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Research progress on the pathogenesis and treatment of cervical spondylotic myelopathy

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Abstract: Cervical spondylotic myelopathy (CSM) is the most serious subtype of cervical spondylosis, which is the main cause of spinal cord dysfunction in middle-aged and elderly people, and the pathogenesis of this CSM is complex, mainly including degenerative aging, dynamic instability, spinal cord ischemia, spinal cord injury, inflammation, apoptosis, and other possible mechanisms. The clinical treatment of the CSM mainly includes conservative treatment and surgical treatment. Conservative treatment includes drugs, acupuncture, moxibustion, traction, physical therapy and manual treatment. Surgical treatment can be divided into anterior surgery, posterior surgery, anterior and posterior combined surgery according to the surgical approach. The choice of treatment regimen should be based on the patient's symptoms, signs, and the results of auxiliary examinations, but how to choose the appropriate treatment plan is still the focus of clinicians. This article focuses on the research progress of the pathogenesis and treatment methods of this disease, in order to provide a reference for the diagnosis and treatment of cervical myelopathy.
Keywords: Cervical spondylotic myelopathy; Spinal canal stenosis; Anterior cervical discectomy and fusion; Posterior cervical surgery
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Cervical spondylotic myelopathy (CSM) is a degenerative disease characterized by the degeneration of the cervical spine and soft tissues around the spinal cord, which causes myeloid symptoms of varying degrees due to compression of the spinal cord or compromised blood supply. While traditionally more prevalent among elderly men, the incidence of CSM is increasingly observed in younger ages. CSM often affects multiple cervical cord segments at the same time, but it most commonly occurs at the C5/6 level, followed by the C3/4 level [1]. The slow onset and long duration of CSM make early detection challenging, yet late-stage manifestations can result in irreversible spinal cord damage, significantly impairing limb function and quality of life. Therefore, understanding its pathogenesis and exploring therapeutic interventions are crucial.

1 Pathogenesis

CSM pathogenesis involves both static and dynamic factors. Static factors are closely related to spinal stenosis, primarily stemming from congenital development and cervical degeneration. Studies indicate that congenital cervical spinal stenosis, particularly when the cervical spinal canal diameter is less than 13 mm, correlates significantly with CSM development [2]. Cervical spine degeneration is characterized by disc herniation, vertebral body osteophyte formation, ossification of the posterior longitudinal ligament, and ligamentum flavum calcification [3]. Dynamic factors, such as repetitive motion, exacerbate the effects of static factors, leading to chronic cervical cord injury.

Prolonged mechanical injury directly damages neurons and glial cells, triggering subsequent pathophysiological changes, including local ischemia, disruption of the blood-spinal cord barrier (BSCB), inflammation, and apoptosis.

1.1 Ischemia

Since the mid-20th century, ischemia has been recognized as a fundamental pathogenetic mechanism leading to spinal cord degeneration, as demonstrated in animal experiments. Ischemia is exacerbated by local vascular malformation and pathological changes within the blood vessels. Yamada *et al.* [4] constructed an animal model of spinal cord ischemia, revealing central pigmentolysis and myelin vacuolization in anterior and posterior horn cells following 20 minutes of spinal cord ischemia. Although such experiments cannot be performed directly in humans, they provide insight into potential pathophysiological mechanisms underlying spinal cord degeneration.

1.2 BSCB

BSCB is a physical barrier between blood and spinal cord parenchyma that prevents toxins, blood cells and pathogens from entering the spinal cord, maintains the homeostasis of the spinal cord parenchyma, and provides the necessary environment for normal neurological function. When the structure and function of the BSCB are damaged, the homeostasis of the spinal cord's internal environment is also disturbed to varying degrees, ultimately leading to neurological deficits [5]. Although there are no effective clinical interventions to restore spinal cord injury resulting from BSCB disruption, research suggests that Sirtuin 1 (SIRT1), a histone deacetylase, protects the endothelial barrier by deacetylating the redox protein p66Shc, and is expected to be a breakthrough in the treatment of spinal cord injury [6].

1.3 Inflammation

When the spinal cord is compressed, the disruption of the BSCB leads to increased vascular permeability of the spinal cord and facilitates the entry of inflammatory cells from the peripheral circulation. Peripheral immune cells, along with cytokines, chemokines, and other mediators produced by microglia, astrocytes, and endothelial cells, guide the inflammatory response of the nerve [7]. Neuroinflammation further exacerbates the degeneration of the spinal cord, creating a vicious cycle.

1.4 Apoptosis

Apoptosis, a programmed cell death process requiring energy and protein synthesis, frequently occurs within hours of cellular inflammation [8]. This process occurs in neurons, oligodendrocytes, microglia, and even astrocytes. While surgical decompression does not completely abrogate apoptosis, it significantly mitigates neuronal apoptosis levels in animal models of CSM, thereby improving neurological function [9].

2 Treatment

CSM should be treated with an individualized plan according to the patient's symptoms, signs and imaging tests, mainly including conservative treatment and surgical treatment. Fehlings *et al.* [10] suggested that prophylactic surgery should not be performed in patients without neurogenic or myeloid symptoms. Conservative treatment can be adopted in patients with mild cases, and surgical interventions should be considered if the conservative treatment is ineffective and the symptoms progress. Patients with moderate or severe CSM can be directly treated with surgery.

2.1 Conservative treatment

2.1.1 Pharmacotherapy

At present, there is no specific drug to cure CSM. Treatment primarily targets symptom management to alleviate patient discomfort and enhance quality of life. Commonly used western medicines include non-steroidal anti-inflammatory drugs, nutritional neurotrophic agents, nerve decongestants, and muscles relaxants. In acute or postoperative scenarios, steroids hormone may be considered. However, prolonged usage at high dosage is cautioned against [11].

According to Chinese medicine, internal factors contributing to CSM are closely linked to liver, spleen, and kidney functions, while external factors encompass wind, cold, dampness, and extended physical labor [12]. Chinese Medicine classifies CSM into five categories: liver and kidney deficiency, qi and blood deficiency, blood stasis and collateral obstruction, dampness and heat invasion, and yin and blood deficiency. Corresponding Chinese herbal medicines are prescribed accordingly [13]. Zhu *et al.* [14] advocated a treatment approach focusing on nourishing the liver and kidney, invigorating qi and blood, and activating blood circulation to remove blood stasis. They have developed the "Yishen Yangsui Prescription" to "nourish the kidneys and marrow, and eliminate bi (obstruction)", and have used this formula for symptomatic treatment of 35 CSM patients. Follow-up observation of changes in spinal cord function showed that the formula had a good effect in treating CSM [15]. Prof. Shi believes that the treatment of CSM should focus on harmonizing qi and blood, activating blood and removing stasis, and nourishing the liver and kidneys. His team used the "Qi-activating and blood-activating kidney-nourishing prescription" formulated by Professor Shi Qi to treat 109 CSM patients and found that this formula had a certain effect on the treatment of mild and moderate CSM through follow-up [16]. Moreover, various scholars have substantiated the efficacy of Chinese medicine in treating mild CSM [17]. Chinese medicine may enhance local spinal cord blood circulation and reduce ischemia, thereby alleviating symptoms.

2.1.2 External treatment

For patients with poor response to oral pharmaco-therapy alone, external interventions are often combined. Common modalities include Chinese medicine physiotherapy such as acupuncture, traction, and manual therapy. Combinations of multiple external therapies are frequently employed to enhance therapeutic outcomes. Wu *et al.* combined acupuncture with *dihuang* drink supplementation to treat 30 CSM patients, noting significant improvement in neck pain and diastasis in the acupuncture group, underscoring acupuncture's therapeutic potential [18]. Prof. Li proposed that standardized Tuina can improve blood circulation in the neck, promote the absorption of edema and inflammation around the nerve roots, and relax muscles, improving the state of cervical spine disorder and reducing mechanical compression. Thirty-four CSM cases treated with Tuina techniques and traction showed symptom alleviation in 30 cases [19]. However, most studies primarily focus on early-stage and mild CSM. For advanced and severe cases where conservative treatment proves ineffective, surgical intervention should be actively considered.

2.2 Surgical treatment

2.2.1 Anterior cervical surgery

Anterior cervical surgery includes anterior cervical discectomy and fusion (ACDF), anterior cervical corpectomy and fusion (ACCF), anterior controllable ante displacement and fusion (ACAF), and artificial cervical disc replacement (ACDR). The Smith-Peterson approach is usually used for the anterior cervical approach, and a transverse incision is usually made in the anterior cervical dermatome to bluntly detach the cervical vastus muscle, and reach the anterior edge of the vertebral body from the gap between the medial border of the sternocleidomastoid muscle, the carotid sheath, and the trachea and esophagus, and then the anterior longitudinal ligament is incised to visualize the vertebral body and the intervertebral discs. The vertebral body and discs are visualized by incision of the anterior longitudinal ligament, and then operated accordingly to different surgical approaches.

The main advantage of ACDF is that it can directly decompress the spinal cord and nerve roots with stable efficacy and safety, which is the gold standard for the treatment of CSM. The shortcomings of ACDF are also more obvious, such as incomplete decompression due to the narrow field of view during the operation, and postoperative complications such as difficulty in swallowing, non-fusion of prosthesis, and sinking of fusion device. To solve these problems, clinicians have optimized the surgical approach and improved the interbody fusion device. The zero-track interbody fusion device is hidden behind the anterior margin of the vertebral body after implantation, which better solves the problem of postoperative dysphagia, and there is no significant difference in the restoration of intervertebral height and cervical spine physiological curvature compared with the traditional ACDF [20]. The 3D-printed interbody fusion device solves the problems of pseudoarthrosis, prosthesis subsidence, and other complications due to its better elasticity modulus, and its micropore and trabecular structure which is easy for the bone tissues to crawl [21].

Compared with ACDF, ACCF has a larger decompression range, a broader field of view, and more complete decompression, which is especially suitable for the cases where the compression mainly comes from the posterior part of the vertebral body, severe stenosis of the cervical canal, and other cases where decompression through the intervertebral space is difficult. However, a large number of studies have shown that in the treatment of multi-segmental CSM, the difference between ACDF and ACCF in terms of fusion rate, JOA score and other efficacies is not statistically significant, and the performance of ACCF in terms of intraoperative hemorrhage, prosthesis settling rate, and complication rate is poorer than that of ACDF [22]. Han *et al.* [23] applied 3D printed artificial vertebral body to ACCF surgery and found that compared with traditional titanium mesh, its contact area with the upper and lower vertebral endplates was larger, stress was more dispersed, and the contact surfaces were more coincidental, which was better able to prevent prosthesis settling.

In 2017, Prof. Shi's team creatively proposed the concept of ACAF based on Yamaura's floating anterior approach, which provides a new idea and method for the surgical treatment of severe cervical posterior longitudinal ligament ossification (OPLL) [24]. This surgical technique achieves decompression of the spinal canal by longitudinally dissecting the vertebral body near the bilateral hook vertebral joints and lifting it anteriorly. Due to the outward position of the groove and the fact that the dura mater is not separated from the posterior longitudinal ligament during the decompression process, the risk of spinal cord injury and cerebrospinal fluid leakage is greatly reduced, and the complications of excessive posterior displacement of the spinal cord, such as the pulling of the nerve roots, are also reduced compared with posterior cervical spine surgery. And the procedure has also achieved good long-term efficacy in clinical [25]. However, there are fewer reports on the complications of ACAF so far, and in-depth study and long-term follow-up are still needed.

Although anterior fusion surgery is effective, the loss of joint mobility (ROM) in the operated segment after fusion and the greatly increased mobility of the adjacent discs can lead to accelerated adjacent segment disease (ASD). Therefore, ACDR was developed for this purpose. The advantage of this procedure is that the ROM of the cervical spine can be preserved while decompressing the cervical spine, which reduces the incidence of ASD in the adjacent vertebrae [26]. The occurrence of heterotopic ossification (HO) of the operated segments after ACDR was first reported in 2005[27]. It has been found that HO does not affect the clinical outcome of ACDR, but due to the occurrence of HO, the ROM of the adjacent segments gradually rises, and the advantage of ACDR in preventing ASD of the adjacent vertebrae gradually shrinks [26]. The limitations of ACDR lie in the long learning curve and the large number of contraindications to the procedure, and it is not appropriate to perform ACDR on patients with more than three surgical segments, cervical instability, degenerative changes in the synovial joints, and allergy to endoprosthetic plants. ACDR is not suitable for patients with more than 3 segments, cervical instability, degeneration of the synovial joints, or allergy to endoprosthesis.

In recent years, microscopes have gradually emerged in anterior cervical spine surgery, and the application of microscopes has solved the problem of the field of vision in anterior cervical spine surgery. First, microscopes provide a stable light source and field of view for the narrow surgical field. Second, microscopes can present the structures in three dimensions, making the surgical operation more delicate, realizing precise hemostasis and decompression, making the operation safer, and at the same time greatly reducing the probability of anterior cervical hematoma and complications [28]. However, the learning curve for microscopy is steeper and spine surgeons need a lot of practice to master microscopic operations.

2.2.2 Posterior cervical spine surgery

Posterior cervical spine surgery mainly includes laminectomy and laminoplasty, the former includes total laminectomy and hemilaminectomy, and laminoplasty has the difference between single-opening and double-opening. The main purpose of the surgery is to indirectly decompress the spinal cord by opening up the posterior wall of the spinal canal and allowing the spinal cord to drift backward away from the pressure-causing objects in front of the spinal canal. The advantages of posterior cervical spine surgery are complete decompression and higher safety, but there are more complications, such as postoperative axial pain, cervical instability, C5 nerve root palsy, and deterioration of neurological function in the long term [29]. In order to reduce the incidence of complications, many scholars have conducted in-depth research and exploration of posterior cervical surgery.

For example, in single-door cervical laminoplasty, three types of fixations, suture suspension, anchoring, and titanium plates, are widely used. Mo *et al.* [30] analyzed a large amount of literature and found that titanium plates were more advantageous than suture suspension or anchoring, with a greater range of motion after cervical spine surgery, and a lower incidence of axial symptoms and C5 nerve root paralysis. Liu *et al.* [31] found that, in the long-term follow-up of 98 patients with CSM who underwent single-door cervical laminoplasty, fixating titanium plates to the lateral block had a lower rate of hinge fracture, and fixation to the plate had less chance of C5 nerve root paralysis and less severity of axial symptoms. hinge fracture rate was lower when fixed to the lateral block, and the probability of C5 nerve root palsy and severity of axial symptoms were less when fixed to the plate.

Although total laminectomy is effective in decompression, it can greatly destabilize the cervical spine, which is not conducive to the long-term recovery of the patients. Ohtonari *et al.* [32] preserved the small joints and the collateral ligaments during laminectomy and demonstrated that the decompression effect of laminectomy was similar to that of conventional laminoplasty, and its imaging performance was not inferior to that of laminoplasty through a noninferiority test. Liu *et al.*[33] observed 68 multisegmental CSM patients and found that laminectomy and decompression combined with internal fixation of lateral screws and rods was better than laminoplasty combined with wire fixation in terms of surgical bleeding, postoperative recovery time, JOA score, physiological curvature recovery, cervical spine mobility, and the incidence of postoperative complications, thus confirming that laminectomy and decompression combined with internal fixation of lateral screws and rods has a definite clinical efficacy.

Although posterior cervical laminectomy and laminoplasty are effective, both require complete exposure of the spinous processes and vertebral plates, and have the shortcomings of being traumatic, bleeding, and prone to complications. For patients with single-stage CSM, open surgery can be endoscopically performed to reduce surgical trauma, and endoscopic laminectomy and laminoplasty (Endo-LOVE) can be used to partially decompress and remove the vertebral plate and synchondrosis in the necessary areas only. Some studies have shown that the use of this technique is safe and effective in the treatment of CSM. However, due to the poor endoscopic field of view, it is prone to instrumentation injury, inadequate hemostasis, and incomplete decompression, which further cause complications such as nerve injury, hematoma formation, and recurrence of the operated segment.

Due to the thinness of the cervical pedicle, manual pinning is prone to deviation, resulting in adverse outcomes. Robotic and navigation-assisted pinning greatly improves pinning accuracy and reduces surgical trauma. Zhang *et al.* [34] analyzed 369 cases of cervical spine surgery with navigation or robotic assistance, and the clinical effect of navigation and robotic-assisted pinning technology is clear. However, there are still some problems with this technique, i.e., it is difficult to accurately attach the data to the target vertebrae during surgery, which may cause the nail placement route to deviate from the planned route. With the continuous development of science and technology, it is believed that spinal surgery will move forward in the direction of more delicate and minimally invasive.

2.2.3 Combined anterior and posterior approach

Anterior approach can better solve the compression from the anterior part of the spinal cord and better maintain the balance of the sagittal and coronal positions of the cervical vertebrae, but when the spinal stenosis is severe, the anterior approach alone has the risk of causing spinal cord injury; whereas, posterior approach can solve the compression from the posterior part of the spinal cord or severe spinal stenosis resulting from extensive anterior approach; and when the responsible gap is more than three and the bone quality is poorer, then the combined anterior and posterior approach should be considered. Patients with poor bone quality [35], or severe anterior compression and severe spinal stenosis, should consider a combined anterior and posterior approach. Kuo *et al.* [36] followed 41 patients who underwent combined anterior and posterior surgery for more than 2 years, and the spinal cord function scores of the patients at the end of the follow-up were significantly improved compared with those of the preoperative period. Although there was a risk of cerebrospinal fluid leakage, the incisions healed well and no adverse long-term complications were found, confirming that combined anterior and posterior surgery has a good long-term clinical outcome.

2.3 Post-operative rehabilitation

In the treatment of CSM, although surgery can instantly relieve the compression of the spinal cord, the damage produced by the long-term compression of the spinal cord, or the irritation symptoms on the spinal cord during decompression during surgery will remain for a period of time after the operation, so postoperative rehabilitation is also a very important part of the treatment process of CSM. Some studies have found that appropriate postoperative interventions can effectively relieve patients' discomfort and accelerate their recovery.

Guo *et al.* [37] applied the Internet telecare model to the postoperative care of CSM, and found that this method performed better than conventional care in relieving symptoms and restoring neurological function. Dong [38] adopted the care model under the concept of rapid rehabilitation surgery for postoperative CSM patients, and compared with conventional care, the implementation of the concept of rapid rehabilitation surgery can to a certain extent promote the recovery of patients, reduce postoperative complications, and alleviate the pain of patients. Liu *et al.* [39] developed an individualized and precise exercise rehabilitation method for cervical spine stabilization through finite element biomechanical analysis of bony structural alterations in CSM patients after implementation of minimally invasive surgery.

3 Summary

Existing studies have mainly concluded that the pathogenesis of CSM is mainly ischemia, blood-spinal cord barrier damage, inflammation and apoptosis caused by spinal cord compression, and most of the clinical treatment plans for this disease are also focused on resolving the spinal cord compression, thus relieving the ischemic state of the spinal cord. However, studies have shown that these therapeutic measures can resolve spinal cord tissue ischemia after relieving spinal cord compression, but they cannot completely terminate spinal cord cell apoptosis, and certain neurological dysfunction still remains and requires prolonged rehabilitation and treatment. The pathogenesis of CSM has not yet been fully clarified, and the current therapeutic goals of spinal cord spondylosis are mainly focused on relieving symptoms, guiding the disease toward benign development, and improving the patient's quality of life and other aspects. Through the previous literature study, it was found that the treatment of this disease is mainly categorized into conservative and surgical treatments. Oral medication alone or combined with external therapies is suitable for most of the patients with mild CSM, but for those who do not have obvious effect of conservative treatment or whose disease continues to progress, surgical treatment should be performed as soon as possible. For limited compression from the ventral side of the spinal cord that does not involve the posterior border of the vertebral body, ACDF surgery can be used to locally decompress the compression; ACCF and ACAF can both relieve ossified compression from the posterior side of the vertebral body, but the difference in efficacy lies in the fact that ACAF is superior to ACCF in terms of complications and recovery of spinal cord function. ACDR surgery can preserve part of the mobility of the operated segments for a short period of time, but long-term follow-up studies have shown that it is more effective for patients with mild CSM than for those with progressive disease. However, long-term follow-up studies have shown that the problem of heterotopic ossification of the operated segments will make the long-term efficacy of this procedure not much different from that of ACDF. Compared with anterior surgery, the biggest advantage of posterior surgery is that it is safer, but there are more postoperative complications than anterior surgery. Combined anterior and posterior surgery is very traumatic, with high blood loss, and it is not recommended to choose this procedure easily if there is not severe compression on both the ventral and dorsal sides of the spinal cord. With the development of science and technology, the input of microscope, robot, navigation system and other equipment makes cervical spine surgery more refined and minimally invasive. Care should be taken in developing a surgical plan that seeks to address the patient's most predominant symptoms with minimal trauma. Postoperative rehabilitation care is also an essential part of the treatment of CSM, which can optimize the surgical effect and reduce the patient's postoperative discomfort to a certain extent. In the future, basic research related to the pathogenesis of CSM and clinical research related to its treatment should be linked together to realize mutual complementarity and common progress.

Conflict of interest: None

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· 研究进展 ·

脊髓型颈椎病发病机制及治疗措施的研究进展

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摘要:脊髓型颈椎病(CSM)是颈椎病中最严重的一个亚型,是造成中老年人群脊髓功能障碍的主要原因。本病发病机制复杂,主要包括退变老化、动态失稳、脊髓缺血、脊髓损伤、炎症、细胞凋亡等可能的机制。治疗方案主要包括保守治疗和手术治疗,保守治疗包括药物、针刺、艾灸、牵引、物理治疗和手法治疗等方式,手术治疗根据手术入路可分为前路手术、后路手术、前后联合手术。治疗方案的选择应结合患者症状、体征以及辅助检查的结果等多方面综合考量,但如何选择适宜的治疗方案仍是临床医生关注的焦点。本文着重探讨该病的发病机制及治疗方法的相关研究进展,为 CSM 的诊断、治疗提供参考。

关键词: 脊髓型颈椎病; 椎管狭窄; 颈椎前路椎间盘切除融合术; 颈椎后路手术
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Research progress on the pathogenesis and treatment of cervical spondylotic myelopathy

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Abstract: Cervical spondylotic myelopathy (CSM) is the most serious subtype of cervical spondylosis, which is the main cause of spinal cord dysfunction in middle-aged and elderly people, and the pathogenesis of this CSM is complex, mainly including degenerative aging, dynamic instability, spinal cord ischemia, spinal cord injury, inflammation, apoptosis, and other possible mechanisms. The clinical treatment of the CSM mainly includes conservative treatment and surgical treatment, conservative treatment includes drugs, acupuncture, moxibustion, traction, physical therapy and manual treatment, surgical treatment can be divided into anterior surgery, posterior surgery, anterior and posterior combined surgery according to the surgical approach. The choice of treatment regimen should be based on the patient's symptoms, signs, and the results of auxiliary examinations, but how to choose the appropriate treatment plan is still the focus of clinicians. This article focuses on the research progress of the pathogenesis and treatment methods of this disease, in order to provide a reference for the diagnosis and treatment of cervical myelopathy.

Keywords: Cervical spondylotic myelopathy; Spinal canal stenosis; Anterior cervical discectomy and fusion; Posterior cervical surgery
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脊髓型颈椎病(cervical spondylotic myelopathy,CSM)是以颈椎和脊髓周围软组织退变为病理基础,压迫脊髓或影响其血供导致脊髓受损而产生不同程度髓性症状的退行性疾病。该病好发于老年男性,但有逐渐年轻化的趋势。CSM 往往同时影响多个颈髓节段,但以 C5/6 水平最为常见,C3/4 水平次之[1]。CSM 发病缓、病程长,早期不易发现,晚期易造成不可逆转的脊髓神经损害,严重影响患者的肢体功能和生活质量,因此对其发病机制和治疗措施的研究十分必要。

1 发病机制

CSM 的致病因素主要包括静态因素和动态因素。静态因素与椎管狭窄密切相关,先天发育和颈椎退变是造成颈椎管

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狭窄的两个主要因素。有研究表明,先天性颈椎管狭窄与 CSM 的发病密切相关,当颈椎椎管直径小于 13 mm 时,CSM 的发病几率明显升高[2]。颈椎退变常见表现有椎间盘突出、椎体骨赘形成、后纵韧带骨化、黄韧带增生钙化等[3]。动态因素则表现为反复运动将静态因素影响放大,致颈髓慢性损伤。

长期机械损伤会对神经元和神经胶质细胞造成直接损伤,进而引发一系列的病理生理学改变。常见的有局部缺血、血-脊髓屏障破坏(blood-spinal cord barrier, BSCB)、炎症和细胞凋亡等。

1.1　*缺血*　自上世纪中叶,就有研究通过动物实验首次证实了缺血是导致脊髓退变的一个重要发病机制。局部血管形变、血管自身病理变化等都会加剧脊髓缺血。Tomonori 等[4]通过构建动物脊髓缺血模型,发现脊髓缺血 20 min 后,即可在前角细胞和后角细胞中可观察到神经元的中心性色素溶解和髓鞘空泡化。虽然此类实验无法直接在人身上进行,但也为人脊髓退变可能的病理生理学机制提供了研究的方向。

1.2　BSCB　是血液和脊髓实质之间的物理屏障,能阻止毒素、血细胞和病原体进入脊髓,维持脊髓实质的稳态,为正常神经功能提供必要的环境。当 BSCB 的结构和功能受到破坏时,脊髓内环境的稳态也会受到不同程度的干扰,最终导致神经功能缺损[5]。虽然目前尚无有效的临床手段来恢复 BSCB 破坏后导致的脊髓损伤,但有研究表明,一种组蛋白脱乙酰酶 Sirtuin 1(SIRT 1)可通过将氧化还原蛋白 p66Shc 脱乙酰化来保护内皮屏障,有望成为治疗脊髓损伤的一个突破口[6]。

1.3　*炎症*　当髓受到压迫时,BSCB 的破坏会导致脊髓血管通透性增加,并促进炎症细胞从外周循环进入,外周来源的免疫细胞与小胶质细胞、星形胶质细胞、内皮细胞所产生的细胞因子、趋化因子等介质共同引导了神经的炎症反应[7]。神经炎症又进一步加剧了脊髓的退变,形成恶性循环。

1.4　*细胞凋亡*　细胞凋亡往往发生在细胞炎症后的几小时内,这是一个需要能量和蛋白质合成的程序化细胞死亡过程[8]。这个过程在神经元、少突胶质细胞、小胶质细胞甚至星形胶质细胞中均有发生。有动物实验结果表明,手术减压并不能完全消除细胞凋亡,但可以明显降低 CSM 动物模型神经细胞的凋亡水平,从而改善神经功能[9]。

2　治　疗

CSM 应根据患者的症状、体征和影像学检查来制定个体化的治疗方案,主要包括保守治疗和手术治疗。Fehlings 等[10]建议,对于没有神经根或髓性症状的患者,不要进行预防性手术;对于轻症患者,可以采用保守治疗,若保守治疗无效且症状进展,则应考虑行手术干预;对中、重度的 CSM 患者可直接行手术治疗。

2.1　*保守治疗*

2.1.1　药物治疗　目前临床尚无特效药物可根治 CSM,只能据其症状给予对症治疗,减轻患者痛苦、提高生活质量,常用的西药主要分为非甾体抗炎药、营养神经药、神经消肿药、肌松药几大类,急性期或术后患者还可考虑应用类固醇激素药物,但此类药物不能长期大量使用[11]。

中医认为本病内因多与肝、脾、肾功能密切相关,外因则有外感风寒湿邪、久劳成损等[12]。常将其分为肝肾亏虚、气血不足、瘀血阻络、湿热浸淫和阴血亏虚 5 种证型,并分别采取相应的中药对症治疗[13]。朱立国等[14]认为治疗当以补益肝肾法、益气补血法、活血通络法进行辨证论治,自拟“益肾养髓方”以“补肾益髓、通络除痹”,并运用此方对 35 例 CSM 患者进行辨证施治,通过随访观察患者的脊髓功能变化,发现该方治疗 CSM 效果良好[15]。施杞教授认为 CSM 的治疗当以调和气血、活血化瘀、补益肝肾,其团队运用施杞教授拟定的“益气活血补肾方”对 109 例 CSM 患者进行治疗随访,最终发现此方对中轻型 CSM 的治疗有一定效果[16]。除此之外,还有学者通过研究也证实了中医对于轻型 CSM 的疗效确切[17]。通过这些研究,考虑中医药取得效果的机制可能是改善了脊髓的局部血液循环、减轻局部缺血,从而缓解症状。

2.1.2　外治法　对于单纯内服药物治疗效欠佳的患者,常结合外治法进行治疗,常用的外治法以中医理疗为主,包括针灸、牵引、手法治疗等。为提高疗效,往往同时使用多种外治法联合施治。吴弢等[18]采取针灸配合地黄饮子加减治疗 CSM 患者 30 例发现,针灸组患者的颈痛、二便情况的改善较明显。李业甫教授则考虑规范的推拿可以通过改善颈部血运来促进水肿神经根周围炎症的吸收,亦可松解肌肉,改善颈椎紊乱状态、减轻机械压迫,并通过推拿手法配合牵引治疗 34 例CSM 患者,其中 30 例均有不适症状的缓解[19]。但无论内治、外治,多数研究针对的是早期、轻症,而对于晚期、重症患者,在保守治疗无效果的情况下,应积极考虑行手术治疗。

2.2　*手术治疗*

2.2.1　颈椎前路手术　颈椎前路手术包括颈椎前路椎间盘切除融合术(anterior cervical discectomy and fusion, ACDF)、颈椎前路椎体次全切除融合术(anterior cervical corpectomy and fusion, ACCF)、颈椎前路椎体骨化物复合体前移融合术(anterior controllable antedisplacement and fusion, ACAF)和人工颈椎间盘置换术(artificial cervical disc replacement, ACDR)。颈椎前路手术入路通常采用 Smith-Peterson 入路,一般选择颈前皮纹作横向切口,钝性分离颈阔肌,从胸锁乳突肌内侧缘间隙,颈动脉鞘与气管、食道间隙抵达椎体前缘,切开前纵韧带即可见椎体和间盘,再根据不同手术方式进行相应操作。

ACDF 的优点在于可以对脊髓和神经根进行直接减压,且具有稳定的疗效和安全性,为治疗 CSM 的金标准。ACDF 的不足也较为明显,如术中因视野狭窄而造成减压不彻底,术后出现吞咽困难、假体不融合、融合器下沉等并发症。为解决这些问题,临床医师对手术方式进行优化,对椎间融合器进行改进。零切迹椎间融合器在植入后隐藏在椎体前缘之后,较好地解决了术后吞咽困难的问题,并且在恢复椎间高度、颈椎生理曲度等方面与传统 ACDF 相比无显著差异[20]。3D 打印椎间融合器因其较好的弹性模量、易于骨组织爬行的微孔小梁结构则较好地解决了假关节形成、假体沉降等并发症[21]。

ACCF 相比于 ACDF 减压范围更大、视野更广阔、减压更

彻底,尤适用于压迫主要来自于椎体后方、颈椎管严重狭窄等经椎间隙减压困难的情况。但大量研究表明,在治疗多节段 CSM 时,ACDF 与 ACCF 在融合率、JOA 评分等疗效方面差异无统计学意义,且 ACCF 在术中出血量、假体沉降率、并发症发生率等方面的表现较 ACDF 欠佳[22]。韩树虹等[23]将 3D 打印人工椎体应用于 ACCF 手术中,发现与传统钛网相比,其与上下椎体终板的接触面积更大,应力更为分散,且接触面更为吻合,能够较好预防假体的沉降。

2017 年,史建刚教授团队创造性地提出 ACAF 的概念,为严重颈椎后纵韧带骨化症(OPLL)的外科治疗提供了新的思路与方法[24]。该术式通过在双侧钩椎关节附近对椎体进行纵向离断并向前方提拉来达到椎管减压的目的,由于其开槽位置偏外且减压过程中未将硬膜与后纵韧带分离,大大降低了脊髓损伤、脑脊液漏的风险,与颈椎后路手术相比又降低了脊髓过度后移导致的神经根牵拉等并发症。且该手术在临床上也取得了不错的远期疗效[25]。但目前为止关于 ACAF 并发症的报道较少,仍需要深入研究及远期随访。

虽然前路融合手术疗效确切,但融合后手术节段的关节活动度(ROM)丧失,相邻椎间盘活动度大大增加,易导致临近节段退变(ASD)加速。因此 ACDR 应运而生。该术式的优势在于可以在减压的同时保留颈椎的 ROM,降低临椎 ASD 的发生率[26]。2005 年首次报道了 ACDR 后手术节段异位骨化的发生[27]。有研究发现手术节段异位骨化并不会对 ACDR 的临床疗效产生影响,但由于手术节段异位骨化的发生,临近节段 ROM 逐渐上升,ACDR 在防止临椎 ASD 的优势也逐渐缩小[26]。ACDR 的局限性在于其学习曲线较长以及手术禁忌证较多,对于手术节段大于 3 个、颈椎不稳、关节突关节退行性变、对内植物过敏的患者则不适宜进行 ACDR 手术。

近年来,显微镜在颈椎前路手术中逐渐崭露头角,显微镜的应用解决了颈椎前路手术视野的问题。首先,显微镜为狭小的手术视野提供了稳定的光源和视野;其次,显微镜可将各结构三维立体的呈现出来,使手术操作更加精细,实现精准止血、精准减压,使手术更加安全,同时也大大降低了颈前血肿和并发症的发生概率[28]。但显微镜的学习曲线较为陡峭,脊柱外科医师需要大量练习才能熟练掌握镜下操作。

2.2.2　颈椎后路手术　颈椎后路手术主要包括椎板切除术和椎板成形术,前者包括全椎板切除术与半椎板切除,椎板成形术又有单开门与双开门之别。手术主要目的是通过打开椎管后壁,使脊髓向后漂移,离开椎管前方致压物从而达到间接减压。颈椎后路手术的优势在于减压彻底、安全性较高,但并发症较多,如术后轴性疼痛、颈椎不稳、C5 神经根麻痹、远期神经功能恶化等[29]。为降低并发症的发生率,许多学者对颈后路手术进行了深入研究探索。

如在单开门颈椎椎板成形术中,缝线悬吊、锚定和钛板三种固定方式被广泛应用。Mo 等[30]对大量文献分析后发现,钛板较缝线悬吊或锚定更有优势,颈椎术后可活动范围较大、轴性症状和 C5 神经根麻痹的发生率较低。Liu 等[31]对 98 例行单开门椎板成形术的 CSM 患者长期随访发现,将钛板固定于侧块时铰链骨折率较低,而固定于椎板时发生 C5 神经根麻痹的概率和轴性症状的严重程度更小。

全椎板切除术虽然减压效果良好,但是会极大破坏颈椎的稳定性,不利于患者术后的远期恢复。Ohtonari 等[32]在椎板切除术中保留了小关节和项韧带,并通过非劣性试验证明通过该方式减压效果与传统椎板成形术相近,并且其影像学表现并不逊色于椎板成形术。Liu 等[33]对 68 名多节段 CSM 患者进行分组观察,发现椎板切除减压联合侧块螺钉棒内固定术在手术出血量、术后恢复时间、JOA 评分、生理曲度恢复、颈椎活动度以及术后并发症发生率等方面的表现均优于椎板成形联合丝线固定术,证实椎板切除减压联合侧块螺钉棒内固定术临床疗效确切。

虽然颈椎后路椎板切除术和椎板成形术效果确切,但都需要完全暴露棘突和椎板,有创伤大、出血多、易发生并发症等不足。对于单阶段 CSM 的患者则可将开放手术内镜化,减小手术创伤,使用内镜下椎板开窗椎管减压术(Endo-LOVE)仅对必要区域椎板和关节突进行部分切除减压。有研究表明使用该技术治疗 CSM 安全有效。但由于内镜下视野较差,易发生器械损伤、止血不充分、减压不彻底等情况,进一步造成神经损伤、血肿形成、手术节段复发等并发症。

由于颈椎的椎弓根较细,手动置钉易产生偏差,造成不良的后果。机器人及导航辅助下置钉大大提高了置钉准确性并减少手术创伤。张琦等[34]研究显示导航及机器人辅助置钉技术在颈椎手术中临床效果确切。但此技术当前仍存在一定问题,即术中难以将数据准确附加于目标椎体,易造成置钉路线与规划路线产生一定偏差。随着科技的不断发展,相信脊柱外科手术也会向更精细、更微创的方向前进。

2.2.3　前后联合入路手术　前路手术可以较好解决来自脊髓前方的压迫,并能较好维持颈椎矢状位和冠状位的平衡,但当椎管狭窄严重时,单纯前路手术有造成脊髓损伤的风险;而后路手术可以解决来自脊髓后方的压迫或广泛的前路压迫所导致的严重椎管狭窄;而当责任间隙大于 3 个,且骨质较差[35],或前路压迫严重致椎管狭窄严重时,则应考虑前后联合入路手术。Kuo 等[36]对 41 例行前后路联合手术患者进行 2 年以上的随访,随访结束时患者的脊髓功能评分均较术前明显改善。虽然有发生脑脊液漏的风险,但切口均愈合良好,且未发现不良的长期并发症,证实了前后路联合手术在临床上有较好的远期疗效。

2.3　术后康复　在 CSM 的治疗中,手术虽然能即时解除脊髓的压迫,但脊髓受到长期压迫后产生的损伤,或手术中减压时对脊髓的刺激症状会在术后残留一段时间,所以术后康复对 CSM 治疗也十分重要。有研究发现,术后给予适当的干预措施可以有效缓解患者不适症状,加快患者康复。

郭淑娟等[37]发现互联网远程护理模式较常规护理在缓解 CSM 术后症状、恢复神经功能方面均表现出色。董姜[38]发现,与常规护理相比较,实施快速康复外科理念可在一定程度上促进患者恢复、降低术后并发症、减轻患者痛苦。刘金玉等[39]通过对实施微创手术后的 CSM 患者骨性结构改变进行有限元生物力学分析,制定个体化的精准运动康复方法,以达

到颈椎稳定的目的。

3 总　结

现有研究主要认为 CSM 的发病机制主要为脊髓受压后导致的缺血、血-脊髓屏障损伤、炎症和细胞凋亡。目前,本病的临床治疗方案也大多着眼于解决脊髓受压,从而缓解脊髓缺血的状态。但研究表明,这些治疗措施在缓解脊髓受压后,虽能解决脊髓组织缺血,但并不能完全终止脊髓细胞的凋亡,仍会残留一定的神经功能障碍,且需要长时间的康复和治疗。CSM 的发病机制尚未完全明确,治疗主要分为保守和手术治疗。单纯口服药物或联合外治手段对大部分轻型 CSM 患者较为适用,但对保守治疗疗效不明显甚或病情继续进展者,应尽早行手术治疗。对于来自脊髓腹侧且不累及椎体后缘的局限性压迫,可行 ACDF 手术进行局部减压;ACCF 与 ACAF 均可以对来自椎体后方的骨化性压迫进行解除,其疗效的区别在于 ACAF 在并发症、脊髓功能恢复程度等方面优于 ACCF;ACDR 手术可以在术后短期内保留手术节段的部分活动度,但远期随访研究表明,手术节段异位骨化的问题会使该手术远期疗效与 ACDF 差距不大;相比于前路手术,后路手术的最大优点即安全性高,但术后并发症较前路更多;前后路联合手术创伤大、失血多,若非脊髓腹背均受压严重,则不建议轻易选择该术式。随着科技的发展,显微镜、机器人、导航系统等设备的投入使颈椎手术更加精细化、微创化。在制定手术方案时应当慎重,争取用最小的创伤解决患者最主要的症状。术后的康复护理也是对 CSM 治疗过程中必不可少的一个环节,可以在一定程度上优化手术效果,减轻患者术后不适症状。未来应将 CSM 发病机制相关的基础研究与治疗相关的临床研究串联起来,实现互助互补,共同进步。

利益冲突　无

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