

**Cerebrovascular Disease  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
1. Mozaffarian D, Benjamin EJ, Go AS, et al. Heart disease and stroke statistics--2015 update: a report from the American Heart Association. <i>Circulation</i> . 2015;131(4):e29-322.	Review/Other-Dx	N/A	To provide heart disease and stroke statistics.	No results stated in abstract.	4
2. Berkhemer OA, Fransen PS, Beumer D, et al. A randomized trial of intraarterial treatment for acute ischemic stroke. <i>N Engl J Med</i> . 2015;372(1):11-20.	Experimental-Tx	500 patients	To assess whether intra-arterial treatment plus usual care would be more effective than usual care alone in patients with a proximal arterial occlusion in the anterior cerebral circulation that could be treated intra-arterially within 6 hours after symptom onset.	The mean age was 65 years (range, 23 to 96), and 445 patients (89.0%) were treated with IV alteplase before randomization. Retrievable stents were used in 190 of the 233 patients (81.5%) assigned to intra-arterial treatment. The adjusted common OR was 1.67 (95% CI, 1.21 to 2.30). There was an absolute difference of 13.5 percentage points (95% CI, 5.9 to 21.2) in the rate of functional independence (modified Rankin score, 0 to 2) in favor of the intervention (32.6% vs 19.1%). There were no significant differences in mortality or the occurrence of symptomatic intracerebral hemorrhage.	1
3. Campbell BC, Mitchell PJ, Kleinig TJ, et al. Endovascular therapy for ischemic stroke with perfusion-imaging selection. <i>N Engl J Med</i> . 2015;372(11):1009-1018.	Experimental-Tx	70 patients	To test whether more advanced imaging selection, recently developed devices, and earlier intervention improve outcomes.	The trial was stopped early because of efficacy after 70 patients had undergone randomization (35 patients in each group). The percentage of ischemic territory that had undergone reperfusion at 24 hours was greater in the endovascular-therapy group than in the alteplase-only group (median, 100% vs 37%; $P<0.001$ ). Endovascular therapy, initiated at a median of 210 minutes after the onset of stroke, increased early neurologic improvement at 3 days (80% vs 37%, $P=0.002$ ) and improved the functional outcome at 90 days, with more patients achieving functional independence (score of 0 to 2 on the modified Rankin scale, 71% vs 40%; $P=0.01$ ). There were no significant differences in rates of death or symptomatic intracerebral hemorrhage.	1

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4. Goyal M, Demchuk AM, Menon BK, et al. Randomized assessment of rapid endovascular treatment of ischemic stroke. <i>N Engl J Med.</i> 2015;372(11):1019-1030.	Experimental-Tx	316 patients	To evaluate rapid endovascular treatment in addition to standard care in patients with acute ischemic stroke with a small infarct core, apoximal intracranial arterial occlusion, and moderate-to-good collateral circulation.	The trial was stopped early because of efficacy. At 22 centers worldwide, 316 participants were enrolled, of whom 238 received intravenous alteplase (120 in the intervention group and 118 in the control group). In the intervention group, the median time from study CT of the head to first reperfusion was 84 minutes. The rate of functional independence (90-day modified Rankin score of 0 to 2) was increased with the intervention (53.0%, vs 29.3% in the control group; $P<0.001$ ). The primary outcome favored the intervention (common OR, 2.6; 95% CI, 1.7 to 3.8; $P<0.001$ ), and the intervention was associated with reduced mortality (10.4%, vs 19.0% in the control group; $P=0.04$ ). Symptomatic intracerebral hemorrhage occurred in 3.6% of participants in intervention group and 2.7% of participants in control group ( $P=0.75$ ).	1
5. Saver JL, Goyal M, Bonafe A, et al. Stent-retriever thrombectomy after intravenous t-PA vs. t-PA alone in stroke. <i>N Engl J Med.</i> 2015;372(24):2285-2295.	Experimental-Tx	196 patients	To establish the efficacy and safety of rapid neurovascular thrombectomy with the stent retriever in conjunction with intravenous t-PA vs intravenous t-PA alone in patients with acute ischemic stroke.	The study was stopped early because of efficacy. At 39 centers, 196 patients underwent randomization (98 patients in each group). In the intervention group, the median time from qualifying imaging to groin puncture was 57 minutes, and the rate of substantial reperfusion at the end of the procedure was 88%. Thrombectomy with the stent retriever plus intravenous t-PA reduced disability at 90 days over the entire range of scores on the modified Rankin scale ( $P<0.001$ ). The rate of functional independence (modified Rankin scale score, 0 to 2) was higher in the intervention group than in the control group (60% vs 35%, $P<0.001$ ). There were no significant between-group differences in 90-day mortality (9% vs 12%, $P=0.50$ ) or symptomatic intracranial hemorrhage (0% vs 3%, $P=0.12$ ).	1
6. American College of Radiology. <i>Manual on Contrast Media</i> . Available at: <a href="http://www.acr.org/Quality-Safety/Resources/Contrast-Manual">http://www.acr.org/Quality-Safety/Resources/Contrast-Manual</a> .	Review/Other-Dx	N/A	Guidance document on contrast media to assist radiologists in recognizing and managing risks associated with the use of contrast media.	N/A	4

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7. Kanal E, Barkovich AJ, Bell C, et al. ACR guidance document on MR safe practices: 2013. <i>J Magn Reson Imaging</i> . 2013;37(3):501-530.	Review/Other-Dx	N/A	Guidance document on MR safety practices to help guide MR practitioners regarding MR safety issues and provide a basis for them to develop and implement their own MR policies and practices.	N/A	4
8. Edjlali M, Roca P, Rabrait C, et al. MR selective flow-tracking cartography: a postprocessing procedure applied to four-dimensional flow MR imaging for complete characterization of cranial dural arteriovenous fistulas. <i>Radiology</i> . 2014;270(1):261-268.	Observational-Dx	8 patients	To assess the feasibility of a selective flow-tracking cartographic procedure applied to 4D flow imaging and to demonstrate its usefulness in the characterization of DAVFs.	Interreader agreement for shunt location on MRIs was perfect (kappa = 1), with good-to-excellent interreader agreement for arterial feeder vessel identification (kappa = 0.97; 95% CI = 0.92, 1.0), and matched in all cases with shunt location defined at DSA. There was good-to-excellent agreement between MR cartography and DSA in the definition of the main feeding arteries (kappa = 0.92; 95% CI = 0.83, 1.0), presence of retrograde flow in dural sinuses (kappa = 1), presence of retrograde cortical venous drainage (kappa = 1), presence of venous ectasia (kappa = 1), and final Cognard classification of DAVFs (kappa = 1, standard error = 0.35).	1
9. Gandhi D, Chen J, Pearl M, Huang J, Gemmete JJ, Kathuria S. Intracranial dural arteriovenous fistulas: classification, imaging findings, and treatment. <i>AJNR Am J Neuroradiol</i> . 2012;33(6):1007-1013.	Review/Other-Dx	N/A	To review intracranial DAVFs.	Intracranial DAVFs are pathologic dural-based shunts and account for 10%–15% of all intracranial AVM. These malformations derive their arterial supply primarily from meningeal vessels, and the venous drainage is either via dural venous sinuses or through the cortical veins. DAVFs have a reported association with dural sinus thrombosis, venous hypertension, previous craniotomy, and trauma, though many lesions are idiopathic. The diagnosis is dependent on a high level of clinical suspicion and high-resolution imaging. Cross-sectional imaging techniques by using CT and MRI aid in the diagnosis, but conventional angiography remains the most accurate method for complete characterization and classification of DAVFs. The pattern of venous drainage observed on dynamic vascular imaging determines the type of DAVF and correlates with the severity of symptoms and the risk of hemorrhage.	4

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10. Iryo Y, Hirai T, Kai Y, et al. Intracranial dural arteriovenous fistulas: evaluation with 3-T four-dimensional MR angiography using arterial spin labeling. <i>Radiology</i> . 2014;271(1):193-199.	Observational-Dx	9 patients	To evaluate whether 3-T 4D ASL-based MRA is useful for the evaluation of shunt lesions in patients with intracranial DAVFs.	On all 4D ASL MRA images, the major intracranial arteries were demonstrated at a temporal resolution of 300 milliseconds. Interobserver agreement was excellent for the fistula site (kappa = 1.00; 95% CI: 1.00, 1.00), moderate for the main arterial feeders (kappa = 0.53; 95% CI: 0.08, 0.98), and good for venous drainage (kappa = 0.77; 95% CI: 0.35, 1.00). Intermodality agreement was excellent for the fistula site and venous drainage (kappa = 1.00; 95% CI: 1.00, 1.00) and good for the main arterial feeders (kappa = 0.80; 95% CI: 0.58, 1.00).	2
11. Nishimura S, Hirai T, Sasao A, et al. Evaluation of dural arteriovenous fistulas with 4D contrast-enhanced MR angiography at 3T. <i>AJNR Am J Neuroradiol</i> . 2010;31(1):80-85.	Observational-Dx	18 consecutive patients	To test the hypothesis that 4D-CE-MRA at 3T enables the same characterization of intracranial DAVFs as DSA.	At DSA, 8 fistulas were located at the transverse sigmoid sinus; 8, at the cavernous sinus; and 2, at the sinus adjacent to the foramen magnum. Interobserver agreement was fair for the main arterial feeders (kappa = 0.59), excellent for the fistula site (kappa = 0.91), and good for venous drainage (kappa = 0.86). Intermodality agreement was moderate for the main arterial feeders (kappa = 0.68) and excellent for the fistula site (kappa = 1.0) and venous drainage (kappa = 1.0).	2
12. Wu H, Block WF, Turski PA, et al. Noncontrast dynamic 3D intracranial MR angiography using pseudo-continuous arterial spin labeling (PCASL) and accelerated 3D radial acquisition. <i>J Magn Reson Imaging</i> . 2014;39(5):1320-1326.	Review/Other-Dx	5 patients	To develop a novel dynamic 3D noncontrast MRA technique that combines dynamic pseudo-continuous ASL, accelerated 3D radial sampling, and time-of-arrival mapping to provide quantitative assessment of arterial flow.	Digital simulations demonstrated reduced image artifacts and improved time-of-arrival accuracy using radial acquisition over Cartesian. Time-of-arrival mapping accuracy is more sensitive to sampling window length than time spacing. Dynamic pseudo-continuous ASL MRA depicted 7 of 8 arterial pedicles, and accurately measured the AVM nidus size when the nidus was compact. The venous drainage in the AVM patients was not consistently visualized.	4

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13. Telischak NA, Detre JA, Zaharchuk G. Arterial spin labeling MRI: clinical applications in the brain. <i>J Magn Reson Imaging</i> . 2015;41(5):1165-1180.	Review/Other-Dx	N/A	To outline the various ASL techniques including advantages and disadvantages of each, methodology for clinical interpretation, and clinical applications with specific examples.	Visualization of CBF has become an important part of neuroimaging for a wide range of diseases. ASL perfusion MRI sequences are increasingly being used to provide MR-based CBF quantification without the need for contrast administration, and can be obtained in conjunction with a structural MRI study. ASL MRI is useful for evaluating cerebrovascular disease including arterio-occlusive disease, vascular shunts, for assessing primary and secondary malignancy, and as a biomarker for neuronal metabolism in other disorders such as seizures and neurodegeneration.	4
14. Easton JD, Saver JL, Albers GW, et al. Definition and evaluation of transient ischemic attack: a scientific statement for healthcare professionals from the American Heart Association/American Stroke Association Stroke Council; Council on Cardiovascular Surgery and Anesthesia; Council on Cardiovascular Radiology and Intervention; Council on Cardiovascular Nursing; and the Interdisciplinary Council on Peripheral Vascular Disease. The American Academy of Neurology affirms the value of this statement as an educational tool for neurologists. <i>Stroke</i> . 2009;40(6):2276-2293.	Review/Other-Dx	N/A	To review and synthesize recent scientific advances regarding the definition, urgency, and evaluation of TIA.	Neuroimaging studies, particularly PWI/DWI MRI, have fundamentally altered our understanding of the pathophysiology of TIA. In routine clinical practice, MRI permits confirmation of focal ischemia rather than another process as the cause of a patient's deficit, improves accuracy of diagnosis of the vascular localization and cause of TIA, and assesses the extent of preexisting cerebrovascular injury. Accordingly, MRI, including diffusion sequences, should now be considered a preferred diagnostic test in the investigation of the patient with potential TIAs. Additional diagnostic workup, including vessel imaging, cardiac evaluation, and laboratory testing, should be completed according to the American Heart Association acute stroke guidelines.	4
15. Kidwell CS, Warach S. Acute ischemic cerebrovascular syndrome: diagnostic criteria. <i>Stroke</i> . 2003;34(12):2995-2998.	Review/Other-Dx	N/A	To review acute ischemic cerebrovascular syndrome.	Clinical trials testing new treatments for acute ischemic stroke or secondary stroke prevention should limit enrollment to patients with "definite" acute ischemic cerebrovascular syndrome whenever feasible.	4

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16. Restrepo L, Jacobs MA, Barker PB, Wityk RJ. Assessment of transient ischemic attack with diffusion- and perfusion-weighted imaging. <i>AJNR Am J Neuroradiol.</i> 2004;25(10):1645-1652.	Review/Other-Dx	22 patients	To test the hypothesis that PWI would substantiate the diagnosis of brain ischemia in an additional proportion of patients with transient neurologic symptoms.	MRI was abnormal in 15 patients (68%): 12 had abnormal DWI, 4 had both DWI and PWI defects (all with a mismatch) and 3 had an isolated PWI abnormality. There were no differences in symptom duration, stroke etiology or cardiovascular risk factors between patients with abnormal MRI and those with unremarkable scan. Patients with mismatch were more likely to need conventional angiography or other cerebrovascular procedures.	4
17. Johnston SC, Gress DR, Browner WS, Sidney S. Short-term prognosis after emergency department diagnosis of TIA. <i>JAMA.</i> 2000;284(22):2901-2906.	Observational-Dx	1707 patients	To determine the short-term risk of stroke and other adverse events after emergency department diagnosis of TIA.	During the 90 days after index TIA, 180 patients (10.5%) returned to the emergency department with a stroke, 91 of which occurred in the first 2 days. Five factors were independently associated with stroke: age >60 years (OR, 1.8; 95% CI, 1.1–2.7; <i>P</i> =.01), diabetes mellitus (OR, 2.0; 95% CI, 1.4–2.9; <i>P</i> <.001), symptom duration longer than 10 minutes (OR, 2.3; 95% CI, 1.3–4.2; <i>P</i> =.005), weakness (OR, 1.9; 95% CI, 1.4–2.6; <i>P</i> <.001), and speech impairment (OR, 1.5; 95% CI, 1.1–2.1; <i>P</i> =.01). Stroke or other adverse events occurred in 428 patients (25.1%) in the 90 days after the TIA and included 44 hospitalizations for cardiovascular events (2.6%), 45 deaths (2.6%), and 216 recurrent TIAs (12.7%).	3

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18. Eliasziw M, Kennedy J, Hill MD, Buchan AM, Barnett HJ. Early risk of stroke after a transient ischemic attack in patients with internal carotid artery disease. <i>CMAJ</i> . 2004;170(7):1105-1109.	Experimental-Tx	1,129 patients	To quantify the early risk of stroke after a TIA in patients with internal carotid artery disease.	For patients with a first-recorded hemispheric TIA (n = 603), the 90-day risk of ipsilateral stroke was 20.1% (95% CI, 17.0%–23.2%), higher than the 2.3% risk (95% CI, 1.0%–3.6%) for patients with a hemispheric stroke (n = 526). The 2-day risks were 5.5% and 0.0%, respectively. Patients with more severe stenosis of the internal carotid artery (>70%) appeared to be at no greater risk of stroke than patients with lesser degrees of stenosis (adjusted HR 1.1, 95% CI, 0.7–1.7). Infarct on brain imaging (adjusted HR 2.1, 95% CI, 1.5–3.0) and the presence of intracranial major-artery disease (adjusted HR 1.9, 95% CI, 1.3–2.7) doubled the early risk of stroke in patients with a hemispheric TIA.	1
19. Kleindorfer D, Panagos P, Pancioli A, et al. Incidence and short-term prognosis of transient ischemic attack in a population-based study. <i>Stroke</i> . 2005;36(4):720-723.	Review/Other-Dx	927 patients	To present the incidence and short-term prognosis of TIA within a large population with a significant proportion of minorities with out-of-hospital TIA.	The overall race, age, and gender-adjusted incidence rate for TIA within our population was 83 per 100,000, with age, race, and gender adjusted to the 1990 US population. Blacks and men had significantly higher rates of TIA than whites and women. Risk of stroke after TIA was 14.6% at 3 months, and risk of TIA/stroke/death was 25.2%. Age, race, and sex were not associated with recurrent TIA or subsequent stroke in our population, but age was associated with mortality.	4
20. Wu CM, McLaughlin K, Lorenzetti DL, Hill MD, Manns BJ, Ghali WA. Early risk of stroke after transient ischemic attack: a systematic review and meta-analysis. <i>Arch Intern Med</i> . 2007;167(22):2417-2422.	Meta-analysis	11 studies	To conduct a systematic review and meta-analysis of observational studies estimating the risk of stroke at 2, 30, and 90 days after TIA and to explore clinical and methodological factors that may explain variability in findings across studies.	Based on a random effects model, the pooled early risk of stroke was 3.5%, 8.0%, and 9.2% at 2, 30, and 90 days after TIA, respectively. Studies reported higher risks when the methodology involved active ascertainment of stroke outcome compared with passive ascertainment. Early risk of stroke was 9.9%, 13.4%, and 17.3% at 2, 30, and 90 days, respectively, when only studies with active outcome ascertainment were considered.	M

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21. Clark TG, Murphy MF, Rothwell PM. Long term risks of stroke, myocardial infarction, and vascular death in "low risk" patients with a non-recent transient ischaemic attack. <i>J Neurol Neurosurg Psychiatry</i> . 2003;74(5):577-580.	Observational-Dx	290 patients	To determine the long term risks of stroke and other vascular events in patients with TIA who survive the initial high risk period.	Median time since last TIA was 3.8 years (interquartile range, 2.2 to 5.8 years). The risk of major vascular events was constant through time. The 10 year risk of first stroke was 18.8% (95% CI, 13.6 to 23.7; 45 events). The 10 year risk of myocardial infarction or death from coronary heart disease was 27.8% (95% CI, 21.8 to 33.3; 67 events) and there was a significant excess of fatal coronary events compared with that expected in the general population (SMR = 1.47; 95% CI, 1.10 to 1.93; P=0.009). A total of 114 patients had at least one major vascular event, with a 10 year risk of any first stroke, myocardial infarction, or vascular death of 42.8% (95% CI, 36.4 to 48.5).	3
22. van Wijk I, Kappelle LJ, van Gijn J, et al. Long-term survival and vascular event risk after transient ischaemic attack or minor ischaemic stroke: a cohort study. <i>Lancet</i> . 2005;365(9477):2098-2104.	Observational-Tx	2,473 participants	To assess the survival status and occurrence of vascular events in 2,473 participants of the Dutch TIA Trial (recruitment in 1986-89; arterial cause of cerebral ischemia).	Follow-up was complete in 2,447 (99%) patients. After a mean follow-up of 10.1 years, 1,489 (60%) patients had died and 1,336 (54%) had had at least 1 vascular event. 10-year risk of death was 42.7% (95% CI, 40.8–44.7). Age and sex-adjusted HRs were 3.33 (2.97–3.73) for age >65 years, 2.10 (1.79–2.48) for diabetes, 1.77 (1.45–2.15) for claudication, 1.94 (1.42–2.65) for previous peripheral vascular surgery, and 1.50 (1.31–1.71) for pathological Q waves on baseline electrocardiogram. 10-year risk of a vascular event was 44.1% (42.0–46.1). After falling in the first 3 years, yearly risk of a vascular event increased over time. Predictive factors for risk of vascular events were similar to those for risk of death.	1
23. Del Zoppo GJ, Saver JL, Jauch EC, Adams HP, Jr. Expansion of the time window for treatment of acute ischemic stroke with intravenous tissue plasminogen activator: a science advisory from the American Heart Association/American Stroke Association. <i>Stroke</i> . 2009;40(8):2945-2948.	Review/Other-Tx	N/A	Guidelines on the expansion of the time window for treatment of acute ischemic stroke with IV t-PA.	No results stated in abstract.	4



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24. Neumann-Haefelin T, Wittsack HJ, Wenserski F, et al. Diffusion- and perfusion-weighted MRI. The DWI/PWI mismatch region in acute stroke. <i>Stroke</i> . 1999;30(8):1591-1597.	Observational- Dx	20 patients	To evaluate the PWI/DWI mismatch region in acute stroke patients and find parameters indicative of both infarct progression and functional impairment.	In 80% of patients the acute DWI lesion was surrounded by regions with abnormal time-to-peak delays (PWI>DWI lesion). A time-to-peak delay of $\geq 6$ s in the mismatch region was found to be associated with lesion enlargement between the initial and follow-up MRI scans. Lesions increased in 9 of 12 patients (75%) in whom the area with time-to-peak delay $\geq 6$ s was larger than the DWI lesion, but they increased in only 1 of 8 (12.5%) of the remaining patients, in whom the area with a time-to-peak delay $\geq 6$ s was smaller than the DWI lesion. The volume of the regions with time-to-peak delays of $\geq 4$ s correlated better with European Stroke Scale ( $r=-0.88$ , $P<0.001$ ) than other PWI (or DWI) volumes, which indicated that a time-to-peak delay of approximately 4 s might be the threshold for functional impairment of brain tissue.	2

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25. Ribo M, Molina CA, Rovira A, et al. Safety and efficacy of intravenous tissue plasminogen activator stroke treatment in the 3- to 6-hour window using multimodal transcranial Doppler/MRI selection protocol. <i>Stroke</i> . 2005;36(3):602-606.	Observational-Tx	135 patients	To study safety and efficacy of t-PA treatment in the 3- to 6-hour window using multimodal TCD/MRI selection criteria.	Of 135 patients, 56 were in the 3- to 6-hour window. Only 13 (23%) patients within 3 to 6 hours did not meet MRI inclusion criteria. Finally, 122 patients were treated with t-PA: A, 79 (65%); B, 43 (35%). Median time to treatment was: A, 136 minutes (range 60 to 180); B, 223 (185 to 360). There were no differences in demographic parameters, baseline National Institutes of Health Stroke Scale (NIHSS) (A, 17; B, 17; $P=0.89$ ), and occlusion location (proximal MCA A, 65.8%; B, 74.4%; $P=0.28$ ). Recanalization rates at 2 hours were similar (A, 49.3%; B, 55.2%; $P=0.33$ ), as were hemorrhagic transformation rates (asymptomatic: A, 18.7%, B, 26.6%, $P=0.43$ ; symptomatic: A, 3.75%, B, 2.38%, $P=0.66$ ). Improvement at discharge was similar in both groups (NIHSS dropped 6.3 points [A] vs 6.1 [B]; $P=0.86$ ). However, the number of patients who benefited from treatment was slightly higher in the 3- to 6-hour group (A, 58.2%; B, 76.2%; $P=0.05$ ), whereas the same rate of patients worsened (A, 11.4%; B, 7.1%; $P=0.46$ ). At 3 months, the rate of independent patients was: A, 42% vs B, 38% ( $P=0.74$ ).	2
26. Fargen KM, Meyers PM, Khatri P, Mocco J. Improvements in recanalization with modern stroke therapy: a review of prospective ischemic stroke trials during the last two decades. <i>J Neurointerv Surg</i> . 2013;5(6):506-511.	Review/Other-Dx	13 trials	To present a review of prospective acute ischemic stroke trials reported in a peer-reviewed forum during the last 20 years to provide insight into the general direction of this rapidly evolving field.	13 prospective trials were included. Regression analyses demonstrated no appreciable change in the median NIHSS score of subjects at the time of enrollment since 1995 ( $P=0.44$ ) and no appreciable improvements in good outcome based on a modified Rankin score of 0-2 at 90 days ( $P=0.66$ ) or mortality at 90 days ( $P=0.55$ ). A significant increase in time from onset of symptoms to treatment among enrolled patients was noted from 1995 to 2012 ( $P=0.03$ ). In addition, a significant improvement in recanalization/reperfusion was noted over the last two decades ( $P=0.02$ ).	4

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27. Mokin M, Khalessi AA, Mocco J, et al. Endovascular treatment of acute ischemic stroke: the end or just the beginning? <i>Neurosurg Focus.</i> 2014;36(1):E5.	Review/Other-Dx	3 trials	To review the evolution of endovascular treatment strategies for the treatment of acute stroke and provide their interpretation of findings and potential limitations of the three recently published randomized trials.	Various endovascular intra-arterial approaches are available for treating patients with acute ischemic stroke who present with severe neurological deficits. Three recent randomized trials-Interventional Management of Stroke (IMS) III, Mechanical Retrieval and Recanalization of Stroke Clots Using Embolectomy (MR RESCUE), and Synthesis Expansion: A Randomized Controlled Trial on Intra-Arterial Versus Intravenous Thrombolysis in Acute Ischemic Stroke (SYNTHESIS Expansion)-evaluated the efficacy of endovascular treatment of acute ischemic stroke and, after failing to demonstrate any significant clinical benefit of endovascular therapies, raised concerns and questions in the medical community regarding the future of endovascular treatment for acute ischemic stroke.	4
28. Nogueira RG, Lutsep HL, Gupta R, et al. Trevo versus Merci retrievers for thrombectomy revascularisation of large vessel occlusions in acute ischaemic stroke (TREVO 2): a randomised trial. <i>Lancet.</i> 2012;380(9849):1231-1240.	Experimental-Tx	178 patients	To compare the efficacy and safety of mechanical thrombectomy with the Trevo Retriever with that of the Merci Retriever in the arterial revascularization of patients with acute ischemic stroke.	Between Feb 3, 2011, and Dec 1, 2011, 88 patients were randomly assigned to the Trevo Retriever group and 90 patients to Merci Retriever group. 76 (86%) patients in the Trevo group and 54 (60%) in the Merci group met the primary endpoint after the assigned device was used (OR 4.22, 95% CI, 1.92–9.69; $P(\text{superiority}) < 0.0001$ ). Incidence of the primary safety endpoint did not differ between groups (13 [15%] patients in the Trevo group vs 21 [23%] in the Merci group; $P = 0.1826$ ).	1

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
29. Saver JL, Jahan R, Levy EI, et al. Solitaire flow restoration device versus the Merci Retriever in patients with acute ischaemic stroke (SWIFT): a randomised, parallel-group, non-inferiority trial. <i>Lancet</i> . 2012;380(9849):1241-1249.	Experimental-Tx	113 total patients	To compare the efficacy and safety of Solitaire with the standard, predicate mechanical thrombectomy device, the Merci Retrieval System.	Between February, 2010, and February, 2011, we randomly allocated 58 patients to the Solitaire group and 55 patients to the Merci group. The primary efficacy outcome was achieved more often in the Solitaire group than it was in the Merci group (61% vs 24%; difference 37% [95% CI, 19–53], OR 4.87 [95% CI, 2.14–11.10]; $P(\text{non-inferiority}) < 0.0001$ , $P(\text{superiority}) = 0.0001$ ). More patients had good 3-month neurological outcome with Solitaire than with Merci (58% vs 33%; difference 25% [6–43], OR 2.78 [1.25–6.22]; $P(\text{non-inferiority}) = 0.0001$ , $P(\text{superiority}) = 0.02$ ). 90-day mortality was lower in the Solitaire group than it was in the Merci group (17 vs 38; difference -21% [-39 to -3], OR 0.34 [0.14-0.81]; $P(\text{non-inferiority}) = 0.0001$ , $P(\text{superiority}) = 0.02$ ).	1
30. Broderick JP, Palesch YY, Demchuk AM, et al. Endovascular therapy after intravenous t-PA versus t-PA alone for stroke. <i>N Engl J Med</i> . 2013;368(10):893-903.	Experimental-Tx	656 participants	To conduct the IMS III trial, an international, phase 3, randomized, open-label clinical trial with a blinded outcome, to test the approach of IV t-PA followed by protocol approved endovascular treatment, as compared with standard IV t-PA.	The study was stopped early because of futility after 656 participants had undergone randomization (434 patients to endovascular therapy and 222 to IV t-PA alone). The proportion of participants with a modified Rankin score of 2 or less at 90 days did not differ significantly according to treatment (40.8% with endovascular therapy and 38.7% with IV t-PA; absolute adjusted difference, 1.5 percentage points; 95% CI, -6.1 to 9.1, with adjustment for the NIHSS score [8–19, indicating moderately severe stroke, or $\geq 20$ , indicating severe stroke]), nor were there significant differences for the predefined subgroups of patients with an NIHSS score of 20 or higher (6.8 percentage points; 95% CI, -4.4 to 18.1) and those with a score of 19 or lower (-1.0 percentage point; 95% CI, -10.8 to 8.8). Findings in the endovascular-therapy and IV t-PA groups were similar for mortality at 90 days (19.1% and 21.6%, respectively; $P = 0.52$ ) and the proportion of patients with symptomatic intracerebral hemorrhage within 30 hours after initiation of t-PA (6.2% and 5.9%, respectively; $P = 0.83$ ).	1

**Cerebrovascular Disease  
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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
31. Ciccone A, Valvassori L, Nichelatti M, et al. Endovascular treatment for acute ischemic stroke. <i>N Engl J Med.</i> 2013;368(10):904-913.	Experimental-Tx	362 patients	To investigate whether endovascular treatment, including the options of a mechanical device and intra-arterial t-PA, is more effective than the currently available treatment with IV t-PA.	A total of 181 patients were assigned to receive endovascular therapy, and 181 IV t-PA. The median time from stroke onset to the start of treatment was 3.75 hours for endovascular therapy and 2.75 hours for IV t-PA ( $P<0.001$ ). At 3 months, 55 patients in the endovascular-therapy group (30.4%) and 63 in the IV t-PA group (34.8%) were alive without disability (OR adjusted for age, sex, stroke severity, and atrial fibrillation status at baseline, 0.71; 95% CI, 0.44 to 1.14; $P=0.16$ ). Fatal or nonfatal symptomatic intracranial hemorrhage within 7 days occurred in 6% of the patients in each group, and there were no significant differences between groups in the rates of other serious adverse events or the case fatality rate.	1
32. Kidwell CS, Jahan R, Gornbein J, et al. A trial of imaging selection and endovascular treatment for ischemic stroke. <i>N Engl J Med.</i> 2013;368(10):914-923.	Experimental-Tx	127 patients	To randomly assign patients within 8 hours after the onset of large vessel, anterior-circulation strokes to undergo mechanical embolectomy (Merci Retriever or Penumbra System) or receive standard care.	Among 118 eligible patients, the mean age was 65.5 years, the mean time to enrollment was 5.5 hours, and 58% had a favorable penumbral pattern. Revascularization in the embolectomy group was achieved in 67% of the patients. 90-day mortality was 21%, and the rate of symptomatic intracranial hemorrhage was 4%; neither rate differed across groups. Among all patients, mean scores on the modified Rankin scale did not differ between embolectomy and standard care (3.9 vs 3.9, $P=0.99$ ). Embolectomy was not superior to standard care in patients with either a favorable penumbral pattern (mean score, 3.9 vs 3.4; $P=0.23$ ) or a nonpenumbral pattern (mean score, 4.0 vs 4.4; $P=0.32$ ). In the primary analysis of scores on the 90-day modified Rankin scale, there was no interaction between the pretreatment imaging pattern and treatment assignment ( $P=0.14$ ).	1

**Cerebrovascular Disease  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
33. Andersen KK, Olsen TS, Dehlendorff C, Kammersgaard LP. Hemorrhagic and ischemic strokes compared: stroke severity, mortality, and risk factors. <i>Stroke</i> . 2009;40(6):2068-2072.	Review/Other-Tx	39,484 patients	To study differences and similarities between patients with hemorrhagic stroke and ischemic stroke with respect to risk factors, stroke severity, and survival.	Of the patients 3,993 (10.1%) had hemorrhagic stroke. Stroke severity was almost linearly related to the probability of having hemorrhagic stroke (2% in patients with the mildest stroke and 30% in those with the most severe strokes). Factors favoring ischemic strokes vs hemorrhagic stroke were diabetes, atrial fibrillation, previous myocardial infarction, previous stroke, and intermittent arterial claudication. Smoking and alcohol consumption favored hemorrhagic stroke, whereas age, sex, and hypertension did not herald stroke type. Compared with ischemic strokes, hemorrhagic stroke was associated with an overall higher mortality risk (HR, 1.564; 95% CI, 1.441–1.696). The increased risk was, however, time-dependent; initially, risk was 4-fold, after 1 week it was 2.5-fold, and after 3 weeks it was 1.5-fold. After 3 months stroke type did not correlate to mortality.	4
34. Endarterectomy for asymptomatic carotid artery stenosis. Executive Committee for the Asymptomatic Carotid Atherosclerosis Study. <i>JAMA</i> . 1995;273(18):1421-1428.	Experimental-Tx	1,659 patients	To determine whether the addition of CEA to aggressive medical management can reduce the incidence of cerebral infarction in patients with asymptomatic carotid artery stenosis.	After a median follow-up of 2.7 years, with 4,657 patient-years of observation, the aggregate risk over 5 years for ipsilateral stroke and any perioperative stroke or death was estimated to be 5.1% for surgical patients and 11.0% for patients treated medically (aggregate risk reduction of 53% [95% CI, 22% to 72%]).	1

**Cerebrovascular Disease  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
35. Barnett HJ, Taylor DW, Eliasziw M, et al. Benefit of carotid endarterectomy in patients with symptomatic moderate or severe stenosis. North American Symptomatic Carotid Endarterectomy Trial Collaborators. <i>N Engl J Med.</i> 1998;339(20):1415-1425.	Experimental-Tx	2,226 patients	To assess the benefit of CEA in patients with symptomatic moderate stenosis, defined as stenosis of <70%.	Among patients with stenosis of 50% to 69%, the 5-year rate of any ipsilateral stroke (failure rate) was 15.7% among patients treated surgically and 22.2% among those treated medically ( $P=0.045$ ); to prevent one ipsilateral stroke during the 5-year period, 15 patients would have to be treated with CEA. Among patients with <50% stenosis, the failure rate was not significantly lower in the group treated with endarterectomy (14.9%) than in the medically treated group (18.7%, $P=0.16$ ). Among the patients with severe stenosis who underwent endarterectomy, the 30-day rate of death or disabling ipsilateral stroke persisting at 90 days was 2.1%; this rate increased to only 6.7% at 8 years. Benefit was greatest among men, patients with recent stroke as the qualifying event, and patients with hemispheric symptoms.	1

**Cerebrovascular Disease  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
36. Brott TG, Hobson RW, 2nd, Howard G, et al. Stenting versus endarterectomy for treatment of carotid-artery stenosis. <i>N Engl J Med.</i> 2010;363(1):11-23.	Experimental-Tx	2,522 patients	To compare the outcomes of carotid-artery stenting with those of CEA among patients with symptomatic or asymptomatic extracranial carotid stenosis.	For 2,502 patients over a median follow-up period of 2.5 years, there was no significant difference in the estimated 4-year rates of the primary end point between the stenting group and the endarterectomy group (7.2% and 6.8%, respectively; HR with stenting, 1.11; 95% CI, 0.81 to 1.51; $P=0.51$ ). There was no differential treatment effect with regard to the primary end point according to symptomatic status ( $P=0.84$ ) or sex ( $P=0.34$ ). The 4-year rate of stroke or death was 6.4% with stenting and 4.7% with endarterectomy (HR, 1.50; $P=0.03$ ); the rates among symptomatic patients were 8.0% and 6.4% (HR, 1.37; $P=0.14$ ), and the rates among asymptomatic patients were 4.5% and 2.7% (HR, 1.86; $P=0.07$ ), respectively. Periprocedural rates of individual components of the end points differed between the stenting group and the endarterectomy group: for death (0.7% vs 0.3%, $P=0.18$ ), for stroke (4.1% vs 2.3%, $P=0.01$ ), and for myocardial infarction (1.1% vs 2.3%, $P=0.03$ ). After this period, the incidences of ipsilateral stroke with stenting and with endarterectomy were similarly low (2.0% and 2.4%, respectively; $P=0.85$ ).	1
37. Grotta JC. Clinical practice. Carotid stenosis. <i>N Engl J Med.</i> 2013;369(12):1143-1150.	Review/Other-Dx	N/A	To review the clinical practice of carotid stenosis.	Carotid intervention (endarterectomy or stenting, depending on the clinical setting) is recommended generally in symptomatic patients with stenosis of more than 70% and in selected asymptomatic low-risk patients and symptomatic patients with stenosis of 50 to 69%.	4



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EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
38. Halliday A, Harrison M, Hayter E, et al. 10-year stroke prevention after successful carotid endarterectomy for asymptomatic stenosis (ACST-1): a multicentre randomised trial. <i>Lancet</i> . 2010;376(9746):1074-1084.	Experimental-Tx	3,120 patients	To assess the long-term effects of successful CEA.	1,560 patients were allocated immediate CEA vs 1,560 allocated deferral of any carotid procedure. The proportions operated on while still asymptomatic were 89.7% vs 4.8% at 1 year (and 92.1% vs 16.5% at 5 years). Perioperative risk of stroke or death within 30 days was 3.0% (95% CI, 2.4–3.9; 26 nondisabling strokes plus 34 disabling or fatal perioperative events in 1979 CEAs). Excluding perioperative events and nonstroke mortality, stroke risks (immediate vs deferred CEA) were 4.1% vs 10.0% at 5 years (gain 5.9%, 95% CI, 4.0–7.8) and 10.8% vs 16.9% at 10 years (gain 6.1%, 2.7–9.4); ratio of stroke incidence rates 0.54, 95% CI, 0.43–0.68, $P < 0.0001$ . 62 vs 104 had a disabling or fatal stroke, and 37 vs 84 others had a nondisabling stroke. Combining perioperative events and strokes, net risks were 6.9% vs 10.9% at 5 years (gain 4.1%, 2.0–6.2) and 13.4% vs 17.9% at 10 years (gain 4.6%, 1.2–7.9). Medication was similar in both groups; throughout the study, most were on antithrombotic and antihypertensive therapy. Net benefits were significant both for those on lipid-lowering therapy and for those not, and both for men and for women up to 75 years of age at entry (although not for older patients).	1

**Cerebrovascular Disease  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
39. Rothwell PM, Eliasziw M, Gutnikov SA, et al. Analysis of pooled data from the randomised controlled trials of endarterectomy for symptomatic carotid stenosis. <i>Lancet</i> . 2003;361(9352):107-116.	Review/Other-Tx	6,092 patients	To determine with as much precision as possible the effectiveness and durability of endarterectomy by degree of carotid stenosis.	Risks of main outcomes in both treatment groups and effects of surgery did not differ between trials. Data for 6,092 patients, with 35,000 patient-years of follow-up, were therefore pooled. Surgery increased the 5-year risk of ipsilateral ischemic stroke in patients with <30% stenosis (n=1,746, absolute risk reduction -2.2%, $P=0.05$ ), had no effect in patients with 30%–49% stenosis (1,429, 3.2%, $P=0.6$ ), was of marginal benefit in those with 50%–69% stenosis (1,549, 4.6%, $P=0.04$ ), and was highly beneficial in those with 70% stenosis or greater without near-occlusion (1,095, 16.0%, $P<0.001$ ). There was a trend towards benefit from surgery in patients with near-occlusion at 2 years' follow-up (262, 5.6%, $P=0.19$ ), but no benefit at 5 years (-1.7%, $P=0.9$ ).	4
40. Wardlaw JM, Chappell FM, Best JJ, Wartolowska K, Berry E. Non-invasive imaging compared with intra-arterial angiography in the diagnosis of symptomatic carotid stenosis: a meta-analysis. <i>Lancet</i> . 2006;367(9521):1503-1512.	Meta-analysis	41 studies	To systematically review the accuracy of noninvasive imaging compared with intra-arterial angiography for diagnosing carotid stenosis in patients with carotid territory ischemic symptoms.	In 41 included studies (2,541 patients, 4,876 arteries), CE-MRA was more sensitive (0.94, 95% CI, 0.88–0.97) and specific (0.93, 95% CI, 0.89–0.96) for 70%–99% stenosis than Doppler US, MRA, and CTA (sensitivities 0.89, 0.88, 0.76; specificities 0.84, 0.84, 0.94, respectively). Data for 50%–69% stenoses and combinations of noninvasive tests were sparse and unreliable. There was heterogeneity between studies and evidence of publication bias.	M

**Cerebrovascular Disease  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
41. Jahromi AS, Cina CS, Liu Y, Clase CM. Sensitivity and specificity of color duplex ultrasound measurement in the estimation of internal carotid artery stenosis: a systematic review and meta-analysis. <i>J Vasc Surg.</i> 2005;41(6):962-972.	Meta-analysis	47 studies	To conduct a systematic review and meta-analysis of the relation between the degree of internal carotid artery stenosis by duplex US criteria and degree of stenosis by angiography.	Variables extracted included internal carotid artery peak systolic velocity, internal carotid artery end diastolic velocity, internal carotid artery/common carotid artery peak systolic velocity ratio, sensitivity and specificity of duplex US scanning for internal carotid artery stenosis by angiography. The Standards for Reporting of Diagnostic Accuracy (STARD) criteria were used to assess study quality. Sensitivity and specificity for duplex US criteria were combined as weighted means by using a random effects model. The threshold of peak systolic velocity $\geq 130$ cm/s is associated with sensitivity of 98% (95% CI, 97% to 100%) and specificity of 88% (95% CI, 76% to 100%) in the identification of angiographic stenosis of $\geq 50\%$ . For the diagnosis of angiographic stenosis of $\geq 70\%$ , a peak systolic velocity $\geq 200$ cm/s has a sensitivity of 90% (95% CI, 84% to 94%) and a specificity of 94% (95% CI, 88% to 97%). For each duplex US threshold, measurement properties vary widely between laboratories and the magnitude of the variation is clinically important. The heterogeneity observed in the measurement properties of duplex US may be caused by differences in patients, study design, equipment, techniques or training.	M
42. Barth A, Arnold M, Mattle HP, Schroth G, Remonda L. Contrast-enhanced 3-D MRA in decision making for carotid endarterectomy: a 6-year experience. <i>Cerebrovasc Dis.</i> 2006;21(5-6):393-400.	Review/Other-Dx	327 patients	To present the radiological characteristics and clinical results of a series of patients operated on the basis of combined US/MRA.	Among 327 patients, preoperative MRA was performed in 278 (85%), DSA in 44 (13.5%) and CTA in 5 (1.5%). Most of DSA studies were performed as emergency for preparation of endovascular therapy or for reasons other than carotid stenosis. 11 additional DSA (3.3%) complemented US/MRA, mostly because diverging diagnosis of subocclusion of ICA. No direct morbidity or intraoperative difficulty was related to preoperative MRA. Combined mortality/major morbidity rate was 0.9% (3 patients) and minor morbidity rate 5.5% (18 patients).	4

**Cerebrovascular Disease  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
43. Honish C, Sadanand V, Fladeland D, Chow V, Pirouzmand F. The reliability of ultrasound measurements of carotid stenosis compared to MRA and DSA. <i>Can J Neurol Sci.</i> 2005;32(4):465-471.	Observational-Dx	140 carotid arteries	To compare reliability of MRA and US modes with DSA in determining degree of internal carotid artery stenosis.	US grading of carotid stenosis can be made more reliable by choosing appropriate parameters. The best combination of sensitivity and specificity for stenosis >70% in our hospital was seen at peak systolic velocity >173 cm/s (sensitivity 0.87, specificity 0.8, PPV 0.70, NPV 0.93, kappa 0.64 and weighted kappa 0.71). MRA kappa was 0.78, (sensitivity 0.75, specificity 1.0, PPV 1.0, NPV 0.85).	2
44. U-King-Im JM, Hollingworth W, Trivedi RA, et al. Cost-effectiveness of diagnostic strategies prior to carotid endarterectomy. <i>Ann Neurol.</i> 2005;58(4):506-515.	Review/Other-Dx	167 patients	To assess the long-term cost-effectiveness of 5 alternative diagnostic strategies for identification of severe carotid stenosis in recently symptomatic patients.	A “selective” strategy, whereby all patients receive Doppler US and CE-MRA (only proceeding to DSA if the CE-MRA is positive and the Doppler US is negative), was most cost-effective. This was both the cheapest imaging and treatment strategy (35,205 dollars per patient) and yielded 6.1590 quality-adjusted life years, higher than 3 alternative imaging strategies. Probabilistic sensitivity analysis demonstrated that there was <10% probability that imaging with either DUS or DSA alone are cost-effective at the conventional 50,000 dollars/quality-adjusted life year threshold. In conclusion, DSA is not cost-effective in the routine diagnostic workup of most patients. Doppler US, with additional imaging in the form of CE-MRA, is recommended, with a strategy of “CE-MRA and selective Doppler US review” being shown to be the optimal imaging strategy.	4

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EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
45. Korn A, Bender B, Thomas C, et al. Dual energy CTA of the carotid bifurcation: advantage of plaque subtraction for assessment of grade of the stenosis and morphology. <i>Eur J Radiol.</i> 2011;80(2):e120-125.	Observational-Dx	36 patients with a total of 46 stenoses	To evaluate the diagnostic value of 3D-multi intensity projection images after subtraction of bone and calcified plaques using dual energy CT for the assessment of carotid bifurcation stenoses.	Grade of the stenosis could be evaluated in all 46 cases in DSA, axial multi planar projections, and 3D-multi intensity projection after bone and calcified plaques. However, in 25 cases grade of the stenosis was not assessable prior to PBS. The average grade of the stenosis increased from DSA (81.4%) to axial multi planar projections (83.5%) to 3D-multi intensity projection before and after bone and calcified plaques (86.5% and 85.6%). The amount of pseudo-occlusions increased in concordance with the grade of the stenosis (0<9<16). Using 3D-multi intensity projection reconstructions, plaque morphology could be evaluated in 32/46 stenoses before bone and calcified plaques and in 44/46 cases after bone and calcified plaques.	2
46. Thomas C, Korn A, Ketelsen D, et al. Automatic lumen segmentation in calcified plaques: dual-energy CT versus standard reconstructions in comparison with digital subtraction angiography. <i>AJR Am J Roentgenol.</i> 2010;194(6):1590-1595.	Observational-Dx	25 patients	To compare the accuracy of visual grading of stenoses after plaque removal with visual grading in standard reconstructions. DSA was used as a reference standard.	The average postprocessing time was 45 seconds. After plaque removal, all 25 relevant and 4 nonrelevant stenoses were correctly detected. Six relevant stenoses were overestimated as complete occlusions. With the standard reconstructions, 2 nonrelevant stenoses were overestimated as relevant. Correlation coefficients (r(2)) for the grading of stenoses after plaque removal and with standard reconstructions vs DSA were 0.7694 and 0.4329, respectively. Vessel contrast enhancement correlated weakly (r(2) = 0.2072) with the accuracy of plaque removal. Dual-energy CT with plaque removal automatically delivers CT luminograms with a high sensitivity for the detection of relevant stenoses and a higher correlation to DSA than standard reconstructions but frequently leads to an overestimation of high-grade stenoses as occlusions. Thus, dual-energy CT plaque and bone removal should be used complementary to standard reconstructions, and not exclusively.	2

**Cerebrovascular Disease  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
47. Tang TY, Howarth SP, Miller SR, et al. The ATHEROMA (Atorvastatin Therapy: Effects on Reduction of Macrophage Activity) Study. Evaluation using ultrasmall superparamagnetic iron oxide-enhanced magnetic resonance imaging in carotid disease. <i>J Am Coll Cardiol</i> . 2009;53(22):2039-2050.	Experimental-Tx	20 patients	To evaluate the effects of low-dose (10 mg) and high-dose (80 mg) atorvastatin on carotid plaque inflammation as determined by ultrasmall superparamagnetic iron oxide-enhanced carotid MRI.	20 patients completed 12 weeks of treatment in each group. A significant reduction from baseline in ultrasmall superparamagnetic iron oxide-defined inflammation was observed in the 80-mg group at both 6 weeks (DeltaSI 0.13; $P=0.0003$ ) and at 12 weeks (DeltaSI 0.20; $P<0.0001$ ). No difference was observed with the low-dose regimen. The 80-mg atorvastatin dose significantly reduced total cholesterol by 15% ( $P=0.0003$ ) and low-density lipoprotein cholesterol by 29% ( $P=0.0001$ ) at 12 weeks.	1
48. U-King-Im JM, Tang TY, Patterson A, et al. Characterisation of carotid atheroma in symptomatic and asymptomatic patients using high resolution MRI. <i>J Neurol Neurosurg Psychiatry</i> . 2008;79(8):905-912.	Observational-Dx	20 symptomatic and 20 asymptomatic patients	To prospectively evaluate differences in carotid plaque characteristics in symptomatic and asymptomatic patients using high resolution MRI.	After exclusion of poor quality images, 109 MRI sections in 18 symptomatic and 19 asymptomatic patients were available for analysis. There were no significant differences in mean luminal stenosis severity (72.9% vs 67.6%; $P=0.09$ ) or plaque burden (median plaque areas 50 mm <sup>2</sup> vs 50 mm <sup>2</sup> ; $P=0.858$ ) between the symptomatic and asymptomatic groups. However, symptomatic lesions had a higher incidence of ruptured fibrous caps (36.5% vs 8.7%; $P=0.004$ ), hemorrhage or thrombus (46.5% vs 14.0%; $P<0.001$ ), large necrotic lipid cores (63.8% vs 28.0%; $P=0.002$ ) and complicated type VI AHA lesions (61.5% vs 28.1%; $P=0.001$ ) compared with asymptomatic lesions. The MRI findings of plaque hemorrhage or thrombus had an OR of 5.25 (95% CI, 2.08 to 13.24) while thin or ruptured fibrous cap (as opposed to a thick fibrous cap) had an OR of 7.94 (95% CI, 2.93 to 21.51) for prediction of symptomatic clinical status.	2

**Cerebrovascular Disease  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
49. Wintermark M, Jawadi SS, Rapp JH, et al. High-resolution CT imaging of carotid artery atherosclerotic plaques. <i>AJNR Am J Neuroradiol.</i> 2008;29(5):875-882.	Observational-Dx	8 patients	To evaluate the ability of multidetector-row CTA to assess the composition and characteristics of carotid artery atherosclerotic plaques with use of histologic examination as the gold standard.	There was a 72.6% agreement between CTA and histologic examination in carotid plaque characterization. CTA showed perfect concordance for calcifications. A significant overlap between densities associated with lipid-rich necrotic core, connective tissue, and hemorrhage limited the reliability of individual pixel readings to identify these components. However, CTA showed good correlation with histologic examination for large lipid cores (kappa = 0.796; $P < .001$ ) and large hemorrhages (kappa = 0.712; $P = .102$ ). CTA performed well in detecting ulcerations (kappa = 0.855) and in measuring the fibrous cap thickness ( $R(2) = 0.77$ ; $P < .001$ ).	2
50. Chen A, Shyr MH, Chen TY, Lai HY, Lin CC, Yen PS. Dynamic CT perfusion imaging with acetazolamide challenge for evaluation of patients with unilateral cerebrovascular steno-occlusive disease. <i>AJNR Am J Neuroradiol.</i> 2006;27(9):1876-1881.	Observational-Dx	15 patients	To assess cerebral hemodynamics by using these parameters and acetazolamide challenge in patients with cerebrovascular steno-occlusive disease.	Significant decreases in CBF (-25.1%, $P = .003$ ) and significant increases in mean transit time (47.1%, $P < .001$ ) were found in stenotic hemispheres. After acetazolamide challenge, significant changes in CBF (-39.5%, $P < .001$ ) and mean transit time (92.9%, $P < .001$ ) were also seen. The acetazolamide test significantly decreased CBF hemispheric ratio (-20.3%, $P < .001$ ) and increased mean transit time hemispheric ratio (30.8%, $P = .002$ ), making both maps more asymmetric. Significance in CBF and mean transit time percent changes ( $P < .001$ and $P = .005$ , respectively) was found between hemispheres. When CBF percent changes were assumed to represent the true determinant of hemodynamic impairment, normal ranges of baseline mean transit time value and mean transit time percent changes demonstrated sensitivities of 66.7% and 100% and specificities of 58.3% and 75%, respectively, for detecting patients with hemodynamic impairment.	4

**Cerebrovascular Disease  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
51. Endo H, Inoue T, Ogasawara K, Fukuda T, Kanbara Y, Ogawa A. Quantitative assessment of cerebral hemodynamics using perfusion-weighted MRI in patients with major cerebral artery occlusive disease: comparison with positron emission tomography. <i>Stroke</i> . 2006;37(2):388-392	Observational-Dx	29 total patients	To validate the accuracy of PWI MRI for detecting hemodynamic impairment by correlating CBV measured by PWI MRI with CVR measured by PET in patients with unilateral major cerebral artery occlusive disease.	A significant negative correlation was observed between PWI MRI-CBV and PET-CVR ( $r=-0.713$ ; $P<0.0001$ ). PWI MRI-CBV higher than the mean +2 SD obtained in normal subjects (15.2 mL/100 g) was defined as elevated and PET-CVR lower than the mean -2 SD obtained in normal subjects (15.1%) was defined as reduced. Assuming the PET-CVR as the true determinant of hemodynamic impairment, PWI MRI-CBV provided 80.0% sensitivity and 91.7% specificity, with 80.0% PPV for detecting patients with reduced CVR.	3
52. Jovin TG, Liebeskind DS, Gupta R, et al. Imaging-based endovascular therapy for acute ischemic stroke due to proximal intracranial anterior circulation occlusion treated beyond 8 hours from time last seen well: retrospective multicenter analysis of 237 consecutive patients. <i>Stroke</i> . 2011;42(8):2206-2211.	Observational-Dx	237 patients	To assess safety, procedural, and clinical outcomes of MRI or CT perfusion imaging-based endovascular therapy in patients with anterior circulation stroke treated beyond 8 hours from time last seen well.	237 patients were identified (mean age, 63.8 +/- 16 years; mean baseline NIHSS, 15 +/- 5.5; mean time last seen well to treatment, 15 +/- 11.2 hours; male gender, 46%). Successful revascularization was achieved in 175/237 (73.84%) patients. Parenchymal hematoma occurred in 21/237 (8.86%) patients. The 90-day mortality rate was 21.5% (51/237). The rate of good outcomes was 45% (100/223) in the 223 patients with available modified Rankin Scale data at 90 days or time of hospital discharge. In multivariate analyses, age (OR, 0.96; 95% CI, 0.94 to 0.98; $P=0.002$ ), admission NIHSS (OR, 0.93; 0.87 to 0.98; $P=0.016$ ), and successful revascularization (OR, 4.32; 1.99 to 9.39; $P<0.0001$ ) were identified as independent predictors of good outcomes.	3



**Cerebrovascular Disease  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
53. Michel P, Ntaios G, Reichhart M, et al. Perfusion-CT guided intravenous thrombolysis in patients with unknown-onset stroke: a randomized, double-blind, placebo-controlled, pilot feasibility trial. <i>Neuroradiology</i> . 2012;54(6):579-588.	Experimental-Tx	12 patients	To design a pilot study to assess feasibility of a trial of PCT-guided thrombolysis in patients with ischemic tissue at risk of infarction and unknown stroke onset.	At baseline, there was a trend towards older age [69.5 (57-78) vs 49 (44-78) years] in the thrombolysis group (n = 6) compared to placebo (n = 6). Regarding feasibility, hospital arrival to treatment delay was above the allowed 2 hours in 3 patients (25%). There were 2 protocol violations (17%) regarding PCT, both underestimating the predicted infarct in patients randomized in the placebo group. No symptomatic hemorrhage or death occurred during the first 7 days. Three of the 4 (75%) and 1 of the 5 (20%) patients were recanalized in the thrombolysis and placebo group respectively. The volume of noninfarcted at-risk tissue was 84 (44-206) cm(3) in the treatment arm and 29 (8-105) cm(3) in the placebo arm.	1
54. Menon BK, Puetz V, Kochar P, Demchuk AM. ASPECTS and other neuroimaging scores in the triage and prediction of outcome in acute stroke patients. <i>Neuroimaging Clin N Am</i> . 2011;21(2):407-423, xii.	Review/Other-Dx	N/A	To summarize ASPECTS and other neuroimaging scores developed for risk prognostication and risk stratification with treatment in patients with acute ischemic stroke.	Neuroimaging scores such as ASPECTS, CBS, leptomeningeal collateral score, pc-ASPECTS, and BASIS help in conveying pathophysiological information in acute ischemic strokes derived from imaging techniques in a simple, easy to use form that helps clinicians in making appropriate treatment decisions and in determining prognosis with reasonable accuracy. These scores also help in creating an easily understandable numerical scale for use in acute ischemic stroke trials. It is, however, imperative that treating physicians understand the limitations of these scales and use them in the appropriate clinical context when making decisions that affect patient management.	4

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
55. Vora NA, Gupta R, Thomas AJ, et al. Factors predicting hemorrhagic complications after multimodal reperfusion therapy for acute ischemic stroke. <i>AJNR Am J Neuroradiol.</i> 2007;28(7):1391-1394.	Observational-Tx	185 patients	To find predictors for hemorrhagic complications in patients with acute ischemic stroke treated with multimodal endovascular therapy.	69 patients (37%) developed postprocedural hemorrhages: 24 (13%) parenchymal hematomas and 45 (24%) hemorrhagic infarctions. Patients with tandem occlusions (OR 4.6 [1.4–6.5], $P < .016$ ), hyperglycemia (OR 2.8 [1.1–7.7], $P < .043$ ), or treated concomitantly with IV t-PA and intra-arterial urokinase (OR 5.1 [1.1–25.0], $P < .041$ ) were at a significant risk for a parenchymal hematoma. Hemorrhagic infarction occurred significantly more in patients presenting with an ASPECTS $\leq 7$ (OR 1.9 [1.3–2.7], $P < .01$ ).	2

**Cerebrovascular Disease  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
56. Saqqur M, Uchino K, Demchuk AM, et al. Site of arterial occlusion identified by transcranial Doppler predicts the response to intravenous thrombolysis for stroke. <i>Stroke</i> . 2007;38(3):948-954.	Observational-Dx	335 patients	To examine clinical outcomes and recanalization rates in a multicenter cohort of stroke patients receiving IV t-PA by site of occlusion localized with bedside TCD.	335 patients had a mean age 69+/-13 years and 48.5% were women (median baseline NIHSS score 16 [range, 3 to 32], mean time to TCD 140+/-84 minutes, and mean time to IV t-PA 145+/-68 minutes). Distal MCA occlusion had an OR of 2 for complete recanalization (50/113 [44.2%], 95% CI: 1.1 to 3.1, <i>P</i> =0.005), proximal MCA 0.7 (49/163 [30%], 95% CI: 0.4 to 1.1, <i>P</i> =0.13), terminal internal carotid artery 0.1 (1/17 [5.9%], 95% CI: 0.015 to 0.8, <i>P</i> =0.015), tandem cervical internal carotid artery/MCA 0.7 (6/22 [27%], 95% CI: 0.3 to 1.9, <i>P</i> =0.5), and basilar artery 0.96 (3 of 10 [30%], 95% CI: 0.2 to 4, <i>P</i> =0.9). Patients with no flow (Thrombolysis in Brain Ischemia 0) at the occlusion site had less probability of complete recanalization than patients with dampened flow (Thrombolysis in Brain Ischemia 3) (OR(adj): 0.256, 95% CI: 0.11 to 0.595, <i>P</i> =0.002). Continuous TCD monitoring was a positive predictor for complete recanalization (OR(adj): 3.02, 95% CI: 1.396 to 6.514, <i>P</i> =0.005). NIHSS score ≤2 at 24 hours was achieved in 66/305 patients (22%): distal MCA 33% (35/107), tandem cervical internal carotid artery/MCA 24% (5/21), proximal MCA 16% (24/155), basilar artery 25% (2/8), and none of the patients with terminal internal carotid artery had dramatic recovery (0%, n=14; <i>P</i> =0.003). Modified Rankin Scale score ≤1 was achieved in 90/260 patients (35%): distal MCA 52% (50/96), proximal MCA 25% (33/131), tandem cervical internal carotid artery/MCA 21% (3/14), terminal internal carotid artery 18% (2/11), and basilar artery 25% (2/8) ( <i>P</i> <0.001). Patients with distal MCA occlusion were twice as likely to have a good long-term outcome as patients with proximal MCA (OR: 2.1, 95% CI: 1.1 to 4, <i>P</i> =0.025).	4

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
57. Dani KA, Thomas RG, Chappell FM, et al. Computed tomography and magnetic resonance perfusion imaging in ischemic stroke: definitions and thresholds. <i>Ann Neurol.</i> 2011;70(3):384-401.	Review/Other-Dx	69 papers	To systematically reviewed CT and MR perfusion imaging in acute ischemic stroke.	Among 7,152 papers, 69 met inclusion criteria for analysis of definitions (49 MR and 20 CT), 21 MR (n = 551), and 10 CT (n = 266) papers, median sample size 22, provided thresholds. We found multiple definitions for tissue states, eg, tissue at risk, 18; nonviable tissue, 12; 16, no definition. Perfusion parameters varied widely; eg, 9 different MR, 6 different CT parameters for the “at risk”/“not at risk threshold.” Median threshold values varied up to 4-fold, eg, for the “at risk”/“not at risk threshold,” median CBF ranged from 18 to 37mL/100g/min; mean transit time from 1.8 to 8.3 seconds relative to the contralateral side. The influence of reperfusion and duration of ischemia could not be assessed.	4
58. Deipolyi AR, Wu O, Macklin EA, et al. Reliability of cerebral blood volume maps as a substitute for diffusion-weighted imaging in acute ischemic stroke. <i>J Magn Reson Imaging.</i> 2012;36(5):1083-1087.	Observational-Dx	58 patients	To assess the reliability of CBV maps as a substitute for DWI MRI in acute ischemic stroke.	Using the full scan duration (110 s), relative regional CBV was increased in most DWI lesions (62%; 95% CI, 48%–74%). Relative regional CBV increased with increasing scan duration ( $P < 0.001$ ). Even with the shortest duration (39.5 s) relative regional CBV was increased in 33% of lesions.	4
59. Fahmi F, Marquering HA, Streekstra GJ, et al. Differences in CT perfusion summary maps for patients with acute ischemic stroke generated by 2 software packages. <i>AJNR Am J Neuroradiol.</i> 2012;33(11):2074-2080.	Observational-Dx	26 consecutive patients	To assess the variability of the area of infarct core and penumbra as presented in summary maps produced by 2 different software packages.	There was a statistically significant difference in infarct core area (-23.6 +/- 25.6 cm(2)) and penumbra area (15.8 +/- 25.3 cm(2)) between the 2 software packages. For all the areas presented in the summary maps, the Bland-Altman interval limit of agreement was larger than 100 cm(2).	2
60. Gonzalez RG. Low signal, high noise and large uncertainty make CT perfusion unsuitable for acute ischemic stroke patient selection for endovascular therapy. <i>J Neurointerv Surg.</i> 2012;4(4):242-245.	Review/Other-Dx	N/A	To review the evidence that led to my current view on the best practices for imaging the stroke patient.	No results stated in abstract.	4

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
61. Gonzalez RG, Copen WA, Schaefer PW, et al. The Massachusetts General Hospital acute stroke imaging algorithm: an experience and evidence based approach. <i>J Neurointerv Surg.</i> 2013;5 Suppl 1:i7-12.	Review/Other-Dx	N/A	To use an experience and evidence based approach to develop the neuroimaging algorithm that best improves outcomes in patients with severe ischemic strokes caused by anterior circulation occlusions.	The Massachusetts General Hospital Neuroradiology Division employed an experience and evidence based approach to develop a neuroimaging algorithm to best select patients with severe ischemic strokes caused by anterior circulation occlusions for IV t-PA and endovascular treatment. Methods found to be of value included the NIHSS, noncontrast CT, CTA and diffusion MRI. Perfusion imaging by CT and MRI were found to be unnecessary for safe and effective triage of patients with severe anterior circulation occlusions. An algorithm was adopted that includes: noncontrast CT to identify hemorrhage and large hypodensity followed by CTA to identify the anterior circulation occlusion; diffusion MRI to estimate the core infarct; and NIHSS in conjunction with diffusion data to estimate the clinical penumbra.	4
62. Kamalian S, Maas MB, Goldmacher GV, et al. CT cerebral blood flow maps optimally correlate with admission diffusion-weighted imaging in acute stroke but thresholds vary by postprocessing platform. <i>Stroke.</i> 2011;42(7):1923-1928.	Observational-Dx	48 consecutive cases	(1) Determine the optimal CT perfusion parameter to define infarct core using various postprocessing platforms; and (2) establish the degree of variability in threshold values between these different platforms.	CBF had the highest accuracy (receiver operating characteristic area under the curve) for all 3 platforms ( $P<0.01$ ). The maximal areas under the curve for each parameter were: absolute CBF 0.88, CBV 0.81, and mean transit time 0.82 and relative CBF 0.88, CBV 0.83, and mean transit time 0.82. Optimal receiver operating characteristic operating point thresholds varied significantly between different platforms (Friedman test, $P<0.01$ ).	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
63. Konstas AA, Goldmakher GV, Lee TY, Lev MH. Theoretic basis and technical implementations of CT perfusion in acute ischemic stroke, part 2: technical implementations. <i>AJNR Am J Neuroradiol.</i> 2009;30(5):885-892.	Review/Other-Dx	N/A	To highlight the need for validation and standardization of important CT perfusion parameters to improve patient outcomes and design future randomized clinical trials that will provide evidence for the importance of the core/penumbra “mismatch” in patient triage for recanalization therapies beyond the current 3-hour therapeutic window for IV thrombolysis.	CT perfusion is a functional imaging technique that provides important information about capillary-level hemodynamics of the brain parenchyma and is a natural complement to the strengths of unenhanced CT and CTA in the evaluation of acute stroke, vasospasm, and other neurovascular disorders. CT perfusion is critical in determining the extent of irreversibly infarcted brain tissue (infarct “core”) and the severely ischemic but potentially salvageable tissue (“penumbra”). This is achieved by generating parametric maps of CBF, CBV, and mean transit time.	4
64. Cheng AL, Batool S, McCreary CR, et al. Susceptibility-weighted imaging is more reliable than T2*-weighted gradient-recalled echo MRI for detecting microbleeds. <i>Stroke.</i> 2013;44(10):2782-2786.	Observational-Dx	9 patients and 21 controls	To investigate the sensitivity and reliability of MRI SWI compared with routine MRI T2*-weighted gradient-recalled echo for cerebral microbleed detection.	In 9 cerebral amyloid angiopathy cases, the raters identified 1,146 total cerebral microbleeds on gradient-recalled echo and 1,432 cerebral microbleeds on SWI. In 22 healthy control subjects, the raters identified ≥1 cerebral microbleeds in 6/22 on gradient-recalled echo (total 9 cerebral microbleeds) and 5/22 on SWI (total 19 cerebral microbleeds). Among cerebral amyloid angiopathy cases, the reliability between raters for cerebral microbleed counts was good for SWI (intraclass correlation coefficient, 0.87) but only moderate for gradient-recalled echo (intraclass correlation coefficient, 0.52). In controls, agreement on the presence or absence of cerebral microbleeds in controls was moderate to good on both SWI (kappa coefficient ranged from 0.57 to 0.74 across the 3 combinations of rater pairs) and gradient-recalled echo (kappa range, 0.31 to 0.70). A review of 114 hypointensities identified as possible cerebral microbleeds indicated that increased detection and reliability on SWI was related to both increased contrast and higher resolution, allowing better discrimination of cerebral microbleeds from the background and better anatomic differentiation from pial vessels.	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
65. Verma RK, Kottke R, Andereggen L, et al. Detecting subarachnoid hemorrhage: comparison of combined FLAIR/SWI versus CT. <i>Eur J Radiol.</i> 2013;82(9):1539-1545.	Observational-Dx	25 patients	To compare the utility of SWI with the established diagnostic techniques CT and FLAIR in their detecting capacity of SAH, and further to compare the combined SWI/FLAIR MRI data with CT to evaluate whether MRI is more accurate than CT.	SAH was detected in a total of 146 subarachnoid regions. CT identified 110 (75.3%), FLAIR 127 (87%), and SWI 129 (88.4%) involved regions. Combined FLAIR and SWI identified all 146 detectable regions (100%). FLAIR was sensitive for frontal-parietal, temporal-occipital and Sylvian cistern SAH, while SWI was particularly sensitive for interhemispheric and intraventricular hemorrhage.	2
66. Lansberg MG, Straka M, Kemp S, et al. MRI profile and response to endovascular reperfusion after stroke (DEFUSE 2): a prospective cohort study. <i>Lancet Neurol.</i> 2012;11(10):860-867.	Review/Other-Dx	138 patients	To establish whether MRI can be used to identify patients who are most likely to benefit from endovascular reperfusion.	138 patients were enrolled. 110 patients had catheter angiography and of these 104 had an MRI profile and 99 could be assessed for reperfusion. 46/78 (59%) patients with target mismatch and 12/21 (57%) patients without target mismatch had reperfusion after endovascular treatment. The adjusted OR for favorable clinical response associated with reperfusion was 8.8 (95% CI, 2.7–29.0) in the target mismatch group and 0.2 (0.0–1.6) in the no target mismatch group ( $P=0.003$ for difference between ORs). Reperfusion was associated with increased good functional outcome at 90 days (OR 4.0, 95% CI, 1.3–12.2) in the target mismatch group, but not in the no target mismatch group (1.9, 0.2–18.7).	4
67. Yoo AJ, Verduzco LA, Schaefer PW, Hirsch JA, Rabinov JD, Gonzalez RG. MRI-based selection for intra-arterial stroke therapy: value of pretreatment diffusion-weighted imaging lesion volume in selecting patients with acute stroke who will benefit from early recanalization. <i>Stroke.</i> 2009;40(6):2046-2054	Observational-Dx	34 consecutive patients	To determine if this threshold could identify patients treated with intra-arterial therapy who would do poorly despite reperfusion.	Among patients with initial infarcts >70 cm <sup>3</sup> , all had poor outcomes despite a 50% recanalization rate with mean infarct growth of 114 cm <sup>3</sup> . These patients also had the largest mean transit time volumes ( $P<0.04$ ). Patients with initial infarct volumes <70 cm <sup>3</sup> who recanalized early had the best clinical outcomes ( $P<0.008$ ) with a 64% rate of modified Rankin Scale score ≤2 and the least infarct growth ( $P<0.03$ ) with mean growth of 18 cm <sup>3</sup> .	3

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EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
68. Sanak D, Nosal V, Horak D, et al. Impact of diffusion-weighted MRI-measured initial cerebral infarction volume on clinical outcome in acute stroke patients with middle cerebral artery occlusion treated by thrombolysis. <i>Neuroradiology</i> . 2006;48(9):632-639.	Observational-Dx	25 consecutive CI patients	To assess the correlation between initial cerebral infarct volume (quantified on DWI MRI) and the resulting clinical outcome in acute stroke patients with MCA (M(1-2) segment) occlusion detected on MRI angiography treated by IV/intra-arterial thrombolysis.	V(DWI-I) ranged from 0.7 to 321 mL. The 24-hour clinical outcome improved significantly ( $P=0.0001$ ) in 87% of patients with a V(DWI-I) $\leq 70$ mL (group 1) and deteriorated significantly ( $P=0.0018$ ) in all patients with a V(DWI-I) $>70$ mL (group 2). The 90-day mortality was 0% in group 1 and 71.5% in group 2. The 90-day clinical outcome was significantly better in group 1 than in group 2 ( $P=0.026$ ).	3
69. Riedel CH, Zimmermann P, Jensen-Kondering U, Stingele R, Deuschl G, Jansen O. The importance of size: successful recanalization by intravenous thrombolysis in acute anterior stroke depends on thrombus length. <i>Stroke</i> . 2011;42(6):1775-1777.	Observational-Dx	138 patients	To investigate if thrombus lengths, measured in thin-slice nonenhanced CT images, can be used to predict the likelihood of a successful recanalization by IV thrombolysis.	In 62 patients, IV thrombolysis resulted in recanalization; among these patients, no thrombus length exceeded 8 mm. The median modified Rankin scale score at hospital discharge was 2. In the remaining 76 patients, thrombus lengths mostly exceeded 8 mm and IV thrombolysis failed in recanalization. These patients were discharged with a median modified Rankin scale score of 5.	4
70. Furlan AJ, Eyding D, Albers GW, et al. Dose Escalation of Desmoteplase for Acute Ischemic Stroke (DEDAS): evidence of safety and efficacy 3 to 9 hours after stroke onset. <i>Stroke</i> . 2006;37(5):1227-1231.	Experimental-Tx	37 patients	To evaluate safety and efficacy of IV desmoteplase in patients with perfusion/diffusion mismatch on MRI, 3 to 9 hours after onset of acute ischemic stroke.	37 patients were randomized and received treatment (intent-to-treat; placebo: n=8; 90 microg/kg: n=14; 125 microg/kg: n=15). No symptomatic intracranial hemorrhage occurred. Reperfusion was achieved in 37.5% (95% CI [8.5; 75.5]) of placebo patients, 18.2% (2.3; 51.8) of patients treated with 90 microg/kg desmoteplase, and 53.3% (26.6; 78.7) of patients treated with 125 microg/kg desmoteplase. Good clinical outcome at 90 days occurred in 25.0% (3.2; 65.1) treated with placebo, 28.6% (8.4; 58.1) treated with 90 microg/kg desmoteplase and 60.0% (32.3; 83.7) treated with 125 microg/kg desmoteplase. In the target population (n=25), the difference compared with placebo increased and was statistically significant for good clinical outcome with 125 microg/kg desmoteplase ( $P=0.022$ ).	1



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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
71. Hacke W, Albers G, Al-Rawi Y, et al. The Desmoteplase in Acute Ischemic Stroke Trial (DIAS): a phase II MRI-based 9-hour window acute stroke thrombolysis trial with intravenous desmoteplase. <i>Stroke</i> . 2005;36(1):66-73.	Experimental-Tx	104 patients	To evaluate the safety and efficacy of IV desmoteplase, a highly fibrin-specific and nonneurotoxic thrombolytic agent, administered within 3 to 9 hours of ischemic stroke onset in patients with perfusion/diffusion mismatch on MRI.	Part 1 was terminated prematurely because of high rates of symptomatic intracranial hemorrhage with desmoteplase (26.7%). In Part 2, the symptomatic intracranial hemorrhage rate was 2.2%. No symptomatic intracranial hemorrhage occurred with placebo in either part. Reperfusion rates up to 71.4% ( $P=0.0012$ ) were observed with desmoteplase (125 microg/kg) compared with 19.2% with placebo. Favorable 90-day clinical outcome was found in 22.2% of placebo-treated patients and between 13.3% (62.5 microg/kg; $P=0.757$ ) and 60.0% (125 microg/kg; $P=0.0090$ ) of desmoteplase-treated patients. Early reperfusion correlated favorably with clinical outcome ( $P=0.0028$ ). Favorable outcome occurred in 52.5% of patients experiencing reperfusion vs 24.6% of patients without reperfusion.	1
72. Gonzalez RG. Current state of acute stroke imaging. <i>Stroke</i> . 2013;44(11):3260-3264.	Review/Other-Dx	N/A	To review the rapid diagnosis of acute stroke, the guidance of treatment using IV administered t-PA, and intra-arterial treatments.	CT and MRI of the patients with acute ischemic stroke provide valuable diagnostic and prognostic information. Neuroimaging can inform on the presence of hemorrhage, vessel occlusion, irreversible injury, and tissue at risk, which helps in making optimal patient management decisions. CT and MRI provide complementary information, and the most comprehensive understanding of the state of the brain in the patient with a stroke syndrome may require both. Much progress has been made in treating stroke, and new insights on stroke physiology provided by imaging suggest that there are major opportunities to treat many more patients effectively.	4

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
73. Donnan GA, Baron JC, Ma H, Davis SM. Penumbra selection of patients for trials of acute stroke therapy. <i>Lancet Neurol.</i> 2009;8(3):261-269.	Review/Other-Dx	N/A	To discuss the background of penumbral selection for therapy, the current status of this approach for several interventions, and areas of future research.	Imaging of the ischemic penumbra is a promising approach to the selection of patients with acute ischemic stroke for trials of intervention at more than 3 hours after onset. Several advances facilitate online assessment of patients for mismatch volumes to improve selection for clinical trials. Furthermore, large mismatch volumes determined with stricter perfusion criteria than the currently used 20% might be required to recruit the most therapeutically responsive patients. To extend the therapeutic time window beyond 3–4.5 hours for alteplase, particularly for times up to 9–12 hours, more phase III randomized, controlled trials that use penumbral selection are needed.	4
74. Kim JT, Yoon W, Park MS, et al. Early outcome of combined thrombolysis based on the mismatch on perfusion CT. <i>Cerebrovasc Dis.</i> 2009;28(3):259-265.	Review/Other-Dx	18 patients	To assess whether combined IV and intra-arterial thrombolysis performed according to the status of tissue based on PCT is beneficial for the early outcome in patients with acute ischemic stroke.	18 patients (11 men) underwent combined IV/intra-arterial thrombolysis. The recanalization rate after combined IV/intra-arterial thrombolysis was 88.9% (TIMI 2, 4; TIMI 3, 12). A good functional outcome at discharge was noted in 12 patients (66.7%). The incidence of symptomatic intracranial hemorrhage was 5.6% (1/18).	4
75. Raaymakers TW, Buys PC, Verbeeten B, Jr., et al. MR angiography as a screening tool for intracranial aneurysms: feasibility, test characteristics, and interobserver agreement. <i>AJR Am J Roentgenol.</i> 1999;173(6):1469-1475.	Observational-Dx	626 patients	Feasibility, test characteristics, and interobserver agreement in evaluation of MR angiograms were assessed by members of the MARS (Magnetic resonance Angiography in Relatives of patients with SAH) Study Group.	33 aneurysms were found in 25 (4%; 95% CI, 3%–6%) of 626 relatives. 13 (8%) of 169 relatives who refused screening had MR-related reasons; an additional 6 persons could not be screened because of contraindications for MRI (pregnancy, n = 1; claustrophobia, n = 5). The PPV of MRA was 100% (95% CI, 79%–100%) for “definite” aneurysms and 58% (95% CI, 28%–85%) for “possible” aneurysms. Sensitivity of MRA was estimated at 83% (95% CI, 65%–94%) and specificity at 97% (95% CI, 94%–98%). Interobserver agreement in the evaluation of MR angiograms was poor (kappa <.30), probably because different diagnostic strategies used by individual observers resulted in different use of the assessment category “possible aneurysm.”	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
76. Ronkainen A, Puranen MI, Hernesniemi JA, et al. Intracranial aneurysms: MR angiographic screening in 400 asymptomatic individuals with increased familial risk. <i>Radiology</i> . 1995;195(1):35-40.	Observational-Dx	37 patients	To evaluate the accuracy and limitations of MRA screening for incidental intracranial aneurysms in healthy individuals with a family history of intracranial aneurysm.	Intracranial aneurysms were detected with MRA in 37 individuals, 32 of whom underwent conventional angiography. Intraobserver consistency was excellent (kappa = 0.96), and interobserver reproducibility was good to excellent (kappa = 0.59–0.82). Both techniques showed similar results in the evaluation of size, localization, and orientation of aneurysms and visibility of the aneurysm neck.	3
77. Dammert S, Krings T, Moller-Hartmann W, et al. Detection of intracranial aneurysms with multislice CT: comparison with conventional angiography. <i>Neuroradiology</i> . 2004;46(6):427-434.	Observational-Dx	50 consecutive patients	To assess the diagnostic accuracy of multislice CT in detection of intracranial aneurysms in patients presenting with subarachnoid or intracranial hemorrhage.	In conventional angiography 51 aneurysms were detected in 41 patients. CTA showed up to 48 aneurysms in 39 patients, depending on the observer. The overall sensitivity of multislice CT was 83.3% for small (<4 mm), 90.6% for medium-size (5–12 mm) and 100% for large (>13 mm) aneurysms. The sensitivity of multislice CTA to medium-size and large intracranial aneurysm is within the upper part of the range reported for helical single-slice CT. However, as small aneurysms may not be found, DSA remains the standard technique for investigation of SAH.	2
78. Jayaraman MV, Mayo-Smith WW, Tung GA, et al. Detection of intracranial aneurysms: multi-detector row CT angiography compared with DSA. <i>Radiology</i> . 2004;230(2):510-518.	Observational-Dx	35 total patients	To prospectively compare the effectiveness of multi-detector row CTA with that of conventional IA-DSA used to detect intracranial aneurysms in patients with nontraumatic acute SAH.	A total of 26 aneurysms were detected at DSA in 21 patients, and no aneurysms were detected in 14 patients. Sensitivity and specificity for CTA were, respectively, 90% and 93% for reader 1 and 81% and 93% for reader 2. The mean diameter of aneurysms detected on CTA images was 4.4 mm, and the smallest aneurysm detected was 2.2 mm in diameter. Aneurysms that were missed at initial interpretation of CTA images were identified at retrospective reading.	1

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
79. Sailer AM, Wagemans BA, Nelemans PJ, de Graaf R, van Zwam WH. Diagnosing intracranial aneurysms with MR angiography: systematic review and meta-analysis. <i>Stroke</i> . 2014;45(1):119-126.	Meta-analysis	12 studies	To evaluate the sensitivity and specificity of MRA in the diagnosis of ruptured and unruptured intracranial aneurysms.	Included studies were of high methodological quality. Studies with larger sample size tended to have higher diagnostic performance. Most studies used TOF MRA technique. Among the 960 patients assessed, 772 aneurysms were present. Heterogeneity with reference to sensitivity and specificity was moderate to high. Pooled sensitivity of MRA was 95% (95% CI, 89%–98%), and pooled specificity was 89% (95% CI, 80%–95%). False-negative and false-positive aneurysms detected on MRA were mainly located at the skull base and MCA. Freehand 3D reconstructions performed by the radiologist significantly increased diagnostic performance. Studies performed on 3 Tesla showed a trend toward higher performance ( $P=0.054$ ).	M
80. van Gijn J, Kerr RS, Rinkel GJ. Subarachnoid haemorrhage. <i>Lancet</i> . 2007;369(9558):306-318.	Review/Other-Dx	N/A	To review SAH.	SAH accounts for only 5% of strokes, but occurs at a fairly young age. Sudden headache is the cardinal feature, but patients might not report the mode of onset. CT brain scanning is normal in most patients with sudden headache, but to exclude SAH or other serious disorders, a carefully planned lumbar puncture is also needed. Aneurysms are the cause of SAH in 85% of cases. The case fatality after aneurysmal hemorrhage is 50%; 1 in 8 patients with SAH dies outside hospital. Rebleeding is the most imminent danger; a first aim is therefore occlusion of the aneurysm. Endovascular obliteration by means of platinum spirals (coiling) is the preferred mode of treatment, but some patients require a direct neurosurgical approach (clipping). Another complication is delayed cerebral ischemia; the risk is reduced with oral nimodipine and probably by maintaining circulatory volume. Hydrocephalus might cause gradual obtundation in the first few hours or days; it can be treated by lumbar puncture or ventricular drainage, dependent on the site of obstruction.	4

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
81. Cortnum S, Sorensen P, Jorgensen J. Determining the sensitivity of computed tomography scanning in early detection of subarachnoid hemorrhage. <i>Neurosurgery</i> . 2010;66(5):900-902; discussion 903.	Observational-Dx	499 patients	To determine the sensitivity of modern CT scanners in detecting SAH and to determine whether there is a continued need for lumbar puncture to exclude the diagnosis.	A total of 499 patients were included. In 203 patients the diagnosis was excluded by a negative CT scan and negative lumbar puncture. 296 patients were found to have a SAH. The diagnosis in 295 of these patients was based on a positive CT scan. In a single patient, on day 6, the diagnosis was based on a positive lumbar puncture. From day 1 to day 5, CT scanning was found to have a sensitivity of 100%. Overall, CT scanning had a sensitivity of 99.7% (95% CI: 98.1%–99.99%).	3
82. Wu Z, Li S, Lei J, An D, Haacke EM. Evaluation of traumatic subarachnoid hemorrhage using susceptibility-weighted imaging. <i>AJNR Am J Neuroradiol</i> . 2010;31(7):1302-1310.	Review/Other-Dx	20 patients	To compare SWI and CT to determine if SWI can show traumatic SAH in different parts of the subarachnoid space.	55 areas with SAH were identified by both CT and SWI. 10 areas were identified by CT only and 13 by SWI only. SAH was recognized on SWI by its very dark signal intensity surrounded by cerebrospinal fluid signal intensity in the sulci or cisterns. Compared with the smooth-looking veins, SAH tended to have a rough boundary and inhomogeneous signal intensity. In many instances, blood in the sulcus left an area of signal intensity loss that had a “triangle” shape. SWI showed 5 more cases of intraventricular hemorrhage than did CT.	4
83. Westerlaan HE, van Dijk JM, Jansen-van der Weide MC, et al. Intracranial aneurysms in patients with subarachnoid hemorrhage: CT angiography as a primary examination tool for diagnosis--systematic review and meta-analysis. <i>Radiology</i> . 2011;258(1):134-145.	Meta-analysis	50 studies; 2 independent reviewers	To calculate the sensitivity and specificity of CTA in the diagnosis of cerebral aneurysms in patients with acute SAH at presentation.	For sensitivity, the selected studies showed moderate heterogeneity. For specificity, low heterogeneity was observed. The majority of the studies (n = 30) used a four-detector row CT scanner. The studies had good methodologic quality. Pooled sensitivity was 98% (95% CI: 97%, 99%), and pooled specificity was 100% (95% CI: 97%, 100%). Potential sources of variability among the studies were variations in the methodologic features (quality score), CT examination procedure (number of rows on the MDCT scanner), the standard of reference used, and the prevalence of ruptured intracranial aneurysms. There was evidence for publication bias, which may have led to overestimation of the diagnostic accuracy of CTA.	M

**Cerebrovascular Disease  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
84. Black PM. Hydrocephalus and vasospasm after subarachnoid hemorrhage from ruptured intracranial aneurysms. <i>Neurosurgery</i> . 1986;18(1):12-16.	Review/Other-Dx	87 patients	To analyze the incidence of hydrocephalus and vasospasm and the relationship between them.	The incidence of hydrocephalus and vasospasm and the relationship between them were analyzed retrospectively in 87 patients with SAH from ruptured intracranial aneurysms. 67% of the patients showed ventricular enlargement on a CT scan done within 30 days of the hemorrhage; in patients whose first scan was done within 3 days of the hemorrhage, 63% seemed to have ventricular enlargement by a neuroradiologist's interpretation. Shunts were required in 14% of the patients because of delayed neurological deterioration or enlarging ventricles; 3% required ventriculostomy shortly after admission. 74% of the patients had angiographic spasm on an angiogram done within the first 30 days after hemorrhage. 62% of the patients had both hydrocephalus and vasospasm; 22% had neither. 5% had hydrocephalus, but no spasm; 11% had spasm, but no hydrocephalus. Hydrocephalus and vasospasm were significantly associated ( $P<0.01$ , chi2).	4

**Cerebrovascular Disease  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
<p>85. Kassell NF, Boarini DJ, Adams HP, Jr., et al. Overall management of ruptured aneurysm: comparison of early and late operation. <i>Neurosurgery</i>. 1981;9(2):120-128.</p>	<p>Review/Other-Dx</p>	<p>61 patients</p>	<p>To analyze the overall management results with 61 consecutive patients admitted within 3 days of SAH from a ruptured intracranial aneurysm.</p>	<p>During the course of this study, the preferred method of management shifted from late surgery (planned at least 7 days after the last hemorrhage) to early surgery (within 4 days of the last hemorrhage). 10 moribund patients were excluded from analysis, leaving 24 in the late group and 27 in the early group. Both groups had comparable patient demographic characteristics and neurological conditions, and their care was supervised by 1 neurosurgeon. A microsurgical intracranial operation was performed on all patients who survived long enough to have surgery. The intraoperative conditions and complications were similar for the 2 groups. The average length of follow-up was 11 months in the late and 9 months in the early group. The overall management results for the late group showed a 42% favorable outcome, a 17% unfavorable outcome, and a 42% mortality. The early group had an 81% favorable outcome, a 7% unfavorable outcome, and an 11% mortality. Patients in both good and poor conditions fared better in the early group. 7 late group patients rebled, compared to none in the early group. The number of medical complications, the length of hospitalization, and the occurrence of symptomatic vasospasm were all greater in the late group. Vasospasm in the early group occurred only postoperatively and, with the aneurysms secured, was treated more aggressively and successfully with hypertensive/hypervolemic therapy than the predominantly operative vasospasm in the late group.</p>	<p>4</p>

**Cerebrovascular Disease  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
86. Donmez H, Serifov E, Kahriman G, Mavili E, Durak AC, Menku A. Comparison of 16-row multislice CT angiography with conventional angiography for detection and evaluation of intracranial aneurysms. <i>Eur J Radiol.</i> 2011;80(2):455-461.	Observational-Dx	112 patients	To compare the diagnostic performance of 16-row multidetector CTA with DSA for the detection and characterization of intracranial aneurysms in patients with nontraumatic SAHs.	A total of 164 aneurysms were detected at DSA in 112 patients, no aneurysms were detected by DSA and multidetector CTA in 16 patients. 8 aneurysms were missed by multidetector CTA. The overall sensitivity, specificity, and accuracy of multidetector CTA on a per-aneurysm basis were 95.1%, 94.1%, and 95%, respectively. According to the size of the aneurysm <3 mm; sensitivity, specificity and diagnostic accuracy of multidetector CTA were 86.1%, 94.1%, 88.6%, respectively.	2
87. McKinney AM, Palmer CS, Truwit CL, Karagulle A, Teksam M. Detection of aneurysms by 64-section multidetector CT angiography in patients acutely suspected of having an intracranial aneurysm and comparison with digital subtraction and 3D rotational angiography. <i>AJNR Am J Neuroradiol.</i> 2008;29(3):594-602.	Observational-Dx	63 subjects	To determine the accuracy of 64-section multislice CTA in aneurysm detection vs combined DSA and 3D rotational angiography.	A total of 41 aneurysms were found in 28 patients. The mean size was 6.09 mm on DSA/3D rotational angiography and 5.98 mm on multislice CTA. Kappa was excellent (0.97) between the aneurysm size on multislice CTA and DSA/3D rotational angiography. Ultimately, 37 aneurysms were detected by DSA/3D rotational angiography in 25 of the 36 patients who underwent conventional angiography. The reviewers noted four 1- to 1.5-mm sessile outpouchings only on 3D rotational angiography; none were considered a source of SAH. One multislice CTA was false positive, whereas one 2-mm aneurysm was missed by CTA. The sensitivity of CTA for aneurysms <4 mm was 92.3%, whereas it was 100% for those 4-10 mm and more than 10 mm, excluding the indeterminate, sessile lesions.	2



**Cerebrovascular Disease  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
88. Agid R, Andersson T, Almqvist H, et al. Negative CT angiography findings in patients with spontaneous subarachnoid hemorrhage: When is digital subtraction angiography still needed? <i>AJNR Am J Neuroradiol.</i> 2010;31(4):696-705.	Observational-Dx	193 patients	To evaluate whether negative findings on CTA can reliably exclude aneurysms in patients with acute SAH.	193 patients with SAH and negative findings on CTA who underwent subsequent DSA were identified. The distribution of blood on unenhanced CT was the following: perimesencephalic hemorrhage in 93 patients, diffuse aneurysmal pattern in 50, no blood on CT (xanthochromic lumbar puncture) in 32, and peripheral sulcal distribution in 18. All patients with perimesencephalic hemorrhage had negative findings on DSA. One patient with no blood on CT had vasculitis on DSA. 6/18 (33%) patients with peripheral blood had vasculitis on DSA. 3 of these were also diagnosed by CTA. All except 1 patient with diffuse aneurysmal blood had negative findings on DSA. 1 patient was diagnosed with an aneurysm on DSA (1/50, 0.5%). Repeat delayed DSA performed in 28 of these patients revealed a small aneurysm in 4 (14%). 5 patients had a complication of DSA (2.6%); 1 was a clinical stroke (0.5%).	3
89. Jagadeesan BD, Delgado Almandoz JE, Kadkhodayan Y, et al. Size and anatomic location of ruptured intracranial aneurysms in patients with single and multiple aneurysms: a retrospective study from a single center. <i>J Neurointerv Surg.</i> 2014;6(3):169-174.	Review/Other-Dx	379 patients	To retrospectively analyze the size of ruptured intracranial aneurysms in patients with single and multiple intracranial aneurysms in order to study this relationship further.	379 patients (281 with a single intracranial aneurysms, Group 1 and 98 with multiple intracranial aneurysms, Group 2) with 419 treated ruptured intracranial aneurysms were included in the study. Very small intracranial aneurysms and small intracranial aneurysms constituted the majority of ruptured intracranial aneurysms in both groups (33.5% and 45.2% in Group 1 and 24.6% and 50.7% in Group 2) and the mean size of the ruptured intracranial aneurysms was not different between the 2 groups. Very small intracranial aneurysms constituted almost two-thirds of all ruptured intracranial aneurysms in certain locations whereas intracranial aneurysms >7 mm in size did not constitute more than a third of the ruptured intracranial aneurysms at any of the arterial locations.	4

**Cerebrovascular Disease  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
90. Dehdashti AR, Rufenacht DA, Delavelle J, Reverdin A, de Tribolet N. Therapeutic decision and management of aneurysmal subarachnoid haemorrhage based on computed tomographic angiography. <i>Br J Neurosurg.</i> 2003;17(1):46-53.	Observational-Dx	100 patients	To evaluate the potential of high quality CTA to replace DSA in cases of ruptured saccular aneurysms and perform early surgical clipping or coiling on the basis of CTA alone.	CTA revealed a total of 118 aneurysms including all ruptured aneurysms. A decision of direct surgical clipping, endovascular coiling or therapeutic abstention was made in 89 cases (89%) on the basis of CTA alone. 61 direct surgical procedures were performed after CTA. 26 cases underwent DSA for immediate endovascular treatment of the ruptured aneurysm. In 11 cases (11%), a DSA was performed prior to the therapeutic decision because of unclear aneurysm. 4 cases were not treated because of initial poor clinical grade. The surgical findings were compared with CTA data and were considered accurate in all but 1 case. All patients underwent postoperative DSA within 10 days after SAH. The sensitivity and the specificity of CTA for the detection of all aneurysms, as compared with postoperative DSA, were 95.1% and 100%, respectively. A total of 6 unruptured aneurysms were missed initially, but were visible retrospectively on CTA in all but 1 case and were found in patients with multiple aneurysms in whom the ruptured aneurysm was detected by CTA. Current quality CTA allows reliable pretreatment planning for the majority of cases of aneurysmal SAH and diminishes the pretreatment evaluation time critically. Complementary pretreatment DSA is required in situations where CTA characteristics of the ruptured aneurysm is unsatisfactory.	3

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EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
<p>91. Hoh BL, Cheung AC, Rabinov JD, Pryor JC, Carter BS, Ogilvy CS. Results of a prospective protocol of computed tomographic angiography in place of catheter angiography as the only diagnostic and pretreatment planning study for cerebral aneurysms by a combined neurovascular team. <i>Neurosurgery</i>. 2004;54(6):1329-1340; discussion 1340-1322.</p>	<p>Review/Other-Dx</p>	<p>223 patients</p>	<p>Since late 2001/early 2002, the combined neurovascular unit of the Massachusetts General Hospital has adopted a prospective protocol of CTA in place of DSA as the only diagnostic and pretreatment planning study for patients with cerebral aneurysms (ruptured and unruptured). The results are obtained during the 12-month period from January 2002 to January 2003.</p>	<p>During the study period, 223 patients with cerebral aneurysms underwent initial diagnostic evaluation for cerebral aneurysm by the combined neurovascular team of Massachusetts General Hospital. Of the 223 patients, 109 patients had confirmed SAH (Group A) and 114 patients did not have SAH (Group B). All of these patients were included in the prospective CTA protocol. Cerebral aneurysm treatment was initiated on the basis of CTA alone in 93 Group A patients (86%), in 89 Group B patients (78%), and in 182 patients (82%) overall. Treatment consisted of surgical clipping in 152 patients (68%), endovascular coiling in 56 patients (25%), endovascular parent artery balloon occlusion in 4 patients (2%), and external carotid artery to internal carotid artery bypass and carotid artery surgical occlusion in 2 patients (1%). 9 patients (4%) did not undergo treatment. The cerebral aneurysm detection rate by CTA was 100% for the presenting aneurysm (ruptured aneurysm in Group A or symptomatic/presenting aneurysm in Group B) in both groups. The detection rate by CTA for total cerebral aneurysms, including incidental multiple aneurysms, was 95.3% in Group A, 98.3% in Group B, and 97% overall. The overall morbidity associated with DSA (pretreatment or as intraoperative or postoperative clip evaluation) was 1 patient (1.3%) with a minor nonneurological complication, 1 patient (1.3%) with a minor neurological complication, and no patients (0%) with a major neurological complication.</p>	<p>4</p>

**Cerebrovascular Disease  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
92. Delgado Almandoz JE, Crandall BM, Fease JL, et al. Diagnostic yield of catheter angiography in patients with subarachnoid hemorrhage and negative initial noninvasive neurovascular examinations. <i>AJNR Am J Neuroradiol.</i> 2013;34(4):833-839.	Observational-Dx	55 patients	To determine the yield of DSA for the detection of causative vascular lesions in this clinical scenario.	55 patients were included in the study, with a mean age of 58.2 years (median, 58 years; range, 25–88 years). 28 patients were men (50.9%), and 27 were women (49.1%). The initial noninvasive examination was a CTA in 47 patients (85.5%) and an MRA in 8 patients (14.5%). 33 patients had diffuse SAH (60%); 11, perimesencephalic SAH (20%); and 11, peripheral sulcal SAH (20%). DSA demonstrated a causative vascular lesion in 6 patients (10.9%), 5 of whom had diffuse SAH (yield of 15.2%) and 1 of whom had peripheral sulcal SAH (yield of 9.1%). No causative vascular lesions were found in patients with perimesencephalic SAH.	3
93. McCormack RF, Hutson A. Can computed tomography angiography of the brain replace lumbar puncture in the evaluation of acute-onset headache after a negative noncontrast cranial computed tomography scan? <i>Acad Emerg Med.</i> 2010;17(4):444-451.	Review/Other-Dx	N/A	To review the recent literature for the prevalence of SAH in emergency department headache patients, the sensitivity of CT for diagnosing acute SAH, and the sensitivity and specificity of CTA for cerebral aneurysms.	SAH prevalence in emergency department headache patients was conservatively estimated at 15%. Representative studies reported CT sensitivity for SAH to be 91% (95% CI = 82% to 97%) and sensitivity of CTA for aneurysm to be 97.9% (95% CI = 88.9% to 99.9%). Based on these data, the posttest probability of excluding aneurysmal SAH after a negative CT/CTA was 99.43% (95% CI = 98.86% to 99.81%).	4
94. van Rooij WJ, Peluso JP, Sluzewski M, Beute GN. Additional value of 3D rotational angiography in angiographically negative aneurysmal subarachnoid hemorrhage: how negative is negative? <i>AJNR Am J Neuroradiol.</i> 2008;29(5):962-966.	Review/Other-Dx	23 patients	To assess the additional diagnostic value of 3D rotational angiography in detecting DSA-occult aneurysms in 23 patients with aneurysmal SAH.	In 18/23 patients (78%), a ruptured small aneurysm was diagnosed on additional 3D rotational angiography. The location of 18 aneurysms was the anterior communicating artery (n = 11), the MCA (n = 3), the posterior communicating artery (n = 2), the ophthalmic artery (n = 1), and the posterior inferior cerebellar artery (n = 1). Aneurysm size was 3 mm in 4, 2 mm in 9, and 1 mm in 5. Of 18 aneurysms, 9 were treated with coil placement; 7 with surgical clipping; and 2 were not treated.	4

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EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
95. Bakker NA, Groen RJ, Foumani M, et al. Repeat digital subtraction angiography after a negative baseline assessment in nonperimesencephalic subarachnoid hemorrhage: a pooled data meta-analysis. <i>J Neurosurg.</i> 2014;120(1):99-103.	Meta-analysis	8 studies; 368 patients	To evaluate the added value of repeat DSA in patients with initial angiographically negative diffuse nonperimesencephalic SAH.	An initial search of the literature yielded 179 studies, 8 of which met the selection criteria. Another 45 patients from the authors' institution were included in the study, providing 368 patients eligible for the pooled analysis. In 37 patients (10.0%, 95% CI, 7.4%–13.6%) an aneurysm was detected on repeat DSA. The timing of the repeat DSA varied from 1 to 6 weeks after the initial DSA. The use of 3D techniques was poorly described among these studies, and no direct comparisons between CTA and DSA were made.	M
96. Chen M. Detection of angiographically occult, ruptured cerebral aneurysms: case series and literature review. <i>J Neurointerv Surg.</i> 2014;6(10):744-747.	Review/Other-Dx	N/A	This case series and literature review illustrates the background and clinical features of ruptured thrombosed cerebral aneurysms.	Thrombosed ruptured cerebral aneurysms have several common anatomic and physiologic mechanisms for their occurrence. They may evade detection if not considered part of a diligent thorough approach that includes careful analysis of the pattern of initial bleeding on noncontrast head CT scan.	4
97. Delgado Almandoz JE, Jagadeesan BD, Refai D, et al. Diagnostic yield of computed tomography angiography and magnetic resonance angiography in patients with catheter angiography-negative subarachnoid hemorrhage. <i>J Neurosurg.</i> 2012;117(2):309-315.	Observational-Dx	77 patients	To determine the yield of CTA and MRA in a prospective cohort of patients with SAH and a negative initial catheter angiogram.	77 patients were included, with a mean age of 52.8 years (median 54 years, range 19–88 years). 50 patients were female (64.9%) and 27 male (35.1%). 43 patients had nonperimesencephalic SAH (55.8%), 29 patients had perimesencephalic SAH (37.7%), and 5 patients had cerebrospinal fluid xanthochromia (6.5%). CTA demonstrated a causative cerebral aneurysm in 4 patients (5.2% yield), all of whom had nonperimesencephalic SAH (9.3% yield). Mean aneurysm size was 2.6 mm (range 2.1–3.3 mm). MRA demonstrated only 1 of these aneurysms. No causative cerebral aneurysms were found in patients with perimesencephalic SAH or cerebrospinal fluid xanthochromia.	2

**Cerebrovascular Disease  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
98. Delgado Almandoz JE, Jagadeesan BD, Refai D, et al. Diagnostic yield of repeat catheter angiography in patients with catheter and computed tomography angiography negative subarachnoid hemorrhage. <i>Neurosurgery</i> . 2012;70(5):1135-1142.	Observational-Dx	72 patients	To determine the yield of repeat catheter angiography in a prospective cohort of patients with SAH and negative initial catheter and CT angiograms.	72 patients were included, with a mean age of 53.1 years (median, 53.5 years; range, 19–88 years). 46 patients were female (63.9%) and 26 male (36.1%). 39 patients had nonperimesencephalic SAH (54.2%), 29 patients had perimesencephalic SAH (40.3%), and 4 patients had cerebrospinal fluid xanthochromia (5.5%). The first repeat catheter angiogram performed 7 days after presentation demonstrated a causative vascular abnormality in 3 patients (yield of 4.2%), 2 of which had nonperimesencephalic SAH (yield of 5.1%), and 1 had perimesencephalic SAH (yield of 3.4%). The second repeat catheter angiogram performed in 43 patients (59.7%) did not demonstrate any causative vascular abnormalities. No causative abnormalities were found in patients with cerebrospinal fluid xanthochromia.	3
99. Lavoie P, Gariépy JL, Milot G, et al. Residual flow after cerebral aneurysm coil occlusion: diagnostic accuracy of MR angiography. <i>Stroke</i> . 2012;43(3):740-746.	Observational-Dx	167 aneurysm evaluations	To estimate the performance measures of MRA in the diagnosis of aneurysm residual flow after coil occlusion.	Class 3 residual flow was seen on DSA follow-up in 27%. The sensitivity and specificity of MRA was 88% (95% CI, 80–94) and 79% (95% CI, 67–88), respectively. The PPV for a Class 3 recurrence was 67% (95% CI, 51–80) and the NPV was 93% (95% CI, 86–97). TOF MRA underestimated the length of the residual flow ( $P=0.039$ ), whereas CE-MRA overestimated its width ( $P<0.0001$ ). MRA sensitivity for a Class 3 residual flow was lower for aneurysms $<6$ mm ( $P=0.01$ ).	2
100. Schaafsma JD, Koffijberg H, Buskens E, Velthuis BK, van der Graaf Y, Rinkel GJ. Cost-effectiveness of magnetic resonance angiography versus intra-arterial digital subtraction angiography to follow-up patients with coiled intracranial aneurysms. <i>Stroke</i> . 2010;41(8):1736-1742.	Review/Other-Dx	310 patients with 341 coiled intracranial aneurysms.	To follow-up patients with coiled intracranial aneurysms, MRA is a promising noninvasive alternative to current standard IA-DXA.	Follow-up with MRA yielded similar life expectancy (MRA, 26.66 years; IA-DXA, 26.63 years; difference, 0.03 years; 95% CI, -0.17–0.23) and quality-adjusted life year (MRA, 10.96; IA-DXA, 10.95; difference, 0.01 quality-adjusted life year; 95% CI, -0.05–0.08) at lower costs (MRA, \$7003; IA-DXA, \$8241 per patient; difference, -\$1238; 95% CI, -2617–36). The expected number of events was comparable except for complications from IA-DXA.	4

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
101. van Amerongen MJ, Boogaarts HD, de Vries J, et al. MRA versus DSA for follow-up of coiled intracranial aneurysms: a meta-analysis. <i>AJNR Am J Neuroradiol.</i> 2014;35(9):1655-1661.	Meta-analysis	51 articles	To perform a systematic review and meta-analysis to evaluate the accuracy of TOF-MRA and CE-MRA in detecting residual flow in the follow-up of coiled intracranial aneurysms.	This meta-analysis has revealed that MRA has a high diagnostic performance when it comes to the detection of residual flow in the follow-up of intracranial aneurysms treated with endovascular coil occlusion and therefore should be routinely used for follow-up. CE-MRA did not perform significantly better than TOF-MRA, indicating that follow-up with the latter should be adequate.	M
102. Kwee TC, Kwee RM. MR angiography in the follow-up of intracranial aneurysms treated with Guglielmi detachable coils: systematic review and meta-analysis. <i>Neuroradiology.</i> 2007;49(9):703-713.	Meta-analysis	16 studies	To systematically review published data on the diagnostic performance of MRA compared with DSA as reference standard in the follow-up of intracranial aneurysms treated with Guglielmi detachable coils.	The inclusion criteria were met by 16 studies. The studies had moderate methodological quality. Pooled sensitivity and specificity of nonenhanced TOF-MRA for the detection of residual flow (within the aneurysmal neck and/or coil mesh) were 83.3% (95% CI 70.3%–91.3%) and 90.6% (95% CI 80.4%–95.8%), respectively. Pooled sensitivity and specificity of CE-MRA for the detection of residual flow were 86.8% (95% CI 71.4%–94.5%) and 91.9% (95% CI 79.8%–97.0%), respectively. All pooled estimates were subject to heterogeneity. There were no statistically significant differences in pooled sensitivity and specificity between TOF-MRA and CE-MRA.	M
103. Attali J, Benaissa A, Soize S, Kadziolka K, Portefaix C, Pierot L. Follow-up of intracranial aneurysms treated by flow diverter: comparison of three-dimensional time-of-flight MR angiography (3D-TOF-MRA) and contrast-enhanced MR angiography (CE-MRA) sequences with digital subtraction angiography as the gold standard. <i>J Neurointerv Surg.</i> 2014.	Observational-Dx	22 patients	To compare the diagnostic accuracy of 3D-TOF-MRA and CE-MRA at 3 T for the evaluation of aneurysm occlusion and parent artery patency after flow diversion treatment, with DSA as the gold standard.	22 patients harboring 23 treated aneurysms were included. Interobserver agreement using simplified scales for occlusion (Montreal) and parent artery patency were higher for DSA (0.88 and 0.61) and CE-MRA (0.74 and 0.55) than for 3D-TOF-MRA (0.51 and 0.02). Intermodality agreement was higher for CE-MRA (0.88 and 0.32) than for 3D-TOF-MRA (0.59 and 0.11). CE-MRA yielded better accuracy than 3D-TOF-MRA for aneurysm remnant detection (sensitivity 83% vs 50%; specificity 100% vs 100%) and for the status of the parent artery (specificity 63% vs 32%; sensitivity 100% vs 100%).	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
104. Villablanca JP, Duckwiler GR, Jahan R, et al. Natural history of asymptomatic unruptured cerebral aneurysms evaluated at CT angiography: growth and rupture incidence and correlation with epidemiologic risk factors. <i>Radiology</i> . 2013;269(1):258-265.	Observational-Dx	165 patients	To characterize the relationship between aneurysm size and epidemiologic risk factors with growth and rupture by using CTA.	Patients (n = 165) with aneurysms (n = 258) had a mean follow-up time of 2.24 years from time of diagnosis. 46/258 (18%) aneurysms in 38 patients grew larger. Spontaneous rupture occurred in 4/228 (1.8%) intradural aneurysms of average size (6.2 mm). Risk of aneurysm rupture per patient-year was 2.4% (95% CI: 0.5%, 7.12%) with growth and 0.2% (95% CI: 0.006%, 1.22%) without growth (P=.034). There was a 12-fold higher risk of rupture for growing aneurysms (P<.002), with high intra- and interobserver correlation coefficients for size, volume, and growth. Tobacco smoking (3.806, 1 degree of freedom; P<.015,) and initial size (5.895, 2 degrees of freedom; P<.051) were independent covariates, predicting 78.4% of growing aneurysms.	4
105. Byrne G, Mut F, Cebra J. Quantifying the large-scale hemodynamics of intracranial aneurysms. <i>AJNR Am J Neuroradiol</i> . 2014;35(2):333-338.	Observational-Dx	210 patients	To objectively characterize these dynamics, classify them, and connect them to aneurysm rupture.	The quantitative classification was compared with a previous qualitative classification performed by visual inspection. Receiver operating characteristic curves provided area-under-the-curve estimates for spatial complexity (0.905) and temporal stability (0.85) to show that the 2 classifications were in agreement. Statistically significant differences were observed in the quantities describing the hemodynamics of ruptured and unruptured intracranial aneurysms. Specifically, ruptured aneurysms had more complex and more unstable flow patterns than unruptured aneurysms. Spatial complexity was more strongly associated with rupture than temporal stability.	3



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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
106. Bederson JB, Connolly ES, Jr., Batjer HH, et al. Guidelines for the management of aneurysmal subarachnoid hemorrhage: a statement for healthcare professionals from a special writing group of the Stroke Council, American Heart Association. <i>Stroke</i> . 2009;40(3):994-1025.	Review/Other-Tx	N/A	To summarize the best available evidence for treatment of patients with aneurysmal SAH and to identify areas of future research.	The current standard of practice calls for microsurgical clipping or endovascular coiling of the aneurysm neck whenever possible. Treatment morbidity is determined by numerous factors, including patient, aneurysm, and institutional factors. Favorable outcomes are more likely in institutions that treat high volumes of patients with SAH, in institutions that offer endovascular services, and in selected patients whose aneurysms are coiled rather than clipped. Optimal treatment requires availability of both experienced cerebrovascular surgeons and endovascular surgeons working in a collaborative effort to evaluate each case of SAH.	4
107. Marshall SA, Kathuria S, Nyquist P, Gandhi D. Noninvasive imaging techniques in the diagnosis and management of aneurysmal subarachnoid hemorrhage. <i>Neurosurg Clin N Am</i> . 2010;21(2):305-323.	Review/Other-Dx	N/A	A review of the literature regarding the use of noninvasive imaging studies to aid in the diagnosis of ruptured intracerebral arterial aneurysms and vasospasm, along with the current published data comparing the gold standard of DSA to these newer modalities.	The management of a SAH and vasospasm presents challenges to the neurosurgeon, neurointensivist, and interventional neuroradiologist. Newer and less invasive modalities for the diagnosis of a SAH and detection of vasospasm are being increasingly used. The current data support use of several of these new techniques in a subset of this population of patients, although DSA still retains its place as the gold standard.	4

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EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
<p>108. Lindegaard KF, Nornes H, Bakke SJ, Sorteberg W, Nakstad P. Cerebral vasospasm diagnosis by means of angiography and blood velocity measurements. <i>Acta Neurochir (Wien)</i>. 1989;100(1-2):12-24.</p>	<p>Observational-Dx</p>	<p>76 patients</p>	<p>To compare the results of angiography and noninvasive Doppler recordings of cerebral artery blood velocity in the diagnosis of cerebral vasospasm.</p>	<p>One radiologist and 1 neurovascular surgeon assessed angiographic spasm visually on a four-level scale. The radiologist's ratings were the term of reference for the study. When there was angiographic spasm of the MCA, the MCA blood velocity was higher and the blood velocity in the distal extracranial internal carotid artery was lower than when MCA spasm was scored as absent. Analysis by Kappa statistics, a measure for the agreement between 2 independent judges with correction for random coincidence, revealed moderate agreement between angiographic spasm and the absolute MCA blood velocity (Kappa = 0.47). However, there was substantial agreement (Kappa = 0.64) between angiographic spasm and the index calculated from dividing the blood velocity in the MCA by the blood velocity in the ipsilateral internal carotid artery. The results indicate that this velocity in the MCA/velocity in the ipsilateral internal carotid artery index gives more appropriate information on MCA spasm. Congenitally asymmetric circles of Willis with 1 wide dominant anterior cerebral artery showed normal blood velocities. In asymmetry induced by vasospasm, the diameter of the major anterior cerebral artery was normal or even reduced, and the blood velocity was significantly elevated. Hence, the agreement between blood velocity recordings and angiographic findings was substantial (Kappa = 0.64) when considering together the findings from both sides of the anterior circle of Willis.</p>	<p>3</p>

**Cerebrovascular Disease  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
109. Proust F, Callonec F, Clavier E, et al. Usefulness of transcranial color-coded sonography in the diagnosis of cerebral vasospasm. <i>Stroke</i> . 1999;30(5):1091-1098.	Observational-Dx	30 patients	To report a prospective comparative study between transcranial color-coded sonography, conventional TCD, and angiography in the diagnosis of cerebral vasospasm after surgical treatment for aneurysm.	The correlation between mean maximum velocity and angiographic diameter was significant for the MCA ( $r=-0.637$ , $P<0.0001$ ), ICA ( $r=-0.676$ , $P<0.0001$ ), and anterior cerebral artery ( $r=-0.425$ , $P<0.01$ ). Transcranial color-coded sonography sensitivity and specificity were higher than those for TCD for MCA (100% and 93%, respectively) and internal carotid artery (100% and 96.6%, respectively). For anterior cerebral artery, the sensitivity and specificity were 71.4% and 84.8%, respectively.	2
110. Swiat M, Weigele J, Hurst RW, et al. Middle cerebral artery vasospasm: transcranial color-coded duplex sonography versus conventional nonimaging transcranial Doppler sonography. <i>Crit Care Med</i> . 2009;37(3):963-968.	Observational-Dx	81 patients	To prospectively compare accuracies of transcranial color-coded duplex sonography and TCD in the diagnosis of MCA vasospasm.	Angiographic MCA narrowing $\leq 50\%$ was found in 21, and $>50\%$ in 10/135 arteries. Accuracy of transcranial color-coded sonography was insignificantly higher than that of TCD in the detection of $\leq 50\%$ and $>50\%$ narrowing, total Az for mean velocity being 0.83 +/- 0.05, 0.77 +/- 0.05, and 0.95 +/- 0.02, 0.86 +/- 0.08, respectively. Sensitivity of transcranial color-coded sonography at commonly used threshold of 120 cm/sec for less advanced MCA spasm was significantly better than that of TCD at similar specificity, 55% vs 39%, $P=0.038$ , whereas at a threshold of 200 cm/sec used for more advanced spasm, sensitivities and specificities of both methods were not different.	1
111. Ionita CC, Graffagnino C, Alexander MJ, Zaidat OO. The value of CT angiography and transcranial doppler sonography in triaging suspected cerebral vasospasm in SAH prior to endovascular therapy. <i>Neurocrit Care</i> . 2008;9(1):8-12.	Review/Other-Dx	55 patients	To evaluate the degree of agreement between TCD and CTA in diagnosing clinical cerebral vasospasm following SAH, and to define the role of CTA in triaging patients prior to DSA and endovascular intervention.	13 patients (24%) had clinical cerebral vasospasm and 42 patients (76%) were asymptomatic. All patients with clinical cerebral vasospasm had also radiological evidence of cerebral vasospasm (agreement 100%). In 35 patients without clinical cerebral vasospasm, both tests agreed for absence of cerebral vasospasm in 28 cases (agreement 83%). The remaining 7 asymptomatic patients had radiological cerebral vasospasm only, in disagreement with clinical absence of cerebral vasospasm (17%).	4

**Cerebrovascular Disease  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
112. Greenberg ED, Gold R, Reichman M, et al. Diagnostic accuracy of CT angiography and CT perfusion for cerebral vasospasm: a meta-analysis. <i>AJNR Am J Neuroradiol.</i> 2010;31(10):1853-1860.	Meta-analysis	9 studies	To perform a meta-analysis of the diagnostic performance of CTA and CTP for vasospasm in patients with aneurysmal SAH by using DSA as the criterion standard.	CTA and CTP searches yielded 505 and 214 manuscripts, respectively. 10 research studies met inclusion criteria for each CTA and CTP search. 6 CTA and 3 CTP studies had sufficient data for statistical analysis. CTA pooled estimates had 79.6% sensitivity (95% CI, 74.9%–83.8%), 93.1% specificity (95% CI, 91.7%–94.3%), 18.1 positive likelihood ratio (95% CI, 7.3–45.0), and 0.2 negative likelihood ratio (95% CI, 0.1-0.4); and CTP pooled estimates had 74.1% sensitivity (95% CI, 58.7%–86.2%), 93.0% specificity (95% CI, 79.6%–98.7%), 9.3 positive likelihood ratio (95% CI, 3.4–25.9), and 0.2 negative likelihood ratio (95% CI, 0.04–1.2). Overall diagnostic ORs were 124.5 (95% CI, 28.4–546.4) for CTA and 43.0 (95% CI, 6.5–287.1) for CTP. Area under the summary receiver operating characteristic analysis curve was 98 +/- 2.0% for CTA and 97 +/- 3.0% for CTP.	M
113. Delgado Almandoz JE, Yoo AJ, Stone MJ, et al. The spot sign score in primary intracerebral hemorrhage identifies patients at highest risk of in-hospital mortality and poor outcome among survivors. <i>Stroke.</i> 2010;41(1):54-60.	Observational-Dx	573 consecutive patients; 3 reviewers	Retrospective study to assess whether the spot sign score can be used to identify primary intracerebral hemorrhage patients who are at highest risk of in-hospital mortality and poor outcome among survivors at 3-month follow-up.	Spot signs identified in 133/573 CT angiograms (23.2%), 11 of which were delayed spot signs (8.3%). The presence of any spot sign increased the risk of in-hospital mortality (55.6%, OR 4.0, 95% CI, 2.6 to 5.9, $P<0.0001$ ) and poor outcome among survivors at 3-month follow-up (50.8%, OR 2.5, 95% CI, 1.4 to 4.3, $P<0.0014$ ). Spot sign score successfully predicted an escalating risk of both outcome measures. In multivariate analysis, the spot sign score was an independent predictor of in-hospital mortality (OR 1.5, 95% CI, 1.2 to 1.9, $P<0.0002$ ) and poor outcome among survivors at 3-month follow-up (OR 1.6, 95% CI, 1.1 to 2.1, $P<0.0065$ ). The spot sign score is an independent predictor of in-hospital mortality and poor outcome among survivors in primary intracerebral hemorrhage.	3

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EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
114. Wada R, Aviv RI, Fox AJ, et al. CT angiography "spot sign" predicts hematoma expansion in acute intracerebral hemorrhage. <i>Stroke</i> . 2007;38(4):1257-1262.	Observational-Dx	39 patients	To assess whether the CTA finding of tiny, enhancing foci (the "spot sign") within hematomas is associated with hematoma expansion and poor clinical outcomes.	13 patients (33%) demonstrated 31 enhancing foci. Baseline clinical variables were similar in both groups. Hematoma expansion occurred in 11 patients (28%) on follow-up. 77% of patients with and 4% without hematoma expansion demonstrated the spot sign ( $P<0.0001$ ). Sensitivity, specificity, PPV, NPV, and likelihood ratio for expansion were 91%, 89%, 77%, 96%, and 8.5, respectively. Interobserver agreement was high ( $\kappa=0.92$ to $0.94$ ). In patients with the spot sign, mean volume change was greater ( $P=0.008$ ), extravasation more common ( $P=0.0005$ ), and median hospital stay longer ( $P=0.04$ ), and fewer patients achieved a good outcome (modified Rankin Scale score $<2$ ), although the latter was not significant ( $P=0.16$ ). No differences in hydrocephalus ( $P=1.00$ ), surgical intervention ( $P=1.00$ ), or death ( $P=0.60$ ) were noted between groups. In multiple regression, the spot sign independently predicted hematoma expansion ( $P=0.0003$ ).	3
115. Lee C, Pennington MA, Kenney CM, 3rd. MR evaluation of developmental venous anomalies: medullary venous anatomy of venous angiomas. <i>AJNR Am J Neuroradiol</i> . 1996;17(1):61-70.	Review/Other-Dx	61 patients	To present characteristic MR findings of DVAs in terms of location of caput and draining veins, to correlate these findings with normal medullary venous anatomy, and to suggest an approach to the evaluation of DVAs by means of MRI.	72 DVAs with 78 draining veins were located: 18 were juxtacortical, 13 were subcortical, and 41 were periventricular or deep. 26 of the DVA caputs were frontal, 16 were parietal, 13 were in the brachium pontis/dentate, 7 were in the temporal lobe, 3 were in the cerebellar hemisphere, 3 were in the occipital lobe, 3 were in the basal ganglia, and 1 was in the pons. The draining veins were superficial in 29 cases and deep in 49. Of the 36 supratentorial deep draining veins, 16 were in the trigone/occipital horn, 11 were in the mid-body of the lateral ventricle, 7 were in the frontal horn, and 2 were in the temporal horn. Among the 14 infratentorial deep draining veins, 5 were in the lateral recess of the fourth ventricle, 4 were anterior transpontine veins, 3 were lateral transpontine veins, and 2 were precentral cerebellar veins.	4

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EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
116. Ruiz DS, Yilmaz H, Gailloud P. Cerebral developmental venous anomalies: current concepts. <i>Ann Neurol.</i> 2009;66(3):271-283.	Review/Other-Dx	N/A	To review current concepts on DVAs with the aim of helping clinicians understand this complex entity.	Cerebral DVAs are the most frequently encountered cerebral vascular malformation, and as such, are frequently reported as fortuitous findings in CT and MR) studies. DVAs are generally considered extreme anatomical variations of the cerebral vasculature, and follow a benign clinical course in the vast majority of cases.	4
117. Santucci GM, Leach JL, Ying J, Leach SD, Tomsick TA. Brain parenchymal signal abnormalities associated with developmental venous anomalies: detailed MR imaging assessment. <i>AJNR Am J Neuroradiol.</i> 2008;29(7):1317-1323.	Observational-Dx	164 patients	To evaluate the prevalence of brain parenchymal signal-intensity abnormalities subjacent to DVA, correlating with DVA morphology and location.	Of the 175 DVAs identified, 28 had associated signal-intensity abnormalities in the drainage territory. 7/28 DVAs with signal-intensity abnormalities were excluded because of significant adjacent white matter signal-intensity changes related to other pathology overlapping the drainage territory. Of the remaining DVAs imaged in this study, 21/168 (12.5%) had subjacent signal-intensity abnormalities. An adjusted prevalence rate of 9/115 (7.8%) was obtained by excluding patients with white matter disease more than minimal in degree. Periventricular location and older age were associated with DVA signal-intensity abnormality.	3
118. Campbell PG, Jabbour P, Yadla S, Awad IA. Emerging clinical imaging techniques for cerebral cavernous malformations: a systematic review. <i>Neurosurg Focus.</i> 2010;29(3):E6.	Review/Other-Dx	N/A	To provide a concise review of the emerging imaging methods used in the clinical diagnosis and treatment of cerebral cavernous malformations.	Prior to the advent of MRI, evaluation of cerebral cavernous malformations was limited to diagnostic angiography and CT. Currently, MRI is the best imaging method to evaluate cerebral cavernous malformations, with T2* gradient-echo sequences being described as the “gold standard.” As the use of more advanced imaging techniques continues to achieve widespread distribution, high-field MRI and SWI MRI are likely to become commonplace for the diagnosis and follow-up of these lesions. Additionally, applications such as diffusion tensor imaging and functional MRI may achieve more relevance as intraoperative navigational modalities for deep-seated lesions in eloquent areas.	4

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EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
119. Smith ER, Scott RM. Cavernous malformations. <i>Neurosurg Clin N Am.</i> 2010;21(3):483-490.	Review/Other-Dx	N/A	To discuss the epidemiology, natural history, diagnosis, treatment and follow-up of children who are found to harbor these lesions.	The management of children with cavernous malformations requires a clear understanding of the natural history of these lesions and the risks of surgical intervention. Presentation is usually hemorrhage, seizure, focal neurologic deficit, or headache. Diagnosis is best made with MRI. Patients with multiple lesions should be referred for genetic evaluation and counseling. Individuals with symptomatic, growing, or hemorrhagic malformations should be considered for surgical resection. Close follow-up after diagnosis and treatment is helpful to identify lesion progression or recurrence.	4
120. Thomas B, Somasundaram S, Thamburaj K, et al. Clinical applications of susceptibility weighted MR imaging of the brain - a pictorial review. <i>Neuroradiology.</i> 2008;50(2):105-116.	Review/Other-Dx	N/A	A pictorial review covering many clinical conditions illustrating its usefulness.	The phase images are useful in differentiating between diamagnetic and paramagnetic susceptibility effects of calcium and blood, respectively. This unique MR sequence will help in detecting occult low flow vascular lesions, calcification and cerebral microbleed in various pathologic conditions and aids in characterizing tumors and degenerative diseases of the brain. This sequence also can be used to visualize normal brain structures with conspicuity.	4
121. Jagadeesan BD, Delgado Almandoz JE, Moran CJ, Benzinger TL. Accuracy of susceptibility-weighted imaging for the detection of arteriovenous shunting in vascular malformations of the brain. <i>Stroke.</i> 2011;42(1):87-92.	Observational-Dx	60 patients	To determine the accuracy of SWI MRI for the detection of arteriovenous shunting in vascular malformations of the brain.	A total of 80 vascular malformations of the brain were identified in the 60 patients included in our study. Of the 29 vascular malformations of the brain with arteriovenous shunting on DSA, 14 were untreated AVM, 10 were previously treated AVM, and 5 were untreated DAVFs. Overall, SWI was 93% sensitive and 98% specific for the detection of arteriovenous shunting in vascular malformations of the brain, with excellent interobserver agreement (kappa=0.94). In the 14 previously treated AVM, SWI was 100% sensitive and specific for the detection of arteriovenous shunting. In the 28 vascular malformations of the brain associated with intracerebral hemorrhage, SWI was 100% sensitive and 96% specific for the detection of arteriovenous shunting.	3

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EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
122. Novakovic RL, Lazzaro MA, Castonguay AC, Zaidat OO. The diagnosis and management of brain arteriovenous malformations. <i>Neurol Clin.</i> 2013;31(3):749-763.	Review/Other-Dx	N/A	To discuss the pathophysiology, natural history, clinical presentations, and current treatment options, including multimodal approaches, for these vascular malformations.	Cerebral AVMs remain a considerable cause of morbidity and mortality and the expanded use of noninvasive brain imaging has led to an increase in identification of these lesions. Challenges remain in management decisions for asymptomatic AVMs, given the poorly defined natural history, and also in selecting optimal treatment in symptomatic AVMs, using single or multimodal therapy. Variations in practice exist due to limited available skill for therapies and lack of rigorous data. Advancements in technologies to treat AVMs and experience will continue to shape management, and continued support and development of randomized controlled trials to elucidate the natural history and compare available treatments is needed.	4
123. Pierot L, Cognard C, Spelle L. [Cerebral arteriovenous malformations: evaluation of the hemorrhagic risk and its morbidity]. <i>J Neuroradiol.</i> 2004;31(5):369-375.	Review/Other-Dx	N/A	To evaluate the hemorrhagic risk and its morbidity in patients.	Evaluation of the hemorrhagic risk associated with intracranial AVM is a keypoint question for physicians involved in the management of these patients. Indeed, this hemorrhagic risk including its morbid-mortality consequences has to be balanced with the therapeutic risk. All the published studies have estimated the annual bleeding risk between 2% to 4%; a first hemorrhagic event is associated with an increased risk of a new bleeding. Mortality associated with AVM bleeding is estimated between 10% to 15%, with a 50% risk of morbidity. Factors associated with an increased risk of bleeding include existence of aneurysms (intranidal or flow related pedicular, proximal or distal) and some venous drainage patterns such as deep venous drainage or venous stenosis.	4



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EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
124. Mossa-Basha M, Chen J, Gandhi D. Imaging of cerebral arteriovenous malformations and dural arteriovenous fistulas. <i>Neurosurg Clin N Am.</i> 2012;23(1):27-42.	Review/Other-Dx	N/A	To discuss the role of conventional as well as advanced imaging modalities that are providing novel ways to characterize these vascular malformations.	Imaging of cerebral AVMs and DAVFs is central to the diagnosis, proper characterization, and evaluation of these lesions. Imaging is helpful in pretreatment planning as well as post-treatment evaluation for residual arteriovenous shunting. DSA remains the gold standard for evaluation of AVM and DAVF, and cone-beam CT is providing improved 3D evaluation. CT and MRI applications are complementary, and provide useful information relating to the association of the vascular lesions to the surrounding intracranial structures as well as physiologic information, which cannot always be adequately evaluated with DSA. Significant improvement in imaging techniques has allowed progressive improvement in temporal and spatial resolution for MRA and CTA techniques, thereby allowing for improved noninvasive evaluation of time-dependent characteristics.	4
125. Mokin M, Dumont TM, Levy EI. Novel multimodality imaging techniques for diagnosis and evaluation of arteriovenous malformations. <i>Neurol Clin.</i> 2014;32(1):225-236.	Review/Other-Dx	N/A	To describe modern noninvasive approaches to diagnosing and evaluating AVMs, including dynamic 4D CT and MRA and perfusion imaging.	Modern noninvasive imaging approaches, such as dynamic 4D CT and MRA, allow excellent visualization of hemodynamic properties of AVMs, which previously could be achieved exclusively with catheter angiography. Whole-brain perfusion can help clinicians recognize certain pathologic phenomena associated with AVMs, such as arterial steal and venous congestion. DSA remains the gold standard for evaluating AVMs, and microcatheter injections provide critical information about each individual pedicle. Several classification systems exist to estimate risk associated with treatment of AVMs. Advances in invasive and noninvasive intraoperative imaging techniques now allow immediate detection of a residual AVM during surgical resection.	4

**Cerebrovascular Disease  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
126. Soize S, Bouquigny F, Kadziolka K, Portefaix C, Pierot L. Value of 4D MR angiography at 3T compared with DSA for the follow-up of treated brain arteriovenous malformation. <i>AJNR Am J Neuroradiol.</i> 2014;35(10):1903-1909.	Observational-Dx	37 patients	To evaluate its usefulness in the follow-up of treated brain AVM.	Between May 2008 and February 2013, 37 patients with a median age of 45 years (interquartile range = 26–55) were prospectively included. Examinations were acquired 36 months (interquartile range = 10–45.5) after the last treatment. Interobserver agreement for brain AVM patency was very good for both 4D MRA (kappa 0.82, 95% CI, .67–.98) and DSA (kappa 0.84, 95% CI, .69–.98). After consensus reading, intermodality agreement for the evaluation of brain AVM patency was good (kappa 0.73, 95% CI, .55–.90). Diagnostic accuracy of 4D MRA for residual brain AVM compared with DSA, reached a sensitivity of 73.7%, specificity 100%, PPV 100%, and NPV 78.3%. Agreements by technique of treatment are also detailed.	3
127. Jagadeesan BD, Delgado Almandoz JE, Benzinger TL, Moran CJ. Postcontrast susceptibility-weighted imaging: a novel technique for the detection of arteriovenous shunting in vascular malformations of the brain. <i>Stroke.</i> 2011;42(11):3127-3131.	Observational-Dx	16 consecutive patients	To determine the utility of postcontrast SWI MRI in the evaluation of vascular malformations of the brain.	A total of 17 vascular malformations of the brain were identified by DSA (9 newly diagnosed AVM, 3 DAVFs, 4 treated AVM with residual arteriovenous shunting, and 1 complex DVA). Postcontrast SWI MRI was 100% sensitive and 100% specific with 100% PPV and 100% NPV for the detection of arteriovenous shunting in these vascular malformations of the brain. The postcontrast SWI MRI signal intensity ratio in the most prominent early draining venous structure was 1.2+/-0.32.	2
128. Chang W, Loecher MW, Wu Y, et al. Hemodynamic changes in patients with arteriovenous malformations assessed using high-resolution 3D radial phase-contrast MR angiography. <i>AJNR Am J Neuroradiol.</i> 2012;33(8):1565-1572.	Observational-Dx	10 patients	To examine hemodynamic data from patients with stable symptoms and those who presented with acute symptoms to identify trends which may help in risk stratification.	Patients with an asymptomatic presentation or mild symptoms (n = 4) had no significant difference in wall shear stress in feeding vessels compared with normal contralateral vessels, whereas patients presenting with hemorrhage, severe headaches/seizures, or focal neurologic deficits (n = 6) had significantly higher wall shear stress in feeding vessels compared with contralateral vessels.	3

**Cerebrovascular Disease  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
129. Narvid J, Do HM, Blevins NH, Fischbein NJ. CT angiography as a screening tool for dural arteriovenous fistula in patients with pulsatile tinnitus: feasibility and test characteristics. <i>AJNR Am J Neuroradiol.</i> 2011;32(3):446-453.	Observational-Dx	7 patients	To determine the sensitivity and specificity of CTA compared with cerebral angiography for DAVF in patients presenting with pulsatile tinnitus.	The presence of arterial feeders showed good test characteristics for screening, with a sensitivity of 86% (95% CI, 42–99) and a specificity of 100% (95% CI, 52–100). A shaggy sinus or tentorium was highly specific: sensitivity of 42% (95% CI, 11–79) and specificity of 100% (95% CI, 56–100). The presence of transcalvarial venous channels demonstrated a poor sensitivity of 29% (95% CI, 5–70) but a high specificity 86% (95% CI, 42–99). CT attenuation of the jugular veins showed statistically significant asymmetry in the DAVF group vs the control group ( $P < .05$ ).	2
130. Alatakis S, Koulouris G, Stuckey S. CT-demonstrated transcalvarial channels diagnostic of dural arteriovenous fistula. <i>AJNR Am J Neuroradiol.</i> 2005;26(9):2393-2396.	Review/Other-Dx	1 patient	To present a case report in which a patient presenting for assessment of pulsatile tinnitus was diagnosed with a DAVF on the basis of the CT findings of resolving otomastoid fluid and the evolution of prominent transcalvarial channels.	Pulsatile tinnitus may be secondary to a large number of pathologic entities, including DAVF. CT is often the primary imaging technique used in the assessment of many cases of pulsatile tinnitus. The presence of transcalvarial channels is of diagnostic significance and may be detected on CT, indicating that further assessment with MRI and DSA is required.	4
131. Saposnik G, Barinagarrementeria F, Brown RD, Jr., et al. Diagnosis and management of cerebral venous thrombosis: a statement for healthcare professionals from the American Heart Association/American Stroke Association. <i>Stroke.</i> 2011;42(4):1158-1192.	Review/Other-Tx	N/A	To provide an overview of cerebral venous sinus thrombosis and to provide recommendations for its diagnosis, management, and treatment.	No results stated in abstract.	4

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EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
132. Ozsvath RR, Casey SO, Lustrin ES, Alberico RA, Hassankhani A, Patel M. Cerebral venography: comparison of CT and MR projection venography. <i>AJR Am J Roentgenol.</i> 1997;169(6):1699-1707.	Observational-Dx	24 patients	To show equivalence or superiority of CT venography compared with the existing test of choice—MR venography—in the evaluation of dural sinus thrombosis and in the identification of cerebral veins and dural sinuses.	Using MR venography, the 2 radiologists diagnosed dural sinus thrombosis in 8 of the 17 patients with suspected dural sinus thrombosis. In these 8 patients, the diagnosis was also made with CT venography. The diagnosis was confirmed by follow-up CT in 4 patients and by follow-up MRI in 2 patients. The maximum-intensity-projection algorithm did not allow direct visualization of thrombus by either the CT or the MRI technique; however, the CT integral display algorithm enabled direct visualization of thrombus on the 3D projection venograms. The systematic comparison of imaging techniques showed that CT venography reliably reveals all cerebral veins and sinuses when they are seen with MR venography. In addition, CT venography more frequently visualizes sinuses or smaller cerebral veins with low flow as compared with MR venography.	3
133. Gupta RK, Bapuraj JR, Khandelwal N, Khurana D. Prognostic indices for cerebral venous thrombosis on CT perfusion: a prospective study. <i>Eur J Radiol.</i> 2014;83(1):185-190.	Observational-Dx	20 patients	To determine the prognostic significance of PCT characteristics of patients with cerebral venous sinus thrombosis and assessed the change in perfusion parameters following anticoagulation therapy.	All patients in this study showed areas of hypoperfusion on CT perfusion. To determine the favorable clinical outcome on basis of perfusion parameters, receiver operating characteristic curve analysis was performed which showed that the optimal threshold for rCBF>60.5%, rCBV>75.5%, and r mean transit time <148.5% correlated with better clinical outcomes. Post treatment perfusion parameters showed significant correlation in core of the lesion ( $P<0.05$ ) than in the periphery.	3

**Cerebrovascular Disease  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
134. Amlie-Lefond C, Bernard TJ, Sebire G, et al. Predictors of cerebral arteriopathy in children with arterial ischemic stroke: results of the International Pediatric Stroke Study. <i>Circulation</i> . 2009;119(10):1417-1423.	Review/Other-Dx	676 subjects with childhood (nonneonatal) arterial ischemic stroke at 30 IPSS centers	To determine the prevalence and predictors of cerebral arteriopathy and focal cerebral arteriopathy among children with arterial ischemic stroke.	Between January 2003 and July 2007, 30 centers within the International Pediatric Stroke Study (IPSS) enrolled 667 children (age, 29 days to 19 years) with arterial ischemic stroke and abstracted clinical and radiographic data. Cerebral arteriopathy and its subtypes were defined using published definitions; focal cerebral arteriopathy was defined as cerebral arterial stenosis not attributed to specific diagnoses such as moyamoya, arterial dissection, vasculitis, or postvaricella angiopathy. We used multivariate logistic regression techniques to determine predictors of arteriopathy and focal cerebral arteriopathy among those subjects who received vascular imaging. Of 667 subjects, 525 had known vascular imaging results, and 53% of those (n=277) had an arteriopathy. The most common arteriopathies were focal cerebral arteriopathy (n=69, 25%), moyamoya (n=61, 22%), and arterial dissection (n=56, 20%). Predictors of arteriopathy include early school age (5 to 9 years), recent upper respiratory infections, and sickle cell disease, whereas prior cardiac disease and sepsis reduced the risk of arteriopathy. The only predictor of focal cerebral arteriopathy was recent upper respiratory infection.	4

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
135. Hajj-Ali RA, Calabrese LH. Diagnosis and classification of central nervous system vasculitis. <i>J Autoimmun.</i> 2014;48-49:149-152.	Review/Other-Dx	N/A	To review the diagnosis and classification of CNS vasculitis.	The diagnostic task for CNS vasculitis is challenging and should include a team of expert diagnosticians in many fields. The advancement in diagnostic modalities demystified many of the mimics of CNS vasculitis. Studies on the diagnostic and follow up roles of high-resolution MRI are such an example. However, a great need exists to expatiate on different aspects of CNS vasculitis such as epidemiologic properties, pathogenesis, diagnostic tools, and management strategies. Substantial work is currently underway, to assess biomarkers to aid in understanding the pathogenesis and to assist in the diagnosis. Multidisciplinary and multicenter collaboration are essential to face these challenges and achieve considerable progress in the coming years.	4

**Cerebrovascular Disease  
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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
136. Cupps TR, Moore PM, Fauci AS. Isolated angiitis of the central nervous system. Prospective diagnostic and therapeutic experience. <i>Am J Med.</i> 1983;74(1):97-105.	Review/Other-Dx	N/A	To report experience with the workup, clinical diagnosis, and successful induction of remission with cyclophosphamide and alternate-day prednisone therapy in 4 patients with isolated angiitis of the CNS.	Isolated angiitis of the CNS is an uncommon clinicopathologic entity characterized by vasculitis restricted to the vessels of the CNS without other apparent systemic vasculitis. Experience with the diagnosis, treatment, and follow-up evaluation in four patients with this disease is presented. Early manifestations of disease include severe headaches, altered mental function, and focal neurologic deficits. The pattern of progression from headaches and altered mental status to multifocal neurologic deficits is particularly suggestive of the diagnosis of vasculitis of the CNS. Systemic symptoms such as fever, myalgia, arthralgia, and arthritis, which occur frequently in other vasculitic syndromes, are generally not present in patients with isolated angiitis of the CNS. No single laboratory study can firmly establish or completely exclude the diagnosis; consequently, tissue diagnosis with biopsy of the brain parenchyma and leptomeninges may be required. In 2 patients, recurrent disease developed despite treatment with corticosteroids alone. Sustained clinical remission was induced in all 4 patients with a regimen of daily cyclophosphamide and alternate-day prednisone therapy. Cyclophosphamide and alternate-day prednisone therapy are considered the treatment of choice in severe, progressive, or corticosteroid-resistant isolated angiitis of the CNS.	4

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EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
137. Salvarani C, Brown RD, Jr., Calamia KT, et al. Primary central nervous system vasculitis: analysis of 101 patients. <i>Ann Neurol.</i> 2007;62(5):442-451.	Review/Other-Dx	101 patients	To analyze the clinical findings, response to therapy, outcome, and incidence of primary CNS vasculitis in a large cohort from a single center.	70 patients were diagnosed by angiography and 31 by CNS biopsy. Three histological patterns were observed during biopsy. Although most patients responded to therapy, an increased mortality rate was observed. Relapses occurred in one-fourth of patients. Mortality rate and disability at last follow-up were greater in those who presented with a focal neurological deficit, cognitive impairment, cerebral infarctions, and angiographic large-vessel involvement but were lower in those with prominent gadolinium-enhanced lesions when evaluated by MRI. The annual incidence rate of primary CNS vasculitis was 2.4 cases per 1,000,000 person-years.	4
138. Jennette JC, Falk RJ, Bacon PA, et al. 2012 revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides. <i>Arthritis Rheum.</i> 2013;65(1):1-11.	Review/Other-Dx	N/A	To report the CHCC2012 revised nomenclature for vasculitides.	Disease names and definitions evolve over time as medical knowledge and understanding advance, which is why CHCC2012 is being proposed to replace CHCC1994. The goals are to make this nomenclature system more relevant and more valuable by including additional categories of vasculitis, and by adjusting names and definitions based on current trends in usage and on advances in the understanding of disease manifestations and mechanisms.	4



**Cerebrovascular Disease  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
139. Appenzeller S, Faria AV, Zanardi VA, Fernandes SR, Costallat LT, Cendes F. Vascular involvement of the central nervous system and systemic diseases: etiologies and MRI findings. <i>Rheumatol Int.</i> 2008;28(12):1229-1237.	Review/Other-Dx	24 patients	To review MRI findings in patients with vascular involvement of the CNS associated with systemic diseases.	24 patients (17 women and 7 men), with mean age of 29.5 years had diagnosis of CNS vasculitis and were included. The clinical presentation was variable, but the most common complaints were headache in 18, focal deficits in 9, disturbances of consciousness in 9, and seizures in 8 patients. Underlying causes for CNS vasculitis were identified in all patients and included systemic lupus erythematosus in 8, tuberculosis in 3, bacterial meningitis in 3, Takayasu arteritis in 2, polyarteritis nodosa in 2, syphilis in 2, drug abuse in 2, yellow fever in 1 and varicella in 1 patient. Nonspecific high intensity T2WI/FLAIR lesions in white matter were the most common finding, present in ten patients. Eight patients had infarctions in large cerebral arteries territory, associated or not with high intensity T2WI/FLAIR small foci. Vascular involvement of the CNS can be found in a great variety of systemic diseases, including rheumatologic, infectious and drug abuse. Clinical findings are unspecific and MRI/MRA may help to establish the correct diagnosis.	4
140. Bekiesinska-Figatowska M. T2-hyperintense foci on brain MR imaging. <i>Med Sci Monit.</i> 2004;10 Suppl 3:80-87.	Observational-Dx	246 patients	To analyze cerebral MRI results in patients.	The following diagnoses were established: widened perivascular spaces in 11 cases, foci most probably associated with brain aging - 21, with migraine -15, ischemic changes -52, vasculitis -12, hypoxic-ischemic changes -8, hemorrhagic foci -11, inflammatory changes - 20, multiple sclerosis -50, central pontine and extrapontine myelinolysis -7, metastases -7, changes caused by radio-and chemotherapy - 8, lesions associated with neurometabolic diseases - 10, CNS degenerative diseases - 13, eclampsia - 1.	3

**Cerebrovascular Disease  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
141. Swartz RH, Bhuta SS, Farb RI, et al. Intracranial arterial wall imaging using high-resolution 3-tesla contrast-enhanced MRI. <i>Neurology</i> . 2009;72(7):627-634.	Review/Other-Dx	37 patients	To review intracranial arterial wall imaging using high-resolution 3T CE-MRI.	Multiplanar T2-weighted fast spin echo and multiplanar T1 FLAIR precontrast and postcontrast images were acquired in 37 patients with focal neurologic deficits. Clinical diagnoses included atherosclerotic disease (13), CNS inflammatory disease (3), dissections (3), aneurysms (3), moyamoya syndrome (2), cavernous angioma (1), extracranial source of stroke (5), and no definitive clinical diagnosis (7). 12 of 13 with atherosclerotic disease had focal, eccentric vessel wall enhancement, 10 of whom had enhancement only in the vessel supplying the area of ischemic injury. Two of 3 with inflammatory diseases had diffuse, concentric vessel wall enhancement. Three of 3 with dissection showed bright signal on T1, and 2 had irregular wall enhancement with a flap and dual lumen.	4
142. von Morze C, Purcell DD, Banerjee S, et al. High-resolution intracranial MRA at 7T using autocalibrating parallel imaging: initial experience in vascular disease patients. <i>Magn Reson Imaging</i> . 2008;26(10):1329-1333.	Review/Other-Dx	10 patients	To apply parallel imaging to 7T TOF MRA studies of normal volunteers and patients with vascular disease, in order to obtain very high resolution (0.12 mm(3)) images within a reasonable scan time.	The technique produced high resolution studies free from discernible reconstruction artifacts in all subjects and provided excellent depiction of vascular pathology in patients.	4

**Cerebrovascular Disease  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
143. Greenan TJ, Grossman RI, Goldberg HI. Cerebral vasculitis: MR imaging and angiographic correlation. <i>Radiology</i> . 1992;182(1):65-72.	Review/Other-Dx	7 patients	To review MRI and angiographic correlation.	Cerebral vasculitis is an unusual disorder with numerous causes. One such entity, noninfectious granulomatous angiitis of the nervous system, is an extremely rare disease with a predilection for leptomeningeal and parenchymal arteries and veins. Isolated involvement of the CNS is characteristic of granulomatous angiitis of the nervous system, which has also been referred to as primary angiitis of the CNS. The results of MRI and angiography in 7 patients with presumed primary angiitis of the CNS were retrospectively analyzed and correlated. MRIs were positive in every case. Characteristically, lesions were multiple, bilateral, and supratentorial. Both gray- and white-matter infarcts were identified in four of seven patients; infarcts were most common in the deep white matter. Primary angiitis of the CNS can also appear as primary parenchymal hemorrhage or simulate low-grade glioma. All lesions identified on MRIs were associated with positive angiographic findings of cerebral vasculitis in the corresponding vascular distribution. However, for 12/33 vascular distributions with angiographic evidence of cerebral vasculitis, no lesions were identified on MRIs. These correlative observations suggest that some patients with proved primary angiitis of the CNS may have normal MRI results.	4

**Cerebrovascular Disease  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
144. Calabrese LH, Furlan AJ, Gragg LA, Ropos TJ. Primary angiitis of the central nervous system: diagnostic criteria and clinical approach. <i>Cleve Clin J Med.</i> 1992;59(3):293-306.	Review/Other-Dx	N/A	To propose a revised set of diagnostic criteria and a practical approach to treatment.	Primary angiitis of the CNS has until recently been considered rare, usually progressive, and untreatable. In 1987, preliminary diagnostic criteria for the disorder were proposed in the hope of gaining a more accurate description of the disease. These criteria were used in reviewing all cases reported in the English language (99 cases) and those seen at The Cleveland Clinic Foundation (9 cases). The disorder is heterogeneous, and has a better prognosis than previously thought. Furthermore, a relatively benign subset of this disorder, termed “benign angiopathy of the CNS,” can be defined on clinical grounds.	4
145. Vollmer TL, Guarnaccia J, Harrington W, Pacia SV, Petroff OA. Idiopathic granulomatous angiitis of the central nervous system. Diagnostic challenges. <i>Arch Neurol.</i> 1993;50(9):925-930.	Review/Other-Dx	39 cases	To determine the frequency of strokes (eg, sudden onset of focal symptoms) as a presenting complication and to determine the sensitivity of angiography and other technologies in detecting vasculitis in histologically proved cases of idiopathic granulomatous angiitis of the CNS, by reviewing the published literature.	Analysis of these cases shows that strokes as presenting complications are rare in idiopathic granulomatous angiitis of the CNS. Most patients present with a diffuse encephalopathy and, when focal symptoms develop, they tend to develop gradually. Including our case, 56% of 41 angiograms performed in 31 reported patients with histologically proved idiopathic granulomatous angiitis of the CNS were abnormal, but only 27% were diagnostic for vasculitis.	4
146. Yuh WT, Ueda T, Maley JE. Perfusion and diffusion imaging: a potential tool for improved diagnosis of CNS vasculitis. <i>AJNR Am J Neuroradiol.</i> 1999;20(1):87-89.	Review/Other-Dx	N/A	To review perfusion and diffusion imaging as a diagnosis of CNS vasculitis.	No results stated in abstract.	4

## Evidence Table Key

### Study Quality Category Definitions

- *Category 1* The study is well-designed and accounts for common biases.
- *Category 2* The study is moderately well-designed and accounts for most common biases.
- *Category 3* There are important study design limitations.
- *Category 4* The study is not useful as primary evidence. The article may not be a clinical study or the study design is invalid, or conclusions are based on expert consensus. For example:
  - a) the study does not meet the criteria for or is not a hypothesis-based clinical study (e.g., a book chapter or case report or case series description);
  - b) the study may synthesize and draw conclusions about several studies such as a literature review article or book chapter but is not primary evidence;
  - c) the study is an expert opinion or consensus document.
- M = Meta-analysis

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Dx = Diagnostic

Tx = Treatment

## Abbreviations Key

3D-TOF = 3D time-of-flight  
ASL = Arterial spin labeling  
AVM = Arteriovenous malformations  
CBF = Cerebral blood flow  
CBV = Cerebral blood volume  
CEA = Carotid endarterectomy  
CE-MRA = Contrast-enhanced magnetic resonance angiography  
CI = Confidence interval  
CNS = Central nervous system  
CT = Computed tomography  
CTA = Computed tomography angiography  
CVR = Cerebrovascular reserve  
DAVF = Dural arteriovenous fistula  
DSA = Digital subtraction angiography  
DVAs = Developmental venous anomalies  
DWI = Diffusion-weighted imaging  
FLAIR = Fluid-attenuated inversion-recovery  
HR = Hazard ratio  
IA-DSA = Intra-arterial digital subtraction angiography  
IV = Intravenous  
MCA = Middle cerebral artery  
MRA = Magnetic resonance angiography  
MRI = Magnetic resonance imaging  
NPV = Negative predictive value  
OR = Odds ratio  
PCT = Perfusion computed tomography  
PET = Positron emission tomography  
PPV = Positive predictive value  
PWI = Perfusion-weighted imaging  
SAH = Subarachnoid hemorrhage  
SD = Standard deviation  
SWI = Susceptibility-weighted imaging  
TCD = Transcranial Doppler  
TIA = Transient ischemic attack  
t-PA = Tissue-type plasminogen activator  
US = Ultrasound