

Research Article

Coiling Techniques in management of Cerebral Aneurysms Preoperative assessment, Outcome and Complications

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Abstract

Background: according to the International Subarachnoid Trial (ISAT), patients with subarachnoid hemorrhage (SAH) fared better with endovascular coiling than those with surgical clipping (Molyneux et al., 2005). With the emergence of flow diversion as a useful technique in management of cerebral aneurysm, endovascular techniques now have many varieties that enable the interventionalist to achieve best outcome. **Objective:** This study aimed to compare the outcome and complications between balloon assisted coiling and the use of Flow diverter stent, also studying the theoretical effect of antiplatelet use in flow diverter group and whether there is an added risk for development of bleeding. **Patients and Methods:** Thirty two patients were included in this study between February/2016 and June/2017. Age range was 25-69 (54± 10.5) for balloon group (Group B =17), 30-68 years old (50.7±10.1) for the Flow diverter group (Group F=15). The females were 10 (58%) in the balloon group and 6 (40%) in the Flow diverter group. No statistically significant difference was found between two groups. Those patient were found to have wide neck aneurysm by either CT cerebral angiography of 4 vessel angiography. Patient undergo preoperative assessment using NIHSS stroke scale, modified Rankin scale, Hunt and Hess scale and modified fisher scale. Post-operative assessment included, modified Rankin scale for clinical outcome and Raymond Roy scale for the degree of obliteration of aneurysm. Follow up study was done after 6 month of the procedure including the same sale to detect the clinical improvement as well as recanalization rate. **Results:** Regarding follow up assessment in clinical outcome, significant improvement occurred in both groups with minimal or no symptoms in 15 out of 17 (88.23%) in the balloon group and 14 out of 15 (93%) in the flow diverter group. Findings show that total obliteration was achieved immediately in most of cases (11 out of 17 in the balloon group, 13 out of 15 in the Flow diverter group). No significant difference between angiographic outcome of immediate and follow up imaging in the case of flow diverter. There is a significant difference between the immediate and follow up score of the balloon group but eventually most of the cases achieve complete obliteration (15 out of 17). Regarding complications, the operation went uneventful for more than 2 thirds of cases in each group. Although thrombotic complication is higher in Flow diverter group (20% for FD Vs 11.8% for B), manifest infarction is paradoxically higher in Balloon group (6.7% for FD Vs 17.6% for B). Hemorrhagic event occurred only once in balloon group (5.9%). For correlation, clinical outcome correlates with radiological outcome (P=0.007 significant level is P<0.001). **Conclusion:** both techniques are safe and effective in management of wide neck cerebral aneurysm with no significant difference between both techniques. Selection of either method is upon the experience of the interventional neurologist's experience and preference.

Key words: Neurointerventional management of cerebral aneurysms , wide-neck cerebral aneurysm, Balloon assisted coiling, Flow diverter stent

Introduction

Microsurgical clipping of intracranial aneurysms has been the historical definitive standard for the treatment of intracranial aneurysms (Le Roux Peter D., 2004). Today's surgical techniques routinely achieve complete exclusion of the aneurysm from the circulation

without compromise of the parent vessel or arterial perforators in a large number of patients. However, there are several risk factors

that may put the patient at increased risk of morbidity and mortality, including aneurysm size and location, patient's age, and the medical

condition of the patient (Wiebers et al., 2003). To overcome some of the limitations of surgical clipping, endovascular treatments have been developed, which have grown considerably in number over the last three decades since the US Food and Drug Administration (FDA) approval of the Guglielmi detachable coil (GDC) in 1995 (Eskridge and Song, 1998).

Both techniques have advantages and disadvantages with the less invasive merit in the side of interventional management. In addition, according to the International Subarachnoid Trial (ISAT), patients with subarachnoid hemorrhage (SAH) fared better with endovascular coiling than those with surgical clipping (Molyneux et al., 2005). With the emergence of flow diversion as a useful technique in management of cerebral aneurysm, endovascular techniques now have many varieties that enable the interventionalist to achieve best outcome. As they are called now you have both deconstructive and reconstructive techniques (Gemmete et al., 2013).

Aim of the work

This study aimed to compare the outcome and complications between two common techniques used to treat wide neck aneurysms, which are balloon assisted coiling and the use of Flow diverter stent, also studying the theoretical effect of antiplatelet use in flow diverter group and whether there is an added risk for development of bleeding.

Material and Method

Thirty-two patients included in this study 16 male patients and 16 female patients' age ranges from 20 years old to 69 years old.

Those where patients admitted to department of Neurology in Matariya teaching hospital, Nasr city insurance hospital and Ain shams university hospitals with a diagnosis of symptomatic cerebral aneurysm mainly subarachnoid hemorrhage. All admitted and operated from February 2016 to June 2017.

Cases from multiple centers are included but all settings are standardized, using the same "angio suite" settings, same device (Artz Zee floor, Siemens, Germany), the same post-operative care protocol and the same team headed by the same experienced neurointerventionalist.

Inclusion criteria:

1. Symptomatic cerebral aneurysm; either ruptured with subarachnoid hemorrhage or unruptured aneurysm with presentation other than hemorrhagic.
2. Wide neck aneurysm by definition, either neck diameter is ≥ 4 mm or dome/neck ratio is less than 2.
3. Age 15-80 years old. Both sexes are included.
4. Good prognostic features; GCS is above or equal to 10, NIHSS score is less or equal to 20, Hunt and Hess scale not more than 4.

Exclusion criteria:

1. History of head trauma.
2. Poor prognostic features; GCS below 10, or Hunt and Hess scale 5.
3. History of any hemostatic disorder
4. History of previous cerebrovascular stroke or any non-aneurysm-induced neuropsychiatric complications.
5. History of uncontrolled complicated metabolic disorders, liver or renal impairment and active viral infection.
6. Hydrocephalic changes that require shunting
7. Fusiform or dissecting aneurysms
8. Giant aneurysm (size > 25 mm)
9. Previous neurosurgical or interventional procedures for the studied aneurysm; retreatment cases.
10. Failure to obtain informed consent from the patient or decision maker.

Methods:

All the patients undergo the following

1. Full medical and neurological history including history of associated comorbidities and risk factors
2. Full Medical & Neurological examination with the required laboratory investigations.
3. Pre-operative assessment including NIHSS score, Hunt and Hess scale and modified Rankin scale.

Hunt and Hess scale is a clinical grading system to predict the prognosis and outcome in patient with subarachnoid hemorrhage ranging from one to 5. A higher grade predicts poor outcome. Modified Rankin scale is used to measure the

degree of disability in patients who had a stroke. It ranges from 0 to 6. Used as measurement of clinical outcome. Higher grade means higher disability.

All patients were subjected to brain CT examination. Entire brain imaging from nasion toinion was done by the use of modern CT device of different models (Toshiba- GE-Philips). Images were interpreted by the radiologists for the diagnosis of SAH and modified Fisher scale assessment.

CT cerebral angiography to detect the presence of aneurysm, site size number and morphology. Digital subtraction angiography is done either during the same setting of therapeutic intervention or in a separate session preoperative; 4-vessel cerebral angiography to detect the aneurysms recording its dimensions, morphology and site, determining that it is wide neck requiring assisted techniques.

In all cases those rules are respected:

1. In cases of Flow diverter, pretreatment with double antiplatelet (Asprin 100 mg and Clopidogril 75 mg).
2. Continuous infusion of heparinized saline in the catheter set for protection against thrombosis
3. Relevant procedural events are recorded including: vasospasm, internal carotid dissection, in stent thrombosis and related infarction, infarction, intra-procedural aneurysm rupture or bleeding even under balloon protection, coil prolapse, coil migration, slipped stent, postoperative disturbed conscious level or hemorrhagic transformation of an infarction due to lytic agent injection after in stent thrombosis or infarctions
4. Immediately after completion of aneurysm obliteration, occlusion of the aneurysm is evaluated with Raymond Roy scale ranging from 1 to 3 where 1 is complete obliteration, 2 is neck remnant and 3 is intra-aneurysmal remnant.
5. Post-operative; enlistment of complications / deficits, also recording of using modified Rankin scale which measures immediate clinical outcome
6. After 6 months, Follow up four vessel angiography is to be done 6 months after the intervention and occlusion is re-evaluated with the same scale and the clinical outcome using modified Rankin scale, as well as recording any event or neurological deficit

Statistical analysis

Data entry and analysis were all done with IBM compatible computer using software SPSS version 23, and graphs were generated using Origin 2018 program. Quantitative data were presented by mean and standard deviation; Independent sample T test was used for parametric quantitative data comparison between the two groups. Paired sample T test was used to compare data pre and post-operative. Qualitative data were presented by frequency distribution. Fisher exact test was used for comparison between qualitative data of the two groups. For nominal ordinal qualitative data i.e. scales Mann Whitney U test for non-parametric quantitative data between the two groups. Pearson correlation method was used to correlate the angiographic outcome with age neck diameter aneurysm size and post-operative clinical outcome.

All tests' Significance level is at P value < 0.05. Pearson correlation significance is at 0.001.

Results

Thirty two patients were included in this study between February/2016 and June/2017. Age range was 25-69 (54 ± 10.5) for balloon group (Group B =17), 30-68 years old (50.7 ± 10.1) for the Flow diverter group (Group F=15). The females were 10 (58%) in the balloon group and 6 (40%) in the Flow diverter group. No statistically significant difference was found between two groups.

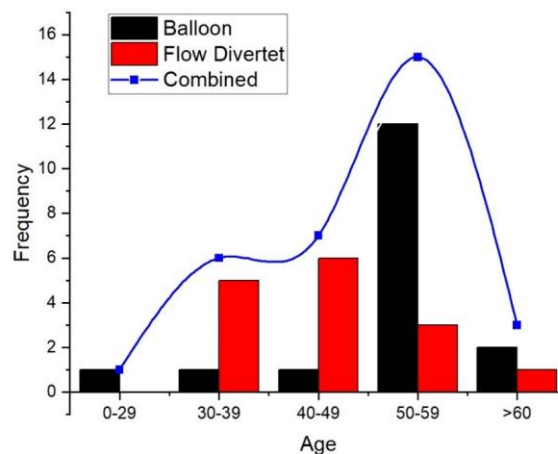


Figure (1): Distribution of age of the patients

For risk factors there was no significant difference between 2 groups.

History of hypertension was positive in 9 patients (52%) and DM 5(31%) in balloon group vs. 5 patients with hypertension and 2 (13.3%) with DM in flow diverter group (33%) (P=0.308). Family history of aneurysm/subarachnoid hemorrhage was positive in 3 patients (17.6%) Group B.

Interestingly, 3 patients have history of Tramadol addiction 2 of them have no other risk factors.

For other risk factors, 3 patients had Family history of hypertension, one had family history of DM, 3 with Ischemic heart disease, 2 with previous stroke, 3 smokers, one patient was HCV positive, one patient had neuro-fibromatosis, one patient with dementia, one patient had history of DVT and seven patients had no relevant medical history.

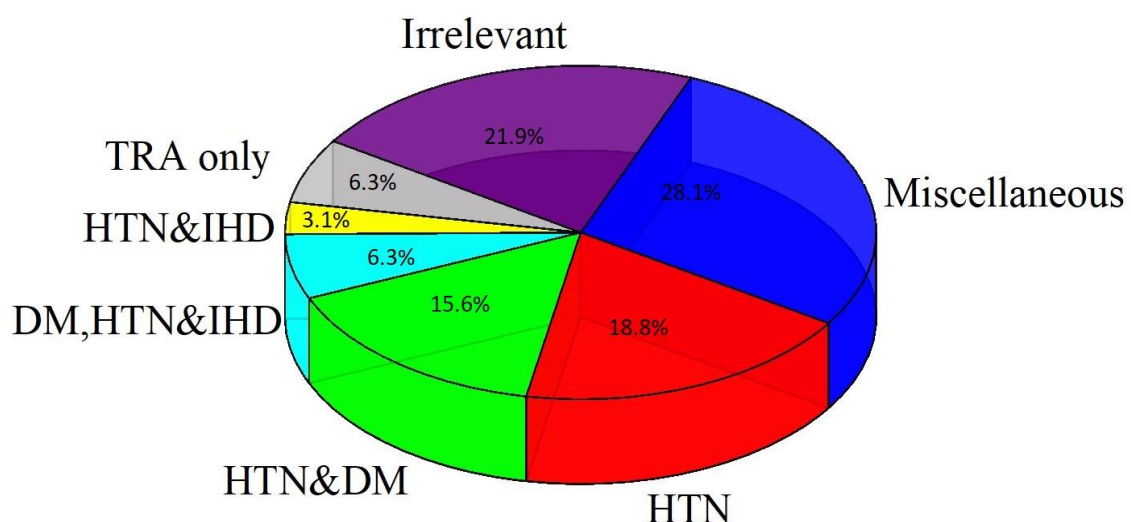


Figure (2): Risk factors in the studied groups

*HTN is for hypertension, DM is for diabetes mellitus, IHD is for ischemic heart disease, TRA is for Tramadol

Headache is the frequent symptom in both groups, while 3rd nerve palsy is more frequent

in FD group. All difference are not statistically significant.

Table (1):Frequency of symptoms in clinical presentation.

Clinical presentation	Balloon (n=17)	Flow Diverter (n=15)	P value
Headache	12(70.6%)	11(73.3%)	1
focal deficit	3(17.6%)	3(20%)	1
Seizures	1(5.9%)	0(0%)	1
Visual field defect	1(5.9%)	1(6.7%)	1
Confusion	3(17.6%)	1(6.7%)	0.603
Diplopia	1(5.9%)	1(6.7%)	1
3rd nerve palsy	1(5.9%)	5(33.3%)	0.076

Four vessel angiography was done for each patient, detecting the site, size and special morphology of aneurysm for each patient. Majority of aneurysms were of anterior circulation origin for both groups. A considerable portion of flow diverter group originated from the carotid artery itself. Eight aneurysms equally distributed in both groups- originated from posterior circulation. No

statistically significant difference between both groups was detected.

For special structural characteristics; 4 patients in balloon groups are bifurcation originating aneurysm, 2 patients had bi-lobed aneurysms, 2 patients had daughter aneurysm. Only one patient in Flow diverter group had an artery originating from aneurysm.

Table (2): Frequency of the aneurysmal site distribution in both groups.

DSA	Balloon (n=17)	Flow Diverter (n=15)	P value
ICA	4(23.5%)	9(60%)	0.070
Cavernous	0(0%)	1(6.7%)	0.469
supraclinoid	2(11.8%)	5(33.3%)	0.209
Paraclinoid	0(0%)	1(6.7%)	0.469
Paraophthalmic	1(5.9%)	0(0%)	0.469
anterior choroidal	0(0%)	1(6.7%)	0.469
other	1 (5.9%)	0 (0%)	0.469
MCA	4(23.5%)	2(13.3%)	0.338
ACA	3(17.6%)	0(0%)	0.229
ACOM	2(11.8%)	0(0%)	0.486
PCOM	3(17.6%)	0(0%)	0.229
PCA	0(0%)	0(0%)	-----
PICA	0(0%)	2(13.3%)	0.212
Tip of basilar	1(5.9%)	0(0%)	1
Vertebral	0(0%)	2(13.3%)	0.212

- Fisher exact test for qualitative data between the two groups
- *: Significant level at P value < 0.05

Aneurysm diameter and neck diameter were measured with dome to neck ratio calculated. All fitting the inclusion criteria with insignificant difference between 2 groups.

Clinical outcome: Comparing the modified Rankin scale in preoperative state, immediate postoperative state and follow up after 6 months, the frequency of each group is shown in the following graphs. In the balloon group, there was statistically significant of the mRS score in the follow up assessment compared to preoperative or immediate post-operative condition ($p < 0.001$). Moreover, in the flow diverter group, the mRS score markedly improved than mRS score immediately after operation ($p < 0.002$). With good outcome defined as modified Rankin scale from 0 to 1 as no or minor symptoms that don't interfere with functionality, good outcome

was 94% in the balloon group versus 93% in the flow diverter group with no statistically significant difference.

Radiological outcome: The flow diverter patients showed no significant difference between immediate and 6 month follow up scores on Raymond ray scale ($p < 0.157$), but balloon group showed significant difference ($p < 0.046$) as shown below. No statistically significant difference between both groups in the Raymond Ray scores, either in immediate or follow up outcome.

Complications: Most of the cases in both groups was uneventful intraoperative and post-operative. Thrombosis events were a little bit higher (3 or 20%) in flow diverter group while manifest infarction is higher in the balloon group (17.6%).

Table (3): The percentage (frequency) of the complications in the studied groups

Complications	Balloon (n=17)	Flow Diverter (n=15)	P value
Uneventful	12(70.6%)	11(73.3%)	1
Manifest infarction	3(17.6%)	1(6.7%)	0.6029
GTC	1(5.9%)	0(0%)	1
Bleeding under balloon protection	1(5.9%)	0(0%)	1
Post operative dCL	1(5.9%)	0(0%)	1
Thrombosis	2(11.8%)	3(20%)	0.6454
Slipped Flow diverter	0(0%)	1(6.7%)	0.469

Correlation: The immediate radiological outcome using Raymond Roy scale was correlated with age, neck diameter and immediate clinical outcome using modified Rankin Scale (mRS)

Here, using Pearson correlation there was significant positive correlation between the immediate clinical outcome with the immediate radiological (Pearson c. 0.467, $p < 0.007$) with no correlation with age or neck diameter

Table (4): Correlation

Immediate radiological outcome (RR scale)	Pearson correlation	Significance
Age	0.157	0.392
Neck diameter	-128	0.486
Immediate mRS	0.467	0.007

Discussion

The flow diverter stent is the application of the findings that highlights the role of reconstruction of the vessel by endoluminal devices such as stent assisted coiling that contribute in aneurysm closure not only by

supporting coils in the aneurysm, but with the diversion of blood flow into its normal path in the vessel away from the aneurysmal sac. Either with the help of coils or without, the flow diverters managed to give better results specially with aneurysms difficult to treat (Mühl-Benninghaus et al., 2017).

Flow diverter stents (FDS) were initially applied to aneurysms that either failed to be treated by other methods or cannot be treated with other methods. It was even advised not to use FDS if the lesion can be treated by other technique due to claimed higher morbidity (Brinjikji et al., 2013; Briganti et al., 2015). Even a trial like FIAT trial that started in 2011 comparing the randomized results of using FDS vs other modalities was withheld due to high mortality and morbidity in outcome (Raymond et al., 2016). Now this concept has changed, FDS is now viewed as an option for many aneurysm types previously treated by other techniques (Al-Mufti et al., 2016).

This study aimed to compare the outcome and complications between two common techniques used to treat wide neck aneurysms, which are balloon assisted coiling and the use of Flow diverter stent, also studying the theoretical effect of antiplatelet use in flow diverter group and whether there is an added risk for development of bleeding.

The following are the most comparable studies that has already been published for outcome and complications of both techniques in comparison as well as every technique alone

A systematic review and meta-analysis was done for studies comparing treatment of cerebral aneurysm using deconstructive techniques (BAC, SAC) versus reconstructive techniques with flow diverter in focus. (Rouchaud et al., 2015)

Another systematic review in 2017 by Yao et al. tested safety and efficacy of flow diverter by combining the result of 10 observational studies in small wide neck aneurysms with comparable

inclusion criteria and the same evaluation scales of clinical and radiological outcome.

Also, Briganti et al., (2017) reported a retrospective study of seven-year experience with flow diverter on 60 patients, results supported the safety and efficacy of flow diverters.

Safety and efficacy of balloon assisted coiling was determined in many studies, namely ATENA and CLARITY study, also in Shapiro review (Shapiro et al., 2008; Pierot et al., 2012).

Other studies enrolled cases that is different in aneurysm type, especially in flow diverter group. This may explain the better outcome and less complication rate in our study than other studies.

Ongoing trials

There are no current published studies specifically comparing both techniques in treatment of intracranial aneurysm. Many ongoing randomized trials comparing the outcome and the complications of flow diverter versus conventional coiling methods, they include:

- 1- LARGE trial (Large aneurysm randomized trial; flow diversion versus traditional endovascular coiling therapy). It is not yet finished or published (Turk et al., 2014).
- 2- EVIDENCE trial (Endovascular treatment of intracranial aneurysm with pipeline versus coils with or without stents) which compares the two techniques in larger than 7 mm aneurysms (Briganti et al., 2015).
- 3- ISAT II trial (The International subarachnoid aneurysm trial II), established in 2013 with ending point arranged in 2024. They enrolled flow diverters as one of the arms of the trial (Darsaut et al., 2013).
- 4- COCOA trial (complete occlusion of coilable intracranial aneurysms trial) it compares PED flow diverter with coiling in small aneurysms (<10 mm) (Al-Mufti et al., 2016).
- 5- MARCO POLO trial (Multicenter randomized controlled trial on selective endovascular aneurysm occlusion with coils versus parent vessel reconstru-

ction with silk stent flow diverter) (Al-Mufti et al., 2016).

Comparison of demographic data of our study with similar studies is in the following table

Table (5): age and number of cases in similar studies

Name of prospective study	Number of patients	Mean age	intervention
Briganti et al.	60	57	PED
Chalouhi et al.	40	52.1	PED
Lin et al.	41	54.9	PED
Yavuz et al.	22	\	PED
Byrne et al.	18	\	SFD
Voigt et al.	27	\	Leo stent
Our study	32(15 FD, 17 BAC)	50.1 FD, 54 BAC	BAC-PED-PFD-SFD

Clinical presentation is similar to literature. Also, preoperative assessment methods were similar to other study designs (Oda et al., 2015)

Outcome: Our study concluded that total obliteration was achieved immediately in 11 out of 17 in the balloon group (64.7%), 13 out of 15 in the Flow diverter group (86.7%), regarding follow up, most of cases in FD group achieved total obliteration with no significant difference between angiographic outcome of immediate

and follow up imaging in the case of flow diverter. This can be explained by good results in immediate evaluation. There is a significant difference between the immediate and follow up score of the balloon group but eventually most of the cases achieve complete obliteration; 15 out of 17, (88.2%).

Table next page summarized the clinical and radiological outcome in different studies including ours in a comparative manner

Table (6): comparison of outcome with other studies

Study\ intervention	Type of study	Immediate total occlusion	Occlusion at 6 month	Mid to long term good outcome
Rouchaud et al. \ deconstructive	Systematic review	77.3%	81%	79.9%
Rouchaud et al.\ FD	Systematic review	53%	90.8%	86%
Yao et al.\ FD	Systematic review	\	84.23%	97.5%
Briganti et al. \ Flow Diverter	retrospective	50%	80%	\
Shapiro et al.\ BAC	Systematic review	70%	79%	\
Our study\ BAC (deconstructive)	prospective	64.7%	88%	94%
Our study\ Flow diverter	prospective	86.7%	93%	93%

Complications: the operation went uneventful for more than two thirds of cases in each group. Although thrombotic complication is higher in Flow diverter group (20% for FD Vs 11.8% for B), manifest infarction is paradoxically higher in Balloon group (6.7% for FD Vs 17.6% for B). Hemorrhagic event occurred only once in balloon group (5.9%).

Similarly, Briganti et al., (2017) reported that 6% of patients experiences non disabling thrombotic events. Also, no recanalization no, rebleeding in all cases. This is very similar to our study (Briganti et al., 2017)

Yao et al. meta-analysis determined that the procedure-related neurologic mortality was 0.87%.(95% CI 0.29%-1.74%) The procedure

related neurologic morbidity rate was 5.22% (3.6-7.1). The ICH rate was 1.42% (0.64-2.49). Ischemic rate was 2.35% (1.31-3.68). The SAH rate was 0.03% (0-0.32). The procedure-related permanent morbidity was 2.41% (0.81-4.83).

Rouchaud et al. meta-analysis had a rate of periprocedural complications of 17% (95% CI 6.3- 27.7%), stroke 11.5% (3.1-19.9), mortality 8.7 (2.1-15.2), morbidity 12.6 (3.3-22) hemorrhage 7.6 (0.8-14.7) for Flow diverter group

For the deconstructive group (Assisted coiling) he reported peri-procedural complications of 26.1% (95% CI 10.6- 41.7 %), stroke 29.1 % (11.9-46.1), mortality 15.1% (3.5-26.7), morbidity 23.4 (8.5-38.2) hemorrhage 12.4 (2.3-22).

Another study compared flow diverter with standard endovascular treatment modalities was published in 2016 studying unruptured carotid ophthalmic aneurysm mainly on 162 patients. The choice of ophthalmic part is to determine the branch patency theory; no procedural related deaths occurred, permanent morbidity was observed in 3.9% of flow diversion group vs 1.6% in the conventional coiling group. Radiological outcome was better in flow diversion group. Complications difference was insignificant but occlusion rate was statistically significant in the favor of flow diverter (Di Maria et al., 2015).

Conclusion

If we eliminate the confounding factors by strict inclusion and exclusion criteria, the results of the balloon assisted coiling and flow diverter stent are comparable with statistically insignificant superiority to the flow diverter group. No rebleeding, rupture or recurrence were noted in both techniques. Both techniques have advantages and disadvantages

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