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Research Progress on Treatment Strategy Selection and Long-Term Prognosis for Severe Intracranial Atherosclerotic Stenosis Undergoing Interventional Therapy

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Abstract: Severe intracranial atherosclerotic stenosis has a high prevalence in Asian populations and represents a major cause of ischemic stroke. Even with intensive pharmacological therapy, patients with this condition remain at substantial risk of stroke recurrence. Endovascular interventional treatment is currently the most typical supplementary therapeutic approach, primarily including balloon angioplasty, stent placement, and drug-coated balloon angioplasty. However, controversies persist in existing studies regarding the selection of the optimal strategy and long-term prognosis. This article reviews the research progress on interventional treatment modalities and long-term prognosis for this disease, so as to provide references for future related studies or clinical practice.

Keywords: severe intracranial atherosclerotic stenosis; plain balloon angioplasty; stent placement; drug-coated balloon; complications

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1. Introduction

Severe intracranial atherosclerotic stenosis can not only cause ischemic stroke but also predispose to stroke recurrence. Moreover, patients remain at risk of recurrent stroke even when adhering to pharmacotherapy. In a 2005 study comparing warfarin and aspirin for the treatment of this disease, Chimowitz MI et al. enrolled 569 patients and found that the one-year incidence of stroke in patients with severe intracranial atherosclerotic stenosis approached 20% [1]. Wang Tao (2022) included 380 patients with severe intracranial atherosclerotic stenosis from eight high-volume centers and extended the follow-up period to three years, finding no significant difference in stroke incidence between combined stent and pharmacological treatment and pharmacological treatment alone, and concluded that pharmacotherapy could serve as the first-line treatment for this disease [2]. In 2015, Zaidat OO et al. compared balloon-expandable stent placement with pharmacotherapy in 112 patients and found that the stroke recurrence rates in the stent group were 24.1% at 30 days and 36.2% at 12 months, both higher than those in the medication group; this trial was terminated early due to futility [3]. Based

on existing studies, although interventional treatment methods for this disease have emerged and been applied, many problems remain to be resolved, such as the optimal treatment strategy and their impact on prognosis, in order to improve treatment efficacy and address the challenges that existing research has been unable to solve.

2. Available Interventional Treatment Options for Severe Intracranial Atherosclerotic Stenosis

2.1. Plain Balloon Angioplasty

Plain balloon angioplasty is the earliest form of interventional therapy applied for severe intracranial atherosclerotic stenosis. Its basic principle is to dilate the stenotic vascular segment using an inflated balloon, thereby improving blood perfusion in the downstream cerebral tissue. The technique is relatively simple to perform and leaves no permanent implant, which helps avoid long-term complications associated with stent placement. However, conventional plain balloon angioplasty has two main disadvantages. First, intra-procedural elastic recoil of the balloon can result in insufficient acute lumen gain, often necessitating subsequent bailout stenting. Second, it carries a considerable risk of long-term restenosis; according to a 2022 study by Luo Jichang et al., when interventional treatment is performed using plain balloon angioplasty alone, the long-term restenosis rate at the target lesion reaches nearly 50% [4]. In recent years, balloon catheter technology has continuously advanced. Rapid-exchange balloon catheters have gradually replaced traditional over-the-wire catheters, thereby simplifying the operational procedure and helping to mitigate elastic recoil during balloon delivery, which further reduces procedural risk.

2.2. Stent Placement

Currently, three typical types of stent placement are employed.

The first type is the self-expanding stent. This technique is the most widely used interventional treatment for severe intracranial atherosclerotic stenosis and has advantages in deliverability and conformability, making it particularly suitable for tortuous intracranial vessels. According to a related study by Bose et al. in 2007, when the Wingspan self-expanding nitinol stent was used for interventional treatment in patients who had failed pharmacotherapy, the mean degree of stenosis decreased from 74.9% to 31.9%, the 30-day rate of stroke or death was 4.5%, and the 6-month rate was 7.1%. This indicates good interventional efficacy, and the stent remains the primary stent device for this disease [5].

The second is the balloon-expandable stent. This type of stent possesses strong radial support force and can effectively reduce the postoperative residual stenosis rate. According to the VISSIT study in 2015, among patients treated with balloon-expandable stents, the perioperative rate of stroke, intracranial hemorrhage, or death within 30 days was approximately 17.2%, and the rate within 12 months was approximately 36.2%, both significantly higher than those in the medication group; the relevant study was terminated early due to a high complication rate. Several existing registry studies in China have reduced the perioperative rate of stroke, intracranial hemorrhage, or death to approximately 4.3% and the one-year stroke rate to 8.9% through measures such as screening for patients with hypoperfusion and extending the procedural time window [6]. This demonstrates that although this method has a relatively low postoperative residual stenosis rate, stringent control over the selection of indications is required to reasonably lower the prognostic risk.

The third is the drug-eluting stent. This type of stent mainly loads antiproliferative drugs (such as sirolimus, paclitaxel, etc.) on the stent surface, which can significantly inhibit the proliferation and migration of vascular smooth muscle cells, and has now been established as a first-line therapy in the coronary intervention field. According to the 2022 NOVA study comparing drug-eluting stents with bare-metal stents, for patients with severe intracranial atherosclerotic stenosis, interventional treatment with drug-eluting stents achieves significantly better outcomes than with bare-metal stents and can markedly reduce the rates of in-stent restenosis and recurrent ischemic stroke.

2.3. Drug-Coated Balloon

The drug-coated balloon is a novel interventional therapy developed in recent years based on the "intervention without implant" concept. This method can rapidly and uniformly transfer antiproliferative drugs to the vessel wall with the aid of an excipient during a single balloon inflation, leaving no permanent implant. In this way, it can effectively avoid thrombus formation caused by foreign body stimulation and reduce the probability of restenosis. Regarding this interventional treatment modality, a number of domestic clinical studies have preliminarily confirmed its effectiveness and safety. For example, the CTR study by Ma et al. in 2025 showed that at six months after intervention with a drug-coated balloon, the incidence of target vessel restenosis was significantly lower than that with stent placement therapy [7].

3. Key Factors Influencing Long-Term Prognosis of Interventional Treatment for Severe Intracranial Atherosclerotic Stenosis

3.1. In-stent restenosis (ISR)

In-stent restenosis (ISR) significantly impacts the long-term prognosis of interventional treatment for severe intracranial atherosclerotic stenosis. After the recanalization of a severely stenotic artery through an interventional approach, whether vascular patency can be maintained over the long term plays a decisive role in both patient prognosis and the risk of stroke recurrence. The primary mechanism of restenosis involves injury to the vascular intima induced by balloon- or stent-based intervention, which triggers smooth muscle cell proliferation or migration and/or excessive extracellular matrix deposition under inflammatory responses, ultimately resulting in neointimal hyperplasia and restenosis.

For patients with severe intracranial atherosclerotic stenosis, the incidence of ISR varies markedly depending on the interventional treatment modality. Compared with traditional bare-metal stent implantation, drug-eluting stents can effectively inhibit neointimal hyperplasia through the sustained release of antiproliferative agents, thereby reasonably reducing the incidence of ISR. Drug-coated balloons, compared with other interventional techniques, are associated with an even lower rate of restenosis after application and demonstrate distinct potential advantages in reducing the long-term risk of restenosis. In addition, if a patient has comorbid diabetes mellitus, the hyperglycemic state may impair vascular endothelial function and enhance platelet adhesion and aggregation, both of which promote excessive neointimal hyperplasia and consequently elevate the risk of ISR [8]. Therefore, during treatment, to improve prognostic outcomes, it is essential not only to rationally determine patient indications and scientifically select the interventional approach, but also to rigorously control the patient's blood glucose, thereby enabling effective prevention and management of such risks.

3.2. Perioperative Complications

Perioperative complications impose significant constraints on the prognosis of interventional treatment for severe intracranial atherosclerotic stenosis. Generally, perioperative complications can be categorized into four main types: first, perforator artery stroke, which typically results from stent placement causing displacement of vascular plaque that occludes the ostium of a perforating branch, and is commonly encountered in interventional treatment of basilar artery stenosis; second, hyperperfusion syndrome, which occurs relatively frequently after abrupt recanalization of severe stenosis, mainly because the autoregulatory function of the distal vasculature cannot adapt to a sudden increase in blood flow, predisposing to cerebral edema or even cerebral hemorrhage; third, acute or subacute thrombosis, which is generally associated with inadequate antiplatelet therapy or poor stent-vessel wall apposition; and fourth, vascular dissection, which is more commonly observed after balloon angioplasty.

Given the impact of perioperative complications, the rational choice of interventional therapy during treatment is critically important. A prospective, randomized controlled trial conducted in 2022 across multiple clinical centers (NOVA) on an intracranial drug-eluting stent system found that, with this interventional approach, the incidence of in-stent restenosis within one year was reduced by 68.5% compared with bare-metal stents. Through judicious patient selection and continuous improvement of interventional techniques, the incidence and severity of perioperative complications can be

effectively controlled, which in turn can significantly reduce stroke recurrence and mortality.

3.3. Patient Selection and Timing of Surgery

For patients with severe intracranial atherosclerotic stenosis, rational patient selection is pivotal to ensuring favorable prognostic outcomes in interventional treatment. Typically, not all patients are suitable for or necessarily require interventional therapy. As a rule, patients considered for interventional treatment should meet the following criteria: first, no marked improvement after intensive medical therapy; second, severe stenosis of the culprit vessel, generally defined as 70%–99%; third, imaging assessment confirming the presence of hemodynamic compromise in the territory supplied by the culprit vessel, or poor compensatory collateral circulation. If these conditions are not met, it is advisable that medical therapy remains the preferred strategy.

In parallel, the appropriate timing of the procedure is also crucial. For patients in the early phase (i.e., within two weeks of symptom onset), the plaque at the lesion site tends to be unstable. Interventional treatment at this stage may lead to plaque dislodgement or perforator occlusion, thereby increasing the risk of complications. Consequently, in recent studies such as BASIS and CASSISS, investigators have predominantly favored scheduling interventional procedures at least three weeks after symptom onset. This approach helps to avoid the acute phase of stroke, thereby reasonably lowering the risk of complications and improving long-term prognostic outcomes.

3.4. Collateral Circulation and Imaging Assessment

During interventional treatment for patients with severe intracranial atherosclerotic stenosis, the status of collateral circulation serves as a critical basis for assessing both the necessity of intervention and long-term prognosis. Theoretically, if the territory supplied by the culprit vessel is adequately compensated by collateral blood flow, the patient may not present with overt ischemic symptoms even in the presence of severe stenosis of the main vessel, and the risk of stroke recurrence would be relatively low. Conversely, if collateral compensation is poor, brain tissue may be susceptible to ischemia at any time, even if the culprit vessel has not reached critical stenosis severity, leading to a higher risk of stroke recurrence.

In light of this, in recent years many scholars internationally have begun to focus on multidimensional imaging evaluation methods and incorporate them into the patient screening process as an essential tool. With sufficiently high-resolution magnetic resonance vessel wall imaging, clinicians can clearly visualize the plaque morphology of the culprit vessel and assess plaque stability based on its characteristics. Furthermore, perfusion imaging enables a scientific evaluation of the hemodynamic status in the supplied territory of the culprit vessel. Alternatively, cerebral angiography can be used to grade the level of collateral circulation. These assessments provide objective evidence for patient selection and offer individualized guidance for treatment strategy decisions in suitable candidates, thereby facilitating interventional procedure planning and preparation, reasonably lowering prognostic risks, and further ensuring favorable long-term outcomes.

4. Conclusion

In summary, the basic treatment for severe intracranial atherosclerotic stenosis is pharmacotherapy. When pharmacotherapy fails to achieve significant improvement, interventional treatment can be adopted. Currently, typical interventional approaches include plain balloon angioplasty, stent implantation, and drug-coated balloon angioplasty. These different interventional methods exhibit significant differences in revascularization efficacy, periprocedural safety, and long-term prognosis. Evidence from existing studies indicates that long-term prognosis is influenced comprehensively by multiple factors, such as restenosis, periprocedural complications, the timing of intervention, collateral circulation, and imaging assessment. Therefore, when implementing interventional treatment, clinicians should rigorously select patients based on their individual conditions, choose the interventional method rationally, and formulate a targeted treatment plan. Only in

this way can the benefits and risks of interventional therapy for patients with severe intracranial atherosclerotic stenosis be maintained in balance. Current related research lacks long-term follow-up evidence in aspects such as high-risk subgroup data and novel interventional devices; the prediction of complications is insufficiently precise; and standardized primary-level diagnosis and treatment approaches have not been widely implemented. Hence, in subsequent studies, investigators in this field should leverage artificial intelligence imaging to construct individualized predictive models for interventional therapy and conduct long-term tracking of patients' treatment and prognosis data using big data and artificial intelligence technologies. Concurrently, novel interventional devices, such as targeted drug-eluting or biodegradable devices, should be developed. Based on these devices, an integrated system combining pharmacotherapy and interventional treatment can be constructed, and complications can be precisely predicted using technologies such as digital twins or artificial intelligence. This will significantly reduce the risk of stroke recurrence and further improve the long-term prognosis and quality of life of patients.

Disclosure statement

The author declares no conflict of interest.

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