EDITORIAL

Safety and efficacy of flow-diverter stents in endovascular treatment of intracranial aneurysm: Interest of the prospective DIVERSION observational study

Endovascular treatment using detachable coils is now a well-established technique for intracranial aneurysms (IA) occlusion following the publication of the results of the International Subarachnoid Aneurysm Trial (ISAT) [1]. However, the treatment of large or giant IA remains challenging with low initial angiographic occlusion rates [2] and high rates of recanalization [2–4].

In this situation, the flow-diverter stents (FDS) appeared recently as an alternative therapeutic option [5]. The concept of these stents is to divert the blood flow allowing progressive aneurysm thrombosis. These devices are deployed in an increasing number of patients. Efficacy of FDS in IA occlusion is high. Szikora et al. reported a complete occlusion and a partial filling at 6 months in 17 and 1 out of 18 patients, respectively [6]. In the series of Lubicz et al., angiographic follow-up at 6 months showed 20 complete occlusions out of 29 aneurysms (69%), 1 neck remnant (3.5%), and 8 incomplete occlusions (27.5%) [7]. In a recent meta-analysis of 29 studies including 1451 patients with 1654 aneurysms, the rate of complete occlusion was 76% at 6 months [8].

However, the safety of FDS remains a crucial concern. The safety results of FDS vary widely across reported studies. In the first Argentine series of 53 patients, no stroke or death were encountered, and 3 patients (5%) experienced transient exacerbations of preexisting cranial neuropathies [9]. In other reports, morbidity and mortality rates after treatment with FDS were found to be high [6,10–16]. In the series of Szikora et al. dealing with 18 patients, one patient died due to rupture of a coexisting aneurysm, one patient experienced abrupt in-stent thrombosis resulting in a transient neuropsychic deficit, and one patient presented visual deficit due to ophthalmic artery occlusion [6]. The same year, Lubicz et al. reported mortality and morbidity rates of 4% (1 out of 26 patients) and 15% (4 patients), respectively [7]. Results from the recent meta-analysis found procedure-related morbidity and mortality of 5% and 4%, respectively [8].

Recently, a major concern was highlighted with delayed aneurysm rupture. In the largest published series of this occurrence, Kulkar et al. reported 13 cases of delayed post-procedural aneurysm rupture [17]. Ten patients developed early aneurysm rupture (mean, 16 days; range, 2–48 days), and 3 delayed ruptures (3–5 months). To date, the mechanism of this event is not well elucidated, but secondary inflammation following intra-aneurysmal thrombus seems to play a key role [18,19]. In addition, delayed ipsilateral intraparenchymal hemorrhage following the technically successful treatment of anterior circulation aneurysms with FDS were also reported [20,21]. Cruz et al. reported 4 cases (8.5%) after the treatment of 47 anterior circulation aneurysms without intraprocedural complication [20].

The DIVERSION study

In this context, the French Society of Neuroradiology in collaboration with the French National regulatory Agency for the Safety of Medicines and Health Products (Agence nationale de sécurité du médicament et des produits de santé – ANSM) have set up in 2012 the DIVERSION study, a prospective, consecutive, observational study conducted in 34 French centers (Table 1). The aim of this study was to evaluate the feasibility, safety and efficacy of FDS for the endovascular treatment of IA at 12 months, as well as prognostic factors for complications.

The study was started in October 8, 2012. Originally planned to include all patients treated with FDS over a one-year period, the inclusion period has recently been extended for an extra year.

The main criteria for inclusion are use of a FDS with or without additional embolic materials, for the treatment of adult patients presenting unruptured or ruptured IA. Patients’ care and follow-up is performed according to the usual practice of each participating center. Especially,
Table 1 Principal investigator sites.

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Description of procedures included during the first year of DIVERSION

During the first 12 months of the study, 283 procedures with FDS were reported by 19 (56%) centers. To date, the data have been completed for 235 of these procedures, corresponding to 272 aneurysms (222 with intradural location and 50 extradural) treated with 321 FDS.

One hundred and seventy-two aneurysms (63%) were treated with the Pipeline Embolization Device ([PED], EV3, Irvine, CA), 77 (28%) with the Silk device (Balt, Montmorency, France), 16 (6%) with the FRED device (Microvention, Tustin, CA), and 7 (3%) with the Surpass device (Stryker Neurovascular, Fremont, CA).

Conclusion

Although safety and efficacy of FDS were reported in small single center-series, there is a current need for more precise information. The absence of randomized controlled trial assessing FDS did not diminish the interest of clinicians, and these devices are increasingly used based on a high efficacy and the possibility to treat large aneurysms with satisfactory results.

In 2010, the occurrence of serious adverse events has led the French and other National Regulatory Agencies to closely follow-up FDS use. There is an obligation for clinicians to systematically report incidents related to medical devices use to the authorities within the vigilance system. However, vigilance remains a small aspect of the post-marketing surveillance process [23]. Post-marketing observational studies are of interest for assessing the safety and efficacy in real practice, and complete device-related data [24], and their number has grown considerably, despite methodological issues.

The DIVERSION study is a large national multicenter and consecutive study designed to guaranty high quality for data collection. Its results should provide better evidence about the current issues concerning FDS. However, safety evaluation relies on several factors including the patient characteristics, the underlying pathology, the aneurysm characteristics and the intervention performed (number and type of FDS, use of coils, etc.). These data will be collected within the DIVERSION study, and complications will be analyzed taking into account these factors.

To answer a more specific issue of whether FDS, compared to usual techniques, improve the safety and efficacy of IA endovascular management, a randomized, prospective, clinical trial has been set up by the hospices civils de Lyon to compare FDS to conventional strategies in patients presenting wide-necked saccular intradural unruptured aneurysms (the EVIDENCE study, NCT01811134).

Disclosure of interest

Benjamin Gory, François Chapuis, Saadia Embarek and Laure Huot declare they have no conflicts of interests concerning this article.

Francis Turjman is consultant for Balt, Covidien, and Codman.
Alain Bonafé is consultant for Covidien, Stryker Neurovascular and Codman.
Laurent Pierot is consultant for Balt, Stryker Neurovascular, Covidien and Microvention.
Laurent Spelle is consultant for Stryker Neurovascular, Covidien and Sequent Medical.
Jérôme Berge is consultant for Penumbra.
Zsolt Kulcsár acts as proctor for companies Balt International, Microvention and Penumbra.
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References


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Available online 31 March 2014