The influence of carotid atherosclerosis on surgical outcomes of patients with cervical spondylotic myelopathy

A retrospective study

Bohan Li, MMa, Shuling Liu, MDb, Yongmei Wang, MDC, Jie Zhao, MMd, Yang Song, MMd, Wen Xu, MMd, Cheng Zhang, MMd, Chunzheng Gao, MDd, Qian Zhao, MMd, Dongjin Wu, MDd.∗

Abstract

The appearance of atherosclerosis in the carotid artery may be suggest the possibility of atherosclerosis in the spinal cord artery, which can cause spinal cord ischemia and further lead to neural element damage.

According to the inclusion and exclude standard, there are 137 patients with cervical spondylotic myelopathy (CSM) incorporating retrospective analysis. These patients were consecutively admitted into The Second Hospital- Cheeloo College of Medicine- Shandong University from January 2016 to December 2018 and have accepted surgical treatment. All patients were examined by color Doppler ultrasound to detect carotid atherosclerosis before surgery. All patients were divided into 2 groups according to the presence or absence of carotid atherosclerosis: carotid atherosclerosis group (n = 88) and noncarotid atherosclerosis group (n = 49).

All patients were followed up for at least 12 months after surgery. Demographic and surgery-related data were collected and analyzed to identify potential factors that affect the surgical outcomes in CSM.

The average age of carotid atherosclerosis group (51 males and 37 females), and noncarotid atherosclerosis group (24 males and 25 females) were 62.02 ± 10.34 years (range, 38–85 years) and 49.61 ± 10.28 years (range, 26–67 years), respectively.

In carotid atherosclerosis group: pre and postoperative modify Japanese Orthopedic Association Scores (mJOA score) were 11.58 ± 1.82 and 14.36 ± 1.64; the recovery rate of mJOA score was 45.57% ± 13.28%. In noncarotid atherosclerosis group: pre and postoperative mJOA score were 12.00 ± 2.11 and 15.04 ± 1.70; the recovery rate of mJOA score was 53.90% ± 13.22%.

Univariate logistic regression analysis demonstrated that gender (P = .004), age ≥ 65 years (P = .001), duration of symptoms ≥ 12 months (P = .040), smoking history (P < .001), preoperative mJOA score ≤ 11 (P = .007) and carotid atherosclerosis (P = .004) were related to poor surgical outcomes. Multivariate logistic regression analysis showed significant correlations between poor surgical outcomes and age ≥ 65 years (P = .047), smoking history (P = .010), preoperative mJOA score ≤ 11 (P = .008) or carotid atherosclerosis (P = .047).

Carotid atherosclerosis may be a risk factor for poor surgical outcomes in CSM.

Abbreviations: CSM = cervical spondylotic myelopathy, mJOA score = modify Japanese Orthopedic Association Scores.

Keywords: age, carotid atherosclerosis, cervical spondylotic myelopathy, modify Japanese Orthopedic Association Scores, prognosis, surgical outcome
1. Introduction

Cervical spondylotic myelopathy (CSM) is one of the most common diseases among middle-aged and elderly people. The exact pathogenesis of CSM is not yet fully understood. Possible mechanisms contributing to CSM include mechanical compression,[1] ischemia,[2,3] the disruption of the blood-spinal cord barrier,[4,5] inflammation[6] and neural cell apoptosis.[7] These complex pathological changes lead to different clinical manifestations, progression and prognosis of CSM patients. CSM is 1 progressive disease, of which the onset is usually insidious. Once the diagnosis is clear, surgery is often recommended to decompress spinal cord. Decompression with or without fixation and fusion is an effective method for the treatment of CSM. However, patients with complete decompression of spinal cord show wide variations in surgical outcomes.[8] Although most patients are satisfied with the outcomes of surgery, there are currently no good indicators to accurately predict the neurological prognosis of surgically treated patients.[9] Previous studies have revealed that age, duration of symptoms, the baseline level of modify Japanese Orthopedic Association Scores (mJOA) score, have revealed that age, duration of symptoms, the baseline level of modify Japanese Orthopedic Association Scores (mJOA) score, hyperintense on T2-weighted in the cervical cord, and diabetes history are related to postoperative functional recovery of patients with CSM.[10,11]

Atherosclerosis is a systemic disease. Severe atherosclerosis can cause vascular stenosis and occlusion, which leads to tissue ischemia. These pathologies may occur in small vessels in spinal cord and result in spinal cord ischemia and neural degeneration.[2,3] Carotid artery is the “window” of the blood vessels throughout the body,[12] which is superficial and easy to check. In recent years, with the development and innovation of modern ultrasound technology and high-frequency transducer, as well as continuously improved quality of ultrasound images, ultrasound technology is widely used in the diagnosis of carotid atherosclerosis due to free invasion, simple operation and no radiation.

The appearance of atherosclerosis in the carotid artery often also suggests the possibility of atherosclerosis in other arteries throughout the body, including the spinal cord artery, which can cause spinal cord ischemia and further lead to neural element damage. In this study, clinical data and surgical results of CSM patients with or without carotid atherosclerosis were analyzed to determine the effect of carotid atherosclerosis on surgical outcomes in CSM.

The purpose of this study was to investigate whether carotid atherosclerosis may affect the prognosis of neurological function after surgery in patients with CSM. According to the results of this study, carotid atherosclerosis may be a risk factor for poor surgical outcomes in patients with CSM.

2. Materials and methods

The study was conducted in accordance with the principles of the Declaration of Helsinki, and the study protocol was approved by the ethics committee of The Second Hospital, Cheloo College of Medicine, Shandong University.

Medical records and radiographs obtained between January 2016 and December 2018 at The Second Hospital, Cheloo College of Medicine, Shandong University were retrospectively reviewed. All patients were diagnosed as CSM by MRI and other imaging examinations combined with clinical manifestations before surgery. The follow-up was less than 12 months, patients with asymptomatic cervical cord compression, previous surgery for CSM, previous or new cerebral infarction, active infection, neoplastic disease, rheumatoid arthritis, ankylosing spondylitis, trauma, concomitant symptomatic lumbar disc herniation and concomitant symptomatic lumbar spinal stenosis were excluded from the study. All patients underwent carotid ultrasound examination (ultrasound equipment: GE-LOGIQ-E9, probe: 11L-D high-frequency probe, frequency range: 6.67 to 10 MHz, detection depth: 50 mm) before surgery. Ultrasound examination was performed by an experienced deputy director physicians or chief physicians trained by the research group according to uniform carotid ultrasound diagnostic criteria.

The demographic data of the patients were collected as follows: gender, age, smoking history, diabetes history, hypertension history, duration of preoperative symptoms, cervical curvature (lordotic, straight, kyphotic),[13] cervical MRI T2 hyperintensity and T1 hypointensity, with or without carotid atherosclerosis. Data related to surgical outcomes were recorded, including surgical approach (anterior/posterior or combined), follow-up time, preoperative mJOA score, postoperative mJOA score and the recovery rate of mJOA score (recovery rate = [postoperative mJOA score-preoperative mJOA score]/[preoperative mJOA score] × 100%). Poor surgical outcome is defined as the recovery rate of mJOA score < 50%.[14] According to the findings of color Doppler ultrasound, the 137 patients included in the study were divided into carotid atherosclerosis group and noncarotid atherosclerosis group. Carotid artery intima-media thickness (cIMT) > 1.2 mm was considered as carotid atherosclerosis. According to the severity of atherosclerosis, it was divided into 4 subgroups, namely groups I-IV. The noncarotid atherosclerosis group was divided into 2 subgroups, group 1 (normal carotid artery) and group 2 (increasing carotid artery intima-media thickness, cIMT≤1.2 mm). Carotid atherosclerosis classification was as follows: Grade I, no plaque; Grade II, unilateral plaque, cIMT≤2 mm; Grade III, unilateral carotid plaque, cIMT>2 mm or bilateral plaque, but at least 1 plaque with cIMT≤2 mm; Grade IV, bilateral plaque, cIMT>2 mm.[15]

All statistical analyses were performed using SPSS 23.0. Numerical variables conforming to normal distribution were reported as the mean ± standard deviation. Numerical variables not conforming to normal distribution were represented as the median (P25, P75). Comparisons between groups were analyzed by Student t test or Mann–Whitney U test. Categorical variables were reported as frequency (%), and comparison between groups was performed using Chi-Squared test or Fisher exact test. Logistic regression analysis was used to determine the predictive factors of poor surgical outcomes. P < .05 was considered statistically significant.

3. Results

One hundred fifty-two consecutive patients with CSM were collected. Fifteen patients were lost to follow-up within 12 months postsurgery and were not included in this study. A total of 137 patients were included in the study, including 75 males and 62 females, with an average age of 57.6 ± 12.2 years and an average follow-up time of 42.6 ± 19.5 months.

For carotid atherosclerosis group, 51 males and 37 females were included; The mean age was 62.02 ± 10.34 years; The 48 patients had smoking history; The 35 and 32 patients were diagnosed with diabetes and hypertension, respectively; The duration of symptoms was 11.00 (5.25, 23.75) months; There were 40, 38 and 10 patients with lordotic, straight and kyphotic cervical curvature, respectively; MRI for cervical spinal cord
showed high signal intensity on T2 in 51 cases and low signal on T1 in 6 cases; For surgical approach, there were 57 cases of anterior approach, 23 cases of posterior approach and 8 cases of anterior combined with posterior approach; The pre and postoperative mJOA score was 11.58 ± 1.82 and 14.36 ± 1.64; The recovery rate of mJOA score was 45.57% ± 13.28%; The follow-up time was 40.08 ± 10.16 months.

Table 1 showed that there was no statistical difference between the 2 groups in terms of the following variables: sex, smoking history, diabetes history, hypertension history, cervical curvature, T2 high signal or T1 low signal in cervical spinal cord, number of lesion levels, duration of symptoms more than 12 months. The duration of symptoms in carotid atherosclerosis group was significantly higher than that of noncarotid atherosclerosis group (11.00 [5.25, 23.75] vs 6.00 [3.00, 13.5], P=.049).

Table 2 showed that there was no significant difference between 2 groups in surgical approach (57/28/3 vs 38/10/1, P=.298), the follow-up time (39.97 ± 10.20 vs 40.08 ± 10.16, P=.949), preoperative mJOA score (11.58 ± 1.82 vs 12.00 ± 2.11, P=.224) and the number of patients with preoperative JOA score ≤11 (31 vs 19, 35.2% vs 38.8%, P=.679). The postoperative mJOA score (14.36 ± 1.64 vs 15.04 ± 1.70, P=.024), the recovery rate of mJOA score (45.57% ± 13.28% vs

### Table 1

| Variable                     | Carotid atherosclerosis group (n=88) | Control group (n=49) | statistic | P value |
|------------------------------|--------------------------------------|----------------------|-----------|---------|
| Gender                       |                                      |                      | 1.023     | .312    |
| Male                         | 51 (58.0%)                           | 24 (49.0%)           |           |         |
| Female                       | 37 (42.0%)                           | 25 (51.0%)           |           |         |
| Age (yr)                     | 62.02 ± 10.34                        | 49.61 ± 10.28        | 6.746     | <.001   |
| Age≥65yr                     | 40 (45.5%)                           | 6 (12.2%)            | 15.564    | <.001   |
| Smoking                      | 48 (53.9%)                           | 24 (48.0%)           | 0.391     | .532    |
| Diabetes                     | 35 (39.3%)                           | 12 (24.0%)           | 3.360     | .067    |
| Hypertension                 | 32 (36.0%)                           | 12 (24.0%)           | 2.115     | .146    |
| Symptom duration (month)     | 11.00 (5.25, 23.75)                  | 6.00 (3.00, 13.5)    | 2.003     | .049    |
| Symptom duration ≥12mo       | 43 (48.9%)                           | 16 (32.7%)           | 3.373     | .064    |
| Affected level               |                                      |                      | 0.001     | .971    |
| single                       | 38 (43.2%)                           | 21 (42.9%)           |           |         |
| multiple                     | 50 (56.8%)                           | 28 (57.1%)           |           |         |
| Cervical alignment           |                                      |                      | 2.101     | .350    |
| Lordotic                     | 40 (45.5%)                           | 27 (55.1%)           |           |         |
| Neutral                      | 38 (43.2%)                           | 15 (30.6%)           |           |         |
| Kyphotic                     | 10 (11.4%)                           | 7 (14.3%)            |           |         |
| T2-weighted hyperintensity   | 51 (58.0%)                           | 20 (40.8%)           | 3.703     | .054    |
| T1-weighted hyperintensity   | 6 (6.8%)                             | 3 (6.1%)             | 0.025     | .875    |

The Independent-Samples t-test was used to assess normally distributed variables, the Mann–Whitney U test was used for non-normally distributed variables, and the Chi-Squared test or Fisher Exact test was used for categorical variables. P<.05 means have statistically significant difference.

### Table 2

| Variable                     | Carotid atherosclerosis group (n=88) | Control group (n=49) | statistic | P value |
|------------------------------|--------------------------------------|----------------------|-----------|---------|
| Surgical approach            |                                      |                      | 2.420     | .298    |
| Anterior                     | 57 (64.8%)                           | 38 (77.6%)           |           |         |
| Posterior                    | 28 (31.8%)                           | 10 (20.4%)           |           |         |
| Combined                     | 3 (3.4%)                             | 1 (2.0%)             |           |         |
| Follow-up (mo)               | 39.97 ± 10.20                        | 40.08 ± 10.16        | 0.064     | .949    |
| Mean preoperative mJOA score | 11.58 ± 1.82                         | 12.00 ± 2.11         | 1.221     | .224    |
| Preoperative mJOA score ≤11  | 31 (35.2%)                           | 19 (38.8%)           | 0.171     | .679    |
| Mean postoperative mJOA score| 14.36 ± 1.64                         | 15.04 ± 1.70         | 2.288     | .024    |
| Mean recovery rate of mJOA score (%) | 45.57 ± 13.28     | 53.90 ± 13.22        | 3.524     | .001    |
| Recovery rate <50%           | 44 (50.0%)                           | 12 (24.50%)          | 8.475     | .004    |

The Independent-Samples t-test was used to assess normally distributed variables, the Mann–Whitney U test was used for non-normally distributed variables, and the Chi-Squared test or Fisher Exact test was used for categorical variables. P<.05 means have statistically significant difference.
53.90% ± 13.22%, P = .001), and the number of patients with the recovery rate of mJOA score < 50% (44 vs 12, 50.00% vs 24.50%, P = .004) in carotid atherosclerosis group were significantly lower than those in noncarotid atherosclerosis group.

As shown in Table 3, univariate logistic regression analysis showed that gender (P = .004), age ≥ 65 years (P = .001), duration of symptoms ≥ 12 months (P = .040), smoking history (P < .001), mJOA score ≤ 11 (P = .007) and carotid atherosclerosis (P = .004) were the predictors of poor surgical outcomes in patients with CSM. Multivariate logistic regression analysis revealed that age ≥ 65 years (P = .047), smoking history (P = .010), mJOA score ≤ 11 (P = .008) and carotid atherosclerosis (P = .047) were related to poor surgical outcomes in patients with CSM.

Table 4 showed that, in noncarotid atherosclerosis group, there was no significant difference regarding surgical outcomes between the 2 subgroups. Difference analysis between 4 subgroups in carotid atherosclerosis group indicated that the severity of carotid atherosclerosis was not related to the functional prognosis of patients with CSM.

Two typical cases of CSM with carotid atherosclerosis are shown in Figure 1 and Figure 2.

Two typical cases of CSM without carotid atherosclerosis are shown in Figure 3 and Fig. 4.

### 4. Discussion

Surgery is an effective method for treatment of CSM, but the recovery of neurological function after surgery is very variable among different patients. Therefore, many researchers have made great efforts to study the prognostic factor of neurological function in CSM patients after surgery. In the evaluation and prediction of postoperative neurological recovery in patients with CSM, researchers expect to identify some preoperative factors to predict the prognosis of postoperative neurological function. According to the results, carotid atherosclerosis is 1 independent risk factor (P = .047) of the recovery of nerve function in CSM patients under surgery. However, the severity of carotid atherosclerosis was not related to the functional prognosis of patients with CSM.

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**Table 3**

| Variable                  | Univariate analysis | Multivariate analysis |
|---------------------------|---------------------|-----------------------|
|                           | β | Odds ratio (95% CI) | P value | β | Odds ratio (95% CI) | P value |
| Male gender               | 1.053 | 2.868 (1.398, 5.884) | .004 | 0.360 | 1.433 (0.563, 3.648) | .450 |
| Age ≥65 yr                | 1.253 | 3.500 (1.669, 7.342) | .001 | 0.885 | 2.423 (1.913, 5.798) | .047 |
| Smoking                   | 1.342 | 3.828 (1.843, 7.953) | < .001 | 1.234 | 3.436 (1.338, 8.821) | .101 |
| Diabetes                  | 0.699 | 2.001 (0.978, 4.136) | .057 |      |                      |        |
| Hypertension              | −0.137 | 0.872 (0.419, 1.815) | .714 |      |                      |        |
| Symptom duration ≥12 mo   | 0.727 | 2.069 (1.033, 4.143) | .040 | 0.685 | 1.983 (0.884, 4.450) | .097 |
| Multiple cervical levels affected | −0.109 | 0.897 (0.451, 1.783) | .757 |      |                      |        |
| Surgical approach         | 0.339 | 1.404 (0.742, 2.685) | .297 |      |                      |        |
| Cervical alignment        | 0.090 | 1.094 (0.670, 1.787) | .718 |      |                      |        |
| T2-weighted hyperintensity| 0.609 | 1.838 (0.920, 3.671) | .085 |      |                      |        |
| T1-weighted hypointensity | 0.635 | 1.887 (0.484, 7.365) | .361 |      |                      |        |
| Preoperative mJOA score ≤11| 0.986 | 2.682 (1.309, 5.493) | .007 | 1.158 | 3.318 (1.359, 7.459) | .008 |
| Carotid atherosclerosis   | 1.126 | 3.083 (1.422, 6.684) | .004 | 0.934 | 2.545 (1.013, 6.391) | .047 |

The Chi-Squared test was used for univariate analysis. *P < .05 was adopted as the enter criterion in each forward stepwise analysis.

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**Table 4**

| Carotid atherosclerosis | β | Odds ratio (95% CI) | P value |
|-------------------------|---|---------------------|---------|
| I ref                   | ref |     | .929 |
| II                      | 0.278 | 1.320 (0.398, 4.378) | .650 |
| III                     | 0.365 | 1.440 (0.439, 4.718) | .547 |
| IV                      | 0.099 | 1.100 (0.341, 3.551) | .873 |

*P < .05 was adopted as the enter criterion in each forward stepwise analysis.

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Figure 1. Patient 1, male, 45 years old. Preoperative carotid ultrasound showed bilateral carotid plaques (A). Preoperative MRI shows the spinal cord was compressed at C5/6, C6/7 with intramedullary T2-weighted hyperintensity (B). Anterior cervical discectomy and fusion were taken for this patient (C). Postoperative MRI showed complete decompression of the cervical spinal cord (D). Modified JOA score of this patient was 11 preoperatively and mJOA score was 14 at the last follow-up after surgery.
Atherosclerosis was not related to the recovery of nerve function in CSM patients. Although there are still controversies, studies have shown that ischemia is one of the important pathophysiological mechanisms of CSM. The damage of spinal cord blood perfusion results in dysfunction and even cell death of oligodendrocytes and neurons. Atherosclerosis and plaque formation can lead to stenosis of spinal artery, hemodynamics changes of spinal artery, reduction of blood supply of spinal cord, and further affect the recovery of patients with CSM after surgery. Most of adult spinal canal is a closed bony canal and the ultrasound produced by the ultrasonic instrument is difficult to penetrate the bone, so it is difficult to detect the spinal artery by the ultrasound. The blood supply of cervical spinal cord mainly comes from vertebral artery. Vertebral artery can be examined by ultrasound, but the part of vertebral artery located in the intervertebral foramen cannot be shown by ultrasound, which cannot completely indicate whether vertebral artery has atherosclerosis and whether it will affect the hemodynamic changes of the spinal artery. Spinal cord angiography and other examinations may increase the economic burden of patients and prolong the treatment time as well as angiography is an invasive examination. In recent years, with the development and innovation of modern ultrasound technology and high-frequency transducer, the quality of ultrasound image is improved significantly.
also improving. Ultrasound technology is widely used in the diagnosis of atherosclerosis due to free invasion, simple operation and no radiation and we can get examination results quickly.

With the development of ultrasound technology, its important role in diagnostic medicine has become increasingly prominent. Color Doppler ultrasound can obtain real-time imaging, realize the dynamic observation of blood flow, measure the blood flow velocity and arterial cross-sectional area. Meanwhile, it is cheap, convenient and fast. Therefore, compared with invasive examinations, color Doppler ultrasound is more suitable for screening vascular lesions.

Carotid artery is one of early-onset sites of atherosclerosis, so it can serve as an ideal and sensitive window to reflect the situation of atherosclerotic throughout the whole body. Carotid atherosclerosis is a risk factor for coronary artery disease. Since the autopsy study by Young et al, the relationship between carotid artery and coronary atherosclerosis has been recognized. Some studies have shown that carotid atherosclerosis is a risk factor for peripheral arterial occlusive diseases and is related to femoral atherosclerosis. (21) Carotid atherosclerosis is also a risk factor for cerebrovascular diseases. Studies by Chemless et al has revealed that carotid atherosclerosis increases the risk of transient ischemic attack. (22)

The above studies demonstrate that carotid atherosclerosis often suggests that other arteries in the body may also have atherosclerosis. The results of this study showed that preoperative carotid atherosclerosis has adverse effects on the surgical outcome of patients with CSM. It is speculated that there are some possible mechanisms contributing to the above results. First, the plaque formation of carotid artery may also indicate the existence of atherosclerosis or even plaque in spinal cord artery. Atherosclerosis or plaque will result in increased vascular fragility, decreased vascular elasticity, lumen stenosis and hemodynamic changes of spinal artery, which affect blood supply to the spinal cord. In addition, external mechanical compression on spinal cord may further damage blood supply of the spinal cord and further affect the functional recovery potential of the injured spinal cord. (23) The recovery potential of spinal cord artery and other compressed vessels after decompression is limited, and atherosclerosis may aggravate this pathological change, which may be one of the reasons why the recovery ratio of spinal cord function in carotid atherosclerosis group is lower than that in noncarotid atherosclerosis group. This study found that the severity of carotid atherosclerosis was not related to the postoperative recovery rate of patients with CSM. The possible reason is that the severity of carotid atherosclerosis cannot fully reflect the severity of spinal atherosclerosis, because the spinal artery is not a branch of the carotid artery, and the changes of carotid artery hemodynamics do not directly affect the spinal cord blood supply. This study also showed that there was no significant difference between the normal carotid artery group and increased carotid intima-media thickness group in surgical outcomes of patients with CSM. One possible explanation is that only increased intima-media thickness of the carotid artery does not affect the hemodynamic changes, the brittleness and elasticity of the blood vessels and blood supply of the spinal cord.

It has been reported that age is an independent risk factor of carotid atherosclerosis. With increasing age, the body’s arteries will naturally become sclerotic and form atherosclerotic plaques. (24) This study also found that the age of patients with carotid atherosclerosis was higher than that of patients without carotid atherosclerosis (62.02 ± 10.34 vs 49.61 ± 10.28). In multivariate logistic regression analysis, age ≥ 65 years was not a predictor of poor surgical outcomes of CSM, which may be due to the correlation between advanced age and carotid atherosclerosis. Some scholars have reported that long-term heavy smoking is a risk factor for carotid atherosclerosis, and smoking can cause atherosclerosis and even plaque formation through a variety of ways. (25,26) Smoking is considered to be a predictor of adverse surgical outcomes in CSM in this study, which may be due to that smoking is likely to cause atherosclerosis, thus affecting the blood supply of the spinal cord and further affecting the recovery of spinal cord nerve function. This study indicated that preoperative mJOA score ≤ 11 is 1 predictor of adverse surgical outcomes in CSM, which is consistent with other studies. (27) Diabetes mellitus has been reported to be 1 risk factor of poor surgical outcomes in CSM. However, the same results were not observed in this study, which may be due to the biased selection of patients.

There are several limitations on this study. This is a retrospective study which means lower evidence level. The sample size of this study is still small and the results need to be further confirmed by expanding the sample size. At present, the specific relationship between carotid atherosclerosis and spinal atherosclerosis is not clear, which should be investigated in future study.

5. Conclusions
The patients with CSM who had carotid atherosclerosis had poorer neurological function recovery after surgery than those without carotid atherosclerosis. Carotid atherosclerosis may be a risk factor for poor surgical outcomes in CSM.

Author contributions
Conceptualization: Dongjin Wu.
Data curation: Shuling Liu, Jie Zhao, Yongmei Wang.
Formal analysis: Bohan Li, Qian Zhao.
Investigation: Yang Song, Wen Xu.
Methodology: Chunzheng Gao, Dongjin Wu.
Project administration: Shuling Liu, Cheng Zhang.
Supervision: Chunzheng Gao, Dongjin Wu.
Visualization: Chunzheng Gao.
Writing – original draft: Bohan Li.
Writing – review & editing: Chunzheng Gao, Dongjin Wu.

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