



Retrospective Cohort Study

Mechanisms of recurrent laryngeal nerve injury near the nerve entry point during thyroid surgery: A retrospective cohort study

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ARTICLE INFO

Keywords:

Thyroid surgery
Recurrent laryngeal nerve
Surgical complication
Intraoperative neuromonitoring
Recovery time

ABSTRACT

Background: The use of intraoperative neuromonitoring (IONM) for visual identification of recurrent laryngeal nerve (RLN) has decreased the rates of RLN injury (RLNI) during thyroid surgery. However, little attention has been paid to RLNI near the nerve entry point (NEP), where most injuries occur. The aim of this study was to determine the mechanism of RLNI near the NEP and to describe the recovery of nerve function.

Methods: Patients undergoing thyroid surgery were analyzed to identify true loss of signal (LOS) by IONM. Follow-up for vocal cord palsy (VCP) was confirmed by a postoperative laryngoscopy. The risk factors for RLNI, the type of RLNI, the prevalence of VCP and the time for VCP recovery were all recorded and analyzed.

Results: We analyzed 3582 at-risk nerves in 2257 surgical patients. The overall rate of RLNI near the NEP in at-risk nerves was 3.2%. RLNI was more likely to occur in nerves with extralaryngeal bifurcation ($p = 0.013$). The distribution of RLNI types, in order of frequency, was traction (52.6%; $n = 61$), compression (38.8%; $n = 45$), thermal (7.8%; $n = 9$), and nerve transection (0.9%; $n = 1$). Complete recovery from VCP was documented in 93.1% ($n = 108$) of RLNI.

Conclusion: Patients with a bifurcated RLN were at a higher risk of RLNI near the NEP than those without bifurcation. Traction and compression injuries occurred most frequently, but would eventually recover. Excessive stretching of the thyroid lobe played a role in RLNIs near the NEP.

1. Introduction

Galen first described the recurrent laryngeal nerve (RLN) in the second century A.D. [1], and for over 100 years thyroid surgeons have highlighted its importance. Recurrent laryngeal nerve injury (RLNI) is a common complication of thyroid surgery that leads to vocal cord palsy (VCP). Unilateral RLNI can cause hoarseness, whereas bilateral RLNI can be life-threatening because it is associated with serious disturbances in respiration. Routine visual identification of the RLN is the most effective way to avoid RLNI. Use of this method has resulted in a lower incidence of RLNI in clinical studies [1–4]. The rate of VCP from RLNI ranges from 4% to 8%, and the rate of permanent VCP is 1%–2% [5,6].

Intraoperative neuromonitoring (IONM) was developed to help identify the RLN to reduce the risk of RLNI [7–12]. It is also used to characterize RLNI when it occurs, especially in traction and compression injuries in which the RLN is visibly intact [13–18]. RLNI can be caused by transection, clamping, ligation, compression, traction, thermal injury, or ischemia [19]. We found that most RLNIs occur near the nerve

entry point (NEP) into the larynx in our practice, and the mechanism of RLNI near the NEP was different than those in other regions. Identification of the RLN has become common practice in recent decades, but little attention is paid to RLNIs that occur near the NEP. This retrospective cohort study was conducted to determine the mechanism of RLNI near the NEP and to describe the recovery of nerve function.

2. Patients and methods

2.1. Patient selection

This retrospective cohort study included data from 2350 patients who underwent total thyroidectomy or total lobectomy as a primary procedure between February 2017 and January 2019. All patients underwent preoperative and postoperative laryngoscopy (within the first 7 days after surgery) to test vocal cord movement. Patients were informed of the study in written and oral form, and they signed informed consent. The study protocol was approved by the Medical Ethics Committee of

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<https://doi.org/10.1016/j.ijso.2020.08.058>

Received 19 May 2020; Received in revised form 22 August 2020; Accepted 26 August 2020

Available online 12 September 2020

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Qilu Hospital of Shandong University (Project identification code: 2018149), and was registered in the ResearchRegistry (UIN: researchregistry5594). This study has been reported in accordance with the STROCSS 2019 Guideline [20]. The design of the study is shown in Fig. 1.

A RLNI near the NEP was defined as an injury occurring within 1 cm of the NEP. Patients were excluded if they had a previous thyroid surgery, preoperative VCP, no record of preoperative or postoperative laryngoscopy, a RLNI cause that could not be explained or identified by IONM, a monitoring device failure, an intentional RLNI because of cancer invasion, or a RLNI that was >1 cm away from the NEP. The mechanism of RLNI and the subsequent recovery of nerve function were documented. Demographic data, surgical anatomy, rate of postoperative VCP, and recovery time were recorded. Surgeons and surgical assistants were not blinded, while the remaining study members were blinded to the surgical method.

2.2. Surgical technique

All operations were performed by two experienced endocrine surgeons. Procedures were performed under general anesthesia. An anterior approach was used to dissect the cricothyroid space and the superior thyroid artery was ligatured to dissociate the thyroid superior pole. The RLN was identified at the level of the inferior thyroid artery and then meticulously dissected along its length, at the same time, the thyroid inferior pole was dissected. The Berry's ligament was then dissected to remove the thyroid lobe.

2.3. IONM and identification of RLNI

Intermittent IONM (3.0 NIM response system EMG Endotracheal Tube; Medtronic, Minneapolis, MN, USA) was used in all operations in a standard four-step procedure to aid in the localization and identification of the RLN and to assess their function during the operation. The International Neural Monitoring Study Group (INMSG) Guidelines were used in the standard equipment setup for induction and maintenance of anesthesia procedures, tube positioning verification tests, and EMG definitions [18]. True loss of signal (LOS) was defined as an absence of the biphasic waveform with a stimulation level of 1.0 mA and an event

threshold of 100 mV. The entire procedure was managed with the troubleshooting algorithm described in the INMSG Guidelines [18,21].

RLN function was assessed after each step of RLN dissection to determine when and where the injury occurred, and the mechanism behind the injury (e.g., traction, compression, thermal, ligation, transection, or clamping injury). To verify the location of the injury, the RLN was tested from the distal portion of the RLN at the NEP with stimulation at 1.0 mA until a signal could not be obtained. Similarly, the RLN was tested from the proximal portion of the exposed nerve to the upper portion until a signal was obtained.

2.4. RLNI mechanisms

Traction and compression injuries may occur simultaneously and it is difficult to distinguish them (Fig. 2). These injuries were confirmed by LOS after medial thyroid retraction and in the absence of other mechanisms of injury. If the RLN was stretched forward, and a disruption of signal was found at the highest point of the nerve or the NEP, then the RLNI was classified as traction injury. When the RLN was not stretched forward and a disruption of signal was found away from the NEP, the RLNI was classified as compression injury. If LOS occurred suddenly after the application of an energy-based device (EBD) near the RLN, then the RLNI was classified as thermal injury. If the nerve was discontinuous, the RLNI was classified as transection injury. In patients where the nerve was pinched by a ligature or clip, the ligature or clip was immediately removed, and the RLNI was classified as ligation injury or clamping injury.

2.5. Follow-up

Postoperative recovery follow-up of all RLNIs was performed by laryngoscopy for up to 6 months. The first postoperative laryngoscopy was performed within 7 days after surgery. Any reduction in vocal cord mobility was defined as a postoperative VCP. When VCP was identified, follow-up was arranged every week for one month and every two weeks thereafter until recovery was confirmed by laryngoscopy. VCP was considered permanent if it persisted for 6 months. Recovery time was defined as the time interval (days) from operation to vocal function recovery during follow-up.

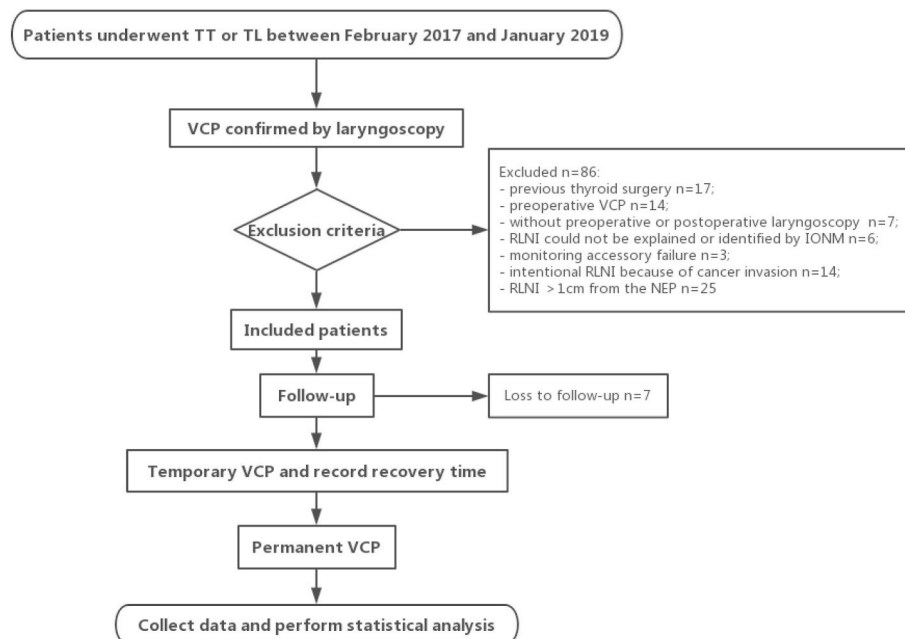


Fig. 1. The flow chart of the study. TT total thyroidectomy, TL total lobectomy, VCP vocal cord palsy, RLNI recurrent laryngeal nerve injury, IONM intraoperative neuromonitoring.

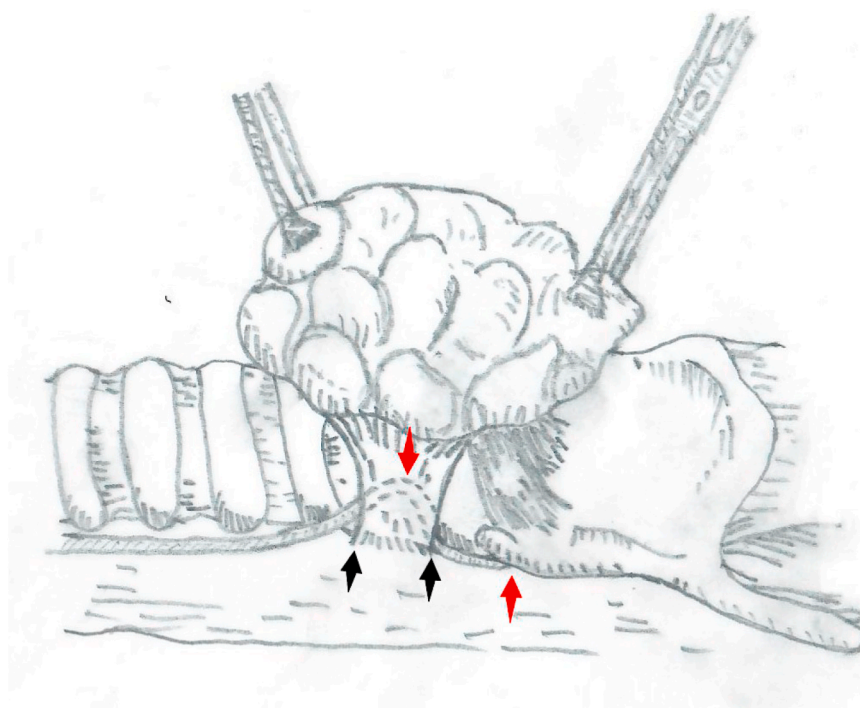


Fig. 2. Excessive traction on the thyroid may cause a RLNI by Berry's ligament, and traction injury (red arrow) and compression injury (black arrow) may occur together. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

2.6. Statistical analysis

We calculated that a total sample size of 2748 at-risk nerves was needed to achieve 80% power at the 5% significance level based on practice experience and the rate of RLNI described in previous publications [5,6], allowing for a 10% loss to follow-up.

The data was analyzed using IBM SPSS Statistics for Windows, version 21.0 (IBM Corp., Armonk, N.Y., USA). Continuous variables were reported as mean \pm standard deviation. A T-test or Mann-Whitney *U* test was used to compare continuous variables, while a Chi-square test or Fisher's exact test was used for categorical variables. Statistical significance was defined as a *p*-value < 0.05 .

3. Results

3.1. Prevalence of RLNI near the NEP

Among the 2350 patients initially enrolled, 7 patients were lost at follow-up. Another 86 patients were excluded (Fig. 1). There were 2257 patients that met the inclusion criteria (1886 females and 371 males, aged 51.9 ± 13.3 years, ranging 19–77). The analysis included 3582 at-risk nerves (1664 right nerves and 1918 left nerves) in 1322 total thyroidectomies and 935 total lobectomies (Table 1).

It was found that age, gender, extent of operations, side, weight of lobe and coexisting Hashimoto's thyroiditis were not associated with RLNI. However, RLNI was more likely to occur in nerves with extralaryngeal bifurcation ($p = 0.013$) (Table 1). One hundred and forty one total instances of RLNI were recorded (including 25 RLNIs with a distance > 1 cm from the NEP), disregarding those caused intentionally due to cancer invasion. One hundred and sixteen nerves (82.3%, 116/141) experienced LOS near the NEP after complete nerve dissection, indicating that the RLNI occurred near the NEP. Postoperative VCP was found in 5.1% (116/2257) of enrolled patients, while the permanent VCP rate was only 0.4% (8/2257). The type of RLNI near the NEP by order of frequency was traction (52.6%; $n = 61$), compression (38.8%; $n = 45$), thermal (7.8%; $n = 9$), and nerve transection (0.9%; $n = 1$)

Table 1

Clinical information of enrolled patients grouped on basis of RLNI.

| Variables | RLNI+ (116 patients, 116 nerves) | RLNI- (2141 patients, 3466 nerves) | P |
|--------------------------------------|--|--|--------|
| Age, (min-max) | 53.4 \pm 11.8 (22–74) | 51.8 \pm 13.4 (19–77) | 0.227 |
| Gender | | | 0.127 |
| Male, n (%) | 25(21.6%) | 346(16.2%) | |
| Female, n (%) | 91(78.4%) | 1795(83.8%) | |
| Procedure | | | 0.339 |
| TT, n (%) | 63(54.3%) | 1259(58.8%) | |
| TL, n (%) | 53(45.7%) | 882(41.2%) | |
| Site | | | 0.721 |
| Left, n (%) | 64(55.2%) | 1854(53.5%) | |
| Right, n (%) | 52(44.8%) | 1612(46.5%) | |
| Extralaryngeal bifurcation, n (%) | 43(37.1%) | 926(26.7%) | 0.013* |
| HT, n (%) | 46(61.3%) | 1533(70.3%) | 0.097 |
| Weight of lobe, g (min- max) | 12.7 \pm 3.5(7–27) | 12.3 \pm 4.5(7–33) | 0.375 |

RLNI recurrent laryngeal nerve injury, TT total thyroidectomy, TL total lobectomy, HT Hashimoto thyroiditis.

* $P < 0.05$.

(Table 2). There were no ligation or clamping injuries.

3.2. Recovery for each type of RLNI

The overall rate of VCP and the mean recovery time for each RLNI type are shown in Table 2. Complete vocal cord function was recovered in 93.1% ($n = 108$) of RLNIs, while 6.9% ($n = 8$) had permanent loss of function. The incidence of temporary VCP was significantly higher in the traction injury and compression injury compared with the thermal injury ($p = 0.001$ and $p = 0.006$, respectively). Recovery time for all types of RLNIs was 37.6 ± 23.3 days. The fastest times were found in traction injury (35.8 ± 19.4 days), followed by compression injury (39.6 ± 22.9 days). Recovery time for temporary RLNI ranged from 10 days

Table 2

Mechanisms and recovery outcomes in RLNI.

| Type of injury | No. N (%) | Permanent VCP n (%) | Temporary VCP n (%) | P* | Recovery time for TVCP days | P+ |
|----------------|-----------|---------------------|---------------------|-------|-----------------------------|-------|
| Traction | 61(52.6%) | 2(3.3%) | 59(96.7%) | 0.001 | 35.8 ± 19.4 | |
| Compression | 45(38.8%) | 2(4.4%) | 43(95.6%) | 0.006 | 39.6 ± 22.9 | 0.365 |
| Thermal | 9(7.8%) | 3(33.3%) | 6(66.7%) | | 41.3 ± 52.2 | 0.585 |
| Transection | 1(0.9%) | 1(100%) | 0(0%) | – | No recovery | – |
| Total | 116 | 8(6.9%) | 108(93.1%) | | 37.6 ± 23.3 | |

RLNI recurrent laryngeal nerve injury, VCP vocal cord palsy, TVCP temporary vocal cord palsy.

P* P-value obtained in comparison between thermal injury and traction injury, compression injury.

P + P-value obtained in comparison between traction injury and compression injury, thermal injury.

for traction/compression injuries to 147 days for thermal injury. Recovery time exceeded 3 months in 4 patients with VCP (one with thermal injury, one with traction injury and two with compression injury). Recovery from VCP was significantly faster in the traction injury compared with the compression and thermal injury, but the difference did not achieve statistical significance ($p = 0.365$ and $p = 0.585$, respectively). The single patient with transection injury did not recover 6 months after the operation. Two patients with traction injury showed impaired vocal cord movement compared with the preoperative measures and they recovered 10 days after the operation. Twelve patients, seven with traction injury and five with compression injury, regained nerve function before wound closure as the tissue band was removed; they retained normal vocal cord movement.

4. Discussion

Among the initial 2350 patients, 82.3% of all RLNI were near the NEP, excluding intentional RLNI from cancer invasion. Visual identification of the RLN during thyroid operations is considered the gold standard of RLN preservation and is associated with lower rates of permanent VCP in many studies [2,3,5,22,23]. These prior studies reported a VCP rate of 3.9%–6.9% with nerve identification compared with 13.1%–21% without nerve identification. However, the permanent VCP rate was only 0.9%–1.2% with visual identification. These results suggest that permanent VCP is less likely to occur if the RLN is clearly identified during the operation. However, visual identification only provides information on structural integrity but not functional integrity. Several studies have shown that RLNI often was not recognized during an operation, even when the integrity of the RLN appeared to be good upon visual inspection [5,24,25]. In these reports, only 7.5%–15% of RLNI were recognized during the operation. IONM during thyroid surgery has advantages in functional outcomes and has become widely accepted as an adjunct to visual identification and a tool to warn surgeons of a risk for a visible RLNI or permanent VCP [13,14,16,18,26–28]. Yet, RLNI still occurs with routine visual identification even combined with IONM. The studies comparing RLNI rates with and without IONM did not show a significant difference, but did indicate a high negative predictive value from 98% to 99.6% for postoperative VCP [6,23,27–29].

The most common variant of the RLN is extralaryngeal bifurcation, which appears in 18.5%–72% of patients in previous studies [30–38]. In this study, the prevalence of extralaryngeal bifurcation was significantly higher in the RLNI positive group. Several other studies have also reported that a bifurcated RLN was more prone to injury if the bifurcation occurred near the Berry's ligament [39–41]. The bifurcated nerve fibers were reported to be thinner and more fragile and were more susceptible to traction injury or compression injury. When the anterior branch was stretched forward by the Berry's ligament, the posterior branch could be mistaken for the RLN trunk, which led to inadvertent injury of the anterior branch. The diameter of the posterior branch may be larger than the anterior branch in some patients [40]. In this circumstance, the posterior branch can appear to be the RLN trunk, which may lead to a transection of the thin anterior branch. Traditionally, the anterior branch has been thought of as the motor branch, though up to 11.5% of

patients have motor fibers in both branches [42]. The functional significance of this is that visual identification and preservation of only the posterior branch of the RLN would lead to vocal cord paralysis. Motor branch nerve injury can only be avoided through careful visual identification and IONM assessment of all RLN branches.

This study found that the most common causes of RLNI near the NEP were traction (52.6%) and compression (38.8%). One study reported 71% of patients had traction injuries and 4.2% had compression injuries [26]. As published elsewhere, there may be many factors in causing of RLNI [43,44]. We concluded that traction injury and compression injury may sometimes occur together, and the severity of the injury depended on which played a greater role.

In this study, the rate of thermal injury near the NEP was 7.8%. Dionigi et al. [26] reported that thermal injury was found in 17% of RLNI. The wide availability of EBDs was expected to increase the incidence of thermal injuries [44]. Therefore, the use of EBDs during thyroidectomy should be standardized to avoid RLNI [45]. The severity of the injury and the recovery outcome depends on temperature and the distance between the RLN and EBDs. It is unlikely that a transection injury caused by misidentification will occur with IONM, but we reported one case in our study. The nerve of this patient was inadvertently transected because the position of the RLN seemed to be vertical to the trachea and it was mistaken for an artery. There was no ligation injury or clamping injury found in this study.

This study confirmed that various RLNI types had very different recovery periods. We noted that traction injury and compression injury caused lower permanent VCP rates than thermal injury and transection injury. Compared with our results, in a previous study, traction injury had a shorter recovery time (27 ± 9 days), lower rates of permanent VCP (1.4%), and a lower rate of physical changes (5%) [26]. As reported by Chiang [5], 94.6% of VCP with intact RLN recovered completely. This experience agreed with our results in which nearly all traction and compression injuries eventually recovered to normal function.

The reason for the high prevalence of traction and compression injuries may be that the thyroid lobe needs to be stretched anteriorly and medially during RLN dissection. The distal portion of the RLN is closer to the trachea and cricoid cartilage, and is more likely to run through the Berry's ligament. Therefore, the distal portion of the RLN may become subject to traction or compression injuries at the Berry's ligament near the NEP. The RLN in approximately 25% of patients runs through the dense fibers of the Berry's ligament [46]. The RLN may be compressed between the trachea and a dense fibrous band or crossing artery, especially within the region of the Berry's ligament [13,46–48]. The influence of the excessive stretching on thermal injury may be that the space between the RLN and thyroid is difficult to release because the fiber of Berry's ligament has high tension. Excessive stretching causes the RLN to become vertical and results in traction or compression injury. Therefore, excessive stretching of the thyroid lobe should be avoided to minimize the risk of RLNI near the NEP. In addition, precise hemostasis and ligation of vessels near the RLN under direct visualization are also necessary to avoid RLNI. A near-total thyroid lobectomy could also be a safe option to minimize the risk of RLNI near the NEP.

A limitation of this study is that there could be many causes of RLNI, especially for traction and compression injuries. It can be hard to

determine which injury caused the RLNI. The mechanical correlation between thyroid traction and RLNI needs additional study.

5. Conclusions

A bifurcated RLN was identified as a risk factor for RLNI near the NEP. Traction and compression injuries were the most common forms of RLNI. The majority of traction and compression injuries may cause temporary VCP, but most would eventually recover. Excessive stretching of the thyroid lobe played an important role in the occurrence of RLNI near the NEP.

Provenance and peer review

Not commissioned, externally peer-reviewed

Data statement

The datasets analyzed during the current study are not publicly available due to the sensitive nature of the informations surveyed in this study but are available from the corresponding author on reasonable request.

Funding

The study was supported by Key Technology Research and Development Program of Shandong Province (grant number 2019GSF108072) and Natural Science Foundation of Shandong Province (grant number ZR2019PH082).

Ethical approval

Research Registration Unique Identifying Number (UIN).

Registry used: ResearchRegistry

Name of the registry: The mechanism and prevention of recurrent laryngeal nerve injury near nerve entry point during thyroid surgery.

Unique Identifying Number (UIN): researchregistry5594.

Hyperlink to the registration: https://www.researchregistry.com/browse-the-registry#home/?view_2_search=researchregistry5594&view_2_page=1 This study has been approved by the Medical Ethics Committee of Qilu Hospital of Shandong University (Project identification code: 2018149).

Author contribution

Nan Liu had the contribution to the paper in study design, data collection, data analysis and writing.

Bin Lv had the contribution to the paper in study design, data collection and data analysis.

Bo Chen, Luchuan Li, Qingdong Zeng, Lei Sheng, Bin Zhang and Weili Liang had the contribution to the paper in data collection and data analysis.

Guarantor

Nan Liu, Bin Lv

CRediT authorship contribution statement

Nan Liu: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Software, Writing - original draft, Writing - review & editing. **Bo Chen:** Data curation, Resources, Supervision, Validation. **Luchuan Li:** Supervision, Project administration. **Qingdong Zeng:** Supervision, Project

administration. **Lei Sheng:** Investigation. **Bin Zhang:** Investigation. **Weili Liang:** Funding acquisition. **Bin Lv:** Conceptualization, Formal analysis, Funding acquisition, Methodology, Project administration, Validation, Writing - review & editing.

Declaration of competing interest

The authors declare no conflict of interest.

Acknowledgment

Supported by the Key Technology Research and Development Program of Shandong Province [grant No. 2019GSF108072] and Natural Science Foundation of Shandong Province [grant No. ZR2019PH082].

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ijssu.2020.08.058>.

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