Selecting the Appropriate First-Line Strategy Based on Hyperdense Vessel Sign in Acute Ischemic Stroke Increases First Pass Recanalization: A Tertiary Center Experience

Uday Bhanu Kovilapu[1] Narendra Jain[2] Atul Mishra[3] Virender Malik[4]

[1] Interventional Radiologist at Department of Radiodiagnosis and Interventional Radiology, Armed Forces Medical College, Pune, Maharashtra, India
[2] Interventional Radiologist at Department of Radiodiagnosis and Interventional Radiology, Command Hospital, Chandi Mandir, Haryana, India
[3] Interventional Radiologist at Department of Radiodiagnosis and Interventional Radiology, Army Hospital (R&R), New Delhi, India
[4] Interventional Radiologist at Department of Radiodiagnosis and Interventional Radiology, Army Institute of Cardiothoracic sciences (AICTS), affiliated to Armed Forces Medical College, Pune, Maharashtra, India

Address for correspondence Virender Malik, MD(Rad), DNB (Rad), DM (Neuroradiology), Intervention Radiologist, Department of Radiodiagnosis and Interventional Radiology, Army Institute of Cardiothoracic sciences (AICTS), Pune - 411040, Maharashtra, India (e-mail: virender2323@gmail.com).

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Abstract

Background: The data pertaining to selecting an optimal first-line strategy (stent retriever [SR] vs. contact aspiration [CA]) based on noncontrast computed tomography (NCCT) in cases of acute ischemic stroke consequent to large vessel occlusion (LVO) is lacking.
Aims: This article studies the influence of hyperdense vessel sign (HVS) in selecting optimal first-line strategy, with intention of increasing first-pass recanalization (FPR).
Methods: Upfront approach at our center is SR technique with rescue therapy (CA) adoption consequent to three failed SR attempts to achieve successful recanalization. Data of patients with acute LVO who underwent mechanical thrombectomy from June 2017 to May 2020 was retrospectively analyzed. Patients were classified into HVS (+) and HVS (–) cohort. Rate of successful recanalization (first pass, early, and final) and efficacy of rescue therapy was assessed between the two cohorts.
Results: Of 52 patients included, 28 and 24 were assigned to the HVS (+) and HVS (–) cohort, respectively. FPR was observed in 50% of HVS (+) and 20.9% of HVS (–) ($p = 0.029$). Early recanalization was documented in 64.2% of HVS (+) and 37.5% of HVS (–) ($p = 0.054$). Rescue therapy need was higher in patients not demonstrating HVS ($p = 0.062$). Successful recanalization was achieved with rescue therapy in 50% of HVS (–) group.
Conclusion: A higher FPR is achievable following individualized first-pass strategy (based on NCCT appearance of clot), instead of a generalized SR first-pass approach. This CT imaging-based strategy is a step closer to achieving primary angiographic goal of FPR.

Keywords
► first-line strategy
► hyperdense vessel sign

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Introduction

Currently, the role of mechanical thrombectomy (MT) as the standard of care in acute ischemic stroke (AIS) consequent to a large vessel occlusion (LVO) is well established.[1] With functional outcome in LVO being profoundly time dependent, achieving first-pass recanalization (FPR) holds paramount importance.[2,3] Currently there is no robust evidence citing significant difference in terms of efficacy or safety between the first-line stent retriever (SR) and contact aspiration (CA) techniques.[4] Though recent studies have suggested that red blood cell (RBC)-rich clot shows better recanalization using SR compared with the CA as the first-line technique,[5] the debate as to the best first-line approach remains unsettled. The currently available data, as a guide to decision making in selecting an optimal first-line MT technique (SR or CA) based on noncontrast computed tomography (NCCT) imaging appearances is at the best sparse.

In this study, we evaluated the influence hyperdense vessel sign (HVS) observed on NCCT has in selecting an optimal individualized first-line approach for MT, with the intention of increasing FPR.

Material and Methods

This retrospective study was performed at a tertiary care center equipped with a “comprehensive stroke” protocol.

Patient Selection and Characteristics

All the clinical and imaging data pertaining to patients with acute LVO who underwent MT using SR or CA approach from June 2017 to May 2020 was reviewed. Patients less than 18 years of age, occlusions involving middle cerebral artery (MCA) distal to M1 bifurcation, vertebrobasilar circulation, and tandem lesions were excluded from the study. Also, patients who underwent MT employing Solumbra technique were not included in the analysis. A total of 52 patients fulfilled the inclusion criteria and were included in the final analysis.

Workflow for Acute Stroke at Our Tertiary Care Center

A stroke neurologist performed an initial assessment, primarily based on the National Institutes of Health Stroke Scale (NIHSS) score. The prethrombectomy evaluation to assess presence of bleed, extent of infarction, and vessel status was done using NCCT with a triple-phase CT angiogram (CTA) for neck and intracranial vessels. Cases with wake-up stroke and late presentations (beyond 6 hours from ictus) underwent MT, provided CT perfusion demonstrated significant mismatch and hence salvageability. If NIHSS score was > 4, imaging ruled out intracranial bleed, and CTA confirmed a LVO, the patient was shifted to interventional laboratory for MT procedure. The intravenous thrombolysis was initiated for patients presenting within 4.5 hours of symptom onset at the discretion of attending stroke physician, after ruling out conventional contraindications to thrombolysis. All procedures were performed by either one or two interventional neuroradiologists, using a biplane angiography system. The upfront approach at our center is SR first technique with adoption of CA technique consequent to three failed SR attempts to achieve modified treatment in cerebral infarction (mTICI) score 2b/3 recanalization. The CA technique employed placement of ACE 68 (large bore aspiration catheter) at the face of the clot and suction aspiration using a Penumbra MAX aspiration pump. The decision for conscious sedation or general anesthesia is individualized (based on patient’s clinical condition) and at the discretion of interventional neuroradiologist.

Retrospective Evaluation of Images

All the NCCT images of 52 patients were evaluated by two neuroradiologists to assess presence or absence of the HVS in the region of LVO. The CTA data was perused to correlate the filling defect with the HVS on NCCT images, thus confirming the clot site. Initially the neuroradiologists were blinded to each other’s imaging conclusions. Subsequently, following consensus meeting between the two neuroradiologists, interobserver agreement for HVS was reached in all cases (kappa: 1).

Angiographic data and follow-up NCCT were reviewed to identify occlusion site, average number of SR passes needed to achieve mTICI 2b/3, mTICI 2b/3 reperfusion after SR strategy, rate of FPR, early recanalization, rescue therapy (switch over to CA), mTICI 2b/3 reperfusion at end of procedure (following CA strategy), incidence of distal embolization using SR technique, and incidence of any or symptomatic intracerebral hemorrhage (ICH).

Postprocedure mTICI grade of $\geq$ 2b was defined as successful recanalization. Early recanalization was defined as recanalization with maximum of two passes of SR. Symptomatic ICH was defined as any intracranial hemorrhage associated with $\geq$ 4 points increase on NIHSS score at 24 hours (Electronic Consolidated Automated Support Criteria).

Statistical Analysis

Quantitative variables were expressed as mean and standard deviation. Qualitative variable were expressed as frequency and percentage. Comparison of continuous variables between two groups was analyzed by Student’s *t*-test. Comparison of continuous variable among more than two categories was analyzed by analysis of variance. Association between qualitative variables was analyzed by chi-square test. A *p*-value of < 0.05 was considered statistically significant. Interobserver agreement for HVS was calculated using kappa statistics. Data were entered in Microsoft Excel and data analysis was performed using SPSS version 22.0.

Results

Of the 52 patients included, 28 and 24 were randomized to HVS (+) and HVS (–) cohort, respectively. Excellent interobserver agreement for HVS was noted using kappa statistics (kappa = 1). All but three patients underwent MT with onset of symptoms being within 6 hours. These three patients (2 HVS+ and 1 HVS–) presented between 6 and 10 hours of symptoms onset and underwent MT following demonstration of brain tissue salvageability on CT perfusion. MT was performed under conscious sedation in 26 (92.9%) of HVS (+) and 22 (91.7%) of HVS (–) cohort, respectively. Two cases underwent the procedure under general anesthesia in each group.

Occlusion involving the terminal internal carotid artery was documented in three patients in each cohort, but affected M1 MCA in 25 (89.3%) and 21 (87.5%) of HVS (+) and HVS (–) cohort, respectively. Intravenous tissue plasminogen activator was administered in 13 (46.4%) and 12 (50%) of HVS (+) and HVS (–) group, respectively. First-pass mTICI 2b/3 recanalization was achieved using SR in 14 (50%) of HVS (+) and 5 (20.9%) of HVS (–) cohorts. Early mTICI 2b/3 recanalization was achieved using SR in 18 (64.2%) of HVS (+) and 9 (37.5%) of HVS (–) cohorts. A total of 7 patients (25%) from HVS (+) needed the rescue therapy (switched over to CA technique) whereas 12 patients (50%) from HVS (–) needed adoption of CA technique consequent to three failed SR attempts to achieve mTICI 2b/3 recanalization. Overall, the CA technique was employed in 19 patients. Following rescue therapy with CA, mTICI 2b/3 recanalization was achieved in 2/7 (28.6%) and 6/12 (50%) of HVS (+) and HVS (–) group, respectively. The rate of distal embolization was 2 (7.1%) in the susceptibility vessel sign (SVS) (+) compared with 4 (16.7%) in the SVS (–) group (►**Table 1**).

The representative cases of HVS (+) and HVS (–) cohort, managed with SR technique and rescue therapy are depicted in ►**Figs. 1** and **2**, respectively.

FPR was observed using SR in 50% of HVS (+) and 20.9% of HVS (–), a statistically significant difference ($p = 0.029$) between the two cohort. The early recanalization (≤ 2 SR passes) was documented in 64.2% of HVS (+) and 37.5% of HVS (–), a near statistically significant difference ($p = 0.054$) between the two cohort. The rate of rescue therapy was much lower in patients demonstrating HVS on NCCT, compared with those in the SVS (–) cohort ($p = 0.062$) (►**Table 1** and ►**Fig. 3**). Also, the incidence of distal embolization was higher in the SVS (–) than in SVS (+) cohort (16.7 vs. 7.1%). No statistically significant difference was noted in the age,

Table 1 Comparison in angiographic outcomes according to hyperdense vessel sign (HVS)

Characteristics	HVS positive (*n* = 28) *n* (%)	HVS negative (*n* = 24) *n* (%)	*p*-Value
Initial NIHSS score, mean (SD)	13.2 (2.7)[a]	14.4 (3.1)[a]	0.142
ASPECTS, mean (SD)	6.2 (1.3)[a]	6.0 (1.1)[a]	0.556
Occlusion site			0.841
-ICA terminus	3/28 (10.7)	3/24 (12.5)	
-M1 MCA	25/28 (89.3)	21/24 (87.5)	
IV t-PA infusion	13/28 (46.4)	12/24 (50.0)	0.797
Anesthesia			0.872
Conscious sedation	26/28 (92.9)	22/24 (91.7)	
GA	2/28 (7.1)	2/24 (8.3)	
SR passes needed to achieve mTICI 2b/3:			
1	14/28 (50.0)	5/24 (20.9)	0.029
2	4/28 (14.3)	4/24 (16.7)	0.812
3	3/28 (10.7)	3/24 (12.5)	0.841
First-pass recanalization	14/28 (50.0)	5/24 (20.9)	0.029
Early recanalization (≤ 2 passes)	18/28 (64.2)	9/24 (37.5)	0.054
mTICI 2b/3 reperfusion after SR strategy	21/28 (75.0)	12/24 (50.0)	0.062
Rescue therapy[b]	7/28 (25.0)	12/24 (50.0)	0.062
mTICI 2b/3 reperfusion post rescue strategy	2/7 (28.6)	6/12 (50.0)	0.075
Overall mTICI 2b/3 reperfusion at end of procedure	23/28 (82.1)	18/24 (75%)	0.530
Distal embolization	2/28 (7.1)	4/24 (16.7)	0.284
ICH at 24 h	2/28 (7.1)	3/24 (12.5)	0.514
Symptomatic ICH	1/28 (3.6)	1/24 (4.2)	0.911

Abbreviations: CA, contact aspiration; GA, general anesthesia; ICA, internal carotid artery; ICH, intracerebral hemorrhage; IV, intravenous; MCA, middle cerebral artery; mTICI, modified treatment in cerebral infarction score; NIHSS, National Institutes of Health Stroke Scale; SD, standard deviation; SR, stent retriever; t-PA, tissue plasminogen activator.
[a]Values indicates mean (SD), rest of values in second and third columns represent numbers (percentage).
[b]Contact aspiration following three failed attempts at recanalization with SR.

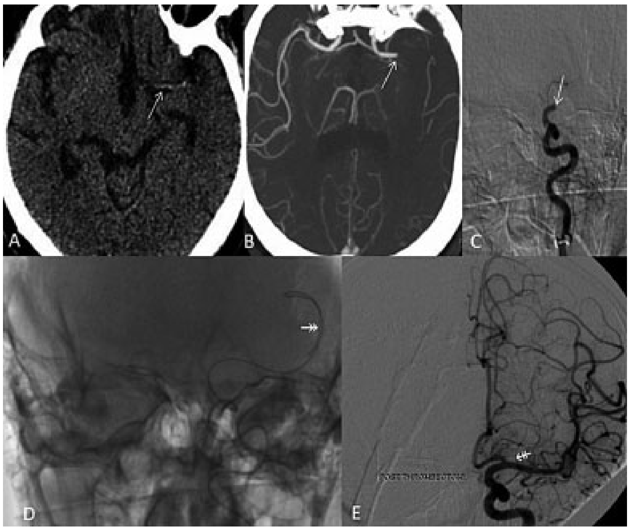

Fig. 1 Successful recanalization using stent retriever (SR) in patient with hyperdense vessel sign (HVS). (**A**) Noncontrast computed tomography (NCCT) image shows presence of HVS in left middle cerebral artery (MCA) (arrow). (**B**) CT angiogram and (**C**) baseline angiography confirmed complete occlusion (arrow in **B** and **C**). (**D**) SR first strategy employed, following navigation of an appropriate microcatheter over a microwire across the occluded segment. Looped microwire tip parked in M2 segment of MCA (two-headed arrow). (**E**) Final angiography demonstrates successful recanalization (arrow with double stroke).

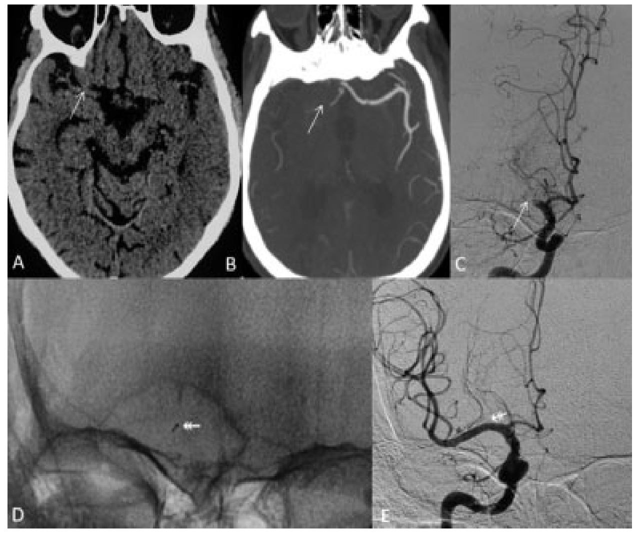

Fig. 2 Successful recanalization following rescue therapy in patient with absent hyperdense vessel sign (HVS). (**A**) Noncontrast computed tomography (NCCT) image shows absence of HVS (arrow). (**B**) CT angiogram and (**C**) baseline angiography demonstrates complete occlusion of M1 segment of right middle cerebral artery (MCA) (arrow in **B** and **C**). (**D**) Contact aspiration attempted consequent to three failed attempts with stent retriever. Depicts tip of ACE 68 aspiration catheter at face of the clot (two-headed arrow). (**E**) Final angiography shows successful recanalization (arrow with double stroke).

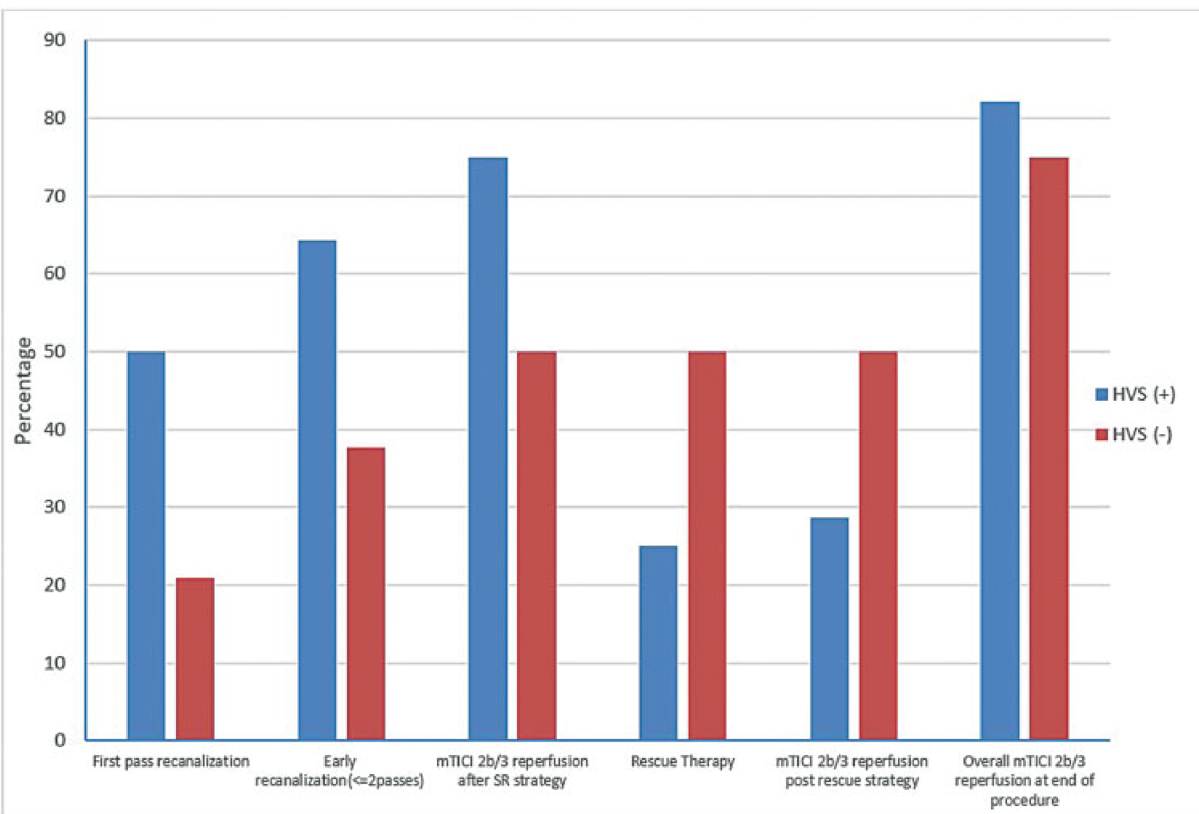

Fig. 3 Bar chart representing angiographic recanalization outcomes with stent retriever (SR) and rescue therapy (contact aspiration consequent to three failed SR attempts) strategies between the two cohort. HVS (+), hyperdense vessel sign present; HVS (–), hyperdense vessel sign absent.

comorbidities, NIHSS and ASPECTS score, use of type of anesthesia, intravenous thrombolysis, and incidence of any or symptomatic ICH between HVS (+) and HVS (–) cohorts (►**Table 1**).

Discussion

Consequent to demonstration of clinical efficacy of MT unequivocally by the multiple landmark randomized clinical trials, presently its role as the standard of care for LVO in AIS is well established.[1,6–9]

Although functional outcome for LVO with MT is definitely superior to intravenous thrombolysis, it is profoundly time dependent.[2,3] Considering therefore the need of early recanalization, FPR is emerging as a key concept in management of AIS.[10,11] Recent studies emphasize the importance of first-pass effect and documented it as an independent prognostic factor in achieving better functional outcome in LVO.[3,11–13] Also, recent literature emphasize the quality of reperfusion to be an important predictor of good clinical outcome, with progressively better clinical outcomes seen from mTICI 2b to 3.[14,15] The multiple passes not only lead to clot compaction, increased time to recanalization, but also to intimal injury and increase in procedure-related complications.[11,16–20]

Therefore, the interventionist must apply a strategy which has the highest likelihood for achieving FPR, based on individual's experience and available literature.

The presence of HVS on NCCT and SVS on gradient-recalled-echo magnetic resonance imaging (MRI) suggests RBC-rich clot, whereas its absence favors a fibrin-predominant occlusive thrombi.[21–24] Also, good concordance between HVS and SVS has been documented in the literature.[21]

The presence of SVS, considered to be due to T2-shortening effect of intracellular deoxyhemoglobin (acute stage of RBC clot), is documented to have a direct correlation with successful recanalization using SR.[25–27] Although studies correlating SVS with clot composition and outcomes (angiographic and clinical) following SR are available, the literature comparing HVS (on NCCT) with angiographic outcome using SR or CA strategy is scarce. Also, CT being a more commonly undertaken investigation in clinical setting of anterior circulation AIS, a first-line strategy (SR or CA) based on clot appearances on CT is more pragmatic and hence warranted. HVS in an appropriate clinical context, is a highly specific, and an early sign of AIS on NCCT.[28] In our study, the two neuroradiologists had an almost perfect interobserver agreement (kappa = 1) for HVS.

Brinjikji et al, based on their systematic review, concluded that clots with a higher mean thrombus Hounsfield unit were more likely to be RBC-rich and showed better angiographic outcome compared with those with lower values.[29] Similarly, in our study HVS presence was observed to be an independent predictor of successful, first pass, as well as early recanalization ($\leq$ 2 SR passes). Such results are biologically plausible with recent data demonstrating improved entrapment of RBC-rich clot in a SR.[12] The favorable recanalization in the HVS (+) cohort noted in our study is in accordance with early recanalization observed in those with SVS sign on MRI.[25–27,30,31] Our results support the premise that RBC-rich clots manifest as HVS and SWS on plain CT and MRI, respectively, and show early recanalization using SR.

A few studies have examined the association between CT attenuation of clot and angiographic outcomes, but not the subgroup analysis to assess and compare efficiency of SR versus CA in those with absent HVS.[32–34] Similar to our results, Froehler et al documented successful recanalization in 79% of patients with HVS, but in only 36% without HVS.[34] However, the thrombectomy in this study was limited to MERCI retriever with no option to switch over to CA (rescue therapy) in those with failed recanalization.

We documented that first-pass mTICI 2b/3 recanalization was achieved using SR in 14 (50%) of HVS (+), but in only 5 (20.9%) of HVS (–) cohort, plausible explanation being the tendency of the fibrin-rich clot to roll out of the SR during retrieval.[30,35] In our study, following rescue therapy with CA (consequent to three failed SR attempts), mTICI 2b/3 recanalization was achieved in 6 (50%) of HVS (–) cohort, with maximum of three CA passes. This observation highlights the effectiveness of aspiration technique in this subgroup of patients.

The incidence of distal embolization was 7.1% in SVS (+) compared with 16.7% in SVS (–) cohort, explained by the higher number of passes needed in the latter.

Although, a recent systematic review and meta-analysis by Boulanger et al suggest no significant difference in terms of efficacy or safety between first-line SR and CA techniques,[4] our study highlights that higher FPR can be achieved if individualized first-pass strategy is employed (based on the appearance of clot on NCCT), instead of a generalized SR first-pass approach.

Some of the limitations of our study include the relatively small number of cases treated, a single-center experience, and the lack of direct analysis of thrombi histologically. Although our study showed high rate of successful recanalization following the rescue therapy with CA (consequent to three failed attempts with SR) in patients with absence of HVS, we cannot definitely comment on the efficacy a CA-based first-line strategy would have yielded if it was applied as the upfront approach for those demonstrating HVS. Further studies employing CA as the first-line strategy are needed to effectively comment on the efficacy the CA technique would have in those with HVS (+). However, being a single-center study, the protocol of adhering to SR as the first strategy in all cases added homogeneity to the cohort.

To our knowledge, there is no other CT-based study, evaluating the influence "HVS" has in selecting an appropriate first approach (ST vs. CA) for MT, with intention of increasing FPR.

Conclusion

The good angiographic recanalization achieved following adoption of rescue therapy with CA technique (consequent to three failed attempts with SR) in the patients demonstrating absence of HVS, support the premise that CA may be considered as the first-line technique in such subset of patients. Our study highlights that higher FPR can be achieved if individualized first-pass strategy is employed (based on the appearance of clot on NCCT), instead of a generalized SR first-pass approach. This CT imaging-based strategy, formulated with our single tertiary center experience, is a step closer to achieving the primary angiographic goal of FPR.

Authors' Contributions

K.U.B.: Concept and design of study, drafting the article, analysis and interpretation of data, critical revision for important intellectual content, final approval of the version to be published.

N.J.: Analysis and interpretation of data, critical revision for important intellectual content, final approval of the version to be published.

A.M.: Analysis and interpretation of data, critical revision for important intellectual content, final approval of the version to be published.

V.M.: Concept and design of study, drafting the article, analysis and interpretation of data, manuscript editing, critical revision for important intellectual content, final approval of the version to be published.

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Note

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Conflict of Interest

There are no conflicts of interest.

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