



Landmark papers in cerebrovascular neurosurgery 2015



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ABSTRACT

The management of cerebrovascular disease has advanced considerably in 2015. Five randomized control trials have firmly established the role of endovascular thrombectomy for ischemic strokes due to large vessel occlusion. The randomized trial of intraarterial treatment for acute ischemic stroke (MR CLEAN) (Berkhemer et al. NEJM 2015;372:11–20) was the first of a series on the topic. There was a total of 5 randomized controlled trials published showing benefit in terms of functional outcomes at 90 days for mechanical thrombectomy including the Endovascular Therapy for Ischemic stroke with perfusion-imaging selection (EXTEND IA) (Campbell et al. NEJM 2015;372:1009–18), the Randomized assessment of rapid endovascular treatment of ischemic stroke (ESCAPE) (Goyal et al. NEJM 2015;372:1019–30) trials, the stent-retriever thrombectomy after IV t-PA is t-PA alone in stroke (SWIFT-PRIME) (Saver et al. NEJM 2015;372:2285–95), and the thrombectomy within 8 h after symptom onset in Ischemic stroke (REVASCAT) trial (Jovin et al. NEJM 2015; 372:2296–306). Six-year results from randomized controlled Barrow Ruptured Aneurysm Trial (BRAT) found no significant difference in functional outcomes in patients ruptured aneurysms treated surgically clippings versus endovascular treatment (Spetzler et al. JNS 2015;123:609–17. The 10-year results of the International Subarachnoid Aneurysm trial (ISAT) reported similar mortality rates and good functional outcomes between clipped and coiled patients (Molyneux et al. Lancet 2015;385:691–7). We also discuss the impact of genome wide sequencing studies in familial aneurysms, the largest publication on stent assisted coiling and flow diverter for aneurysms and noteworthy papers relevant to Moyamoya and cavernous malformations (Yang et al. Neurosurgery 2015;77:241–7).

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1. Introduction

A plethora of high quality papers were published in cerebrovascular neurosurgery in 2015. Most spectacularly, five randomized controlled trials comparing endovascular thrombectomy for acute ischemic stroke due to large vessel occlusion to standard treatment were published (MR CLEAN, EXTEND IA, ESCAPE, SWIFT-PRIME, and REVASCAT) [1–5]. The 10-year follow up results of the International Subarachnoid Aneurysm Trial (ISAT) and 6-year results of the Barrow Ruptured Aneurysm Trial (BRAT) were also published. We also highlight several other important studies relevant to cerebrovascular neurosurgery published this year, particularly those looking at safety and efficacy of flow diverters for treatment of cerebral aneurysms.

2. Methods

We searched, human, English language publications, in MEDLINE (PubMed and Ovid), EMBASE, CINAHL, Google Scholar, and the Cochrane Library from January 1st 2015 to December 31st, 2015. We used, in various relevant combinations, keywords and MeSH terms pertinent to the area of interest: clinical trial, cerebrovascular, stroke, cavernous malformation, cavernoma, Moyamoya, aneurysm, unruptured, rupture, endovascular, flow diverter, microsurgical clipping, arteriovenous malformation, anti-platelet therapy, arteriovenous fistula, ischemia, stroke, cerebrovascular accident, and infarct. Identified articles were then selected based on a combination; of study type (high quality clinical trials were preferentially selected), number of patients, impact factor of the journal, clinical impact on field (as determined by the senior authors; JMM, CJG, AJT, CSO; all qualified neurosurgeons).

3. Results

Search term results included 337 articles relating to ‘clinical trials’ in the ‘cerebrovascular’ field. Various combination of ‘aneurysm’ with other search terms yielded 330 relevant articles. Search terms relating to ‘endovascular clinical trials’ in the management of ‘stroke’ yielded 123 articles. Searching for ‘cerebrovascular cavernous malformation’ yielded 17 articles. ‘Cerebrovascular moyamoya’ yielded 89 articles. AVM and AVF searches yielded 132 articles. The abstracts of all identified articles were then reviewed and a short list of articles to feature in this paper was then produced as outlined in the methods section. In total 17 articles relating to aneurysm, 1 article relating to anti-platelet agents, 4 articles relating to AVM management, 1 article relating to CCF treatment, 1 article to moyamoya management, 6 articles relating to mechanical thrombectomy for stroke and 2 articles relating to cavernous malformations were included in the final manuscript.

3.1. Cerebral aneurysms

3.1.1. Genetic risk factors for cerebral aneurysms

Genome wide association studies have focused on the role of common variants associated with cerebral aneurysms. Whereas common variants individually may have a small effect on aneurysm risk, high-throughput sequencing enables the identification of rare variants with large effects on aneurysm risk. Members of 7 families of European American descent with the highest density of aneurysms were recruited as part of the International Familial Intracranial Aneurysm Study underwent whole exome sequencing (WES) identifying 68 variants in 68 genes of which 5 variants were found in 2 families. RNA expression in aneurysmal tissue and control cerebrovascular tissue was analyzed in patients independent of the families included in the WES. Of the 68 genes identified using WES, 1 gene (TMEM132B) was differentially expressed in aneurysms versus control tissue. TMEM132B encodes transmembrane protein 132B, a protein of unknown function. Further studies will be necessary to validate and characterize the variants identified [6].

3.1.2. Endovascular treatment of cerebral aneurysms

A number of important articles pertinent to the endovascular management of cerebral aneurysms were published in 2015. In one of the largest series to date, safety and efficacy of primary coil embolization was compared to stent-assisted coiling in 563 aneurysms. Rates of thromboembolic and hemorrhagic complications did not differ between primary coiling and stent-assisted coiling [7]. Thromboembolic complications in patients that underwent stent assisted coiling of ruptured and unruptured aneurysms was 8.6% and 3.8%, respectively. Recanalization was significantly higher in patients that underwent primary coiling at a rate of 17.8% and 15.2% for ruptured and unruptured aneurysms, respectively. The issue of recanalization and subsequent need for re-treatment after endovascular treatment of aneurysm prompted the development of the Aneurysm Recanalization Stratification Scale [8]. The scale incorporates aneurysm-related and treatment-related features predicting the risk for retreatment and was validated in 1543 patients from 5 large neurovascular centers in the United States and Canada [9]. Aneurysm size of greater than 10 mm (+2 points), rupture (+2 points), intraaneurysmal thrombus (+2 points), and incomplete embolization (+1 point for Raymond Roy 2 and +2 for Raymond Roy 3) at initial treatment increased the risk for retreatment. Stent-assisted coiling (-1 point), and to an even greater degree flow diversion using the Pipeline Embolization Device (PED, Covidien – Ev3, Plymouth, MN) (-2 points), decreased the risk (points subtracted). Whereas the probability of retreatment for a score of -2 was 4.9%, a score of 7 was found to require treatment in 100% of patients.

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