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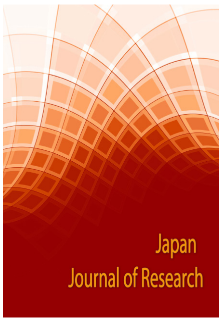

Is Chronic Neck Pain Associated With Disc Degeneration in The Young Population? A Perspective From The Modified Grading System on Cervical Disc Degeneration

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Abbreviations: CNP: chronic neck pain; MRI: magnetic resonance imaging; CSF: cerebral spinal fluid; SC: spinal cord; BMI: body mass index; VAS: visual analogue scale; NDI: neck disability index; ACDF: anterior cervical discectomy and fusion; TNF: tumor necrosis factor; IL: interleukin

Abstract

In order to investigate whether the chronic neck pain is associated with cervical disc degeneration, a case-control study was carried out. To facilitate statistical analysis, it is necessary to quantify the degree of cervical intervertebral disc degeneration using a grading system. Therefore, a modified grading system for cervical disc degeneration was proposed based on cervical magnetic resonance image (MRI). Several doctors were invited to review the images on two separate occasions and classify the cervical disc degeneration grades of all subjects according to the new grading method. The intra-observer agreement for this new grading system was excellent (K>0.8), and the inter-observer agreement was substantial (K>0.6). There was no significant difference in the distribution of cervical disc degeneration grades between the two groups (P=0.863>0.05). The new cervical disc degeneration grading system demonstrates excellent reliability and suggests there is no correlation between the occurrence of CNP and disc degeneration.

Highlights

- A modified grading system for cervical disc degeneration based on MRI images was established for young CNP subjects, demonstrating good inter- and intra-observer agreement and high reproducibility
- Women were more prone to CNP
- The causes of pain might be multifactorial and not related to cervical disc degeneration.

Introduction

Chronic neck pain (CNP) is the second most prevalent spinal pathology worldwide, following lower back pain. It significantly impacts patients' quality of life and adds an economic burden to society [1-3] Surgery is required for only a small percentage of CNP patients with clear pathological changes, such as atlantoaxial osteoarthritis, high cervical radiculopathies (C3-4), or cervical pseudarthrosis, and so on. [4] The majority of patients with pain of undefined etiology are classified as chronic nonspecific neck pain or chronic mechanical neck pain if the pain persists for more than three months, both abbreviated as CNP. These patients are typically managed by physicians specializing in rehabilitation or pain medicine [5,6] Many CNP patients are middle-aged or elderly, with their cervical spine magnetic resonance imaging (MRI)s often showing varying degrees of degenerative changes and sometimes compression of the spinal cord and/or nerve roots. Some studies suggest a link between CNP and intervertebral disc degeneration [7] However, in young patients, particularly those under 35year old,

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cervical MRIs are not routinely employed as they rarely show signs of nerve compression, making it difficult to clarify the potential pathology of the cervical spine or determine if their pain is associated with cervical disc degeneration. MRI had been widely used in clinical practice due to its non-invasive nature and lack of radiation. It not only aided in the development of surgical plans but also provided accurate assessments of disc degeneration, especially early lesions. Therefore, this study aimed to address this gap by conducting cervical MRIs in young CNP patients and healthy controls, and by validating a modified grading method for cervical disc degeneration to determine if their CNP is related to disc degeneration.

Materials and methods

Sample population

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013), and was approved by the Ethics Committee of Beijing Jishuitan Hospital (No. K2022094-00). Informed consent was taken from all the participants. From October 2022 to March 2023, CNP patients and healthy subjects were recruited from students at a university, screened according to the inclusion and exclusion criteria, and all subjects were scheduled to undergo cervical MRI. (1) Inclusion criteria for the control group: (i) age: 20 to 35 years old; (ii) no neck pain within the past 1 year; and (iii) no structural deformity of the motor system in the subjects. Exclusion criteria: (i) the occurrence of body pain within the past week; (ii) with musculoskeletal abnormalities; (iii) a history of surgery and trauma; (iv) suffering from tumor, fracture, cervical intervertebral disc herniation, etc.; (v) claustrophobic patients. Those who meet any of the above are excluded.

Inclusion criteria for the CNP group: (i) age: 20 to 35 years old; (ii) complaints of recurrent neck pain and/or stiffness; (iii) pain duration ≥ 3 months. Exclusion criteria: (i) neck pain associated with spinal cord and/or radiculopathy; (ii) neck pain caused by other reasons such as tumor or infection, etc.; (iii) a history of neck trauma or surgery, or congenital spinal deformity; (iv) exercise that has been performed 3 months prior to the enrolment, or has already been performed, or is intended to be performed during the period of the present study that may improve the CNP, e.g., swimming, yoga and fitness; (v) claustrophobic patients.

Imaging technique

MRIs of the cervical spine were acquired from a 1.5T MRI scanner (Signa Mr360; GE Corp. BSN, MA) in supine neutral position. A standard imaging protocol was used, which included sagittal T1-weighted fast spin-echo sequences [repetition time (TR)/echo time (TE), 499/8.4 ms; slice thickness, 3.0 mm; field of view, 21 cm; matrix, 300 cm; and field of view, 1.5 cm. view, 21 cm; matrix, 300x192; and number of excitations (NEX), 2] and T2-weighted fast relaxation fast spin-echo sequences (TR/TE, 2281/124 ms; slice thickness, 3.0 mm; field of view, 21cm; matrix, 288x256; and NEX, 2). Axial T2-weighted fast spin-echo sequences were also acquired [repetition time (TR)/echo time (TE), 2816/103.8 ms; slice thickness, 3.0 mm; field of view, 20 cm; matrix, 288×256; and NEX, 2. view, 20 cm; matrix, 288x192; and number of excitations (NEX), 2].

Table 1. *Grading System for Cervical Intervertebral Disc Degeneration*

Grade	Nucleus Signal Intensity	Nucleus Structure	Border of Nucleus	Disc Height
0	Hyperintense	Homogeneous, white	Clear	Normal
1	Intermediate	Inhomogeneous, white	Clear	Normal
2	Hypointense	Inhomogeneous, gray to black	Unclear	Normal
3	Hypointense	Inhomogeneous, gray to black	Unclear	Decreased

CSF, cerebrospinal fluid; SC, spinal cord

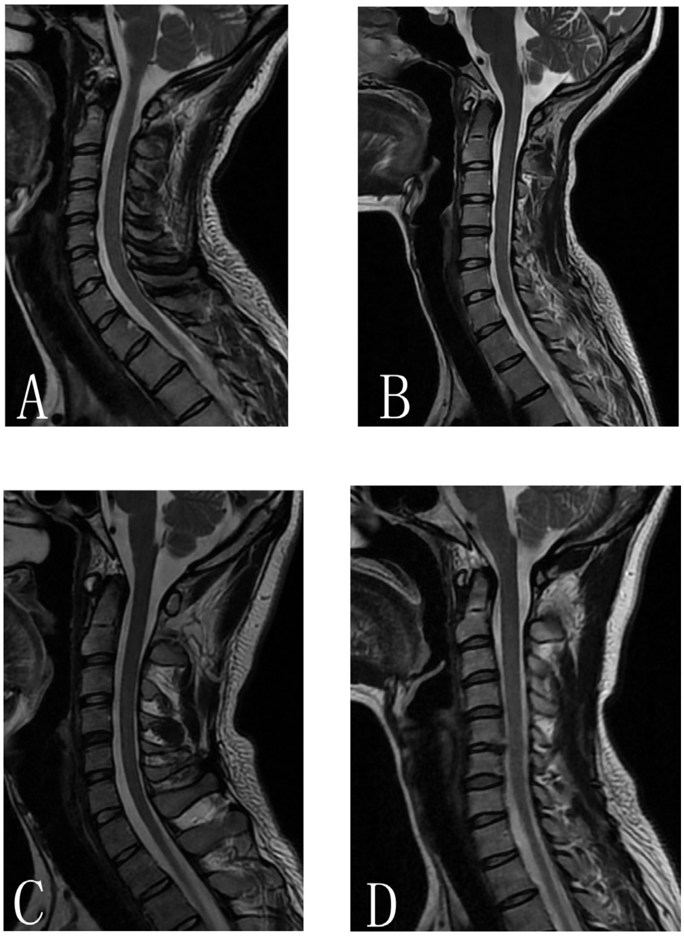

Figure 1. *Grading system for cervical disc degeneration. A, Grade 0: All the nucleus signal intensities in every cervical disc (from C2/3 to C6/7) were hyperintense, similar to cerebrospinal fluid (CSF), with a homogeneous and white nucleus structure, and the border of nucleus is clear with normal disc height. B, Grade 1: The C4/5 disc was the most degenerated level compared to other levels in the entire cervical spine, with an intermediate nucleus signal intensity similar to the spinal cord (SC), an inhomogeneous and white nucleus structure, and the border of nucleus is clear with normal disc height. C, Grade 2: The C4/5 disc was the most degenerated level compared to other levels in the entire cervical spine, with a hypointense nucleus signal intensity lower than the spinal cord (SC), an inhomogeneous nucleus structure that was grey to black, and the border of nucleus is unclear with normal disc height. D, Grade 3: The C5/6 disc was the most degenerated level compared to other levels in the entire cervical spine, with a hypointense nucleus signal intensity lower than the spinal cord (SC), an inhomogeneous nucleus structure that was grey to black, and the border of nucleus is unclear with decreased disc height.*

Image assessment

All assessments of disk degeneration were made with T2-weighted images. The mid-sagittal slice was chosen to determine the disk height, nucleus intensity and structure. Based on the clinical experience and related articles [8-11], we proposed a modified cervical disc degeneration grading system, especially tailored for the young CNP patients (Table 1, Figure 1). The grading was based on the nucleus pulposus signal and its structure as well as disc height. Since young people were not the most prevalent population for cervical disc herniation, disc herniation was not included in the classification of this staging system. To further explore the reliability of this grading system and its practicality in common clinical practice, two radiologists and two spine surgeons from two hospitals were asked to evaluate all the participants' MRI pictures independently. AII of them have more than 10 years of experience in their field. All the MRIs were analyzed by these observers on different environment with an interval of one month. An illustration with a grading system (Table 1) and a handout of typical sample MRI (Figure 1) were provided to the observers during image review. If one subject had different grades from C2/3 to C6/7, he/she would be classified as the highest grading classification. For example, when a participant had C3/4 disc degeneration for grade 0, C4/5 and C5/6 for grade 2, C6/7 for grade 3, the participant would be classified as cervical disc degeneration for grade 3. Finally, to investigate the exact distribution of disc degeneration among participants with and without CNP, a consensus on the grading system was reached for each participant after a panel discussion, once all observers had completed their MRI evaluations.

Data analysis

The Kolmogorov-Smirnov and Shapiro-Wilk tests were used to assess the normality of age and BMI data. Data with normal distribution were described as the mean ±standard deviation, while non-normally distributed data were described as the median (inter-quartile range, IQR). Differences in age and BMI were compared between the two groups using the independent sample t-test and Mann-Whitney U test, respectively. The gender was compared with the Pearson X2 test. The reliability of this novel cervical disc degeneration grading system was investigated using agreement percentage and Kappa statistics for each observer. The reliability of this novel cervical disc degeneration grading system was investigated using agreement percentage and Kappa statistics for each observers (intra-observer reliability) and among the observers (interobserver reliability). According to the rules suggested by Landis and Koch [12], the agreement was rated as follows: poor, K 0 to 0.2; fair, K 0.21 to 0.4; moderate, K 0.41 to 0.60; substantial, K 0.61 to 0.80; and excellent, K > 0.81. A value of 1 meant absolute agreement, whereas 0 suggested agreement no better than chance. The intra-observer and interobserver agreements were calculated using SPSS 22.0 (IBM Corp., Armonk, NY, USA). The frequency of disagreement was analyzed for each grade. Differences in the distribution of grading diagnoses were compared between the CNP and control groups using the independent samples Mann-Whitney U test. A P value <0.05 was considered statistically significant.

Results

A total of 78 participants were recruited for this study, with 39 participants in each group. Age was normally distributed, with an average age of 25 ± 2.22 years (range, 20-32 years) in the control group, and 24.23 ± 2.31 years (range, 20-30 years) in the CNP group. Participants in the control group were older than those in the CNP group, and the difference was statistically significant (P=0.027 <0.05). BMI had a skewed distribution, with a median of 21.60 (19.80, 23.80) in the control group and 20.80 (19.10, 22.90) in the CNP group. The difference in BMI between the two groups was not statistically significant (P=0.219 >0.05). Regarding gender distribution, the control group included 20 females and 19 males, while the CNP group comprised 29 females and 10 males, indicating that females were significantly more predisposed to CNP than males (P=0.035 <0.05). According to the modified grading method for cervical disc degeneration: 4 patients were classified as grade 0, 22 as grade 1, 13 as grade 2, and none as grade 3 in the CNP group; while 2 as grade 0, 25 as grade 1, 11 as grade 2, and 1 as grade 3 in the control group. Table 2 summarized the frequency at which each grade of disc degeneration was evaluated by the 4 observers. Regardless of whether they were in the CNP group or the control group, the participants tended to develop Grade 1 and Grade 2 cervical disc degeneration, which suggested that only few young people suffered from Grade 3 severe disc degeneration no matter they suffered from CNP or not. Table 3 summarized the K value for intra- and interobserver agreements. The intra-observer agreement for each of the 4 observers was excellent, with K values ranging from 0.885 to 0.953. The interobserver agreement was expected to be slightly lower than the intra-observer agreement. However, this agreement remained substantial-excellent, with K values ranging from 0.705 to

Table 2. *Cervical Disc Degeneration Grading in 4 Observers*

Observers / Grades	0	1	2	3
A1	6	43	28	1
A2	6	46	25	1
B1	6	51	20	1
B2	5	53	19	1
C1	5	50	22	1
C2	6	50	21	1
D1	5	50	22	1
D2	5	51	21	1
Average	6 (7.7%)	49 (62.8%)	22 (28.2%)	1 (1.3%)
Consensus	6 (7.7%)	47 (60.2%)	24 (30.8%)	1 (1.3%)

Table 3. *Interobserver and Intra-oberver Reliability*

Intra-observer	K	Interob-server (1)	K (1)	Interob-server (2)	K (2)
A1-A2	0.938	A1-B1	0.705	A2-B2	0.755
		A1-C1	0.809	A2-C2	0.828
B1-B2	0.953	A1-D1	0.809	A2-D2	0.758
		B1-C1	0.886	B2-C2	0.837
C1-C2	0.910	B1-D1	0.840	B2-D2	0.952
D1-D2	0.885	C1-D1	0.863	C2-D2	0.840
		Whole	0.795	Whole	0.811

K (1): the Kappa value in the first round among the 4 observers
K (2): the Kappa value in the second round among the 4 observers

Table 4. *Consistency Among 4 Observers for Each Grading*

Grade	K (1)	K (2)
0	0.772	0.772
1	0.773	0.796
2	0.815	0.829
3	1.000	1.000

K (1): the Kappa value in the first round among the 4 observers
K (2): the Kappa value in the second round among the 4 observers

0.952. The whole K-value for the interobserver reliability in the first round was 0.795, which was very close to 0.8 (excellent). The whole K-value for the second round was 0.811, which had reached the excellent standard. This indicated that this grading system also had very good interobserver consistency. Table 4 showed the substantial consistency among the 4 observers for each grading type (0-3) in both reviews for the first and second rounds (K>0.77). The determination of grade 0 had the lowest interobserver consistency (K=0.772). This was likely because the rules required the MRI findings of all cervical discs to conform to the standards of grade 0 for a subject to be classified as grade 0. Therefore, observers must carefully assess 5 segments (C2/3-C6/7) and also made consistent comparisons before reaching a conclusion. This was unlike other grades, where observers only needed to assess the most degenerated disc segment to make a decision. Thus, in the determination of grade 0, as the number of segments assessed increased, the consistency among 4 observers inevitably decreased. Finally, according to the independent samples Mann-Whitney U test, there was no significant difference in the distribution of disc degeneration grades between the CNP and control groups (P=0.863 >0.05), suggesting that severe disc degeneration did not tend to occur more frequently in the CNP group but was distributed evenly between both groups.

Discussion

In this study, a case-control study for CNP was conducted among young college students. Both CNP patients and healthy controls underwent cervical MRI. Using our modified cervical disc degeneration grading system and inviting several radiologists and spine surgeons to perform two separate readings of the films, we found that this grading method had excellent reliability. By examining the distribution pattern of different cervical disc degenerations between the two groups (CNP group and healthy control group), we found no concentration of severe grades of cervical disc degeneration in the CNP group. There was no significant difference in the distribution of cervical disc degeneration grades between the two groups, suggesting no correlation between the occurrence of CNP and cervical disc degeneration in the young population. Additionally, demographic analysis revealed that females were more likely to develop CNP compared to males. This may be due to women having weaker muscle strength and endurance than men, making prolonged periods of desk work more likely to cause neck muscle fatigue, leading to pain. Finally, although the age of the control group was higher than that of the CNP group with a statistically significant difference (P=0.027 < 0.05), the mean age of the control group was 25 ± 2.22 years compared to 24.23 ± 2.31 years in the CNP group, a difference of less than one year. In terms of data analysis, the data between the two groups were so close that small differences could cause statistically significant differences, which would be negligible in a clinical study.

As people age, disc degeneration became inevitable, characterized by a progressive loss of water and proteoglycan content. This degeneration was reflected in reduced signal intensity on T2 images of cervical MRI and a mixed internal structure where the nucleus pulposus and annulus fibrosus were poorly demarcated. With further degeneration, the disc might collapse due to increased dehydration, leading to a high degree of signal loss [11,13-15]. Research on cervical disc degeneration classification, especially those focusing on reproducibility, was relatively limited. Kolstad [16] used MRI of the cervical spine to classify cervical disc degeneration based on nucleus pulposus signal intensity, disc protrusion, and bone marrow signals adjacent to the discs. This classification system comprised 12 types, ranging from A to L. The height of the cervical discs was also measured using X-ray, to define the relationship between MRI-classified cervical disc degeneration and disc height measured from radiographs. Their X-ray measurement method was not only accurate but also verified that the X-ray measurements strongly correlated with the disc height changes observed by MRI. This finding supports the feasibility of using MRI as a disc height measurement tool in this study. However, their study classified cervical disc degeneration into 12 subtypes, which proved to be overly complicated, resulting in low interobserver agreement. The K-values were only 0.44 and 0.45, indicating poor reproducibility.

Jacobs [8] had also developed a grading system for cervical disc degeneration using cervical MRI. This system comprises grade 0 (normal height compared to C2-3, with or without a cleft in the nucleus pulposus), grade 1 (dark disc, with normal height), grade 2 (collapsed disc, little or no osteophytes), and grade 3 (collapsed disc, many osteophytes). Despite good inter- and intra-observer agreement in Jacobs' study, no study had confirmed that osteophytes adjacent to the disc in the posterior aspect of the cervical vertebral body were secondary to disc height loss. The exact cause of osteophyte formation remained unclear and might be related to chronic disc injury, inflammatory response, and local instability [17,18]. Through large-sample cervical X-ray studies, Tao [19] found that loss of cervical disc height and the formation of cervical osteophytes were common radiographic manifestations of cervical degeneration and were closely related to age, with prevalence rates of 44.2% (699/1581) and 47.3% (748/1581), respectively. The prevalence of disc height loss was slightly lower than that of osteophyte formation. Therefore, Tao's study did not support Jacobs' theory that osteophyte formation was secondary to disc height loss. In the cervical intervertebral disc degeneration classification proposed by Miyazaki [9], the "Distinction of Nucleus and Annulus" was divided into three grades: clear, unclear, and lost. However, during actual image evaluation, we found that the categories of "unclear" and "lost" were easily confused and difficult to define clearly. Therefore, in order to make this grading system more intuitive and easier to apply, we simplified the "Border of Nucleus" into only two categories: clear and unclear. In another cervical intervertebral disc degeneration classification system proposed by Suzuki [11] he referenced the methods of Matsumoto [20] and Walraeven [21] using a 25% disc height loss as the criterion: if the height loss was ≤25%, it would be classified as Grade 1 or Grade 2; if the height loss was >25%, it would be classified as the most severe degeneration, Grade 3. However, none of these authors provided any anatomical basis or explanation for why 25% was chosen as the cutoff. In fact, once disc height became to lost, it indicated that the internal structure of the disc had already undergone severe and irreversible degeneration, leading to a reduction in its overall load-bearing capacity. Since load-bearing was the most fundamental function of the intervertebral disc, impairment of this function also indicated severe degeneration. Therefore, in this study tailored for young college students, whose cervical intervertebral discs should normally have intact load-bearing function, any observed disc height loss was automatically classified as the most severe grade of disc degeneration in this modified grading system.

In 2020, an estimated 203 million people globally suffered from chronic neck pain (CNP), making it the fourth leading cause of disability and the twenty-first in terms of global pain burden. Despite this high prevalence, the precise etiology of CNP remained unclear [22,23]. Research suggested that the causes of CNP might be multifactorial, including muscle strain, lack of exercise, degenerative or inflammatory changes in the discs, joints, ligaments, or nerves, whiplash injuries from car accidents, sports or work-related activities, and psychosocial factors [24-26]. This lack of clarity might be compounded by the fact that patients often received multidisciplinary treatments without effective communication among different specialists. Unlike patients with cervical spondylotic myelopathy who might be directly referred to spine surgeons for surgical intervention, CNP patients often consulted various disciplines, including pain medicine, physiotherapy, rehabilitation, and even psychiatry. These specialists might have differing opinions and treatment approaches based on their unique professional backgrounds. For example, Dr. Peng [7], a spine surgeon, posited that cervical disc degeneration could lead to neck pain. Degeneration of these discs could release cytokines such as tumor necrosis factor (TNF) and interleukins (IL), causing inflammation of nerve endings and resulting in pain. Numerous studies had shown that for patients with cervical spondylotic myelopathy or radiculopathy, whether they undergo anterior cervical discectomy and fusion (ACDF) or disc replacement surgery, relief from spinal cord/nerve compression was associated with the resolution of neck pain, reinforcing the role of intervertebral discs in causing neck pain [27-30]. However, physiotherapist Falla [31] found through electromyography that CNP patients exhibited significantly reduced amplitude of deep cervical flexor movements during cranio-cervical flexion compared to asymptomatic patients, with an increased amplitude in compensatory superficial cervical flexors. This suggested that dysfunction of the deep cervical flexors may contribute to CNP. Kraatz [32], in a systematic review, identified increased workload, work stress, and job control as factors contributing to neck pain. On the other hand, physiotherapist Jahre [25] found that in young patients with chronic non-specific neck pain, factors such as being female, having a high BMI, poor physical activity, prolonged computer use, and high work stress were not significant risk factors for pain. Therefore, the complexity in diagnosing CNP might require future resolution through better interdisciplinary collaboration among doctors in different fields.

The first limitation was that only 78 subjects were included in the study, and only two radiologists and two spine surgeons were invited to read the films. To increase the reproducibility and persuasiveness of this grading system, future studies should include more young subjects and invite more spine surgeons and radiologists to perform multiple rounds of film readings. The second limitation was that the grading system only records the presence or absence of CNP symptoms, but did not account for the duration of pain, frequency of pain episodes, intensity of pain, or triggers of pain. Future studies needed to analyze these symptoms in conjunction with imaging to further investigate the relationship between the clinical presentation and the newly established grading system, and to provide targeted treatments.

Conclusion

In this study, a modified grading system for cervical disc degeneration based on MRI images was established for young CNP subjects, demonstrating good inter- and intra-observer agreement and high reproducibility. Women were more prone to CNP, and the causes of pain might be multifactorial and not related to cervical disc degeneration. Therefore, even for CNP patients with persistent symptoms, the decision to undergo surgical treatment should be made carefully.

Declaration

Ethics approval and consent to participate

This study was reviewed and approved by the Institutional Review Board of Jishuitan Hospital (No. K2022094-00). All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Written informed consent was obtained from individual participants.

Consent for publication

All data published here are under the consent for publication. Written informed consent was obtained from all individual participants included in the study.

Availability of data and materials

The datasets generated and/or analyzed during the current study are not publicly available because the data were collected from university instead of hospital; however, the data are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Study conception and design: Jianze Liu, Ning Zhang, Da He. Data collection: Kebin Cheng, Luxin Lou, Yushuang Zhang, Kai Yan. Analysis and interpretation: Fangfang Duan, Xianglong Li. Manuscript preparation: Nan Li, Jiangzhen Guo, Chunjing Tao.

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