CANADIAN STROKE BEST PRACTICE RECOMMENDATIONS

Acute Stroke Management Evidence Tables

Seventh Edition, Update 2022

Section 4: Emergency Department Evaluation and Management of Patients with Transient Ischemic Attack and Acute Stroke – Neurovascular Imaging

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Published Guidelines

Guideline	Recommendations
Turc G, Bhogal P, Fischer U, et al. **European Stroke Organisation (ESO)—European Society for Minimally Invasive Neurological Therapy (ESMINT) guidelines on mechanical thrombectomy in acute ischaemic stroke endorsed by Stroke Alliance for Europe (SAFE).** ***Eur Stroke J* 2019;4(1):6-12.**	PICO 8: For adults with LVO related acute ischaemic stroke, does selection of MT candidates based on a particular ASPECTS or infarct core volume threshold compared with no specific threshold: – improve identification of patients with a therapy effect of MT on functional outcome? – decrease the risk of symptomatic intracerebral hemorrhage? *Recommendations* • In the 0-6 hour time window, we recommend MT plus best medical management (BMM) (including IVT whenever indicated) over BMM alone in LVO related anterior circulation stroke patients without evidence of extensive infarct core (e.g. ASPECTS 6 on non-contrast CT scan or infarct core volume 70 ml). Quality of evidence: High ⊕⊕⊕⊕, Strength of recommendation: Strong ↑↑ • In the 6-24 hour time window, we recommend MT plus BMM (including IVT whenever indicated) over BMM alone in LVO related anterior circulation stroke patients fulfilling the selection criteria of DEFUSE-3* or DAWN**, including estimated volume of infarct core. Quality of evidence: Moderate ⊕⊕⊕, Strength of recommendation: Strong ↑↑ • We recommend that anterior circulation stroke patients with extensive infarct core (e.g. ASPECTS 70 ml or >100 ml) be included in RCTs comparing mechanical thrombectomy plus best medical management versus best medical management alone. Quality of evidence: Very Low ⊕, Strength of recommendation: - PICO 9: For adults with LVO related acute ischaemic stroke, does selection of MT candidates based on advanced perfusion, core, or collateral imaging compared with no advanced imaging: • improve identification of patients with a therapy effect of mechanical thrombectomy on functional outcome? • decrease the risk of symptomatic intracerebral hemorrhage? *Recommendations* • In adult patients with anterior circulation LVO-related acute ischaemic stroke presenting from 0-6 hours from time last known well, advanced imaging is not necessary for patient selection. Quality of evidence: Moderate ⊕⊕⊕, Strength of recommendation: Weak ↓ • In adult patients with anterior circulation LVO-related acute ischaemic stroke presenting beyond 6 hours from time last known well, advanced imaging selection is necessary. Quality of evidence: Moderate ⊕⊕⊕, Strength of recommendation: Strong ↑↑
Powers WJ, Rabinstein AA, Ackerson T, Adeoye OM, Bambakidis NC, Becker K, Biller J, Brown M, Demaerschalk BM, Hoh B, Jauch EC, Kidwell CS, Leslie-Mazwi TM, Ovbiagele B, Scott PA, Sheth KN, Southerland AM, Summers DV, Tirschwell DL; on behalf of the American Heart Association Stroke Council. **Guidelines for the early management of patients**	**2. Emergency Evaluation & Treatment** **2.1. Stroke Scales** 1. The use of a stroke severity rating scale, preferably the NIHSS, is recommended. (Class 1; LOE B-NR). **2.2. Head & Neck Imaging** 1. All patients with suspected acute stroke should receive emergency brain imaging evaluation on first arrival to a hospital before initiating any specific therapy to treat AIS (Class 1; LOE A). 2. Systems should be established so that brain imaging studies can be performed as quickly as possible in patients who may be candidates for IV fibrinolysis or mechanical thrombectomy or both. (Class 1; LOE B-NR).

Guideline	Recommendations
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.** **(selected)**	3. Noncontrast CT (NCCT) is effective to exclude ICH before IV alteplase administration. Class 1; LOE A 4. Magnetic resonance (MR) imaging (MRI) is effective to exclude ICH before IV alteplase administration. Class 1. LOE-B-NR. 5. CTA with CTP or MR angiography (MRA) with diffusion-weighted magnetic resonance imaging (DW-MRI) with or without MR perfusion is recommended for certain patients. (Class I; LOE A).
Clinical Guidelines for Stroke Management 2017. Melbourne (Australia): National Stroke Foundation.	Strong Recommendation All patients with suspected stroke who are candidates for reperfusion therapies should undergo brain imaging immediately. All other suspected stroke patients should have an urgent brain CT or MRI (‘urgent’ being immediately where facilities are available and preferably within 60 minutes). Weak recommendation Updated In patients with suspected stroke and TIA, MRI is more sensitive and specific than non-contrast CT and is the preferred modality when diagnostic confirmation is required. Practice statement Consensus-based recommendation New Either CT or MRI are acceptable acute imaging options but these need to be immediately accessible to avoid delaying reperfusion therapies. Strong recommendation New If using CT to identify hyperdense thrombus, thin slice (< 2 mm) noncontrast CT should be used rather than the standard 5 mm slices to improve diagnostic sensitivity for vessel occlusion. Weak recommendation New CT perfusion imaging may be used in addition to routine imaging to improve diagnostic and prognostic accuracy. Strong recommendation Updated • All patients who would potentially be candidates for endovascular thrombectomy should have vascular imaging from aortic arch to cerebral vertex (CTA or MRA) to establish the presence of vascular occlusion as a target for thrombectomy and to assess proximal vascular access. • All other patients with carotid territory symptoms who would potentially be candidates for carotid re-vascularisation should have early vascular imaging to identify stenosis in the ipsilateral carotid artery. CT angiography (if not already performed as part of assessment for reperfusion therapies), Doppler ultrasound or contrast-enhanced MR angiography are all reasonable options depending on local experience and availability.

Evidence Tables

Neurovascular Imaging Using Non Contast CT and MRI

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Brunser et al. 2013 **Chile** **Prospective study**	NA	842 patients admitted to the Emergency Department of a single institution between 2004 and 2011 with suspected acute ischemic stroke. Mean age of persons with confirmed stroke was 71.1 years, 55.7% were women.	The test characteristics of DWI to identify patients with acute ischemic stroke were examined. A final diagnosis of ischemic stroke was made based on patient history, clinical examination, and the evolution of typical vascular brain damage, viewed on CT/DWI, or on follow-up imaging, or if an occluded vessel was observed in the symptomatic territory.	**Primary outcomes:** Sensitivity, specificity, accuracy, positive and negative likelihood ratios	A final diagnosis of ischemic stroke was made in 729, while 113 were stroke mimics. Of 729 patients with a diagnosis of stroke, 609 (88.6%) had a DWI performed, of which 551 (90.4%) had an image compatible with an ischemic stroke. Of 113 patients with a diagnosis of stroke mimic, 103 had a DWI performed, of which 3 showed abnormal findings. Among patients with a suspected ischemic stroke, DWI had a sensitivity of 90% (95% CI, 87.9–92.6), and specificity of 97% (95 CI%, 91.8–99). Accuracy was 95%. The positive likelihood ratio was of 31 (95% CI, 10.1–94.7), and the negative likelihood ratio was 0.1 (95% CI, 0.077–0.126).
Brazzelli et al. 2009 **UK** **Cochrane Review**	NA	8 studies met the inclusion criteria (7 of the 8 evaluated CT and MRI (DWI – diffusion weighted) for ischemic stroke and 2 of the 8 studies evaluated MRI for hemorrhagic stroke). A total of 226 patients were included. Mean age was 65.1 yrs.	All studies that compared the diagnostic accuracy of MRI and CT for either ischemic or hemorrhagic stroke were included in the review.	**Primary outcomes**: Sensitivity and specificity of the diagnostic tests reported separately for diagnosing ischemic stroke and hemorrhagic stroke.	**Diagnosis of Ischemic stroke (DWI and CT):** **DWI**: Sensitivity 0.99 (95% CI 0.23 to 1.00); Specificity 0.92 (95% CI 0.83 to 0.97). **CT**: Sensitivity 0.39 (95% CI 0.16 to 0.69); Specificity 1.00 (95% CI 0.94 to 1.00). **Diagnosis of Hemorrhagic stroke (MRI – DWI and GRE):** **DWI**: (1 study) Sensitivity: 1.00 (95% CI 0.91 to 1.00); Specificity: 1.00 (95% CI 0.91 to 1.00). **GRE/DWI**: (1 study) Sensitivity: 0.83 (0.52 to 0.98); Specificity: 1.00 (95% CI 0.95 to 1.00). **GRE**: (1 study) Sensitivity: 1.00 (0.91 to 1.00); Specificity: 0.98 (0.87 to 1.00).

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					Cautions: Authors indicate the presence of possible selection bias of patients. Most studies did not include patients who were "stroke mimics". This may explain the high specificity and question the usefulness of the findings.
Chalela et al. 2007 **USA** **Prospective study**	NA	356 patients admitted to a single facility from 2000-2002 for emergency assessment of suspected acute stroke. Median age was 76 years.	The accuracy of non-contrast CT and MRI (with diffusion-weighted and susceptibility weighted images) for the detection of total stroke, ischemic stroke and ICH, was assessed. Scans were independently interpreted by four experts, who were unaware of clinical information, MRI-CT pairings, and follow-up imaging. The final diagnosis was established by the patient's hospital record during admission.	**Primary outcomes:** Sensitivity, specificity	The median time from symptom onset to MRI imaging was 367 minutes; the median time from symptom onset to CT imaging was 390 min. 217 patients had a final diagnosis of stroke. Acute stroke was detected in 185 patients (52%; 95% CI 47–58) with MRI and in 59 patients (17%; 13–21) with CT. Ischemic stroke was detected in 164 patients (46%; 95% CI 41–51) with MRI and in 35 patients (10%; 95% CI 7-14) with CT. Intracranial hemorrhage was detected in 23 patients (6%; 95% CI 4-10) with MRI and in 25 patients (7%; 95% CI 5-10) with CT. Relative to final diagnosis, the sensitivity and specificity of MRI to detect any stroke was 83% (95% CI 78%–88%) and 97% (95% CI 92%–99%) Relative to final diagnosis, the sensitivity and specificity of CT to detect any stroke was 26% (95% CI 20%–32%) and 98% (95% CI 93%–99%). Among patients with an ischemic stroke who received a scan within 3 hours of stroke onset the sensitivity and specificity of MRI was 73% and 92%, respectively. The corresponding values for CT scan were 12% and 100%.

CT Perfusion Imaging To Idenify Ischemic Stroke

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Shen et al. 2017 **China** **Systematic review & meta-analysis**	8 studies were of high quality	27 studies including 2,168 patients presenting with possible acute ischemic stroke. The percentage of patients with confirmed ischemic stroke ranged from 20-100%.	The diagnostic accuracy of CT perfusion (CTP) was compared with non-enhanced computed tomography (NCCT) and computed tomography angiography (CTA) in detecting acute ischemic stroke. The reference standard in all studies was a follow-up CT or MRI	**Primary outcomes:** Sensitivity, specificity	All patients underwent CTP within 24 hours of symptom onset. In 12 studies, patients received imaging within 6 hours. Using data from 18 studies, the pooled sensitivity of CTP to identify ischemic stroke was 82% (95% CI 75–88%), the specificity was 96% (95% CI 89–99%). 10 studies compared the accuracy of CTP with NCCT. The sensitivity of NCCT ranged from 15% to 86%. The specificity was 100%. No summary pooled estimate was reported. 7 studies compared the accuracy of CTP with CTA. The sensitivity of CTA ranged from 56% to100%, and the specificity was 100%. There was no significant difference between CTP and CTA in the pooled sensitivities and specificities. The authors concluded CTP is more accurate than NCCT and has similar accuracy to CTA in detecting acute ischemic stroke, although the evidence is not strong.
Biesbroek et al. 2013 **The Netherlands** **Systematic review & meta-analysis**	QUADAS scores ranged from 5-13 (median score 11)	15 studies including 1,107 patients with possible ischemic stroke. Mean NIHSS score, when reported, ranged from 8.3 to 13.2	The diagnostic value of CTP for detecting ischemic stroke was assessed. The reference standard was follow-up MRI-DWI (n=4), follow-up MRI or follow-up CT (n=11).	**Primary outcomes:** Sensitivity, specificity	All patients underwent CTP within 48 hours of symptom onset. In 8 studies, patients received imaging within 6 hours. The pooled sensitivity of CTP was 80% (95% CI: 72–86%), specificity was 95% (95% CI: 86–98%). Sensitivities in individual studies ranged from 50% to 100%, specificities ranged from 70% to 100%. The percentage of patients with confirmed stroke ranged from 37% to 100%.

Diagnostic Utility of NCCT and CTP in Posterior Circulation

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Katyal et al. 2021 **Australia** **Systematic review & meta-analysis**	Risk of bias was assessed as low in 11 studies, using the Jadad scale.	14 studies (9 diagnostic and 5 prognostic) including 2,074 adult patients, diagnosed with posterior circulation acute ischemic stroke. Median age ranged from 57 to 71 years.	Diagnostic/prognostic utility of CTP and NCCT to identify patients who are likely to experience favorable outcomes following reperfusion therapy was assessed using pooled sensitivity (SENS) and specificity (SPEC), and area under the curve (AUC).	**Primary outcomes:** SN, SP, AUC	The diagnostic accuracy of CTP was comparable to NCCT (AUC_{CTP}: 0.90 [95% CI 0.87–0.92] vs. AUC_{NCCT}: 0.96 [95% CI 0.94– 0.97]). The pooled sensitivity of CTP was higher compared with NCCT ($SENS_{CTP}$: 72% [95% CI 57%–83%] vs. $SENS_{NCCT}$: 25% [95% CI 17%–35%]) ($p < 0.001$), The pooled specificity of CTP was lower compared with NCCT ($SPEC_{CTP}$: 90% [95% CI 83%–94%] vs. $SPEC_{NCCT}$: 96% [95% CI 95%– 98%]). Meta-analysis of the diagnostic accuracy of individual perfusion maps (such as CBF, CBV, MTT, or TTP) could not be performed.

Imaging Techniques Used for EVT Selection

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Sarraj et al. 2022 **USA** **Pooled patient-level meta-analysis**	The risk of bias in the nonrandomized studies was low to moderate, assessed using the ROBINS-I tool, and low in the RCTs assessed using the ROB 2 tool.	517 patients included in 3 RCTs (EXTEND-IA, EXTEND-and IA-TNK parts 1 and 2) and 2 prospective nonrandomized studies (INSPIRE and SELECT) with isolated M2 occlusions. Median age was 72 years, 47.5% were women. Median baseline NIHSS score was 11. Median ASPECTs was 9.	The overall outcomes of patients treated with EVT (n=195) vs. best medical management (n=322) were compared, as were the outcomes of patients with favourable mismatch profile vs. without favourable mismatch profile. A favourable mismatch profile was defined as a mismatch ratio of ≥1.8 and mismatch volume of ≥15ml.	**Primary outcome:** Functional independence (mRS 0-2) at 90 days **Secondary outcomes:** Distribution of mRS scores at 90 days, excellent functional outcome (mRS 0-1) at 90 days **Safety outcomes:** sICH, neurological worsening (decrease of ≥4 NIHSS points) at 24 hours and mortality	Patients who received EVT treatment were significantly younger (75 vs. 71 years), had a higher median NIHSS score (13 vs. 10) and had more critically hypoperfused brain (72 vs. 49 mL). In the overall adjusted analysis, the odds of functional independence were significantly higher in the EVT group (68.3% vs 61.6%; OR=2.42, 95% CI 1.25–4.67) as were the odds in a shift toward better functional outcome (adjusted cOR = 2.02, 95% CI = 1.23– 3.29) at 90-day follow-up. The odds of 90-day mortality were also reduced significantly in the EVT group (5% vs. 10%; adj OR=0.32, 95% CI 0.12–0.87). There were no significant differences between groups on any other outcomes. *Patients with favourable perfusion mismatch profile* The odds of functional independence were significantly higher in the EVT group (70.7% vs. 61.3%; aOR = 2.29, 95% CI 1.09–4.79). Mortality

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					was significantly lower in the EVT group (3% vs. 9.8%). *Patients without favourable perfusion mismatch profile* There was no significant difference in functional independence between groups (EVT=43.8% vs. MM = 62.7%), or on any other secondary or safety outcomes.
Nguyen et al. 2022 **USA** **Prospective study**	NA	1,604 patients included in the CT for Late Endovascular Reperfusion (CLEAR) study, recruited from 15 sites in 5 countries undergoing EVT in the extended time window (6 to 24 hours), with NIHSS scores ≥6, occlusion of the ICA or proximal MCA (M1/M2 segments), and a prestroke mRS score of 0 to 2. Median age was 70 years, 53% were women.	The outcomes of patients selected according to 3 imaging modalities were compared: MRI (n=318), CTP (n=752) and CT (n=534). If both NCCT and CTP were used, the patient was classified as selected by CTP. If both CTP and MRI were used, the patient was classified as selected by MRI.	**Primary outcome:** Distribution of mRS scores at 90 days **Secondary outcomes:** Functional independence (mRS 0-2) at 90 days, 90-day mortality and sICH Analyses were adjusted for age, baseline NIHSS score, sex, baseline mRS scores, hypertension, atrial fibrillation, diabetes, transfer status, intravenous thrombolysis, baseline ASPECTS, site of occlusion, and time last seen well to arterial puncture.	Median APECTS score was 8. There was no significant difference in 90-day ordinal mRS shift between patients selected by CT vs CTP (OR=0.95, 95% CI 0.77-1.17) or CT vs MRI (OR=0.95, 95% CI 0.8-1.13). The odds of functional independence at 90 days were similar between patients selected by CTP and NCCT (OR=0.90, 95% CI 0.70-1.16). The odds were significantly lower for patients selected by MRI vs. NCCT (OR=0.79, 95% CI, 0.63-0.98). Overall, 6.3% of patients had sICH, with similar percentages across the 3 cohorts (NCCT, 8.1% vs. CTP, 5.8% vs. MRI, 4.7%). 90-day mortality was similar across the 3 groups (NCCT, 23.4% vs. CTP,21.1% vs. MRI, 19.5%).
Albers et al. 2021 **USA** **Pooled Analysis of AURORA data**	NA	505 patients from 6 trials (DAWN, DEFUSE 3, REVASCAT, RESILIENT, ESCAPE and POSITIVE) in which patients were randomized between 6 and 24 hours after they were last known well, to receive treatment with EVT (n=266) or best medical care (control, n=239). The mean age of EVT patients was 68	The benefits of EVT treatment were assessed based on the outcomes of 3 assembled imaging groups: 1) clinical mismatch subgroup (mismatch between clinical defect and size of early infarction), 2) a target perfusion mismatch subgroup (mismatch between size of perfusion lesion and size of early infarction),	**Primary outcome:** Ordinal change in 90-day mRS scores Analyses were adjusted for age, sex, baseline NIHSS score, site of occlusion, ASPECTS result, and time from stroke onset to randomization	The majority of data came from patients enrolled in the DAWN (n=163) and DEFUSE 3 (n=180) trials. 373 patients (73.9%) had imaging profiles (clinical mismatch and/or perfusion mismatch) that could both be assessed, and 132 patients (26.1%) had undetermined imaging profiles. Of 372 patients with both imaging profiles and 90-day mRS scores available, 359 patients met the criteria for the target perfusion mismatch profile, 295 met the criteria for the clinical mismatch profile, and 283 patients met the criteria for both the target perfusion and clinical mismatch profiles.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
		years, 55% were women. The mean age for medical care patients was 69 years, 52.7% were men. The mean baseline NIHSS score was 16.4 in the EVT group and 17.2 in the control group The mean baseline ASPECTS score was 7.8 in the EVT group and 7.5 in the control group.	and 3) an undetermined profile subgroup. 124 patients were selected based on MRI data, and the remaining patients were selected using CT or CTP data.		Among patients in the clinical mismatch subgroup and patients in the target perfusion mismatch subgroup, EVT was associated with significant reduction in disability at 90 days (OR= 3.57, 95% CI 2.29-5.57 and OR= 3.13, 95% CI 2.10-4.66, respectively). There was no significant reduction in disability among patients with an undetermined imaging profile in those who received EVT (OR=1.59, 95% CI 0.82-3.06).
Nogueira et al. 2021 **USA** **Prospective study**	NA	Patients from the Trevo Retriever Registry with occlusions involving the intracranial internal carotid or the M1- or M2-segments of the MCA, premorbid mRS score 0 to 2 and time to treatment 0 to 24 hours.	Patients were categorized according to treatment times within the early (0–6 hour) or extended (6–24 hour) window as well as imaging modality NCCT ± CTA or NCCT ± CTA and CTP, and their outcomes compared.	**Primary outcomes:** Good outcome (mRS 0-2) at 90 days, successful reperfusion (grade 2b or 3 mTICI), symptomatic ICH, 90-day mortality	*Early window* In the early window, 332 patients were included who underwent NCCT±CTA alone while 373 patients also underwent CTP. There were no significant differences between groups for a good outcome (55.9% vs. 60.6%, P=0.202), mortality (13.0% vs 10.5%, P=0.302), successful reperfusion (92.8% vs 91.7%, P=0.593), or sICH (1.8% versus 2.4%, P=0.613). There were no significant differences in 90-day functional disability (mRS ordinal shift: adj OR=0.936, 95% CI 95% CI, 0.709–1.238) or independence (adj OR=1.178, 95% CI, 0.833–1.666) across the CTP and NCCT±CTA groups. *Extended Window* In the extended window group, 67 patients underwent NCCT±CTA alone while 180 also underwent CTP. There were no significant differences between groups in 90-day good outcome (60.6% vs 54.7%, P=0.412), 90-day mortality (9.0% vs 11.1%, P=0.624), successful reperfusion (95.5% vs 93.9%, P=0.622), or sICH (1.5% vs 0.6%, P=0.470).

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					There were no significant differences between groups in 90-day functional disability (adj OR= 0.983, 95% CI, 0.81–1.662) or independence (adj OR=0.640, 95% CI, 0.318–1.289).
Almekhlafi et al. 2020 **Canada** **Retrospective study**	NA	86 patients with late-window (≥ 6 hours) large vessel occlusion stroke included in the PRove-IT study. Median age was 71 years, 49% were women.	The utility of collateral imaging using multiphase CTA vs. CT perfusion imaging (CTP) in selecting late window patients for EVT, was examined. In separate sessions, using random patient ordering, the same 2 readers scored the NCCT ASPECTS and then the collateral score on mCTA to determine whether a patient was a candidate for endovascular therapy (EVT).	**Primary outcome:** Early neurologic improvement (defined as ≥50% drop in the NIHSS score during 24 hours) and 90-day functional independence (mRS score of 0–2)	The median time from last known well/stroke symptom onset to baseline CT was 9.6 hours. 35 patients (40.7%) received EVT, while 51 (59.3%) were treated conservatively. Of the patients who received EVT, 25 (71%) were successfully reperfused. Good functional outcome was achieved in 16/35 (47%) of EVT patients. Of the 83 patients in this cohort with available 90-day outcomes, 63 (75.9%) patients were considered eligible for EVT according to the mCTA criteria, compared with 58 patients (69.9%) according to the DEFUSE-3 criteria and only 32 patients (38.6%) according to DAWN criteria. Among the 35 EVT treated patients, 33 (94.3%) were considered good EVT candidates according to the mCTA criteria compared with 28 patients (80%), according to DEFUSE-3 criteria, and 18 patients (51.4%), according to DAWN criteria for EVT eligibility. All imaging paradigms performed well in predicting 90-day functional outcome. C-statistics were 0.86 for mCTA (<3 vs. ≥3), 0.84 for Defuse 3 criteria and 0.83 for DAWN criteria. The imaging paradigms for early neurological improvement were not as good. C statistics were 0.80 for mCTA (<3 vs. ≥3), 0.74 for Defuse 3 criteria and 0.71 for DAWN criteria. Patients who had favorable mCTA and Defuse 3 imaging profiles had significantly better 90-day functional outcome when they were treated with

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					EVT.
Sarraj et al. 2020 **USA** **Prospective study** ***Optimizing Patient's Selection for Endovascular Treatment in Acute Ischemic Stroke (SELECT) Study***	NA	361 adult patients recruited from 9 sites with large-vessel occlusions presenting within 24 hours from last known well and NIHSS score ≥6.	Patients received a prespecified imaging evaluation (CT, CTA, and CTP with RAPID software mismatch determination). At the discretion of the treating physician 285 received EVT and 76 received medical management. An independent, blinded, neuroimaging core laboratory adjudicated favorable imaging profiles based on predefined criteria (CT: ASPECTS ≥ 6, CTP: regional cerebral blood flow (< 70ml with mismatch ratio ≥ 1.2 and mismatch volume ≥ 10ml).	**Primary outcome:** Functional independence (mRS 0-2) at 90 days, moderate functional dependence (mRS score - 3), sICH, neurological worsening, infarct growth, final infarct volume	Among patients who were treated with EVT, 87.0% had favorable CTs, 91% favorable CTPs, 81% both favorable CT and CTP profiles, 16% discordant, and 3% both unfavorable. Having a favorable profile on both CT and CTP significantly increased the odds of receiving thrombectomy compared to discordant profiles (adjusted [adj] OR = 3.97, 95% CI = 1.97–8.01, p < 0.001). 58% of the patients with favorable profiles on both CT and CTA achieved functional independence compared to 38% in discordant profiles and 0% when both were unfavorable (p < 0.001 for trend). The odds of functional independence were similar between favorable CT vs. favorable CTP profiles (CT = 56% vs CTP = 57%, adj OR = 1.91, 95% CI = 0.40–9.01, p = 0.41). *Subgroup of 105 patients with large ischemic cores (Sarraj et al. 2019)* 71 patients had ASPECTS ≤ 5, 74 had scores of ≥50 cm^3 on CTP and 40 had large cores on both CT and CTP imaging. 62 patients were treated with EVT, 43 with medical management. A significantly higher number of patients treated with EVT achieved functional independence (31% vs. 14%, OR=3.27, 95% CI, 1.11-9.62, p= .03). EVT was associated with better functional outcomes (common OR, 2.12, 95% CI, 1.05-4.31, P = .04), less infarct growth (44 vs 98 mL; P = .006), and smaller final infarct volume (97 vs 190 mL; P = .001), compared with medical management. The odds of functional independence decreased

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					per each 10-cm^3 increase in core volume (adjusted OR, 0.58, 95% CI, 0.39-0.87, P = .007) and per hour of treatment delay (adjusted OR, 0.60, 95% CI, 0.36-0.99, P = .045). Of 10 patients who had EVT with core volumes >100 cm^3, none had a favorable outcome
Leslie-Mazwi et al. 2019 **USA** **Pre-specified subgroup analysis of RCT**	NA	182 patients from the DEFUSE 3 trial, who were ineligible for treatment EVT using DAWN criteria (including baseline NIHSS score ≥10, clinical imaging mismatch via MR-DWI or CTP-rCBF, with criteria based on age, core infarct size). In contrast, DEFUSE-3 criteria included NIHSS of ≥6, initial infarct volume (ischemic core) <70 mL, a ratio of volume of ischemic tissue (penumbra) to infarction of ≥1.8, and an absolute volume of potentially reversible ischemia of ≥15 mL.	Subgroups of patients were compared with the DEFUSE 3 non-DAWN and entire DEFUSE 3 cohorts. Reasons for DAWN exclusion in DEFUSE 3 were infarct core too large (n=33), NIHSS score 6 to 9 (n=31), and mRS score of 2 (n=13).	**Primary outcome:** Functional independence (mRS 0-2) at 90 days **Secondary outcomes:** Angiographic, radiological, and safety	Of the 182 patients enrolled in the DEFUSE 3 trial, the eligibility overlap with DAWN criteria was 62%. 71 patients enrolled DEFUSE 3 were non-DAWN–eligible. For core too large (CTL) patients (n=33), the median 24-hour infarct volume was significantly greater compared with the core-not-too-large (CNTL, n=149) patients (119 vs. 31.5 mL, p<0.001). Median infarct growth was significantly greater in the CTL group (83.9 vs. 23.8 mL, p<0.001). There were no significant differences between groups (CTL vs. CNTL) in the percentage of patients who were independent at day 90 (24% vs. 32%, p=0.37), 90-day mortality (18% vs. 20%, p=0.8) or the incidence of symptomatic ICH (9% vs. 5%, p=0.39). For patients with CTL, after adjustment for prognostic factors of age and NIHSS, the odds of mRS 0-2 at 90 days were significantly higher for patients treated with mechanical thrombectomy vs. medical management (OR=20.9, 95% CI, 1.3–337.8). For patients with baseline NIHSS scores of 6-9 (n=31), the median NIHSS score was significantly lower compared with the rest of the DEFUSE 3 cohort (8 vs. 18, p<0.001). A significantly higher percentage of the NIHSS 6-9 patients were functionally independent at day 90 (74% vs. 22%, p<0.001) and significantly fewer were dead at 90

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					days (6% vs. 23%, p=0.024).
Desai et al. 2018 **USA** **Retrospective study**	NA	204 patients admitted to a single comprehensive stroke center from November 2014 to February 2017, with acute ischemic stroke, 6–24 hours after last known well with NIHSS score ≥6.	Patients were screened for trial eligibility using DAWN/DEFUSE-3 trial criteria. Those meeting the criteria were divided into 3 groups: DAWN eligible (n=45), DEFUSE-3 eligible (n=47), and non-DAWN non-DEFUSE-3 (NDND, n=142). Characteristics and outcomes were compared between the groups.	**Primary outcome:** mRS 0-2 at 90 days **Secondary outcome:** Stroke-related mortality **Primary safety outcomes:** Symptomatic ICH (sICH), neurological deterioration (an increase in NIHSS score of ≥4 points within 36 hours from treatment)	The most common reasons for not meeting trial criteria (NDND group, n=142) included: ischemic core >70mL (38%), baseline mRS >2 (27%), absence of clinical core mismatch or target mismatch on perfusion imaging (23%), and/or distal occlusions (MCA-M2) (22%). 37 (26%) trial ineligible patients with LVO received off-label EVT. 26 of the DAWN eligible patients and 24 of the DEFUSE-3 group received EVT. *NDND EVT group vs. DAWN EVT group* A significantly higher percentage of patients in the DAWN EVT experienced early neurological recovery (15% vs. 9%, p<0.01). 14% of patients in the DAWN EVT group had a mRS score of 0-2 compared with 11% in the NDND group (p=0.054). sICH was 8% in the NDND group compared with 4% in the DAWN group (p=0.49). Stroke related mortality was 15% (DAWN) vs. 24% NDND (p=0.38). *NDND EVT group vs. DEFUSE-3 EVT group* There were no significant differences between groups on any of the outcomes (early neurological improvement, mRS 0-2, sICH or stroke-related mortality).

Effect of Ischaemic Core Volume on Functional Outcome

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Campbell et al. 2019 Hermes Collaborators **Australia**	Risk of bias was low in all trials	1,764 patients included in 7 RCTs comparing EVT vs. medical management. (MR CLEAN, ESCAPE, EXTEND IA, SWIFT PRIME, REVASCAT, THRACE, PISTE). Mean	The association of ischaemic core and penumbral volumes with 90-day mRS score was assessed. Before treatment with	**Primary outcome:** Functional independence (mRS score 0-2) at 90 days	CTP was available and assessable for 591 (34%) patients and diffusion MRI for 309 (18%) patients. The odds of functional independence were significantly lower in patients who had CTP vs. those who had diffusion MRI, after adjustment for ischaemic core volume.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Systematic review & meta-analysis		age was 65·6 years, 53% were men. Median baseline NIHSS score was 17. Median ASPECTs score was 8.	either EVT or medical therapy, ischaemic core was estimated, by CTP as relative cerebral blood flow <30% of normal brain blood flow, or by MRI as an apparent diffusion coefficient < 620 µm²/s. Critically hypoperfused tissue was estimated as the volume of tissue with a CTP time to maximum >6 seconds. Mismatch volume was calculated as critically hypoperfused tissue volume minus ischaemic core volume.		Increasing ischaemic core volume was associated with reduced likelihood of functional independence (CTP: OR 0·77 [0·69–0·86] per 10 mL, diffusion MRI: OR 0·87 [0·81–0·94] per 10 mL). In patients with CTP with >50% endovascular reperfusion (n=186), increasing age, age, increasing NIHSS score, increasing ischaemic core volume, and imaging-to-reperfusion time were independently associated with functional improvement Estimated ischaemic core volume was independently associated with functional independence and functional improvement but did not modify the treatment benefit of endovascular thrombectomy over standard medical therapy.

ASPECTS-based Selection for Late Window EVT

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Nannoni et al. 2022 **Switzerland** **Retrospective study**	NA	337 patients admitted to 2 stroke centres (2010-2018) with acute ischemic stroke, 6–24 h after last known well with NIHSS score of ≥10 and an internal carotid artery or M1 occlusion. Median age was 73 years, 52% were women. Median NIHSS score was 18. Median baseline ASPECTs score was 7.	The outcomes of 4 patient groups were compared: 1) clinical-ASPECTS mismatch positive who received EVT treatment (n=146); 2) patients who received EVT treatment, but were mismatch negative (n=72), 3) patients who were mismatch positive and no EVT (n=50) and 4) patients who were mismatch negative and no EVT (n=69). Positive mismatch was	**Primary outcome:** Ordinal shift analysis of mRS scores at 90 days. **Secondary outcomes:** Improvement of NIHSS at 24 hours from the baseline and symptomatic ICH (sICH)	*Late EVT vs. no EVT* 218 patients were treated with EVT. Of these, 146 were mismatch +ve and 72 were mismatch -ve. Late EVT treatment was associated with a significantly better outcome in patients who were mismatch +ve (adjusted OR=2.83; 95% CI, 1.48–5.58) but not in mismatch -ve patients (aOR=1.32, 95%CI 0.61–2.84). *Mismatch positive vs. mismatch negative* 119 patients were not treated with EVT. Of these, 50 were mismatch +ve and 69 were mismatch -vs. There was no association between mismatch +ve patients who received EVT and mismatch -ve patients who did not receive EVT.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
			defined as NIHSS ≥10 and ASPECTs ≥7 or NIHSS ≥20 and ASPECTs ≥5, using NCCT or diffusion-weighted MRI on admission.		The greatest improvement in mean NIHSS score at 24 hours was in the mismatch +ve/EVT+ group (-6 points). The greatest frequency of sICH was in the mismatch-ve/EVT + group (19%).
Nagel et al. 2019 **Germany** **Retrospective study**	NA	390 patients identified from a prospective database (2014-2017) with LVO and NIHSS >5 and ASPECTs >5, with premorbid mRS 0-1, who underwent EVT within 24 hours of symptoms onset. Median age was 74 years, 53% were women. Median baseline NIHSS score was 16.	The outcomes of patients presenting within 6 hours (n=283) of symptom onset and those presenting ≥6 hours (n=107), were compared	**Primary outcome**: Good outcome (mRS 0-2) at 90 days **Safety outcomes:** Mortality on day 90 and symptomatic intracranial hemorrhage (sICH)	Of 107 late window strokes, 76 received imaging using DWI and MRP or CTP of whom 62 had mismatch >1.2 and 14 with no mismatch. 31 patients received CT or CTA only. 44.9% of patients in both groups had a good outcome. 15.2% of patients in the early window died vs. 14% in the late group. 6.0% of patients in the early window had a sICH vs. 5.6% in the late group. Independent predictors of good outcome (regardless of group) were decreasing age, decreasing NIHSS score, increasing ASPECTs score, general anesthesia and successful recanalization

MRI following Minor Stroke or TIA

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Coutts et al. 2019 **Canada** **Prospective study** ***Diagnosis of Uncertain-Origin***	NA	1,028 patients ≥18 years who experienced nonmotor or nonspeech minor focal neurologic events of any duration or motor or speech symptoms of short duration (5 minutes), with no previous stroke and	All patients received an MRI within 8 days of enrollment. Following a diagnosis based on MRI findings with an axial DWI sequence (using local protocols), follow-up was conducted at 1 year to	**Primary outcome:** The proportion of participants with acute stroke detected on brain MRI scans **Secondary outcomes:** Recurrent ischemic stroke, death, MI and TIA at 1 year	Median time from symptom onset to neurologic assessment was 50 hours. Median time from symptom onset to MRI was 102 hours. 139 patients (13.5%) had acute infarcts based on MRI findings. Of 740 patients with a normal neurological exam, 79 (10.1%) were DWI +ve. Of 149 abnormal clinical exams that were thought to be indicative of stroke, 50 (33.6%) were DWI +ve. Of

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Benign Transient Neurological Symptoms (DOUBT) study		NIHSS score of ≤3 who were referred to a neurologist within 8 days of symptom onset. Mean age was 63 years, 51% were women.	determine if there had been a death or recurrent stroke.		139 patients with abnormal clinical exams, 10 (15.2%) were DWI +ve. 92 patients (8.9%) had a single lesion, and 47 (4.6%) had multiple DWI-positive lesions. Factors associated with a higher risk of DWI +ve scan were older age, male sex, motor or speech symptoms on presentation, persistent symptoms, no history of a similar prior event, and abnormal results of neurologic examination at time of evaluation. The final diagnosis after all investigations were completed was minor stroke or TIA in 382 individuals (37.2%). The final diagnosis (ischemic vs nonischemic cause) was unchanged after all investigations in 720 individuals (70.0%), revised from nonischemic to ischemic in 79 (7.7%), and revised from ischemic to nonischemic in 229 (22.3%). There were 7 recurrent strokes, 9 TIAs, 9 deaths and 4 MIs.

Abbreviations

AUC: area under curve	ASPECTS: Alberta Stroke Program Early CT Score	CA: concealed allocation
CI: confidence interval	CTA: Computed tomography angiography	CTP: computed tomographic perfusion
DWI: diffusion-weighted imaging	EVT: endovascular therapy	ITT: intention-to-treat
mRS: modified Rankin Scale	mTICI: modified treatment in cerebral infarction	NA: not assessed
OR: odds ratio	RR: relative risk	SN: sensitivity
SP: specificity		

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