# Endovascular Aneurysm Treatment with the Numen Coil Embolization System: A Prospective Randomized Controlled Open-Label Multicenter Noninferiority Trial in China

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■ OBJECTIVE: **We investigated the safety and efficacy of the Numen coil compared with the Axium coil in the treatment of intracranial aneurysms.**

■ METHODS: **Because CATCH (Coil Application Trial in China) is a prospective randomized controlled open-label noninferiority trial conducted in 10 centers across China, patients who fulfilled the inclusion and exclusion criteria were randomized 1:1 to either a test group (Numen) or a control group (Axium). The primary outcome was based on successful aneurysm occlusion at 6 months follow-up, whereas secondary outcomes included technical success, the recanalization and retreatment rates, and the rate of serious adverse events (SAEs) at 6 months and 12 months follow-up.**

■ RESULTS: **Between August 2017 and December 2019, 350 patients presenting with 350 aneurysms were enrolled and randomized. Per-protocol analysis showed that the successful aneurysm occlusion rate at 6 months was 91.18% for the test group compared with 91.85% in the control group, with a difference of −0.68% ($P = 0.8419$), and the overall mortality during the 30-day follow-up period was 1.19% and 1.81% in the test and control group, respectively, showing no significant difference between the 2 groups ($P = 0.6837$), whereas the SAE incidence during the 12-month follow-up period was 12.50% and 17.47% in the test and control groups, respectively, which was not statistically significant ($P = 0.2222$).**

■ CONCLUSIONS: **This trial showed that the Numen coil was noninferior to the Axium coil in terms of intracranial aneurysm embolization and can be considered as a safe and effective coil for treating patients with intracranial aneurysm in clinical practice.**

## INTRODUCTION

Neurovascular embolization coils were one of the first medical devices for treating intracranial aneurysms via an endovascular approach as early as the 1970s. Since ISAT (International Subarachnoid Aneurysm Trial), a large prospective randomized controlled for 2143 patients with neurosurgical clipping or intravascular embolization, suggested that coil

**Key words**
- Aneurysm
- Coil
- Complication
- Device

**Abbreviations and Acronyms**
**3D**: Three-dimensional
**CATCH**: Coil Application Trial in China
**FAS**: Full analysis set
**PPS**: Per-protocol set
**SS**: Safety set
**SAE**: Serious adverse event

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embolization was superior to surgical clipping in terms of disability, mortality, and incidence of epilepsy regardless of postoperative recurrence,[1,2] coil embolization has become the first-line treatment for intracranial aneurysms instead of surgical interventions.

Additive designing, processing, and manufacturing techniques provide a greater coil optimization in terms of delivery performance and method of use as well as achieving better angiographic outcomes. It was also reported that the hydrogel coil expansion through the blood hydrogel immediately increases the density,[3] whereas the biodegradable polyglycolic/polylactic acid coil increases the aneurysm embolization rate by escalating the inflammatory response at the neck of the aneurysm.[4] However, these bioactive modified coils do not show superior long-term stability compared with bare-metal coils.[3-6]

Although several technologies have rapidly developed over the past decades for treating aneurysms, coil embolization with the incorporation of bare-metal coils still accounts for the largest proportion of aneurysm-treating devices, such as the introduction of Numen coil (MicroPort NeuroTech, Shanghai, China), a new electric detachable bare-metal coil made of platinum-tungsten alloys, that has passed all major preclinical studies, namely, product design and quality inspection as well as animal risk analysis studies.

Therefore, a multicenter randomized controlled trial was conducted in China to assess the safety and effectiveness of the Numen coil by comparing its efficacy with the Axium coil (Medtronic, Minneapolis, Minnesota, USA), which is one of the most widely used coils in China for treating intracranial aneurysms.

## METHODS

### Study Design and Patients

A prospective multicenter open-label randomized controlled trial, CATCH (Coil Application Trial in China), was conducted in 10 centers across China and included patients aged 18–80 years, with a single untreated intracranial saccular aneurysm (maximum diameter of the target aneurysm, 24 mm; Hunt and Hess scale score, ≤III; modified Rankin Scale score ≤2), ruptured or unruptured aneurysms indicated for both test group (Numen coil embolization) as well as control group (Axiumcoil embolization) treatment options, and scheduled for a single-sitting primary coiling treatment; patients who had previously received other intravascular interventional therapies for the target aneurysm were excluded. All patients gave written informed consent or, if consent was not attained, written assent was obtained from their medical decision makers. The design and implementation of the clinical trial were in accordance with the ethical guidelines determined by the Declaration of Helsinki and complied with the relevant provisions of China's current regulation of Good Clinical Practice for Medical Devices with ISO14155 standards.

A total of 334 enrolled CATCH trial patients' data were included in the full analysis set (FAS), except for 16 patients who were excluded because of withdrawal of informed consent (5 patients), nonconformance with inclusion and exclusion criteria (8 patients), and nonuse of the coil (3 patients) according to their random allocation.

### Randomization and Masking

Because the random numbers and devices assignment was conducted by Data Acquisition Station for the Interactive Web Response System, the dynamic randomization performed by minimization method controlled the balance of 4 influencing factors: neck, diameter, location, and state of rupture of the aneurysm.

An independent core laboratory that comprised 3 members qualified in neuroimaging or with equivalent qualifications, located at the Sixth People's Hospital, Shanghai determined the results of the primary and secondary efficacy end points by assessing and correlating angiograms according to the modified 3-point Raymond scale. Although the collated digital copies of angiogram images were further sent to assessors masked to allocation and treatment received at the independent core laboratory for analysis, the investigator's judgment about the patient's imaging results only used was to guide the the patient's clinical treatment as well as the selection of the following treatment.

An independent clinical events committee comprising 3 clinical experts was responsible for reviewing and adjudicating all deaths and serious adverse events (SAEs) pertaining to the trial; SAE was defined as any adverse event that resulted in death or serious deterioration in a patient's health during the clinical trial, including a life-threatening illness or injury, permanent impairment of a body structure or a bodily function, and hospitalization or prolongation of existing hospitalization.

### Procedures

All procedures were performed under general anesthesia via a transfemoral approach that included a heparin dose at 100 units/kg for maintaining an activated clotting time of 250–350 seconds throughout the procedure after sheath placement, followed by placement of a suitable guiding catheter in the internal carotid artery or vertebral artery. Subsequently, coils were delivered into the target aneurysm through the Numen catheter and other auxiliary devices and later detached after satisfactory placement. It was also suggested that the test or control group coil length used in each aneurysm should be ≥50% of the total length, whereas balloon-assisted and stent-assisted coiling could be used for wide-neck aneurysms (neck >4 mm or dome/neck <2), thus using all major stents except the flow diverter and covered stent. It was further advised to use a single detachment controller to detach the same coil a maximum of 5 times followed by replacement of either detachment controller or the coil apart from other possible remedial measures that might be used to continue the procedure because of detachment failure; subsequently, all relevant data were recorded such as location and size of the aneurysm, aneurysmal neck width and shape, and diameter of the parent artery as well as the treatment results.

### Outcome Measurements

The considered primary outcome was a successful occlusion rate at 6 months postoperative follow-up, which was defined as the occlusion degree of an aneurysm with a Raymond scale score of either I or II, whereas the secondary outcomes included the complete occlusion rates at both 6 and 12 months as well as the recanalization rate at 6 months follow-up after treatment. Moreover, the complete occlusion was defined as an aneurysm

occlusion degree with a Raymond score of I, whereas the recanalization rate was defined as the percentage of patients with a decreased aneurysm occlusion degree at the follow-up period compared with the immediate postoperative period. Digital subtraction angiography was used to evaluate the aneurysm occlusion degree immediately and 6 months after treatment, whereas magnetic resonance angiography was used at the 12 months follow-up period.

The safety outcome measurements included the retreatment rate as well as the clinical outcome worsening rate at and 12 months postoperatively and procedure-related or device-related adverse events at 30 days and 6 and 12 months after the treatment, whereas the clinical outcome worsening rate was defined as the proportion of patients with a modified Rankin Scale score >2 with ≥1 point higher than the preprocedure score. The obtained evaluation results were the final score of those patients who had not completed either 6 or 12 months of follow-up because of death or SAEs related to the surgical procedure or the treatment device. All SAEs were assessed by the clinical events committee, whereas non-SAEs were assessed by the principal investigator.

### Statistical Analysis

Based on a comprehensive literature review and clinical experience, the primary end point (successful occlusion rate 6 months after the procedure) was set as 85% whereas the noninferiority boundary was set as 12.5%; as a 1-tailed test having the significance level of $\alpha = 0.025$ and power $(1-\beta) = 80\%$. As calculated by Power Analysis & Sample Size software (NCSS, LLC. Kaysville, Utah, USA), 260 patients were randomized in a 1:1 ratio (130 in each group), although considering the patient withdrawal rate, previously, 336 patients were planned for the study enrollment (168 in each group).

The FAS was the set of patients who were recruited, treated, and had baseline assessment data based on the intention-to-treat principle, whereas patients with missing occlusion degree results of the aneurysms 6 months postoperatively were considered to have unsuccessful occlusion. The per-protocol set (PPS) was athe subset of the FAS that included those patients who had received the treatment prescribed in the protocol, and their primary outcome observation data could be easily obtained, with no significant violation of the trial protocol. The safety set (SS) was the set of patients who were treated after randomization and had ≥1 safety evaluation. Because effectiveness analysis was performed in both the FAS and the PPS subgroups, all baseline demographic data were analyzed in the FAS subgroup, whereas a safety analysis was performed in the SS subgroup. Although proportions were used for categorical variables, and medians with interquartile ranges were used for continuous variables, the categorical variables were compared between study arms using the $\chi^2$ test or a Fisher exact test, whereas either the t test or a Mann-Whitney rank test was used for assessing continuous variables according to the data distribution.

The Cochran-Mantel-Haenszel $\chi^2$ test stratified by research centers was used to compare the difference in outcome between the 2 groups, and the bilateral 95% confidence interval was also calculated, suggesting that if the lower range of the intervals was greater than −12.5%, the successful occlusion rate of aneurysms in the experimental group was not inferior to that in the control group, followed by calculating the 95% confidence intervals of the 2 groups and listing the corresponding contingency table data that considered $P < 0.05$ a statistically significant difference between the 2 groups.

The statistical analysis process was conducted at the Department of Health Statistics, affiliated with the Fourth Military Medical University. Because the statistical analyses were performed with the statistical software package SPSS version 19 (IBM Corp., Armonk, New York, USA), all tests were 2-sided, and a $P$ value <0.05 was considered to be statistically significant. An independent data and safety monitoring committee had unrestricted data access and monitored the progress of the trial. The trial registration number (ClinicalTrials.gov) was NCT02990156.

## RESULTS

### Patients' Disposition and Characteristics

Of 350 patients presenting with 350 aneurysms enrolled and randomized between August 8, 2017 and December 21, 2019, 5 withdrew consent and 11 violated the trial protocol and did not undergo the procedure, whereas the remaining 334 patients underwent all necessary procedures (Numen, $n = 168$; Axium, $n = 166$), and formed our FAS and SS subgroups based on a modified intention-to-treat principle. Among all 334 treated patients, 271 were included in the PPS whereas 54 were lost to the primary end point follow-up, 5 exceeded the 6 months follow-up time, and 4 were deemed ineligible because 3 in the test group were treated with the Axium coil and 1 in the control group did not use the Axium coil; a comparison of the baseline characteristics between the 2 groups in the FAS showed similar distributions. The details are shown in **Figure 1** and **Table 1**.

### Primary Outcome

Primary outcome data based on core laboratory data sets were available for 271 patients (PPS) because the successful occlusion rate was 91.18% (124/136) in the test group compared with 91.85% (124/135) in the control group, resulting in a difference of −0.68% (−7.31%, 5.96%; $P = 0.8419$), which matched with the noninferiority criteria. The details are shown in **Table 2**.

### Secondary Outcome

Because core laboratory angiographic outcomes at 6 months follow-up were available for 271 patients, the complete occlusion rate was 60.29% (82/136) in the test group compared with 57.04% (77/135) in the Axium control group, whereas no statistically significant difference was observed between the 2 groups ($P = 0.5861$). The details are shown in **Table 2**.

The recanalization rate (follow-up at 6 months) was 8.33% (11/132) for the test group compared with 5.43% (7/129) for the Axium control group; thus, no statistically significant difference was noted between the 2 groups ($P = 0.3541$). The details are shown in **Table 2**.

Core laboratory angiographic outcomes at 12 months follow-up were available for 242 patients; the complete occlusion rate of the test group was 70.94% (83/117) compared with 65.60% (82/125) in the Axium control group. Henceforth, there was no statistically significant difference between the 2 groups ($P = 0.3728$). The details are shown in **Table 2**.

### Adverse Events

At 6 months follow-up, 2 patients in the control group accepted retreatment (2/160, 1.25%) whereas retreatment was not required in the test group and thus, no significant difference was observed between the 2 groups (P = 0.2431); at the 12 months follow-up, 2 patients in the control group accepted retreatment (2/156, 1.28%) and retreatment was not required in the test group, and hence, there was no statistically significant difference between the 2 groups (P = 0.2460). The details are shown in Table 3.

Clinical follow-up data at 6 months were available for 330 patients; the clinical outcome worsening rate for the test group was 3.01% (5/166) compared with 4.88% (8/164) in the Axium control group, thus showing no statistically significant difference between the 2 groups (P = 0.3836), whereas in the clinical follow-up data at 12 months available for 319 patients, the clinical outcome worsening rate was 2.50% (4/160) for the test group compared with 5.03% (8/159) in the Axium control group, showing no statistically significant difference between the 2 groups (P = 0.2348). The details are shown in Table 4.

Although 19 patients were present in the test group with an incidence of 10.71% and 22 patients in the control group with an incidence of 13.25% during the 12 months follow-up period because of procedure-related adverse events, the difference between the 2 groups was not statistically significant (P = 0.6201).

The incidence of SAEs during the 12 months follow-up period was 12.50% (21/168) and 17.47% (29/166) in the test and control groups, respectively, thereby suggesting that no statistically significant difference was noted between the 2 groups (P = 0.2222). Similarly, the incidence of procedure-related SAEs was 5.36% (9/168) and 7.23% (12/166) in the test and control groups, respectively, showing that there was no statistically significant difference between the 2 groups (P = 0.5078), whereas the device-related SAEs incidence was 1.79% (3/168) and 3.61% (6/166) in the test and control groups, respectively, thereby showing that there was no statistically significant difference between the 2 groups (P = 0.3348). The details are given in Table 5.

The overall mortality during the 30 days follow-up period was 1.19% (2/168) and 1.81% (3/166) in the test and control groups, respectively, and no statistically significant difference was observed between the 2 groups (P = 0.6837). It was also observed that mortality was proportional to the procedure used in 1.19% (2/168) and 1.20% (2/166) of patients in the test and control groups, respectively, hence showing no statistically significant difference between the 2 groups (P = 1.0000), whereas the device mortality was 0.60% and 1.20% in the test and control groups, respectively, showing no statistically significant difference between the 2 groups (P = 0.6216) and, thus, an absence of mortality during the 6 months or 12 months follow-up period. The details are shown in Table 5.

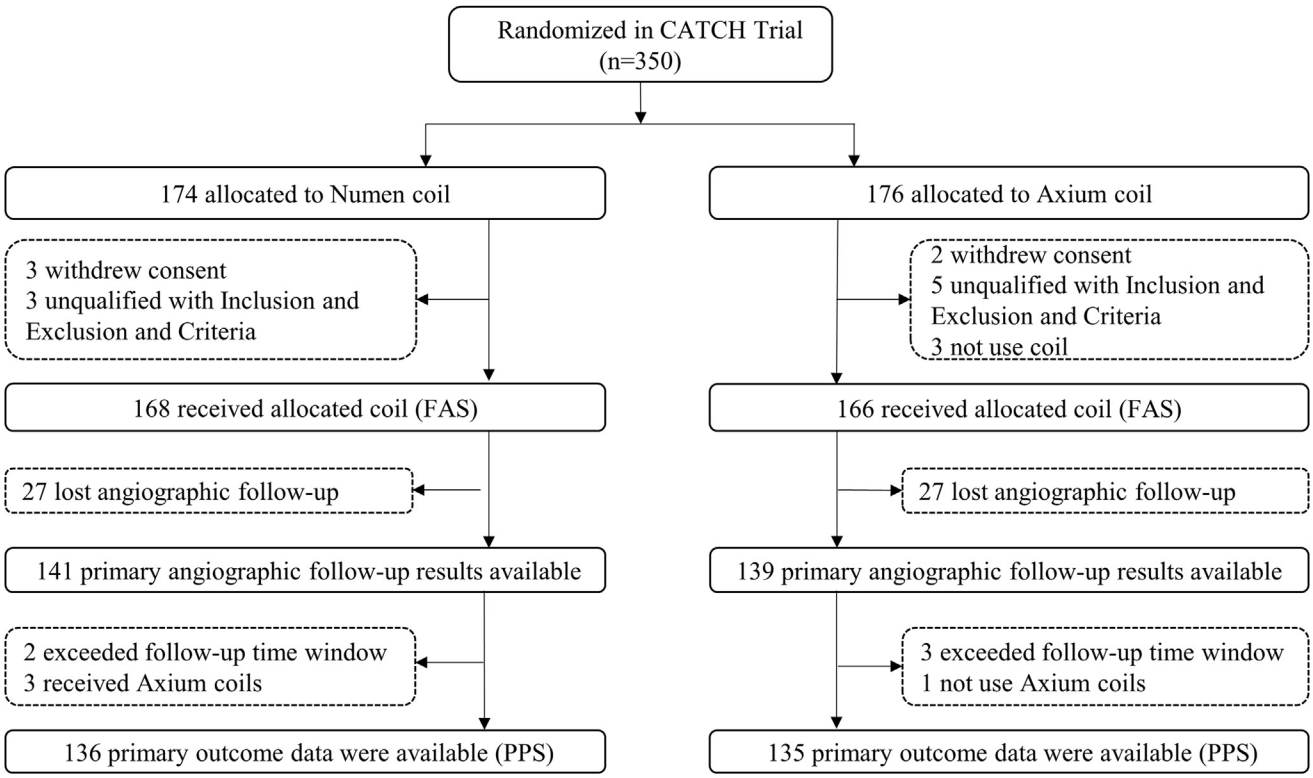


**Figure 1.** Trial profile. FAS, full analysis set; PPS, per-protocol set.

**Table 1.** Baseline Characteristics of the Modified Intention-To-Treat Population

| | NeuroTech Coils (N = 168) | Axium Coils (N = 166) | *P* Value |
|---|---|---|---|
| Gender | | | 0.7082 |
| Female | 106 (63.10) | 108 (65.06) | |
| Male | 62 (36.9) | 58 (34.94) | |
| Age (years), mean ± standard deviation | 57.47 ± 10.84 | 56.15 ± 9.94 | 0.2445 |
| Medical history | | | |
| Cerebral infarction | 27 (16.07) | 28 (16.87) | 0.7844 |
| Coronary artery disease | 6 (3.57) | 10 (6.02) | 0.2940 |
| Hypertension | 85 (50.6) | 88 (53.01) | 0.6585 |
| Hypercholesterolemia | 18 (10.71) | 13 (7.83) | 0.3640 |
| Diabetes | 14 (8.33) | 12 (7.23) | 0.7064 |
| Current/previous smoking | 39 (23.21) | 32 (19.28) | 0.5680 |
| Current/previous drinking | 34 (20.24) | 23 (13.86) | 0.2764 |
| Baseline rupture status | | | 0.7552 |
| Yes | 46 (27.38) | 48 (28.92) | |
| No | 122 (72.62) | 118 (71.08) | |
| Total (missing) | 168 (0) | 166 (0) | |
| Hubnt and Hess grade of patients with ruptured aneurysms | | | 0.4244 |
| I | 22 (47.83) | 20 (41.67) | |
| II | 20 (43.48) | 21 (43.75) | |
| III | 4 (8.7) | 7 (14.58) | |
| Total (missing) | 46 (0) | 48 (0) | |
| Aneurysm location | | | |
| Anterior | 165 (98.21) | 165 (99.4) | |
| Posterior | 3 (1.79) | 1 (0.6) | |
| C3 | 8 (4.76) | 4 (2.41) | |
| C5 | 15 (8.93) | 8 (4.82) | |
| C6 | 44 (26.19) | 47 (28.31) | |
| C7 | 50 (29.76) | 48 (28.92) | |
| Anterior cerebral artery | 3 (1.79) | 4 (2.41) | |
| Middle cerebral artery | 13 (7.74) | 13 (7.83) | |
| Anterior communicating artery | 32 (19.05) | 41 (24.7) | |
| Basilar artery | 3 (1.79) | 1 (0.6) | |
| Total (missing) | 168 (0) | 166 (0) | |
| Target aneurysm size (mm), mean ± standard deviation | 6.26 ± 3.10 | 5.98 ± 2.91 | 0.3931 |
| Total (missing) | 168 (0) | 165 (1) | |
| Size of aneurysm neck (mm), mean ± standard deviation | 3.74 ± 1.89 | 3.66 ± 1.56 | |
| Total (missing) | 167 (1) | 165 (1) | |
| Assist device used | | | 0.7261 |
| Balloon | 6 (6.12) | 4 (4.30) | |
| Stent | 91 (92.86) | 87 (93.55) | |
| Balloon and stent | 1 (1.02) | 2 (2.15) | |
| Total (missing) | 98 (0) | 93 (0) | |

Values are number (%) except where indicated otherwise.

## DISCUSSION

In this prospective randomized controlled open-label multicenter noninferiority study trial conducted in China, the safety and effectiveness of Numen coils were compared with Axium coils for endovascular treatment of patients with intracranial aneurysms. Our study results showed that Numen coils were comparable to Axium coils in terms of successful occlusion rate as well as the marginal occurrence of procedural adverse events in intracranial aneurysm embolization procedure, thus providing robust evidence for the safety and efficacy of Numen coils in treating intracranial aneurysms.

According to the primary end point of successful occlusion rate (Raymond score I or II), our treatment results were superior to CCT (Cerecyte Coil Trial) and MAPS (Matrix and Platinum Science) trial results and similar to the GREAT trial. It was also reported that CCT noted a successful occlusion rate of 59% and 54% for Cerecyte and bare platinum coil, respectively, at 6 months follow-up,[5] followed by a complete to near-complete occlusion rate of 64.6% and 67.7% for Matrix[2] and bare platinum coils, respectively, at 12 ± 3 months,[4] whereas the GREAT trial reported the initial angiographic outcome as 74% and 75% for the second-generation HydroCoil Embolic System (MicroVention Inc., Aliso Viejo, California, USA) and bare platinum coil, respectively.[3] Several past literary insights have shown that the primary outcomes in FAS analysis conducted in the CATCH trial were 76.79% and 77.11% for the Numen group and Axium group, respectively, at the 6 months follow-up period, whereas a recently reported study of 5 years of MAPS trial[7] expressed that patients with Raymond score I and II occlusion were at very low risk of delayed hemorrhage and all due efforts should be made to achieve this level of occlusion. At the 12 months follow-up period, the rebleeding rate was 1.2% in the CATCH trial, suggesting that our clinical trial patients might be at a lower risk of delayed hemorrhage, and, hence, long-term follow-up was required to substantiate this.

Although coil embolization is widely used to treat both ruptured and unruptured intracranial aneurysms, relatively higher recurrence rates after coiling remain as one of the major drawbacks of this technique.[8] In our study trial, because the recanalization rate was 8.33% in the test and 5.43% in the control group and the retreatment rate was 1.28% in the control group, without any patient receiving retreatment in the test group, these rates were

**Table 2.** Initial and Follow-Up Angiographic Outcome Based on Core Laboratory Assessed

| | Modified Intention-to-Treat | | | Per-Protocol Analysis | | |
|---|---|---|---|---|---|---|
| | Numen Coils (N = 168), n (%) | Axium Coils (N = 166), n (%) | *P* Value | Numen Coils (N = 136), n (%) | Axium Coils (N = 135), n (%) | *P* Value |
| Immediate Raymond scores | | | 0.6258 | | | 0.9398 |
| I | 66 (40.74) | 57 (35.63) | | 44 (33.33) | 38 (29.46) | |
| II | 79 (48.77) | 91 (56.88) | | 71 (53.79) | 80 (62.02) | |
| III | 17 (10.49) | 12 (7.50) | | 17 (12.88) | 11 (8.53) | |
| Total (missing) | 162 (6) | 160 (6) | | 132 (4) | 129 (6) | |
| 6-month Raymond scores | | | 0.4187 | | | 0.6597 |
| I | 86 (60.99) | 77 (55.40) | | 82 (60.29) | 77 (57.04) | |
| II | 43 (30.50) | 51 (36.69) | | 42 (30.88) | 47 (34.81) | |
| III | 12 (8.51) | 11 (7.91) | | 12 (8.82) | 11 (8.15) | |
| Total (missing) | 141 (27) | 139 (27) | | 136 (0) | 135 (0) | |
| 6-month successful occlusion | | | 0.9442 | | | 0.8419 |
| Yes | 129 (76.79) | 128 (77.11) | | 124 (91.18) | 124 (91.85) | |
| No | 39 (23.21)* | 38 (22.89)* | | 12 (8.82) | 11 (8.15) | |
| Total (missing) | 168 (0) | 166 (0) | | 136 (0) | 135 (0) | |
| 6-month complete occlusion | | | 0.3424 | | | 0.5861 |
| Yes | 86 (60.99) | 77 (55.40) | | 82 (60.29) | 77 (57.04) | |
| No | 55 (39.01) | 62 (44.60) | | 54 (39.71) | 58 (42.96) | |
| Total (missing) | 141 (27) | 139 (27) | | 136 (0) | 135 (0) | |
| 6-month recanalization | | | 0.3623 | | | 0.3541 |
| Yes | 11 (8.03) | 7 (5.26) | | 11 (8.33) | 7 (5.43) | |
| No | 126 (91.97)† | 126 (94.74)† | | 121 (91.67)† | 122 (94.57)† | |
| Total (missing) | 137 (31) | 133 (33) | | 132 (4) | 129 (6) | |
| 12-month Raymond scores | | | 0.3916 | | | 0.4499 |
| I | 91 (71.09) | 87 (65.41) | | 83 (70.94) | 82 (65.60) | |
| II | 32 (25.00) | 43 (32.33) | | 29 (24.79) | 40 (32.00) | |
| III | 5 (3.91) | 3 (2.26) | | 5 (4.27) | 3 (2.40) | |
| Total (missing) | 128 (40) | 133 (33) | | 117 (19) | 125 (10) | |
| 12-month complete occlusion | | | 0.3246 | | | 0.3728 |
| Yes | 91 (71.09) | 87 (65.41) | | 83 (70.94) | 82 (65.60) | |
| No | 37 (28.91) | 46 (34.59) | | 34 (29.06) | 43 (34.40) | |
| Total (missing) | 128 (40) | 133 (33) | | 117 (19) | 125 (10) | |

*The cases missing for the primary end point successful aneurysm occlusion rate at 6 months after procedures were filled up by cases of unsuccessful occlusion.
†If the Raymond score immediately after procedures or the Raymond score at 6 months after procedures were missing, the recanalization would be defined as missing.

remarkably lower compared with other randomized controlled trials.[3-6,9,10] Among the various factors potentially affecting aneurysm recurrence, low packing density is a well-known predisposing factor for aneurysm recanalization,[11-13] the value of which was 44.91% in the test and 44.30% in the control group of the CATCH trial (**Supplementary Table 2**), which was superior to those found in randomized controlled trials using other modified and bare platinum coils.[3-6,9,10] This crucial observation corroborates the findings from the GREAT trial, which also showed a correlation between packing density and angiographic recurrences for both the hydrogel and the control arms of the study.[10]

**Table 3.** Retreatment in the Modified Intention-To-Treat Population

| | Numen Coils (N = 168), n (%) | Axium Coils (N = 166), n (%) | *P* Value |
|---|---|---|---|
| 6-month retreatment | | | |
| Yes | 0 (0.00) | 2 (1.25) | 0.2431 |
| No | 164 (100.0) | 158 (98.75) | |
| Total (missing) | 164 (4) | 160 (6) | |
| 12-month retreatment | | | |
| Yes | 0 (0.00) | 2 (1.28) | 0.2460 |
| No | 158 (100.0) | 154 (98.72) | |
| Total (missing) | 158 (10) | 156 (10) | |

**Table 4.** Clinical Outcome of Patients at 6 and 12 Months Follow-Up in the Modified Intention-to-Treat Population

| | Numen Coils, n (%) | Axium Coils, n (%) | *P* Value |
|---|---|---|---|
| Baseline mRS score | | | |
| 0 | 99 (59.28) | 87 (52.73) | 0.1660 |
| 1 | 55 (32.93) | 58 (35.15) | |
| 2 | 12 (7.19) | 19 (11.52) | |
| 4 | 1 (0.60) | 1 (0.61) | |
| Total (missing) | 167 (1) | 165 (1) | |
| 6 months follow-up mRS score | | | |
| 0 | 147 (88.55) | 140 (85.37) | 0.3691 |
| 1 | 12 (7.23) | 13 (7.93) | |
| 2 | 1 (0.60) | 2 (1.22) | |
| 3 | 0 (0.00) | 1 (0.61) | |
| 4 | 4 (2.41) | 4 (2.44) | |
| 5 | 1 (0.60) | 1 (0.61) | |
| 6 | 1 (0.60) | 3 (1.83) | |
| Total (missing) | 166 (2) | 164 (2) | |
| 12 months follow-up mRS score | | | |
| 0 | 148 (92.50) | 144 (90.57) | 0.5051 |
| 1 | 7 (4.38) | 4 (2.52) | |
| 2 | 0 (0.00) | 2 (1.26) | |
| 3 | 0 (0.00) | 3 (1.89) | |
| 4 | 3 (1.88) | 3 (1.89) | |
| 5 | 1 (0.63) | 0 (0.00) | |
| 6 | 1 (0.63) | 3 (1.89) | |
| Total (missing) | 160 (8) | 159 (7) | |
| 6 months follow-up worsened clinical outcome | | | |
| No | 161 (96.99) | 156 (95.12) | 0.3836 |
| Yes | 5 (3.01) | 8 (4.88) | |
| Total (missing) | 166 (2) | 164 (2) | |
| 12 months follow-up worsened clinical outcome | | | |
| No | 156 (97.50) | 151 (94.97) | 0.2348 |
| Yes | 4 (2.50) | 8 (5.03) | |
| Total (missing) | 160 (8) | 159 (7) | |

The last evaluation results of patients who failed to complete the 6 months and 12 months follow-up because of death or procedure-related or device-related serious adverse events were used as the final results.
mRS, modified Rankin Scale.

Because the application of intracranial stents makes it possible for wide-necked and complex aneurysms to be treated with coil embolization, this approach not only improves the complete occlusion rate but also significantly reduces the recurrence rate,[14,15] which was also substantiated by the CATCH trial, in which the complete occlusion rate of aneurysms at 12 months follow-up was significantly higher than that at 6 months follow-up, whereas the recurrence rate was markedly lower, thus implying that because 54.2% patients underwent the stent-assisted coiling technique in our study, this treatment could significantly improve the aneurysm occlusion rate and reduce the rate of recurrence. Another observation in our study was that the symptomatic cerebral infarction incidence was 4.76% in the test and 6.02% in the Axium coil group, which further asserted that although stent-assisted Numen coiling can achieve a superior aneurysm embolization effect, their continuous use might increase the risk of cerebral infarction, especially the risk of acute in-stent thrombosis.

Coil softness represents its ability to fill an aneurysm. Usually, the coil softness is evaluated by the physical properties of the metal springs. The inverse of its softness, coil stiffness, is proportional to its spring constant (k). A smaller value of k means a softer embolization coil. However, there are several different ways to calculate spring constant (k). In our study, the value of k could be presented as follows:

$$k = \text{spring stiffness} \propto \frac{d^4}{D^3}, \frac{d}{D}, \frac{d^4}{D}$$

where $d$ is the stock wire diameter and $D$ is the secondary structure diameter (coil outer diameter).

Because bare platinum coils remain the mainstay therapy for intracranial aneurysms, recently, interest has developed in enhancing their mechanical attributes to make them safer, softer, and easier to deploy. Many types of bare-metal coils, including Axium, Target, Orbit, and Microplex coils, are clinically available, with different characteristics, including structure, softness, transportability, and ease of use.[14,15] Among all these characteristics, softness is an important index that represents the ability to fill an aneurysm and is determined by the interplay of several physical properties of the metal springs such as the coil stiffness parameter, which is proportional to the spring constant (k), thereby implying that a smaller value of $k$ indicates a softer embolization coil.[16,17] If the structural attributes of widely available coils are taken into account, both Numen and

**Table 5.** Summary of Serious Adverse Events within 12 months in the Modified Intention-to-Treat Population

| | Numen Coils (N = 168), n (%) | Axium Coils (N = 166), n (%) | *P* Value |
|---|---|---|---|
| All SAEs | 21 (12.5) | 29 (17.47) | 0.2222 |
| Procedure-related SAEs | 9 (5.36) | 12 (7.23) | 0.5078 |
| Device-related SAEs | 3 (1.79) | 6 (3.61) | 0.3348 |
| Neurologic complications | 12 (7.14) | 16 (9.64) | 0.411 |
| Symptomatic intracranial hemorrhage | 1 (0.60) | 2 (1.20) | 0.6216 |
| Aneurysm rupture or rebleeding | 1 (0.60) | 1 (0.60) | 1.000 |
| Symptomatic cerebral Infarction | 8 (4.76) | 10 (6.02) | 0.610 |
| Others (e.g., hydrocephalus) | 2 (1.19) | 3 (1.81) | 0.6837 |
| Death | 2 (1.19) | 3 (1.81) | 0.6837 |
| Procedure-related death | 2 (1.19) | 2 (1.20) | 1.0000 |
| Device-related death | 1 (0.60) | 2 (1.20) | 0.6216 |

SAE, serious adverse event.

Axium coils have 2 types of coil shapes: three-dimensional (3D) and helical. Furthermore, Numen coils possess 2 different 3D coil shapes, 3/4 loops and 1/2 loops; it is perceived that the 3D coil with 3/4 loops is formed by a series of Ω-shaped loops, providing a stable framing and uniform figuration in aneurysms, whereas the 3D coil with 1/2 loops is fabricated by a series of Ω-shaped and S-shaped loops, which are incorporated for conformable framing, dense filling, and safe finishing. In our study, the evaluation of all the spring constant (k) values of both the Numen and Axium coils with different 3D shapes (**Supplementary Table 1**) made it evident that the Numen coils with 3/4 loops (Numen Frame) were equivalent to or harder than Axium coils, whereas the Numen coils with 1/2 loops (Numen Finish) were softer than Axium coils (**Supplementary Figure 1** shows the results of a bench test simulating aneurysm wall pressure between Numen coils and other coils). Because it was assumed that softer coils make coiling safer, it was also consistent with our findings that the Numen coils (Numen Finish) are softer than Axium coils and might reduce the risk of procedure-related complications to a certain extent; however, our study results showed the incidence of the procedure-related complications as 5.36%, which was slightly lower in the Numen coil group and was not statistically significant.

Of the many physical attributes, 1 essential component for optimized functioning of the coil is its competency, which is put to use while framing, filling, and finishing coils. Our findings suggest that 112 patients (66.67%) in the test group underwent complete embolization exclusively with Numen coils, whereas 87 patients (52.41%) in the control group underwent embolization only with Axium coils, which was lower than that with Numen coils, thus indicating that Numen coils have a satisfactory performance throughout the aneurysm embolization process right from initial framing step to the gradual finishing phase (**Supplementary Table 3**).

Moreover, this might be a study limitation because the nonavailability of primary outcome data for 54 patients (27 each in the test and control groups) in FAS analysis led to a sensitivity analysis being performed for an additional 54 patients in the analysis population with missing primary outcome data stating that the probability of the test group was not inferior to that of the control group at 73.09%.

## CONCLUSIONS

This trial showed that the Numen coil was noninferior to the Axium coil in terms of successful occlusion rate as well as the marginal occurrence of procedure-related or device-related adverse events in treating intracranial aneurysms. The Numen coil is a safe and effective alternative to conventional surgical options for treating patients with intracranial aneurysm in clinical practice. Additional analysis of long-term follow-up after coil embolization will surely be beneficial. It might also be imperative to summarize the experience of Numen coils in postmarketing real-world studies for productive outcomes in the near future.

## CRediT AUTHORSHIP CONTRIBUTION STATEMENT

**Rui Zhao:** Methodology, Coordinated the trial, Formal analysis, Writing – original draft, Implementation of the study, Data curation, Approved the report for publication. **Guoli Duan:** Methodology, Coordinated the trial, Formal analysis, Writing – original draft, Implementation of the study, Data curation, Approved the report for publication. **Pengfei Yang:** Methodology, Coordinated the trial, Formal analysis, Writing – original draft, Implementation of the study, Data curation, Approved the report for publication. **Tianxiao Li:** Methodology, Supervised the performance of all radiological measurements and their interpretation, Implementation of the study, Data curation, Approved the report for publication. **Sheng Guan:** Methodology, Supervised the performance of all radiological measurements and their interpretation, Implementation of the study, Data curation, Approved the report for publication. **Hua Yang:** Methodology, Supervised the performance of all radiological measurements and their interpretation, Implementation of the study, Data curation, Approved the report for publication. **Zhenwei Zhao:** Methodology, Supervised the performance of all radiological measurements and their interpretation, Implementation of the study, Data curation, Approved the report for publication. **Xingen Zhu:** Methodology, Supervised the performance of all radiological measurements and their interpretation, Implementation of the study, Data curation, Approved the report for publication. **Guobiao Liang:** Methodology, Supervised the performance of all radiological measurements and their interpretation, Implementation of the study, Data curation, Approved the report for publication. **Xin Wu:** Methodology, Supervised the performance of all radiological measurements and their interpretation, Implementation of the study, Data curation, Approved the report for publication. **Bing Leng:**

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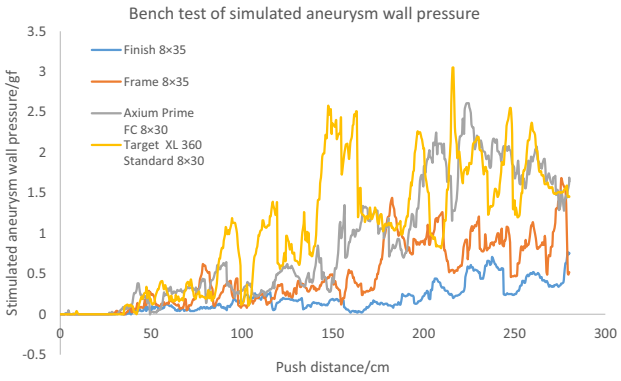
## SUPPLEMENTARY DATA




**Supplementary Figure 1.** Results of a Bench Test Simulated Aneurysm Wall Pressure Between Numen Coils and Other Coils.

**Supplementary Table 1.** Values of Spring Constant (*k*) of the Numen and Axium Coils with Three-Dimensional Shapes

| Coils (mm) | Coil Length (cm) | Coil Outer Diameter (inch) | d/D | $d^4/D^3$ | $d^4/D$ |
|---|---|---|---|---|---|
| Numen Finish | | | | | |
| 1—2 | 2—8 | 0.0100 | 125 | 62 | 40 |
| 2.5—5 | 3—20 | 0.0100 | 150 | 129 | 83 |
| 6—8 | 10—35 | 0.0100 | 175 | 238 | 154 |
| Numen Frame | | | | | |
| 4—6 | 6—25 | 0.0120 | 167 | 235 | 218 |
| 7—10 | 12—40 | 0.0130 | 173 | 296 | 323 |
| 11—20 | 27—58 | 0.0140 | 214 | 750 | 948 |
| 22—24 | 56—70 | 0.0140 | 250 | 1389 | 1756 |
| Axium 3D | | | | | |
| 2—3.5 | 2—15 | 0.0115 | 130 | 85 | 72 |
| 4—6 | 6—20 | 0.0125 | 160 | 208 | 210 |
| 7—10 | 15—30 | 0.0135 | 167 | 265 | 311 |

**Supplementary Table 2.** The Packing Density of CATCH Clinical Trial

| | Modified Intention-to-Treat | | | Per-Protocol Analysis | | |
|---|---|---|---|---|---|---|
| | Numen Coils (N = 168) | Axium Coils (N = 166) | *P* Value | Numen Coils (N = 136) | Axium Coils (N = 135) | *P* Value |
| Packing density, mean ± standard deviation | 44.91 ± 31.98 | 44.30 ± 22.33 | 0.8426 | 44.31 ± 30.86 | 44.64 ± 22.80 | 0.9982 |

**Supplementary Table 3.** The Comparison of 100% Use Coil Ratio

| | Modified Intention-to-Treat | | |
|---|---|---|---|
| | Numen Coils (N = 168), n (%) | Axium Coils (N = 166), n (%) | *P* Value |
| 100% use coil ratio | | | 0.0079 |
| Yes | 112 (66.67) | 87 (52.41) | |
| No | 56 (33.33) | 79 (47.59) | |