This is an Accepted Manuscript for *The Journal of Laryngology & Otology*

DOI: 10.1017/S0022215124001683

Investigation of vocal cord palsy etiology- timing and relevance of imaging

Bahareh Bakhshaie Philipsen[1], Jacob Mølstrøm[2], Camilla Slot Mehlum[2], Gitte Bjørn Hvilsom[1]

Affiliation

1) Department of Head & Neck Surgery, Departments at Zealand University Hospital, Lykkebækvej 1, 4600 Køge, Denmark

2) Department of Head & Neck Surgery and Audiology, Odense University Hospital, J.B. Winsløws vej 4, 5000 Odense C, Denmark

Author 1: Bahareh B. Philipsen, MD, Consultant, Clinical associate professor

Author 1: Jacob Mølstrøm, MD

Author 2: Camilla Slot Mehlum, MD, PhD, Consultant, Clinical associate professor

Author 3: Gitte Bjørn Hvilsom, MD, PhD, Consultant, Clinical associate professor

Corresponding author

Bahareh Bakhshaie Philipsen , Department of ORL - Head & Neck Surgery and Audiology, Zealand University Hospital, Lykkebækvej 1, 4600 Køge, Denmark

bphilipsen@health.sdu.dk; Phone no. 004531329298. ORCID: 0000-0002-4889-458X

Abstract

Objective

We aimed to evaluate imaging modalities utilized in patients with vocal cord palsy (VCP) of unknown etiology, emphasizing the significance of timing and diagnostic yield.

Methods

We conducted a retrospective review of medical records of patients diagnosed with VCP of unknown etiology after their initial clinical examination between 2005 and 2016.

Results

In our cohort, 46 out of 173 (27%) patients were diagnosed with malignancies. All malignancies were identified during the initial imaging examination, except for one patient.

Diagnostic imaging facilitated the diagnosis in 36% of the patients. Computed Tomography (CT) of the neck and chest and full-body Positron Emission Tomography-Computed Tomography (PET-CT) presented the highest overall diagnostic yield of 36% and 35%, respectively.

Conclusion

We recommend that patients with initial CT of the neck and upper chest or PET-CT combined with Magnetic Resonance Imaging without pathological findings, are followed without additional imaging examinations, unless new relevant symptoms arise.

https://doi.org/10.1017/S0022215124001683 Published online by Cambridge University Press

Keywords

Vocal cord palsy, vocal cord paralysis, vocal cord paralyses, MRI, CT, PET, ultrasound, follow-up

INTRODUCTION

Vocal cord palsy (VCP) can be the initial and sole symptom of head and neck cancer (HNC).[1] Since time to treatment play a crucial role in cancer survival [2], an efficient diagnostic workup is essential. Malignancies have been reported to account for as much as 57 % of VCP etiologies.[1, 3-5] However, a broad range of neurological, traumatic, and other benign conditions may also cause VCP.[1] Considering the variety of causes of VCP, various imaging modalities are used in the diagnostic investigation. Additionally, even after a comprehensive examination, the etiology might remain unknown, categorizing the VCP as idiopathic.[1]

An optimal protocol for investigation and follow-up of VCP has been discussed for decades without a consensus on the initial diagnostic approach or the extend and duration of the follow-up in cases of indeterminate etiology.[6-9] Despite this apparent lack of agreement upon practices, it is of great importance to identify malignancies or other severe, treatable causes of VCP.

The aim of this retrospective study was to assess the diagnostic yield of imaging modalities utilized in probing the causes of VCP with initially unknown etiology and to evaluate the performance of an extensive follow-up protocol in order to improve future investigation and optimize the use of resources.

METHODS

The patients

In 2007, the Danish National Board of Health, in collaboration with national multidisciplinary cancer groups and the Danish Regions, introduced fast-track clinical pathway solutions to reduce unnecessary waiting times. This initiative was founded on so called "package solutions", which incorporated pre-scheduled slots for outpatient assessments, imaging, and diagnostic surgical procedures.[10, 11] Based on the well-known risk of underlying malignancy, all patients with a newly diagnosed VCP are referred to this fast track programme. Patients with VCP are diagnosed by flexible fiberoptic laryngoscopy or videostroboscopy. These examinations are supplemented with a chest X-ray (CXR) or computed tomography (CT) of the neck and chest, ultrasound (US) of the neck, and magnetic resonance imaging (MRI) of the neck and brainstem. If no pathology is identified, the patient is categorized with idiopathic VCP. In our department, the CT of the neck and chest was replaced by full-body positron emission tomography (PET-CT) in 2012.

If no cause was determined during the initial investigation and the VCP persisted, patients underwent repeated clinical phoniatric follow-ups and after six months new imaging; CT of the neck and chest and/or MRI of neck and brainstem to detect potential cases of late-manifesting extra-laryngeal disease.[5]

In 2020, the guidelines for the fast-track program for HNC were revised by the Danish Health Authority. Since 1st of October 2020, it has been mandatory to conduct a US of the neck and either a CT of the neck and chest or a PET-CT for all patients entering the fast-track program if no other obvious causes of VCP are found during the patient´s initial consultation.

https://doi.org/10.1017/S0022215124001683 Published online by Cambridge University Press

Study design:

In this retrospective study, we reviewed the records of all patients diagnosed with VCP at the Department of Otorhinolaryngology - Head and Neck Surgery, Odense University Hospital (OUH), Denmark, over a 12-year period from January 1st, 2005, to December 31st, 2016. The study received approval from the Regional Scientific Ethical Committee for Southern Denmark (17/21199) and the National Committee on Health Research Ethics (3-3013-2237/1).

Data sources:

The primary data source was patient medical records. All relevant records were identified and accessed on-site at OUH using the International Classification of Diseases, version 10 (ICD-10) codes for VCP (J38.0, J38.01 and J38.02).

Data collection:

Patient's medical records were retrospectively reviewed by two members of the research team. Data were extracted on the following variables: age at diagnosis, gender, side of VCP, symptoms, date of the initial consultation regarding VCP, imaging modalities utilized, diagnostic findings, follow-up setup, and final conclusion regarding cause of VCP. All data were compiled into a secure, access-logged database using Research Electronic Data Capture (REDCap) tools, hosted at Odense Patient Explorative Network (OPEN) at OUH.

Study population:

https://doi.org/10.1017/S0022215124001683 Published online by Cambridge University Press

During the study period, we identified 678 patients diagnosed with VCP. Of these, 173 (26%) were eligible patients with an initially undetermined etiology.

The diagnosis of VCP was established based on findings from flexible laryngoscopy or rigid videostroboscopy.

Inclusion criteria: Patients diagnosed with VCP where on evident cause was discerned following the initial clinical assessment.

Exclusion criteria: Patients aged below 16 years, cases with direct association between surgical trauma and the onset of VCP, and patients previously diagnosed with cancer invading structures along the course of the affected recurrent nerve. In case of an obvious relation between surgical iatrogenic trauma and VCP was apparent, further diagnostic imaging was deemed redundant, leading to the exclusion of such cases from the study.

Statistical analysis:

The diagnostic yield was calculated as the proportion of procedures with pathological findings to the total number of procedures performed. Descriptive statistics were utilized to describe demographic data. The Mann-Whitney U test and Chi Square test were employed for the comparison of continuous and categorical variables, respectively. The statistical tests were two-sided, with a P value of <0.05 considered statistically significant. All statistical analyses were conducted using Stata 17 (StataCorp. 2021. College Station, TX: StataCorp LLC).

https://doi.org/10.1017/S0022215124001683 Published online by Cambridge University Press

RESULTS

Out of 173 eligible patients, 156 (90%) presented with unilateral VCP, with 111 (71%) being left-sided and 45 (29%) right-sided. The remaining 17 patients (10%) had bilateral VCP. The mean age was 62 (range 16-92) years. On average, patients were followed for seven months (range 0-36). Patient characteristics are presented in *table 1*.

After completed imaging examinations, both initial and follow-up, 46 of the 173 patients (27%) were diagnosed with malignant disease. Men had a one-in-three probability of a malignancy, while women had a one-in-five probability. The etiologies of VCP are detailed in *Table 2.*

The majority of the malignancies originated from the lungs, 24/46 (52%), followed by the breast, 6/46 (13%), and the esophagus, 6/46 (13%), while the remaining 10/46 (22%) patients had miscellaneous cancers. Disseminated disease to the neck and/or mediastinal lymph nodes were identified in 14/24 patients with lung cancer, 6/6 patients with breast cancer, 4/6 patients with esophageal cancer, 2/2 patients with kidney cancer, 1/2 with thyroid cancer, and 1/1 with skin cancer. *Table 3* provides a comprehensive outline of the imaging modalities used to diagnose malignancy in each patient.

A total of 127 (73%) patients either had a specific benign etiology or remained idiopathic without signs of malignancy during follow-up. In 16/173 (9%) patients with VCP, diagnostic imaging found a specific causative structural benign disorder: Five with intracerebral disease (two patients with Chiari malformation, two with cerebral apoplexy and one with a meningioma), four patients with aortic disease, and seven with goiter, of which six patients underwent hemithyroidectomy. In 13/173 (8%) patients with normal imaging findings, VCP was assumed to be caused by medical conditions comprising infectious disorders, Parkinson's

https://doi.org/10.1017/S0022215124001683 Published online by Cambridge University Press

disease, radiotherapy complications, neck trauma, and vocal cord fixation due to rheumatoid arthritis. The cause of VCP was classified as idiopathic in the remaining 98/173 (57%) patients.

In patients with unilateral VCP, malignancies were detected in 32% of those with left-sided and 18% with right-sided VCP.

For the subgroup with bilateral VCP, two out of 17 patients had malignant diseases (lymphoma and lung cancer), two had specific benign diseases (one Chiari malformation and one Parkinson's disease) and 13 were idiopathic.

In our study, the majority (89%) underwent neck US, followed by CT of the neck and chest (68%), MRI of the neck and brainstem, (57%), CXR (47%), PET-CT (23%), and cerebral MRI (8%). Diagnostic imaging resulted in diagnoses in 62/173 (36%) patients. The CT of the neck and upper chest, as well as the PET-CT, demonstrated the highest overall diagnostic yield at 36% and 35%, respectively. In the patients who underwent PET-CT, no pathological etiologies underlying VCP were detected that were not identified on CT of the neck and upper chest. For patients presenting with specific benign disorders, the CT of the neck and upper chest and MRI of the neck and brainstem outperformed other modalities with a diagnostic yield of 14% and 9%, respectively. While the MRI proved pivotal in identifying cerebral lesions, such findings were infrequent. In the subset of patients diagnosed with malignant conditions, the CT of the neck and upper chest and the PET-CT achieved the highest diagnostic yield at 97% and 100%, respectively. Notably, in a case involving a patient with disseminated kidney cancer (patient no. 43, *Table 3*), both the CT and MRI revealed potential metastatic lesions in the left lung and right jugular foramen. However, the subsequent PET-

CT was instrumental in pinpointing the primary kidney lesion. The remaining imaging modalities rendered considerably lower diagnostic yield when identifying underlying malignancies. *Table 4* delineates the diagnostic yields associated with each employed imaging modality.

Following the initial imaging, 100/173 (58%) patients remained diagnostically unresolved. Of these patients, 42 patients regained normal vocal cord mobility upon follow-up, eleven patients declined further examination, four patients failed to appear, and one patient had died due to heart disease. Of the remaining 42 patients, 10 showed partial improvement in their VCP, while 32 persisted with immobility. Follow-up imaging for these 42 patients identified extralaryngeal pathology in two cases. For one patient (no. 30, Table 3), the initial imaging examination included neck US, CXR, and MRI of the neck and brainstem. However, a follow-up a CT of neck and upper chest detected a proximal esophageal carcinoma. The second patient initially underwent US and CT of neck and upper chest. On follow-up, an MRI of the cerebrum revealed a cerebellopontine angle meningioma. Notably, these two patients were diagnosed in 2005 and 2007, a time when PET-CT and MRI of the neck and brainstem were not yet incorporated into the standard preliminary assessment.

Upon reviewing the medical records of patients with VCP categorized as idiopathic, we found no indications of late-emerging conditions that could be associated with the onset of VCP.

https://doi.org/10.1017/S0022215124001683 Published online by Cambridge University Press

DISCUSSION

We retrospectively evaluated a cohort of 173 patients with VCP of initially unknown etiology and evaluated the use and diagnostic yield of the imaging modalities applied at initial assessment and during follow-up.

Our cohort consisted of 90% unilateral VCP (64% left-sided and 26% right-sided) and 10% bilateral VCP, a distribution comparable to other studies.[6, 8, 12, 13] Malignant etiology was diagnosed in 27% of our cases, a specific benign etiology in 16%, leaving 57% of our cohort with idiopathic VCP.

The most frequently reported malignancies causing VCP are thyroid, pulmonary, and esophageal carcinomas, as well as mediastinal metastasis [13-16], consistent with our findings. The reported proportion of idiopathic VCP varies from 3 to 76% [5, 12, 14, 16], reflecting the discrepancies in investigation approaches. Diagnostic tools should possess high sensitivity for detecting occult diseases, but cost-effectiveness must also be considered. CXR, CT, MRI, and neck US have been applied in the investigation of VCP for decades.[9, 14]

CT of neck and upper chest is considered standard care when evaluating patients with VCP.[14] In our study, we observed a total diagnostic yield of CT of the neck and upper chest of 36%, compared to 97% in the subgroup diagnosed with malignancy. Comparable findings have been observed in several other studies. In a prospective study, Gupta J et al.[4] reported on 120 patient with vocal cord paralysis, wherein a CT from the base of skull to the chest revealed malignancy in 34% of the patients. Bilici et al.[6] reported diagnostic yields for CT of the neck and chest of 24.5% and 30.9%, respectively. However, Paddle et al.[8] presented a case series with chart review determining the diagnostic yield of CT in patients with presumed idiopathic unilateral vocal fold paresis, reporting a diagnostic yield of just 2.9% in a study of 174

https://doi.org/10.1017/S0022215124001683 Published online by Cambridge University Press

patients, thus arguing against routine CT. This opinion was supported by the retrospective study of Badia et al.[17], who reported a diagnostic yield of CT of neck and chest of a mere 1.7% in 60 patients with presumed idiopathic, unilateral vocal fold paresis.

Bilateral VCP is more commonly attributed to lesions in the central nervous system, especially in the medulla oblongata, such as demyelinating diseases, infections, and both benign and malignant intraaxial tumors.[18] MRI provides superior resolution, especially in the brainstem and skull base compared to CT [6, 14], making it ideal for detecting lesions in the central nervous system causing VCP. In our study, an MRI scan of the neck and brainstem was conducted in all patients with bilateral VCP, while 84/156 (54%) patients with unilateral VCP underwent an MRI scan of the neck and brainstem. We observed a total diagnostic yield for MRI of the neck and brainstem of 10% (10/99). Additionally, MRI contributed to the detection of metastatic neck disease in five patients. In our cohort, an MRI of the cerebrum was performed only in 14 patients, with a diagnostic yield of 7% (1/14). Between 2012 and 2016, an MRI scan of the neck and brainstem was conducted in 35/41 (85%) patients.

PET-CT has been established as an effective and sensitive diagnostic tool for detection for malignancies, demonstrating a significant capability to rule out malignancy in patients with VCP.[19, 20] However, in certain lesions, it can be challenging to differentiate between benign and malignant etiologies. [21, 22] Asymmetrical fluorodeoxyglucose uptake in vocal cords is a well-known finding in patients with VCP.[17] Increased uptake in the contralateral, unaffected vocal cord is often observed due to heightened physiological activity serving as a compensatory mechanism.[18]

In a systematic review by Rohde et al.[23] that compared the diagnostic accuracy of PET-CT to standard conventional imaging for patients with head and neck squamous cell carcinoma, the

https://doi.org/10.1017/S0022215124001683 Published online by Cambridge University Press

meta-analysis showed a pooled sensitivity and specificity for PET-CT of 89.3% and 89.5%, respectively. In contrast, standard conventional imaging displayed a sensitivity of 71.6% and specificity of 78.0%. Thomassen et al.[20] conducted a retrospective study on 65 patients referred for PET-CT due to paresis or paralysis of one or both vocal cords. The results of the PET-CT were compared against clinical evaluations and histopathological findings. Their findings underscored the utility of PET-CT, showing a sensitivity of 100% and highlighting its efficacy in excluding malignancy. Importantly, biopsy-confirmed malignancy (either newly diagnosed or relapsed) was identified as the cause of VCP in 42% of these patients. However, it´s worth noting that in 12% of cases, the PET-CT results were false positive, leading to a series of potentially unnecessary investigations.

During our study period, new guidelines for the diagnostic evaluation of VCP were implemented in 2012, leading to a varied imaging approaches within our cohort. From January 2012 to December 2016, 38/41 (93%) patients with VCP of undetermined etiology underwent PET-CT examinations during this timeframe (data not presented). In our analysis, the full-body PET-CT showed the highest diagnostic yield of 100% in the 46 patients with malignant diseases, though the overall yield was 35%.

In Denmark, neck US is a routine procedure in all ENT departments and is incorporated into the fast-track evaluation during the initial examination.[5] US offers high sensitivity and serves as a precise imaging tool for differential diagnosis of neck pathologies, especially thyroid pathologies.[16] In cases where thyroid lesions are located deep within in the posterior part of the thyroid lobe, VCP can be the primary manifestation. The strength of US lies in its accessibility, cost-effectiveness, and lack of radiation exposure. Nevertheless, potential

https://doi.org/10.1017/S0022215124001683 Published online by Cambridge University Press

interobserver variability should be acknowledged.[16] Our study found the diagnostic yield of neck US to be 7% (11/155) in all patients. Still, it was 24% (10/41) in patients with malignant neck and/or mediastinum conditions, 67% for lymphoma cases (2/3), and 100% for all thyroid diseases (9/9). This suggests that patients with thyroid lesions might not require additional imaging. Bilici et al.[6] reported a diagnostic yield of neck US at 26.2%, advocating for neck US and CT of the chest as initial assessment tools for unilateral vocal fold paralysis. Wang et al.[16] reported the significance of neck US, including the thyroid gland, as the primary imaging approach for unilateral vocal fold paralysis.

As for follow-up protocols, no consensus has been reached and various strategies have been suggested throughout the years. El Badaway et al.[3] followed 62 patients, all of whom underwent initial CT of the neck and chest without discernible pathological findings. Clinical evaluations were performed with six month intervals, and no additional positive findings were observed during the follow-up period spanning 18 to 66 months. In a review, Tsikoudas et al.[24] argued that patients with initial CT scans without pathological findings should receive subsequent follow-up without additional imaging, unless specific symptoms emerged. In a retrospective study, Noel et al.[7] found that 90% of 207 patients with idiopathic VCP maintained their diagnosis after 60 months with 42% of the cohort monitored beyond a year. They suggested annual clinical evaluation, resorting to imaging only when new symptoms manifest. In our study, 42 of 173 patients (24%) were qualified for imaging follow-up. Among these, two with persistent symptoms were diagnosed with disease during follow-up. One patient´s CT of the neck and chest unveiled an esophageal carcinoma, which had not been initially CT-scanned. For another patient, an MRI of the cerebrum found a benign

cerebral tumor during the follow-up. In summary, the diagnostic yield at 6 months follow-up was below 5%. Importantly, we did not discover any late-emerging malignancies disease in the idiopathic group. This insight is pivotal as it spares patients from extensive examinations, associated concerns, and can help curtail healthcare expenditures.

In 2021, as a result of this current study, our regional guideline for follow-up underwent a revision. Now, CT scans of the neck and chest and MRIs of neck and brainstem are not routinely performed at the six-month follow-up but only when clinically indicated.

Based on our results, we suggest the workup of patients with unilateral and bilateral vocal cord palsy as illustrated in Figure 1.

Strengths and limitations

During our study period, revised guidelines for the diagnostic evaluation of VCP were implemented, leading to varied imaging examinations within our cohort.

Upon reviewing the medical records of patients in the idiopathic group, we did not identify any additional cases of late-onset disease that could have precipitated VCP. We consider the extended five-year follow-up period to be one of the strengths of our study.

Conclusion

In our study, CT of the neck and upper chest and PET-CT demonstrated comparable diagnostic yields in detecting underlying extra-laryngeal pathology. While our data did not reveal an advantage, MRI remains a suitable modality for identifying lesions within the central nervous system responsible for VCP. We suggest that patients with initial normal

https://doi.org/10.1017/S0022215124001683 Published online by Cambridge University Press

findings on CT, PET-CT, or MRI be monitored without subsequent imaging unless new relevant symptoms manifest.

Acknowledgements

None

Financial Support

This research received no specific grant from any funding agency, commercial or not-for-profit sectors

References

1 Chen, HC, Jen, YM, Wang, CH, Lee JC, Lin, YS. Etiology of vocal cord paralysis. ORL J Otorhinolaryngol Relat Spec 2007;69:167-71
2 Chen, Z, King, W, Pearcey, R, Kerba, M, Mackillop, WJ. The relationship between waiting time for radiotherapy and clinical outcomes: a systematic review of the literature. Radiother Oncol 2008;87:3-16
3 El Badawey, MR, Punekar, S, Zammit-Maempel, I. Prospective study to assess vocal cord palsy investigations. Otolaryngol Head Neck Surg 2008;138:788-90
4 Gupta, J, Varshney, S, Bist, SS, Bhagat, S. Clinico-etiolological study of vocal cord paralysis. Indian J Otolaryngol Head Neck Surg 2013;65:16-9
5 Mehlum, CS, Faber, CE, Grøntved, AM, Andersen, P. [Vocal fold palsy--investigation and follow-up]. Ugeskr Laeger 2009;171:113-7
6 Bilici, S, Yildiz, M, Yigit, O, Misir, E. Imaging Modalities in the Etiologic Evaluation of Unilateral Vocal Fold Paralysis. J Voice 2019;33:813.e1-.e5
7 Noel, JE, Jeffery, CC, Damrose, E. Repeat Imaging in Idiopathic Unilateral Vocal Fold Paralysis: Is It Necessary? Ann Otol Rhinol Laryngol 2016;125:1010-4
8 Paddle, PM, Mansor, MB, Song, PC, Franco, RA, Jr. Diagnostic Yield of Computed Tomography in the Evaluation of Idiopathic Vocal Fold Paresis. Otolaryngol Head Neck Surg: 2015 153:414-9
9 MacGregor, FB, Roberts, DN, Howard, DJ, Phelps, PD. Vocal fold palsy: a re-evaluation of investigations. J Laryngol Otol 1994;108:193-6

10 Roennegaard, AB, Rosenberg, T, Bjørndal, K, Sørensen, JA, Johansen J, Godballe C. The Danish Head and Neck Cancer fast-track program: a tertiary cancer centre experience. Eur J Cancer 2018;90:133-9
11 Sorensen, JR, Johansen, J, Gano, L, Sørensen, JA, Larsen, SR, Andersen, PB A "package solution" fast track program can reduce the diagnostic waiting time in head and neck cancer. Eur Arch Otorhinolaryngol 2014;271:1163-70
12 Terris, DJ, Arnstein, DP, Nguyen, HH. Contemporary evaluation of unilateral vocal cord paralysis. Otolaryngol Head Neck Surg 1992;107:84-90
13 Seyed Toutounchi, SJ, Eydi, M, Golzari, SE, Ghaffari, MR, Parvizian, N. Vocal cord paralysis and its etiologies: a prospective study. J Cardiovasc Thorac Res 2014;6:47-50
14 Kang, BC, Roh, JL, Lee, JH, Jung, JH, Choi, SH, Nam, SY. Usefulness of computed tomography in the etiologic evaluation of adult unilateral vocal fold paralysis. World J Surg 2013;37:1236-40
15 Glazer, HS, Aronberg, DJ, Lee, JK, Sagel, SS. Extralaryngeal causes of vocal cord paralysis: CT evaluation. AJR Am J Roentgenol 1983;141:527-31
16 Wang, CP, Chen, TC, Lou, PJ, Yang, TL, Hu, YL, Shieh, MJ. Neck ultrasonography for the evaluation of the etiology of adult unilateral vocal fold paralysis. Head Neck 2012;34:643-8
17 Badia, PI, Hillel, AT, Shah, MD, Johns, MM, Klein, AM. Computed tomography has low yield in the evaluation of idiopathic unilateral true vocal fold paresis. Laryngoscope 2013;123:204-7
18 Dankbaar, JW, Pameijer, FA. Vocal cord paralysis: anatomy, imaging and pathology. Insights Imaging 2014;5:743-51
19 Rohde, M, Nielsen, AL, Pareek, M, Johansen, J, Sørensen, JA, Diaz, A. A PET/CT-Based Strategy Is a Stronger Predictor of Survival Than a Standard Imaging Strategy in Patients with Head and Neck Squamous Cell Carcinoma. J Nucl Med 2018;59:575-81
20 Thomassen, A, Nielsen, AL, Lauridsen, JK, Blomberg, BA, Hess, S, Petersen H. FDG-PET/CT can rule out malignancy in patients with vocal cord palsy. Am J Nucl Med Mol Imaging 2014;4:193-201
21 Heller, MT, Meltzer, CC, Fukui, MB, Rosen, CA, Chander, S, Martinelli, MA. Superphysiologic FDG Uptake in the Non-Paralyzed Vocal Cord. Resolution of a False-Positive PET Result with Combined PET-CT Imaging. Clin Positron Imaging 2000;3:207-11
22 Minamimoto, R, Kubota, K, Morooka, M, Ito, K, Mitsumoto, T, Okasaki, M. Reevaluation of FDG-PET/CT in patients with hoarseness caused by vocal cord palsy. Ann Nucl Med 2012;26:405-11
23 Rohde, M, Dyrvig, AK, Johansen, J, Sørensen, JA, Gerke, O, Nielsen, AL. 18F-fluoro-deoxy-glucose-positron emission tomography/computed tomography in diagnosis of head and neck squamous cell carcinoma: a systematic review and meta-analysis. Eur J Cancer 2014;50:2271-9
24 Tsikoudas, A, Paleri, V, El-Badawey, MR, Zammit-Maempel, I. Recommendations on follow-up strategies for idiopathic vocal fold paralysis: evidence-based review. J Laryngol Otol 2012;126:570-3

Bullet Point Summary

- The optimal protocol for investigation and follow-up on vocal cord palsy (VCP) with undetermined etiology has been discussed for decades.
- Of the 173 patients with VCP in our study, 27% were diagnosed with malignancy.
- In 45 out of 46 cases, malignancies were detected during the initial imaging investigation.
- Post-initial imaging, 58% patients had an unresolved diagnosis.
- 42 patients underwent follow-up imaging, identifying two additional patients with extralaryngeal pathology, in both cases, the initial imaging procedure had been incomplete.
- CT of the neck and upper chest, along with full-body PET-CT, demonstrated similarly high diagnostic yields for identifying underlying extra-laryngeal pathology.

https://doi.org/10.1017/S0022215124001683 Published online by Cambridge University Press

Table 1: Characteristics of patients with vocal cord palsy of unknown etiology after initial clinical examination.

Characteristics	Overall, n (%)	Benign etiology*, n (%)	Malignant etiology, n (%)	P-value
Patients	173	127 (73.4)	46 (26.6)	
Sex				0.09
Male	83 (48.0)	56 (67.5)	27 (32.5)	
Female	90 (52.0)	71 (78.9)	19 (21.1)	
Mean age, years (range)	62 (16-92)	61 (16-92)	66 (29-85)	0.005
Side of palsy				0.06
Right	45 (26.0)	37 (82.2)	8 (17.8)	
Left	111 (64.2)	75 (67.6)	36 (32.4)	
Bilateral	17 (9.8)	15 (88.2)	2 (11.8)	
Mean follow-up, mo. (range)	7 (0-36)	8 (0-36)	6 (0-18)	0.002

*Specific benign diagnosis or idiopathic after investigation
Percentages in the benign and malignant columns should be interpreted horizontally.
n, number; mo., month

https://doi.org/10.1017/S0022215124001683 Published online by Cambridge University Press

Table 2: Etiology of vocal cord palsy

Diagnosis	Unilateral VCP No. Patients (%*)	Bilateral VCP No. Patients (%*)	Total No. Patients (%*)
Malignant etiology			
Lung			
Primary tumor	11 (6.4)	1 (0.6)	12 (6.9)
Metastasis	12 (6.9)	-	12 (6.9)
Esophageal			
Primary tumor	1 (0.6)	-	1 (0.6)
Metastasis	5 (2.9)	-	5 (2.9)
Breast			
Metastasis	6 (3.5)	-	6 (3.5)
Lymphoma	2 (1.2)	1 (0.6)	3 (1.8)
Laryngeal			
Primary tumor	2 (1.2)	-	2 (1.2)
Thyroid			
Primary tumor	2 (1.2)	-	2 (1.2)
Kidney			
Metastasis	2 (1.2)	-	2 (1.2)
Skin			
Metastasis	1 (0.6)	-	1 (0.6)
Total malignant	44 (25.4)	2 (1.2)	46 (26.6)
Specific benign etiology			
Neurological			
Chiari malformation	1 (0.6)	1 (0.6)	2 (1.2)
Cerebrovaskular disease	2 (1.2)	-	2 (1.2)
Intracerebral tumor	1 (0.6)	-	1 (0.6)

https://doi.org/10.1017/S0022215124001683 Published online by Cambridge University Press

Parkinson´s disease	-	1 (0.6)	1 (0.6)
Neuroborreliosis	1 (0.6)	-	1 (0.6)
Radiotherapy of benign spinal tumor	1 (0.6)	-	1 (0.6)
Other			
Goiter*	7 (4.0)	-	7 (4.0)
Blunt trauma	2 (1.2)	-	2 (1.2)
Radiotherapy of benign mediastinal tumor	1 (0.6)	-	1 (0.6)
Sarcoidosis	1 (0.6)	-	1 (0.6)
Aortic aneurism	3 (1.7)	-	3 (1.7)
Aortitis	1 (0.6)	-	1 (0.6)
Vincristine-induced	1 (0.6)	-	1 (0.6)
Rheumatic disease	4 (2.3)	-	4 (2.3)
Herpes zoster infection	1 (0.6)	-	1 (0.6)
Total specific benign	27 (15.6)	2 (1.2)	29 (16.8)
Idiopathic	85 (49.1)	13 (7.5)	98 (56.6)
Total	156 (90.2)	17 (9.8)	173 (100)

Percentage of the 173 patients with vocal cord palsy.
*Subsequent hemithyroidectomy in 6/7 cases, all with benign histology

https://doi.org/10.1017/S0022215124001683 Published online by Cambridge University Press

Table 3: Diagnostic imaging results at initial and follow-up examinations in patients with malignant etiology of vocal cord palsy.

Patient No.	Malignant disease	US neck I/F	CXR I/F	CT neck/chest I/F	MRI neck/brainstem I/F	MRI cerebrum I/F	PET/CT I/F
1	Lung	-/-	N/-	M/-	N/-	-/-	-/-
2	Lung	-/-	M/-	M/-	-/-	-/-	-/-
3	Lung	N/-	N/-	M/-	-/-	-/-	-/-
4	Lung	N/-	N/-	M/-	-/-	-/-	-/-
5	Lung	S/-	M/-	M/-	-/-	-/-	-/-
6	Lung	-/-	-/-	M/-	-/-	-/-	-/-
7	Lung	S/-	-/-	M/-	-/-	-/-	M/-
8	Lung	S/-	N/-	M/-	-/-	-/-	-/-
9	Lung	N/-	M/-	M/-	-/-	-/-	-/-
10	Lung	-/-	M/-	M/-	-/-	-/-	-/-
11	Lung	-/-	M/-	-/-	-/-	-/-	-/-
12	Lung	-/-	M/-	M/-	-/-	-/-	-/-
13	Lung	N/-	M/-	-/-	S/-	-/-	-/-
14	Lung	N/-	M/-	M/-	-/-	-/-	-/-
15	Lung	N/-	-/-	-/-	-/-	-/-	M/-
16	Lung	N/-	-/-	M/-	S/-	-/-	-/-
17	Lung	N/-	-/-	-/-	-/-	-/-	M/-

https://doi.org/10.1017/S0022215124001683 Published online by Cambridge University Press

18	Lung	N/-	M/-	M/-	N/-	-/-	-/-
19	Lung	N/-	-/-	M/-	-/-	-/-	-/-
20	Lung	N/-	-/-	-/-	-/-	-/-	M/-
21	Lung	N/-	N/-	M/-	-/-	-/-	-/-
22	Lung	N/-	N/-	M/-	N/-	-/-	-/-
23	Lung	N/-	N/-	M/-	-/-	-/-	-/-
24	Lung	S/-	-/-	M/-	-/-	-/-	-/-
25	Esophagus	N/-	-/-	-/-	-/-	-/-	M/-
26	Esophagus	N/-	N/-	M/-	-/-	-/-	-/-
27	Esophagus	N/-	-/-	M/-	-/-	-/-	-/-
28	Esophagus	N/-	-/-	M/-	-/-	-/-	-/-
29	Esophagus	S/-	-/-	-/-	-/-	-/-	M/-
30	Esophagus	N/N	N/-	-/-	N/-	-/-	-/M
31	Breast	N/-	-/-	M/-	-/-	-/-	-/-
32	Breast	S/-	-/-	-/-	-/-	-/-	M/-
33	Breast	S/-	-/-	-/-	-/-	-/-	M/-
34	Breast	N/-	N/-	M/-	-/-	-/-	-/-
35	Breast	N/-	-/-	M/-	-/-	-/-	-/-
36	Breast	N/-	-/-	M/-	N/-	-/-	-/-
37	Lymphoma	N/-	S/-	M/-	-/-	-/-	-/-
38	Lymphoma	M/-	-/-	-/-	S/-	-/-	M/-
39	Lymphoma	M/-	-/-	-/-	-/-	-/-	M/-

https://doi.org/10.1017/S0022215124001683 Published online by Cambridge University Press

40	Thyroid	M/-	-/-	M/-	-/-	-/-	-/-
41	Thyroid	M/-	-/-	M/-	-/-	N/-	-/-
42	Kidney	S/-	S/-	-/-	S/-	-/-	M/-
43	Kidney	-/-	N/-	S/-	S/-	-/-	M/-
44	Laryngeal	S/-	-/-	-/-	M/-	-/-	M/-
45	Laryngeal	N/-	N/-	M/-	M/-	-/-	-/-
46	Skin	S/-	-/-	M/-	-/-	-/-	-/-

I: Initial examination; F: Follow-up examination

M: Malignant diagnosis found; N: No malignant diagnosis found; S: suspicious findings; -: Imaging modality not applied.

US: ultrasonography, CT: computed tomography, MRI: magnetic resonance imaging, PET/CT: Positron emission tomography–computed tomography, CXR: chest x-ray

https://doi.org/10.1017/S0022215124001683 Published online by Cambridge University Press

Table 4: Diagnostic yield of the imaging modalities.

Imaging modality	Specific benign diagnosis (%)	Malignant diagnosis (%)	Overall (%)
US neck	7/116 (6.0)	4/39 (10.3)	11/155 (7.1)
CXR	1/59 (1.7)	9/23 (39.1)	10/82 (12.2)
CT neck/ upper chest	12/86 (13.9)	31/32 (96.9)	43/118 (36.4)
MRI neck/brainstem	8/87 (9.2)	2/12 (16.7)	10/99 (10.1)
MRI cerebrum	1/13 (7.7)	0/1 (0.0)	1/14 (7.1)
PET-CT	0/26 (0.0)	14/14 (100)	14/40 (35.0)

US, ultrasonography; CT, computed tomography, MRI, magnetic resonance imaging;

PET/CT, positron emission tomography–computed tomography; CXR, chest x-ray

https://doi.org/10.1017/S0022215124001683 Published online by Cambridge University Press

This is an Accepted Manuscript for *The Journal of Laryngology & Otology*

DOI: 10.1017/S0022215124001683

Figure 1: Our recommended assessment for a patient with newly diagnosed vocal cord palsy includes the following steps: