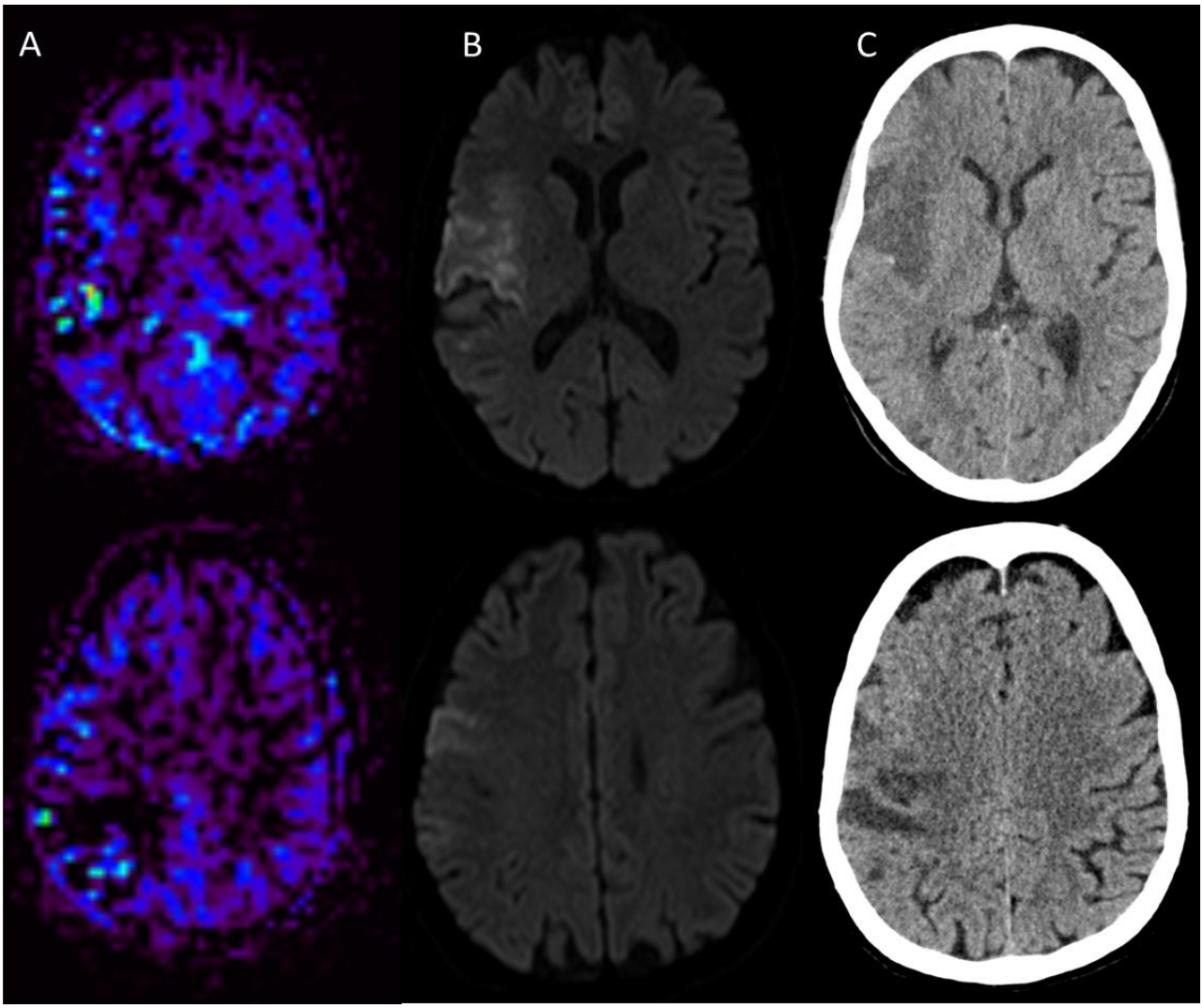


Figure 10.

Admission MRI and follow-up CT of one patient. PcASL shows the areas of globally hypoperfused tissue with leptomeningeal collaterals in the right frontal and perirolandic region (A), while the ischemic core on DWI involve only the right inferior and middle frontal gyri (B). The follow up CT shows a final infarct area, which appears wider than the non-viable tissue seen on DWI and overlapping with the hypoperfused area on rCBF map (C).



11. Supplementary Figures

Figure I.

Study flowchart of analysis 1 (sensitivity and specificity of CTP for the detection of AIS). Abbreviations: AIS: acute ischemic stroke; CTP: computed tomography perfusion; CSC: comprehensive stroke center; mCT: multimodal computed tomography; ASPECTS: Alberta Stroke Program Early CT Score; CT/MRI: computed tomography/magnetic resonance imaging; IVT rT-PA: intravenous thrombolysis with recombinant tissue plasminogen activator; EVT: endovascular treatment.

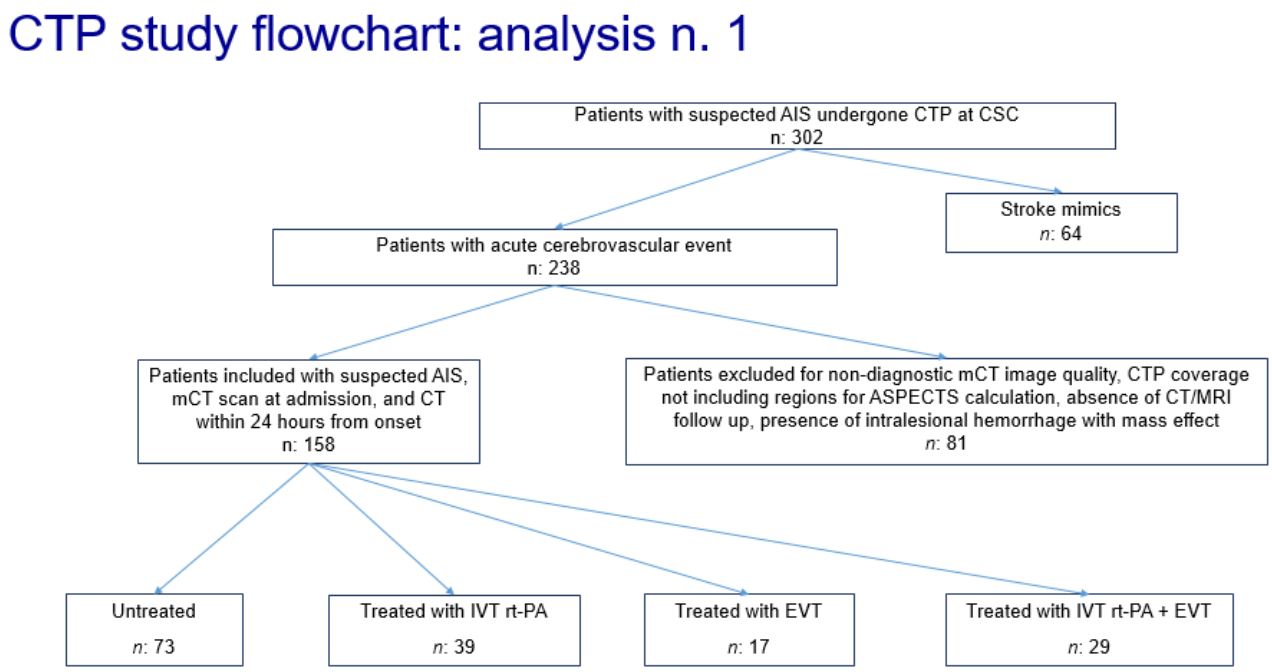


Figure II.

Study flowchart of analysis 2 (reliability of CTP to identify total hypoperfusion area and ischemic core/penumbra ratio using Tmax/Tmax mismatch). Abbreviations: CTP: computed tomography perfusion; TICI: modified Thrombolysis in Cerebral Ischemia; FCR: favorable clinical response; EVT: endovascular treatment.

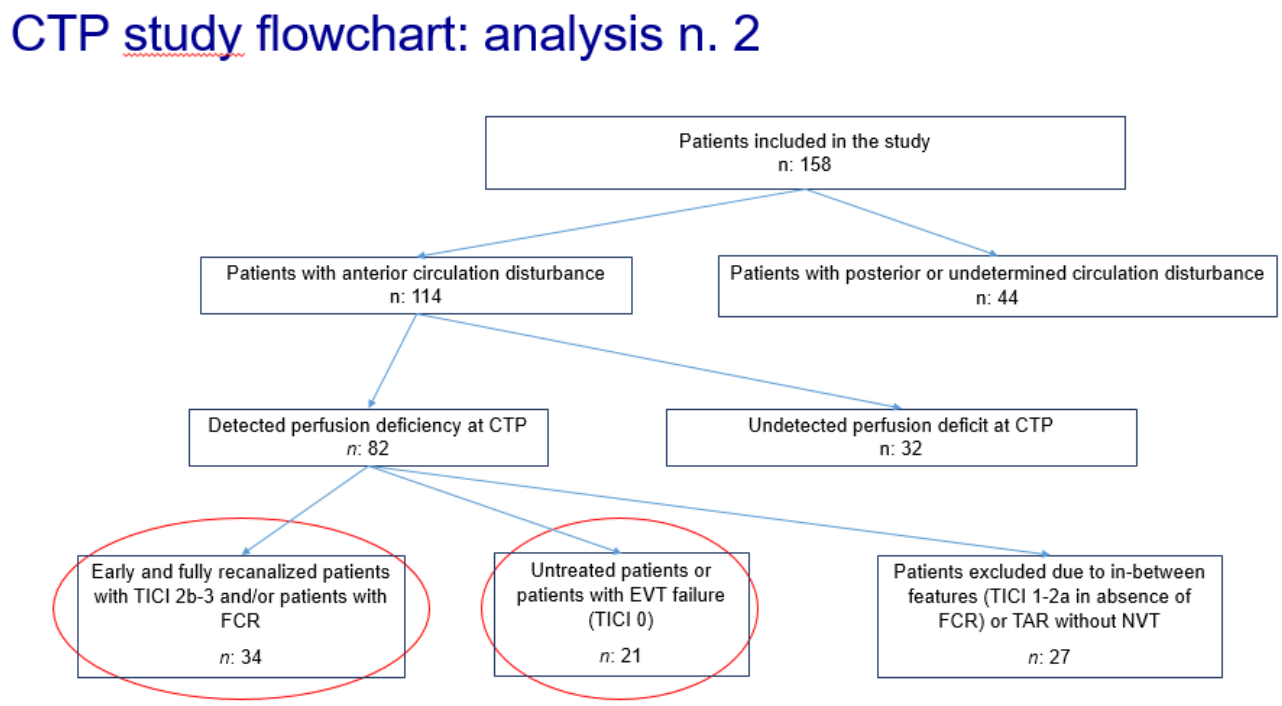


Figure III.

Illustrative examples of non-viable tissue overestimating final infarct in patients with early recanalization. Perfusion maps and follow-up CT of two patients. On the superior row, perfusion maps with a threshold of Tmax>16s show the automatically outlined areas of critically hypoperfused tissue in left temporal and insular lobe (case 1, A) and in left fronto-temporal region (case 2, B). On inferior row, the corresponding follow up CT show a final infarct area, which appears smaller than the hypoperfused area on CTP, involving just the insular cortex in the first case and the fronto-insular lobe in the latter (C and D, respectively).

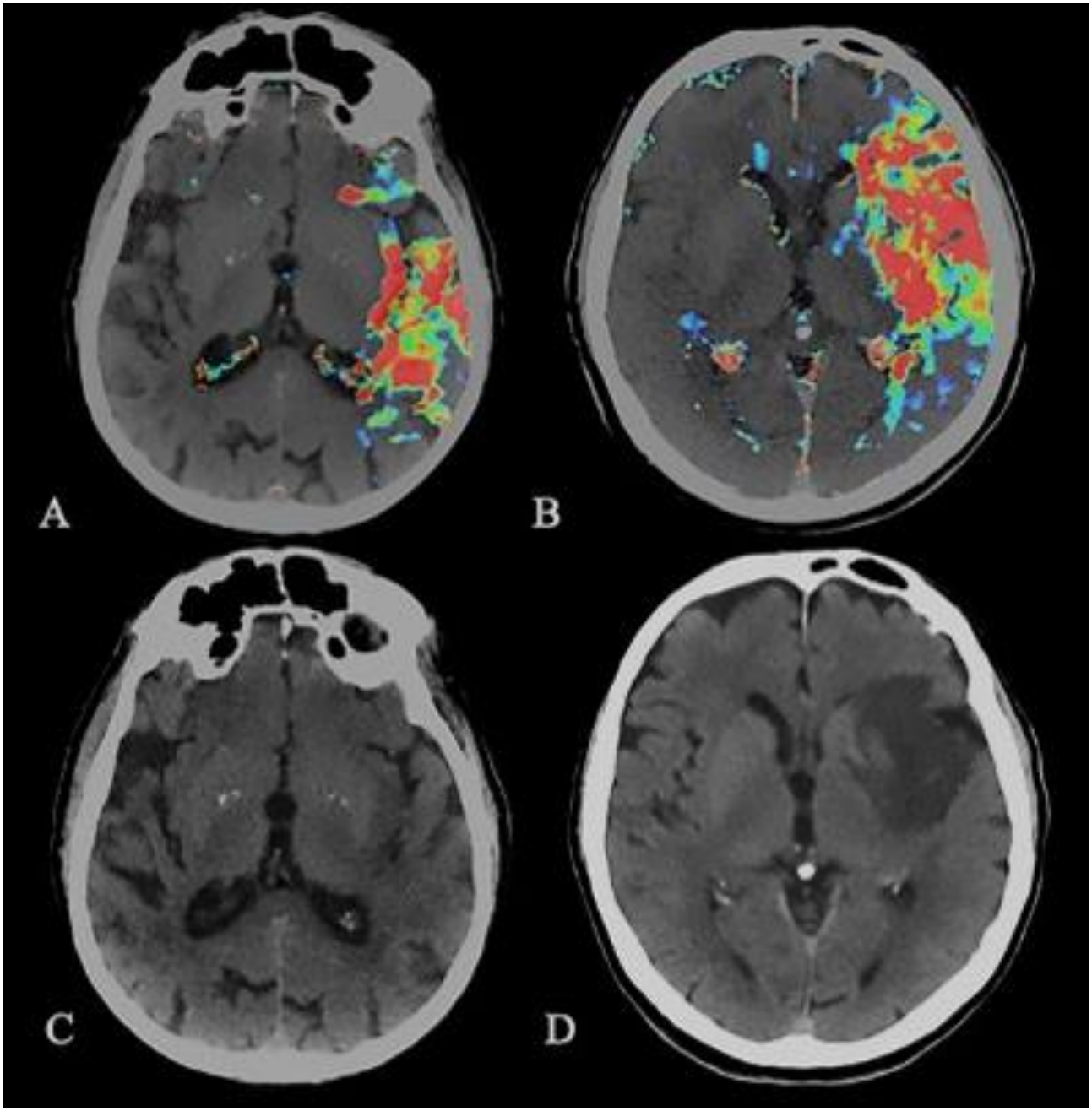


Figure IV.

Reliability of CTP to identify total hypoperfusion area and ischemic core/penumbra ratio using Tmax/Tmax mismatch. Correlation coefficients and linear regression analysis of volume discrepancy between FIA, NVT, and TAR. Linear regression line is shown with the accompanying R2 value, showing significant correlation

between the follow-up CT volume and perfusion deficit at CTP, considering Tmax 16s in favorable outcome group (A) and Tmax 9.5s in unfavorable outcome group (B).

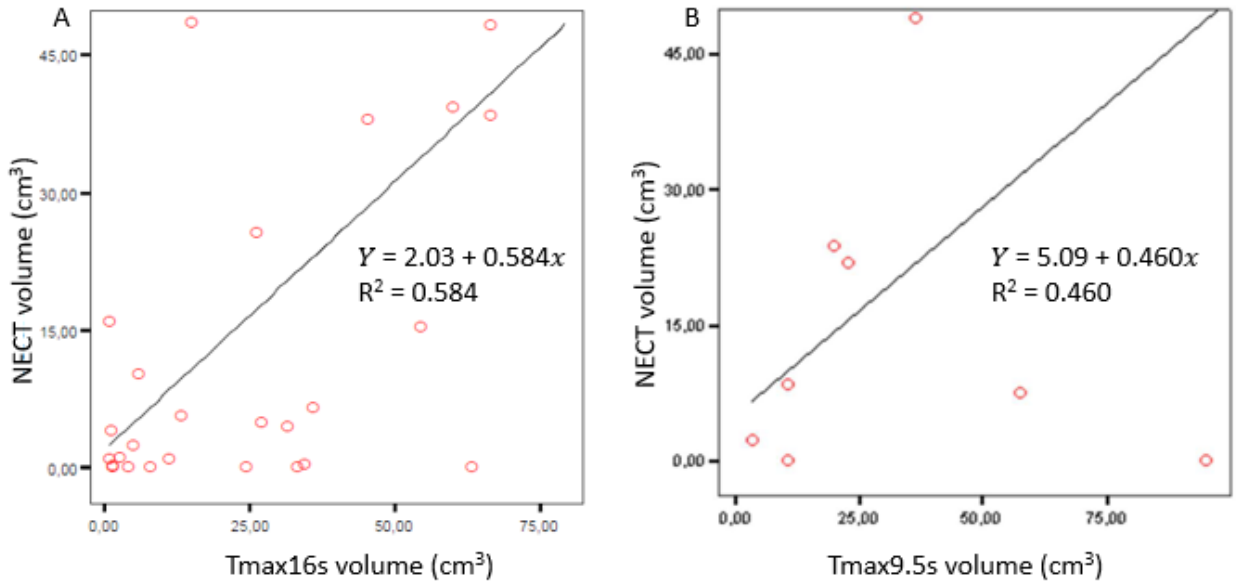


Figure V.

Study flowchart of analysis 1 (sensitivity and specificity of FAST MRI for the detection of AIS). Abbreviations: AIS: acute ischemic stroke; CTP: computed tomography perfusion; CSC: comprehensive stroke center; mCT: multimodal computed tomography; ASPECTS: Alberta Stroke Program Early CT Score; CT/MRI: computed tomography/magnetic resonance imaging; IVT rT-PA: intravenous thrombolysis with recombinant tissue plasminogen activator; EVT: endovascular treatment.

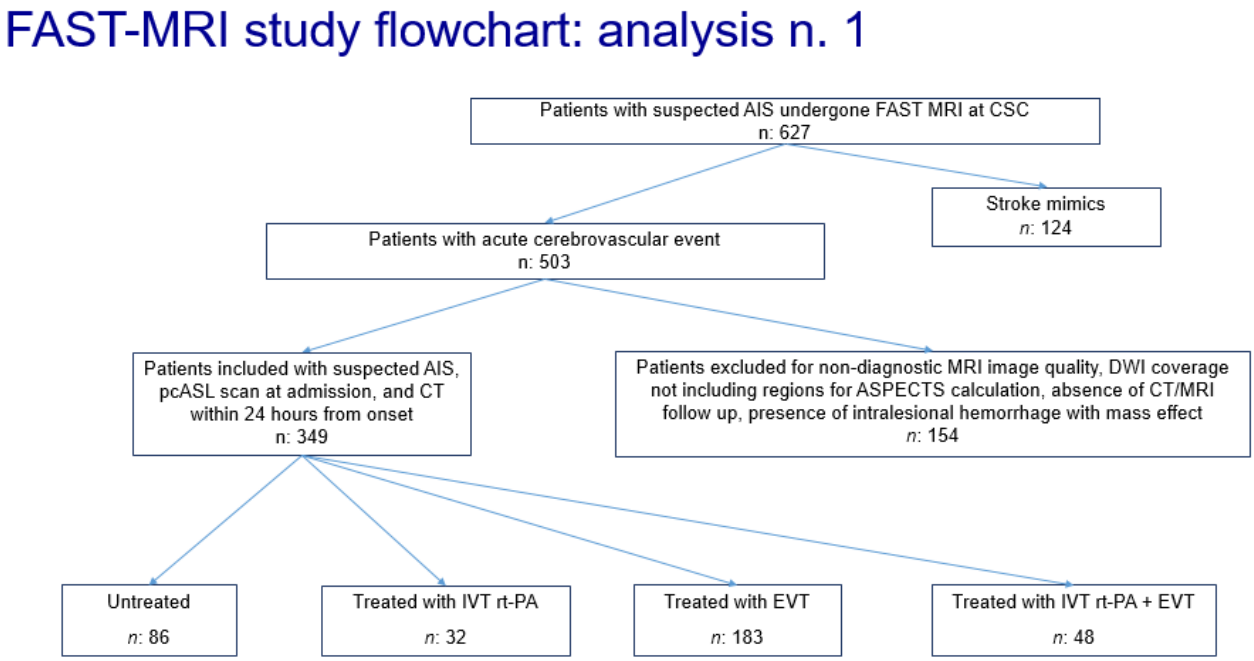


Figure VI.

Study flowchart of analysis 2 (reliability of FAST MRI to identify total hypoperfusion area and ischemic core/penumbra ratio using Tmax/Tmax mismatch). Abbreviations: CTP: computed tomography perfusion; TICI: modified Thrombolysis in Cerebral Ischemia; FCR: favorable clinical response; EVT: endovascular treatment.

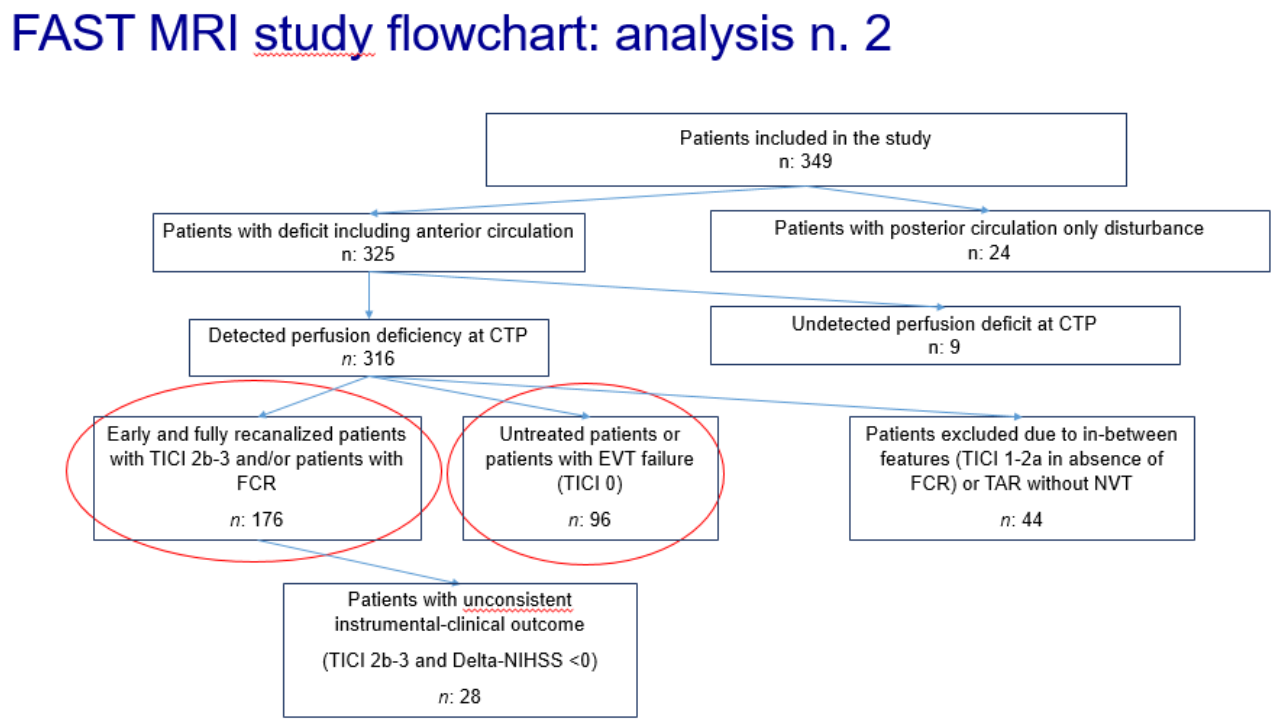
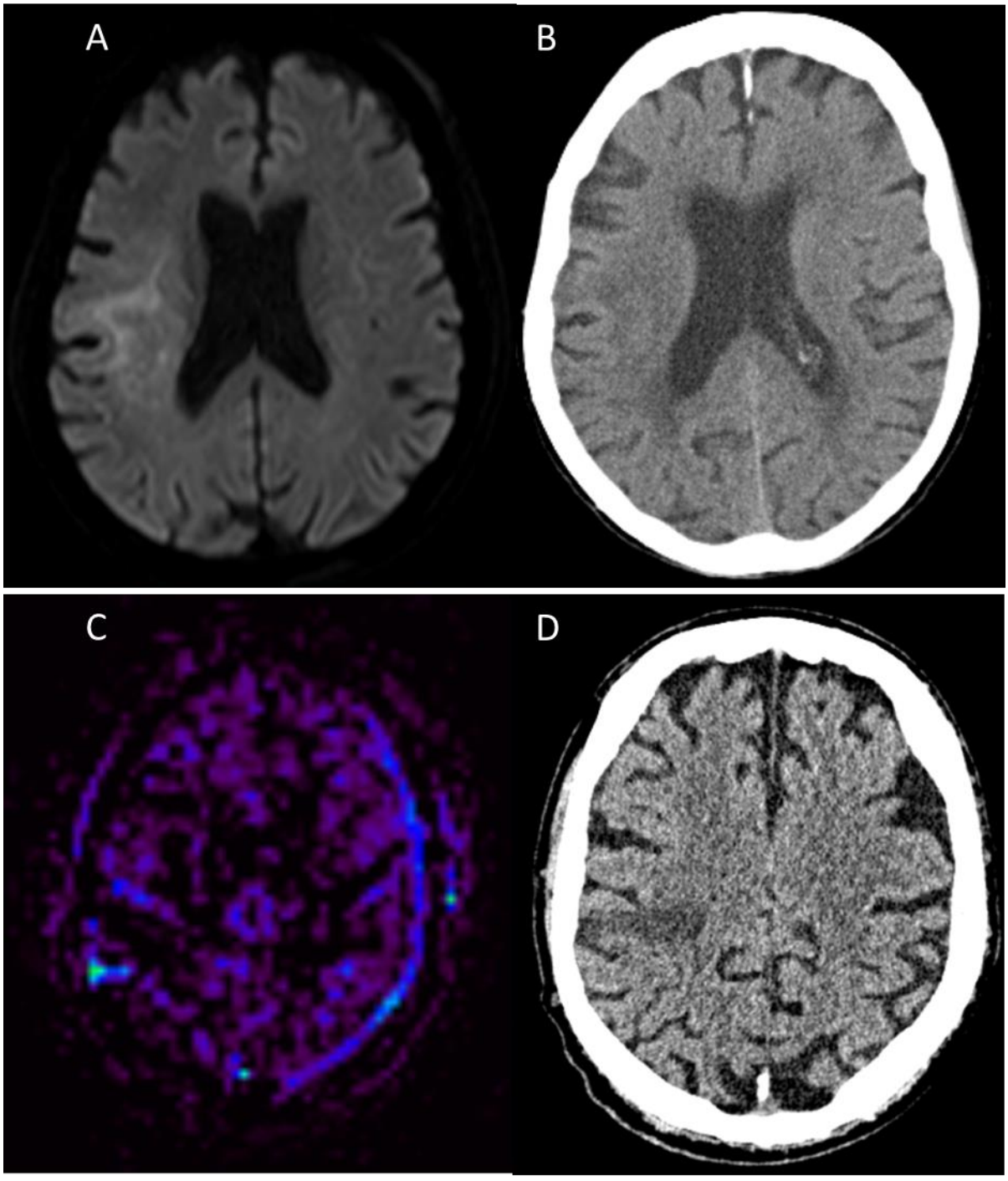


Figure VII.

Illustrative examples of non-viable tissue in patients with early recanalization and tissue at risk in a patient with failure of treatment, respectively overestimating the final infarct. Admission MRI and follow-up CT of two patients. On the superior row, DWI shows the non-viable tissue in right semioval centre and M5 territory (A), while the corresponding follow up CT shows only a slightly hypodense area in the middle frontal gyrus (B). On inferior row, the pcASL shows a reduced rCBF in pre-central, superior parietal lobule and precuneous region (C); the corresponding follow up CT shows a final infarct area, which appears smaller than the hypoperfused area on CTP, involving just the pre-cental gyrus (C and D, respectively).



12. Tables

Table Ia.

Sensitivity and specificity of CTP for the detection of AIS. Four groups of treatment: untreated (U); treated with intravenous thrombolysis with recombinant tissue plasminogen activator (IVT); treated with endovascular therapy (EVT); treated with IVT and EVT combined (IVT+EVT). Quantitative data analysis (QN): age; National Institute of Health Stroke Scale (NIHSS) on admission (A), discharge (D), and the difference between the two evaluations (Δ); time in relation to computed tomography perfusion (CTP), considering time between onset of symptoms and CTP (O-to-CTP, minutes), time between CTP and the achievement of recanalization (CTP-to-R, minutes), time between CTP and early (within 48 hours) computed tomography control (CTP-to-eCT, hours), time between CTP and late CT control (CTP-to-lCT, days), and time between CTP and magnetic resonance imaging (MRI), if performed (CTP-to-MRI, days); mean (M), standard deviation (SD), median (Md), range (R), and interquartile range (IQR) are reported for every variables; post-hoc analysis for differences between groups was applied, in order to calculate the p value (p); *post-hoc a,b vs c,d. †post-hoc a vs b,c,d.

	TREATMENT															
	U			**IVT**			**EVT**			**IVT+EVT**			**Total**			
no.	73			39			17			29			158			
QN	Md	R	IQR	Md	R	IQR	Md	R	IQR	Md	R	IQR	Md	R	IQR	p
Age																
	75	47-98	21	78	32-99	19	72	46-90	20.5	78	41-92	18	76	32-99	19.25	0.803
NIHSS																
A	3	0-23	5	6	0-24	4.25	14	1-19	13	8	0-23	11	5	0-24	8	0.015*
D	0	0-30	1	1	0-22	4	4	0-20	10.5	2	0-23	9	1	0-30	4	0.712
Δ	2	-44	4	3	-18	4	7	-30	10.5	5	-32	8.5	2	-44	6	0.108
Time																
O-to-CTP	/	/	/	113	55-388	103	140	27-663	133.5	119	69-324	145	119	27-663	116	0.429
CTP-to-R	/	/	/	/	/	/	146	90-407	63.5	141	74-851	68.5	141	74-851	66	0.862
CTP-to-eCT	32	12-48	21	25	16-38	4	25	15-35	8.5	25.5	17-36	5	26	12-48	8	0.001†
CTP-to-lCT	5	2-72	5.75	7	3-150	11.5	6	2-17	4.5	7	2-70	6.25	6	2-150	6	0.069
CTP-to-MRI	4	1-26	5.25	3	1-20	4	/	/	/	/	/	/	3	1-26	4	0.606

Table Ib.

Sensitivity and specificity of CTP for the detection of AIS. Four groups of treatment: untreated (U); treated with intravenous thrombolysis with recombinant tissue plasminogen activator (IVT); treated with endovascular therapy (EVT); treated with IVT and EVT combined (IVT+EVT). Categorical data analysis (QL): gender (male: M; female: F); circulation territory infarction (CTI), divided in anterior (A), posterior (P), and undetermined (U, further divided into A and P, using the OCSP classification); presence of perfusion deficit (PD), divided into negative (N) and positive results (Y), furtherly divided in hypoperfusion with inclusion of non-viable tissue (NVT-i) and hypoperfusion with tissue at risk only (TAR-o)detection; detection of ischemic lesion at early radiologic assessment (ERAID; no: N; yes: Y; not available: NA); detection of ischemic lesion at late radiologic assessment (LRAID; no: N; yes: Y; not available: NA), with division in computer tomography (CT) and magnetic resonance imaging (MRI) detection; concerning patient treated with EVT, with or without IVT, Thrombolysis in Cerebral Ischemia (TICI) reperfusion grade was reported from 0 (failure) to 3 (complete recanalization); relative (R%) and total (T%) percentages were reported in presence of splitted data; chi-square (χ2) and p-value (p) were reported if they could be calculated.

			TREATMENT								
			U	**IVT**	**EVT**	**IVT+EVT**		**Total**			
		no.	73	39	17	29		158			
QL			no.	no.	no.	no.	no.	T%	R%	p	χ^2
Gender		M	40	21	9	11	81	51.27%		0.466	2.551
		F	33	18	8	18	77	48.73%			
CTI	A		35	34	16	29	114	72.15%		<0.001	49.669
	P		5	4	1	0	10	6.33%			
	U		33	1	0	0	34	21.52%			
		OCSP-A	28	1	0	0	29	18.35%	85.29%		
		OCSP-P	5	0	0	0	5	3.16%	14.71%		
PD	N		45	18	0	1	64	40.51%		<0.001	47.205
	Y	NVT-i	23	16	16	26	81	51.27%			
		TAR-o	5	5	1	2	13	8.22%			
ERAID	N		30	20	5	10	65	41.1%		<0.001	30.029
	Y		21	19	11	18	69	47.3%			
	NA		22	0	1	1	24	15.2%			
LRAID	N		20	9	4	5	38	24.1%		<0.026	14.378
	Y		21	19	12	14	66	41.8%			
		CT	13	12	11	14	50	31.65%	75.75%		
		MRI	8	7	1	0	16	10.13%	24.24%		
	NA		32	11	1	10	54	34.2%			
TICI		0	/	/	1	2	3	6.52%			
		1	/	/	2	1	3	6.52%			
		2a	/	/	3	9	12	26.08%			
		2b	/	/	7	7	14	30.43%			
		3	/	/	4	10	14	30.43%			

Table II.

Sensitivity and specificity of CTP for the detection of AIS. Four groups of treatment: untreated (U); treated with intravenous thrombolysis with recombinant tissue plasminogen activator (IVT); treated with endovascular therapy (EVT); treated with IVT and EVT combined (IVT+EVT). Ischemic area detection rate: number and percentage of infarcts identified by early computed tomography (CT) within 48 hours or at late control only. For the latter group, we distinguished CT and magnetic resonance imaging (MRI) detections, reporting relative (R%) and total (T%) percentages.

	TREATMENT						
	U	**IVT**	**EVT**	**IVT+EVT**	**Total**		
no.	73	39	17	29	158		
Ischemic area detection						T%	R%
No	38	15	4	10	67	42.41%	
CT control ≤48	21	19	11	18	69	43.67%	
Late control only	14	5	2	1	22	13.92%	
CT	8	0	1	1	10	6.33%	45.45%
MRI	6	5	1	0	12	7.59%	54.54%

Table III.

Sensitivity and specificity of CTP for the detection of AIS. CTP for the detection of AIS divided for circulation territory.

Circulation territory	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value	Accuracy
Anterior TAR	76.19%	64.41%	75.29%	65.52%	71.33%
NVT included	75.0%	74.51%	82.19%	65.52%	74.81%
Posterior TAR	100.0%	75.0%	77.78%	100.0%	86.67%
NVT included	100.0%	75.0%	75.0%	100.0%	85.71%
Total TAR	78.02%	65.67%	75.53%	68.75%	72.78%
NVT included	76.74%	74.58%	81.48%	68.75%	75.86%

Table IV.

Reliability of CTP to identify total hypoperfusion area and ischemic core/penumbra ratio using Tmax/Tmax mismatch. Inclusion/exclusion criteria for group a) and b). Group c) represented patients excluded from sample.

	Inclusion criteria	**Exclusion criteria**
	Anterior circulation disturbance Detected perfusion deficit at CTP	Posterior or undetermined circulation disturbance Undetected perfusion deficit at CTP
Group a)	Treated patients TICI 2b-3 FCR	Untreated patients TICI 0 TAR without NVT
Group b)	Untreated patients TICI 0	Treated patients with TICI ≠ 0 TAR without NVT
Group c)	TICI 1-2a in absence of FCR TAR without NVT	a) and b) characteristics

Table V.

Reliability of CTP to identify total hypoperfusion area and ischemic core/penumbra ratio using Tmax/Tmax mismatch. Categorical data analysis (QL): treatments (untreated: U; treated with intravenous thrombolysis with recombinant tissue plasminogen activator: IVT; treated with endovascular therapy: EVT; treated with IVT and EVT combined: IVT+EVT); first CT check for the determination of FIA, divided in relation to time from the CTP study: within 48 hours; between 48 h and 6 days; after 6 days. Two groups of outcome: favorable and unfavorable.

	OUTCOME					
QL	Favorable		Unfavorable		χ^2	P value
Treatment	no.	%	no.	%		
U	0	0.0%	18	85.7%		
IVT	5	14.7%	0	0.0%		
EVT	10	29.4%	1	4.8%		
IVT+EVT	19	55.9%	2	9.5%		
Total	34		21		43.482	<0.001
CTP-to-first-CT						
≤48 h	34	100.0%	17	81.0%		
>48 h < 6 d	0	0.0%	2	9.5%		
≥6 d	0	0.0%	2	9.5%		
Total	34		21		6.984	<0.030

Table VI.

Reliability of CTP to identify total hypoperfusion area and ischemic core/penumbra ratio using Tmax/Tmax mismatch. Qualitative data analysis (QL) for degree of final infarct area (FIA) in computed tomography perfusion (CTP) in patients with TICI 2b-3 or FCR after EVT; inclusion of FIA in non-viable tissue (NVT) and tissue at risk (TAR) are considered, respectively. Time between CTP assessment and recanalization in patients with TICI 2b-3 or FCR after EVT, according to median and interquartile ranges: very early recanalization (VER: within 109.5 minutes); early recanalization (ER: after 109.5 minutes but within 127.5 minutes); late recanalization (LR: after 127.5 minutes). Because of the small sample size, p value could not be established.

	CTP-to-recanalization time						
QL	VER (≤109.5)		ER (≤127.5)		LR (>127.5)		TOT
Inclusion of NVT in FIA	no.	%	no.	%	no.	%	
No FIA	5	62.5%	2	28.57%	3	21.43%	10
NVT>FIA	2	25.0%	4	57.14%	8	57.14%	14
NVT=FIA	0	0.0%	1	12.29%	0	0.0%	1
NVT<FIA	1	12.5%	0	0.0%	3	21.43%	4
Inclusion of TAR in FIA							
No FIA	5	62.5%	2	28.57%	3	21.43%	10
TAR>FIA	3	37.5%	5	71.43%	10	71.43%	18
TAR=FIA	0	0.0%	0	0.0%	1	7.14%	1
TAR<FIA	0	0.0%	0	0.0%	0	0.0%	0
TOT	8		7		14		29

Table VII.

Reliability of CTP to identify total hypoperfusion area and ischemic core/penumbra ratio using Tmax/Tmax mismatch. Volumetric data for quantitative assessment of discrepancy between final infarct area (FIA), non-viable tissue (NVT) and tissue at risk (TAR). Volume measurement reported both for final infarct lesion using follow-up nonenhanced computed tomography (NECT) and for perfusion deficit detected with CTP. Considering the premises of our analysis, we compared FIA and NVT using Tmax 16s in patients with favorable clinical response and/or TICI 2b-3 (favorable outcome group, A), as well as we assessed the correlation between FIA and TAR using Tmax 9.5s in patients with TICI 0 or untreated (unfavorable outcome group, B).

Outcome group	Tmax 9,5	Tmax 16	Follow-up NECT
	Volume (cm3)		
A	15,51	4,81	2,5
A	129	33,12	0
A	30,65	7,85	0
B	87,8	29,75	80,3
A	167	79,29	95,4
A	30,63	0,65	16
A	21,89	3,97	0
B	3,28	1,14	2,4
A	118	26,91	5
A	144	66,41	48,3
A	130	54,42	15,4
A	60,53	26,2	25,7
B	172	108	94,5
B	36,29	20,55	49
B	57,55	14,88	7,5
A	34,05	11,09	0,9
A	4,27	0,9	0,9
B	22,78	12,14	22
A	15,92	1,08	4,2
A	101	31,35	4,6
A	28,54	5,7	10,4
A	160	60,16	39,2
A	138	63,17	0
A	154	35,76	6,5
A	99,36	45,26	38
A	15,58	2,52	1,1
A	70,48	14,9	48,7
A	72,25	13,2	5,7
A	151	66,55	38,5
B	19,74	6,48	23,8
B	10,53	1,42	0
A	72,76	24,38	0
A	75,96	1,38	0,3
A	49,3	23,23	81,5
B	94,95	53,6	0
A	17,07	1,39	0
B	10,42	6,81	8,5
A	106	34,37	0,4

Table VIII.

Sensitivity and specificity of FAST MRI for the detection of AIS. FAST MRI for the detection of AIS divided for circulation territory.

Circulation territory	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value	Accuracy
Anterior perfusion deficit	96,46%	10,00%	97,32%	7,69%	93,98%
TAR detected	95,95%	10,00%	96,93%	7,69%	84,82%
FAST MRI	100,00%	10,00%	97,41%	100,00%	97,13%
Posterior perfusion deficit	96,46%	10,00%	97,32%	7,69%	93,98%
TAR detected	95,95%	10,00%	96,93%	7,69%	84,82%
FAST MRI	100,00%	10,00%	97,41%	100,00%	97,13%
Total perfusion deficit	96,46%	10,00%	97,32%	7,69%	93,98%
TAR detected	95,95%	10,00%	96,93%	7,69%	84,82%
FAST MRI	100,00%	10,00%	97,41%	100,00%	97,13%

Table IX.

Reliability of MRI to identify total hypoperfusion area and ischemic core/penumbra ratio using DWI/pcASL mismatch. Inclusion/exclusion criteria for group a) and b). Group c) considered both excluded patients and those with unconsistent interventional-clinical outcome.

	Inclusion criteria	**Exclusion criteria**
	Anterior circulation disturbance Detected perfusion deficit at pcASL	Posterior or undetermined circulation disturbance Undetected perfusion deficit at pcASL
Group a)	Treated patients TICI 2b-3 FCR	Untreated patients TICI 0 TAR without NVT
Group b)	Untreated patients TICI 0	Treated patients with TICI ≠ 0 TAR without NVT
Group c)	TAR without NVT TICI 1-2a in absence of FCR TICI 2b-3 and Delta-NIHSS <0	a) and b) characteristics

Table X.

Reliability of MRI to identify total hypoperfusion area and ischemic core/penumbra ratio using DWI/pcASL mismatch. Qualitative data analysis (QL) for degree of final infarct area (FIA) in magnetic resonance imaging (MRI) in patients with TICI 2b-3 or FCR after EVT; inclusion of FIA in non viable tissue (NVT) and tissue at risk (TAR) are considered, respectively. Time between MRI assessment and recanalization in patients wth TICI 2b-3 or FCR after EVT, according to median and interquartile ranges: very early recanalization (VER: within 112.5 minutes); early recanalization (ER: after 144 minutes but within 180 minutes); late recanalization (LR: after 180 minutes). Because of the small sample size, p value could not be established.

	pcASL-to-recanalization time						
QL	VER (≤112.5)		ER (≤144)		LR (>180)		TOT
Inclusion of NVT in FIA	no.	%	no.	%	no.	%	
No FIA	0	0%	0	0%	4	100%	4
NVT>FIA	2	22,2%	3	33,3%	4	44,4%	9
NVT=FIA	31	31,31%	57	57,58%	11	11,11%	99
NVT<FIA	6	13,64%	24	54,55%	14	31,82%	44
Inclusion of TAR* in FIA							
*NV	4		4		3		11
No FIA	0	0%	0	0%	3	100%	3
TAR>FIA	31	25,20%	69	56,10%	23	18,70%	123
TAR=FIA	4	22,22%	10	55,56%	4	22,22%	18
TAR<FIA	0	0%	1	100%	0	0%	1
TOT	39		84		33		156

Missing Values Quantitative

Univariate Statistics

	N	Missing	
		Count	Percent
Sex (S)	349	0	.0
INTERVENTION	349	0	.0
Occluded vessel	349	0	.0
Side	349	0	.0
Circulation	349	0	.0
Perfusion deficit	349	0	.0
Ischemic lesion at CT/MR control	349	0	.0
Anatomical inclusion of hypoperfused area in the ischemic lesion at CT/MR control	349	0	.0
DWI core inclusion in FIA	349	0	.0
pcASL penumbra inclusion in FIA	319	30	8.6
TICI	220	129	37.0
Successful EVT treatment	220	129	37.0
Favourable Clinical Response	349	0	.0
TOAST	349	0	.0
Smoking	303	46	13.2
Former Smoker	299	50	14.3
Diabetes	329	20	5.7
Previous Stroke TIA	328	21	6.0
Coronary artery disease	334	15	4.3
Ejection fraction (EF)≤40%	280	69	19.8

Hyperlipemia	328	21	6.0
Malignant neoplasia (K)_Hystory	327	22	6.3
Known_Atrial_Fibrillation (AF)	338	11	3.2
Newonset_AF	338	11	3.2
Hypertension	328	21	6.0
Carotid_Stenosis_left	274	75	21.5
Carotid_Stenosis_right	274	75	21.5
Stenosis dicho (<50/≥50%)	349	0	.0
Carotid intima-media thickness (CIMT) qualitative	260	89	25.5
Antihypertensive	327	22	6.3
Statins	324	25	7.2
Anticoagulants	327	22	6.3
Antiplatelet	327	22	6.3
Antibiotics	326	23	6.6
Insulin	326	23	6.6
Beta_blockers	327	22	6.3

Descriptive Qualitative

		Count	Column N %	Table N %
S	Male	161	46.1%	46.1%
	Female	188	53.9%	53.9%
INTERVENTION	Not Treated	86	24.6%	24.6%
	IVT	32	9.2%	9.2%
	EVT	183	52.4%	52.4%
	Bridging	48	13.8%	13.8%
Occluded vessel	ACA	3	0.9%	0.9%
	MCA	209	59.9%	59.9%

	T-Carotids	32	9.2%	9.2%
	ICA Intra	7	2.0%	2.0%
	ICA extra	32	9.2%	9.2%
	Tandem	33	9.5%	9.5%
	Combined (MCA+ACA/PCA	9	2.6%	2.6%
	VB	24	6.9%	6.9%
Side	Right	144	41.3%	41.3%
	Left	198	56.7%	56.7%
	Bilateral	7	2.0%	2.0%
Circulation	Posterior	24	6.9%	6.9%
	Anterior	321	92.0%	92.0%
	Posterior+Anterior	4	1.1%	1.1%
Perfusion deficit (Yes/No)	No	13	3.7%	3.7%
	Yes	293	84.0%	84.0%
	Yes No Penumbra	43	12.3%	12.3%
Ischemic lesion at CT/MR control (Yes/No)	No	10	2.9%	2.9%
	Yes	339	97.1%	97.1%
Anatomical inclusion of hypoperfused area in the ischemic lesion at CT/MR control (Yes/No)	No	3	0.9%	0.9%
	Yes	346	99.1%	99.1%
DWI Core inclusion in FIA	Partial (Core Higher)	23	6.6%	6.6%
	Complete (core equal)	213	61.0%	61.0%
	Higher (Ischemia>Core)	103	29.5%	29.5%
	No FIA	10	2.9%	2.9%
pcASL Penumbra inclusion in FIA	Partial (Penumbra higher)	194	60.8%	60.8%
	Complete (Penumbra equal)	106	33.2%	33.2%

	Higher (Ischemia>Penumbra)	7	2.2%	2.2%
	No FIA	12	3.8%	3.8%
TICI	0	27	12.3%	12.3%
	1	3	1.4%	1.4%
	2a	14	6.4%	6.4%
	2b	51	23.2%	23.2%
	2c	55	25.0%	25.0%
	3	70	31.8%	31.8%
Successful EVT treatment (Yes/No)	TICI 0-2a	44	20.0%	20.0%
	TICI 2b-3	176	80.0%	80.0%
Favourable Clinical Response	No	245	70.2%	70.2%
	Yes	104	29.8%	29.8%
TOAST	Athero	86	24.6%	24.6%
	Cardio	102	29.2%	29.2%
	Small vessels	10	2.9%	2.9%
	Other Causes	14	4.0%	4.0%
	Undetermined (multiple causes)	8	2.3%	2.3%
	Undetermined (iter not completed)	129	37.0%	37.0%
Smoking	No	230	75.9%	75.9%
	Yes	73	24.1%	24.1%
Former_Smoker	No	246	82.3%	82.3%
	Yes	53	17.7%	17.7%
Diabetes	No	247	75.1%	75.1%
	Yes	82	24.9%	24.9%
Previous_Stroke/TIA	No	277	84.5%	84.5%
	Yes	51	15.5%	15.5%

Coronary_artery_disease	No	282	84.4%	84.4%
	Yes	52	15.6%	15.6%
EF≤40%	No	259	92.5%	92.5%
	Yes	21	7.5%	7.5%
Hyperlipemia	No	197	60.1%	60.1%
	Yes	131	39.9%	39.9%
K_Hystory	No	283	86.5%	86.5%
	Yes	44	13.5%	13.5%
Known_Atrial_Fibrillation	No	260	76.9%	76.9%
	Yes	78	23.1%	23.1%
Newonset_AF	No	298	88.2%	88.2%
	Yes	40	11.8%	11.8%
Hypertension	No	77	23.5%	23.5%
	Yes	251	76.5%	76.5%
Carotid_Stenosis_left	No	78	28.5%	28.5%
	<50%	127	46.4%	46.4%
	50-70%	33	12.0%	12.0%
	>70%	18	6.6%	6.6%
	Occlusion	18	6.6%	6.6%
Carotid_Stenosis_right	No	69	25.2%	25.2%
	<50%	136	49.6%	49.6%
	50-70%	31	11.3%	11.3%
	>70%	18	6.6%	6.6%
	Occlusion	20	7.3%	7.3%
Stenosis dicho	<50%	205	58.7%	58.7%
	≥50%	69	19.8%	19.8%
	2	75	21.5%	21.5%
CIMT qual	Normal	48	18.5%	18.5%

	Mild	77	29.6%	29.6%
	Moderated	71	27.3%	27.3%
	Severe	64	24.6%	24.6%
Antihypertensive	No	96	29.4%	29.4%
	Yes	231	70.6%	70.6%
Statins	No	203	62.7%	62.7%
	Yes	121	37.3%	37.3%
Anticoagulants	No	282	86.2%	86.2%
	Yes	45	13.8%	13.8%
Antiplatelet	No	219	67.0%	67.0%
	Yes	108	33.0%	33.0%
Antibiotics	No	320	98.2%	98.2%
	Yes	6	1.8%	1.8%
Insulin	No	309	94.8%	94.8%
	Yes	17	5.2%	5.2%
Beta_blockers	No	235	71.9%	71.9%
	Yes	92	28.1%	28.1%

Descriptive Quantitative Variables

	Mean	Median	Percentile 25	Percentile 75	Missing	Maximum	Minimum
Age	73	75	66	83	0	99	30
Time between onset of symptoms and pcASL	5.0	4.1	2.8	6.1	36	21.0	1.0
Time between pcASL and reperfusion	2.2	2.2	1.7	2.9	124	15.5	-6.7
Time between pcASL and CT/MR control	41.7	27.8	23.0	38.0	30	336.0	4.7
NIHSS admission	11	11	6	16	0	27	0
NIHSS discharge	11	5	2	13	0	42	0

Δ NIHSS	1	2	0	7	0	21	-42
EF	56	55	55	60	69	70	25
RBC	4320000	4310000	3930000	4700000	4	6320000	2390000
HCT	37.92	38.00	34.00	41.00	6	52.90	23.00
Hb	13.38	12.90	11.55	13.90	5	95.62	3.70
WBC	9942	9200	7500	11800	2	31300	3400
Neutrophils	72.1	74.0	64.0	81.0	2	93.0	23.0
Lymphocytes	20.3	19.0	12.0	27.0	3	62.0	3.0
Neu Count	6927.19	6420.00	4823.00	8490.00	135	17660.70	1701.50
Lym Count	1786.14	1591.10	1116.00	2231.00	135	8740.00	223.20
NLR	5.20	3.95	2.44	6.67	136	30.00	.59
Platelets	230911	222000	185000	267000	2	610000	67000
CRP	2.25	.65	.20	2.00	48	71.00	.03
PT	86.18	87.00	80.00	96.00	27	135.00	13.00
APTT	29.49	29.20	27.30	31.45	29	47.90	1.60
INR	1.13	1.08	1.02	1.13	26	4.86	.83
LDL	101.2	97.0	75.0	123.0	32	216.0	25.0
HDL	48	46	38	56	32	106	19
Triglycerides	104	92	71	123	34	458	5
Cholesterol	176	177	148	200	29	302	70
Na	139	139	137	141	7	173	122
K	4.16	4.10	3.80	4.50	7	6.90	1.00
Az	48	41	32	54	5	328	13
Cr	1.07	.90	.80	1.20	5	11.00	.05
Ca	8.99	9.04	8.50	9.50	211	10.83	4.60
Systolic_Blood_Pressure	148	145	131	160	54	240	90
Dyastolic_Blood_Pressure	81	80	70	90	53	170	45
Heart_Rate	79	78	69	88	54	150	40

Blood_Oxygen	97	97	96	98	64	100	82
Blood_Glucose	139	129	110	152	63	363	72
pre-stroke mRS	1	0	0	1	80	4	0
3-month mRS	3	2	1	4	120	6	0

Oneway

Warnings

Post hoc tests are not performed for Time between pcASL and reperfusion because at least one group has fewer than two cases.

Descriptives

		N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum
						Lower Bound	Upper Bound		
Age	Not Treated	86	74.47	11.045	1.191	72.10	76.83	43	96
	IVT	32	68.34	16.206	2.865	62.50	74.19	30	90
	EVT	183	73.72	13.308	.984	71.77	75.66	33	95
	Bridging	48	72.58	13.815	1.994	68.57	76.59	43	99
	Total	349	73.25	13.204	.707	71.86	74.64	30	99
Time between onset of symptoms and pcASL	Not Treated	79	5.739	3.6425	.4098	4.923	6.555	1.0	20.5
	IVT	29	4.779	3.0029	.5576	3.637	5.922	1.6	12.7
	EVT	161	4.814	3.1467	.2480	4.324	5.303	1.0	21.0
	Bridging	44	4.564	2.9549	.4455	3.665	5.462	1.2	16.0
	Total	313	5.009	3.2550	.1840	4.647	5.371	1.0	21.0
Time between pcASL and reperfusion	Not Treated	0	.	.	.	.	.	.	.

	IVT	28	.404	2.5989	.4912	-.604	1.411	-6.7	3.0
	EVT	151	2.734	1.2691	.1033	2.530	2.938	1.0	13.7
	Bridging	46	1.752	2.6252	.3871	.973	2.532	-4.5	15.5
	Total	225	2.243	1.9779	.1319	1.983	2.503	-6.7	15.5
Time between pcASL and CT/MR control	Not Treated	85	72.731	67.6386	7.3364	58.141	87.320	4.7	336.0
	IVT	30	26.087	9.9292	1.8128	22.379	29.794	5.1	52.9
	EVT	161	30.759	27.1652	2.1409	26.531	34.987	7.3	312.0
	Bridging	43	32.298	23.4646	3.5783	25.076	39.519	12.5	163.0
	Total	319	41.711	44.8823	2.5129	36.767	46.655	4.7	336.0
NIHSS admission	Not Treated	86	11.42	7.376	.795	9.84	13.00	0	27
	IVT	32	8.53	5.124	.906	6.68	10.38	2	22
	EVT	183	11.12	6.081	.449	10.23	12.01	0	26
	Bridging	48	12.13	6.252	.902	10.31	13.94	0	26
	Total	349	11.09	6.405	.343	10.42	11.77	0	27
NIHSS discharge	Not Treated	86	15.47	15.089	1.627	12.23	18.70	0	42
	IVT	32	4.84	7.874	1.392	2.00	7.68	0	42
	EVT	183	10.13	12.007	.888	8.38	11.88	0	42
	Bridging	48	7.29	10.076	1.454	4.37	10.22	0	42
	Total	349	10.57	12.679	.679	9.24	11.91	0	42
Δ NIHSS	Not Treated	86	-4.05	11.868	1.280	-6.59	-1.50	-36	13
	IVT	32	3.69	8.014	1.417	.80	6.58	-31	18
	EVT	183	.99	10.681	.790	-.57	2.55	-42	17
	Bridging	48	4.83	10.628	1.534	1.75	7.92	-27	21
	Total	349	.52	11.126	.596	-.65	1.70	-42	21
EF	Not Treated	61	54.20	8.797	1.126	51.94	56.45	25	65

	IVT	23	58.26	4.158	.867	56.46	60.06	50	65
	EVT	154	55.27	7.405	.597	54.09	56.45	25	65
	Bridging	42	56.90	6.622	1.022	54.84	58.97	35	70
	Total	280	55.53	7.473	.447	54.65	56.41	25	70
CIMT	Not Treated	42	1.1738	.21647	.03340	1.1064	1.2413	.60	1.60
	IVT	19	1.0579	.28346	.06503	.9213	1.1945	.60	1.70
	EVT	149	1.1812	.22997	.01884	1.1440	1.2184	.60	1.60
	Bridging	40	1.1063	.22480	.03554	1.0344	1.1781	.60	1.50
	Total	250	1.1586	.23331	.01476	1.1295	1.1877	.60	1.70
RBC	Not Treated	85	4480823.53	626605.009	67964.856	4345667.96	4615979.10	3010000	6010000
	IVT	32	4675625.00	590947.503	104465.747	4462565.70	4888684.30	3290000	6320000
	EVT	181	4185082.87	617049.988	45864.964	4094580.71	4275585.03	2390000	6150000
	Bridging	47	4306595.74	619404.611	90349.448	4124731.74	4488459.75	2680000	5950000
	Total	345	4320000.00	636896.545	34289.357	4252556.81	4387443.19	2390000	6320000
HCT	Not Treated	84	39.6345	5.32723	.58125	38.4784	40.7906	26.00	52.90
	IVT	31	40.6226	3.81066	.68441	39.2248	42.0203	32.00	47.00
	EVT	181	36.6337	5.26969	.39169	35.8608	37.4066	23.00	50.00
	Bridging	47	37.9979	4.86436	.70954	36.5696	39.4261	26.00	49.00
	Total	343	37.9160	5.31224	.28683	37.3519	38.4802	23.00	52.90
Hb	Not Treated	84	14.3229	9.18443	1.00210	12.3297	16.3160	8.20	95.62
	IVT	32	18.0303	17.54676	3.10186	11.7040	24.3566	9.70	85.00
	EVT	181	12.2525	1.93817	.14406	11.9682	12.5368	3.70	16.80
	Bridging	47	12.9021	1.69134	.24671	12.4055	13.3987	8.40	17.50
	Total	344	13.3843	7.31650	.39448	12.6084	14.1602	3.70	95.62
WBC	Not Treated	85	9979.53	4094.246	444.083	9096.42	10862.64	3400	31300

	IVT	32	9722.81	3033.409	536.236	8629.15	10816.47	5700	18800
	EVT	182	10063.74	3639.613	269.786	9531.41	10596.07	4270	23000
	Bridging	48	9558.13	2781.649	401.496	8750.42	10365.83	3700	19000
	Total	347	9941.73	3592.739	192.868	9562.39	10321.07	3400	31300
Neutrophils	Not Treated	85	70.212	12.9772	1.4076	67.413	73.011	23.0	90.0
	IVT	32	70.531	10.8508	1.9182	66.619	74.443	50.0	90.0
	EVT	182	74.122	10.9385	.8108	72.522	75.722	32.0	93.0
	Bridging	48	68.604	13.0494	1.8835	64.815	72.393	41.0	88.0
	Total	347	72.070	11.9208	.6399	70.811	73.328	23.0	93.0
Lymphocytes	Not Treated	84	22.119	10.7057	1.1681	19.796	24.442	5.0	62.0
	IVT	32	22.313	10.4339	1.8445	18.551	26.074	5.0	43.0
	EVT	182	18.592	9.3665	.6943	17.222	19.962	3.0	54.0
	Bridging	48	22.521	11.4111	1.6470	19.207	25.834	4.0	46.0
	Total	346	20.337	10.2239	.5496	19.256	21.418	3.0	62.0
Neu Count	Not Treated	85	8634.6235	15000.61236	1627.04485	5399.0664	11870.1807	1610.00	141410.00
	IVT	32	6833.9375	2385.10139	421.63034	5974.0167	7693.8583	3190.00	12032.00
	EVT	182	7464.8571	3149.51090	233.45728	7004.2093	7925.5050	2112.00	18400.00
	Bridging	48	6870.7500	2273.20402	328.10874	6210.6804	7530.8196	1702.00	10836.00
	Total	347	7611.0346	7837.72447	420.75109	6783.4829	8438.5863	1610.00	141410.00
Lym Count	Not Treated	84	2323.0833	2909.89934	317.49605	1691.5965	2954.5702	432.00	26850.00
	IVT	32	2196.5625	1163.62900	205.70249	1777.0295	2616.0955	285.00	5076.00
	EVT	182	1893.7582	1236.46347	91.65277	1712.9129	2074.6036	295.00	8680.00
	Bridging	48	1964.1458	1345.68684	194.23316	1573.3991	2354.8926	345.00	8740.00
	Total	346	2035.7572	1800.39307	96.78973	1845.3850	2226.1295	285.00	26850.00
NLR	Not Treated	84	4.6300	3.48659	.38042	3.8734	5.3866	.98	18.00

	IVT	32	4.4056	3.63282	.64220	3.0959	5.7154	1.20	18.00
	EVT	182	5.4846	4.18957	.31055	4.8718	6.0973	.50	30.00
	Bridging	48	5.0192	3.77515	.54490	3.9230	6.1154	.91	18.00
	Total	346	5.1127	3.92911	.21123	4.6973	5.5282	.50	30.00
Platelets	Not Treated	85	226576.47	72422.598	7855.334	210955.28	242197.66	67000	495000
	IVT	32	246562.50	46555.508	8229.929	229777.45	263347.55	153000	348000
	EVT	182	231368.13	72975.449	5409.300	220694.73	242041.53	73000	610000
	Bridging	48	226416.67	79283.717	11443.619	203395.07	249438.26	111000	511000
	Total	347	230910.66	71675.937	3847.766	223342.71	238478.62	67000	610000
CRP	Not Treated	76	3.6000	9.14628	1.04915	1.5100	5.6900	.06	71.00
	IVT	24	1.0283	.98017	.20008	.6144	1.4422	.10	3.23
	EVT	159	2.0445	4.32564	.34305	1.3670	2.7221	.07	42.90
	Bridging	42	1.3114	1.85638	.28645	.7329	1.8899	.03	9.29
	Total	301	2.2540	5.66035	.32626	1.6119	2.8960	.03	71.00
PT	Not Treated	74	88.2635	15.92066	1.85074	84.5750	91.9520	31.00	121.00
	IVT	28	87.9643	14.40546	2.72238	82.3784	93.5501	42.00	112.00
	EVT	174	83.9937	19.92596	1.51058	81.0121	86.9752	13.00	134.00
	Bridging	46	90.0000	14.97702	2.20824	85.5524	94.4476	60.00	135.00
	Total	322	86.1783	18.06892	1.00694	84.1972	88.1593	13.00	135.00
APTT	Not Treated	72	30.4278	4.25409	.50135	29.4281	31.4274	11.20	42.90
	IVT	28	29.4964	2.12925	.40239	28.6708	30.3221	24.10	34.50
	EVT	174	29.3730	4.98286	.37775	28.6274	30.1186	1.60	47.90
	Bridging	46	28.4717	3.19984	.47179	27.5215	29.4220	20.80	35.60
	Total	320	29.4916	4.43584	.24797	29.0037	29.9794	1.60	47.90
INR	Not Treated	74	1.0966	.17843	.02074	1.0553	1.1380	.92	2.23

	IVT	28	1.0957	.14791	.02795	1.0384	1.1531	.94	1.76
	EVT	175	1.1658	.39742	.03004	1.1065	1.2251	.83	4.86
	Bridging	46	1.0683	.09212	.01358	1.0409	1.0956	.87	1.28
	Total	323	1.1300	.31175	.01735	1.0958	1.1641	.83	4.86
LDL	Not Treated	74	104.811	35.7410	4.1548	96.530	113.091	46.0	195.0
	IVT	30	115.700	30.2429	5.5216	104.407	126.993	60.0	176.0
	EVT	169	97.479	34.9062	2.6851	92.178	102.780	25.0	216.0
	Bridging	44	99.182	31.1204	4.6916	89.720	108.643	57.0	177.0
	Total	317	101.151	34.4904	1.9372	97.340	104.963	25.0	216.0
HDL	Not Treated	74	46.76	13.370	1.554	43.66	49.85	23	88
	IVT	30	46.13	9.001	1.643	42.77	49.49	32	67
	EVT	169	48.83	15.894	1.223	46.41	51.24	19	106
	Bridging	44	47.23	12.748	1.922	43.35	51.10	25	80
	Total	317	47.87	14.362	.807	46.28	49.45	19	106
Triglycerides	Not Treated	74	110.15	47.906	5.569	99.05	121.25	41	330
	IVT	28	118.50	37.950	7.172	103.78	133.22	55	234
	EVT	169	99.94	50.136	3.857	92.33	107.55	5	344
	Bridging	44	101.16	67.929	10.241	80.51	121.81	44	458
	Total	315	104.16	51.689	2.912	98.43	109.89	5	458
Cholesterol	Not Treated	75	180.67	40.654	4.694	171.31	190.02	80	284
	IVT	30	192.73	32.035	5.849	180.77	204.70	132	258
	EVT	171	171.55	43.772	3.347	164.94	178.16	70	302
	Bridging	44	172.66	36.785	5.546	161.48	183.84	118	265
	Total	320	175.83	41.518	2.321	171.26	180.39	70	302
Na	Not Treated	85	138.92	4.127	.448	138.03	139.81	126	151

	IVT	32	138.28	4.214	.745	136.76	139.80	127	146
	EVT	178	138.37	4.501	.337	137.70	139.03	122	173
	Bridging	47	139.87	4.003	.584	138.70	141.05	128	148
	Total	342	138.70	4.331	.234	138.24	139.16	122	173
K	Not Treated	85	4.1534	.59798	.06486	4.0244	4.2824	2.60	5.80
	IVT	32	4.1187	.45397	.08025	3.9551	4.2824	3.10	5.00
	EVT	178	4.2044	.63137	.04732	4.1110	4.2978	1.00	6.90
	Bridging	47	4.0166	.48011	.07003	3.8756	4.1576	3.00	5.20
	Total	342	4.1579	.59064	.03194	4.0951	4.2207	1.00	6.90
Az	Not Treated	85	49.62	29.330	3.181	43.30	55.95	13	184
	IVT	32	41.81	14.132	2.498	36.72	46.91	17	76
	EVT	180	50.52	35.818	2.670	45.25	55.78	13	328
	Bridging	47	42.72	17.511	2.554	37.58	47.86	17	90
	Total	344	48.42	30.831	1.662	45.15	51.69	13	328
Cr	Not Treated	85	1.0784	.57023	.06185	.9554	1.2013	.30	3.70
	IVT	32	1.2688	1.79218	.31681	.6226	1.9149	.50	11.00
	EVT	180	1.0564	.67780	.05052	.9567	1.1561	.05	6.60
	Bridging	47	.9796	.33825	.04934	.8803	1.0790	.05	2.00
	Total	344	1.0711	.79368	.04279	.9869	1.1553	.05	11.00
Ca	Not Treated	31	9.2606	.72506	.13022	8.9947	9.5266	7.52	10.77
	IVT	6	8.9467	.58725	.23975	8.3304	9.5630	8.20	9.65
	EVT	80	8.8958	.91163	.10192	8.6929	9.0986	4.60	10.83
	Bridging	21	8.9590	.54601	.11915	8.7105	9.2076	7.50	9.77
	Total	138	8.9896	.82003	.06981	8.8515	9.1276	4.60	10.83
Systolic_Blood_Pressure	Not Treated	66	154.18	26.630	3.278	147.64	160.73	100	240

	IVT	24	148.29	21.155	4.318	139.36	157.22	107	194
	EVT	166	145.20	21.250	1.649	141.95	148.46	90	195
	Bridging	39	146.23	24.055	3.852	138.43	154.03	112	200
	Total	295	147.60	23.092	1.344	144.95	150.25	90	240
Dyastolic_Blood_Pressure	Not Treated	67	85.36	17.912	2.188	80.99	89.73	55	170
	IVT	24	80.25	10.975	2.240	75.62	84.88	60	100
	EVT	166	79.60	13.887	1.078	77.47	81.73	45	120
	Bridging	39	77.67	12.359	1.979	73.66	81.67	57	111
	Total	296	80.70	14.681	.853	79.02	82.38	45	170
Heart_Rate	Not Treated	69	82.51	16.750	2.017	78.48	86.53	50	133
	IVT	24	81.00	13.536	2.763	75.28	86.72	53	115
	EVT	164	77.87	14.047	1.097	75.70	80.03	40	150
	Bridging	38	79.00	17.789	2.886	73.15	84.85	56	138
	Total	295	79.35	15.240	.887	77.61	81.10	40	150
Blood_Oxygen	Not Treated	65	96.71	2.082	.258	96.19	97.22	91	100
	IVT	20	97.55	1.538	.344	96.83	98.27	94	100
	EVT	162	96.69	2.339	.184	96.33	97.05	82	100
	Bridging	38	97.05	1.610	.261	96.52	97.58	92	100
	Total	285	96.80	2.152	.127	96.55	97.05	82	100
Blood_Glucose	Not Treated	63	150.73	58.533	7.375	135.99	165.47	72	340
	IVT	22	123.27	32.226	6.871	108.98	137.56	80	212
	EVT	161	140.94	46.649	3.676	133.68	148.20	72	363
	Bridging	40	123.45	26.890	4.252	114.85	132.05	76	190
	Total	286	139.29	47.201	2.791	133.80	144.79	72	363
pre-stroke mRS	Not Treated	44	1.30	1.534	.231	.83	1.76	0	4

	IVT	18	.50	.786	.185	.11	.89	0	2
	EVT	162	.52	.900	.071	.38	.66	0	4
	Bridging	45	.38	.912	.136	.10	.65	0	4
	Total	269	.62	1.064	.065	.49	.75	0	4
3-month mRS	Not Treated	44	4.09	2.044	.308	3.47	4.71	0	6
	IVT	24	1.83	1.494	.305	1.20	2.46	0	6
	EVT	128	2.57	2.003	.177	2.22	2.92	0	6
	Bridging	33	2.12	1.867	.325	1.46	2.78	0	6
	Total	229	2.72	2.061	.136	2.45	2.99	0	6

ANOVA

		Sum of Squares	df	Mean Square	F	Sig.
Age	Between Groups	958.306	3	319.435	1.846	.139
	Within Groups	59713.505	345	173.083		
	Total	60671.811	348			
Time between onset of symptoms and pcASL	Between Groups	58.527	3	19.509	1.857	.137
	Within Groups	3247.048	309	10.508		
	Total	3305.575	312			
Time between pcASL and reperfusion	Between Groups	142.190	2	71.095	21.500	.000
	Within Groups	734.082	222	3.307		
	Total	876.272	224			

Time between pcASL and CT/MR control	Between Groups	112233.449	3	37411.150	22.304	.000
	Within Groups	528352.854	315	1677.311		
	Total	640586.304	318			
NIHSS admission	Between Groups	270.375	3	90.125	2.220	.086
	Within Groups	14005.504	345	40.596		
	Total	14275.880	348			
NIHSS discharge	Between Groups	3661.147	3	1220.382	8.053	.000
	Within Groups	52282.383	345	151.543		
	Total	55943.530	348			
Δ NIHSS	Between Groups	3047.709	3	1015.903	8.755	.000
	Within Groups	40033.334	345	116.039		
	Total	43081.043	348			
EF	Between Groups	369.533	3	123.178	2.235	.084
	Within Groups	15210.239	276	55.110		
	Total	15579.771	279			
CIMT	Between Groups	.388	3	.129	2.418	.067
	Within Groups	13.166	246	.054		
	Total	13.554	249			
RBC	Between Groups	9548591071003.803	3	3182863690334.601	8.349	.000

	Within Groups	129990608928996.220	341	381204131756.587		
	Total	139539200000000.020	344			
HCT	Between Groups	773.104	3	257.701	9.840	.000
	Within Groups	8878.098	339	26.189		
	Total	9651.202	342			
Hb	Between Groups	1007.517	3	335.839	6.580	.000
	Within Groups	17353.667	340	51.040		
	Total	18361.184	343			
WBC	Between Groups	11427543.894	3	3809181.298	.293	.830
	Within Groups	4454661418.642	343	12987351.075		
	Total	4466088962.536	346			
Neutrophils	Between Groups	1712.184	3	570.728	4.125	.007
	Within Groups	47456.568	343	138.357		
	Total	49168.752	346			
Lymphocytes	Between Groups	1174.908	3	391.636	3.839	.010
	Within Groups	34887.021	342	102.009		
	Total	36061.929	345			
Neu Count	Between Groups	138575542.471	3	46191847.490	.750	.523
	Within Groups	21116178439.114	343	61563202.446		
	Total	21254753981.585	346			

Lym Count	Between Groups	11678143.973	3	3892714.658	1.203	.309
	Within Groups	1106610101.633	342	3235702.052		
	Total	1118288245.607	345			
NLR	Between Groups	61.157	3	20.386	1.324	.266
	Within Groups	5264.921	342	15.395		
	Total	5326.078	345			
Platelets	Between Groups	10443600774.872	3	3481200258.291	.676	.567
	Within Groups	1767110629772.679	343	5151926034.323		
	Total	1777554230547.551	346			
CRP	Between Groups	218.036	3	72.679	2.298	.078
	Within Groups	9393.838	297	31.629		
	Total	9611.874	300			
PT	Between Groups	1913.349	3	637.783	1.971	.118
	Within Groups	102888.659	318	323.549		
	Total	104802.008	321			
APTT	Between Groups	113.397	3	37.799	1.938	.123
	Within Groups	6163.470	316	19.505		
	Total	6276.867	319			
INR	Between Groups	.515	3	.172	1.778	.151

	Within Groups	30.779	319	.096		
	Total	31.294	322			
LDL	Between Groups	9790.358	3	3263.453	2.790	.041
	Within Groups	366118.374	313	1169.707		
	Total	375908.732	316			
HDL	Between Groups	355.596	3	118.532	.572	.634
	Within Groups	64826.839	313	207.115		
	Total	65182.435	316			
Triglycerides	Between Groups	11816.404	3	3938.801	1.481	.220
	Within Groups	827121.660	311	2659.555		
	Total	838938.063	314			
Cholesterol	Between Groups	13901.453	3	4633.818	2.732	.044
	Within Groups	535966.747	316	1696.097		
	Total	549868.200	319			
Na	Between Groups	94.189	3	31.396	1.684	.170
	Within Groups	6303.390	338	18.649		
	Total	6397.579	341			
K	Between Groups	1.374	3	.458	1.316	.269
	Within Groups	117.586	338	.348		
	Total	118.960	341			

Az	Between Groups	3836.699	3	1278.900	1.350	.258
	Within Groups	322197.182	340	947.639		
	Total	326033.881	343			
Cr	Between Groups	1.687	3	.562	.892	.446
	Within Groups	214.380	340	.631		
	Total	216.067	343			
Ca	Between Groups	3.013	3	1.004	1.510	.215
	Within Groups	89.112	134	.665		
	Total	92.125	137			
Systolic_Blood_Pressure	Between Groups	3896.064	3	1298.688	2.472	.062
	Within Groups	152882.736	291	525.370		
	Total	156778.800	294			
Dyastolic_Blood_Pressure	Between Groups	2017.509	3	672.503	3.189	.024
	Within Groups	61568.329	292	210.850		
	Total	63585.838	295			
Heart_Rate	Between Groups	1119.040	3	373.013	1.616	.186
	Within Groups	67166.295	291	230.812		
	Total	68285.336	294			
Blood_Oxygen	Between Groups	16.138	3	5.379	1.164	.324

	Within Groups	1298.859	281	4.622		
	Total	1314.996	284			
Blood_Glucose	Between Groups	24366.155	3	8122.052	3.751	.011
	Within Groups	610605.173	282	2165.267		
	Total	634971.329	285			
pre-stroke mRS	Between Groups	24.642	3	8.214	7.811	.000
	Within Groups	278.681	265	1.052		
	Total	303.323	268			
3-month mRS	Between Groups	116.262	3	38.754	10.236	.000
	Within Groups	851.852	225	3.786		
	Total	968.114	228			

Post Hoc Tests

Multiple Comparisons

Bonferroni

Dependent Variable	(I) INTERVENTION	(J) INTERVENTION	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval Lower Bound	95% Confidence Interval Upper Bound
Age	Not Treated	IVT	6.121	2.724	.152	-1.11	13.35
		EVT	.749	1.720	1.000	-3.81	5.31
		Bridging	1.882	2.370	1.000	-4.41	8.17
	IVT	Not Treated	-6.121	2.724	.152	-13.35	1.11

		EVT	-5.372	2.521	.203	-12.06	1.32
		Bridging	-4.240	3.002	.953	-12.21	3.73
	EVT	Not Treated	-.749	1.720	1.000	-5.31	3.81
		IVT	5.372	2.521	.203	-1.32	12.06
		Bridging	1.133	2.133	1.000	-4.53	6.79
	Bridging	Not Treated	-1.882	2.370	1.000	-8.17	4.41
		IVT	4.240	3.002	.953	-3.73	12.21
		EVT	-1.133	2.133	1.000	-6.79	4.53
Time between onset of symptoms and pcASL	Not Treated	IVT	.9599	.7038	1.000	-.909	2.829
		EVT	.9256	.4453	.231	-.257	2.108
		Bridging	1.1756	.6098	.329	-.444	2.795
	IVT	Not Treated	-.9599	.7038	1.000	-2.829	.909
		EVT	-.0344	.6539	1.000	-1.771	1.702
		Bridging	.2157	.7754	1.000	-1.843	2.275
	EVT	Not Treated	-.9256	.4453	.231	-2.108	.257
		IVT	.0344	.6539	1.000	-1.702	1.771
		Bridging	.2500	.5514	1.000	-1.214	1.714
	Bridging	Not Treated	-1.1756	.6098	.329	-2.795	.444
		IVT	-.2157	.7754	1.000	-2.275	1.843
		EVT	-.2500	.5514	1.000	-1.714	1.214
Time between pcASL and CT/MR control	Not Treated	IVT	46.6439*	8.6973	.000	23.552	69.736
		EVT	41.9716*	5.4910	.000	27.393	56.550
		Bridging	40.4329*	7.6642	.000	20.084	60.782
	IVT	Not Treated	-46.6439*	8.6973	.000	-69.736	-23.552
		EVT	-4.6723	8.1442	1.000	-26.295	16.951
		Bridging	-6.2110	9.7426	1.000	-32.078	19.656
	EVT	Not Treated	-41.9716*	5.4910	.000	-56.550	-27.393
		IVT	4.6723	8.1442	1.000	-16.951	26.295

		Bridging	-1.5387	7.0303	1.000	-20.204	17.127
	Bridging	Not Treated	-40.4329*	7.6642	.000	-60.782	-20.084
		IVT	6.2110	9.7426	1.000	-19.656	32.078
		EVT	1.5387	7.0303	1.000	-17.127	20.204
NIHSS admission	Not Treated	IVT	2.887	1.319	.176	-.61	6.39
		EVT	.298	.833	1.000	-1.91	2.51
		Bridging	-.706	1.148	1.000	-3.75	2.34
	IVT	Not Treated	-2.887	1.319	.176	-6.39	.61
		EVT	-2.589	1.221	.208	-5.83	.65
		Bridging	-3.594	1.454	.084	-7.45	.26
	EVT	Not Treated	-.298	.833	1.000	-2.51	1.91
		IVT	2.589	1.221	.208	-.65	5.83
		Bridging	-1.005	1.033	1.000	-3.75	1.74
	Bridging	Not Treated	.706	1.148	1.000	-2.34	3.75
		IVT	3.594	1.454	.084	-.26	7.45
		EVT	1.005	1.033	1.000	-1.74	3.75
NIHSS discharge	Not Treated	IVT	10.621*	2.549	.000	3.86	17.39
		EVT	5.334*	1.609	.006	1.06	9.60
		Bridging	8.173*	2.218	.002	2.29	14.06
	IVT	Not Treated	-10.621*	2.549	.000	-17.39	-3.86
		EVT	-5.287	2.359	.154	-11.55	.97
		Bridging	-2.448	2.809	1.000	-9.90	5.01
	EVT	Not Treated	-5.334*	1.609	.006	-9.60	-1.06
		IVT	5.287	2.359	.154	-.97	11.55
		Bridging	2.839	1.996	.935	-2.46	8.14
	Bridging	Not Treated	-8.173*	2.218	.002	-14.06	-2.29
		IVT	2.448	2.809	1.000	-5.01	9.90
		EVT	-2.839	1.996	.935	-8.14	2.46

Δ NIHSS	Not Treated	IVT	-7.734*	2.231	.004	-13.65	-1.82
		EVT	-5.036*	1.408	.002	-8.77	-1.30
		Bridging	-8.880*	1.941	.000	-14.03	-3.73
	IVT	Not Treated	7.734*	2.231	.004	1.82	13.65
		EVT	2.698	2.064	1.000	-2.78	8.18
		Bridging	-1.146	2.458	1.000	-7.67	5.38
	EVT	Not Treated	5.036*	1.408	.002	1.30	8.77
		IVT	-2.698	2.064	1.000	-8.18	2.78
		Bridging	-3.844	1.747	.171	-8.48	.79
	Bridging	Not Treated	8.880*	1.941	.000	3.73	14.03
		IVT	1.146	2.458	1.000	-5.38	7.67
		EVT	3.844	1.747	.171	-.79	8.48
EF	Not Treated	IVT	-4.064	1.816	.156	-8.89	.76
		EVT	-1.076	1.123	1.000	-4.06	1.91
		Bridging	-2.708	1.488	.420	-6.66	1.25
	IVT	Not Treated	4.064	1.816	.156	-.76	8.89
		EVT	2.988	1.659	.437	-1.42	7.40
		Bridging	1.356	1.926	1.000	-3.76	6.47
	EVT	Not Treated	1.076	1.123	1.000	-1.91	4.06
		IVT	-2.988	1.659	.437	-7.40	1.42
		Bridging	-1.632	1.292	1.000	-5.07	1.80
	Bridging	Not Treated	2.708	1.488	.420	-1.25	6.66
		IVT	-1.356	1.926	1.000	-6.47	3.76
		EVT	1.632	1.292	1.000	-1.80	5.07
CIMT	Not Treated	IVT	.11591	.06396	.427	-.0542	.2860
		EVT	-.00740	.04042	1.000	-.1149	.1001
		Bridging	.06756	.05111	1.000	-.0684	.2035
	IVT	Not Treated	-.11591	.06396	.427	-.2860	.0542

		EVT	-.12331	.05636	.178	-.2732	.0266
		Bridging	-.04836	.06446	1.000	-.2198	.1231
	EVT	Not Treated	.00740	.04042	1.000	-.1001	.1149
		IVT	.12331	.05636	.178	-.0266	.2732
		Bridging	.07496	.04120	.420	-.0346	.1845
	Bridging	Not Treated	-.06756	.05111	1.000	-.2035	.0684
		IVT	.04836	.06446	1.000	-.1231	.2198
		EVT	-.07496	.04120	.420	-.1845	.0346
RBC	Not Treated	IVT	-194801.471	128052.269	.775	-534618.77	145015.82
		EVT	295740.656*	81184.079	.002	80299.30	511182.01
		Bridging	174227.785	112229.589	.729	-123600.25	472055.82
	IVT	Not Treated	194801.471	128052.269	.775	-145015.82	534618.77
		EVT	490542.127*	118400.715	.000	176337.54	804746.72
		Bridging	369029.255	141503.906	.057	-6485.17	744543.68
	EVT	Not Treated	-295740.656*	81184.079	.002	-511182.01	-80299.30
		IVT	-490542.127*	118400.715	.000	-804746.72	-176337.54
		Bridging	-121512.872	101078.318	1.000	-389748.34	146722.60
	Bridging	Not Treated	-174227.785	112229.589	.729	-472055.82	123600.25
		IVT	-369029.255	141503.906	.057	-744543.68	6485.17
		EVT	121512.872	101078.318	1.000	-146722.60	389748.34
HCT	Not Treated	IVT	-.98806	1.07545	1.000	-3.8421	1.8660
		EVT	3.00082*	.67562	.000	1.2078	4.7938
		Bridging	1.63665	.93220	.480	-.8372	4.1105
	IVT	Not Treated	.98806	1.07545	1.000	-1.8660	3.8421
		EVT	3.98888*	.99474	.000	1.3490	6.6287
		Bridging	2.62471	1.18407	.164	-.5176	5.7670
	EVT	Not Treated	-3.00082*	.67562	.000	-4.7938	-1.2078
		IVT	-3.98888*	.99474	.000	-6.6287	-1.3490

		Bridging	-1.36417	.83780	.626	-3.5875	.8592
	Bridging	Not Treated	-1.63665	.93220	.480	-4.1105	.8372
		IVT	-2.62471	1.18407	.164	-5.7670	.5176
		EVT	1.36417	.83780	.626	-.8592	3.5875
Hb	Not Treated	IVT	-3.70746	1.48413	.078	-7.6460	.2311
		EVT	2.07037	.94319	.173	-.4327	4.5734
		Bridging	1.42073	1.30138	1.000	-2.0328	4.8743
	IVT	Not Treated	3.70746	1.48413	.078	-.2311	7.6460
		EVT	5.77783*	1.37004	.000	2.1420	9.4136
		Bridging	5.12818*	1.63737	.011	.7830	9.4734
	EVT	Not Treated	-2.07037	.94319	.173	-4.5734	.4327
		IVT	-5.77783*	1.37004	.000	-9.4136	-2.1420
		Bridging	-.64964	1.16959	1.000	-3.7535	2.4542
	Bridging	Not Treated	-1.42073	1.30138	1.000	-4.8743	2.0328
		IVT	-5.12818*	1.63737	.011	-9.4734	-.7830
		EVT	.64964	1.16959	1.000	-2.4542	3.7535
WBC	Not Treated	IVT	256.717	747.427	1.000	-1726.69	2240.13
		EVT	-84.207	473.446	1.000	-1340.57	1172.15
		Bridging	421.404	650.663	1.000	-1305.23	2148.03
	IVT	Not Treated	-256.717	747.427	1.000	-2240.13	1726.69
		EVT	-340.924	690.807	1.000	-2174.08	1492.23
		Bridging	164.688	822.450	1.000	-2017.81	2347.18
	EVT	Not Treated	84.207	473.446	1.000	-1172.15	1340.57
		IVT	340.924	690.807	1.000	-1492.23	2174.08
		Bridging	505.611	584.747	1.000	-1046.10	2057.32
	Bridging	Not Treated	-421.404	650.663	1.000	-2148.03	1305.23
		IVT	-164.687	822.450	1.000	-2347.18	2017.81
		EVT	-505.611	584.747	1.000	-2057.32	1046.10

Neutrophils	Not Treated	IVT	-.3195	2.4395	1.000	-6.793	6.154
		EVT	-3.9102	1.5453	.071	-8.011	.190
		Bridging	1.6076	2.1237	1.000	-4.028	7.243
	IVT	Not Treated	.3195	2.4395	1.000	-6.154	6.793
		EVT	-3.5907	2.2547	.673	-9.574	2.393
		Bridging	1.9271	2.6844	1.000	-5.196	9.051
	EVT	Not Treated	3.9102	1.5453	.071	-.190	8.011
		IVT	3.5907	2.2547	.673	-2.393	9.574
		Bridging	5.5178*	1.9086	.025	.453	10.582
	Bridging	Not Treated	-1.6076	2.1237	1.000	-7.243	4.028
		IVT	-1.9271	2.6844	1.000	-9.051	5.196
		EVT	-5.5178*	1.9086	.025	-10.582	-.453
Lymphocytes	Not Treated	IVT	-.1935	2.0981	1.000	-5.761	5.374
		EVT	3.5273	1.3322	.051	-.008	7.063
		Bridging	-.4018	1.8275	1.000	-5.251	4.448
	IVT	Not Treated	.1935	2.0981	1.000	-5.374	5.761
		EVT	3.7207	1.9360	.333	-1.417	8.858
		Bridging	-.2083	2.3050	1.000	-6.325	5.908
	EVT	Not Treated	-3.5273	1.3322	.051	-7.063	.008
		IVT	-3.7207	1.9360	.333	-8.858	1.417
		Bridging	-3.9291	1.6388	.102	-8.278	.420
	Bridging	Not Treated	.4018	1.8275	1.000	-4.448	5.251
		IVT	.2083	2.3050	1.000	-5.908	6.325
		EVT	3.9291	1.6388	.102	-.420	8.278
Neu Count	Not Treated	IVT	1800.68603	1627.30546	1.000	-2517.6102	6118.9822
		EVT	1169.76639	1030.79209	1.000	-1565.5932	3905.1259
		Bridging	1763.87353	1416.62969	1.000	-1995.3633	5523.1104
	IVT	Not Treated	-1800.68603	1627.30546	1.000	-6118.9822	2517.6102

		EVT	-630.91964	1504.03106	1.000	-4622.0890	3360.2497
		Bridging	-36.81250	1790.64703	1.000	-4788.5598	4714.9348
	EVT	Not Treated	-1169.76639	1030.79209	1.000	-3905.1259	1565.5932
		IVT	630.91964	1504.03106	1.000	-3360.2497	4622.0890
		Bridging	594.10714	1273.11668	1.000	-2784.2966	3972.5109
	Bridging	Not Treated	-1763.87353	1416.62969	1.000	-5523.1104	1995.3633
		IVT	36.81250	1790.64703	1.000	-4714.9348	4788.5598
		EVT	-594.10714	1273.11668	1.000	-3972.5109	2784.2966
Lym Count	Not Treated	IVT	126.52083	373.67894	1.000	-865.1085	1118.1502
		EVT	429.32509	237.27378	.428	-200.3268	1058.9770
		Bridging	358.93750	325.47000	1.000	-504.7601	1222.6351
	IVT	Not Treated	-126.52083	373.67894	1.000	-1118.1502	865.1085
		EVT	302.80426	344.81049	1.000	-612.2171	1217.8256
		Bridging	232.41667	410.51936	1.000	-856.9759	1321.8092
	EVT	Not Treated	-429.32509	237.27378	.428	-1058.9770	200.3268
		IVT	-302.80426	344.81049	1.000	-1217.8256	612.2171
		Bridging	-70.38759	291.87162	1.000	-844.9254	704.1502
	Bridging	Not Treated	-358.93750	325.47000	1.000	-1222.6351	504.7601
		IVT	-232.41667	410.51936	1.000	-1321.8092	856.9759
		EVT	70.38759	291.87162	1.000	-704.1502	844.9254
NLR	Not Treated	IVT	.22437	.81507	1.000	-1.9386	2.3873
		EVT	-.85456	.51755	.598	-2.2280	.5188
		Bridging	-.38917	.70992	1.000	-2.2731	1.4947
	IVT	Not Treated	-.22437	.81507	1.000	-2.3873	1.9386
		EVT	-1.07894	.75211	.914	-3.0748	.9169
		Bridging	-.61354	.89543	1.000	-2.9897	1.7627
	EVT	Not Treated	.85456	.51755	.598	-.5188	2.2280
		IVT	1.07894	.75211	.914	-.9169	3.0748

		Bridging	.46539	.63663	1.000	-1.2240	2.1548
	Bridging	Not Treated	.38917	.70992	1.000	-1.4947	2.2731
		IVT	.61354	.89543	1.000	-1.7627	2.9897
		EVT	-.46539	.63663	1.000	-2.1548	1.2240
Platelets	Not Treated	IVT	-19986.029	14886.524	1.000	-59489.63	19517.57
		EVT	-4791.661	9429.644	1.000	-29814.62	20231.30
		Bridging	159.804	12959.270	1.000	-34229.54	34549.15
	IVT	Not Treated	19986.029	14886.524	1.000	-19517.57	59489.63
		EVT	15194.368	13758.814	1.000	-21316.68	51705.42
		Bridging	20145.833	16380.766	1.000	-23322.96	63614.62
	EVT	Not Treated	4791.661	9429.644	1.000	-20231.30	29814.62
		IVT	-15194.368	13758.814	1.000	-51705.42	21316.68
		Bridging	4951.465	11646.419	1.000	-25954.03	35856.96
	Bridging	Not Treated	-159.804	12959.270	1.000	-34549.15	34229.54
		IVT	-20145.833	16380.766	1.000	-63614.62	23322.96
		EVT	-4951.465	11646.419	1.000	-35856.96	25954.03
CRP	Not Treated	IVT	2.57167	1.31683	.311	-.9259	6.0692
		EVT	1.55547	.78428	.290	-.5276	3.6386
		Bridging	2.28857	1.08132	.211	-.5835	5.1606
	IVT	Not Treated	-2.57167	1.31683	.311	-6.0692	.9259
		EVT	-1.01619	1.23159	1.000	-4.2873	2.2550
		Bridging	-.28310	1.43908	1.000	-4.1054	3.5392
	EVT	Not Treated	-1.55547	.78428	.290	-3.6386	.5276
		IVT	1.01619	1.23159	1.000	-2.2550	4.2873
		Bridging	.73310	.97570	1.000	-1.8584	3.3246
	Bridging	Not Treated	-2.28857	1.08132	.211	-5.1606	.5835
		IVT	.28310	1.43908	1.000	-3.5392	4.1054
		EVT	-.73310	.97570	1.000	-3.3246	1.8584

PT	Not Treated	IVT	.29923	3.99094	1.000	-10.2962	10.8946
		EVT	4.26984	2.49635	.529	-2.3576	10.8973
		Bridging	-1.73649	3.37727	1.000	-10.7027	7.2297
	IVT	Not Treated	-.29923	3.99094	1.000	-10.8946	10.2962
		EVT	3.97061	3.66262	1.000	-5.7532	13.6944
		Bridging	-2.03571	4.31150	1.000	-13.4822	9.4107
	EVT	Not Treated	-4.26984	2.49635	.529	-10.8973	2.3576
		IVT	-3.97061	3.66262	1.000	-13.6944	5.7532
		Bridging	-6.00632	2.98214	.269	-13.9235	1.9109
	Bridging	Not Treated	1.73649	3.37727	1.000	-7.2297	10.7027
		IVT	2.03571	4.31150	1.000	-9.4107	13.4822
		EVT	6.00632	2.98214	.269	-1.9109	13.9235
APTT	Not Treated	IVT	.93135	.98361	1.000	-1.6801	3.5428
		EVT	1.05479	.61886	.536	-.5883	2.6979
		Bridging	1.95604	.83361	.117	-.2572	4.1693
	IVT	Not Treated	-.93135	.98361	1.000	-3.5428	1.6801
		EVT	.12344	.89927	1.000	-2.2641	2.5110
		Bridging	1.02469	1.05859	1.000	-1.7858	3.8352
	EVT	Not Treated	-1.05479	.61886	.536	-2.6979	.5883
		IVT	-.12344	.89927	1.000	-2.5110	2.2641
		Bridging	.90125	.73220	1.000	-1.0427	2.8452
	Bridging	Not Treated	-1.95604	.83361	.117	-4.1693	.2572
		IVT	-1.02469	1.05859	1.000	-3.8352	1.7858
		EVT	-.90125	.73220	1.000	-2.8452	1.0427
INR	Not Treated	IVT	.00091	.06892	1.000	-.1821	.1839
		EVT	-.06915	.04307	.656	-.1835	.0452
		Bridging	.02836	.05832	1.000	-.1265	.1832
	IVT	Not Treated	-.00091	.06892	1.000	-.1839	.1821

		EVT	-.07006	.06322	1.000	-.2379	.0978
		Bridging	.02745	.07445	1.000	-.1702	.2251
	EVT	Not Treated	.06915	.04307	.656	-.0452	.1835
		IVT	.07006	.06322	1.000	-.0978	.2379
		Bridging	.09751	.05147	.354	-.0391	.2341
	Bridging	Not Treated	-.02836	.05832	1.000	-.1832	.1265
		IVT	-.02745	.07445	1.000	-.2251	.1702
		EVT	-.09751	.05147	.354	-.2341	.0391
LDL	Not Treated	IVT	-10.8892	7.4025	.854	-30.544	8.765
		EVT	7.3315	4.7674	.751	-5.327	19.990
		Bridging	5.6290	6.5108	1.000	-11.658	22.916
	IVT	Not Treated	10.8892	7.4025	.854	-8.765	30.544
		EVT	18.2207*	6.7758	.045	.230	36.211
		Bridging	16.5182	8.0978	.253	-4.983	38.019
	EVT	Not Treated	-7.3315	4.7674	.751	-19.990	5.327
		IVT	-18.2207*	6.7758	.045	-36.211	-.230
		Bridging	-1.7025	5.7884	1.000	-17.072	13.666
	Bridging	Not Treated	-5.6290	6.5108	1.000	-22.916	11.658
		IVT	-16.5182	8.0978	.253	-38.019	4.983
		EVT	1.7025	5.7884	1.000	-13.666	17.072
HDL	Not Treated	IVT	.623	3.115	1.000	-7.65	8.89
		EVT	-2.072	2.006	1.000	-7.40	3.25
		Bridging	-.471	2.740	1.000	-7.74	6.80
	IVT	Not Treated	-.623	3.115	1.000	-8.89	7.65
		EVT	-2.695	2.851	1.000	-10.27	4.88
		Bridging	-1.094	3.407	1.000	-10.14	7.95
	EVT	Not Treated	2.072	2.006	1.000	-3.25	7.40
		IVT	2.695	2.851	1.000	-4.88	10.27

		Bridging	1.601	2.436	1.000	-4.87	8.07
	Bridging	Not Treated	.471	2.740	1.000	-6.80	7.74
		IVT	1.094	3.407	1.000	-7.95	10.14
		EVT	-1.601	2.436	1.000	-8.07	4.87
Triglycerides	Not Treated	IVT	-8.351	11.442	1.000	-38.73	22.03
		EVT	10.208	7.189	.940	-8.88	29.30
		Bridging	8.990	9.818	1.000	-17.08	35.06
	IVT	Not Treated	8.351	11.442	1.000	-22.03	38.73
		EVT	18.559	10.522	.473	-9.38	46.50
		Bridging	17.341	12.467	.991	-15.76	50.44
	EVT	Not Treated	-10.208	7.189	.940	-29.30	8.88
		IVT	-18.559	10.522	.473	-46.50	9.38
		Bridging	-1.218	8.728	1.000	-24.39	21.96
	Bridging	Not Treated	-8.990	9.818	1.000	-35.06	17.08
		IVT	-17.341	12.467	.991	-50.44	15.76
		EVT	1.218	8.728	1.000	-21.96	24.39
Cholesterol	Not Treated	IVT	-12.067	8.897	1.000	-35.69	11.55
		EVT	9.117	5.704	.666	-6.03	24.26
		Bridging	8.008	7.821	1.000	-12.76	28.77
	IVT	Not Treated	12.067	8.897	1.000	-11.55	35.69
		EVT	21.184	8.152	.059	-.46	42.83
		Bridging	20.074	9.751	.242	-5.81	45.96
	EVT	Not Treated	-9.117	5.704	.666	-24.26	6.03
		IVT	-21.184	8.152	.059	-42.83	.46
		Bridging	-1.109	6.962	1.000	-19.59	17.37
	Bridging	Not Treated	-8.008	7.821	1.000	-28.77	12.76
		IVT	-20.074	9.751	.242	-45.96	5.81
		EVT	1.109	6.962	1.000	-17.37	19.59

Na	Not Treated	IVT	.636	.896	1.000	-1.74	3.01
		EVT	.552	.569	1.000	-.96	2.06
		Bridging	-.955	.785	1.000	-3.04	1.13
	IVT	Not Treated	-.636	.896	1.000	-3.01	1.74
		EVT	-.084	.829	1.000	-2.28	2.12
		Bridging	-1.591	.990	.653	-4.22	1.04
	EVT	Not Treated	-.552	.569	1.000	-2.06	.96
		IVT	.084	.829	1.000	-2.12	2.28
		Bridging	-1.507	.708	.204	-3.39	.37
	Bridging	Not Treated	.955	.785	1.000	-1.13	3.04
		IVT	1.591	.990	.653	-1.04	4.22
		EVT	1.507	.708	.204	-.37	3.39
K	Not Treated	IVT	.03466	.12233	1.000	-.2900	.3593
		EVT	-.05097	.07776	1.000	-.2573	.1554
		Bridging	.13682	.10721	1.000	-.1477	.4213
	IVT	Not Treated	-.03466	.12233	1.000	-.3593	.2900
		EVT	-.08563	.11325	1.000	-.3862	.2149
		Bridging	.10215	.13518	1.000	-.2566	.4609
	EVT	Not Treated	.05097	.07776	1.000	-.1554	.2573
		IVT	.08563	.11325	1.000	-.2149	.3862
		Bridging	.18779	.09673	.318	-.0689	.4445
	Bridging	Not Treated	-.13682	.10721	1.000	-.4213	.1477
		IVT	-.10215	.13518	1.000	-.4609	.2566
		EVT	-.18779	.09673	.318	-.4445	.0689
Az	Not Treated	IVT	7.811	6.385	1.000	-9.13	24.75
		EVT	-.893	4.051	1.000	-11.64	9.86
		Bridging	6.900	5.596	1.000	-7.95	21.75
	IVT	Not Treated	-7.811	6.385	1.000	-24.75	9.13

		EVT	-8.704	5.906	.849	-24.38	6.97
		Bridging	-.911	7.055	1.000	-19.63	17.81
	EVT	Not Treated	.893	4.051	1.000	-9.86	11.64
		IVT	8.704	5.906	.849	-6.97	24.38
		Bridging	7.793	5.043	.739	-5.59	21.18
	Bridging	Not Treated	-6.900	5.596	1.000	-21.75	7.95
		IVT	.911	7.055	1.000	-17.81	19.63
		EVT	-7.793	5.043	.739	-21.18	5.59
Cr	Not Treated	IVT	-.19040	.16469	1.000	-.6274	.2466
		EVT	.02196	.10450	1.000	-.2554	.2993
		Bridging	.09870	.14434	1.000	-.2843	.4817
	IVT	Not Treated	.19040	.16469	1.000	-.2466	.6274
		EVT	.21236	.15234	.985	-.1919	.6166
		Bridging	.28910	.18199	.679	-.1939	.7721
	EVT	Not Treated	-.02196	.10450	1.000	-.2993	.2554
		IVT	-.21236	.15234	.985	-.6166	.1919
		Bridging	.07674	.13007	1.000	-.2684	.4219
	Bridging	Not Treated	-.09870	.14434	1.000	-.4817	.2843
		IVT	-.28910	.18199	.679	-.7721	.1939
		EVT	-.07674	.13007	1.000	-.4219	.2684
Ca	Not Treated	IVT	.31398	.36371	1.000	-.6600	1.2880
		EVT	.36490	.17253	.218	-.0971	.8269
		Bridging	.30160	.23048	1.000	-.3156	.9188
	IVT	Not Treated	-.31398	.36371	1.000	-1.2880	.6600
		EVT	.05092	.34518	1.000	-.8735	.9753
		Bridging	-.01238	.37750	1.000	-1.0233	.9986
	EVT	Not Treated	-.36490	.17253	.218	-.8269	.0971
		IVT	-.05092	.34518	1.000	-.9753	.8735

		Bridging	-.06330	.19995	1.000	-.5988	.4722
	Bridging	Not Treated	-.30160	.23048	1.000	-.9188	.3156
		IVT	.01238	.37750	1.000	-.9986	1.0233
		EVT	.06330	.19995	1.000	-.4722	.5988
Systolic_Blood_Pressure	Not Treated	IVT	5.890	5.464	1.000	-8.62	20.40
		EVT	8.977*	3.335	.045	.12	17.84
		Bridging	7.951	4.629	.522	-4.35	20.25
	IVT	Not Treated	-5.890	5.464	1.000	-20.40	8.62
		EVT	3.087	5.006	1.000	-10.21	16.38
		Bridging	2.061	5.947	1.000	-13.74	17.86
	EVT	Not Treated	-8.977*	3.335	.045	-17.84	-.12
		IVT	-3.087	5.006	1.000	-16.38	10.21
		Bridging	-1.026	4.079	1.000	-11.86	9.81
	Bridging	Not Treated	-7.951	4.629	.522	-20.25	4.35
		IVT	-2.061	5.947	1.000	-17.86	13.74
		EVT	1.026	4.079	1.000	-9.81	11.86
Dyastolic_Blood_Pressure	Not Treated	IVT	5.108	3.454	.842	-4.07	14.28
		EVT	5.756*	2.102	.039	.17	11.34
		Bridging	7.692	2.925	.054	-.08	15.46
	IVT	Not Treated	-5.108	3.454	.842	-14.28	4.07
		EVT	.648	3.171	1.000	-7.78	9.07
		Bridging	2.583	3.767	1.000	-7.42	12.59
	EVT	Not Treated	-5.756*	2.102	.039	-11.34	-.17
		IVT	-.648	3.171	1.000	-9.07	7.78
		Bridging	1.936	2.584	1.000	-4.93	8.80
	Bridging	Not Treated	-7.692	2.925	.054	-15.46	.08
		IVT	-2.583	3.767	1.000	-12.59	7.42
		EVT	-1.936	2.584	1.000	-8.80	4.93

Heart_Rate	Not Treated	IVT	1.507	3.600	1.000	-8.06	11.07
		EVT	4.641	2.180	.205	-1.15	10.43
		Bridging	3.507	3.069	1.000	-4.65	11.66
	IVT	Not Treated	-1.507	3.600	1.000	-11.07	8.06
		EVT	3.134	3.320	1.000	-5.69	11.95
		Bridging	2.000	3.961	1.000	-8.52	12.52
	EVT	Not Treated	-4.641	2.180	.205	-10.43	1.15
		IVT	-3.134	3.320	1.000	-11.95	5.69
		Bridging	-1.134	2.735	1.000	-8.40	6.13
	Bridging	Not Treated	-3.507	3.069	1.000	-11.66	4.65
		IVT	-2.000	3.961	1.000	-12.52	8.52
		EVT	1.134	2.735	1.000	-6.13	8.40
Blood_Oxygen	Not Treated	IVT	-.842	.550	.760	-2.30	.62
		EVT	.016	.316	1.000	-.82	.86
		Bridging	-.345	.439	1.000	-1.51	.82
	IVT	Not Treated	.842	.550	.760	-.62	2.30
		EVT	.859	.510	.558	-.50	2.21
		Bridging	.497	.594	1.000	-1.08	2.08
	EVT	Not Treated	-.016	.316	1.000	-.86	.82
		IVT	-.859	.510	.558	-2.21	.50
		Bridging	-.361	.388	1.000	-1.39	.67
	Bridging	Not Treated	.345	.439	1.000	-.82	1.51
		IVT	-.497	.594	1.000	-2.08	1.08
		EVT	.361	.388	1.000	-.67	1.39
Blood_Glucose	Not Treated	IVT	27.457	11.523	.107	-3.16	58.08
		EVT	9.786	6.915	.949	-8.59	28.16
		Bridging	27.280*	9.407	.024	2.28	52.28
	IVT	Not Treated	-27.457	11.523	.107	-58.08	3.16

		EVT	-17.671	10.577	.575	-45.77	10.43
		Bridging	-.177	12.351	1.000	-32.99	32.64
	EVT	Not Treated	-9.786	6.915	.949	-28.16	8.59
		IVT	17.671	10.577	.575	-10.43	45.77
		Bridging	17.494	8.221	.205	-4.35	39.34
	Bridging	Not Treated	-27.280*	9.407	.024	-52.28	-2.28
		IVT	.177	12.351	1.000	-32.64	32.99
		EVT	-17.494	8.221	.205	-39.34	4.35
pre-stroke mRS	Not Treated	IVT	.795*	.287	.036	.03	1.56
		EVT	.777*	.174	.000	.31	1.24
		Bridging	.918*	.217	.000	.34	1.50
	IVT	Not Treated	-.795*	.287	.036	-1.56	-.03
		EVT	-.019	.255	1.000	-.70	.66
		Bridging	.122	.286	1.000	-.64	.88
	EVT	Not Treated	-.777*	.174	.000	-1.24	-.31
		IVT	.019	.255	1.000	-.66	.70
		Bridging	.141	.173	1.000	-.32	.60
	Bridging	Not Treated	-.918*	.217	.000	-1.50	-.34
		IVT	-.122	.286	1.000	-.88	.64
		EVT	-.141	.173	1.000	-.60	.32
3-month mRS	Not Treated	IVT	2.258*	.494	.000	.94	3.57
		EVT	1.521*	.340	.000	.62	2.43
		Bridging	1.970*	.448	.000	.78	3.16
	IVT	Not Treated	-2.258*	.494	.000	-3.57	-.94
		EVT	-.737	.433	.540	-1.89	.42
		Bridging	-.288	.522	1.000	-1.68	1.10
	EVT	Not Treated	-1.521*	.340	.000	-2.43	-.62
		IVT	.737	.433	.540	-.42	1.89

		Bridging	.449	.380	1.000	-.56	1.46
	Bridging	Not Treated	-1.970*	.448	.000	-3.16	-.78
		IVT	.288	.522	1.000	-1.10	1.68
		EVT	-.449	.380	1.000	-1.46	.56

*. The mean difference is significant at the 0.05 level.

Custom Tables

Warnings

Pairwise comparisons are requested but no eligible subtables are found in table "1".

Table 1

		INTERVENTION															
		Not Treated				IVT				EVT				Bridging			
		Count	Column N %	Table N %	Row N %	Count	Column N %	Table N %	Row N %	Count	Column N %	Table N %	Row N %	Count	Column N %	Table N %	Row N %
S	Male	46	53.5%	13.2%	28.6%	15	46.9%	4.3%	9.3%	78	42.6%	22.3%	48.4%	22	45.8%	6.3%	13.7%
	Female	40	46.5%	11.5%	21.3%	17	53.1%	4.9%	9.0%	105	57.4%	30.1%	55.9%	26	54.2%	7.4%	13.8%
Occluded vessel	ACA	2	2.3%	0.6%	66.7%	1	3.1%	0.3%	33.3%	0	0.0%	0.0%	0.0%	0	0.0%	0.0%	0.0%
	MCA	48	55.8%	13.8%	23.0%	25	78.1%	7.2%	12.0%	101	55.2%	28.9%	48.3%	35	72.9%	10.0%	16.7%
	T-Carotids	7	8.1%	2.0%	21.9%	0	0.0%	0.0%	0.0%	22	12.0%	6.3%	68.8%	3	6.3%	0.9%	9.4%
	ICA Intra	2	2.3%	0.6%	28.6%	1	3.1%	0.3%	14.3%	4	2.2%	1.1%	57.1%	0	0.0%	0.0%	0.0%
	ICA extra	10	11.6%	2.9%	31.3%	1	3.1%	0.3%	3.1%	17	9.3%	4.9%	53.1%	4	8.3%	1.1%	12.5%
	Tandem	4	4.7%	1.1%	12.1%	0	0.0%	0.0%	0.0%	25	13.7%	7.2%	75.8%	4	8.3%	1.1%	12.1%
	Combined (MCA+ACA/PCA)	4	4.7%	1.1%	44.4%	0	0.0%	0.0%	0.0%	4	2.2%	1.1%	44.4%	1	2.1%	0.3%	11.1%
	VB	9	10.5%	2.6%	37.5%	4	12.5%	1.1%	16.7%	10	5.5%	2.9%	41.7%	1	2.1%	0.3%	4.2%

Side	Right	38	44.2%	10.9%	26.4%	13	40.6%	3.7%	9.0%	74	40.4%	21.2%	51.4%	19	39.6%	5.4%	13.2%
	Left	47	54.7%	13.5%	23.7%	18	56.3%	5.2%	9.1%	105	57.4%	30.1%	53.0%	28	58.3%	8.0%	14.1%
	Bilateral	1	1.2%	0.3%	14.3%	1	3.1%	0.3%	14.3%	4	2.2%	1.1%	57.1%	1	2.1%	0.3%	14.3%
Circulation	Posterior	9	10.5%	2.6%	37.5%	4	12.5%	1.1%	16.7%	10	5.5%	2.9%	41.7%	1	2.1%	0.3%	4.2%
	Anterior	76	88.4%	21.8%	23.7%	27	84.4%	7.7%	8.4%	172	94.0%	49.3%	53.6%	46	95.8%	13.2%	14.3%
	Posterior+Anterior	1	1.2%	0.3%	25.0%	1	3.1%	0.3%	25.0%	1	0.5%	0.3%	25.0%	1	2.1%	0.3%	25.0%
Perfusion deficit (Yes/No)	No	9	10.5%	2.6%	69.2%	2	6.3%	0.6%	15.4%	2	1.1%	0.6%	15.4%	0	0.0%	0.0%	0.0%
	Yes	52	60.5%	14.9%	17.7%	19	59.4%	5.4%	6.5%	176	96.2%	50.4%	60.1%	46	95.8%	13.2%	15.7%
	Yes No Penumbra	25	29.1%	7.2%	58.1%	11	34.4%	3.2%	25.6%	5	2.7%	1.4%	11.6%	2	4.2%	0.6%	4.7%
Ischemic lesion at CT/MR control (Yes/No)	No	2	2.3%	0.6%	20.0%	2	6.3%	0.6%	20.0%	5	2.7%	1.4%	50.0%	1	2.1%	0.3%	10.0%
	Yes	84	97.7%	24.1%	24.8%	30	93.8%	8.6%	8.8%	178	97.3%	51.0%	52.5%	47	97.9%	13.5%	13.9%
Anatomical inclusion of hypoperfused area in the ischemic lesion at CT/MR control (Yes/No)	No	1	1.2%	0.3%	33.3%	0	0.0%	0.0%	0.0%	2	1.1%	0.6%	66.7%	0	0.0%	0.0%	0.0%
	Yes	85	98.8%	24.4%	24.6%	32	100.0%	9.2%	9.2%	181	98.9%	51.9%	52.3%	48	100.0%	13.8%	13.9%
DWI Core inclusion in FIA	Partial (Core Higher)	6	7.0%	1.7%	26.1%	1	3.1%	0.3%	4.3%	13	7.1%	3.7%	56.5%	3	6.3%	0.9%	13.0%
	Complete (core equal)	56	65.1%	16.0%	26.3%	26	81.3%	7.4%	12.2%	100	54.6%	28.7%	46.9%	31	64.6%	8.9%	14.6%
	Higher (Ischemia>Core)	22	25.6%	6.3%	21.4%	3	9.4%	0.9%	2.9%	65	35.5%	18.6%	63.1%	13	27.1%	3.7%	12.6%
	No FIA	2	2.3%	0.6%	20.0%	2	6.3%	0.6%	20.0%	5	2.7%	1.4%	50.0%	1	2.1%	0.3%	10.0%
pcASL Penumbra inclusion in FIA	Partial (Penumbra higher)	23	30.3%	7.2%	11.9%	12	37.5%	3.8%	6.2%	125	74.4%	39.2%	64.4%	34	79.1%	10.7%	17.5%
	Complete (Penumbra equal)	48	63.2%	15.0%	45.3%	18	56.3%	5.6%	17.0%	33	19.6%	10.3%	31.1%	7	16.3%	2.2%	6.6%
	Higher (Ischemia>Penumbra)	2	2.6%	0.6%	28.6%	0	0.0%	0.0%	0.0%	4	2.4%	1.3%	57.1%	1	2.3%	0.3%	14.3%
	No FIA	3	3.9%	0.9%	25.0%	2	6.3%	0.6%	16.7%	6	3.6%	1.9%	50.0%	1	2.3%	0.3%	8.3%
TICI	0	0	0.0%	0.0%	0.0%	0	0.0%	0.0%	0.0%	23	13.1%	10.5%	85.2%	4	9.3%	1.8%	14.8%
	1	0	0.0%	0.0%	0.0%	0	0.0%	0.0%	0.0%	3	1.7%	1.4%	100.0%	0	0.0%	0.0%	0.0%
	2a	0	0.0%	0.0%	0.0%	0	0.0%	0.0%	0.0%	13	7.4%	5.9%	92.9%	1	2.3%	0.5%	7.1%

	2b	0	0.0%	0.0%	0.0%	0	0.0%	0.0%	0.0%	39	22.2%	17.7%	76.5%	12	27.9%	5.5%	23.5%
	2c	0	0.0%	0.0%	0.0%	0	0.0%	0.0%	0.0%	44	25.0%	20.0%	80.0%	11	25.6%	5.0%	20.0%
	3	0	0.0%	0.0%	0.0%	1	100.0%	0.5%	1.4%	54	30.7%	24.5%	77.1%	15	34.9%	6.8%	21.4%
Successful EVT treatment (Yes/No)	TICI 0-2a	0	0.0%	0.0%	0.0%	0	0.0%	0.0%	0.0%	39	22.2%	17.7%	88.6%	5	11.6%	2.3%	11.4%
	TICI 2b-3	0	0.0%	0.0%	0.0%	1	100.0%	0.5%	0.6%	137	77.8%	62.3%	77.8%	38	88.4%	17.3%	21.6%
Favourable Clinical Response	No	86	100.0%	24.6%	35.1%	17	53.1%	4.9%	6.9%	119	65.0%	34.1%	48.6%	23	47.9%	6.6%	9.4%
	Yes	0	0.0%	0.0%	0.0%	15	46.9%	4.3%	14.4%	64	35.0%	18.3%	61.5%	25	52.1%	7.2%	24.0%
TOAST	Athero	14	16.3%	4.0%	16.3%	6	18.8%	1.7%	7.0%	51	27.9%	14.6%	59.3%	15	31.3%	4.3%	17.4%
	Cardio	24	27.9%	6.9%	23.5%	7	21.9%	2.0%	6.9%	58	31.7%	16.6%	56.9%	13	27.1%	3.7%	12.7%
	Small vessels	8	9.3%	2.3%	80.0%	2	6.3%	0.6%	20.0%	0	0.0%	0.0%	0.0%	0	0.0%	0.0%	0.0%
	Other Causes	4	4.7%	1.1%	28.6%	0	0.0%	0.0%	0.0%	7	3.8%	2.0%	50.0%	3	6.3%	0.9%	21.4%
	Undetermined (multiple causes)	7	8.1%	2.0%	87.5%	0	0.0%	0.0%	0.0%	1	0.5%	0.3%	12.5%	0	0.0%	0.0%	0.0%
	Undetermined (iter not completed)	29	33.7%	8.3%	22.5%	17	53.1%	4.9%	13.2%	66	36.1%	18.9%	51.2%	17	35.4%	4.9%	13.2%
Smoking	No	39	60.9%	12.9%	17.0%	17	81.0%	5.6%	7.4%	143	82.7%	47.2%	62.2%	31	68.9%	10.2%	13.5%
	Yes	25	39.1%	8.3%	34.2%	4	19.0%	1.3%	5.5%	30	17.3%	9.9%	41.1%	14	31.1%	4.6%	19.2%
Former_Smoker	No	53	82.8%	17.7%	21.5%	17	81.0%	5.7%	6.9%	138	81.2%	46.2%	56.1%	38	86.4%	12.7%	15.4%
	Yes	11	17.2%	3.7%	20.8%	4	19.0%	1.3%	7.5%	32	18.8%	10.7%	60.4%	6	13.6%	2.0%	11.3%
Diabetes	No	49	64.5%	14.9%	19.8%	21	87.5%	6.4%	8.5%	137	75.3%	41.6%	55.5%	40	85.1%	12.2%	16.2%
	Yes	27	35.5%	8.2%	32.9%	3	12.5%	0.9%	3.7%	45	24.7%	13.7%	54.9%	7	14.9%	2.1%	8.5%
Previous_Stroke/TIA	No	60	78.9%	18.3%	21.7%	18	75.0%	5.5%	6.5%	156	86.2%	47.6%	56.3%	43	91.5%	13.1%	15.5%
	Yes	16	21.1%	4.9%	31.4%	6	25.0%	1.8%	11.8%	25	13.8%	7.6%	49.0%	4	8.5%	1.2%	7.8%
Coronary_artery_disease	No	65	81.3%	19.5%	23.0%	25	86.2%	7.5%	8.9%	151	84.4%	45.2%	53.5%	41	89.1%	12.3%	14.5%
	Yes	15	18.8%	4.5%	28.8%	4	13.8%	1.2%	7.7%	28	15.6%	8.4%	53.8%	5	10.9%	1.5%	9.6%
EF≤40%	No	57	93.4%	20.4%	22.0%	23	100.0%	8.2%	8.9%	140	90.9%	50.0%	54.1%	39	92.9%	13.9%	15.1%
	Yes	4	6.6%	1.4%	19.0%	0	0.0%	0.0%	0.0%	14	9.1%	5.0%	66.7%	3	7.1%	1.1%	14.3%
Hyperlipemia	No	49	64.5%	14.9%	24.9%	14	58.3%	4.3%	7.1%	110	60.8%	33.5%	55.8%	24	51.1%	7.3%	12.2%
	Yes	27	35.5%	8.2%	20.6%	10	41.7%	3.0%	7.6%	71	39.2%	21.6%	54.2%	23	48.9%	7.0%	17.6%

K_Hystory	No	65	86.7%	19.9%	23.0%	19	79.2%	5.8%	6.7%	159	87.8%	48.6%	56.2%	40	85.1%	12.2%	14.1%
	Yes	10	13.3%	3.1%	22.7%	5	20.8%	1.5%	11.4%	22	12.2%	6.7%	50.0%	7	14.9%	2.1%	15.9%
Known_Atrial_Fibrillation	No	59	72.8%	17.5%	22.7%	27	87.1%	8.0%	10.4%	130	72.6%	38.5%	50.0%	44	93.6%	13.0%	16.9%
	Yes	22	27.2%	6.5%	28.2%	4	12.9%	1.2%	5.1%	49	27.4%	14.5%	62.8%	3	6.4%	0.9%	3.8%
Newonset_AF	No	74	91.4%	21.9%	24.8%	29	93.5%	8.6%	9.7%	157	87.7%	46.4%	52.7%	38	80.9%	11.2%	12.8%
	Yes	7	8.6%	2.1%	17.5%	2	6.5%	0.6%	5.0%	22	12.3%	6.5%	55.0%	9	19.1%	2.7%	22.5%
Hypertension	No	13	17.1%	4.0%	16.9%	8	33.3%	2.4%	10.4%	42	23.2%	12.8%	54.5%	14	29.8%	4.3%	18.2%
	Yes	63	82.9%	19.2%	25.1%	16	66.7%	4.9%	6.4%	139	76.8%	42.4%	55.4%	33	70.2%	10.1%	13.1%
Carotid_Stenosis_left	No	10	21.7%	3.6%	12.8%	12	52.2%	4.4%	15.4%	41	25.3%	15.0%	52.6%	15	34.9%	5.5%	19.2%
	<50%	20	43.5%	7.3%	15.7%	9	39.1%	3.3%	7.1%	79	48.8%	28.8%	62.2%	19	44.2%	6.9%	15.0%
	50-70%	12	26.1%	4.4%	36.4%	2	8.7%	0.7%	6.1%	16	9.9%	5.8%	48.5%	3	7.0%	1.1%	9.1%
	>70%	3	6.5%	1.1%	16.7%	0	0.0%	0.0%	0.0%	12	7.4%	4.4%	66.7%	3	7.0%	1.1%	16.7%
	Occlusion	1	2.2%	0.4%	5.6%	0	0.0%	0.0%	0.0%	14	8.6%	5.1%	77.8%	3	7.0%	1.1%	16.7%
Carotid_Stenosis_right	No	8	17.4%	2.9%	11.6%	9	39.1%	3.3%	13.0%	36	22.2%	13.1%	52.2%	16	37.2%	5.8%	23.2%
	<50%	28	60.9%	10.2%	20.6%	13	56.5%	4.7%	9.6%	80	49.4%	29.2%	58.8%	15	34.9%	5.5%	11.0%
	50-70%	7	15.2%	2.6%	22.6%	1	4.3%	0.4%	3.2%	19	11.7%	6.9%	61.3%	4	9.3%	1.5%	12.9%
	>70%	1	2.2%	0.4%	5.6%	0	0.0%	0.0%	0.0%	14	8.6%	5.1%	77.8%	3	7.0%	1.1%	16.7%
	Occlusion	2	4.3%	0.7%	10.0%	0	0.0%	0.0%	0.0%	13	8.0%	4.7%	65.0%	5	11.6%	1.8%	25.0%
Stenosis dicho	<50%	36	41.9%	10.3%	17.6%	22	68.8%	6.3%	10.7%	116	63.4%	33.2%	56.6%	31	64.6%	8.9%	15.1%
	≥50%	10	11.6%	2.9%	14.5%	1	3.1%	0.3%	1.4%	46	25.1%	13.2%	66.7%	12	25.0%	3.4%	17.4%
	Missing value	40	46.5%	11.5%	53.3%	9	28.1%	2.6%	12.0%	21	11.5%	6.0%	28.0%	5	10.4%	1.4%	6.7%
CIMT qual	Normal	5	11.6%	1.9%	10.4%	7	35.0%	2.7%	14.6%	27	17.4%	10.4%	56.3%	9	21.4%	3.5%	18.8%
	Mild	15	34.9%	5.8%	19.5%	8	40.0%	3.1%	10.4%	40	25.8%	15.4%	51.9%	14	33.3%	5.4%	18.2%
	Moderated	13	30.2%	5.0%	18.3%	2	10.0%	0.8%	2.8%	42	27.1%	16.2%	59.2%	14	33.3%	5.4%	19.7%
	Severe	10	23.3%	3.8%	15.6%	3	15.0%	1.2%	4.7%	46	29.7%	17.7%	71.9%	5	11.9%	1.9%	7.8%
Antihypertensive	No	18	23.7%	5.5%	18.8%	9	37.5%	2.8%	9.4%	55	30.4%	16.8%	57.3%	14	30.4%	4.3%	14.6%
	Yes	58	76.3%	17.7%	25.1%	15	62.5%	4.6%	6.5%	126	69.6%	38.5%	54.5%	32	69.6%	9.8%	13.9%
Statins	No	52	69.3%	16.0%	25.6%	12	50.0%	3.7%	5.9%	117	65.0%	36.1%	57.6%	22	48.9%	6.8%	10.8%

	Yes	23	30.7%	7.1%	19.0%	12	50.0%	3.7%	9.9%	63	35.0%	19.4%	52.1%	23	51.1%	7.1%	19.0%
Anticoagulants	No	66	86.8%	20.2%	23.4%	21	87.5%	6.4%	7.4%	149	82.8%	45.6%	52.8%	46	97.9%	14.1%	16.3%
	Yes	10	13.2%	3.1%	22.2%	3	12.5%	0.9%	6.7%	31	17.2%	9.5%	68.9%	1	2.1%	0.3%	2.2%
Antiplatelet	No	54	71.1%	16.5%	24.7%	15	62.5%	4.6%	6.8%	118	65.6%	36.1%	53.9%	32	68.1%	9.8%	14.6%
	Yes	22	28.9%	6.7%	20.4%	9	37.5%	2.8%	8.3%	62	34.4%	19.0%	57.4%	15	31.9%	4.6%	13.9%
Antibiotics	No	75	98.7%	23.0%	23.4%	23	95.8%	7.1%	7.2%	177	98.3%	54.3%	55.3%	45	97.8%	13.8%	14.1%
	Yes	1	1.3%	0.3%	16.7%	1	4.2%	0.3%	16.7%	3	1.7%	0.9%	50.0%	1	2.2%	0.3%	16.7%
Insulin	No	69	90.8%	21.2%	22.3%	24	100.0%	7.4%	7.8%	171	95.0%	52.5%	55.3%	45	97.8%	13.8%	14.6%
	Yes	7	9.2%	2.1%	41.2%	0	0.0%	0.0%	0.0%	9	5.0%	2.8%	52.9%	1	2.2%	0.3%	5.9%
Beta_blockers	No	62	81.6%	19.0%	26.4%	17	70.8%	5.2%	7.2%	120	66.7%	36.7%	51.1%	36	76.6%	11.0%	15.3%
	Yes	14	18.4%	4.3%	15.2%	7	29.2%	2.1%	7.6%	60	33.3%	18.3%	65.2%	11	23.4%	3.4%	12.0%

Pearson Chi-Square Tests

		INTERVENTION
S	Chi-square	2.788
	df	3
	Sig.	.425
Occluded vessel	Chi-square	34.559
	df	21
	Sig.	.032*,b,c
Side	Chi-square	.882
	df	6
	Sig.	.990b,c
Circulation	Chi-square	7.733
	df	6
	Sig.	.258b,c
Perfusion deficit (Yes/No)	Chi-square	76.704

	df	6
	Sig.	.000[*,b]
Ischemic lesion at CT/MR control (Yes/No)	Chi-square	1.524
	df	3
	Sig.	.677[b,c]
Anatomical inclusion of hypoperfused area in the ischemic lesion at CT/MR control (Yes/No)	Chi-square	.903
	df	3
	Sig.	.825[b,c]
DWI Core inclusion in FIA	Chi-square	13.046
	df	9
	Sig.	.161[b,c]
pcASL Penumbra inclusion in FIA	Chi-square	62.208
	df	9
	Sig.	.000[*,b,c]
TICI	Chi-square	5.368
	df	10
	Sig.	.865[b,c]
Successful EVT treatment (Yes/No)	Chi-square	2.647
	df	2
	Sig.	.266[b,c]
Favourable Clinical Response	Chi-square	54.701
	df	3
	Sig.	.000[*]
TOAST	Chi-square	47.608
	df	15
	Sig.	.000[*,b,c]
Smoking	Chi-square	13.659
	df	3

	Sig.	.003*
Former_Smoker	Chi-square	.683
	df	3
	Sig.	.877
Diabetes	Chi-square	9.076
	df	3
	Sig.	.028*
Previous_Stroke/TIA	Chi-square	5.575
	df	3
	Sig.	.134
Coronary_artery_disease	Chi-square	1.459
	df	3
	Sig.	.692
EF≤40%	Chi-square	2.513
	df	3
	Sig.	.473b
Hyperlipemia	Chi-square	2.271
	df	3
	Sig.	.518
K_Hystory	Chi-square	1.469
	df	3
	Sig.	.689
Known_Atrial_Fibrillation	Chi-square	11.809
	df	3
	Sig.	.008*
Newonset_AF	Chi-square	4.098
	df	3
	Sig.	.251

Hypertension	Chi-square	4.065
	df	3
	Sig.	.255
Carotid_Stenosis_left	Chi-square	21.974
	df	12
	Sig.	.038*,b
Carotid_Stenosis_right	Chi-square	18.363
	df	12
	Sig.	.105b
Stenosis dicho	Chi-square	53.357
	df	6
	Sig.	.000*
CIMT qual	Chi-square	14.472
	df	9
	Sig.	.106
Antihypertensive	Chi-square	2.065
	df	3
	Sig.	.559
Statins	Chi-square	7.140
	df	3
	Sig.	.068
Anticoagulants	Chi-square	7.232
	df	3
	Sig.	.065
Antiplatelet	Chi-square	.979
	df	3
	Sig.	.806
Antibiotics	Chi-square	.893

	df	3
	Sig.	.827[b,c]
Insulin	Chi-square	4.653
	df	3
	Sig.	.199[b]
Beta_blockers	Chi-square	6.485
	df	3
	Sig.	.090

Results are based on nonempty rows and columns in each innermost subtable.

*. The Chi-square statistic is significant at the .05 level.

b. More than 20% of cells in this subtable have expected cell counts less than 5. Chi-square results may be invalid.

c. The minimum expected cell count in this subtable is less than one. Chi-square results may be invalid.

Comparisons of Column Proportions[c]

		INTERVENTION			
		Not Treated (A)	IVT (B)	EVT (C)	Bridging (D)
S	Male				
	Female				
Occluded vessel	ACA			.[a]	.[a]
	MCA				
	T-Carotids		.[a]		
	ICA Intra				.[a]
	ICA extra				
	Tandem		.[a]		

	Combined (MCA+ACA/PCA		.[a]		
	VB				
Side	Right				
	Left				
	Bilateral				
Circulation	Posterior				
	Anterior				
	Posterior+Anterior				
Perfusion deficit (Yes/No)	No	C(.001)			.[a]
	Yes			A(.000) B(.000)	A(.000) B(.000)
	Yes No Penumbra	C(.000) D(.003)	C(.000) D(.002)		
Ischemic lesion at CT/MR control (Yes/No)	No				
	Yes				
Anatomical inclusion of hypoperfused area in the ischemic lesion at CT/MR control (Yes/No)	No		.[a]		.[a]
	Yes		.[a]		.[a]
DWI Core inclusion in FIA	Partial (Core Higher)				
	Complete (core equal)		C(.029)		
	Higher (Ischemia>Core)			B(.020)	
	No FIA				
pcASL Penumbra inclusion in FIA	Partial (Penumbra higher)			A(.000) B(.000)	A(.000) B(.002)
	Complete (Penumbra equal)	C(.000) D(.000)	C(.000) D(.002)		
	Higher (Ischemia>Penumbra)		.[a]		

	No FIA				
TICI	0	.[a,b]	.[a,b]		
	1	.[a,b]	.[a,b]		.[a]
	2a	.[a,b]	.[a,b]		
	2b	.[a,b]	.[a,b]		
	2c	.[a,b]	.[a,b]		
	3	.[a,b]	.[a,b]		
Successful EVT treatment (Yes/No)	TICI 0-2a	.[a,b]	.[a,b]		
	TICI 2b-3	.[a,b]	.[a,b]		
Favourable Clinical Response	No	.[a]			
	Yes	.[a]			
TOAST	Athero				
	Cardio				
	Small vessels			.[a]	.[a]
	Other Causes		.[a]		
	Undetermined (multiple causes)	C(.001)	.[a]		.[a]
	Undetermined (iter not completed)				
Smoking	No			A(.003)	
	Yes	C(.003)			
Former_Smoker	No				
	Yes				
Diabetes	No				
	Yes				
Previous_Stroke/TIA	No				
	Yes				
Coronary_artery_disease	No				
	Yes				

EF≤40%	No		.[a]		
	Yes		.[a]		
Hyperlipemia	No				
	Yes				
K_Hystory	No				
	Yes				
Known_Atrial_Fibrillation	No				A(.026) C(.014)
	Yes	D(.026)		D(.014)	
Newonset_AF	No				
	Yes				
Hypertension	No				
	Yes				
Carotid_Stenosis_left	No		C(.046)		
	<50%				
	50-70%	C(.027)			
	>70%		.[a]		
	Occlusion		.[a]		
Carotid_Stenosis_right	No				
	<50%				
	50-70%				
	>70%		.[a]		
	Occlusion		.[a]		
Stenosis dicho	<50%			A(.005)	
	≥50%			B(.033)	
	2	C(.000) D(.000)			
CIMT qual	Normal				

	Mild				
	Moderated				
	Severe				
Antihypertensive	No				
	Yes				
Statins	No				
	Yes				
Anticoagulants	No				C(.049)
	Yes			D(.049)	
Antiplatelet	No				
	Yes				
Antibiotics	No				
	Yes				
Insulin	No		.[a]		
	Yes		.[a]		
Beta_blockers	No				
	Yes				

Results are based on two-sided tests. For each significant pair, the key of the category with the smaller column proportion appears in the category with the larger column proportion.

Significance level for upper case letters (A, B, C): .05[c]

a. This category is not used in comparisons because its column proportion is equal to zero or one.

b. This category is not used in comparisons because the sum of case weights is less than two.

c. Tests are adjusted for all pairwise comparisons within a row of each innermost subtable using the Bonferroni correction.

Part 1.1 – *Prognostic accuracy of DWI-pcASL protocol for the detection of AIS*

Analysis of non-parametric variables with Bonferroni correction

Nonparametric Tests

Hypothesis Test Summary

	Null Hypothesis	Test	Sig.[a,b]	Decision
1	The distribution of NLR is the same across categories of INTERVENTO.	Independent-Samples Kruskal-Wallis Test	.095	Retain the null hypothesis.
2	The distribution of Neu Count is the same across categories of INTERVENTO.	Independent-Samples Kruskal-Wallis Test	.705	Retain the null hypothesis.
3	The distribution of Lym Count is the same across categories of INTERVENTO.	Independent-Samples Kruskal-Wallis Test	.147	Retain the null hypothesis.
4	The distribution of Neutrophils is the same across categories of INTERVENTO.	Independent-Samples Kruskal-Wallis Test	.011	Reject the null hypothesis.
5	The distribution of Lymphocytes is the same across categories of INTERVENTO.	Independent-Samples Kruskal-Wallis Test	.017	Reject the null hypothesis.

a. The significance level is .050.

b. Asymptotic significance is displayed.

Independent-Samples Kruskal-Wallis Test

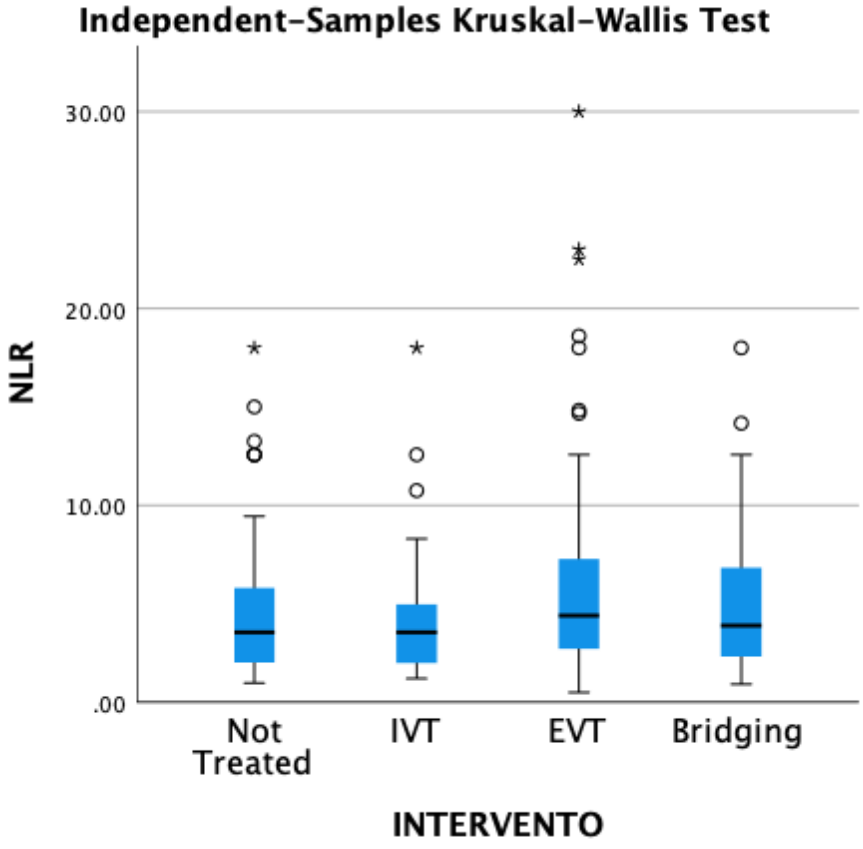
NLR across INTERVENTION

Independent-Samples Kruskal-Wallis Test Summary

Total N	346
Test Statistic	6.379[a,b]
Degree Of Freedom	3
Asymptotic Sig.(2-sided test)	.095

a. The test statistic is adjusted for ties.

b. Multiple comparisons are not performed because the overall test does not show significant differences across samples.



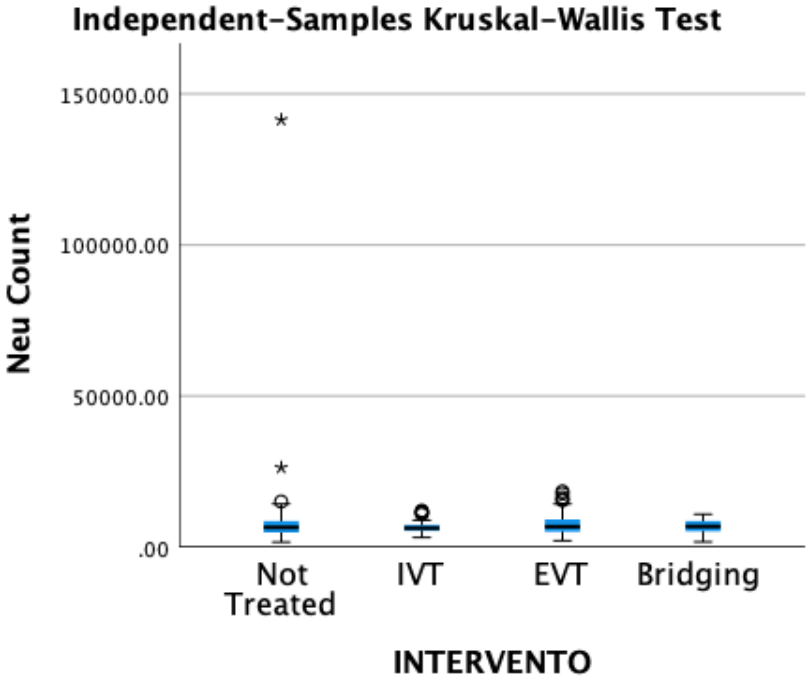
Neu Count across INTERVENTION

Independent-Samples Kruskal-Wallis Test Summary

Total N	347
Test Statistic	1.400[a,b]
Degree Of Freedom	3
Asymptotic Sig.(2-sided test)	.705

a. The test statistic is adjusted for ties.

b. Multiple comparisons are not performed because the overall test does not show significant differences across samples.



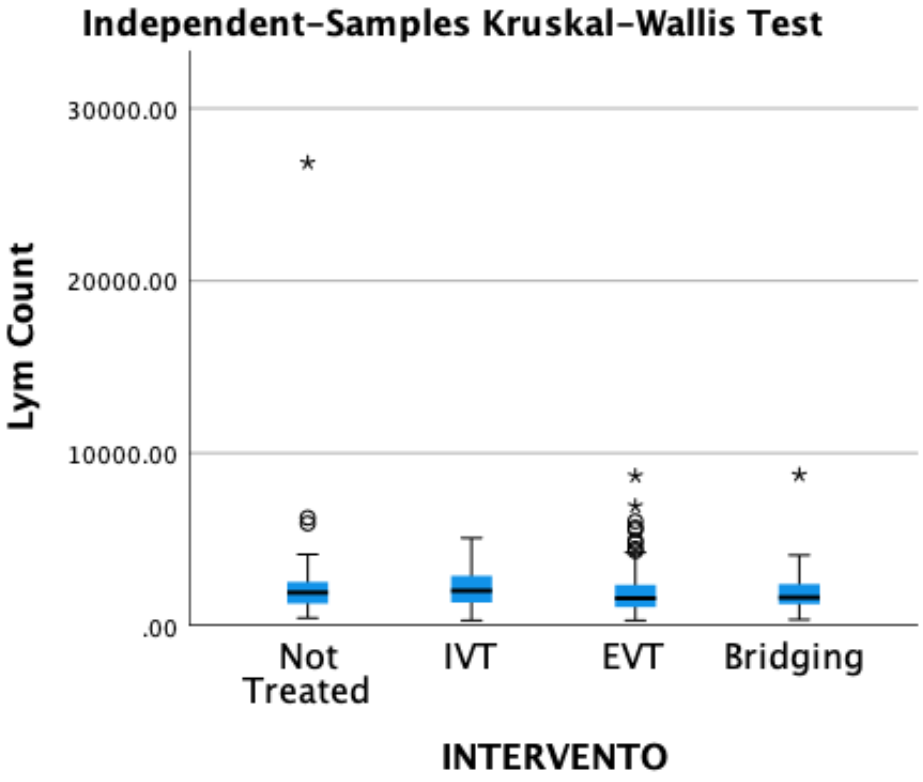
Lym Count across INTERVENTION

Independent-Samples Kruskal-Wallis Test Summary

Total N	346
Test Statistic	5.369[a,b]
Degree Of Freedom	3
Asymptotic Sig.(2-sided test)	.147

a. The test statistic is adjusted for ties.

b. Multiple comparisons are not performed because the overall test does not show significant differences across samples.

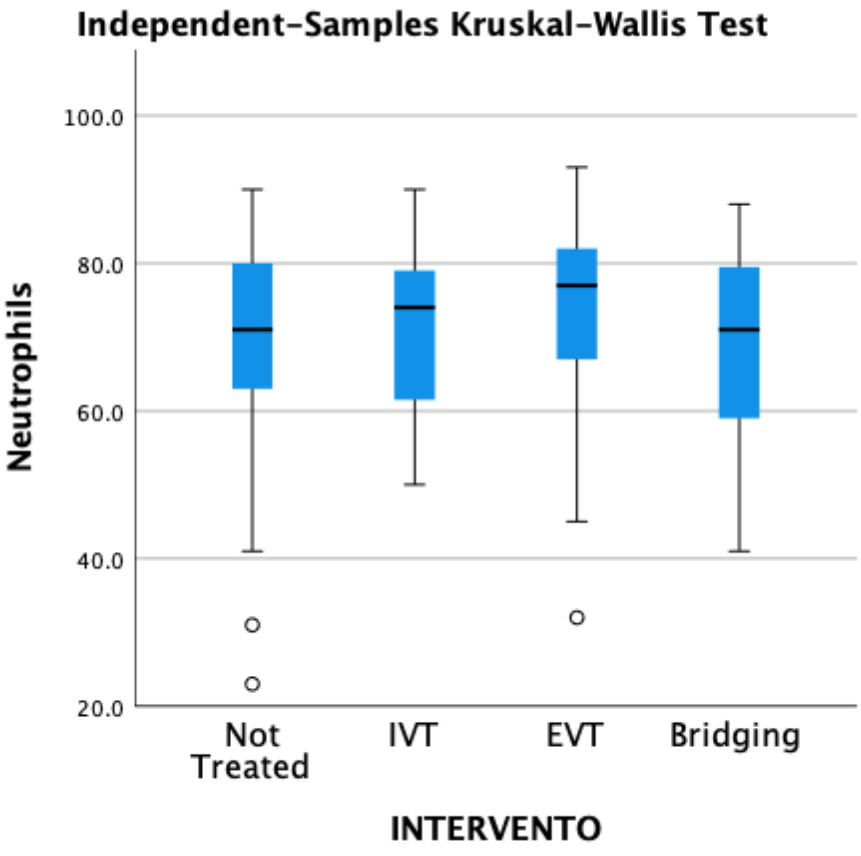


Neutrophils across INTERVENTION

Independent-Samples Kruskal-Wallis Test Summary

Total N	347
Test Statistic	11.058[a]
Degree Of Freedom	3
Asymptotic Sig.(2-sided test)	.011

a. The test statistic is adjusted for ties.



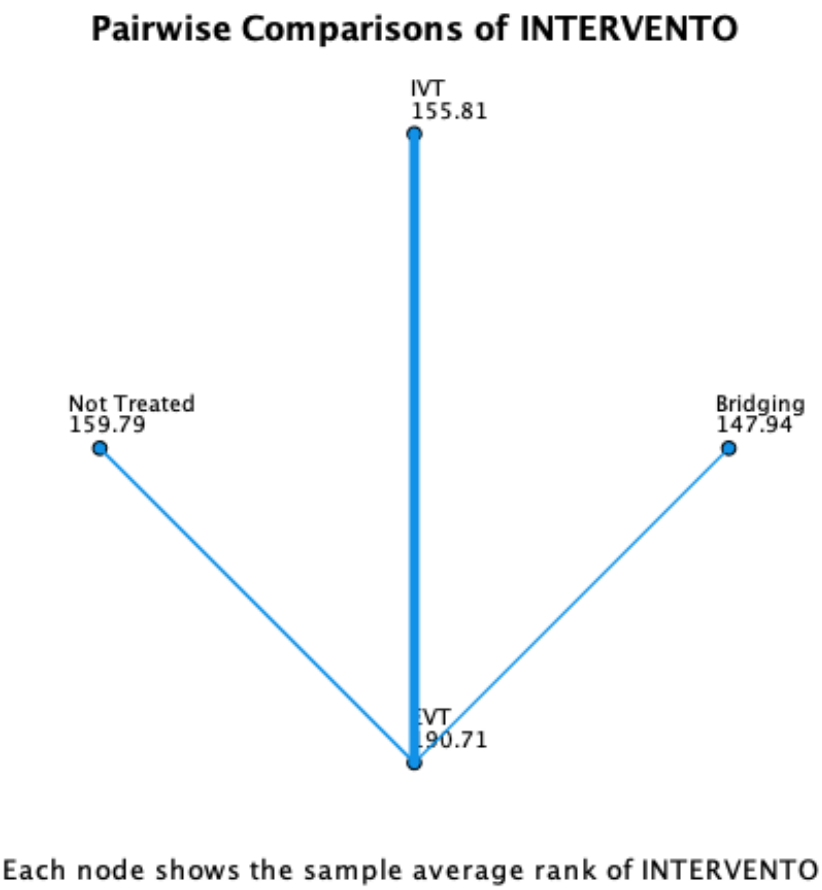
Pairwise Comparisons of INTERVENTION

Sample 1-Sample 2	Test Statistic	Std. Error	Std. Test Statistic	Sig.	Adj. Sig.[a]
Bridging-IVT	7.875	22.883	.344	.731	1.000
Bridging-Not Treated	11.851	18.103	.655	.513	1.000
Bridging-EVT	42.771	16.269	2.629	.009	.051
IVT-Not Treated	3.976	20.795	.191	.848	1.000
IVT-EVT	-34.896	19.220	-1.816	.069	.417
Not Treated-EVT	-30.921	13.172	-2.347	.019	.113

Each row tests the null hypothesis that the Sample 1 and Sample 2 distributions are the same.

Asymptotic significances (2-sided tests) are displayed. The significance level is .050.

a. Significance values have been adjusted by the Bonferroni correction for multiple tests.

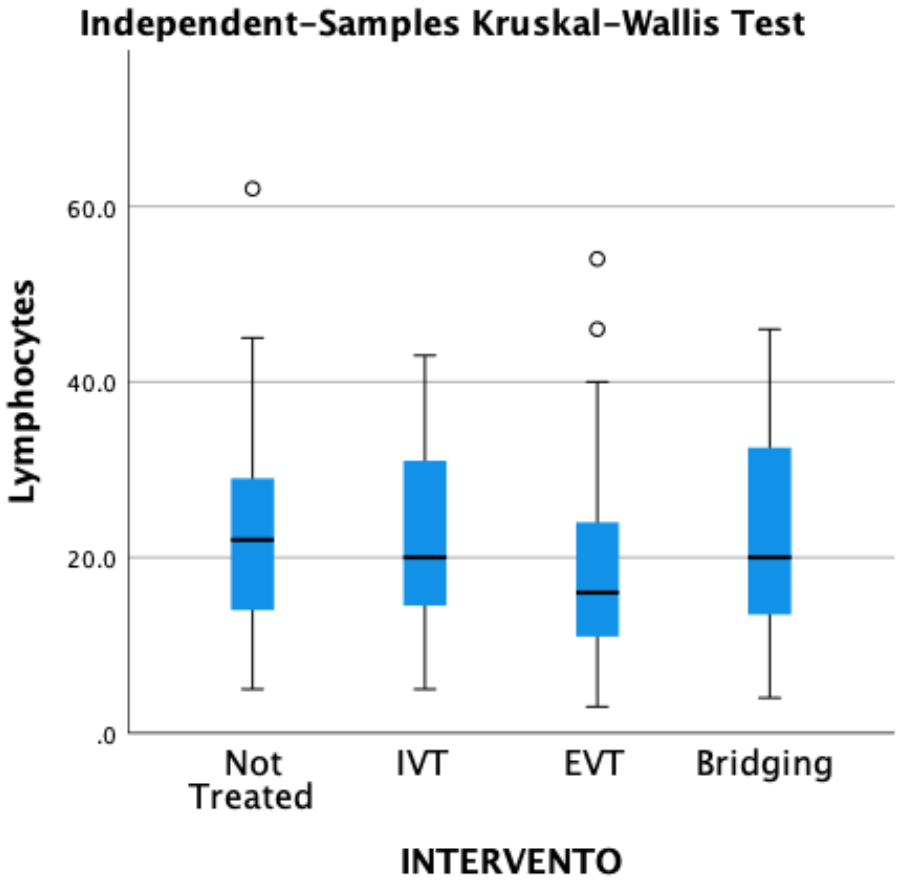


Lymphocytes across INTERVENTION

Independent-Samples Kruskal-Wallis Test Summary

Total N	346
Test Statistic	10.235[a]
Degree Of Freedom	3
Asymptotic Sig.(2-sided test)	.017

a. The test statistic is adjusted for ties.



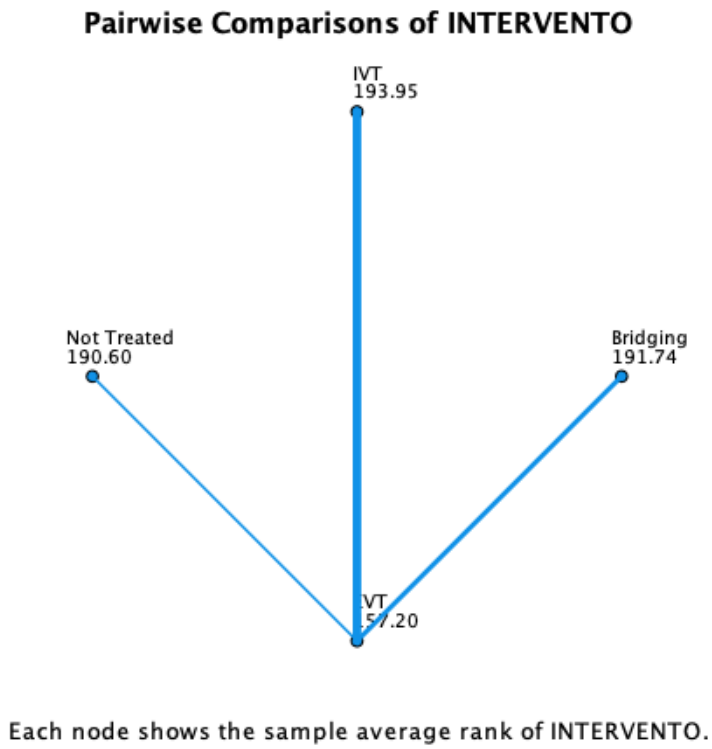
Pairwise Comparisons of INTERVENTION

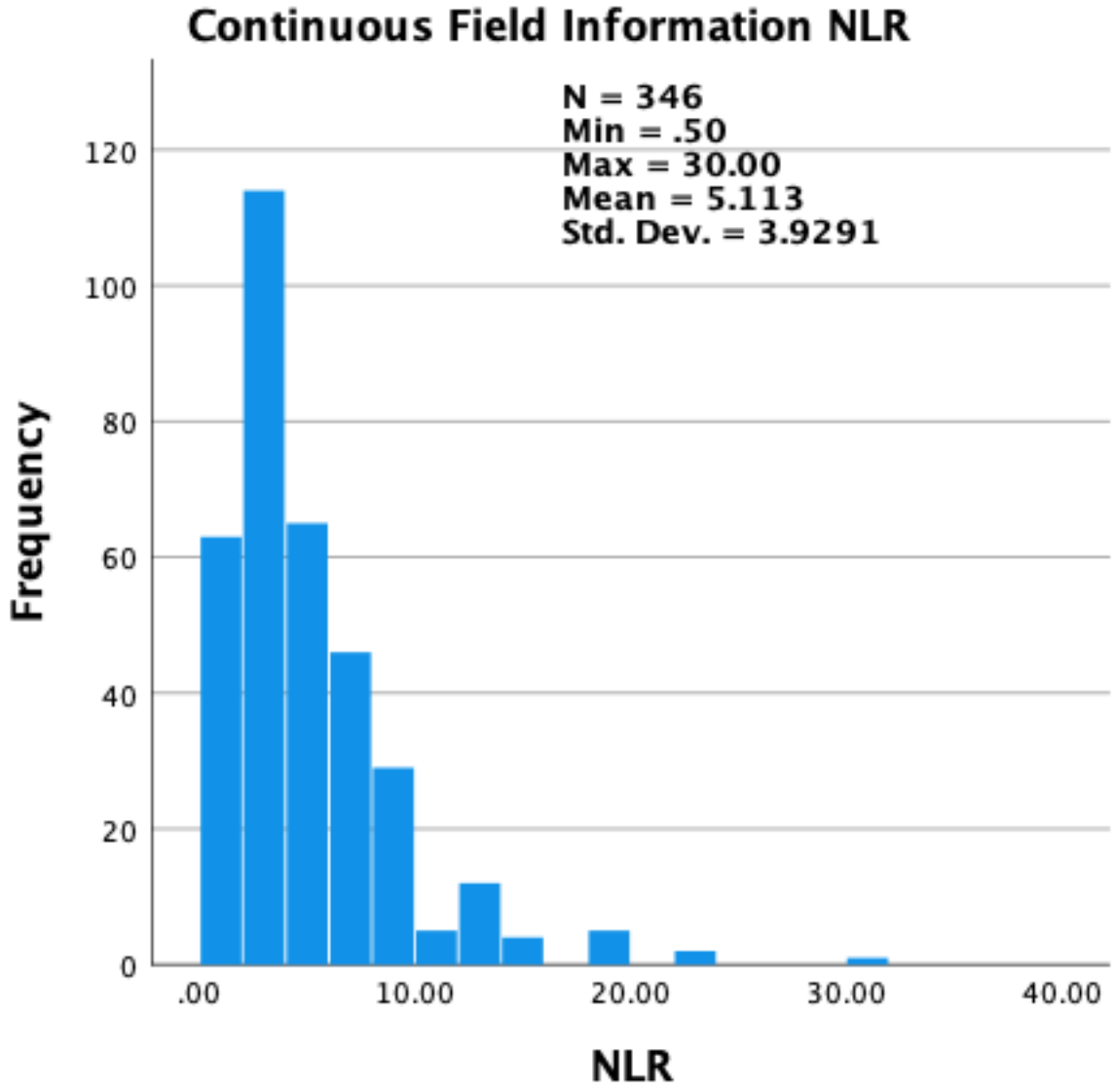
Sample 1-Sample 2	Test Statistic	Std. Error	Std. Test Statistic	Sig.	Adj. Sig.[a]
EVT-Not Treated	33.401	13.186	2.533	.011	.068
EVT-Bridging	-34.539	16.220	-2.129	.033	.199
EVT-IVT	36.753	19.162	1.918	.055	.331
Not Treated-Bridging	-1.138	18.087	-.063	.950	1.000
Not Treated-IVT	-3.352	20.766	-.161	.872	1.000
Bridging-IVT	2.214	22.813	.097	.923	1.000

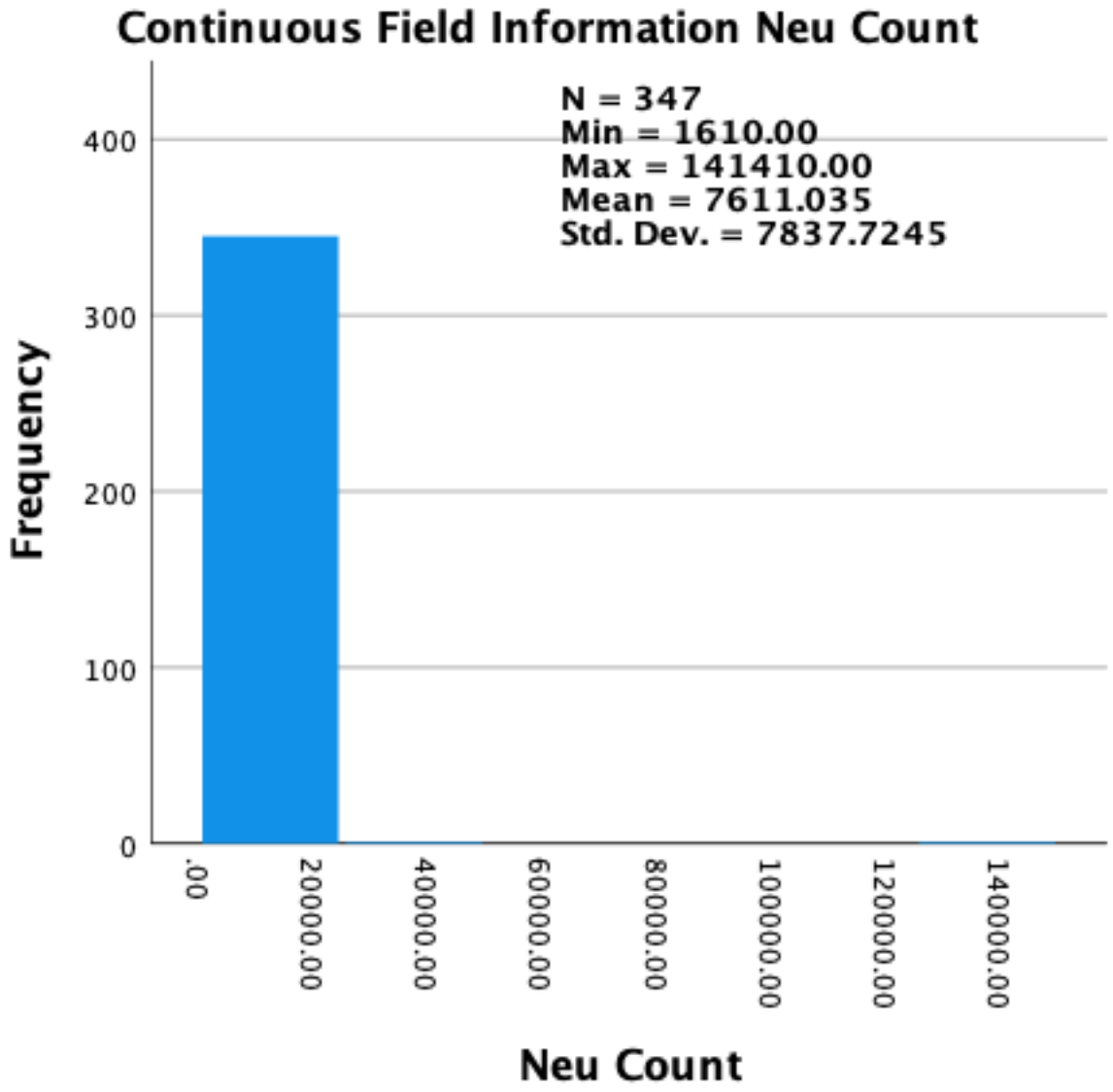
Each row tests the null hypothesis that the Sample 1 and Sample 2 distributions are the same.

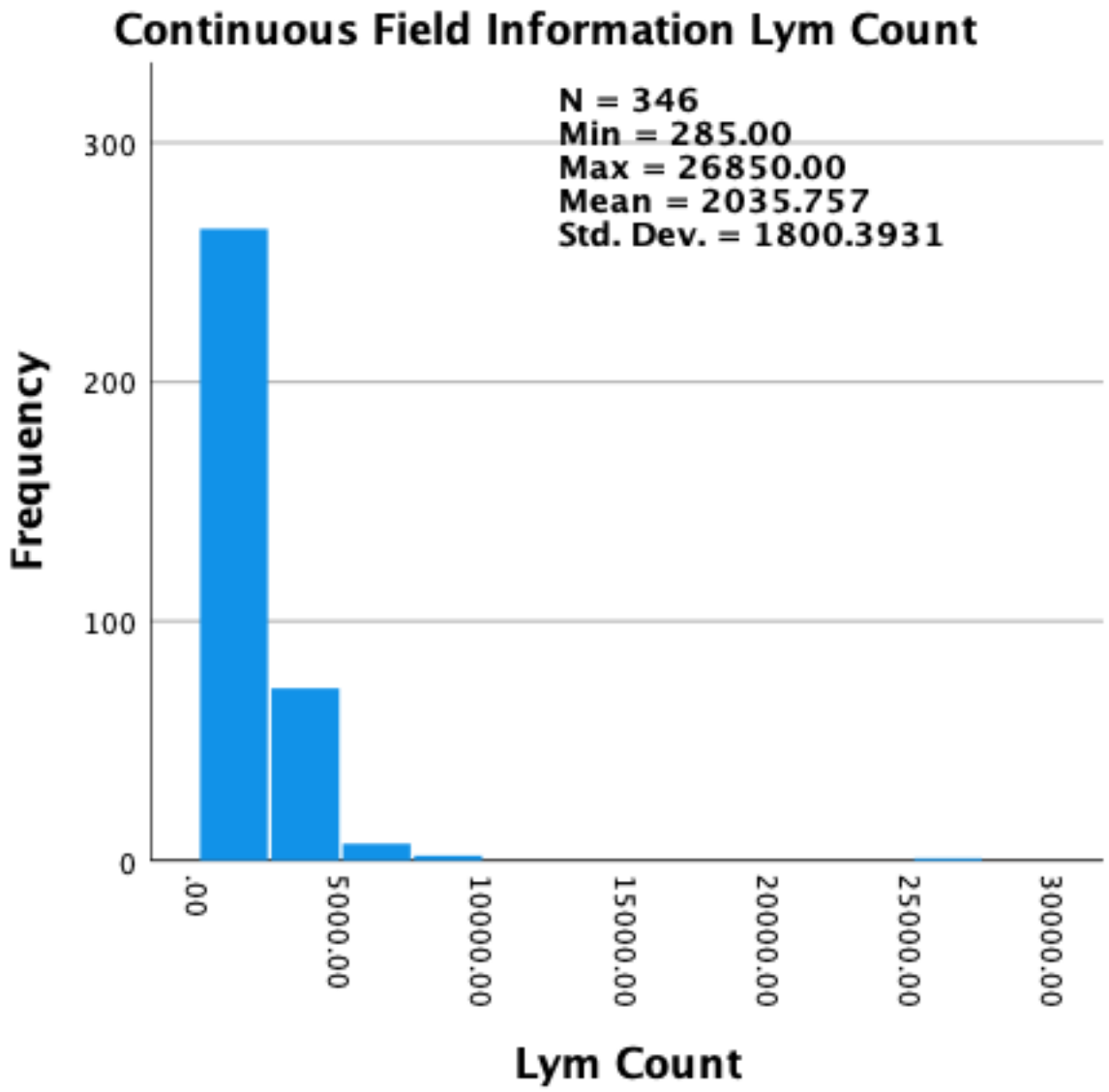
Asymptotic significances (2-sided tests) are displayed. The significance level is .050.

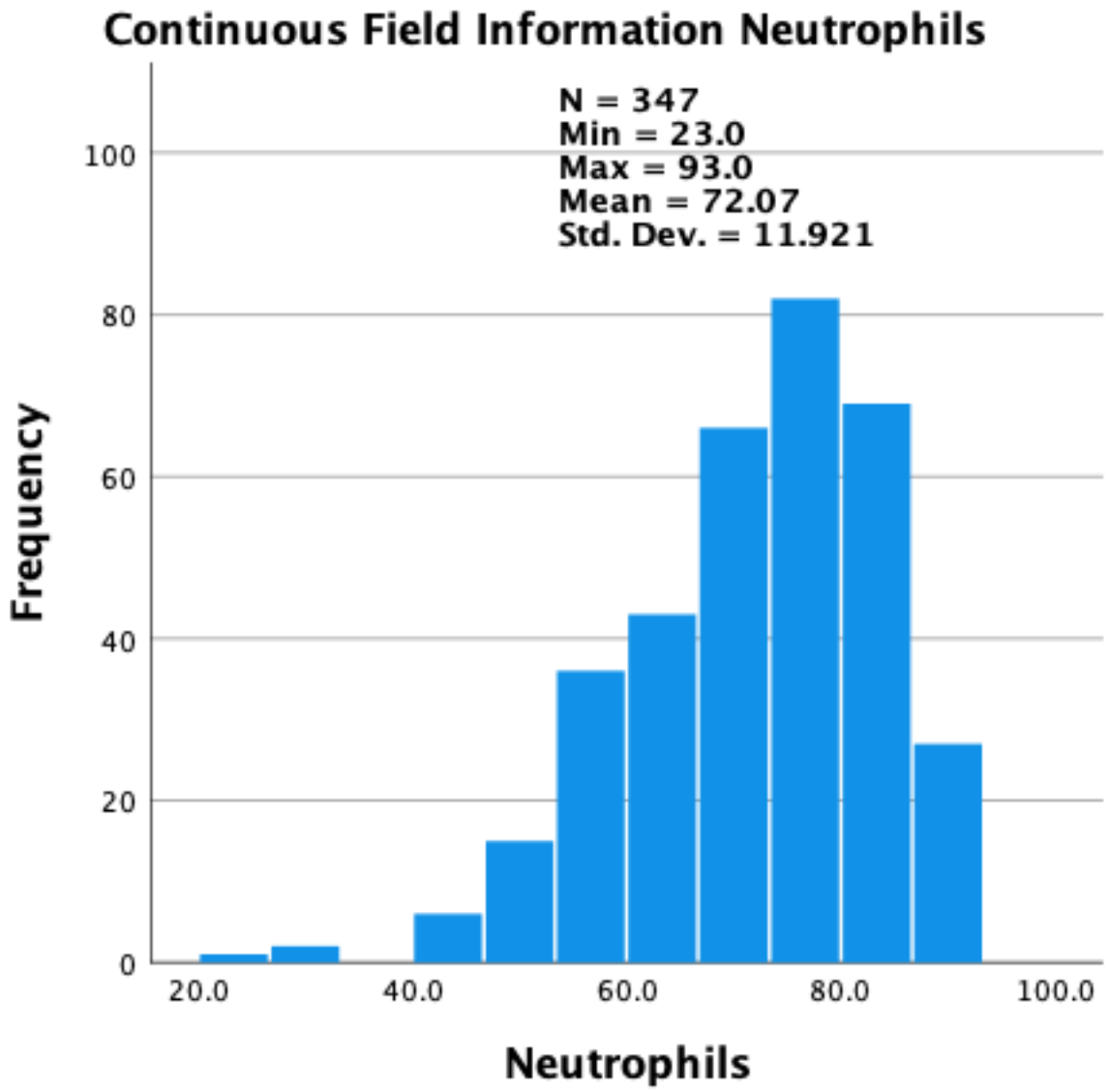
a. Significance values have been adjusted by the Bonferroni correction for multiple tests.

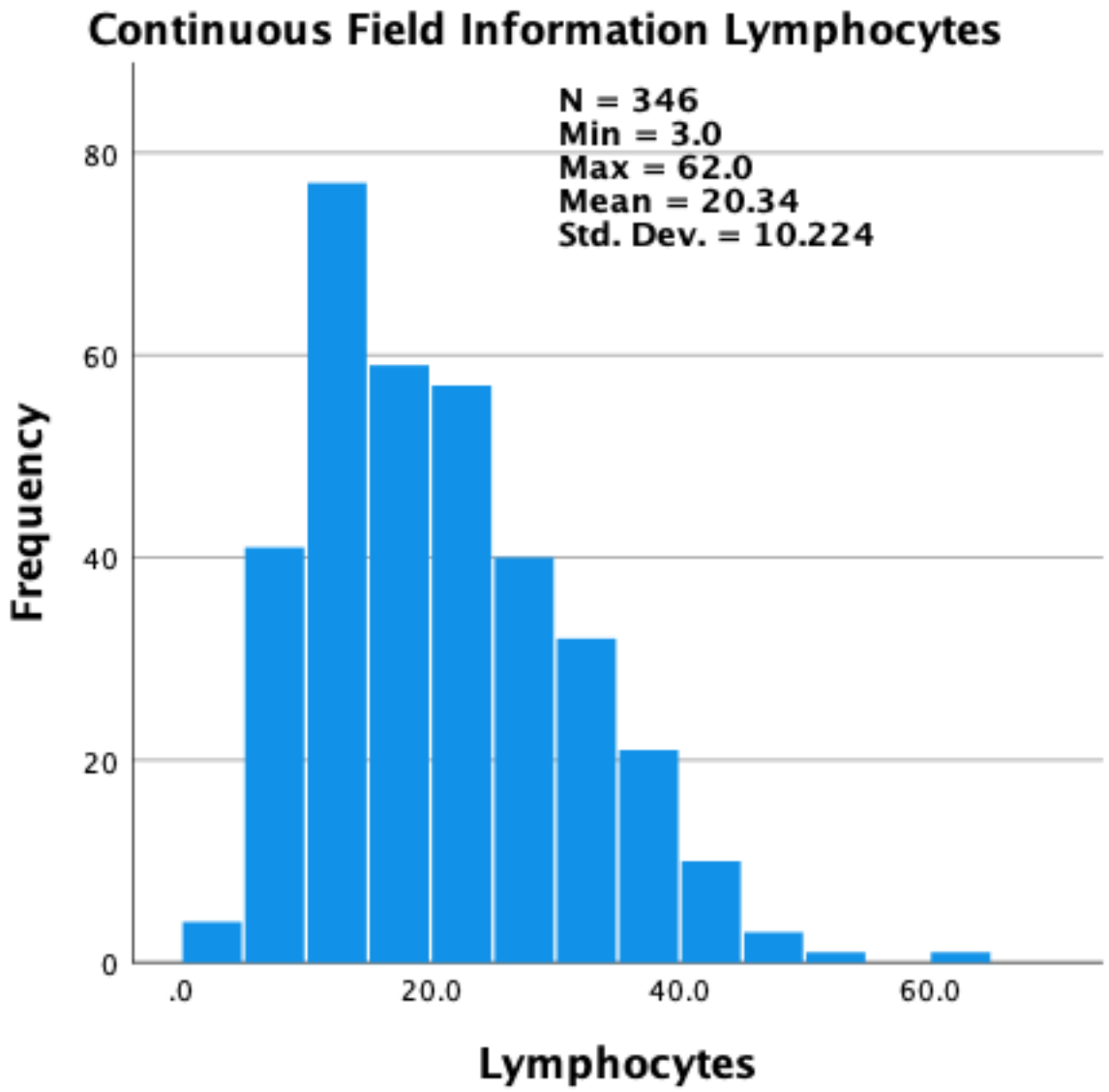


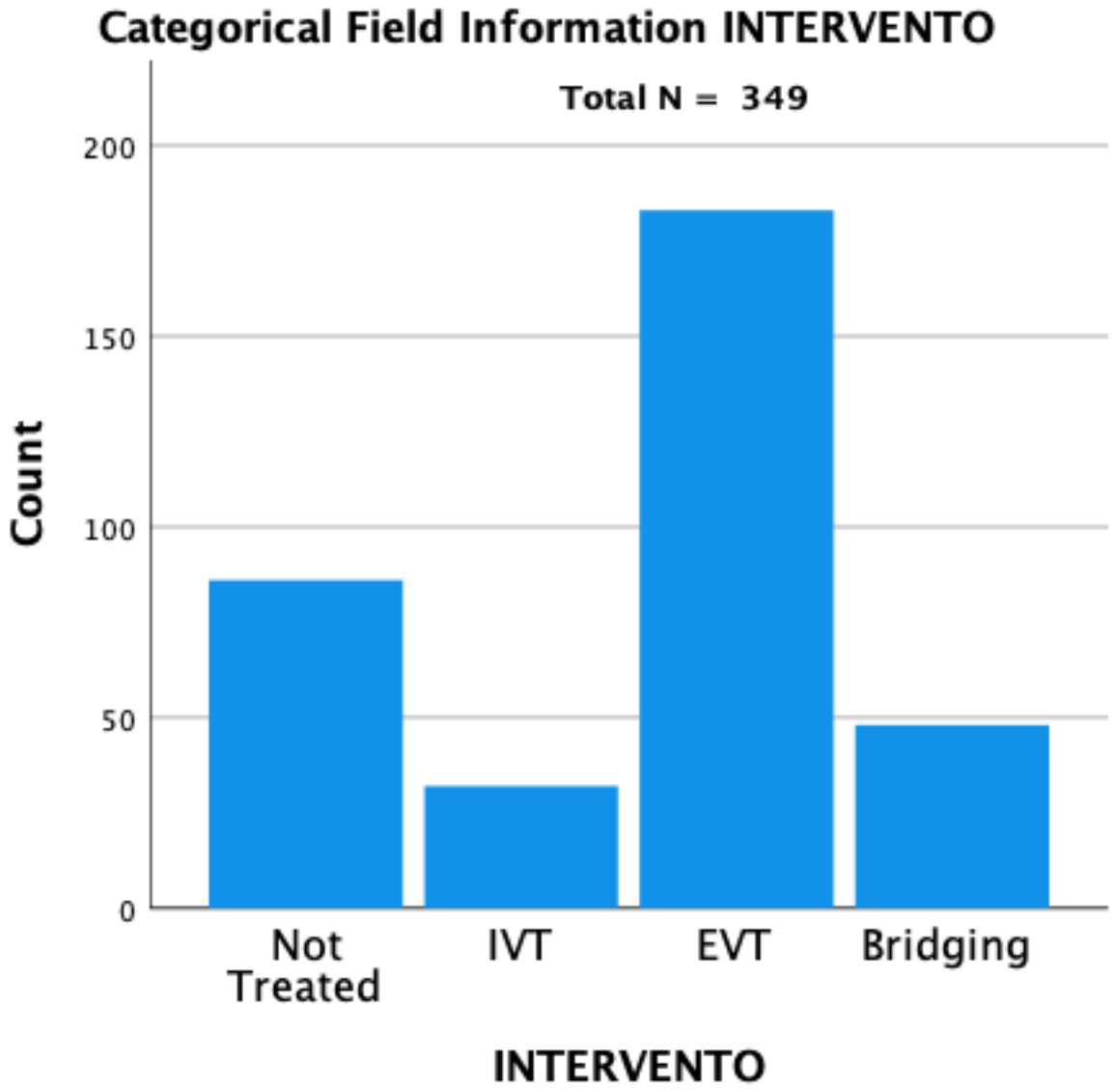

Continuous Field Information NLR
N = 346
Min = .50
Max = 30.00
Mean = 5.113
Std. Dev. = 3.9291
Frequency
120
100
80
60
40
20
0
.00
10.00
20.00
30.00
40.00
NLR


Continuous Field Information Neu Count
N = 347
Min = 1610.00
Max = 141410.00
Mean = 7611.035
Std. Dev. = 7837.7245
Frequency
400
300
200
100
0
.00
20000.00
40000.00
60000.00
80000.00
100000.00
120000.00
140000.00
Neu Count


Continuous Field Information Lym Count
N = 346
Min = 285.00
Max = 26850.00
Mean = 2035.757
Std. Dev. = 1800.3931
Frequency
300
200
100
0
.00
5000.00
10000.00
15000.00
20000.00
25000.00
30000.00
Lym Count


Continuous Field Information Neutrophils
N = 347
Min = 23.0
Max = 93.0
Mean = 72.07
Std. Dev. = 11.921
Frequency
100
80
60
40
20
0
20.0
40.0
60.0
80.0
100.0
Neutrophils


Continuous Field Information Lymphocytes
N = 346
Min = 3.0
Max = 62.0
Mean = 20.34
Std. Dev. = 10.224
Frequency
80
60
40
20
0
.0
20.0
40.0
60.0
Lymphocytes


Categorical Field Information INTERVENTO
Total N = 349
Count
200
150
100
50
0
Not Treated
IVT
EVT
Bridging
INTERVENTO

Part 2 – *Reliability of FAST MRI HSIP to identify total hypoperfusion area and ischemic core/penumbra ratio using DWI/pcASL mismatch*.

Custom Tables

		Count	Column N %
Clinical/instrumental outcome	Not Treated	96	35.3%
	Favorable (TICI2b-3 and/or FCR)	148	54.4%
	Not consistent (TICI2b-3 and Delta NIHSS<0)	28	10.3%
Sex (S)	Male	122	44.9%
	Female	150	55.1%
INTERVENTION	Not treated	70	25.7%
	IVT	10	3.7%
	EVT	149	54.8%
	Bridging	43	15.8%
Occluded vessel	ACA	2	0.7%
	MCA	180	66.2%
	Carotid terminal	30	11.0%
	ICA intra	4	1.5%
	ICA extra	24	8.8%
	Tandem	26	9.6%
	Combined (MCA+ACA)	6	2.2%
	VB	0	0.0%
Side	Right	113	41.5%
	Left	157	57.7%
	Bil	2	0.7%
Perfusion deficit (Yes/No)	Yes	242	89.0%
	Yes No penumbra	30	11.0%

Ischemic lesion at CT/MR control (Yes/No)	No	7	2.6%
	Yes	265	97.4%
Anatomical Anatomical Anatomical inclusion of hypoperfused area in the ischemic lesion at CT/MR control (Yes/No)	No	2	0.7%
	Yes	270	99.3%
DWI Core inclusion in FIA	Partial (core higher)	15	5.5%
	Complete (core equal)	168	61.8%
	Higher (ischemia>core)	82	30.1%
	No FIA	7	2.6%
pcASL Penumbra inclusion in FIA	Partial (penumbra higher)	163	65.7%
	Complete (penumbra equal)	73	29.4%
	Higher (ischemia>penumbra)	4	1.6%
	No FIA	8	3.2%

Multivariate analysis (MVA)

Univariate Statistics

		Missing	
	N	Count	Percent
Anatomical inclusion of hypoperfused area in the ischemic lesion at CT/MR control	272	0	.0
DWI Core inclusion in FIA	272	0	.0
pcASL Penumbra inclusion in FIA	248	24	8.8
Clinical/instrumental outcome	272	0	.0

S	272	0	.0
INTERVENTION	272	0	.0
Occluded vessel	272	0	.0
Side	272	0	.0
Perfusion deficit	272	0	.0
Ischemic lesion at CT/MR control	272	0	.0

Custom Tables (quantitative variables)

	Mean	Median	Percentile 25	Percentile 75	Missing	Maximum	Minimum
AGE	74	76	66	84	0	99	33
Time between onset of symptoms and pcASL	4.9	4.1	2.7	6.1	28	21.0	1.0
Time between pcASL and reperfusion	2.4	2.3	1.8	2.9	96	15.5	-3.7
Time between pcASL and reperfusion (min)	145.26	138.00	105.00	177.00	96	930.00	-222.00
Time between pcASL and CT/MR control	41.3	27.9	22.6	40.5	23	336.0	4.7

Oneway

Descriptives

						95% Confidence Interval for Mean			
		N	Mean	Std. Deviation	Std. Error	Lower Bound	Upper Bound	Minimum	Maximum
AGE	Not Treated	96	73.73	12.188	1.244	71.26	76.20	43	96

	Favorable (TICI2b-3 and/or FCR)	148	73.57	13.549	1.114	71.37	75.77	33	95
	Not consistent (TICI2b-3 and Delta NIHSS<0)	28	76.64	12.514	2.365	71.79	81.50	46	99
	Total	272	73.94	12.965	.786	72.39	75.49	33	99
Time between onset of symptoms and pcASL	Not Treated	86	5.516	3.5110	.3786	4.764	6.269	1.0	20.5
	Favorable (TICI2b-3 and/or FCR)	135	4.475	2.7404	.2359	4.008	4.941	1.0	21.0
	Not consistent (TICI2b-3 and Delta NIHSS<0)	23	4.683	2.9198	.6088	3.420	5.945	1.5	15.3
	Total	244	4.861	3.0762	.1969	4.474	5.249	1.0	21.0
Time between pcASL and reperfusion	Not Treated	5	2.360	1.2818	.5732	.768	3.952	1.0	4.1
	Favorable (TICI2b-3 and/or FCR)	145	2.380	1.9049	.1582	2.067	2.693	-3.7	15.5
	Not consistent (TICI2b-3 and Delta NIHSS<0)	26	2.535	1.0684	.2095	2.103	2.966	-.1	5.0
	Total	176	2.402	1.7860	.1346	2.137	2.668	-3.7	15.5
Time between pcASL and reperfusion (min)	Not Treated	5	141.6000	76.90774	34.39419	46.1064	237.0936	60.00	246.00
	Favorable (TICI2b-3 and/or FCR)	145	144.1655	115.77337	9.61445	125.1618	163.1692	-222.00	930.00
	Not consistent (TICI2b-3 and Delta NIHSS<0)	26	152.0769	64.10611	12.57224	126.1839	177.9699	-6.00	300.00
	Total	176	145.2614	108.44216	8.17414	129.1288	161.3939	-222.00	930.00
Time between pcASL and CT/MR control	Not Treated	91	62.244	60.7206	6.3653	49.598	74.890	4.7	336.0
	Favorable (TICI2b-3 and/or FCR)	134	30.157	16.8917	1.4592	27.270	33.043	5.1	163.0
	Not consistent (TICI2b-3 and Delta NIHSS<0)	24	24.558	7.2045	1.4706	21.516	27.601	15.6	44.6
	Total	249	41.344	41.8453	2.6518	36.121	46.567	4.7	336.0

ANOVA

		Sum of Squares	df	Mean Square	F	Sig.
AGE	Between Groups	229.348	2	114.674	.681	.507
	Within Groups	45323.711	269	168.490		
	Total	45553.059	271			
Time between onset of symptoms and pcASL	Between Groups	57.793	2	28.897	3.107	.047
	Within Groups	2241.645	241	9.301		
	Total	2299.438	243			
Time between pcASL and reperfusion	Between Groups	.536	2	.268	.083	.920
	Within Groups	557.663	173	3.223		
	Total	558.199	175			
Time between pcASL and reperfusion (min)	Between Groups	1448.904	2	724.452	.061	.941
	Within Groups	2056499.074	173	11887.278		
	Total	2057947.977	175			
Time between pcASL and CT/MR control	Between Groups	63282.561	2	31641.281	20.982	.000
	Within Groups	370972.531	246	1508.018		
	Total	434255.093	248			

Post Hoc Tests

Multiple Comparisons

Bonferroni

Dependent Variable	(I) Clinical/instrumental outcome	(J) Clinical/instrumental outcome	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
AGE	Not Treated	Favorable (TICI2b-3 and/or FCR)	.162	1.701	1.000	-3.94	4.26

		Not consistent (TICI2b-3 and Delta NIHSS<0)	-2.914	2.788	.891	-9.63	3.80
	Favorable (TICI2b-3 and/or FCR)	Not Treated	-.162	1.701	1.000	-4.26	3.94
		Not consistent (TICI2b-3 and Delta NIHSS<0)	-3.075	2.675	.754	-9.52	3.37
	Not consistent (TICI2b-3 and Delta NIHSS<0)	Not Treated	2.914	2.788	.891	-3.80	9.63
		Favorable (TICI2b-3 and/or FCR)	3.075	2.675	.754	-3.37	9.52
Time between onset of symptoms and pcASL	Not Treated	Favorable (TICI2b-3 and/or FCR)	1.0415*	.4208	.042	.027	2.056
		Not consistent (TICI2b-3 and Delta NIHSS<0)	.8337	.7159	.736	-.892	2.560
	Favorable (TICI2b-3 and/or FCR)	Not Treated	-1.0415*	.4208	.042	-2.056	-.027
		Not consistent (TICI2b-3 and Delta NIHSS<0)	-.2078	.6880	1.000	-1.866	1.451
	Not consistent (TICI2b-3 and Delta NIHSS<0)	Not Treated	-.8337	.7159	.736	-2.560	.892
		Favorable (TICI2b-3 and/or FCR)	.2078	.6880	1.000	-1.451	1.866
Time between pcASL and reperfusion	Not Treated	Favorable (TICI2b-3 and/or FCR)	-.0200	.8167	1.000	-1.994	1.954
		Not consistent (TICI2b-3 and Delta NIHSS<0)	-.1746	.8767	1.000	-2.294	1.945
	Favorable (TICI2b-3 and/or FCR)	Not Treated	.0200	.8167	1.000	-1.954	1.994
		Not consistent (TICI2b-3 and Delta NIHSS<0)	-.1546	.3824	1.000	-1.079	.770
	Not consistent (TICI2b-3 and Delta NIHSS<0)	Not Treated	.1746	.8767	1.000	-1.945	2.294
		Favorable (TICI2b-3 and/or FCR)	.1546	.3824	1.000	-.770	1.079
Time between pcASL and reperfusion (min)	Not Treated	Favorable (TICI2b-3 and/or FCR)	-2.56552	49.59271	1.000	-122.4551	117.3240
		Not consistent (TICI2b-3 and Delta NIHSS<0)	-10.47692	53.24151	1.000	-139.1874	118.2336

	Favorable (TICI2b-3 and/or FCR)	Not Treated	2.56552	49.59271	1.000	-117.3240	122.4551
		Not consistent (TICI2b-3 and Delta NIHSS<0)	-7.91141	23.22034	1.000	-64.0462	48.2234
	Not consistent (TICI2b-3 and Delta NIHSS<0)	Not Treated	10.47692	53.24151	1.000	-118.2336	139.1874
		Favorable (TICI2b-3 and/or FCR)	7.91141	23.22034	1.000	-48.2234	64.0462
Time between pcASL and CT/MR control	Not Treated	Favorable (TICI2b-3 and/or FCR)	32.0872*	5.2750	.000	19.372	44.802
		Not consistent (TICI2b-3 and Delta NIHSS<0)	37.6856*	8.9110	.000	16.206	59.165
	Favorable (TICI2b-3 and/or FCR)	Not Treated	-32.0872*	5.2750	.000	-44.802	-19.372
		Not consistent (TICI2b-3 and Delta NIHSS<0)	5.5984	8.6074	1.000	-15.150	26.346
	Not consistent (TICI2b-3 and Delta NIHSS<0)	Not Treated	-37.6856*	8.9110	.000	-59.165	-16.206
		Favorable (TICI2b-3 and/or FCR)	-5.5984	8.6074	1.000	-26.346	15.150

*. The mean difference is significant at the 0.05 level.

Custom Tables (qualitative variables)

Warnings

Pairwise comparisons are requested but no eligible subtables are found in table "1".

Table 1

		Clinical/instrumental outcome								
		Not Treated			Favorable (TICI2b-3 and/or FCR)			Not consistent (TICI2b-3 and Delta NIHSS<0)		
		Count	Row N %	Column N %	Count	Row N %	Column N %	Count	Row N %	Column N %
S	Male	49	40.2%	51.0%	58	47.5%	39.2%	15	12.3%	53.6%

	Female	47	31.3%	49.0%	90	60.0%	60.8%	13	8.7%	46.4%
INTERVENTION	Not treated	70	100.0%	72.9%	0	0.0%	0.0%	0	0.0%	0.0%
	IVT	0	0.0%	0.0%	10	100.0%	6.8%	0	0.0%	0.0%
	EVT	23	15.4%	24.0%	105	70.5%	70.9%	21	14.1%	75.0%
	Bridging	3	7.0%	3.1%	33	76.7%	22.3%	7	16.3%	25.0%
Occluded vessel	ACA	2	100.0%	2.1%	0	0.0%	0.0%	0	0.0%	0.0%
	MCA	57	31.7%	59.4%	107	59.4%	72.3%	16	8.9%	57.1%
	Carotid terminal	10	33.3%	10.4%	17	56.7%	11.5%	3	10.0%	10.7%
	ICA intra	1	25.0%	1.0%	3	75.0%	2.0%	0	0.0%	0.0%
	ICA extra	14	58.3%	14.6%	6	25.0%	4.1%	4	16.7%	14.3%
	Tandem	7	26.9%	7.3%	14	53.8%	9.5%	5	19.2%	17.9%
	Combined (MCA+ACA)	5	83.3%	5.2%	1	16.7%	0.7%	0	0.0%	0.0%
	VB	0	0.0%	0.0%	0	0.0%	0.0%	0	0.0%	0.0%
Side	Right	46	40.7%	47.9%	54	47.8%	36.5%	13	11.5%	46.4%
	Left	49	31.2%	51.0%	94	59.9%	63.5%	14	8.9%	50.0%
	Bil	1	50.0%	1.0%	0	0.0%	0.0%	1	50.0%	3.6%
Perfusion deficit (Yes/No)	Yes	74	30.6%	77.1%	141	58.3%	95.3%	27	11.2%	96.4%
	Yes No penumbra	22	73.3%	22.9%	7	23.3%	4.7%	1	3.3%	3.6%
Ischemic lesion at CT/MR control (Yes/No)	No	1	14.3%	1.0%	6	85.7%	4.1%	0	0.0%	0.0%
	Yes	95	35.8%	99.0%	142	53.6%	95.9%	28	10.6%	100.0%
Anatomical Anatomical inclusion of hypoperfused area in the ischemic lesion at CT/MR control (Yes/No)	No	2	100.0%	2.1%	0	0.0%	0.0%	0	0.0%	0.0%
	Yes	94	34.8%	97.9%	148	54.8%	100.0%	28	10.4%	100.0%
DWI Core inclusion in FIA	Partial (core higher)	4	26.7%	4.2%	10	66.7%	6.8%	1	6.7%	3.6%
	Complete (core equal)	56	33.3%	58.3%	99	58.9%	66.9%	13	7.7%	46.4%
	Higher (ischemia>core)	35	42.7%	36.5%	33	40.2%	22.3%	14	17.1%	50.0%
	No FIA	1	14.3%	1.0%	6	85.7%	4.1%	0	0.0%	0.0%

pcASL Penumbra inclusion in FIA	Partial (penumbra higher)	31	19.0%	36.9%	115	70.6%	83.9%	17	10.4%	63.0%
	Complete (penumbra equal)	47	64.4%	56.0%	16	21.9%	11.7%	10	13.7%	37.0%
	Higher (ischemia>penumbra)	3	75.0%	3.6%	1	25.0%	0.7%	0	0.0%	0.0%
	No FIA	3	37.5%	3.6%	5	62.5%	3.6%	0	0.0%	0.0%

Pearson Chi-Square Tests

		Clinical/instrumental outcome
S	Chi-square	4.266
	df	2
	Sig.	.118
INTERVENTION	Chi-square	177.717
	df	6
	Sig.	.000[*,b]
Occluded vessel	Chi-square	23.446
	df	12
	Sig.	.024[*,b,c]
Side	Chi-square	8.176
	df	4
	Sig.	.085[b,c]
Perfusion deficit (Yes/No)	Chi-square	21.397
	df	2
	Sig.	.000[*]
Ischemic lesion at CT/MR control (Yes/No)	Chi-square	2.932
	df	2

	Sig.	.231[b,c]
Anatomical Anatomical inclusion of hypoperfused area in the ischemic lesion at CT/MR control (Yes/No)	Chi-square	3.694
	df	2
	Sig.	.158[b,c]
DWI Core inclusion in FIA	Chi-square	13.612
	df	6
	Sig.	.034[*,b,c]
pcASL Penumbra inclusion in FIA	Chi-square	56.908
	df	6
	Sig.	.000[*,b,c]

Results are based on nonempty rows and columns in each innermost subtable.

*. The Chi-square statistic is significant at the .05 level.

b. More than 20% of cells in this subtable have expected cell counts less than 5. Chi-square results may be invalid.

c. The minimum expected cell count in this subtable is less than one. Chi-square results may be invalid.

Comparisons of Column Proportions[b]

		Clinical/instrumental outcome		
		Not Treated (A)	Favorable (TICI2b-3 and/or FCR) (B)	Not consistent (TICI2b-3 and Delta NIHSS<0) (C)
S	Male			
	Female			
INTERVENTION	Not treated		.[a]	.[a]
	IVT	.[a]		.[a]

	EVT		A	A
	Bridging		A	A
Occluded vessel	ACA		.[a]	.[a]
	MCA			
	Carotid terminal			
	ICA intra			.[a]
	ICA extra	B		
	Tandem			
	Combined (MCA+ACA)	B		.[a]
	VB	.[a]	.[a]	.[a]
Side	Right			
	Left			
	Bil		.[a]	
Perfusion deficit (Yes/No)	Yes		A	
	Yes No penumbra	B		
Ischemic lesion at CT/MR control (Yes/No)	No			.[a]
	Yes			.[a]
Anatomical Anatomical inclusion of hypoperfused area in the ischemic lesion at CT/MR control (Yes/No)	No		.[a]	.[a]
	Yes		.[a]	.[a]
DWI Core inclusion in FIA	Partial (core higher)			
	Complete (core equal)			
	Higher (ischemia>core)	B		B
	No FIA			.[a]
pcASL Penumbra inclusion in FIA	Partial (penumbra higher)		A C	
	Complete (penumbra equal)	B		B

	Higher (ischemia>penumbra)			.[a]
	No FIA			.[a]

Results are based on two-sided tests. For each significant pair, the key of the category with the smaller column proportion appears in the category with the larger column proportion.

Significance level for upper case letters (A, B, C): .05

a. This category is not used in comparisons because its column proportion is equal to zero or one.

b. Tests are adjusted for all pairwise comparisons within a row of each innermost subtable using the Bonferroni correction.