CLINICAL ARTICLE

Anterior Cervical Decompression and Fusion Surgery for Cervical Spondylosis with Concomitant Tinnitus: A Multicenter Prospective Cohort Study

Liang Yang, MD[1,2], Yongchao Li, MD[2], Xiaodong Pang, MD, PhD[2], Duanming Li, MD[2], Ye Wu, MD, PhD[3], Xiongsheng Chen, MD, PhD[4], Baogan Peng, MD, PhD[2]

[1]Department of Orthopaedics, Featured Medical Center of Chinese People's Armed Police Forces, Tianjing, [2]Department of Orthopaedics, The Third Medical Center of Chinese PLA General Hospital and [3]Department of Orthopaedics, Beijing 304th Hospital, Beijing and [4]Spine Center, Department of Orthopaedics, Shanghai Changzheng Hospital, Second Affiliated Hospital of Naval Medical University, Shanghai, China

Objective: Cervical spondylosis is often accompanied by tinnitus. Up to now, there is a lack of large samples and prospective studies to investigate the effect of anterior cervical decompression and fusion (ACDF) on tinnitus associate with cervical spondylosis. To this end, we performed a prospective cohort study to assess the effectiveness of ACDF on the relief of tinnitus.

Methods: This was a multicenter, prospective, cohort clinical study. Between August 2017 and August 2018, 174 patients with cervical spondylosis accompanied by tinnitus were enrolled, with a follow-up of 12 months. Among the 174 patients, 142 received anterior cervical surgery (surgery group) and 32 received conservative treatment (conservative group). The primary end point was the mean change in scores on the tinnitus functional index (TFI). The secondary end points included tinnitus loudness, modified Japanese orthopaedic association scores (mJOA) for spinal cord function, and visual analogue scale (VAS) for neck pain. All the above indexes were measured before treatments and at 1, 3, 6, and 12 months after treatments. One-way analysis of variance and paired samples *t*-test was adopted for statistical analysis.

Results: The TFI score was reduced immediately after cervical decompression surgery (from 54.7 ± 15.6 to 32.3 ± 12.5, $P < 0.001$) and this was sustained at 12 months ($P < 0.001$). The TFI score of the conservative group also decreased (from 53.9 ± 16.8 to 45.2 ± 13.6, $P < 0.001$), but the effect was not maintained at 12 months ($P = 0.069$). There was a significant improvement in tinnitus loudness (from 5.2 ± 1.6 to 2.6 ± 1.9, $P < 0.001$), mJOA (from 12.0 ± 1.6 to 14.2 ± 1.6, $P < 0.001$), and VAS for neck pain (from 58.5 ± 9.6 to 22.0 ± 16.4, $P < 0.001$) in the surgical group. Improvements in the surgical group were statistically significantly greater than that in the conservative group ($P < 0.001$).

Conclusion: This study indicates that anterior cervical surgery can relieve tinnitus in patients with cervical spondylosis and that tinnitus is an accompanying manifestation of cervical spondylosis.

Key words: Anterior cervical decompression and fusion; Cervical disc degeneration; Cervical somatosensory; Cervical spondylosis; Tinnitus

Introduction

Tinnitus is a common and annoying symptom, and is the sensation of hearing a sound in the absence of an internal or external source, so it is also regarded as an auditory hallucination similar to central nervous pain.[1,2] The prevalence of tinnitus is about 10% to 15% of the total

Address for correspondence Baogan Peng, MD, PhD, Department of Orthopaedics, The Third Medical Center of Chinese PLA General Hospital, 69 Yongding Road, Haidian District, Beijing, China Tel: 86-010-57976611; Fax: 86-010-57976638; Email: pengbaogan76611@163.com
Xiongsheng Chen, MD, PhD, Spine Center, Department of Orthopaedics, Shanghai Changzheng Hospital, Second Affiliated Hospital of Naval Medical University, 415 Fengyang Road, Huangpu District, Shanghai, China Tel: +86 -021-81885633; Email: cxspine@smmu.edu.cn
Liang Yang and Yongchao Li are co-first authors.
Received 26 May 2022; accepted 11 October 2022

population, which can seriously affect quality of life.[3] In the group of patients with chronic tinnitus, a subgroup called cervicogenic somatic tinnitus (CST) can be defined, which is related to the somatosensory system of the cervical spine.[4–12] A large number of basic studies have found the neural connection between the neck somatosensory system and the cochlear nucleus (CN).[13–17] The exact prevalence of CST is unclear, but previous studies have shown that CST accounts for 36.7% to 43% of total tinnitus patients.[6,18] The prevalence of cervical dysfunction in CST patients is much higher than that in other chronic subjective tinnitus patients.[7] Thus, CST is thought to be associated with cervical dysfunction.[6,7,19]

As cervical spondylosis is the most common disease of cervical dysfunction,[20] tinnitus in patients with cervical spondylosis has special value. In a retrospective study of total disc replacement in the treatment of cervical myelopathy and/or radiculopathy, 22.6% (30/133) of patients had tinnitus symptoms.[21] Recent studies have found that a large number of Ruffini corpuscles[22,23] and nociceptors[23–25] grow into the degenerative cervical intervertebral disc. It is suggested that the former is related to dizziness, while the latter is related to chronic neck pain.[26,27] Inflammatory mediators and cytokines have been shown to significantly increase in degenerative cervical discs, which can make these mechanoreceptors of cervical discs more sensitive to mechanical stimuli.[28] These mechanoreceptors may produce abundant somatic information and influence auditory perception, causing CST. If so, anterior cervical decompression and fusion (ACDF) surgery can effectively treat cervical spondylosis patients with CST by eliminating the abnormal somatic inputs generated by increased these mechanoreceptors in the degenerative cervical disc. In fact, a recently published narrative review and meta-analysis based on retrospective studies found that tinnitus symptoms associated with cervical spondylosis was significantly relieved after cervical compression.[29] To date, there is a lack of large sample and prospective study to investigate the effect of ACDF surgery on CST associate with cervical spondylosis. To this end, our aim was to undertake a prospective cohort study to analyze the process by which anterior cervical decompression relieves tinnitus and to explore the pathogenesis of this form of tinnitus.

Methods

Study Design

This was a multicenter, prospective, cohort clinical study (Trial registry number: ChiCTR-ONC-17012027). Patients were recruited from three third class hospitals. Ethics committee approval was sought and obtained at each institution (Institutional Review Board number: 2017022). The authors vouch for the completeness and accuracy of the data and analyses and for the fidelity of the study to the protocol.

Study Population

Between August 2017 and August 2018, 656 patients with cervical spondylotic radiculopathy and/or myelopathy were enrolled in three spinal centers. After more than three months of conservative treatment, they did not have any improvement, suitable for ACDF due to severe neurological dysfunction or intolerable symptoms. Among them, 174 patients who were accompanied by CST were collected in this study. All prospective participants underwent a complete audio-logical, ENT, and neurological investigation to rule out possible treatable causes for their tinnitus and provided written informed consent. A total of 142 patients (81.6%) underwent ACDF (surgery group). The remaining 32 patients refused surgery due to fear or other reasons and continued to receive conservative treatment (conservative group). A total of 158 cases (90.8%) were followed-up for one year, including 130 cases (91.5%) in the surgery group and 28 cases (87.5%) in the conservative group.

The inclusion criteria were as follows: (i) 18 to 55 years old, with typical clinical manifestations of cervical radiculopathy and/or myelopathy; (ii) cervical spinal cord or nerve root compression showed by MRI; (iii) tinnitus with or without other symptoms, such as dizziness, headache, blurred vision, and nausea; and (iv) referring to the diagnostic criteria of CST by Sanchez *et al.*, the occurrence time or increase of tinnitus is consistent with neck pain[4]; Tinnitus duration in all patients was longer than 3 months. Exclusion criteria were as follows: (i) patients with a history of cervical injury or surgery; (ii) patients with neurological diseases, vestibular diseases, temporomandibular disorders or any other possible treatable causes for tinnitus; (iii) those with congenital or developmental abnormalities of the cervical spine; and (iv) and those who were unable to comply with the study or took medication that may cause tinnitus. The study was in line with the Declaration of Helsinki and was approved by the ethical review committees of all participating hospitals. Informed written consent was obtained from all patients.

Treatment

Decompression and fusion segments depended on clinical manifestations and corresponding nerve root and/or spinal cord compressions shown on MRI. The choice of surgery levels was determined by a senior spine surgeon at each center (Baogan Peng, Ye Wu, and Xiongsheng Chen, respectively). Anterior cervical interbody fusion was performed with a cage which was filled with autogenous bone obtained by local decompression and anterior plate fixation. The operative segments ranged from C2/3 to C7/T1 (Table 1). Conservative treatment included physiotherapy, intermittent fixation of the cervical collar, and oral medications including non-steroidal anti-inflammatory drugs, analgesics, and muscle relaxants.

End Points

The primary efficacy end point was the mean change in scores on the tinnitus functional index (TFI)[30] from baseline to 12 months in the surgical group, as compared with the mean change in the conservative group. Scores on the TFI

were taken at baseline for both groups, and at 1, 3, 6, and12 months of follow-up.

The study was also powered for assessment of a secondary efficacy end point: Assessment of tinnitus loudness ("How loud is your tinnitus?": 0 = "no tinnitus" and 10 = "as loud as imaginable") was analyzed by visual analogue scale (VAS) which was asked before (pre) and directly after (post) the intervention, and at 3, 6, and 12 months of follow-up.[31] Other end points included neurological function improvement assessed by the modified Japanese orthopaedic association (mJOA) score[26] and relief of neck pain measured by 100 mm VAS score. In addition, according to the patient's self-assessment of therapeutic efficacy, the results were classified as "free of tinnitus," "improved" or "not improved."

Baseline data included age, sex, TFI score, tinnitus VAS score, mJOA score, neck pain VAS score, cervical spondylosis classification, and diseased cervical disc segment were collected before treatment. Re-evaluation was performed at 1, 3, 6, and 12 months, respectively, after treatment.

Statistical Analysis

Means, standard deviations, and 95% confidence intervals in TFI score, tinnitus VAS score, neck pain VAS score, and mJOA score from baseline were calculated. One way ANOVA was used to compare the two groups. Analyses of factors associated with improvements in the two treatment groups over 12 months were conducted with linear regression. Comparisons of TFI score, VAS score for tinnitus, VAS score for neck pain and mJOA at baseline, 1, 3, 6, and 12 months within groups were conducted with paired-samples *t*-test. The significance level was set at $P < 0.05$. SPSS version 23.0 (IBM, Quarry Bay, Hong Kong) was used to analyze the data.

Results

Tinnitus Functional Index (TFI)

After treatment, the comparison of TFI scores at each time point between the two groups showed significant differences. After cervical decompression, TFI scores of the surgery group decreased immediately ($P < 0.001$) and lasted for 12 months (Tables 2 and 3 and Fig. 1, $P < 0.001$). The TFI score of the conservative group also decreased ($P < 0.001$), but the improvement did not last for 12 months ($P = 0.069$). Improvements in the surgical group were statistically significantly greater than that in the conservative group (Table 4, $P < 0.001$). Linear regression with the outcome of changes and independent variables group (surgery vs. conservative) showed that the improvements were significantly associated with group (Table 5, $P < 0.001$). Besides, in order to explore the influence of surgical segments on tinnitus improvement, we divided the surgery patients into two subgroups, single segment (n = 74, 56.9%) and multi-segment (more than 2 segments, n = 56, 43.1%) and compared the TFI scores between the two subgroups at baseline and 12 months. There was no significant difference in TFI scores between the two subgroups (55.7 ± 16.9 and 53.4 ± 13.8 at baseline, $P = 0.053$; 33.0 ± 14.4 and 32.7 ± 14.0 at 12 months, $P = 0.626$). As most of the lesions occurred in the lower cervical spine in this study (only one case was C2/3, and the others were C3/4-C7/T1), we were unable to compare the differences in the improvement of tinnitus in patients with degenerative changes in the upper and lower cervical spine.

Visual Analogue Scale (VAS) of Tinnitus

The VAS scores of tinnitus in the surgical group decreased immediately ($P < 0.001$) and lasted for 12 months (Tables 2 and 3 and Fig. 1, $P < 0.001$). The VAS scores of tinnitus in the conservative group also decreased ($P < 0.001$), but the improvement did not last for 12 months ($P = 0.283$). However, the VAS scores of tinnitus in the surgical group were significantly lower than that in the conservative group at each time point (Fig. 2, $P < 0.001$).

Modified Japanese Orthopaedic Association (mJOA) Score

The mJOA scores in the surgical group were 12.0 and 14.2 at baseline and 12 months, respectively, while those in the conservative group were 12.9 and 13.0 at baseline and 12 months. Compared with the baseline score, the mJOA score of the

TABLE 1 Comparison of participant characteristics of the two treatment groups at baseline

Characteristic	Surgery group (n = 142)	Conservative group (n = 32)	*P*
Sex, female, n (%)	81(57.0%)	14(43.8%)	0.17
Age (y)	46.7 (6.3)	47.1 (4.8)	0.09
TFI	54.5 (15.3)	52.7 (16.7)	0.42
VAS for tinnitus	5.2 (1.6)	5.3 (1.3)	0.09
VAS for neck pain	58.4 (9.6)	55.4 (7.4)	0.80
mJOA	12.0 (1.6)	12.9 (1.5)	0.73
Type of CS			
CSM	85 (59.9%)	19 (59.4%)	
CSR	27 (19.0%)	8 (25.0%)	
Mixed CS	30 (21.1%)	5 (15.6%)	
Diseased level	n = 223	n = 48	
C2/3	1 (0.4%)	0 (0%)	
C3/4	15(6.7%)	2 (4.2%)	
C4/5	54 (24.2%)	12 (25.0%)	
C5/6	91 (40.8%)	18 (37.5%)	
C6/7	57 (25.6%)	13 (27.1%)	
C7/T1	5 (2.2%)	3 (6.3%)	

Notes: Data are mean (SD) or number (%). Comparison of means among two groups (significant at $p < 0.05$).; Abbreviations: CS, cervical spondylosis; CSM, cervical spondylotic myelopathy; CSR, cervical spondylotic radiculopathy; Mixed CS, mixed cervical spondylosis; mJOA, modified Japanese orthopaedic association scores; SD, standard deviation; TFI, tinnitus functional index; VAS, visual analogue scale.

TABLE 2 Comparison of changes in outcome measures over 12 months for each treatment group

Measure	Group	Baseline mean (SD)	1 month mean (SD)	12 months mean (SD)	1 month vs. baseline Mean diff (95% CI)	1 month vs. baseline p	12 months vs. baseline Mean diff (95% CI)	12 months vs. baseline P
TFI	SG	54.7 (15.6)	32.3 (12.5)	32.9 (14.2)	22.4 (19.3, 25.5)	0.000*	21.9 (18.8, 25.0)	0.000*
	CG	53.9 (16.8)	45.2 (13.6)	50.6 (15.2)	8.8 (4.7, 12.8)	0.000*	3.3 (−0.3, 6.9)	0.069
VAS for tinnitus	SG	5.2 (1.6)	2.9 (1.7)	2.6 (1.9)	2.3 (2.0, 2.7)	0.000*	2.6 (2.3, 3.0)	0.000*
	CG	5.4 (1.2)	4.6 (1.0)	5.2 (1.1)	0.8 (0.5, 1.1)	0.000*	0,2 (−0.2, 0.5)	0.283
VAS for pain	SG	58.5 (9.6)	28.4 (18.7)	22.0 (16.4)	30.1 (27.1, 33.2)	0.000*	36.5 (33.7, 39.3)	0.000*
	CG	54.8 (7.6)	38.2 (5.1)	43.1 (6.6)	16.5 (14.2, 18.8)	0.000*	11,7 (8.4, 15.0)	0.000*
mJOA	SG	12.0 (1.6)	14.0 (1.5)	14.2 (1.6)	−2.0 (−2.2, −1.7)	0.000*	−2.2 (−2.4, −1,9)	0.000*
	CG	12.9 (1.6)	13.3 (1.3)	13.0 (1.5)	−0.4 (−0.8, 0)	0.062	−0.1 (−0.7, 0.5)	0.721

Abbreviations: 95% CI, 95% confidence interval; CG, conservative group; Mean diff, difference among groups for the least squares mean; mJOA, modified Japanese orthopaedic association scores; SD, standard deviation; SG, surgery group; TFI, tinnitus functional index; VAS, visual analogue scale.; * $p < 0.05$

TABLE 3 All outcome measures over 12 months for each treatment group (mean ± SD)

Measure	Group	Baseline	1 Month	3 Months	6 Months	12 Months
TFI	SG	54.7 (15.6)	32.3 (12.5)	33.0 (12.3)	33.1 (13.4)	32.9 (14.2)
	CG	53.9 (16.8)	45.2 (13.6)	49.4 (14.1)	49.8 (14.7)	50.6 (15.2)
VAS for tinnitus	SG	5.2 (1.6)	2.9 (1.7)	2.6 (1.8)	2.5 (1.8)	2.6 (1.9)
	CG	5.4 (1.2)	4.6 (1.0)	5.0 (1.3)	5.0 (1.2)	5.2 (1.1)
VAS for pain	SG	58.5 (9.6)	28.4 (18.7)	23.8 (16.4)	22.7 (16.0)	22.0 (16.4)
	CG	54.8 (7.6)	38.2 (5.1)	42.8 (6.7)	43.3 (6.7)	43.1 (6.6)
mJOA	SG	12.0 (1.6)	14.0 (1.5)	14.1 (1.5)	14.2 (1.6)	14.2 (1.6)
	CG	12.9 (1.6)	13.3 (1.3)	13.1 (1.4)	13.0 (1.5)	13.0 (1.5)

Abbreviations: CG, conservative group; mJOA, modified Japanese orthopaedic association scores; SD, standard deviation; SG, surgery group; TFI, tinnitus functional index; VAS, visual analogue scale.

surgery group was significantly improved at each time point after treatment (Tables 2 and 3, $P < 0.001$). There was no significant improvement in mJOA score in the conservative treatment group at each time point ($P > 0.05$). After 12 months of treatment, the increase of mJOA score in the surgery group reached the lowest clinically significant difference (1 to 2 points),[32] while that in the conservative group did not reach it.

Visual Analogue Scale (VAS) of Neck Pain

The mean neck pain intensity on VAS in both groups was greater than 54 mm before treatment, indicating severe pain.[33] After treatment, the pain in both groups was significantly reduced, lasting for 12 months ($P < 0.001$). The neck pain score of the surgery group was significantly lower than that of the conservative group at each time point after treatment (Fig. 3, $P < 0.001$). The average pain intensity in the surgical group decreased from severe at baseline to mild (VAS score < 30 mm) after treatment. The conservative group changed from severe to moderate (VAS 30 mm to 54 mm) after treatment (Tables 2 and 3).

Patients' Rating of the Treatment

After 12 months of follow-up, 35 cases (26.9%) in the surgery group felt "free of tinnitus," 80 cases (61.5%) felt "improved," and 15 cases (11.5%) felt "not improved." In the conservative group, no one felt "free of tinnitus," 12 cases (42.9%) felt "improved" and 16 cases (57.1%) felt "not improved."

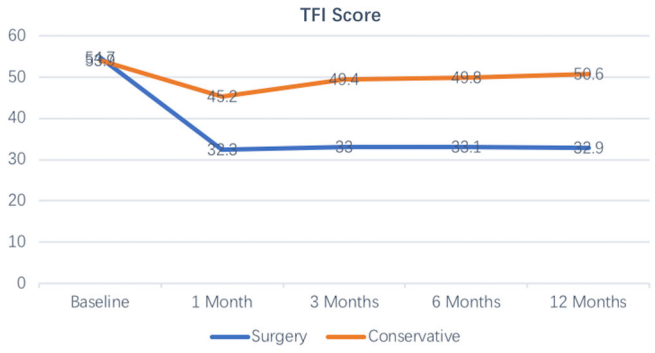

Fig. 1 Changes of tinnitus functional index (TFI) over time in both groups

TABLE 4 Comparison of improvements in the two treatment groups over 12 months

Improvements	Surgery group (n = 130)	Conservative group (n = 28)	*P*
TFI (baseline−1 month)	22.4 (18.0)	8.8 (10.4)	0.000
TFI (baseline−3 month)	21.7 (17.5)	4.6 (10.1)	0.000
TFI (baseline−6 month)	21.6 (18.0)	4.1 (9.5)	0.000
TFI (baseline−12 month)	21.9 (18.0)	3.3 (9.3)	0.000
VAS for tinnitus (baseline−1 month)	2.3 (2.1)	0.8 (0.8)	0.000
VAS for tinnitus (baseline−3 month)	2.7 (2.1)	0.4 (0.9)	0.000
VAS for tinnitus (baseline−6 month)	2.7 (2.2)	0.4 (0.9)	0.000
VAS for tinnitus (baseline−12 month)	2.6 (2.2)	0.2 (0.9)	0.000
mJOA (1 month–baseline)	2.0 (1.3)	0.4 (1.1)	0.000
mJOA (3 month–baseline)	2.1 (1.3)	0.3 (1.2)	0.000
mJOA (6 month–baseline)	2.1 (1.3)	0.2 (1.4)	0.000
mJOA (12 month–baseline)	2.2 (1.4)	0.1 (1.6)	0.000
VAS for pain (baseline−1 month)	30.0 (17.7)	16.5 (5.9)	0.000
VAS for pain (baseline−3 month)	34.7 (15.4)	12.0 (8.6)	0.000
VAS for pain (baseline−6 month)	35.8 (15.5)	11.5 (9.1)	0.000
VAS for pain (baseline−12 month)	36.5 (16.2)	11.7 (8.5)	0.000

Notes: Data are mean (SD). Comparison of means of improvements among two groups (significant at $p < 0.05$).; Abbreviations: mJOA, modified Japanese orthopaedic association scores; SD, standard deviation; TFI, tinnitus functional index; VAS, visual analogue scale.

Complications

Eight patients had mild dysphagia and six patients had hoarseness immediately after operation, but all of the symptoms disappeared within 1 month after conservative treatment. Three patients developed C5 nerve root paralysis, and the symptoms disappeared within 3 months after conservative treatment. There were no other surgical complications, such as infection, implant loosening and falling off, and aggravation of neurological symptoms.

Discussion

The current study suggests that anterior cervical surgery can effectively improve the symptoms of tinnitus associated with cervical spondylosis, which is significantly better than conservative treatment. The TFI score was reduced immediately after cervical decompression surgery and this was sustained for 12 months. The TFI score of the conservative group also decreased, but the effect did not last for 12 months. Nervous function improved significantly in the surgery group, but not in the conservative group (Tables 2 and 3). In the surgery group, there was a positive correlation between lower TFI score and higher mJOA score at each follow-up time point. But there was no correlation between the two in the conservative group. This indicated that the improvement of tinnitus in the surgery group was related to anterior cervical decompression surgery.

TABLE 5 Linear regression with the outcome of changes and independent variables group (surgery vs. conservative)

	Unadjusted		Adjusted	
Improvements	Coefficient	*P*	Coefficient	*P*
TFI (baseline−1 month)	−0.297	0.000	−0.277	0.000
TFI (baseline−3 months)	−0.372	0.000	−0.355	0.000
TFI (baseline−6 months)	−0.371	0.000	−0.353	0.000
TFI (baseline−12 months)	−0.390	0.000	−0.373	0.000
VAS for tinnitus (baseline−1 month)	−0.288	0.000	−0.306	0.000
VAS for tinnitus (baseline−3 months)	−0.406	0.000	−0.419	0.000
VAS for tinnitus (baseline−6 months)	−0.410	0.000	−0.424	0.000
VAS for tinnitus (baseline−12 months)	−0.417	0.000	−0.430	0.000
mJOA (1 month–baseline)	−0.429	0.000	−0.334	0.000
mJOA (3 months–baseline)	−0.476	0.000	−0.392	0.000
mJOA (6 months–baseline)	−0.474	0.000	−0.414	0.000
mJOA (12 months–baseline)	−0.488	0.000	−0.414	0.000
VAS for pain (baseline−1 months)	−0.306	0.000	−0.278	0.000
VAS for pain (baseline−3 months)	−0.515	0.000	−0.483	0.000
VAS for pain (baseline−6 months)	−0.538	0.000	−0.500	0.000
VAS for pain (baseline−12 months)	−0.533	0.000	−0.493	0.000

Notes: Data are expressed as standardized coefficients beta. The independent variables are groups (surgery vs. conservative), adjusted for age, sex, and corresponding baseline data.; Abbreviations: TFI, tinnitus functional index; VAS, visual analogue scale; mJOA, modified Japanese orthopaedic association scores.

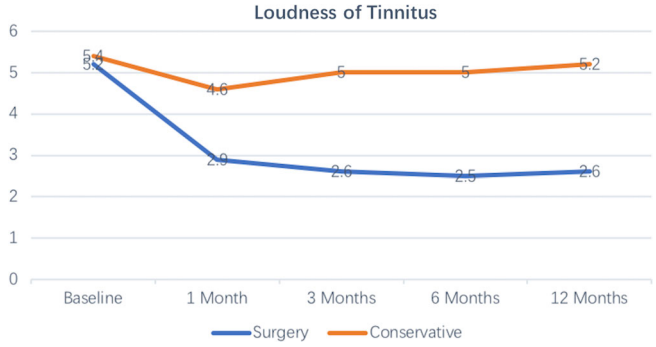

Fig. 2 Changes of tinnitus loudness (VAS scores) over time in both groups

Diagnostic Criteria of CST and Patient Selection

In this study, CST patients were included according to the diagnostic criteria of Sanchez *et al.*[4] However, as the focus of this study was CST population, the diagnosis was more limited than the initial criteria of somatic tinnitus. We excluded patients with head and neck trauma, as well as patients with temporomandibular disorders. After excluding other causes of tinnitus, the criterion 4 "temporal coincidence of appearance or increase of both pain and tinnitus" was used for the main diagnosis of CST. In fact, a recent study found that the simultaneous onset or increase and decrease of tinnitus and neck pain are most proposed to use as a single criterion for identifying patients with a certain influence on their tinnitus.[11]

As these patients we selected have severe neurological dysfunction or intolerable symptoms, it is obvious that a randomized controlled trial is not feasible in logic and ethics. Nevertheless, the clinical effect of this study cannot exclude some factors, such as placebo and Hawthorne effects.[34] However, we compared the effect of patients who did not agree with the surgery (conservative group) with that of the surgery group. Although the number of conservative group patients was not large, this conclusion can be more reliable. In addition, as this study was a prospective multicenter study, the external validity of this result was higher than that of a single-center study.

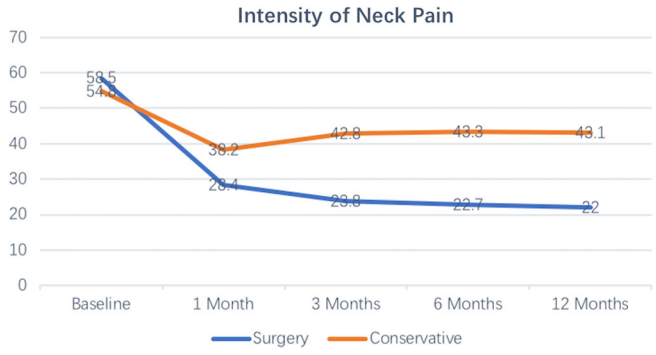

Fig. 3 Changes of intensity of neck pain (VAS scores) over time in both groups

Pathogenesis of CST

Tinnitus is a sound perception without external acoustic stimulation.[3] For years, tinnitus has been thought to be caused almost entirely by abnormal neuronal activity in the auditory pathway. However, researchers have concluded more often that in some people tinnitus can be induced or regulated through somatosensory systems, especially through cervical somatosensory system.[5–7,11,15,19,35] The somatosensory information of the cervical spine is transmitted to spinal trigeminal nucleus and dorsal column nucleus through the afferent fibers, the cell bodies of which are located in the dorsal root and trigeminal ganglia.[17] Secondary somatosensory neurons projecting to the cochlear nucleus are located in the trigeminal and the dorsal column nuclei.[36,37] In addition, some projections of spinal trigeminal and dorsal column nuclei converge with those of cochlear nucleus in the inferior colliculus. The projected cells of the inferior colliculus are mainly derived from the trigeminal and the dorsal column nuclei.[37] Stimulation of cervical dorsal root ganglia or trigeminal ganglia elicits excitation in some dorsal cochlear nucleus neurons.[15] Modulation of cervical somatosensory inputs on firing rate and synchrony of dorsal cochlear nucleus neurons is thought to be related to CST physiologically.[15] Therefore, the regulation of tinnitus by stimulating the somatosensory system may be achieved by activating the auditory areas through non-classical pathways.[4]

The connection between proprioceptive afferents in the neck and cochlear nucleus has been found.[38] In previous basic studies, Yang *et al.*[22,23] found that a large number of Ruffini corpuscles grew into the degenerative cervical disc. It is well known that Ruffini corpuscles, as a type of proprioceptors, are normally distributed around joints and sense the movement and direction of joints.[39] Further clinical studies have shown that a large number of Ruffini corpuscles in the degenerative cervical disc are associated with cervicogenic dizziness,[23,40] which is due to a strong connection between the cervical dorsal roots and the vestibular nuclei through the cervical proprioceptors.[27] For the same reason, we propose that in our study, the abnormal proprioceptive signals generated by Ruffini corpuscles may be transmitted to the cochlear nucleus, resulting in CST.

Neck Pain and CST

Degenerative cervical disc has scientifically been considered as a major source of neck pain.[25,26] Consistent with previous clinical studies,[4–12] the current study found that the main feature in our patients was the temporal coincidence of the onset or relief of both neck pain and tinnitus. But animal studies suggest a lack of direct nociceptive projections from the cervical somatosensory system to the auditory system.[13,15,36] Thus, theoretically, neck pain is unlikely to drive tinnitus directly. However, there are other cortico-cortical

pathways that are sensitive to pain and may cause somatic tinnitus.[41] In addition, neck pain has an effect on changes of cervical proprioceptive information from muscle spindles.[20,27,42] Both static and dynamic γ-motoneurons are excited by input of muscle nociceptive afferents, which were strong enough to increase the sensitivity of muscle spindles.[43,44] And in this circumstance, the sensitized muscle nociceptors and spindles will generate a positive feedback loop, which will result in a lot of abnormal somatic information, thereby resulting in CST.

Spinal Cord Function and CST

In our current study, we found some interesting phenomena. Some patients with cervical myelopathy, their spinal cord function was severely impaired, but their CST was not. In contrast, some patients with cervical radiculopathy, where only one nerve root was compressed, had severe CST. These confusing phenomena may be related to the severity of the inflammatory response and the number of Ruffini corpuscles and nociceptors growing in the degenerated cervical disc.

Strengths and Limitations

To our knowledge, the current study is the first large sample, multicenter prospective cohort study to investigate the effect of ACDF on concomitant tinnitus associated with cervical spondylosis. Nevertheless, there are several potential limitations in our research that should be mentioned. First, in this study, surgical patients were selected based on their cervical radiculopathy and/or myelopathy rather than tinnitus. That is to say, the main purpose of choosing ACDF surgery is to improve the symptoms of cervical myelopathy and/or radiculopathy. Therefore, the results cannot be interpreted as all patients with cervical myelopathy and/or radiculopathy complicated by CST should be treated with anterior cervical decompression surgery. Only those patients with cervical spondylosis complicated by CST who have reached the indication of surgical decompression due to cervical myelopathy and/or radiculopathy can be treated with ACDF. Second, the pathogenesis of CST may be multifactorial. Most of the studies related to CST, including this study, are clinical studies and cannot provide direct and convincing evidence to confirm the pathogenesis of CST. However, this study provides a direction for relevant basic research. In addition, the diagnosis and treatment of CST are still controversial among some scholars. In most literatures, the diagnostic criteria of CST are based on the criteria proposed by Sanchez *et al.*[4], and Michiels *et al.*[9] In 2018, the expert consensus on CST diagnostic criteria was published,[9] which also agreed with the diagnostic criteria proposed by Sanchez *et al.*[4] In our study, the diagnosis of CST also refers to the diagnostic criteria proposed by Sanchez *et al.* However, the diagnosis of CST, including expert consensus, is mainly based on symptoms and exclusivity, and further research is needed to explore its more detailed diagnostic criteria. Lastly, our study only completed a one-year follow-up, and further long-term follow-up is needed to confirm the efficacy of ACDF in the treatment of CST.

Conclusions

Our study indicates that ACDF can alleviate tinnitus associated with cervical spondylosis. Relief of tinnitus following anterior cervical surgery may be attributed to the excision of the degenerative cervical disc, removal of ingrown Ruffini corpuscles and nociceptors, thereby eliminating abnormal cervical somatosensory inputs. These clinical findings support previous basic science researches on the pathophysiology of tinnitus associated with cervical spondylosis.

Acknowledgments

We are grateful to the patients, the nurses and the staff who participated in this study.

Author Contributions

Bao-gan Peng and Xiong-sheng Chen designed and supervised the study, Liang Yang, Yong-chao Li and Bao-gan Peng drafted the manuscript, Liang Yang, Yong-chao Li, Xiao-dong Pang, Ye Wu and Xiong-sheng Chen carried out data analysis, Liang Yang, Yong-chao Li, Xiao-dong Pang, Duan-ming Li, Ye Wu and Xiong-sheng Chen performed data collection. The author(s) read and approved the final manuscript.

Ethical Statement

All patients provided written informed consent. The study was approved by the local ethics committee of the Third Medical Center of Chinese PLA General Hospital, Shanghai Changzheng Hospital and Beijing 304th Hospital.

References

1. De Ridder D, Schlee W, Vanneste S, et al. Tinnitus and tinnitus disorder: theoretical and operational definitions (an international multidisciplinary proposal). Prog Brain Res. 2021;260:1–25.
2. Dalrymple SN, Lewis SH, Philman S. Tinnitus: diagnosis and management. Am Fam Physician. 2021;103:663–71.
3. Baguley D, McFerran D, Hall D. Tinnitus. Lancet. 2013;382:1600–7.
4. Sanchez TG, Rocha CB. Diagnosis and management of somatosensory tinnitus: review article. Clinics (Sao Paulo). 2011;66:1089–94.
5. Oostendorp RA, Bakker I, Elvers H, et al. Cervicogenic somatosensory tinnitus: an indication for manual therapy? Part 1: theoretical concept. Man Ther. 2016;23:120–3.
6. Michiels S, Van de Heyning P, Truijen S, De Hertogh W. Diagnostic value of clinical cervical spine tests in patients with cervicogenic somatic tinnitus. Phys Ther. 2015;95:1529–35.
7. Michiels S, De Hertogh W, Truijen S, Van de Heyning P. Cervical spine dysfunctions in patients with chronic subjective tinnitus. Otol Neurotol. 2015;36:741–5.
8. Bousema EJ, Koops EA, van Dijk P, Dijkstra PU. Association between subjective tinnitus and cervical spine or temporomandibular disorders: a systematic review. Trends Hear. 2018;22:2331216518800640.
9. Michiels S, Ganz Sanchez T, Oron Y, et al. Diagnostic criteria for somatosensory tinnitus: a Delphi process and face-to-face meeting to establish consensus. Trends Hear. 2018;22:2331216518796403.

10. Van der Wal A, Michiels S, Van de Heyning P, et al. Treatment of somatosensory tinnitus: a randomized controlled trial studying the effect of orofacial treatment as part of a multidisciplinary program. J Clin Med. 2020;9:705.
11. Michiels S, Cardon E, Gilles A, Goedhart H, Vesala M, Schlee W. Somatosensory tinnitus diagnosis: diagnostic value of existing criteria. Ear Hear. 2021;43:143–9.
12. Michiels S, Van de Heyning P, Truijen S, Hallemans A, De Hertogh W. Does multi-modal cervical physical therapy improve tinnitus in patients with cervicogenic somatic tinnitus? Man Ther. 2016;26:125–31.
13. Zhan X, Pongstaporn T, Ryugo DK. Projections of the second cervical dorsal root ganglion to the cochlear nucleus in rats. J Comp Neurol. 2006;496:335–48.
14. Levine RA, Nam EC, Melcher J. Somatosensory pulsatile tinnitus syndrome: somatic testing identifies a pulsatile tinnitus subtype that implicates the somatosensory system. Trends Amplif. 2008;12:242–53.
15. Shore S, Zhou J, Koehler S. Neural mechanisms underlying somatic tinnitus. Prog Brain Res. 2007;166:107–23.
16. Young ED, Nelken I, Conley RA. Somatosensory effects on neurons in dorsal cochlear nucleus. J Neurophysiol. 1995;73:743–65.
17. Levine RA, Abel M, Cheng H. CNS somatosensory-auditory interactions elicit or modulate tinnitus. Exp Brain Res. 2003;153:643–8.
18. Abel MD, Levine RA. Muscle contractions and auditory perception in tinnitus patients and nonclinical subjects. Cranio. 2004;22:181–91.
19. Reisshauer A, Mathiske-Schmidt K, Kuchler I, Umland G, Klapp BF, Mazurek B. Functional disturbances of the cervical spine in tinnitus. HNO. 2006; 54:125–31.
20. Hain TC. Cervicogenic causes of vertigo. Curr Opin Neurol. 2015;28:69–73.
21. Sun YQ, Zheng S, Yu J, Yan K, Tian W. Effect of total disc replacement on atypical symptoms associated with cervical spondylosis. Eur Spine J. 2013;22: 1553–7.
22. Yang L, Yang C, Pang X, et al. Mechanoreceptors in diseased cervical intervertebral disc and vertigo. Spine (Phila Pa 1976). 2017;42:540–6.
23. Yang L, Chen J, Yang C, Pang X, Li D, Wu B, et al. Cervical intervertebral disc degeneration contributes to dizziness: a clinical and immunohistochemical study. World Neurosurg. 2018;119:e686–93.
24. Wu B, Yang L, Peng B. Ingrowth of nociceptive receptors into diseased cervical intervertebral disc is associated with discogenic neck pain. Pain Med. 2019;20:1072–7.
25. Peng B, Bogduk N. Cervical discs as a source of neck pain. An analysis of the evidence. Pain Med. 2019;20:446–55.
26. Peng B, DePalma MJ. Cervical disc degeneration and neck pain. J Pain Res. 2018;11:2853–7.
27. Peng B. Cervical vertigo: historical reviews and advances. World Neurosurg. 2018;109:347–50.
28. Risbud MV, Shapiro IM. Role of cytokines in intervertebral disc degeneration: pain and disc content. Nat Rev Rheumatol. 2014;10:44–56.
29. Garg K, Aggarwal A. Effect of cervical decompression on atypical symptoms cervical spondylosis-a narrative review and meta-analysis. World Neurosurg. 2022;157(207–217):e201.
30. Meikle MB, Henry JA, Griest SE, et al. The tinnitus functional index: development of a new clinical measure for chronic, intrusive tinnitus. Ear Hear. 2012;33:153–76.
31. Vanneste S, Plazier M, Van de Heyning P, De Ridder D. Transcutaneous electrical nerve stimulation (TENS) of upper cervical nerve (C2) for the treatment of somatic tinnitus. Exp Brain Res. 2010;204:283–7.
32. Tetreault L, Nouri A, Kopjar B, Cote P, Fehlings MG. The minimum clinically important difference of the modified Japanese orthopaedic association scale in patients with degenerative cervical myelopathy. Spine (Phila Pa 1976). 2015;40: 1653–9.
33. Collins SL, Moore RA, McQuay HJ. The visual analogue pain intensity scale: what is moderate pain in millimetres? Pain. 1997;72:95–7.
34. Sedgwick P, Greenwood N. Understanding the Hawthorne effect. BMJ. 2015; 351:h4672.
35. Sanchez TG, da Silva LA, Brandao AL, Lorenzi MC, Bento RF. Somatic modulation of tinnitus: test reliability and results after repetitive muscle contraction training. Ann Otol Rhinol Laryngol. 2007;116:30–5.
36. Zhou J, Shore S. Projections from the trigeminal nuclear complex to the cochlear nuclei: a retrograde and anterograde tracing study in the Guinea pig. J Neurosci Res. 2004;78:901–7.
37. Zhou J, Shore S. Convergence of spinal trigeminal and cochlear nucleus projections in the inferior colliculus of the Guinea pig. J Comp Neurol. 2006;495: 100–12.
38. Kanold PO, Young ED. Proprioceptive information from the pinna provides somatosensory input to cat dorsal cochlear nucleus. J Neurosci. 2001;21: 7848–58.
39. Abraira VE, Ginty DD. The sensory neurons of touch. Neuron. 2013;79: 618–39.
40. Peng B, Yang L, Yang C, Pang X, Chen X, Wu Y. The effectiveness of anterior cervical decompression and fusion for the relief of dizziness in patients with cervical spondylosis: a multicentre prospective cohort study. Bone Joint J. 2018; 100-B:81–7.
41. Ward J, Vella C, Hoare DJ, Hall DA. Subtyping somatic tinnitus: a cross-sectional UK cohort study of demographic, clinical and audiological characteristics. PLoS One. 2015;10:e0126254.
42. Peng B, Yang L, Li Y, Liu T, Liu Y. Cervical proprioception impairment in neck pain-pathophysiology, clinical evaluation, and management: a narrative review. Pain Ther. 2021;10:143–64.
43. Liu TH, Liu YQ, Peng BG. Cervical intervertebral disc degeneration and dizziness. World J Clin Cases. 2021;9:2146–52.
44. Wilkinson KA. Molecular determinants of mechanosensation in the muscle spindle. Curr Opin Neurobiol. 2022;74:102542.