Surgical versus non-surgical interventions for vocal cord nodules (Review)

Pedersen M, McGlashan J

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# Table of Contents

ABSTRACT .................................................. 1  
PLAIN LANGUAGE SUMMARY ................................ 1  
BACKGROUND ................................................. 2  
OBJECTIVES .................................................. 2  
CRITERIA FOR CONSIDERING STUDIES FOR THIS REVIEW ................. 2  
SEARCH METHODS FOR IDENTIFICATION OF STUDIES ...................... 3  
METHODS OF THE REVIEW ................................... 3  
DESCRIPTION OF STUDIES .................................... 4  
METHODOLOGICAL QUALITY .................................... 4  
RESULTS ....................................................... 4  
DISCUSSION .................................................... 4  
AUTHORS’ CONCLUSIONS ..................................... 5  
POTENTIAL CONFLICT OF INTEREST ................................. 6  
ACKNOWLEDGEMENTS ......................................... 6  
SOURCES OF SUPPORT ....................................... 6  
REFERENCES ................................................... 6  
TABLES ......................................................... 8  
   Characteristics of excluded studies .............................. 8  
ADDITIONAL TABLES .......................................... 9  
   Table 01. ADDITIONAL SEARCH STRATEGIES .......................... 9  
GRAPHS AND OTHER TABLES ................................... 9  
INDEX TERMS .................................................. 9  
COVER SHEET .................................................. 9
Surgical versus non-surgical interventions for vocal cord nodules (Review)

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ABSTRACT

Background
Vocal cord nodules are bilateral, benign, callous-like growths of the mid-portion of the membranous vocal folds. They are of variable size and are characterised histologically by thickening of the epithelium with a variable degree of inflammation in the underlying superficial lamina propria. They characteristically produce hoarseness, discomfort and an unstable voice when speaking or singing.

Objectives
To assess the effectiveness of surgery versus non-surgical interventions for vocal cord nodules.

Search strategy
Our search included the Cochrane Ear, Nose and Throat Disorders Group Trials Register, the Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library, Issue 4 2006), MEDLINE (1950 to 2007) and EMBASE (1974 to 2007). The date of the last search was January 2007.

Selection criteria
Randomised and quasi-randomised trials comparing any surgical intervention for vocal cord nodules with non-surgical treatment or no treatment.

Data collection and analysis
No suitable trials were identified.

Main results
No studies fulfilled the inclusion criteria.

Authors’ conclusions
There is a need for high quality randomised controlled trials to evaluate the effectiveness of surgical and non-surgical treatment of vocal cord nodules.

PLAIN LANGUAGE SUMMARY

Surgery versus non-surgical interventions (voice therapy, medical treatment) for the resolution of vocal cord nodules.

Vocal cord nodules are benign, callous-like growths on the vocal cords. Symptoms include hoarseness, throat discomfort, pain and an unstable voice when speaking or singing. They can be caused by ‘voice abuse’ (prolonged shouting or singing above the individual’s own range) but may also be caused by infection, allergy or acid reflux.

Vocal cord nodules can be surgically removed but may also be treated with non-surgical voice therapy interventions (e.g. voice retraining, rest or hygiene advice) or
Vocal cord nodules are bilateral, benign, callous-like growths of variable size found at the mid-part of the membranous vocal cords. They are characterised mainly by thickening of the epithelium with a variable degree of inflammatory reaction in the underlying superficial lamina propria (Nagata 1983).

Symptoms, prevalence and aetiology
Vocal nodules cause hoarseness, throat discomfort or pain which varies with the amount of voice use. This results in an unstable and unpredictable voice, which can affect quality of life, particularly in professional voice users such as singers (Lacina 1972). The prevalence of nodules in the general population is not known but it has been reported as being the cause of hoarseness in up to 23.4% of children (Silverman 1975), 0.5% to 1.3% of ENT clinic attendances (Böhme 1969; Nagata 1983) and 6% of phoniatric clinic attendances. The prevalence of nodules in female teachers was found to be 43% of 218 cases with dysphonia, in a population of 1046 female teachers in a study in Spain (Urrutikoetxea 1995). It has been reported that teachers speak for an average of 102 minutes per eight hours (Masuda 1993). Nodules were found in 25% of hoarse singers (Lacina 1972).

The aetiology of vocal nodules is not known, but traditionally they are thought to be due to 'voice abuse' and psychological factors, especially in children. Other medical conditions, such as infection, allergy and reflux may also play a role (Hugh-Munier 1990). In a study of 20 adult females, voice abuse was considered to be the cause of vocal nodules (Yamaguchi 1986). The abuse was characterised by strain in the neck and shoulder region, hard glottal attack, loud voice in the chest register and singing above the individual’s range. The definition of vocal abuse is however subjective, although attempts have been made to define objective deviations (Xu 1991; Pedersen 1997). The impact stress of phonation appears to be important both clinically and in laboratory models of vocal cord nodules (Jiang 1994). In boys it is recognised that nodules resolve spontaneously at puberty (Seidner 1982; Håkansson 1984).

Diagnosis
The accepted method for the diagnosis of nodules is endoscopic laryngeal examination (allowing visualisation of the vocal cords during phonation and respiration). Examination with a stroboscope gives additional information about the vibratory and closure patterns of the vocal cords and helps exclude other vocal cord pathology, for example intracordal cysts. Stroboscopy is considered a nec-
a control group but no adequate randomisation procedure) and quasi-randomised trials were also identified.

**Types of participants**

Children and adults with visually confirmed vocal cord nodules. We planned to include studies where the clinical diagnosis had been reached by examination of the vocal cords by indirect laryngoscopy, rigid or fibre-optic endoscopy or micro-laryngoscopy. Stroboscopy was not considered mandatory.

**Types of intervention**

Non-surgical versus surgical interventions.

Non-surgical measures included one or more of the following:

1. medical/pharmacological treatment of infections, allergy and gastroesophageal acid reflex;
2. vocal hygiene advice (including alterations in working environment);
3. reduction of ‘voice abuse’;
4. voice re-training;
5. voice rest;
6. observation alone.

Surgical treatment was removal of the nodules by:

1. direct microsurgical techniques;
2. indirect microsurgical techniques;
3. laser excision;
4. laser ablation.

**Types of outcome measures**

**Primary outcome measures**

1. Perceptual scoring of voice quality (both by the patient and the investigator)
2. Quality of life, for example, return to singing career or other vocally demanding profession

**Secondary outcome measures**

1. Assessment of conditions associated with nodules (see under non-surgical types of interventions)
2. Objective assessment of the vocal cords and of vocal function in individuals with nodules:
   a) visual appearance of the vocal cords;
   b) scoring of roughness, breathiness and overall hoarseness of the voice with perceptual measures;
   c) acoustic measures of continuous speech or sustained vowels and phonetograms;
   d) fundamental frequency with jitter and shimmer;
   e) aerodynamic measurements.

Desirable time points of outcome assessment were: short-term, one month; medium-term, six months; long-term, 1 to 5 years.

**Search methods for identification of studies**

See: Cochrane Ear, Nose and Throat Disorders Group methods used in reviews.


The Cochrane Central Register of Controlled Trials (CENTRAL) was searched using the terms:

1. VOICE DISORDERS explode all trees (MeSH)
2. GRANULOMA LARYNGEAL single term (MeSH)
3. VOCAL CORDS [pa] single term (MeSH)
4. vocal* NEAR (nodul* OR callus* OR thickening* OR lesion* OR granuloma*)
5. voice NEAR (nodul* OR callus* OR thickening* OR lesion* OR granuloma*)
6. laryn* NEAR (nodul* OR callus* OR thickening* OR lesion* OR granuloma*)
7. glotti* NEAR (nodul* OR callus* OR thickening* OR lesion* OR granuloma*)
8. #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7

Strategies for all other databases were modelled on the CENTRAL version and can be found in Table 01. Terms were combined with the highly sensitive search strategy designed by The Cochrane Collaboration for identifying randomised controlled trials and controlled clinical trials in MEDLINE, and with an adapted version in EMBASE.

Reference lists of identified publications were scanned for additional trials and authors contacted as necessary. In addition, the reference lists of any previous reviews of the subject and the authors' own files were scanned for relevant studies. During the preparation of the original version of this review, the PEVOC III conference 1999 and the XXIrd conference of the Union of European Phoniatricians 1999 were attended, but no further references were obtained.

**Methods of the review**

**Study selection**

The full text articles of the retrieved trials were reviewed by two authors and the inclusion criteria applied independently. Any
differences in opinion about which studies to include in the review were resolved by discussion between the two authors.

No suitable trials were identified for inclusion in this review. Should such trials become available the following methods will be applied:

**Data extraction**
Data from the studies will be independently extracted by the two authors using standardised data forms. Data will be extracted so as to allow an intention-to-treat analysis. After all the data forms are filled in, all first authors of the trials to be included and possibly included will receive a copy for comments. Where data are missing, the review authors will write to the authors of the study requesting the missing data.

**Quality assessment**
The quality of all trials will be assessed independently by the two authors. Differences will be resolved by discussion. A modification of the method by Schulz et al is planned (Schulz 1995).

The selected studies will be assessed for the following characteristics:

1. the adequacy of the randomisation process and of allocation concealment (A: adequate, B: uncertain, C: not adequate);
2. the potential for selection bias after allocation to study group, i.e. losses to follow up and whether analysis was by intention-to-treat;
3. whether there was blinding of outcome assessors to the participants' study group;
4. quality of the outcome assessment (A: adequate).

Studies will be graded A, B or C for their overall methodological quality:

A: minimisation of bias in all four categories above, i.e. adequate randomisation; few losses to follow up and intention-to-treat analysis, blinding of outcome assessors, high quality outcome assessment;
B: each of the criteria in A partially met;
C: one or more of the criteria in A not met.

**Data analysis**
Data analysis will be by intention-to-treat. If data are of sufficient quality (categories A and B) they will be combined to give a summary of effect, otherwise data will not be combined. Study quality will be used in a sensitivity analysis. If the data permit, analysis will be carried out separately for different types of voice treatment, as well as considering surgical versus non-surgical treatment of nodules as a whole.

Study outcomes are likely to be measured in a variety of ways using several categorical variables. Data may be dichotomised if appropriate. Statistical advice will be sought to determine the best way of presenting and summarising the data.

**Description of Studies**
A total of 295 studies were identified through electronic searching for the update of this review in 2006. For the original review, handsearching of more than 250 pre-1966 papers was also carried out. From the full search results, eighteen full text papers were obtained for further evaluation. Of these ten were not relevant to the review, and the remaining eight were excluded. Details of the excluded studies, with reasons for exclusion can be found in the table of 'Characteristics of Excluded Studies'. All excluded studies were randomised controlled trials and all, or a proportion of, the participants in each trial had vocal cord nodules. The studies were excluded because they compared different surgical techniques (e.g. microspot CO\textsubscript{2} laser versus excision), different regimens of voice therapy (e.g. traditional voice therapy versus transnasal flexible laryngoscopy assisted voice therapy), or other interventions for nodules (e.g. acupuncture). No randomised controlled trials were identified which compared surgical with non-surgical interventions and therefore no studies met the inclusion criteria for this review.

**Methodological Quality**
Not applicable.

**Results**
No studies were found which satisfied the inclusion criteria for this review.

**Discussion**
A comprehensive search strategy was used for the review. No studies were excluded due to language. While several attempts were made to identify unpublished works, it is still possible that some studies will have been missed. However, the absence of eligible studies for review was not due to restricted selection criteria.

A large number of studies describing either the aetiology, methods for diagnosis or treatment of vocal cord nodules were identified. A major problem highlighted by these descriptive studies is the lack of consensus on the definition of vocal cord nodules and relationship with possible aetiological factors. Not all patients with vocal nodules are symptomatic and some may like the quality of voice that the nodules give them. Out of 65 asymptomatic singing students Lundy found two with nodules diagnosed with video-stroboscopy (Lundy 1999). Malmgren et al did not find a strong association between the patient’s and Speech Therapist’s perception of the voice after treatment and the size or change in size of the vocal nodules (Malmgren 1990). This raises the question of whether the endoscopic appearance of vocal cords is actually

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Surgical versus non-surgical interventions for vocal cord nodules (Review) 4
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an appropriate outcome measure in spite of it being one of the most widely used. A variety of other outcome measures were used to assess the effectiveness of the interventions, many of which were subjective and there was often no reference to validation. Some studies used psychological and quality of life measures, and a few used perceptual measures and objective voice measurements. There were problems with many of the studies considered for this review in that they had methodological and statistical errors such as inconsistent definitions of key variables, inadequate sample size, no confidence limits, short or missing follow up, too many separate endpoints and missing data.

Although it is taught that vocal cord nodules form as a result of 'voice abuse', this is increasingly recognised as being a being a rather simplistic view. Firstly nodules have a heterogenous appearance ranging from diffuse swellings where the histological abnormality seems to be more concentrated in the superficial lamina propria to tiny discrete whitish lesions representing focal epithelial thickening. These various types may not necessarily have the same aetiology or prognosis and further studies need to be performed to determine the causative factors now that the lesions can be better visualised with newer imaging techniques.

Secondly, the point at which nodules become pathological may depend on the individual's perception of their voice and the demands on their voice. As with any organ it is possible to improve its physical performance with training and optimisation of the environment in which it is expected to function. However there are likely to be physical limits to the sound production (in terms of stamina, pitch range, loudness, timbre and fine control) based on the anatomical and physiological limitations of the individual's vocal apparatus. It may be necessary to recognise that the vocal demands are in fact too great for the individual, or the individual's larynx, in their chosen working environment (the amount of background noise or vocal cord irritation from a pollutant). These factors may be as important as, if not more important than, the intervention itself in determining the success of a treatment.

Thirdly there are no gold standards in objective outcome measures of voice treatment and often there is poor correlation between the more objective and subjective measures of assessment. The aims of treatment need to be carefully defined, e.g. resolution of nodules on endoscopic examination, improvement in levels of impairment, activity and participation, acoustic, perceptual and aerodynamic measurements. Whatever measurements are chosen they must be as objective as possible, but also have real relevance to patients.

There is evidence from non-randomised intervention studies (Verdolini 1994; Yamaguchi 1986; Holmberg 2001) that both speech therapy techniques and surgery (Bouchayer 1988; Wendler 1971; Keilmann 1997) are effective. However it is not clear how patients should be selected. Although speech therapy is first line treatment, there is no consensus as to which of the techniques employed by speech therapists are most effective nor for how long they should be used. The techniques range from improving vocal hygiene, behaviour modification and 'abuse' reduction, to vocal retraining and psychological support. It is likely that more than one factor usually requires intervention and that this should be individualised. Future studies would benefit from attempts at quantifying or at least defining each of these factors.

There is a general consensus that surgical treatment of the nodules should aim at removing the minimum amount of mucosa from the vocal cord. Whether cold surgical techniques are better than laser treatment has not been determined with certainty but with newer instruments the surgical result is more likely to be dependent on the skill and experience of the surgeon rather than the tool.

The role of postoperative voice therapy is unclear with some claiming that recurrence is more likely without it. The chance of recurrence is likely to depend on compliance with pre-operative instructions in speech therapy techniques, anatomical, physiological, environmental and psychological factors. Some are likely to be cured with or without postoperative voice therapy and some will suffer further recurrence in spite of it.

There is no doubt that vocal nodules are a difficult condition to study and treat when the aetiology is not fully understood. In addition there are no robust objective measures of vocal function and there are many variables that can affect the outcome of an intervention. More patient orientated outcome measures are being developed and their value is being slowly defined.

Authors' Conclusions

Implications for practice

There is no evidence from randomised controlled trials, on which to base reliable conclusions about the comparative effectiveness of surgical versus non-surgical interventions for the management of patients with vocal cord nodules.

Implications for research

There is a need for a carefully designed prospective randomised controlled study to determine which patients should be selected for primary voice therapy and which would benefit from surgery. Although voice therapy is usually chosen as primary treatment it may not necessarily be the most cost effective way of managing this condition. Voice therapy usually requires a prolonged period of treatment while surgery potentially removes the causative lesions restoring the anatomical configuration of the vocal folds. However there are potential risks of surgery and failures have been reported if the underlying causative factors are not addressed. In addition it may be that patients would rather explore the more conservative approaches before submitting themselves to surgery. It may be important to determine patient views before investing in such a study.
POTENTIAL CONFLICT OF INTEREST

None known.

ACKNOWLEDGEMENTS

We wish to thank Kasper Højby Nielsen from the Danish National Library of Science and Medicine, Jenny Bellorini and Christine Clar from the Cochrane ENT Group and Mirko Tos of the ENT Department, Gentofte University Hospital, Copenhagen, for their help.

Martin Burton was the inspiring tutor of the review.

SOURCES OF SUPPORT

External sources of support

• No sources of support supplied

Internal sources of support

• No sources of support supplied

REFERENCES

References to studies excluded from this review

Benninger 2000

Carding 1998

Hörmann 1999

Mashima 2003

Ragab 2005

Rattenbury 2004

Wang 2005

Yiu 2006

Additional references

Bouchayer 1988

Böhme 1969
Surgical versus non-surgical interventions for vocal cord nodules (Review)

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Fex 1994  

Hocevar 1997  

Holmberg 2001  

Hugh-Munier 1997  

Håkansson 1984  

Jiang 1994  

Keilmann 1997  

Kleinasser 1991  

Kuhn 1998  

Lacina 1972  

Lundy 1999  

Malmgren 1990  

Masuda 1993  

McFarlane 1990  

Murry 1992  

Nagata 1983  

Pedersen 1997  

Remacle 1999  

Schulz 1995  

Seidner 1982  

Silverman 1975  

Urrutikoetxea 1995  

Verdolini 1994  

Wendler 1971  

Xu 1991  

Yamaguchi 1986  
## Characteristics of excluded studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
</tr>
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</table>
| Benninger 2000 | ALLOCATION: Randomised controlled trial  
PARTICIPANTS: Patients (18 years and older) with vocal cord nodules, polyps, mucous retention cysts or polypoid degeneration of the vocal fold(s)  
INTERVENTIONS: Microspot CO2 laser excision versus microdissection |
| Carding 1998  | ALLOCATION: Randomised controlled trial  
PARTICIPANTS: Patients with non-organic dysphonia (including minor laryngeal lesions such as insignificant vocal cord oedema, non-fibrous nodules, chronic laryngitis and dysphonia plicae ventriculares (false cord phonation)  
INTERVENTIONS: Direct (voice) therapy versus indirect therapy versus no treatment |
| Hörmann 1999  | ALLOCATION: Randomised controlled trial  
PARTICIPANTS: 44 adult patients with benign lesions of the vocal fold such as polyps, Reinke's oedema or vocal cord nodules not amenable to conservative treatment  
INTERVENTIONS: Conventional phonosurgery versus laser surgery |
| Mashima 2003  | ALLOCATION: Randomised controlled trial  
PARTICIPANTS: 72 patients with voice disorders, including 31 with vocal cord nodules  
INTERVENTION: Conventional voice therapy versus remote voice therapy delivered via a real-time audio-video monitoring system |
| Ragab 2005    | ALLOCATION: Randomised controlled trial  
PARTICIPANTS: 50 patients with benign superficial vocal cord lesions (20 vocal cord nodules)  
INTERVENTIONS: Cold knife versus radiosurgical excision |
| Rattenbury 2004 | ALLOCATION: Randomised controlled trial  
PARTICIPANTS: 50 patients with muscle tension dysphonia (patients with minor vocal cord lesions e.g. minor vocal cord nodules, were included)  
INTERVENTIONS: Traditional voice therapy versus transnasal flexible laryngoscopy (TFL) assisted voice therapy |
| Wäng 2005     | ALLOCATION: Randomised controlled trial  
PARTICIPANTS: 80 patients with vocal cord nodules  
INTERVENTIONS: Acupuncture versus Chinese herbs versus Western medicine |
| Yiu 2006      | ALLOCATION: Randomised controlled trial  
PARTICIPANTS: 54 patients (female) with dysphonia associated with benign pathological changes (13 nodules)  
INTERVENTION: Acupuncture versus placebo (sham acupuncture) |
Table 01. ADDITIONAL SEARCH STRATEGIES

<table>
<thead>
<tr>
<th>MEDLINE (DataStar)</th>
<th>EMBASE (DataStar)</th>
<th>LILACS/mRCT/IndMed</th>
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<tr>
<td>1. VOICE-DISORDERS.DE.</td>
<td>1. LARYNX-DISORDER.DE.</td>
<td>((dysphoni% OR laryngospasm% OR voice disorder% OR laryngeal dystonia) AND (botulin% OR botox% OR dysport% OR oculinum% OR myobloc% OR neurobloc% OR botb% OR cs bot%) OR vistabel%))</td>
</tr>
<tr>
<td>2. LARYNGISMUS.DE.</td>
<td>2. LARYNX-SPASM.DE.</td>
<td></td>
</tr>
<tr>
<td>3. (SPASM$4 OR SPASTIC OR FLACCID OR HYPERKINETIC OR RESPIRATORY OR LARYNGOSPASM$4) NEAR DYSPHONI$2</td>
<td>4. DYSPHONI$2</td>
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<td>4. PHONATION ADJ DISORDER$1 OR LARYNGEAL ADJ DYSTONIA OR NEUROLOGICS2 ADJ VOICE ADJ DISORDER$1</td>
<td>5. PHONATION ADJ DISORDER$1 OR LARYNGEAL ADJ DYSTONIA</td>
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<td>6. PHONATION ADJ DISORDER$1 OR NEUROLOGIC ADJ VOICE ADJ DISORDER$1</td>
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<td>11. 8 AND 11</td>
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This review has no analyses.
JULIAN MCGLASHAN: protocol development, trials searching, quality assessment of trials, data extraction, data analysis, review development.

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<th><strong>Issue protocol first published</strong></th>
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<tr>
<td><strong>Review first published</strong></td>
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</tr>
<tr>
<td><strong>Date of most recent amendment</strong></td>
<td>23 May 2007</td>
</tr>
<tr>
<td><strong>Date of most recent SUBSTANTIVE amendment</strong></td>
<td>02 January 2001</td>
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</tbody>
</table>

**What's New**

Full searches were carried out again 19th January 2007. No new studies which met our inclusion criteria were identified.

<table>
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<th><strong>Date new studies sought but none found</strong></th>
<th>19 January 2007</th>
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<tbody>
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<td><strong>Date new studies found but not yet included/excluded</strong></td>
<td>Information not supplied by author</td>
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<tr>
<td><strong>Date new studies found and included/excluded</strong></td>
<td>Information not supplied by author</td>
</tr>
<tr>
<td><strong>Date authors' conclusions section amended</strong></td>
<td>Information not supplied by author</td>
</tr>
</tbody>
</table>

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Cochrane Ear, Nose and Throat Disorders Group

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