Rescue Therapy in Endovascualr Treatment for Acute Ischemic Stroke Due to Large Artery Atherosclerosis

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Abstract

Background and purpose Safety and predictors of rescue therapy in patients with acute ischemic stroke due to large artery atherosclerosis still remain unclear. This study aimed to test safety of rescue therapy and evaluate predictors of it after failed mechanical thrombectomy.

Methods This retrospective study enrolled consecutively 245 patients with acute ischemic stroke treated by endovascular treatment from March 2016 to April 2019 in a single stroke center. We analyzed the clinical data and laboratory test for safety and predictors of rescue therapy. Binary logistic analysis was applied to confirm the independently relationship.

Results There were totally 145 patients enrolled among 245 patients. Rescue therapy was independently associated with the excellent outcome [p=0.048, adjusted OR: 2.655, 95%CI: 1.008 – 6.989] and longer procedure time of endovascular treatment [p=0.004, adjusted OR: 3.722, 95%CI: 1.519-9.122], but there was no significance on complications and mortality. Prestrike incidence [p=0.004, adjusted OR:4.427, 95%CI:1.618-12.114], use of rt-PA [p=0.003, adjusted OR:4.792, 95%CI:1.688-13.602], tandem occlusion [p=0.001, adjusted OR:0.021, 95%CI:0.002-0.194], PLT [p=0.012, adjusted OR:3.234, 95%CI:1.289-8.113], P-LCR>42.3% [p=0.031, adjusted OR:0.132, 95%CI:0.021-0.827] were independent predictors of rescue therapy.

Conclusions Rescue therapy for acute ischemic stroke due to large artery atherosclerosis costs more procedure time of endovascular treatment, but it can successfully recanalize the occlusive large artery and is independently related to the excellent clinical outcome without increasing ICH, sICH, reocclusion and others. Prestroke incidence, use of rt-PA, tandem occlusion, PLT and P-LCR may be independent predictors of rescue therapy in acute ischemic stroke due to large artery atherosclerosis.

Introduction

After safety and efficient of mechanical thrombectomy proved by 5 randomized clinical trials, Mechanical thrombectomy was widely recommended by the most neurologists for acute ischemic stroke[1–5]. However, according to a meta-analysis of the randomized clinical trials, the recanalization failure was 29%[6], and recanalization failure is still the most focused problem. As we known, successful recanalization is the key to the good outcome for patients with acute ischemic stroke.[7] In all causes of stroke, large artery atherosclerosis is most common in Asian patients[8], and unsuccessful recanalization is more attributed to large artery atherosclerosis which is more susceptible to artery reocclusion during or after successful mechanical thrombectomy[9, 10].

Rescue therapy, including balloon angioplasty, stenting and intra-artery thrombolysis, can prevent artery reocclusion during mechanical thrombectomy or after mechanical thrombectomy in real world, especially balloon angioplasty and stenting which are used most widely. Although only intracranial stenting for failed mechanical thrombectomy have been reported before[11], balloon angioplasty is also used as rescue therapy[12]. However, safety of balloon angioplasty and stenting for failed mechanical thrombectomy which are treated as rescue therapy, and which kind of factors can lead to rescue therapy in patients with acute ischemic stroke due to large artery atherosclerosis still remain unclear. Additional, use of rescue therapy is also controversial in the recent relevant guideline[13]. Now, this retrospectively clinical study aims to explore to the safety of balloon angioplasty and stenting as rescue therapy for failed mechanical thrombectomy and the factors led to rescue therapy in patients with acute ischemic stroke due to large artery atherosclerosis.

Methods

Patients Enrollment and Data Collection

This retrospective clinical study enrolled consecutively 246 patients with acute ischemic stroke treated by endovascular treatment from March 2016 to April 2019 in Second Affiliated Hospital of Harbin Medical University, and it was approved by the ethic committees of Second Affiliated Hospital of Harbin Medical University.

All patients conformed to the indications of endovascular thrombectomy for acute ischemic stroke: (1) Diagnosed with acute ischemic stroke; (2) A large intracranial artery occlusion; (3)Aged ≥18 years; (4) The premorbid modified Rankin Scale (mRS) score of <2; (5) The pretreatment National Institutes of Health Stroke Scale (NIHSS) score ≥6 and Alberta Stroke Program Early Computed Tomography Score (ASPECTS) ≥6; (6) Treated within 6 hours of stroke onset, or treated within 6 to 16 hours which meet DAWN or DEFUSE 3 eligibility criteria[14, 15]; (7) Diagnosed without concomitantly potential intracranial hemorrhagic diseases, such as aneurysm or arteriovenous malformation. And we further filtrated the required patients based on the following included criteria: patients with acute ischemic stroke due to large artery atherosclerosis based on TOAST classification[16]. All patients were separated from mechanical thrombectomy group and rescue therapy group for further data analysis.

All data obtained from Second Affiliated Hospital of Harbin Medical University mainly included clinical data and laboratory data. Clinical data mainly contained age, sex(male), previous medical history, smoking defined as a patient who had smoked continuously for 6 months with ≥1 cigarette per day and assessment for the severity of patients, such as admission NIHSS by physical examination and ASPECTS by a cranial computed tomography scans (CT) or magnetic resonance imaging (MRI). Moreover, patients treated with recombinant tissue plasminogen activator (rt-PA) before endovascular treatment, symptom onset to groin puncture time (OTP), number of patients treated within 6 h to 16h, and occlusion sites, judged by computed tomography angiography (CTA) or magnetic resonance angiography (MRA), and confirmed by digital substraction angiography (DSA), were also included. The complications included by intracranial hemorrhage (ICH), symptomatic intracranial hemorrhage (sICH), reocclusion and others such as ischemia reperfusion damage and distal embolism. The modified Rankin Scale (mRS) at 90 days after endovascular treatment for the outcome of patients was usually assessed by telephone follow-up, and mRS 0-2 was considered as functional independence[17]. In addition, the clinical outcome assessed by mRS at 90 days in this study mainly included the excellent outcome (mRS 0-1), the favorable outcome (mRS 0-2) and mortality. Laboratory data from blood routine examination tested by Second Affiliated Hospital of Harbin Medical University mainly contained platelet amount (PLT), mean platelet volume (MPV), plateletocrit (PCT), Platelet distribution width (PDW) and platelet -larger cell ratio (P-LCR), and we analyzed the ratio of laboratory tests on related platelets beyond the normal range between rescue therapy and mechanical thrombectomy, such as MPV, PCT, PDW, or P-LCR. The factors analysis on rescue therapy included all above data except the aspects of complications and mRS at 90 days which were analyzed on safety of rescue therapy in endovascular treatment.

Procedure and Post-procedure on Endovascular Treatment

Endovascular treatment was performed under local anesthesia or general anesthesia in all enrolled patients. The enrolled patients would be treated with intravenous rt-PA treatment within 4.5 hours of symptom onset, and direct thrombectomy without intravenous rt-PA treatment beyond 4.5 hours from symptom onset was also performed in some patients. Mechanical thrombectomy was performed by SOLUMBRA technique, that is stent retriever combined with the non-contact aspiration technique with intracranial support catheter for all enrolled patients[18]. Modified Thrombolysis in Cerebral Infarction Score (mTICI) 2b or 3 would be considered as successful recanalization[19], and if the occlusion sites were not successfully recanalized after three attempts of stent retriever, rescue therapy would be adopted[20]. Balloon angioplasty and stenting were performed at the discretion of operator. Briefly, balloon angioplasty would be first attempted after failed mechanical thrombectomy, and stenting would be adopted after failed recanalization with balloon angioplasty. Furthermore, Patients with tandem lesion were adopted by carotid stenting with antithrombotic agents for the proximal occlusion based on the previous report[21], which was not defined as rescue therapy in this study.

Because the stroke cause of all enrolled patients with acute ischemic stroke in this study were large artery atherosclerosis based on TOAST classification. Tirofiban as the main anti-platelet therapy was injected through intravenous treatment in this single center[22].

Image Analysis

Patients after endovascular treatment received CT or MRI within 48 hours or any symptoms of functional impairment happened again after endovascular treatment. And image analysis after endovascular treatment mainly included ICH, sICH and reocclusion. ICH was diagnosed and classified according to Heidelberg Bleeding Classification by CT after endovascular thrombectomy[23], and sICH was diagnosed when ICH followed any of the following conditions: (1) NIHSS score increased >4 points than that immediately before worsening; (2) NIHSS score increased >2 points in 1 category; deterioration led to intubation, hemicraniectomy, external ventricular drain placement, or any other major interventions. Reocclusion was primarily evaluated by MRA, and further confirmed by DSA. Two physicians reviewed the CT and MRI results independently. In case of disagreement, a third physician was invited for a final decision.

Statistical Analysis

Statistical analysis was performed with SPSS 22.0 (IBM, Armonk, NY).

All categorical variables were presented as number and frequency (%), and continuous variables were presented as the median and interquartile range (IQR). Student T test or Mann-Whitney U test for continuous variables, χ2 or Fisher exact tests for categorical variables on univariable analysis and multivariate binary logistic regression analysis was performed for independent relationship, we included variables with a potential association (p<0.1) in the univariate analysis. p<0.05 was considered as statistical significance with adjusted odds ratio (OR) and 95% confidence interval (95%CI).

Results

There were totally 145 patients enrolled in this study among 245 patients with acute ischemic stroke from March 2016 to April 2019 in Second Affiliated Hospital of Harbin Medical University. Notably, all enrolled patients were treated by mechanical thrombectomy with SOLITAIRE FR (Medtronic, USA), and balloon angioplasty with GATEWAY (Boston Scientific, USA) and stenting with SOLITAIRE AB (Medtronic, USA) were adopted in patients treated by rescue therapy. 87 patients in mechanical thrombectomy group and 58 patients in rescue therapy group were analyzed with the factor's analysis on rescue therapy and safety of rescue therapy in endovascular treatment. Collected data of all enrolled patients were showed in Table 1.

As the Table 1 shown, all of the enrolled patients with acute ischemic stroke due to large artery atherosclerosis were successful recanalized. There was significant difference on groin puncture to recanalization time between rescue therapy group and mechanical thrombectomy group in Figure 1[90min (70min-147.5min) vs 75min (52.5min-100min), p=0.013]. Complications included ICH [12.1% vs 17.2%, p=0.395], sICH [8.6% vs 11.5%, p=0.578], reocclusion [3.4% vs 4.6%, p=1.000] and others [10.3% vs 4.6%, p=0.316] were not all significant between rescue therapy and mechanical thrombectomy in Figure 2. The clinical outcome of all enrolled patients after endovascular treatment between mechanical thrombectomy and rescue therapy was shown in Figure 3. The favorable outcome [43.1% vs 36.8%, p=0.445] and mortality [31.0% vs 28.7%, p=0.767] showed insignificance between these both groups, but the excellent outcome [37.9% vs 20.6%, p=0.023] of both groups showed significance. In binary logistic regression analysis, rescue therapy was independently associated with the excellent outcome [p=0.048, adjusted OR: 2.655, 95%CI: 1.008 – 6.989] and longer time of the procedure of endovascular treatment [p=0.004, adjusted OR: 3.722, 95%CI: 1.519-9.122]. All above analysis results shows that rescue therapy can solve effectively the failed mechanical thrombectomy without increasing significantly the incidence of complications than mechanical thrombectomy, but rescue therapy costs more time on the procedure of endovascular treatment. The favorable outcome and mortality of patients treated by rescue therapy is not significantly more than mechanical thrombectomy, but the excellent clinical outcome of patients is independently correlated with rescue therapy. Thus, it suggests that although rescue therapy needs more time to recanalize the occlusion artery, it is safe after failed mechanical thrombectomy.

We also analyzed all clinical risk factors and laboratory test on related platelets in Table 2. There was no difference between patients treated by rescue therapy and mechanical thrombectomy on age [61(52-67) vs 62(56-68), p=0.359], male [74.1% vs 83.9%, p=0.15] and smoking [50.0% vs 44.8%, p=0.541]. This part of data also showed no difference on medical history of patients, including hypertension [74.1% vs 64.4%, p=0.216], diabetes mellitus [24.1% vs 20.7%, p=0.624], coronary artery disease (CAD) [13.8% vs 13.8%, p=1.000], prestrike incidence [34.5% vs 20.7%, p=0.064]. On aspect of pre-procedure assessment of endovascular treatment, those were also insignificant between both group on admission NIHSS [13 (9-19) vs 14 (11-19), p=0.27], ASPECTS [9 (8-10) vs 8 (8-9), p=0.466] and symptom onset to groin puncture time [266.5 min (182 min-359 min) vs 292 min (196.5 min-389 min), p=0.285]. In this study, some patients with acute ischemic stroke received endovascular treatment beyond standard time window, which was within 6 hours after symptom onset, and these patients met DAWN or DEFUSE 3 eligibility criteria[14, 15]. Thus, we analyzed this part of patients who were defined as patients with time beyond time window, and this factor was also insignificant between rescue therapy and mechanical thrombectomy [24.1% vs 31.0%, p=0.366]. Patients treated by rt-PA before endovascular treatment between rescue therapy and mechanical thrombectomy showed significantly difference [37.9% vs 18.4%, p=0.009]. According to primary judgement from CTA or MRA and final confirmation from DSA, the occlusion sites in this both groups mainly contained internal carotid artery (ICA) [29.3% vs 16.1%], middle cerebral artery (MCA) [24.1% vs 31.0%], basilar artery (BA) [34.5% vs 24.1%] and vertebral artery (VA) [10.3% vs 2.3%]. The occlusion sites were not significant between patients treated by rescue therapy and mechanical thrombectomy [p=0.102]. However, tandem occlusion, only enrolled in the endovascular treatment for the distal intracranial artery occlusion, was significant between rescue therapy group and mechanical thrombectomy group [1.7% vs 26.4%, p<0.001]. There were also the significant difference on some laboratory tests on related platelets between both groups, including platelet amount (PLT*10^9) [225(194-269) vs 206(151-253), p=0.036], plateletocrit (PCT>17.0) [1.7% vs 10.3%, p=0.045], platelet-larger cell ratio (P-LCR>42.3%) [3.4% vs 18.4%, p=0.008], but mean platelet volume (MPV>11.0fl) [46.6% vs 56.3%, p=0.129] and platelet distribution width (PDW>0.23%) [70.7% vs 57.5%, p=0.107] showed no difference between rescue therapy and mechanical thrombectomy.

In multivariate binary logistic regression analysis, we analyzed all factors with a potential association (p<0.1) after univariate analysis in Table 3. Prestrike incidence [p=0.004, adjusted OR:4.427, 95%CI:1.618-12.114], use of rt-PA [p=0.003, adjusted OR:4.792, 95%CI:1.688-13.602], tandem occlusion [p=0.001, adjusted OR:0.021, 95%CI:0.002-0.194], PLT [p=0.012, adjusted OR:3.234, 95%CI:1.289-8.113], platelet-larger cell ratio(P-LCR>42.3%) [p=0.031, adjusted OR:0.132, 95%CI:0.021-0.827] were independent predictors of rescue therapy after multivariate analysis.

Discussion

It has been reported by the clinical randomized trials for a few years that mechanical thrombectomy is safe and efficient for acute ischemic stroke. Although it effectively improves recanalization of intracranial occlusion arteries, the unsuccessful recanalization is still common, especially patients with acute ischemic stroke due to large artery atherosclerosis. In real world, rescue therapy is mainly applied to the unsuccessful recanalization after mechanical thrombectomy, but the reports about rescue therapy are relatively rare. This study not only reports safety of rescue therapy, but rescue therapy is independently associated with prestroke incidence, use of rt-PA, distal artery embolism in tandem occlusion, platelet amount (PLT) and platelet-larger cell ratio(P-LCR).

Rescue therapy was applied to recanalized failed mechanical thrombectomy in this study, and all of the patients through failed mechanical thrombectomy were successfully recanalized after rescue therapy. It reveals that rescue therapy actually solves the unsuccessful recanalization after mechanical thrombectomy without the significant increasing reocclusion. Although Yoonkyung Chang, et al reported rescue stenting for failed mechanical thrombectomy was efficient and safe and Byung Moon Kim reported balloon angioplasty was also efficient, balloon angioplasty and stenting both have been commonly applied as rescue therapy[11, 12]. There are few reports on whether rescue therapy including balloon angioplasty and stenting are safe, but this study suggests the thoughts on safety of rescue therapy that balloon angioplasty and stenting can improve patients` clinical outcome and cannot increase the incidence of ICH or sICH. However, it is interesting that rescue therapy is only independently associated with the excellent clinical outcome (mRS 0–1), not with the favorable clinical outcome. Longer procedure time of rescue therapy may be the reason, because the previous reports suggested shortening recanalization time of endovascular treatment affected the clinical outcome. Although rescue therapy can develop successful recanalization rate, it is not the first choice for acute ischemic stroke. Rescue therapy was applied after failed mechanical thrombectomy, that is still the existence of occlusion or below mTICI 2b after 3 attempts of stent retriever, to inevitably increase the procedure time of endovascular time in this study. Nevertheless, it showed the importance of rescue therapy that the excellent clinical outcome was still associated with rescue therapy under longer recanalization time. Further study for decreasing he procedure time of endovascular treatment for better clinical outcome can focus on whether it is feasible that rescue therapy may be applied after failed mechanical thrombectomy with single attempts of stent retriever in patients with acute ischemic stroke due to large artery atherosclerosis who are susceptible to rescue therapy.

Yang-Ha Hwang, et al reported that in situ thrombo-occlusion with underlying intracranial atherosclerotic disease may contribute to residual stenosis which leads to instant or delayed reocclusion in intracranial large artery atherosclerosis disease[24]. It may be that residual stenosis exists in patients with acute ischemic stroke due to large artery atherosclerosis who were ever subjected to ischemic stroke[25]. One of causes led to rescue therapy in large artery atherosclerosis is repeatedly reocclusion during the procedure, and residual stenosis in patients with prestroke incidence may be the key to the repeatedly reocclusion. Thus, rescue therapy may be actually more easily to happen to patients with prestroke incidence.

Although endovascular treatment has been verified on efficacy and safety for acute ischemic stroke due to large artery occlusion, use of rt-PA is not denied in the recent guideline[13]. However, it is always controversial on whether patients receive rt-PA in pre-procedure of endovascular treatment. Urs Fischer, et al discussed from the positive and negative viewpoints on direct mechanical thrombectomy or combined intravenous and mechanical thrombectomy, the arguments against using of rt-PA before endovascular treatment mainly focused on recanalization rates, safety, peri-interventional techniques and thrombus fragility and thrombus migration[26]. In this study, the results revealed patients with acute ischemic stroke due to large artery atherosclerosis receiving rt-PA in the pre-procedure of endovascular may be more susceptible to failed mechanical thrombectomy and compelled to receive rescue therapy. The main reason that large artery atherosclerosis evolves to artery occlusion is mainly atherosclerotic plaques disruption that triggers a series of clotting reaction, including platelet activation, adherence and aggregation, and the activating tissue factors[27]. when patients with acute ischemic stroke due to large artery atherosclerosis receive rt-PA before the procedure of endovascular treatment, it may lead to platelet activation or convert fibrinogen to fibrin and indirectly make repeatedly reocclusion during the procedure[28]. Even now we cannot deny the worth of rt-PA in endovascular treatment for acute ischemic stroke, but it can be further studied on which kind of patients with acute ischemic stroke should be treated by intravenous rt-PA before endovascular treatment for facilitating the operation and better clinical outcome.

The data from this study showed recanalizing distal artery occlusion in tandem occlusion might tend to adopt mechanical thrombectomy instead of rescue therapy. Although many operators in real world agree with the fact that recanalizing the distal artery occlusion with mechanical thrombectomy is not more difficult than the proximal occlusion, there are few reports on the reasons why cause this fact. On the contrary, most of the recent reports focus on how to safely and efficiently recanalize the tandem occlusion[29–31]. Histopathologic analysis of the thrombi in the distal artery from the proximal artery occlusion in tandem occlusion may be associated with higher recanalization rates with mechanical thrombectomy in the distal occlusion for further study.

Platelets play a role in evolving from large artery atherosclerosis to occlusion[32, 33], so we analyzed the laboratory test on platelets of patients at admission in this study, that is high PLT and low P-LCR may be related to rescue therapy. Pascal J. Mosimann, et al reported unexpected early reocclusion after successful mechanical thrombectomy was influenced by high platelet amount at admission, and they explained the residual embolic fragments at the occlusion site after mechanical thrombectomy may act as kernels to adhere the higher concentration of circulating platelets for the new thrombi formation at the same site[34]. This point is same as repeatedly reocclusion, treated by rescue therapy, in patients with acute ischemic stroke due to large artery atherosclerosis during the procedure of endovascular treatment, and further verifies that high PLT may be actually the predictor of rescue therapy. However, patients with high P-LCR in the preprocedure may be more susceptible to mechanical thrombectomy instead of rescue therapy. Cengiz Beyan, et al found P-LCR, measuring more than 12 fl in volume, could contain fraction of platelet precursors without displaying the capability of aggregation[35]. It may be that patients with acute ischemic stroke due to large artery atherosclerosis who have higher P-LCR are not easier to exist the situation that reocclusion at the thrombectomy site, which is not suitable for rescue therapy.

Limitations

There are some limitations as a retrospective analysis from a single center. Firstly, all enrolled patients were collected from Second Affiliated Hospital of Harbin Medical University, the data with limitation of sample size from a single center also exist statistical bias. Moreover, although it was independently relationship between rescue therapy and prestroke incidence from this study, there were little information on whether patients with prestroke incidence received antiplatelet medical treatment or which kinds of antiplatelet medical treatment were applied in those patients before endovascular treatment. Patients treated by endovascular treatment beyond 6 hours according to DAWN or DEFUSE 3 eligibility criteria were totally enrolled as a varies for analysis on rescue therapy and mechanical thrombecomty because of not large enough sample size, it can be more persuasive that dividing time period beyond 6 hours for further analysis.

Conclusions

In conclusion, although rescue therapy for acute ischemic stroke due to large artery atherosclerosis, including balloon angioplasty and stenting, costs more procedure time of endovascular treatment, but it can successfully recanalize the occlusion sites after failed mechanical thrombectomy without increasing complications, such as intracranial hemorrhage, symptomatic intracranial hemorrhage, reocclusion and others. And rescue therapy is associated with the excellent clinical outcome. Prestroke incidence, use of rt-PA, tandem occlusion, platelet amount and platelet-large cell ratio may be independent predictors of rescue therapy in acute ischemic stroke due to large artery atherosclerosis, that is patients with prestroke incidence, using of rt-PA before endovascular treatment and higher platelet amount may be susceptible to rescue therapy, as well as patients with the distal artery occlusion in tandem occlusion and higher platelet-large cell ratio may be susceptible to mechanical thrombectomy.

Declarations

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Disclosure Statement:

The authors have nothing to disclosure.

Conflict of interest statement:

The authors declare that they have no competing interests.

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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Tables

Table 1: Clinical data and laboratory data of all enrolled patients

	All patients(N=145)
Age	61(54-67)
Male	116(80.0%)
Hypertension	99(68.3%)
Diabetes mellitus	32(22.1%)
CAD	20(13.8%)
Prestroke Incidence	38(26.2%)
Smoking	68(46.9%)
Admission NHISS	14(11-19)
ASPECTS	8(8 - 9)
Symptom onset to groin puncture time,min	284(194-367)
Treatment beyond time window	41(28.3%)
Use of rt-PA	38(26.2%)
Occlusion sites	
ICA	31(21.4%)
MCA	41(28.3%)
BA	41(28.3%)
VA	8(5.5%)
Tandem Occlusion	24(16.6%)
Successful recanlization	145(100%)
Groin puncturetime to recanalization,min	80(55-115)
Balloon angioplasty	28(19.3%)
Stenting	30(20.7%)
Complications	
ICH	22(15.2%)
sICH	15(10.3%)
Reocclusion	4(2.8%)
others	10(6.9%)
mRS at 90 days	
0 - 1	40(27.6%)
0 - 2	57(39.3%)
Mortality	43(29.7%)
Laborary test	
PLT	214(171-255)
MPV(>11.0fl)	66(45.5%)
PCT(>17.0)	10(6.9%)

PDW(>0.23%)	91(62.8%)
P-LCR(>42.3%)	18(12.4%)

Table 2: Univariate analysis between rescue therapy and mechanical thrombectomy

	Rescue Therapy(N=58)	Mechanical Thrombectomy(N=87)	p value
Age	61(52-67)	62(56-68)	0.359
Male	43(74.1%)	73(83.9%)	0.150
Smoking	29(50%)	39(44.8%)	0.541
Hypertension	43(74.1%)	56(64.4%)	0.216
Diabetes mellitus	14(24.1%)	18(20.7%)	0.624
CAD	8(13.8%)	12(13.8%)	1.000
Prestroke Incidence	20(34.5%)	18(20.7%)	0.064
Admission NHISS	13(9-19)	14(11-19)	0.270
ASPECTS	9(8-10)	8(8-9)	0.466
Symptom onset to puncture time,min	266.5(182-359)	292(196.5-389)	0.285
Treatment beyond time window	14(24.1%)	27(31.0%)	0.366
Use of rt-PA	22(37.9%)	16(18.4%)	**0.009**
Occlusion sites			0.102
ICA	17(29.3%)	14(16.1%)	
MCA	14(24.1%)	27(31.0%)	
BA	20(34.5%)	21(24.1%)	
VA	6(10.3%)	2(2.3%)	
Tandem Occlusion	1(1.7%)	23(26.4%)	**<0.001**
Laborary test			
PLT*10^9	225(194-269)	206(151-253)	**0.036**
MPV(>11.0fl)	27(46.6%)	49(56.3%)	0.129
PCT(>17.0)	1(1.7%)	9(10.3%)	**0.045**
PDW(>0.23%)	41(70.7%)	50(57.5%)	0.107
P-LCR(>42.3%)	2(3.4%)	16(18.4%)	**0.008**

Table 3: Multivariate analysis on predictors of rescue therapy

	p value	adjusted OR	95%CI
Prestroke Incidence	**0.004**	4.427	1.618-12.114
Use of rt-PA	**0.003**	4.792	1.688-13.602
Tandem Occlusion	**0.001**	0.021	0.002-0.194
PLT	**0.012**	3.234	1.289-8.113
PCT(>17.0)	0.549	0.449	0.033-6.142
P-LCR(>42.3%)	**0.031**	0.132	0.021-0.827

Figures

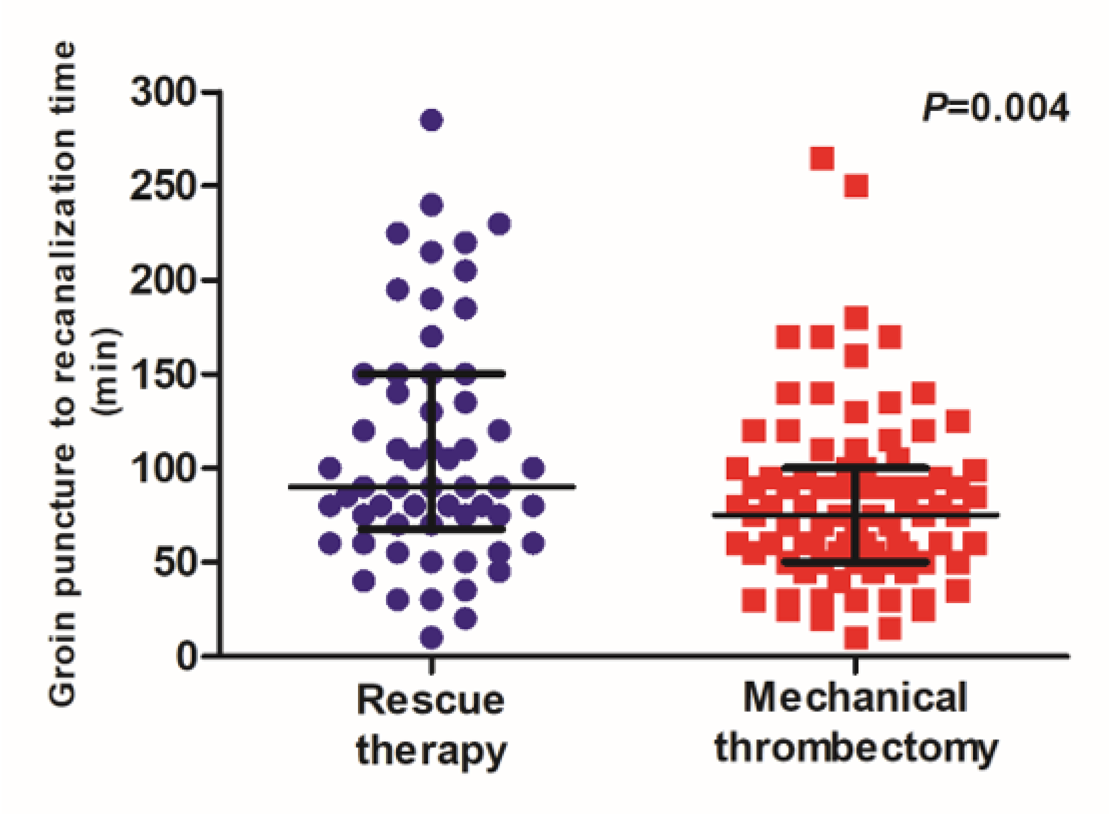

Figure 1

Comparison of rescue therapy and mechanical thrombectomy on groin puncture to recanalization time: There was significant difference on groin puncture to recanalization time between rescue therapy group and mechanical thrombectomy group from univariate analysis [90min (70min-147.5min) vs 75min (52.5min-100min), p=0.013]. Rescue therapy was independently associated with longer time of the procedure of endovascular treatment from multivariate binary logistic analysis [p=0.004, adjusted OR: 3.722, 95%CI: 1.519-9.122].

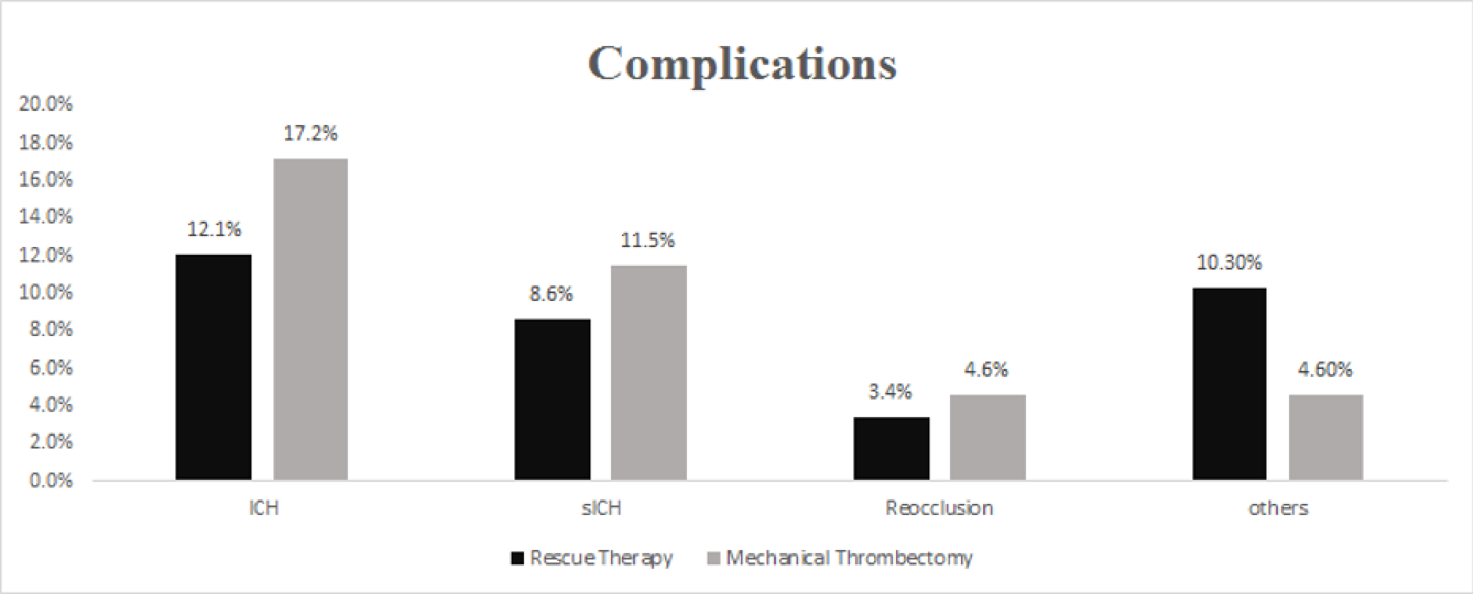

Figure 2

Comparison of rescue therapy and mechanical thrombectomy on complications of endovascular treatment: Complications included ICH [12.1% vs 17.2%, p=0.395], sICH [8.6% vs 11.5%, p=0.578], reocclusion [3.4% vs 4.6%, p=1.000] and others (ischemic reperfusion damage and distal embolism) [10.3% vs 4.6%, p=0.316] were not significant between rescue therapy and mechanical thrombectomy.

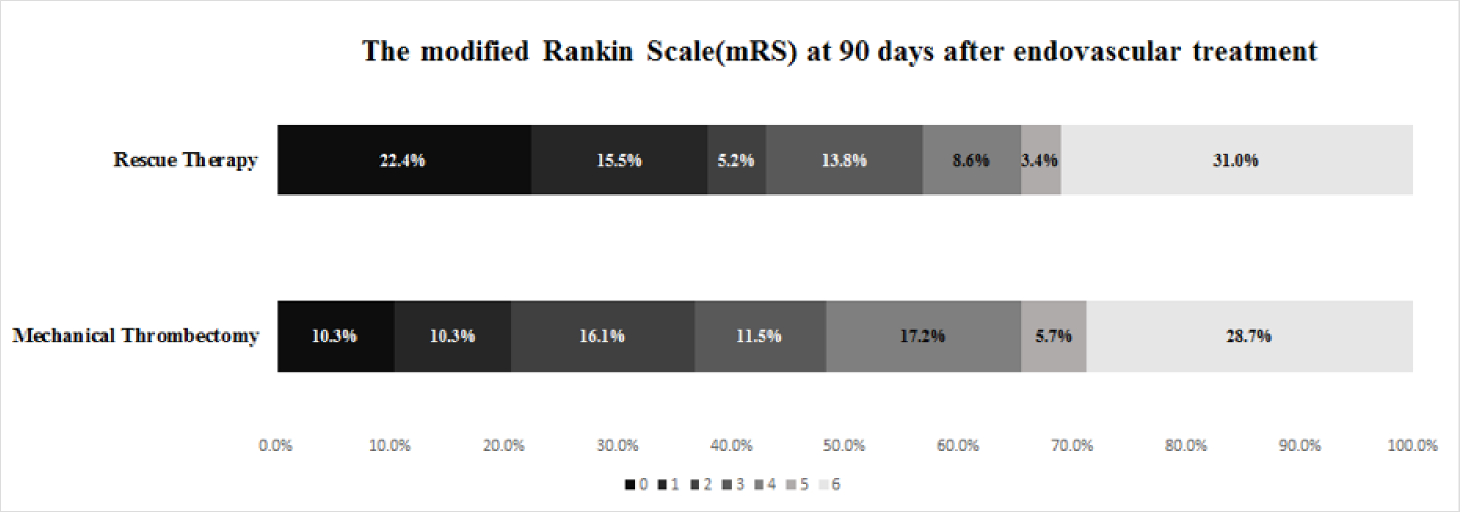

Figure 3

Comparison of rescue therapy and mechanical thrombectomy on mRS at 90 days after endovascular treatment: The favorable outcome (mRS 0-2) [43.1% vs 36.8%, p=0.445] and mortality [31.0% vs 28.7%, p=0.767] showed insignificance between these both groups, but the excellent outcome [37.9% vs 20.6%, p=0.023] of both groups showed significance from univariate analysis. Rescue therapy was independently associated with the excellent outcome (mRS 0-1) from multivariate binary logistic analysis [p=0.048, adjusted OR: 2.655, 95%CI: 1.008 – 6.989].