Tasks in Diagnosis of Ischemic Stroke

Subjects: Neuroimaging
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Stroke is undoubtedly challenging medically and has great social and economic impact. Population-based studies have shown that the incidence of stroke in high-income countries decreased significantly between the years 1970–2000, and that the incidence continues to decrease with a current annual rate of 1–1.5%. Since the year 2000, mortality rates from stroke have fallen in all members of the Organization for Economic Co-operation and Development (OECD) and partner countries, with an average reduction of 52%. The explanation for this is a reduction in risk factors, primarily smoking, and improvement in the quality of medical care.

MRI CT Ischemic Stroke

1. First Task: To Rule Out Intracranial Hemorrhage

CT is a basic imaging method in the diagnostic workflow of stroke patients. CT is widely available, could examine nearly all patients included non-cooperating ones, a CT brain scan is very fast, being acquired in seconds. The advantage of non-enhanced CT (NECT) is the lack of absolute contraindications; generally speaking, in the acute setting, pregnancy is not considered a contraindication. For years, NECT has served as the gold standard method for detecting intracranial hemorrhage. NECT, with high sensitivity, is able to identify a small amount of acute blood in the brain parenchyma as well as in the extra-axial spaces such as the subarachnoid, subdural, epidural and intraventricular spaces [1]. However, NECT is not the only method which is sovereign in the diagnosis of acute intracerebral hemorrhage (ICH). MRI, especially with the help of T2 susceptibility-weighted imaging (T2 SWI) and diffusion-weighted imaging (DWI), is able to detect hyperacute/acute ICH with excellent accuracy [2][3]. However, in some cases, conventional MRI is not able to distinguish between calcifications and hemorrhage; thus, both pathologies are hypointense on T2 SWI and sometimes calcifications may be hyperintense on T1-weighted sequences similarly as subacute hematoma. However, quantitative susceptibility mapping is a novel postprocessing technique that may successfully solve that diagnostic problem [4]. Moreover, in comparison to NECT, MRI has higher sensitivity in the detection of subacute or chronic ICH as well as microhemorrhages [3]. The sensitivity of NECT in the detection of microbleeds is especially poor [5]. MRI is also more sensitive than NECT in detecting hemorrhagic transformation of infarction [5].

The detection of aneurysmal subarachnoid hemorrhage (SAH) is not as straightforward as the detection of ICH; there are pitfalls primarily related to time factors as well as the amount of hemorrhage. NECT detection of SAH depends on the attenuation (in Hounsfield units) of blood in the cerebrospinal fluid [6]. This attenuation depends on the amount of blood mixed with cerebrospinal fluid, on the hematocrit and hemoglobin level, and on the level of hemoglobin degradation. The sensitivity of NECT for SAH within first 6 h after stroke event onset is 99% [6].

However, the sensitivity of NECT in the days following stroke onset decreases moderately; after 5 to 7 days from the acute SAH event, the sensitivity of NECT decreases sharply [7]. Therefore, in the case of strong suspicion of SAH, other methods must be applied. One of the methods able to satisfactorily solve this problem is lumbar puncture, which has often been required to show xanthochromia and confirm SAH [7]. However, with the advantage of modern imaging methods such as MRI, invasive lumbar puncture may be avoided. MRI of the brain, with use of T2-weighted fluid-attenuated inversion recovery (T2 FLAIR), DWI and T2 SWI sequences, is very sensitive in the detection of both acute and subacute SAH, with a sensitivity of approximately 98% [8]. The reason for this high sensitivity in the detection of subacute SAH is the ability of T2 FLAIR sequences to show even minimal protein in the cerebrospinal fluid [9]. Moreover, another advantage of MRI is the possibility to identify other potential causes of the patient's acute status that may mimic stroke, called stroke mimics. There are however some disadvantages of MRI that limit its use as a method of the first choice. MRI scans take considerably longer; currently the duration of a single sequence typically minutes, with complete brain protocols generally requiring about 15 min. Furthermore, there are contraindications to MRI, both relative and absolute, as well as motion and metal artifacts may reduce the yield of scans.

2. Second Task: To Identify Potential Large Vessel Occlusion and Its Localization

The fact that EVT is currently the standard of care in case of AIS with LVO has been stressed previously. Potential candidates for EVT should be screened for the presence and localization of LVO [10]. CT angiography (CTA) is a fast and suitable tool; a disadvantage of CTA is the necessity of intravenous iodinated contrast agent application, which brings potential adverse effects. Monophasic CTA should be performed from the aortic arch to the brain vertex. There is also the potential for multiphase extension as well as repeating the scan. Monophasic CTA acquired at peak arterial phase typically provides the exact localization of occlusion and a "road map" for EVT navigation. It may also provide basic assessment of collaterals; however, there is the considerable risk of collateral underestimation due to the early time of acquisition. CTA sensitivity for intracranial occlusion detection has been reported as high as 100% [11]. Distal occlusion may, however, be missed by inexperienced raters. According to a recent study by Fasen et al., as many as 20% of LVOs were surprisingly missed on initial CTA evaluation; non-radiologists were more likely to miss LVO compared with radiologists/neuroradiologists, and M2 MCA occlusion was more likely to be missed compared with proximal occlusions [12]. Multiphasic CTA solves these limitations, as equilibrium venous phase and late venous phase may be added to common acquisitions during peak arterial phase (monophasic CTA) [13][14]. Calcified emboli may also be a source of misinterpretation and thus are frequently overlooked [12][15]. The most common potential sources of calcified emboli are calcified aortic stenosis, carotid atherosclerotic plaque and mitral annular calcifications [15]. Careful evaluation of NECT while searching for calcified density in the branches of MCA may be helpful [15]. Moreover, EVT by stent retriever in the case of calcified emboli is less effective, with greater potential for severe periprocedural adverse events [16]. An important pitfall in the CTA evaluation of extracranial occlusion must be mentioned; hard calcified atherosclerotic plaques may cause difficulties in the differentiation between near-occlusion and occlusion. Near occlusion is often under-reported in clinical practice [17].

MRI is another method that may be used in the evaluation of potential LVO and its localization. There are two technical possibilities in MR angiography (MRA); native or unenhanced MRA primarily using the time of flight (TOF) technique, the second is contrast enhanced MRA (CEMRA) with intravenous gadolinium-based contrast agent (GBCA) administration. Briefly, the TOF technique visualizes flow and is based on the phenomenon of the inflow effect of fresh hydrogen protons entering an imaging slice. On the TOF technique the morphology of the vessel is not seen; however, moving blood is depicted. For better visualization, the source data may be reconstructed using maximum intensity projection (MIP) or volume rendering reconstruction (VRT). There are, however, some pitfalls and limitations to TOF. The TOF method is based on the detection of flow; however, slow flow or flow from parallel vessels may be desaturated like stationary (non-moving) tissues and signals from vessels may be lost. Moreover, turbulent flow may cause spin-dephasing and unexpectedly short T2 relaxation resulting again in signal loss. The same may happen in the case of retrograde arterial flow. TOF sensitivity to intracranial stenosis or occlusion detection is lower than CTA sensitivity; 70% sensitivity for stenosis detection, 87% sensitivity for occlusion detection, and approximately 59% positive predictive value for occlusion has been reported [10]. TOF 3D MRA may be as well affected by some T1 hyperintense structures or objects such as hematomas that may be visible and may affect or limit image quality. Moreover, interpretation of the exam may be partly or completely impossible due to patient motion. Another disadvantage is that the sequence generally takes minutes to acquire.

CEMRA is a technique involving T1-weighted spoiled gradient-echo sequences after intravenous administration of GBCA. Single- or multi-phasic data may be acquired. The source data may again be used for MIP and VRT 3D reconstructions. CEMRA removes above-mentioned limitations of different flow artifacts. Disadvantages of CEMRA is the need for GBCA application [18]. A recent study unsurprisingly showed that, in the case of AIS with LVO, CEMRA detects arterial occlusions better than TOF MRA and when combined with other MRI morphological sequences, is better able to assess thrombus length and localization [19].

3. The Third Task: To Estimate the Ischemic Core

There are several possibilities for both CT and MRI in the assessment or estimation of potential acute ischemic changes and estimation of the ischemic core. For these purposes, the Alberta stroke program early CT score (ASPECTS) was developed. ASPECTS should be evaluated on NECT. ASPECTS is simply a semiquantitative score that assesses the extent of early ischemic changes in the territory of the MCA [20]. The territory of the MCA is divided into 10 regions, and one point is subtracted for each area where early signs of ischemia are detected, such as hypodensities or blurring. ASPECTS evaluation seems simple; however, there are a number of pitfalls and limitations. Acute ischemic changes within the first hours of stroke onset may be very subtle, as the morphological background of those changes is cytotoxic oedema. The evaluation of these subtle changes on NECT requires an experienced neuroradiologist. It is not surprising that interobserver and intraobserver variability in ASPECTS evaluation is suboptimal [21]. Therefore, automated software based on machine learning was developed to avoid the subjectivity of raters. Initially, some radiologists expressed skepticism with respect to the utility of such software; however, it was soon proven that the automated software is not inferior to evaluation by radiologists [22]. The undeniable advantage of automated software is its speed.

Initially ASPECTS was used for the selection patients that would profit from IVT; thus, ASPECTS grading was proven as an independent predictor of functional outcome [20][23]. Recently, ASPECTS has been used for the selection of subjects for EVT; an ASPECTS score > 6 is a key factor in selecting patients with AIS with LVO in the early time window, up 6 h from stroke onset, that should benefit from acute EVT [24]. It has repeatedly been proven that, in the early time window, ASPECTS ≥ 6 is associated with good clinical outcome and predicts functional independence after EVT [25][26][27]. Conversely, in the case of ASPECTS in the range of 0–5, the benefit EVT is not clear [28]. The role of ASPECTS in selecting AIS patients in the late time window, more than 6 h from last known well (LKW), has not been widely established; the preferred diagnostic imaging method for patient selection is CT perfusion (CTP) or MRI with DWI and MR perfusion (MRP) [29][30]. However, it could be found that some studies that have shown ASPECTS grading as an independent predictor of good clinical outcome in AIS patients in the late or unknown time window, and consider ASPECTS a suitable criterion in selecting patients for EVT in the late time window [31][32].

ASPECTS is not the same as the stroke core volume. In some studies, great variability between specific ASPECTS grade and the cerebral blood volume (CBV) on CTP has been found [25][26]. The explanation is straightforward as each region of the MCA territory in ASPECTS evaluation has a different volume, one point on ASPECTS always means a different brain volume. Finally, some studies have reported that the ischemic core on CTP does not correlate with the definitive infarction volume, at least in the early time window; this topic is discussed in the next paragraphs. However, in a recent study by Nannoni et al. that included 1046 subjects, moderate correlation between ASPECTS and the core volume on CTP in AIS was reported; the correlation was stronger in subjects with LVO and in a subgroup of patients in the late time window [27]. There are several other variables beside the time window and LVO presence that influenced ASPECTS. Pre-stroke statin use positively influences collateral perfusion and is associated with higher ASPECTS scores [27]. In contrast, hyperglycemia at admission is associated with poorer ASPECTS scores [27]. This finding is in concordance with previously-published studies that showed hyperglycemia is associated with early infarct expansion [33]. Unsurprisingly, good collaterals are also associated with higher ASPECTS scores [27].

CTP is an established method used to evaluate the viability of brain tissue. CTP distinguishes ischemic core from penumbra (potentially salvageable tissue) by measuring blood perfusion in cerebral regions following intravenous contrast agent injection. Cerebral blood flow (CBF), CBV and mean transit time (MTT) are basic parameters determined by CTP analysis and are used for ischemic core and penumbra calculations. Software calculates absolute CBF in mL/100 g/min and CBV in mL/100 g for all voxels; however, relative values (rCBF, rCBV) in percentages (%) are also calculated. Standard ischemic core delineation is rCBF < 30% in comparison with the healthy, non-affected hemisphere [34]. Evaluation of CTP data using CT postprocessing software is often a complicated process, therefore automated software based on artificial intelligence was developed to avoid this limitation; its undeniable advantage is its speed.

Although CTP has been used for decades, its results were often controversial [35]. However, the DAWN and DEFUSE 3 trials figuratively resuscitated CTP, as they used CTP-calculated penumbra volume as a predictive factor for clinical outcome in patients treated with EVT in the late time window [29][30]. However, as was mentioned

above, there is evidence that the ischemic core on CTP poorly correlates with the definitive ischemic volume in patients with AIS with LVO after successful urgent EVT, at least in the time window up to 6 h from AIS onset [34][36][37]. Moreover, some authors have reported significant overestimation of initial core volume on CTP, which was romantically called a “ghost infarct” [38][39]. Despite the above mentioned, DAWN or DEFUSE 3 indication criteria for EVT in the late time window are still used. However, there are studies that bring some data implying that can be possibly standed without CTP. Desai et al. analyzed clinical outcomes of subjects who did not meet DAWN and DEFUSE 3 inclusion criteria and received off-label EVT in the late time window; 30% of treated patients achieved functional independence at 3 months [40]. Moreover, Alexandre et al. treated 49 patients with LVO in anterior circulation in the time window longer than 6 h and did not use CPT at all [41]. In 77% of subjects, recanalization was successful and 18 of 49 treated patients achieved functional independence at 3 months after treatment [41]. The possibilities with MRI are similar to CTP, and MRP is also one of the methods available in the diagnostic spectrum. MRP is based on the detection of signal decrease due to the susceptibility effect of GBCA during the passage GBCA through the intracerebral vessels. The signal decrease observed per voxel is directly proportional to the concentration of gadolinium in the vessels; rCBV, rCBF, MTT and TTP may be calculated from the source data and used for perfusion map construction [42].

MRI with DWI and T2 FLAIR sequences is definitively the best method in acute ischemic core volume assessment; their sensitivity and specificity have been repeatedly proven. DWI detects hyperacute ischemic changes at the stage of cytotoxic edema, which appears at the moment of Na^+/K^+ ATPase failures, when water molecules translocate from the extracellular to the intracellular space. Moreover, in cytotoxic edema the volume of the cell increases and extracellular space decreases, restricting the free diffusion of water molecules. Hyperacute ischemic changes are detectable as early as minutes to hours from arterial occlusion [42]. The area of high signal intensity on DWI does not unequivocally mean ischemic core, as cytotoxic edema itself may be reversible [43]. Later when cell membrane disruption develops and vasogenic edema appears, not only DWI but also T2 signal increases and positivity on T2 FLAIR appears, which indicates the onset of irreversible ischemic changes [42]. ASPECTS could be also evaluated by the same way as on NECT on DWI that precisely depicts the extend of acute ischemia, this evaluation is simply called DWI-ASPECTS and has also been incorporated into clinical practice [44].

References

1. Aygun, N.; Masaryk, T.J. Diagnostic imaging for intracerebral hemorrhage. Neurosurg. Clin. N. Am. 2002, 13, 313–334.
2. Fiebach, J.B.; Schellinger, P.D.; Gass, A.; Kucinski, T.; Siebler, M.; Villringer, A.; Olkers, P.; Hirsch, J.G.; Heiland, S.; Wilde, P.; et al. Stroke magnetic resonance imaging is accurate in hyperacute intracerebral hemorrhage: A multicenter study on the validity of stroke imaging. Stroke 2004, 35, 502–506.

3. Kidwell, C.S.; Chalela, J.A.; Saver, J.L.; Starkman, S.; Hill, M.D.; Demchuk, A.M.; Butman, J.A.; Patronas, N.; Alger, J.R.; Latour, L.L.; et al. Comparison of MRI and CT for detection of acute intracerebral hemorrhage. JAMA 2004, 292, 1823–1830.
4. Ciraci, S.; Gumus, K.; Doganay, S.; Dundar, M.S.; Kaya Ozcora, G.D.; Gorkem, S.B.; Per, H.; Coskun, A. Diagnosis of intracranial calcification and hemorrhage in pediatric patients: Comparison of quantitative susceptibility mapping and phase images of susceptibility-weighted imaging. Diagn. Interv. Imaging 2017, 98, 707–714.
5. Haller, S.; Vernooij, M.W.; Kuijer, J.P.A.; Larsson, E.M.; Jäger, H.R.; Barkhof, F. Cerebral Microbleeds: Imaging and Clinical Significance. Radiology 2018, 287, 11–28.
6. Dubosh, N.M.; Bellolio, M.F.; Rabinstein, A.A.; Edlow, J.A. Sensitivity of Early Brain Computed Tomography to Exclude Aneurysmal Subarachnoid Hemorrhage: A Systematic Review and Meta-Analysis. Stroke 2016, 47, 750–755.
7. Cortnum, S.; Sørensen, P.; Jørgensen, J. Determining the sensitivity of computed tomography scanning in early detection of subarachnoid hemorrhage. Neurosurgery 2010, 66, 900–902; discussion 903.
8. Shimoda, M.; Hoshikawa, K.; Shiramizu, H.; Oda, S.; Matsumae, M. Problems with diagnosis by fluid-attenuated inversion recovery magnetic resonance imaging in patients with acute aneurysmal subarachnoid hemorrhage. Neurol. Med. Chir. 2010, 50, 530–537.
9. Verma, R.K.; Kottke, R.; Andereggen, L.; Weisstanner, C.; Zubler, C.; Gralla, J.; Kiefer, C.; Slotboom, J.; Wiest, R.; Schroth, G.; et al. Detecting subarachnoid hemorrhage: Comparison of combined FLAIR/SWI versus CT. Eur. J. Radiol. 2013, 82, 539–545.
10. Almekhlafi, M.A.; Kunz, W.G.; Menon, B.K.; McTaggart, R.A.; Jayaraman, M.V.; Baxter, B.W.; Heck, D.; Frei, D.; Derdeyn, C.P.; Takagi, T.; et al. Imaging of Patients with Suspected Large-Vessel Occlusion at Primary Stroke Centers: Available Modalities and a Suggested Approach. AJNR 2019, 40, 396–400.
11. Bash, S.; Villablanca, J.P.; Jahan, R.; Duckwiler, G.; Tillis, M.; Kidwell, C.; Saver, J.; Sayre, J. Intracranial vascular stenosis and occlusive disease: Evaluation with CT angiography, MR angiography, and digital subtraction angiography. Am. J. Neuroradiol. 2005, 26, 1012–1021.
12. Fasen, B.A.C.M.; Heijboer, R.J.J.; Hulsmans, F.H.; Kwee, R.M. CT Angiography in Evaluating Large-Vessel Occlusion in Acute Anterior Circulation Ischemic Stroke: Factors Associated with Diagnostic Error in Clinical Practice. Am. J. Neuroradiol. 2020, 41, 607–611.
13. Yu, A.Y.; Zerna, C.; Assis, Z.; Holodinsky, J.K.; Randhawa, P.A.; Najm, M.; Goyal, M.; Menon, B.K.; Demchuk, A.M.; Coutts, S.B.; et al. Multiphase CT angiography increases detection of anterior circulation intracranial occlusion. Neurology 2016, 87, 609–616.

14. Menon, B.K.; d'Esterre, C.D.; Qazi, E.M.; Almekhlafi, M.; Hahn, L.; Demchuk, A.M.; Goyal, M. Multiphase CT Angiography: A New Tool for the Imaging Triage of Patients with Acute Ischemic Stroke. Radiology 2015, 275, 510–520.
15. Walker, B.S.; Shah, L.M.; Osborn, A.G. Calcified cerebral emboli, a "do not miss" imaging diagnosis: 22 new cases and review of the literature. AJNR 2014, 35, 1515–1519.
16. Dobrocky, T.; Piechowiak, E.; Cianfoni, A.; Zibold, F.; Roccatagliata, L.; Mosimann, P.; Jung, S.; Fischer, U.; Mordasini, P.; Gralla, J. Thrombectomy of calcified emboli in stroke. Does histology of thrombi influence the effectiveness of thrombectomy? J. Neurointerv. Surg. 2018, 10, 345–350.
17. Johansson, E.; Gu, T.; Aviv, R.I.; Fox, A.J. Carotid near-occlusion is often overlooked when CT angiography is assessed in routine practice. Eur. Radiol. 2020, 30, 2543–2551.
18. Riederer, S.J.; Stinson, E.G.; Weavers, P.T. Technical Aspects of Contrast-enhanced MR Angiography: Current Status and New Applications. Magn. Reson. Med. Sci. 2018, 17, 3–12.
19. Dhundass, S.; Savatovsky, J.; Duron, L.; Fahed, R.; Escalard, S.; Obadia, M.; Zuber, K.; Metten, M.A.; Mejdoubi, M.; Blanc, R.; et al. Improved detection and characterization of arterial occlusion in acute ischemic stroke using contrast enhanced MRA. J. Neuroradiol. 2020, 47, 278–283.
20. Barber, P.A.; Demchuk, A.M.; Zhang, J.; Buchan, A.M. Validity and reliability of a quantitative computed tomography score in predicting outcome of hyperacute stroke before thrombolytic therapy. ASPECTS Study Group. Alberta Stroke Programme Early CT Score. Lancet 2000, 355, 1670–1674.
21. Farzin, B.; Fahed, R.; Guilbert, F.; Poppe, A.Y.; Daneault, N.; Durocher, A.P.; Lanthier, S.; Boudjani, H.; Khoury, N.N.; Roy, D.; et al. Early CT changes in patients admitted for thrombectomy: Intrarater and interrater agreement. Neurology 2016, 87, 249–256.
22. Nagel, S.; Sinha, D.; Day, D.; Reith, W.; Chapot, R.; Papanagiotou, P.; Warburton, E.A.; Guyler, P.; Tysoe, S.; Fassbender, K.; et al. e-ASPECTS software is non-inferior to neuroradiologists in applying the ASPECT score to computed tomography scans of acute ischemic stroke patients. Int. J. Stroke 2017, 12, 615–622.
23. Hill, M.D.; Buchan, A.M.; Canadian Alteplase for Stroke Effectiveness Study (CASES) Investigators. Thrombolysis for acute ischemic stroke: Results of the Canadian Alteplase for Stroke Effectiveness Study. CMAJ 2005, 172, 1307–1312.
24. Powers, W.J.; Rabinstein, A.A.; Ackerson, T.; Adeoye, O.M.; Bambakidis, N.C.; Becker, K.; Biller, J.; Brown, M.; Demaerschalk, B.M.; Hoh, B.; et al. Guidelines for the Early Management of Patients with Acute Ischemic Stroke: 2019 Update to the 2018 Guidelines for the Early Management of Acute Ischemic Stroke: A Guideline for Healthcare Professionals from the American Heart Association/American Stroke Association. Stroke 2019, 50, e344–e418.

25. Haussen, D.C.; Dehkharghani, S.; Rangaraju, S.; Rebello, L.C.; Bouslama, M.; Grossberg, J.A.; Anderson, A.; Belagaje, S.; Frankel, M.; Nogueira, R.G. Automated CT Perfusion Ischemic Core Volume and Noncontrast CT ASPECTS (Alberta Stroke Program Early CT Score): Correlation and Clinical Outcome Prediction in Large Vessel Stroke. Stroke 2016, 47, 2318–2322.
26. Olive-Gadea, M.; Martins, N.; Boned, S.; Carvajal, J.; Moreno, M.J.; Muchada, M.; Molina, C.A.; Tomasello, A.; Ribo, M.; Rubiera, M. Baseline ASPECTS and e-ASPECTS Correlation with Infarct Volume and Functional Outcome in Patients Undergoing Mechanical Thrombectomy. J. Neuroimaging 2019, 29, 198–202.
27. Nannoni, S.; Ricciardi, F.; Strambo, D.; Sirimarco, G.; Wintermark, M.; Dunet, V.; Michel, P. Correlation between ASPECTS and Core Volume on CT Perfusion: Impact of Time since Stroke Onset and Presence of Large-Vessel Occlusion. Am. J. Neuroradiol. 2021, 42, 422–428.
28. Goyal, M.; Menon, B.K.; van Zwam, W.H.; Dippel, D.W.; Mitchell, P.J.; Demchuk, A.M.; Dávalos, A.; Majoie, C.B.; van der Lugt, A.; de Miquel, M.A.; et al. Endovascular thrombectomy after large-vessel ischaemic stroke: A meta-analysis of individual patient data from five randomised trials. Lancet 2016, 387, 1723–1731.
29. Albers, G.W.; Lansberg, M.G.; Kemp, S.; Tsai, J.P.; Lavori, P.; Christensen, S.; Mlynash, M.; Kim, S.; Hamilton, S.; Yeatts, S.D.; et al. A multicenter randomized controlled trial of endovascular therapy following imaging evaluation for ischemic stroke (DEFUSE 3). Int. J. Stroke 2017, 12, 896–905.
30. Jovin, T.G.; Ribo, M.; Pereira, V.; Furlan, A.; Bonafe, A.; Baxter, B.; Gupta, R.; Lopes, D.; Jansen, O.; Smith, W.; et al. Diffusion-weighted imaging or computerized tomography perfusion assessment with clinical mismatch in the triage of wake up and late presenting strokes undergoing neurointervention with Trevo (DAWN) trial methods. Int. J. Stroke 2017, 12, 641–652.
31. Nagel, S.; Herweh, C.; Pfaff, J.A.R.; Schieber, S.; Schönenberger, S.; Möhlenbruch, M.A.; Bendszus, M.; Ringleb, P.A. Simplified selection criteria for patients with longer or unknown time to treatment predict good outcome after mechanical thrombectomy. J. Neurointerv. Surg. 2019, 11, 559–562.
32. Konstas, A.A.; Minaeian, A.; Ross, I.B. Mechanical Thrombectomy in Wake-Up Strokes: A Case Series Using Alberta Stroke Program Early CT Score (ASPECTS) for Patient Selection. J. Stroke Cerebrovasc. Dis. 2017, 26, 1609–1614.
33. Shimoyama, T.; Kimura, K.; Uemura, J.; Saji, N.; Shibazaki, K. Elevated glucose level adversely affects infarct volume growth and neurological deterioration in non-diabetic stroke patients, but not diabetic stroke patients. Eur. J. Neurol. 2014, 21, 402–410.
34. Geuskens, R.R.; Borst, J.; Lucas, M.; Boers, A.M.; Berkhemer, O.A.; Roos, Y.B.; van Walderveen, M.A.; Jenniskens, S.F.; van Zwam, W.H.; Dippel, D.W.; et al. Characteristics of Misclassified CT Perfusion Ischemic Core in Patients with Acute Ischemic Stroke. PLoS ONE 2015, 10, e0141571.

35. Mazzei, M.A.; Preda, L.; Cianfoni, A.; Volterrani, L. CT perfusion: Technical developments and current and future applications. Biomed. Res. Int. 2015, 2015, 397521.
36. Kremenova, K.; Holesta, M.; Peisker, T.; Girsa, D.; Weichet, J.; Lukavsky, J.; Malikova, H. Is limited-coverage CT perfusion helpful in treatment decision-making in patients with acute ischemic stroke? Quant. Imaging. Med. Surg. 2020, 10, 1908–1916.
37. Tsang, A.C.O.; Lenck, S.; Hilditch, C.; Nicholson, P.; Brinjikji, W.; Krings, T.; Pereira, V.M.; Silver, F.L.; Schaafsma, J.D. Automated CT. Perfusion Imaging Versus Non-contrast CT for Ischemic Core Assessment in Large Vessel Occlusion. Clin. Neuroradiol. 2020, 30, 09–14.
38. Martins, N.; Aires, A.; Mendez, B.; Boned, S.; Rubiera, M.; Tomasello, A.; Coscojuela, P.; Hernandez, D.; Muchada, M.; Rodríguez-Luna, D.; et al. Ghost Infarct Core and Admission Computed Tomography Perfusion: Redefining the Role of Neuroimaging in Acute Ischemic Stroke. Interv. Neurol. 2018, 7, 513–521.
39. Boned, S.; Padroni, M.; Rubiera, M.; Tomasello, A.; Coscojuela, P.; Romero, N.; Muchada, M.; Rodríguez-Luna, D.; Flores, A.; Rodríguez, N.; et al. Admission CT perfusion may overestimate initial infarct core: The ghost infarct core concept. J. Neurointerv. Surg. 2017, 9, 66–69.
40. Desai, S.M.; Rocha, M.; Molyneaux, B.J.; Starr, M.; Kenmuir, C.L.; Gross, B.A.; Jankowitz, B.T.; Jovin, T.G.; Jadhav, A.P. Thrombectomy 6-24 hours after stroke in trial ineligible patients. J. Neurointerv. Surg. 2018, 10, 1033–1037.
41. Alexandre, A.M.; Pedicelli, A.; Valente, I.; Scarcia, L.; Giubbolini, F.; D'Argento, F.; Lozupone, E.; Distefano, M.; Pilato, F.; Colosimo, C. May endovascular thrombectomy without CT perfusion improve clinical outcome? Clin. Neurol. Neurosurg. 2020, 198, 106207.
42. Schaefer, P.W. Applications of DWI in clinical neurology. J. Neurol. Sci. 2001, 186 (Suppl. 1), 25–35.
43. Malikova, H.; Kremenova, K.; Budera, P.; Herman, D.; Weichet, J.; Lukavsky, J.; Osmancik, P. Silent strokes after thoracoscopic epicardial ablation and catheter ablation for atrial fibrillation: Not all lesions are permanent on follow-up magnetic resonance imaging. Quant. Imaging Med. Surg. 2021, 11, 3219–3233.
44. Barber, P.A.; Hill, M.D.; Eliasziw, M.; Demchuk, A.M.; Pexman, J.H.; Hudon, M.E.; Tomanek, A.; Frayne, R.; Buchan, A.M.; ASPECTS Study Group. Imaging of the brain in acute ischaemic stroke: Comparison of computed tomography and magnetic resonance diffusion-weighted imaging. J. Neurol. Neurosurg. Psychiatry 2005, 76, 1528–1533.