

Title: Vocal Nodules management.

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Abstract

Vocal fold nodules present the voice clinic team with a number of clinical dilemmas which are not as simple as previously thought. The definition, aetiology, prevalence and diagnosis are all poorly understood. Furthermore, treatment evidence for both behavioural and surgical approaches is weak. This paper reviews the published evidence pertaining to all of these aspects. Specific areas of uncertainty that remain include: poorly defined nomenclature, the natural history of paediatric vocal nodules, the establishment of criteria to measure successful treatment, optimal configuration of speech therapy regimens and the rationale for surgical intervention. The authors suggest the development of evidence-based guidelines for UK practice.

Definition:

Pedersen and McGlashan (1) defined vocal nodules as “bilateral, benign, callous-like growths of variable size found at the mid-part of the membranous vocal cords”. They are characterised by thickening of the epithelium with a variable degree of inflammatory reaction in the underlying superficial lamina propria (2; Figure 1). The characteristic morphological changes of the epithelium are easily seen during routine laryngeal outpatient endoscopy, especially if stroboscopy is used to highlight the mucosal waves during phonation (3). As might be expected, therefore, nodules interfere with the vibratory behaviour of the vocal folds creating increased aperiodicity of vibration and consequential deterioration in voice quality and durability (4). Vocal fold nodules are found in both adults and children.

Aetiology:

The aetiology of vocal nodules is unknown although the histological changes have been linked with repetitive mucosal injury due to laryngeal hyperfunction and vocal abuse (1). Impact stress is highest at the site of greatest contact of the vocal folds in laboratory models (5,6). However, there is a wide range of additional or contributory casual factors including certain infections, chronic inflammatory disorders, allergy and reflux (7).

Prevalence and risk factors:

To our knowledge, the only substantial prevalence data is from a South Korean national health survey (n = 19,636) which reports an observed rate of 1.31% (8), although the criteria for diagnosis are not defined. In general, vocal nodules are described more frequently in women than men, and a hormonal cause for this difference has been hypothesised (9). Other risk factors include occupations with high vocal demand (7) and specific personality and psychological traits (10,11). They

are also frequently reported in children, where strong associations are reported with hearing loss and behavioural difficulties (13.14).

Diagnosis

Pedersen and McGlashan (1) recognised that “the lack of consensus on the definition of vocal fold nodules and relationship with possible etiological factors” was a major problem. Furthermore, not all patients with vocal nodules are symptomatic and indeed some may actually like the quality of voice that the nodules give them. Rosen (3) presented a diagnostic paradigm for benign vocal fold lesions wherein vocal fold nodules were described as bilateral without any requirement for symmetry. Rosen (3) states that a key stroboscopic prerequisite for the diagnosis of vocal fold nodules is “normal, or minimal impairment of, vibratory properties of the mucosa”. However, interestingly, Mansuri’s systematic review (14) of non-medical treatments for vocal nodules included 7 studies (total n = 21) that did not employ diagnostic stroboscopy and a further 3 studies did not describe the diagnostic criteria at all. The main clinical problem is that modern outpatient diagnostic methods show the condition to be rather rare, and that over-diagnosis and/or misdiagnosis was likely commonplace historically. For both of these latter reasons, there is a paucity of information on which to base treatment plans and prognosis.

Symptoms:

The presence of vocal nodules results in dysphonia characterised by hoarseness, breathiness and a lower habitual pitch (15). Other common symptoms are reduced vocal range, vocal fatigue, dryness and throat discomfort (14). These voice difficulties commonly lead to lost time at work, reduced productivity and impaired quality of life (4). Dysphonia adversely affects employment, leading to disability as voice and speech are essential for effective communication, self-assertion and

persuasion- all of which are key criteria for professional success even in the electronic age (16).

Treatment strategies and evidence

Behavioral voice therapy approaches

There is no Level 1 evidence for the efficacy of treatment of patients with vocal fold nodules. The most recent relevant Cochrane review (1) was able to report evidence from non-randomised interventional studies (Levels 2-4) only. The authors concluded that both behavioural voice therapy and laryngeal microsurgery were effective treatments. However, there was uncertainty as to which patients should be selected for primary voice therapy and which would most benefit from surgery. Despite this, most clinicians endorse voice therapy as the primary treatment modality, reserving microsurgery for cases where significant vocal limitations remain after optimal behavioural management (17,18). Voice therapy treatment programmes for vocal fold nodules vary in emphasis and approach but most include at least three basic components: (1) education of the patient regarding behaviours and practices that produce, maintain and/or exacerbate the nodules; (2) elimination of maladaptive behaviours that enable the lesions to form further exacerbate the dysphonia; and (3) modification of any concomitant speaker-specific and situation-specific behaviours which further exacerbate the condition (19,20). It is unclear from the literature which of these components in isolation or in combination enables the most efficacious therapy approach.

The evidence base for the efficacy of voice therapy for patients with vocal nodules has developed chronologically and consistently. Preliminary single case and small group studies reported important therapeutic effects using various combinations of therapy techniques (21,22,23,24,25,26). Several subsequent group comparison design studies reported on treatment efficacy for larger groups of patients with “non-

organic voice disorders” (or similar terms) which included patients with vocal fold nodules (27,28). However, it was not possible to extrapolate the specific data on the vocal nodules patients from the broader findings. Mansuri (14) further reported that existing studies suffered from high heterogeneity of populations, methods and outcomes. However several recent studies represent higher quality methodology and provide evidence for optimal intensity of voice therapy (29), the long term benefits of intensive versus traditional voice therapy (30), and the implementation of tele-practice in treating adult patients with vocal nodules (29). The most comprehensive evidence on children is a retrospective cohort study (n= 67) (31) which reported that resolution was almost universal in this population within five years of diagnosis but the time to resolution was proportional to the size of the nodules at the outset (negative) and the use of targeted voice therapy (positive). However, children received a varied mixture of treatments including behavioural voice therapy and surgery in this study.

Surgical approaches

High definition vocal fold visualisation techniques (32,33) permit detailed evaluation and management of cord lesions whilst preserving the overlying glottis epithelium which thus enables optimal vocal outcomes from surgery. However, the consequence of improved visualisation has been the recognition that true vocal nodules are uncommon in adults (Rosen, 2012). Thus, where once the majority of non-malignant bilateral vocal cord lesions were labelled as “nodules”, and often removed with older, less precise instruments, without prior trials of conservative therapy, now treatment, largely non-surgical or minimally invasive, can be tailored precisely to the underlying pathology.

Johns et al (34) reviewed the literature on the surgical management of vocal nodules and found no evidence for surgery being a first-line treatment. The authors concluded that non-medical treatments should be applied wherever possible. Pedersen and McGlashan's Cochrane review of medical and surgical treatment of vocal fold nodules was first published in 2002, but after three updates, the latest of which was 2012, there were still no randomised controlled trials identified on which to base therapeutic recommendations. Pedersen and McGlashan restricted their consideration of surgical removal of the nodules by one of four methods: direct microsurgery, indirect microsurgery, laser excision, and laser ablation. This was reasonable given the constraints of a Cochrane review, but excluded various injection techniques which might be considered minimally invasive surgery or even, by some, non-surgical medical treatments. Rosen et al (3) concluded that adult patients with highly-characterised benign vocal fold nodules responded to non-surgical treatment and none required surgical exploration. In addition, the authors stated that any bilateral vocal fold lesion that did not respond to voice therapy cannot, by definition, be vocal fold nodules.

The evidence for the efficacy of surgery for all types of vocal fold lesions is limited. Benninger (33) reported a small (n=37) randomised trial comparing the use of the CO₂ laser with that of steel microinstruments only as surgical options for patients with a variety of benign vocal fold lesions. There was no significant difference in perceptual and observed voice outcomes at three months' follow-up, but diagnoses were not restricted to nodules. Nardone's review of 67 children diagnosed with vocal nodules found that those undergoing surgery (unspecified type) had a faster

resolution rate than other groups (one year versus three years for voice therapy and five for behavioural modification alone: 34). However, there were only three children in the surgery group, making firm conclusions elusive.

“Minimally invasive” injection treatments have only been addressed in small uncontrolled studies. They include Tateya’s study of 27 patients treated with peroral injection of steroids, of which 17 experienced complete resolution (35). However, the reported incidence of spontaneous resolution and lack of blinding and controls are significant confounders. Similar qualifications apply to studies of the use of botulinum toxin injections to induce 'voice rest' in patients with recalcitrant nodules, reviewed by Allen and Belafsky (36). Botulinum toxin has a significant side-effect profile which many may not find acceptable. Hsiung (31) hypothesised that augmenting vocal cords after microsurgical removal of nodules reduced “generalised tension” and thereby recurrence. Again, this is a limited uncontrolled study without further evidential support.

Areas of Uncertainty

- *Nomenclature*: The current literature is severely hampered by poorly defined nomenclature and diagnostic processes (3). A recent study identified at least seven sub-types of benign mid-membranous vocal fold lesions identified using modern high definition endoscopy, all of which potentially require a different management approach (37).
- *Natural history of paediatric vocal nodules*: There is no evidence that childhood nodules extend into adolescence or increase the likelihood of adult nodules. Adults who had vocal fold nodules as children do not appear to have as great a propensity for symptomatic voice disorders than other adults (38,39). However, behavioural and surgical treatments remain common practice for children with vocal fold nodules (38) and no evidence-based treatment decision algorithm has been devised to date to our knowledge.
- *Criteria for successful treatment*: as with other spontaneously relapsing and remitting conditions, it is difficult to define a successful outcome sufficient to enable meaningful comparisons between reports and trials. The matter is further complicated by the fact that some people with nodules appear to have little or no subjective disability whilst others may be severely impacted (40). Therefore, the question of what criteria define a clinically significant vocal nodule and what constitutes successful treatment remains open.
- *Speech therapy regimens*: whilst the evidence base for primary voice therapy is now reasonably well-established, there remain important areas of uncertainty. These include the long-term benefits of therapy and the precise treatment regimens, such as optimal duration, intensity and compliance (30).

- The evidence for the efficacy of surgery *per se*, and choice of surgical (including minimally invasive injection) technique is poor with the great majority of patients' responding to voice therapy alone and no substantial evidence for one surgical (including injection) technique over the others. Until such evidence emerges, it seems reasonable that all non-surgical options should be exhausted first, especially voice therapy, and, if this fails, the least morbid surgical treatment possible may be considered.

Guidelines

A search for evidence-based guidelines relating to diagnosis and management of vocal nodules from official societies (including American Speech-Language-Hearing Association and American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNS) in the US and European Laryngological Society and British Laryngological Association in Europe) revealed no results. However, the *AAO-HNS* are publishing clinical practice guidelines for the management of hoarseness (41) whilst the British Voice Association present an informal overview of pathogenesis and management (42) and guidance for parents on the care of children with vocal nodules (43). Vocal nodules-specific, fully evidence-based guidance should be developed.

Conclusions and Recommendations

Vocal nodules are common in children, where they usually require no treatment, and rare in adults. There is no evidence that childhood nodules transition into adult problems. Symptomatic adults, such as the receptionist above, respond to specialised voice therapy, though optimal regimens are yet to be determined. In the rare cases of patients that fail to respond to voice therapy, plus lifestyle modification and optimised reflux management where appropriate, a cautious approach to surgery is proposed with all potential side-effects considered. Microsurgery and various injections are amongst the options. A trial of surgery versus voice therapy would appear to be less required than adequately powered trials comparing voice therapy techniques. Robust and regularly updated, evidence-based, international guidelines are required.

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