

Clinical Outcomes and Factors of Single Attempt of Stent Retrieval during Endovascular Thrombectomy for Acute Ischemic Stroke

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Abstract

Backgrounds: Single attempt of stent retrieval during endovascular thrombectomy (EVT) seems to be associated with favorable clinical outcomes of patients with acute ischemic stroke (AIS), but the relationship between single attempt and clinical outcomes or complications have not been characterized. In addition, the factors related to single retrieval attempts during EVT are undefined. Here, we investigated the relationship between single attempt of stent retrieval and the clinical outcomes or complications after EVT, and further investigated the factors associated with single attempt of stent retrieval in AIS patients.

Methods: This study enrolled consecutive patients with AIS treated by EVT with second-generation stent retriever devices from April 2016 to April 2019. Attempts of EVT were classified as single or multiple attempts of stent retrieval after filtrating all enrolled patients based on inclusion and exclusion criteria. We analyzed the clinical outcomes and complications between single attempt of stent retrieval and multiple attempts of stent retrieval, and the factors independently associated with a single attempt were identified through logistical regression analysis.

Results: We enrolled 143 patients, including 69 patients with single attempt of stent retrieval and 74 patients with multiple attempts of stent retrieval. More patients with single attempt of stent retrieval reached favorable clinical outcomes ($p = 0.016$; adjusted OR [95%CI]: 2.652 [1.204-5.843]), and patients with single attempts of stent retrieval showed as a lower incidence of symptomatic intracranial hemorrhage (sICH) ($p = 0.046$; adjusted OR [95%CI]: 0.192 [0.038-0.973]). Diabetes mellitus ($p = 0.026$; adjusted OR [95%CI]: 2.871 [1.137-7.249]) was independently associated with single attempt of EVT with stent retrieval.

Conclusions: Single attempt of stent retrieval during EVT can decrease incidence of sICH and improve favorable clinical outcomes of patients with AIS. Those with diabetes mellitus may be more prone to single attempt of stent retrieval during EVT.

Introduction

Endovascular thrombectomy (EVT) is a safe procedure for patients with acute ischemic stroke (AIS) due to intracranial artery occlusions [1–5]. Second-generation stent retriever devices such as Solitaire have increased the rates of recanalization in patients with AIS than ever [6]. However, higher recanalization cannot completely ensure favorable clinical outcomes after EVT. Recently, lots of studies start to focus on how to improve favorable clinical outcomes and decrease complications for patients with AIS treated by EVT.

3 to 4 attempts of stent retrieval can reduce the chances of recanalization and increase the risk of complications based on the previous studies [7], and multiple attempts of stent retrieval can lead to a poor prognosis for AIS patients [8, 9]. Single attempt of EVT with stent retrieval seems to be associated with favorable clinical outcomes, but the relationship between single attempt and clinical outcomes or complications have not been investigated. In addition, the factors associated with single attempt of stent retrieval in EVT also remain undefined. In this study, we investigated the relationship between single attempt of stent retrieval and the clinical outcomes or complications after EVT, and further investigated the factors associated with single attempt of stent retrieval in AIS patients.

Methods

Patients Enrollment

Consecutive patients with AIS were treated by EVT from April 2016 to April 2019 in our institute. The study was approved by the ethics committees of the Second Affiliated Hospital of Harbin Medical University and all patients received written consent before EVT.

Patients conformed to the typical criteria of EVT for AIS, namely: (1) AIS diagnosis; (2) large intracranial artery occlusions; (3) Aged ≥ 18 years; (4) Premorbid modified Rankin Scale (mRS) scores < 2 ; (5) National Institute of Health Stroke Scale (NIHSS) scores ≥ 6 and Alberta Stroke Program Early Computed Tomography Score (APECTS) ≥ 6 ; (6) EVT within 6 h of stroke onset or treated 6 to 16 h upon DAWN or DEFUSE 3 eligibility criteria [10, 11]; (7) No findings on concomitant intracranial hemorrhagic disease, including aneurysm or arteriovenous malformations. Meanwhile, Patients were selected according to the following inclusion criteria: intracranial artery occlusion after EVT successfully recanalized and subsequently defined as a modified Thrombolysis in Cerebral Infarction (mTICI) score of 2b or 3 [12]. Exclusion criteria: rescue therapies performed due to the failure of recanalization, including stent implantation, balloon angioplasty or intra-arterial thrombolysis. According to attempts of EVT, all enrolled patients in this study were divided into single attempt of stent retrieval or multiple attempts.

Preoperative Evaluation and Treatment

Cranial computed tomography scans were performed on each patient to exclude intracranial hemorrhage (ICH) and to estimate the volume of infarction tissues for APECTS assessments before EVT. Physical examinations were used to evaluate the NIHSS scores. To determine the occurrence of large intracranial artery occlusions, such as internal carotid artery (ICA), M1 segment of the middle cerebral artery (M1), M2 segment of the middle cerebral artery (M2), and basilar artery (BA), were confirmed via computed tomography angiography, magnetic resonance angiography, and digital-subtraction angiography. According to 2018 AHA/ASA guidelines for AIS, patients with no history of hemorrhagic disease needed to receive intravenous treatment (IVT) before EVT within 4.5 h of symptom presentation or directly receive EVT in the absence of IVT beyond 4.5 h [13].

Endovascular Procedure

We performed EVT under local or general anesthesia. Thrombectomy was performed using the SOLUMBRA technique, in which a stent retriever was combined with a non-contact aspiration technique using intracranial catheter support, designed to reduce the incidence of distal embolization [14]. EVT using a second-generation stent retriever did not exceed 3 attempts. Finally, mTICI 2b or 3 were deemed as a successful recanalization.

Those with tandem lesions received carotid stenting in proximal occlusions and thrombectomy in distal occlusions [15]. The number of stent retrievals were recorded only in distal occlusions.

Postoperative Evaluation

Cranial computed tomography scans were performed within 48 h or during any functional impairment following EVT. Cranial computed tomography scans data were reviewed by two independent physicians, with disagreements resolved by a third party. Post-procedural evaluations included the incidence of complications and clinical outcomes. ICH was classified using Heidelberg Bleeding Classifications via cranial computed tomography scans analysis [16], sICH was diagnosed when the following occurred: (1) Increase in NIHSS scores of ≥ 4 points; (2) NIHSS scores ≥ 2 points in category 1; major interventions such as hemicraniectomy, deterioration, intubation, and external ventricular drain placement. The mRS at 90 days post-treatment was evaluated through telephone communication and follow-up. Scores of 0–2 were deemed as favorable clinical outcomes [17].

Data Collection and Factor Definition

Clinical and laboratory data were obtained and registered in case report forms. Clinical data was recorded including baseline characteristics, complications and clinical outcomes. Complications including ICH, sICH and others and clinical outcomes based on mRS were recorded to analyze the relationship between single attempt of stent retrieval and favorable clinical outcomes or incidence of complications. Baseline characteristics including age, male sex, hypertension (defined by a history of hypertension), diabetes mellitus (defined by a history of diabetes mellitus), a history of cerebral ischemic stroke, smokers (continuously for ≥ 6 months having ≥ 1 cigarette per day), NIHSS scores, symptom onset to groin puncture time (OTP), ASPECTS, number of patients with IVT prior to EVT and stroke causes judged by TOAST classifications [18] and laboratory data including blood and biochemical examinations prior to EVT were evaluated for factors associated with single attempt of stent retrieval.

Statistics

Data were analyzed using SPSS 22.0. Numbers and frequencies were used to represent categorical variables (%). The median and interquartile range (IQR) were used to represent continuous variables. Continuous variables were compared with a Student's T test or Mann-Whitney U test. Categorical data were compared with a χ^2 or Fisher exact tests via univariable analysis. For multivariable analysis, potential factors ($p < 0.1$) were assessed via binary logistic regression. p -values < 0.05 were deemed significant.

Results

Of the enrolled patients, 143/245 with AIS were treated through EVT from April 2016 to April 2019 based on the inclusion and exclusion criterion, including 69 patients treated by single attempt of stent retrieval and 74 patients treated by multiple attempts (Fig. 1). All patients were treated with second generation stent retrievers, including Solitaire (Medtronic, Irvine, CA, USA). Clinical data and laboratory data in all enrolled patients were shown in Table 1. Notably, all patients with intravenous thrombolysis prior to EVT were treated with tissue-type plasminogen activator (t-PA).

Table 1
Characteristics of All Enrolled Patients

	All patients(n = 143)
Baseline Characteristics	
Age, median (IQR)	62(56–69)
Male sex, n (%)	105(73.4%)
Hypertension, n (%)	86(60.1%)
Diabetes Mellitus, n (%)	30(21.0%)
Atrial Fibrillation, n (%)	44(30.8%)
History of ischemic stroke, n (%)	29(20.3%)
Smoking, n (%)	56(39.2%)
NIHSS score, median (IQR)	14(11–18)
ASPECTS, median (IQR)	8(8–10)
OTP (min), median (IQR)	264(197–355)
EVT beyond time window	32(22.4%)
IVT, n (%)	34(23.8%)
Occlusion sites, n (%)	
ICA	25(17.5%)
M1	64(44.8%)
M2	5(3.5%)
BA	28(19.6%)
Distal Occlusion in Tandem Occlusion	21(14.7%)
Stroke cause, n (%)	
LAA	72(50.3%)
Cardioembolic	44(30.8%)
Others	27(18.9%)
Baseline measurement in laboratory test	
Leukocyte level*10 ⁹ /L, median (IQR)	9.40(7.65–11.8)
Neutrophil level*10 ⁹ /L, median (IQR)	7.35(5.50–9.92)

	All patients(n = 143)
Lymphocyte level*10 ⁹ /L, median (IQR)	1.45(1.02–1.90)
NLR, median (IQR)	5.67(2.97–8.49)
Serum glucose(mmol/L), median (IQR)	7.36(6.00-10.02)
Complications	
ICH	38(26.6%)
sICH	21(14.7%)
others	5(3.5%)
Clinical Outcomes	
Favorable clinical outcomes, n (%)	48(33.6%)
Mortality, n (%)	34(23.8%)

Table 2 showed clinical outcomes and incidence of complications following univariable and multivariable analysis. More patients with the favorable clinical outcome (mRS 0–2) were treated through single attempt of stent retrieval than those through multiple attempts ($p = 0.02$). Patients treated through single attempt of stent retrieval showed as lower incidence of ICH ($p = 0.005$) and sICH ($p = 0.001$) compared to the multiple attempts group. The mortality ($p = 0.181$) and the incidence of other complications ($p = 0.406$), including reocclusion, distal embolization or ischemic refusion damage, did not differ between single and multiple attempts of stent retrieval. Table 2 also showed that single attempt of stent retrieval was not independently related to the incidence of ICH ($p = 0.876$; adjusted OR [95%CI]: 0.914 [0.294–2.843]), but was independently related to the incidence of sICH ($p = 0.046$; adjusted OR [95%CI]: 0.192 [0.038–0.973]). The favorable clinical outcomes were independently associated with single attempt of stent retrieval ($p = 0.016$; adjusted OR [95%CI]: 2.652 [1.204–5.843]). This suggested that single attempt of stent retrieval could decrease the incidence of sICH and improve favorable clinical outcomes compared with multiple attempts.

Table 2

Single Attempt of Stent Retrieval for Complications and Prognosis of Acute Ischemic Stroke

	Univariable Analysis			Multivariable Analysis		
	Single attempt (n = 69)	Multiple attempts(n = 74)	P value	P value	Adjusted OR	95%CI
Complications						
ICH	11(15.9%)	27(36.5%)	0.005	0.876	0.914	0.294– 2.843
sICH	3(4.3%)	18(24.3%)	0.001	0.046	0.192	0.038– 0.973
others	1(1.4%)	4(5.4%)	0.406	/	/	/
Clinical Outcomes						
Favorable clinical outcomes, n (%)	32(46.4%)	16(21.6%)	0.002	0.016	2.652	1.204– 5.843
Mortality, n (%)	13(18.8%)	21(28.4%)	0.181	/	/	/

To further analyze the factors associated with single attempt of stent retrieval, the detailed characteristics of the patients were assessed in Table 3. There were no significance differences between single and multiple attempts of stent retrieval upon the analysis of most factors through univariable analysis including age ($p = 0.400$), male ($p = 0.100$), hypertension ($p = 0.124$), atrial fibrillation ($p = 0.419$), a history of ischemic stroke ($p = 0.404$), smoking ($p = 0.726$), NIHSS scores ($p = 0.968$), ASPECTS ($p = 0.270$), symptom onset to groin puncture time ($p = 0.182$), endovascular treatment beyond the time window ($p = 0.563$), intravenous thrombolysis (IVT) ($p = 0.873$), occlusion sites ($p = 0.154$), distal occlusion in tandem occlusion ($p = 0.377$), stroke causes ($p = 0.692$), leukocyte levels ($p = 0.374$), neutrophil levels ($p = 0.222$), lymphocyte levels ($p = 0.864$), neutrophil to lymphocyte ratio (NLR) ($p = 0.241$) and blood glucose levels ($p = 0.076$). Only diabetes mellitus showed significant differences between single and multiple attempts of stent retrieval ($p = 0.023$). Table 3 shows the multivariable analysis of the independent factors for single attempt of stent retrieval and its associated factors ($p < 0.1$). Blood glucose levels were not independent an independent factor related to single attempt of stent retrieval ($p = 0.135$; adjusted OR [95%CI]: 1.745 [0.841–3.620]), whilst single attempt was associated with diabetes mellitus ($p = 0.026$; adjusted OR [95%CI]:2.871 [1.137–7.249]). However, blood glucose levels only differed in those with or without diabetes mellitus, which may influence the data. We therefore divided patients into those with diabetes mellitus and those without diabetes mellitus and further analyzed the relationship between blood glucose levels and stent retrieval. Figure 2A showed no significant differences in blood glucose levels between single and multiple attempts of stent retrieval in patients with diabetes mellitus (11.29 [10.37–14.22] versus 11.0 [8.42–12.66], $p = 0.221$). Figure 2B also showed a non-significant difference in patients without diabetes mellitus (6.53 [5.89–8.20] versus 6.77 [5.72–8.23], $p = 0.662$). Subgroup

analysis suggested that blood glucose levels were not related to single attempt of stent retrieval, and that only diabetes mellitus represent an independent factor for single attempt.

Table 3

Univariable Analysis and Multivariable Analysis on Single Attempt and Multiple Attempts of Stent Retrieval

	Univariable Analysis		Multivariable Analysis			
	Single attempt (n = 69)	Multiple attempts(n = 74)	P value	P value	Adjusted OR	95%CI
Baseline Characteristics						
Age, median (IQR)	62(56–67)	64(56–71)	0.4	/	/	/
Male sex, n (%)	55(79.7%)	50(67.6%)	0.1	/	/	/
Hypertension, n (%)	46(66.7%)	40(54.1%)	0.124	/	/	/
DM, n (%)	20(29.0%)	10(13.5%)	0.023	0.026	2.871	1.137–7.249
AF, n (%)	19(27.5%)	25(33.8%)	0.419	/	/	/
History of ischemic stroke, n (%)	16(23.2%)	13(17.6%)	0.404	/	/	/
Smoking, n (%)	26(37.7%)	30(40.5%)	0.726	/	/	/
NIHSS score, median (IQR)	14(11–18)	14(11–17)	0.968	/	/	/
ASPECTS, median (IQR)	9(8–10)	8(7–10)	0.27	/	/	/
OTP (min), median (IQR)	254(178–350)	275(216–360)	0.182	/	/	/
EVT beyond time window	14(20.3%)	18(24.3%)	0.563	/	/	/
IVT, n (%)	16(23.2%)	18(24.3%)	0.873	/	/	/
Occlusion sites, n (%)			0.154	/	/	/
ICA	7(10.1%)	18(24.3%)				
M1	32(46.4%)	32(43.2%)				
M2	2(2.9%)	3(4.1%)				
BA	16(23.2%)	12(16.2%)				
Distal Occlusion in Tandem Occlusion	12(17.4%)	9(12.2%)	0.377	/	/	/
Stroke cause, n (%)			0.692	/	/	/
LAA	37(53.6%)	35(47.3%)				

	Univariable Analysis		Multivariable Analysis			
Cardioembolic	19(27.5%)	25(33.8%)				
Others	13(18.8%)	14(18.9%)				
Baseline measurement in laboratory test			/	/	/	
Leukocyte level*10 ⁹ /L, median (IQR)	9.20(7.50–11.60)	9.60(7.83-12)	0.374	/	/	/
Neutrophil level*10 ⁹ /L, median (IQR)	6.90(5.38–9.74)	7.54(5.61–10.36)	0.222	/	/	/
Lymphocyte level*10 ⁹ /L, median (IQR)	1.43(1.01–1.98)	1.48(1.02–1.86)	0.864	/	/	/
NLR, median (IQR)	4.79(2.67–8.40)	5.98(3.41–8.87)	0.241	/	/	/
Serum glucose(mmol/L), median (IQR)	7.69(6.04–10.52)	6.89(5.79–8.95)	0.076	0.135	1.745	0.841–3.620

Discussion

In previous studies, no more than three attempts of stent retrieval during EVT were deemed optimal to ensure high recanalization rates to decrease the risk of complications. Although no more than three attempts of stent retrieval can ensure relatively high recanalization rates and decrease complications for favorable clinical outcomes, increasing attempts lead to hemorrhagic transformation after EVT due to the increased likelihood of artery injury by retriever devices that target the lesions, which can worsen the prognosis of AIS patients [19]. Thus, single attempt of stent retrieval should be advocated.

In this study, we also found that patients with diabetes mellitus were independently associated with single attempt of stent retrieval. It should be noted that all diabetic patients were confirmed before admission and all of them received the same medicine treatment before EVT. However, admission with randomized blood glucose levels from blood biochemical examinations were not independently related to single attempt of stent retrieval by univariable, multivariable, or even subgroup analysis. High blood glucose levels may exist in patients without diabetes mellitus due to stress reactions after symptom onset, but only admission blood glucose levels may represent potential factors associated with the attempts of stent retrieval. Table 3 showed the admission glucoses assessed by multivariable analysis, which was identified as a potential factor by univariable analysis, but not as an independent factor, suggesting that the admission blood glucose levels were not the reason why diabetes mellitus patients tended to receive single attempt of stent retrieval. In contrast, an abnormal status in patients with diabetes mellitus may explain the occurrence of single attempt of stent retrieval. It was previously shown

that thrombus and stents are adhesive due to the fibrin networks of the dense thrombus surface, determined by a range of initiators of thrombus formation [20]. Patients with diabetes mellitus show accelerated clot initiation caused by platelet activity and hypercoagulation, and adverse reaction milieu characteristics due to diabetes mellitus lead to a dysregulated clotting system [21, 22]. In addition, diabetes mellitus indicates the formation of more compact fibrin networks in the thrombi [23], whilst red blood cells in the thrombi are mainly captured by fibrin networks during thrombi formation[24]. Meanwhile, it was found that the histopathological structure of the thrombi is dictated by high levels of red blood cells that contribute to high recanalization rates and single attempt of stent retrieval [25, 26]. This supports the high occurrence of single stent retrievals in diabetes mellitus patients. However, no direct evidence has reported the relationship between diabetes mellitus and red blood cells in intracranial thrombi. This study explains the primary reason for single attempt of stent retrieval caused by diabetes mellitus, and further studies should focus on the mechanism of diabetes mellitus in intracranial thrombi formation and the relationship between diabetes mellitus and red blood cells in the intracranial thrombi.

This clinical retrospective analysis had some limitations. Statistical bias may have occurred as all patients were enrolled from a single center and the sample size was limited. Moreover, we had little information on whether patients with a history of ischemic stroke received antiplatelet therapy and the nature of that therapy prior to EVT. We only recorded preoperative laboratory findings to evaluate factors associated with single attempt of stent retrieval in EVT, and changes in blood composition should also be noted.

In conclusion, single attempt of stent retrieval in EVT can decrease the rates of sICH and improve the functional outcome of AIS patients. Diabetes mellitus was identified as an independent factor associated with single attempt of stent retrieval. Namely, patients with diabetes mellitus may receive single stent retrievals during EVT for AIS.

Abbreviations

EVT: Endovascular Thrombectomy; AIS: Acute Ischemic Stroke; mRS: modified Rankin Scale; NIHSS: National Institute of Health Stroke Scale; APECTS: Alberta Stroke Program Early Computed Tomography Score; mTICI: modified Thrombolysis in Cerebral Infarction; ICH: Intracranial Hemorrhage; sICH: symptomatic Intracranial Hemorrhage; ICA: Internal Carotid Artery; M1: M1 segment of the middle cerebral artery; M2: M2 segment of the middle cerebral artery; BA: Basilar Artery; IVT: Intravenous Treatment; OTP: Symptom Onset to Groin Puncture Time; IQR: Interquartile Range; LAA: Large Artery Arteriosclerosis; t-PA: Tissue-type Plasminogen Activator; NLR: Neutrophil to Lymphocyte Ratio;

Declarations

Ethical approval and consent to participate

This study was approved by the Ethics Committee of the Second Affiliated Hospital of Harbin Medical University (HMU). All patients received written consent before endovascular thrombectomy. This study conformed to the standards set by the Declaration of Helsinki and was approved by the medical ethics committee of HMU. The study participants agreed to participate and provided written informed consent.

Consent for publication

Not applicable.

Conflict of interest statement:

The authors declare that they have no competing interests.

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Author Contributions

Ruiyan Li provide the funding;

Ruiyan Li, Mingli Liu, Yang Liu designed the research study;

Mingli Liu, Yang Liu collected the clinical data;

Mingli Liu, Yang Liu and Lin Lin analyzed the data;

Ruiyan Li, Yongli Li and Yan Feng contributed to the procedure of operation and related clinical work;

Mingli Liu wrote the paper;

Rui wang and Jinqun Cai revised the paper.

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None

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Figures

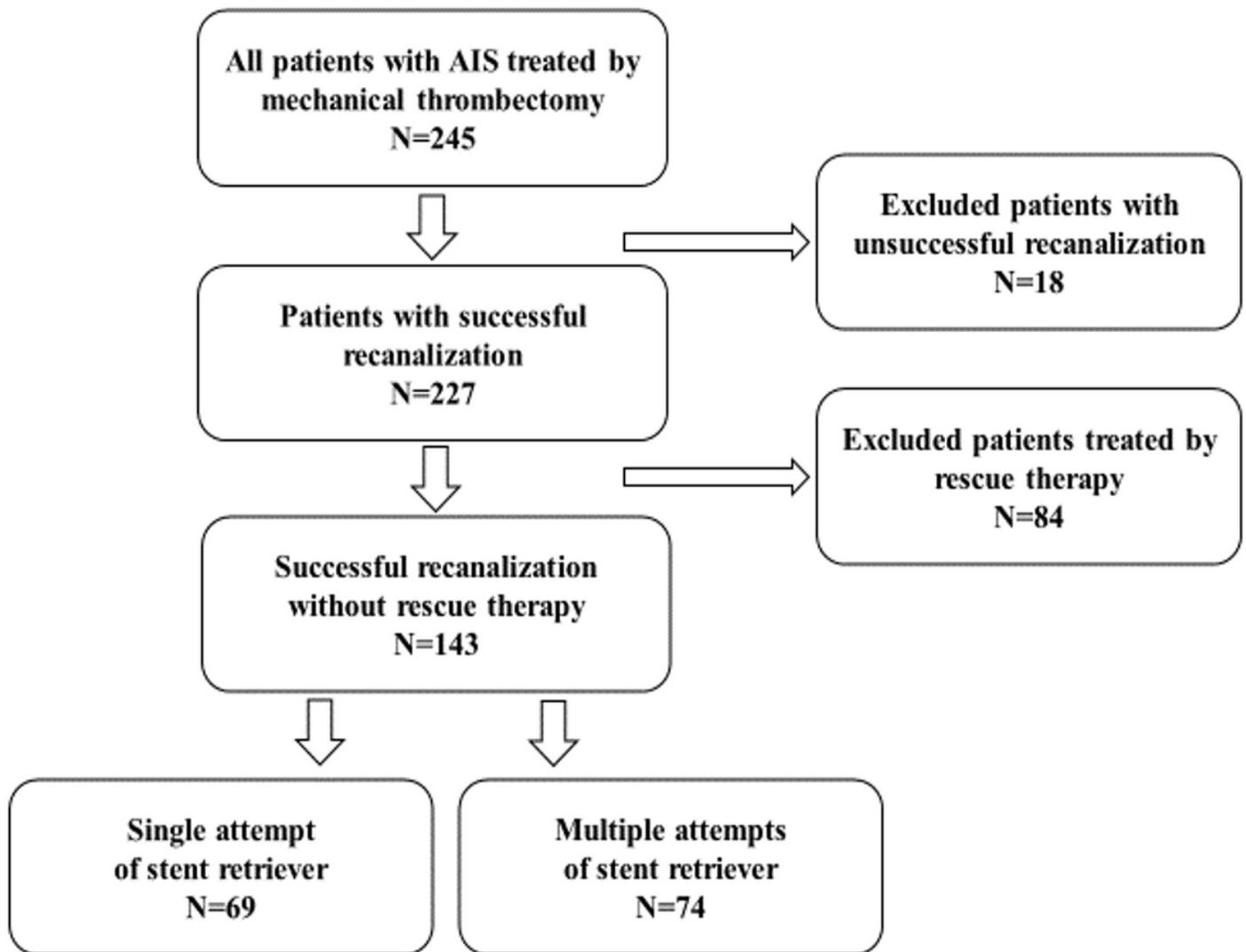


Figure 1

Inclusion and Exclusion Flow Chart. Recanalization was defined as mTICI 2b or 3; Rescue therapies included balloon angioplasty, stent implantation or intra-arterial thrombolysis.

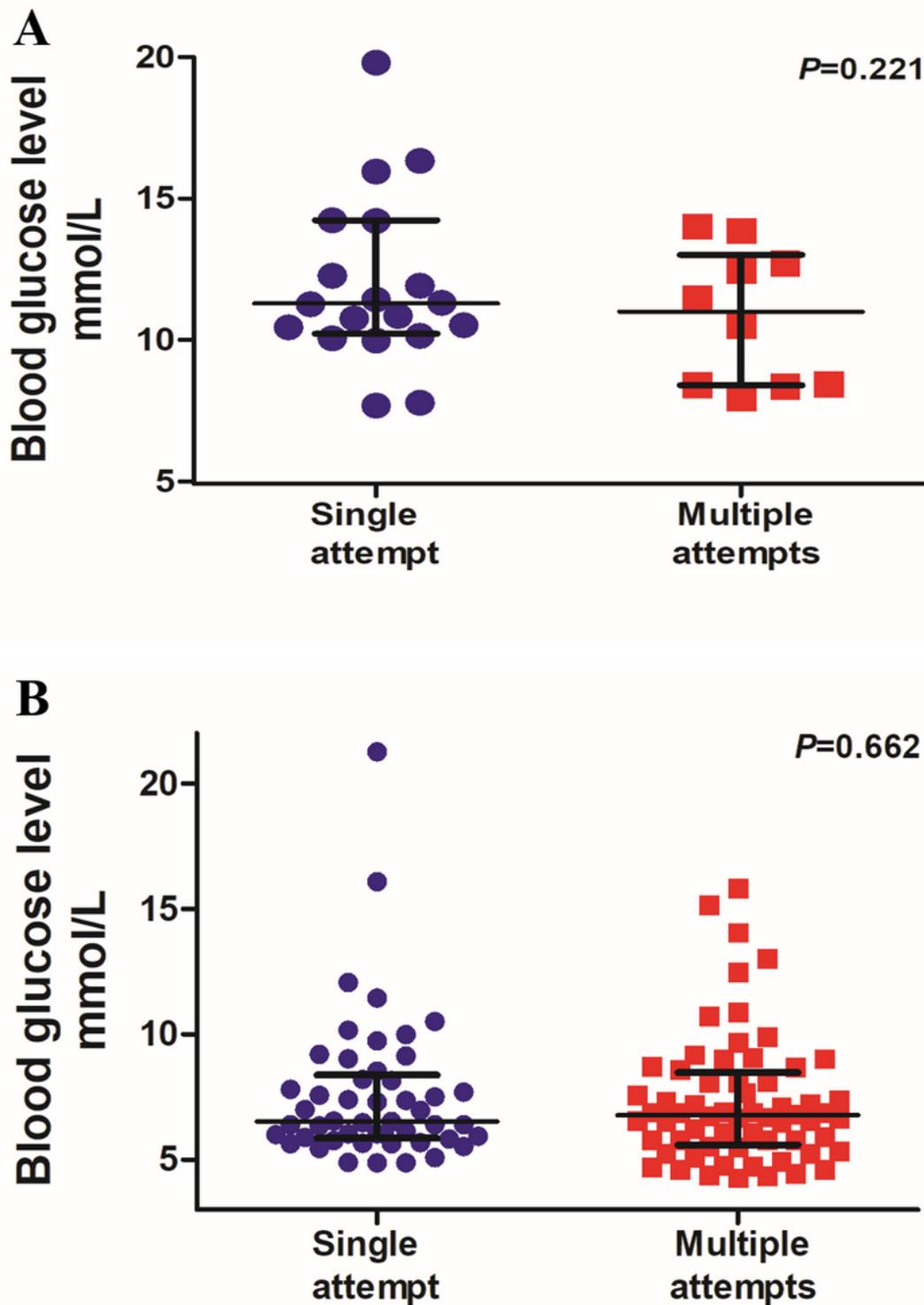


Figure 2

Relationship between Stent Retrieval and Blood Glucose Levels. A. No significant differences in blood glucose levels were observed between single and multiple attempts of stent retrieval in patients with diabetes mellitus [11.29 (10.37-14.22) versus 11.0 (8.42-12.66), $p=0.221$]. B. No significant differences in blood glucose levels were observed between single and multiple attempts of stent retrieval in patients without diabetes mellitus [6.53 (5.89-8.20) versus 6.77 (5.72-8.23), $p=0.662$].