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# Incidence and predictors of futile recanalisation after endovascular therapy in acute vertebrobasilar artery occlusion patients: insight from the ANGEL-ACT registry

Dapeng Sun ,[1] Xinguang Yang,[1,2] Xiaochuan Huo ,[3] Raynald - ,[1] Baixue Jia ,[1] Xu Tong ,[1] Anxin Wang,[4] Ning Ma ,[1] Feng Gao,[1] Dapeng Mo ,[1] Zhongrong Miao[1]

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DS and XY contributed equally.

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For numbered affiliations see end of article.

**Correspondence to**
Dr Zhongrong Miao;
zhongrongm@163.com

Dr Xiaochuan Huo;
huoxiaochuan@126.com

## ABSTRACT

**Objectives** To identify the occurrence rate and predictors of futile recanalisation after endovascular therapy (EVT) for acute vertebrobasilar artery occlusion (VBAO).

**Methods** Participants of the Endovascular Treatment Key Technique and Emergency Workflow Improvement of Acute Ischaemic Stroke (ANGEL-ACT) registry were selected for the analysis. Futile recanalisation was defined as patients did not achieve a 90-day good outcome (modified Rankin Scale ≤3) despite successful recanalisation (modified Treatment in Cerebral Ischaemia Scale ≥2b) after the procedure. Multivariable logistic regression analysis was conducted to find independent predictors of futile recanalisation in VBAO patients undergoing EVT.

**Results** Three hundred and fifteen patients with VBAO who achieved successful recanalisation after EVT were included in current analysis, of whom, 155 (49.2%) suffered futile recanalisation, and 160 achieved effective recanalisation. After the multivariable analysis, we found admission National Institutes of Health Stroke Scale (NIHSS) ≥19 (OR 4.81, 95% CI 2.76 to 8.39, p<0.001), platelet-lymphocyte ratio (PLR) ≥162.2 (OR 1.93, 95% CI 1.14 to 3.27, p=0.001), onset-to-puncture time (OTP) ≥334 min (OR 2.15, 95% CI 1.25 to 3.68, p=0.005) and use of general anesthesia (GA) (OR 1.87, 95% CI 1.09 to 3.22, p=0.024) were associated with futile recanalisation.

**Conclusions** Futile recanalisation after EVT occurred 49.2% of VBAO patients in the ANGEL-ACT registry. NIHSS≥19, PLR≥162.2, OTP≥334 min and use of GA were independent predictors of futile recanalisation.

### WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ There is little literature about futile recanalisation after endovascular therapy (EVT) for vertebrobasilar artery occlusion (VBAO), especially in the Asian population. Age, initial National Institutes of Health Stroke Scale, Posterior Circulation Alberta Stroke Programme Early CT Score, intravenous thrombolysis, number of passes ≤3 and first pass modified Treatment in Cerebral Ischaemia Scale 2b-3 reperfusion were reported as associated independently with futile recanalisation after EVT for VBAO previously.

### WHAT THIS STUDY ADDS

⇒ We observed that futile recanalisation occurred in 49.2% of patients with VBAO, and added platelet-lymphocyte ratio ≥162.2, onset-to-puncture time ≥334 min and use of general anesthesia as the new predictors of futile recanalisation.

### HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ The rate and several predictors of futile recanalisation after EVT for VBAO have been identified in this analysis, which could add them to the global data.

## INTRODUCTION

Whether endovascular therapy (EVT) is superior to medical therapy for acute ischaemic stroke (AIS) caused by acute vertebrobasilar artery occlusion (VBAO) is still unclear. At present, four randomised controlled trials (RCTs) have been completed. BEST (Basilar Artery Occlusion Endovascular Intervention vs Standard Medical Treatment) and BASICS (Basilar Artery International Cooperation Study) RCTs did not find the superiority of EVT for VBAO.[1 2] However, the other RCTs in China, BAOCHE (Basilar Artery Occlusion Chinese Endovascular Trial) and ATTENTION (Endovascular Treatment for Acute Basilar Artery Occlusion), found that EVT could lead to better outcomes than medical therapy in VBAO patients.[3 4] Among the four RCTs, the successful recanalisation rate in the EVT group varied from 71% to 93% and 90-day good outcome (modified Rankin Scale(mRS) 0–3) rate after EVT varied from 42% to 46%.[1–4] Therefore, there were still some VBAO patients who did not achieve a good outcome at 90 days despite successful

recanalisation after EVT, which we call futile recanalisation. Futile recanalisation of EVT in AIS caused by large-vessel occlusion in the anterior circulation has been explored by many studies.[5] However, regarding the VBAO, especially in the Asian population, the studies are still scarce.[6–11]

Therefore, we conducted an analysis using the data from a Chinese, nationwide, prospective, multicentre, registry database, aiming to explore the rate and predictors of futile recanalisation in VBAO patients undergoing EVT.

## METHODS

### Study population

ANGEL-ACT registry (Endovascular Treatment Key Technique and Emergency Workflow Improvement of Acute Ischaemic Stroke) is a multicentre, prospective registry study, carried out from November 2017 to March 2019 at 111 sites in 26 Chinese provinces. Data were used from the above registry. The exclusion criteria and inclusion criteria, imaging interpretation method, and data collection method were reported previously.[12] The inclusion and exclusion criteria of the current study were that: inclusion criteria: (1) age ≥18 years old; (2) AIS due to LVO; (3) the patient or the patient's legal representative signed the informed consent; (4) undergoing EVT; exclusion criteria: (1) EVT records unavailable; (2) unsuccessful recanalisation; (3) mRS missing at 90 days; (4) posterior cerebral artery occlusion and (5) anterior circulation stroke.

### Data collection

ANGEL-ACT registry collected all information prospectively, such as medical history, demographic characteristics, laboratory results, baseline National Institutes of Health Stroke Scale (NIHSS), vital signs, periprocedural management, procedural variables, key time points and clinical outcomes at 90 days assessed by mRS. The investigators received training and got the qualification certificates to record NIHSS and mRS. By the phone interview, only investigators blinded to all clinical information evaluated mRS at 90 days on the protocol of standardised interview.

ANGEL-ACT registry had an independent neuroimaging core lab to assess all imaging that included digital subtraction angiography, baseline MRI/MR angiography, CT/ CT angiography and CT after the procedure. The imaging interpretation included underlying intracranial atherosclerotic disease, tandem lesion, intraprocedural complications, modified Treatment in Cerebral Ischaemia Scale (mTICI)[13] after the procedure, baseline Posterior Circulation Alberta Stroke Programme Early CT Score (PC-ASPECTS) and haemorrhage transformation after the procedure.

### Futile recanalisation and effective recanalisation

We defined futile recanalisation as VBAO patients experiencing a 90-day poor outcome (mRS 4–6) despite successful recanalisation (mTICI≥2b) after EVT and effective recanalisation as VBAO patients achieving a 90-day good outcome (mRS≤3) with successful recanalisation after EVT.

### Statistical analysis

We used numbers (percentages) to express categorical variables and median (IQR) to express continuous variables. The Mann-Whitney test and Pearson $\chi^2$ test/Fisher's exact test were performed as univariable analyses to perform the comparison of baseline and procedure variables between the futile recanalisation and effective recanalisation groups. Before multivariable analysis, the variance inflation factors were calculated to assess the multicollinearity among the variables with p<0.10 in the univariable analysis. Next, in order to identify the best cut-off values of onset-to-puncture time (OTP), NIHSS, baseline neutrophil-lymphocyte ratio (NLR), procedure duration and baseline platelet-lymphocyte ratio (PLR), to predict futile recanalisation, we performed receiver operating characteristic analyses. Then we converted the NIHSS, PLR, NLR, OTP and procedure duration into two categorical variables according to the best cut-off values. Finally, in order to identify the independent predictors of futile recanalisation, we conducted binary logistic regression analysis with back-stepwise including NLR, PLR, NIHSS, OTP, procedure duration, use of general anaesthesia (GA) and heparin. All statistical analyses were conducted by the SAS software (V.9.4, SAS Institute). A p<0.05 (two tailed) is considered statistical significance.

## RESULTS

As shown in figure 1, 315 of 1793 patients with VBAO in the ANGEL-ACT registry who achieved successful recanalisation were included in this analysis, of whom, 155 experienced futile recanalisation and 160 achieved effective recanalisation.

As shown in table 1, patients with futile recanalisation had higher admission NIHSS (29 (19–35) vs 15 (8–26), p<0.001), higher admission PLR (179.4 (125.8–230.7) vs 149.0 (103.1–215.7), p=0.026), higher admission NLR (7.8 (3.8–11.7) vs 5.8 (3.1–9.3), p=0.018), a higher rate of use of GA (64.5% vs 51.3%, p=0.017) and OTP (341 (230–439) min vs 275 (185–399) min, p=0.007) than those with effective recanalisation.

As shown in table 2, online supplemental file 1, we identified that admission NIHSS≥19 (OR 4.81, 95% CI 2.76 to 8.39, p<0.001), PLR≥162.2 (OR 1.93, 95% CI 1.14 to 3.27, p=0.001), OTP≥334 min (OR 2.15, 95% CI 1.25 to 3.68, p=0.005) and use of GA (OR 1.87, 95% CI 1.09 to 3.22, p=0.024) were related to the futile reperfusion after EVT for VBAO patients after the multivariable logistic analysis .

## DISCUSSION

We found that futile recanalisation of EVT occurred in 49.2% of patients with VBAO, which was similar to the

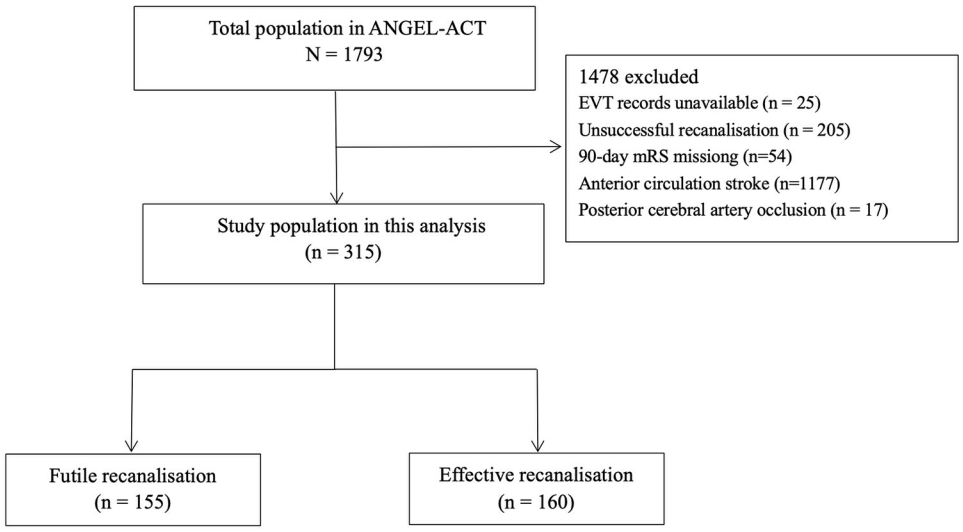


**Figure 1** Flow chart of patient selection. ANGEL-ACT; Endovascular Treatment Key Technique and Emergency Workflow Improvement of Acute Ischaemic Stroke; EVT, endovascular treatment; mRS, modified Rankin scale.

ETIS (Endovascular Treatment in Ischaemic Stroke) registry reported (49.5%) and lower than the BASILAR (Endovascular Treatment for Acute Basilar Artery Occlusion Study) registry reported (62.8%).[10 11] Furthermore, the use of GA, admission NIHSS≥19, PLR≥162.2 and OTP≥334 min could predict independently futile recanalisation after EVT for VBAO.

Several previous studies have investigated the rate and independent predictors of futile recanalisation in VBAO patients undergoing EVT.[6–11] However, the definition of futile recanalisation only in the ETIS registry and BASILAR registry was the same as our study (successful recanalisation after EVT with good outcome (90-day mRS 0–3)).[7 10 11] ETIS registry and BASILAR registry reported that age, initial NIHSS, PC-ASPECTS, intravenous thrombolysis, number of passes≤3, first pass mTICI 2b-3 reperfusion, diabetes mellitus, NLR, procedure duration, incomplete recanalisation and collateral circulation were associated with futile recanalisation.[7 10 11] Our study added that PLR≥162.2, OTP≥334 min and the use of GA as the new predictors of futile recanalisation of EVT for VBAO.

PLR is an easily available parameter before the procedure. Previous studies demonstrated that high admission PLR could predict poor outcomes in patients with AIS.[14–16] Our study first demonstrated that PLR≥162.2 was an independent predictor of futile recanalisation. PLR has been reported as a biomarker that could reflect the inflammation intensity and the thrombotic pathways synthetically.[17] Immune system is activated once AIS occurs. Then the lymphocytes are suppressed, and lymphocyte counts decrease.[18] Low lymphocyte count is a general feature of an inflammatory process, which has been proven by both clinical and animal studies, can also accelerate atherosclerotic progression.[19] Platelets play a critical role in atherosclerotic plaque development, atherosclerotic plaque destabilisation and atherosclerotic plaque rupture, and also in circulating arterial platelet–fibrin thrombus formation.[20] The proinflammatory chemokines released by platelets participate in thrombosis and inflammation, which is also important in the formation of thrombus in reaction to endothelial cell erosion or atherosclerosis plaque rupture.[14] Moreover, when the platelets are activated, they can release inflammatory mediators, which could also aggravate inflammation reaction at the vascular lesion site.[21] Furthermore, platelets also can be in conjunction with neutrophils and fibrinogen, which can damage the blood-brain barrier.[15] Additionally, Li *et al* demonstrated that PLR was associated with a high risk of stroke-related pneumonia, which may also be a reason for poor outcomes of AIS.[22] In summary, it is reasonable and understandable that PLR was associated with the futile recanalisation after EVT for VBAO.

Several previous studies have found that a longer OTP could predict poor outcomes after EVT for VBAO.[23–27] Regarding futile recanalisation, OTP≥334 min was found to be one independent predictor of it in our cohort, which was similar to what Ouyang *et al* reported (futile recanalisation was defined as 90-day mRS 0–2 with successful recanalisation), although different definitions of futile recanalisation in the two studies.[9] Therefore, shortening the time delay before the procedure should be highlighted during the treatment, including early identification of stroke, fast arrival at the stroke centre and rapid intrahospital transport.

The best anaesthesia strategy during the procedure in patients with VBAO is still unknown. Recently, a two-centre RCT demonstrated that VBAO patients undergoing EVT with GA had a similar 90-day mRS 0–2 rate with those with conscious sedation (CS).[28] Similarly, both the BASILR registry and ETIS registry also suggested GA could lead to similar clinical outcomes with local anaesthesia (LA)/CS in VBAO patients after EVT.[29 30] Unlike them, several other studies found GA was associated with poor outcomes in such patients.[25 31] Our study further

**Table 1** Baseline and procedure characteristics of patients with futile recanalisation and effective recanalisation

| Baseline and procedure variables | Futile recanalisation (n=155) | Effective recanalisation (n=160) | P value |
|---|---|---|---|
| Age, years, median (IQR) | 64 (55–72) | 64 (54–72) | 0.499 |
| Male sex, n (%) | 120 (77.4) | 130 (81.3) | 0.401 |
| Admission mode, n (%) | | | 0.490 |
| Mothership | 90 (58.1) | 99 (61.9) | |
| Drip and ship | 65 (41.9) | 61 (38.1) | |
| Hypertension, n (%) | 105 (67.7) | 113 (70.6) | 0.580 |
| DM, n (%) | 37 (23.9) | 33 (20.6) | 0.488 |
| Hyperlipidaemia, n (%) | 18 (11.6) | 26 (16.3) | 0.235 |
| Coronary heart disease, n (%) | 26 (16.8) | 25 (15.6) | 0.782 |
| Atrial fibrillation, n (%) | 21 (13.6) | 23 (14.4) | 0.832 |
| Prior stroke, n (%) | 44 (28.4) | 44 (27.5) | 0.861 |
| Smoking history, n (%) | | | 0.233 |
| Never smoking | 83 (53.6) | 76 (47.5) | |
| Previous smoking | 11 (7.1) | 20 (12.5) | |
| Current smoking | 61 (39.4) | 64 (40.0) | |
| SBP, mmHg | 150 (135–167) | 153 (136–164) | 0.644 |
| Admission NIHSS* | 29(19-35) | 15(8-26) | **<0.001** |
| Admission PC-ASPECTS† | 9 (6–10) | 9 (7–10) | 0.149 |
| Serum glucose, mmol/L, median (IQR) | 7.9 (6.6–10.5) | 7.5 (6.4–10.1) | 0.355 |
| Blood WCC, $\times 10^9$/L, median (IQR) | 10.3 (8.2–13.4) | 10.0 (8.0–12.5) | 0.113 |
| NLR, median (IQR) | 7.8 (3.8–11.7) | 5.8 (3.1–9.3) | **0.018** |
| PLR, median (IQR) | 179.4 (125.8–230.7) | 149.0 (103.1–215.7) | **0.026** |
| PLT, $\times 10^9$/L, median (IQR) | 221.5 (184.0–251.0) | 216.0 (182.0–262.0) | 0.967 |
| Prior use of antiplatelet agents, n (%) | 24 (15.5) | 33 (20.6) | 0.236 |
| Prior use of anticoagulants, n (%) | 3 (1.9) | 5 (3.1) | 0.723 |
| Prior IVT, n (%) | 38(24.5) | 45(28.1) | 0.467 |
| Tandem occlusion, n (%) | 33 (21.3) | 23 (14.4) | 0.109 |
| Underlying ICAD, n (%) | | | 0.760 |
| Yes | 76 (49.0) | 73 (45.6) | |
| No | 63 (40.7) | 67 (41.9) | |
| Undetermined | 16 (10.3) | 20 (12.5) | |
| TOAST subtypes, n (%) | | | 0.106 |
| Large artery atherosclerosis | 96 (61.9) | 108 (67.5) | |
| Cardioembolism | 29 (18.7) | 30 (18.8) | |
| Other or unknown | 22 (14.2) | 21 (13.1) | |
| Undetermined | 8 (5.2) | 1 (0.6) | |
| General anaesthesia, n (%) | 100 (64.5) | 82 (51.3) | **0.017** |
| Heparin, n (%) | 89 (57.4) | 75 (46.9) | 0.061 |
| GP IIb/IIIa receptor inhibitor, n (%) | 109 (70.3) | 99 (61.9) | 0.114 |
| Stent retriever as first line, n (%) | 107 (69.0) | 105 (65.6) | 0.519 |
| Direct aspiration as first line, n (%) | 10 (6.5) | 6 (3.8) | 0.275 |
| Direct aspiration+stent retriever as first-line | 13 (8.4) | 18 (11.3) | 0.394 |
| IAT, n (%) | 13 (8.4) | 12 (7.5) | 0.771 |
| Rescue balloon/ stenting angioplasty, n (%) | 51 (32.9) | 48 (30.0) | 0.579 |
| Complete recanalisation, n (%) | 104 (67.1) | 111 (69.4) | 0.664 |
| No. of MT passes, median (IQR) | 1 (1–2) | 1 (1–2) | 0.151 |
| OTP, min, median(IQR) | 341 (230–439) | 275 (185–399) | **0.007** |
| Procedure duration, min, median(IQR) | 96(60-145) | 84(53-120) | 0.058 |

Continued

**Table 1** Continued

| Baseline and procedure variables | Futile recanalisation (n=155) | Effective recanalisation (n=160) | P value |
|---|---|---|---|

Bold values indicate statistical significance.
*Two missing data.
†Six missing data.
‡
DM, diabetes mellitus; IAT, intra-arterial thrombolysis; ICAD, intracranial atherosclerotic disease; IVT, intravenous thrombolysis; MT, mechanical thrombectomy; NIHSS, National Institute of Health Stroke Scale; NLR, neutrophil to lymphocyte ratio; OTP, Onset-to-puncture time; PC-ASPECTS, Posterior Circulation Alberta Stroke Programme Early CT Score; PLR, platelet to lymphocyte ratio; PLT, platelet; SBP, systolic blood pressure; TOAST, Trial of ORG 10172 in Acute Stroke Treatment; WCC, white cell count.

**Table 2** Independent predictors of futile recanalisation

| Predictors | Unadjusted OR (95% CI) | P value | Adjusted OR (95% CI) | P value |
|---|---|---|---|---|
| Admission NIHSS | | | | |
| ≥19 vs <19 | 4.01 (2.47 to 6.51) | <0.001 | 4.81 (2.76 to 8.39) | <0.001 |
| PLR | | | | |
| ≥162.2 vs <162.2 | 2.18 (1.35 to 3.52) | 0.002 | 1.93 (1.14 to 3.27) | 0.001 |
| OTP | | | | |
| ≥334 min vs <334 min | 2.17 (1.38 to 3.43) | 0.001 | 2.15 (1.25 to 3.68) | 0.005 |
| General anaesthesia | | | | |
| Yes vs no | 1.73 (1.10 to 2.72) | 0.018 | 1.87 (1.09 to 3.22) | 0.024 |

NIHSS, National Institute of Health Stroke Scale; OTP, onset-to-puncture time; PLR, platelet to lymphocyte ratio.

found that GA was related to the futile recanalisation of EVT for VBAO. Long-time delay to recanalisation, blood pressure reduction and other undesirable physiologic effects such as changes in immune reaction, loss of airway reflexes and respiratory depression more frequently occur in GA, which may explain the association.[28 32 33] However, the anaesthesia protocol of the ANGEL-ACT registry recommended that LA was the first-line anaesthesia strategy, using CS when necessary. GA should be used if the patient is expected to cooperate poorly during the procedure even with the use of CS, or with high-risk airway conditions, or with high-risk CS, which may bias our finding. Therefore, future large, multicentre RCTs are required to validate this finding.

## Limitations

Our study had several limitations. First, our study is an observational study, which might introduce a selection bias. Second, some potential predictors such as blood pressure during the procedure, pons-midbrain index,[34] baseline infarct volum and collateral circulation (posterior circulation CT angiography score or Basilar Artery on CT Angiography Score) were not collected, which may bias our conclusions. Third, all participants in our study are limited to Chinese. Hence, the conclusions may not be generalised to other races easily.

## CONCLUSIONS

Futile recanalisation in the ANGEL-ACT registry was observed in 49.2% of the VBAO patients who achieved successful recanalisation after EVT. Moreover, we found that the predictors of futile recanalisation were admission NIHSS≥19, PLR≥162.2, OTP≥334 min and the use of GA.

**Author affiliations**
[1]Interventional Neuroradiology, Department of Neurology, Beijing Tiantan Hospital, Captial Medical University, Beijing, China
[2]Department of Neurology, Sun Yat-Sen Memorial Hospital, Guangzhou, Guangdong, China
[3]Cerebrovascular Disease Department, Neurological Disease Center, Beijing Anzhen Hospital, Capital Medical University, Beijing, China
[4]China National Clinical Research Center for Neurological Diseases, Beijing Tiantan Hospital, Capital Medical University, Beijing, China

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**Competing interests** None declared.

**Patient consent for publication** Not applicable.

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**ORCID iDs**
Dapeng Sun http://orcid.org/0000-0001-6321-5381
Xiaochuan Huo http://orcid.org/0000-0003-1264-5132
Raynald - http://orcid.org/0000-0002-4749-3514
Baixue Jia http://orcid.org/0000-0001-8782-5344
Xu Tong http://orcid.org/0000-0002-3277-6941
Ning Ma http://orcid.org/0000-0002-4909-7048
Dapeng Mo http://orcid.org/0000-0001-6641-5573

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