ORIGINAL ARTICLE

Velopharyngeal function and nasalance score in post-radiation nasopharyngeal carcinoma patients

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ABSTRACT

Introduction: Voice production and speech impairment in head and neck cancer patients can be experienced due to tumors or therapy such as radiotherapy. Velopharyngeal fibrosis in post-radiation nasopharyngeal carcinoma (NPC) patients can disrupt the velopharyngeal closure during speech, causing hypernasality. This study aims to determine the characteristics and proportions of the nasalance score in post-radiation NPC patients with or without resonance disorder.

Materials and Methods: This research is a descriptive study using cross-sectional techniques, followed by retrospective data collection of post-radiation NPC patients at Dr. Cipto Mangunkusumo General Hospital for the period July-August 2023. The parameter assessed is the nasalance score using a nasometer, the velopharyngeal dysfunction assessed with flexible laryngoscopy, and the hypernasality assessed by a 15 years' experienced speech therapist.

Results: The nasalance score in the Gajah 1 test obtained a median of 14 (7-22), for the mean value of Hantu 1 test was 39.8% ± 4.5, and for the mean value of Sengau test was 62.2 ± 6.9, with a nasalance score cut point in Gajah 1 test between normal resonance and hypernasal was 15.5% and in Hantu 1 test was 42.5%. Gender and radiation dose to the pharyngeal constrictor muscle tend to have a significant relationship with resonance disorder in post-radiation NPC patients.

Conclusion: A prospective study is needed in NPC patients with pre- and post-radiation assessment and follow-up evaluation to assess the effects of radiation which includes all relevant functional aspects of voice and speech.

KEYWORDS:
Nasopharyngeal carcinoma, radiation, nasalance score, hypernasality, velopharyngeal dysfunction

INTRODUCTION

Voice production is essential for verbal communication and social interaction, serving as a reflection of an individual's identity and personality, which significantly impacts their well-being and quality of life. [1,2]

The velopharynx (VP) plays a vital role in speech and voice generation. Dysfunction in the velopharynx, whether caused by nerve issues, structural abnormalities, or functional impairments, can lead to resonance problems such as hypernasality.[3,4] Additionally, individuals with head and neck cancer may experience difficulties in voice production and speech due to tumors or treatments like radiotherapy.

Radiotherapy works by inhibiting tumor cell growth through various molecular mechanisms and can be used alone or in combination with surgery and/or chemotherapy.[5] According to Dorr et al. and Kraaijenga et al.[6] the risk of side effects on normal tissues near the targeted area depends on the radiation dose and the amount of healthy tissue exposed.[7] High doses of radiation not only destroy tumor cells but can also affect normal cells, potentially causing tissue fibrosis, hypovascularity, and hypocellularity.[8] In patients with nasopharyngeal carcinoma (NPC), VP is at risk of radiation side effects due to its proximity to the tumor being targeted. A study by Xiao-song et al.[9] examined 16 post-radiation NPC patients with velopharyngeal dysfunction who had received an average radiation dose of 70 Gy. The dysfunction resulted in velopharyngeal insufficiency caused by atrophy and fibrosis, the common side effects of radiotherapy.

Nasometry, an acoustic tool that measures speech nasality through a nasalance score, is often used to assess the impact of therapies or procedures on speech. Numerous studies have explored velopharyngeal function and resonance in head and neck cancer patients. However, there is still no data on the characteristics and proportions of nasalance scores in post-radiation NPC patients, whether they have resonance disorders or not. Therefore, research is needed to assess nasalance scores and velopharyngeal dysfunction in these patients.

MATERIALS AND METHODS

Study design and participants

This descriptive study was conducted using a cross-sectional approach at the Ear, Nose, Throat, Head, and Neck Surgery Outpatient Clinic and Radiation Oncology Unit of Cipto Mangunkusumo General Hospital. The study was conducted from June to September 2023 and involved 37 post-radiation NPC patients.

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Table I: Subject Distribution of Study Population (N=37)

Characteristics of study population	Frequency	Percentage (%)
Gender		
Male	23	62.2
Female	14	37.8
Age Group		
18 – 45 years old	17	45.9
46 – 59 years old	20	54.1
Median (Range) Age	47.0	18 – 59
Treatment Modality		
Radiation	1	2.7
CRT	13	35.1
NAC and CRT	16	43.2
CRT and adjuvant chemotherapy	6	16.2
NAC, CRT, and adjuvant chemotherapy	1	2.7
Tumor size		
T1	5	13.5
T2	15	40.5
T3	7	18.9
T4	10	27
Time from the last radiation		
3 months - 1 year	17	45.9
More than 1 year	20	54.1
Median (Range) Time from the last radiation in month	14	3 – 120
Resonance disorder		
Normal	29	78.4
Hypernasal	8	21.6
Velopharyngeal dysfunction		
Velopharyngeal dysfunction	13	35.1
Coronal	5	38.5
Circular	4	30.8
Sagittal	4	30.8
Normal VP	24	64.9
Nasalance score (Median/Mean and SD/Range)		
Median (Range) Gajah 1 test	14,0	7 – 22
Mean ± SD Hantu 1 test	39.8	± 4.5
Mean ± SD Hantu 1 test	62.2	± 6.9
Radiation dose (Median/Mean and SD/Range)		
Mean ± SD PCM radiation dose cGy	6091.3	± 311.7
Median (Range) Soft palate radiation dose cGy	6836.0	5535 – 7125

CRT, chemoradiation; NAC, neo-adjuvant chemotherapy; PCM, pharyngeal constrictor muscle; VP, velopharynx.

Table II: Subject distribution by resonance disorder (N=37)

Distribution	Resonance Disorder		p-value
	Hypernasal (N=8)	Normal (N=29)	
Gender			
Male	2	21	0.035[a]
Female	6	8	
Age Group			
18 – 45 years old	3	12	>0.999[a]
46 – 59 years od	5	17	
NAC			
Yes	5	12	0.428[a]
No	3	17	
Adjuvant chemotherapy			
Yes	2	5	0.631[a]
No	6	24	
Time from the last radiation in month (Median and Range)	15 (4-85)	12 (3-120)	0.502[b]
PCM radiation dose cGy (Mean ± SD)	6292.66 ± 277.2	6035.77 ± 301.6	0.037[c]
Soft palate radiation dose cGy (Median and Range)	6909 (6752-7070)	6919 (6045-7125)	0.957[b]
Velopharyngeal dysfunction			
Coronal	3	2	
Sagittal	2	2	
Circular	2	2	
Normal velopharynx	1	23	

NAC, neo-adjuvant chemotherapy; PCM, pharyngeal constrictor muscle
[a]Fisher's exact test, [b]Mann-Whitney test, [c]Independent t-test

Table III: Characteristics of study population with velopharyngeal dysfunction (N=37)

Characteristic	Velopharyngeal dysfunction		p-value
	Velopharyngeal dysfunction (N=13)	Normal VP (N=24)	
Gender			
Male	6	17	0.171[a]
Female	7	7	
Age Group			
18 – 45 years old	6	9	0.730[a]
46 – 59 years old	7	15	
Time from the last radiation in month (Median and Range)	14 (3-78)	13,5 (3-120)	0.838[b]
PCM radiation dose cGy (Mean ± SD)	6195 ± 334.6	6035 ± 290.4	0.139[c]
Soft palate radiation dose cGy (Median and Range)	6941 (6752-7125)	6918 (6045-7111)	0.276[b]

PCM, pharyngeal constrictor muscle.
[a]Fisher's exact test, [b]Mann-Whitney test, [c]Independent t-test

Table IV: Nasalance score based on type test and resonance disorder (N=37)

Nasalence score (%)	Resonance disorder				p-value
	Hypernasal (N=8)		Normal (N=29)		
	Mean	SD	Mean	SD	
Gajah 1 test	17.5	± 3.9	13.3	± 4.2	0.01
Hantu 1 test	44.0	± 5.1	38.6	± 5.6	0.02
Sengau test	65.3	± 8.5	61.4	± 6.3	0.15

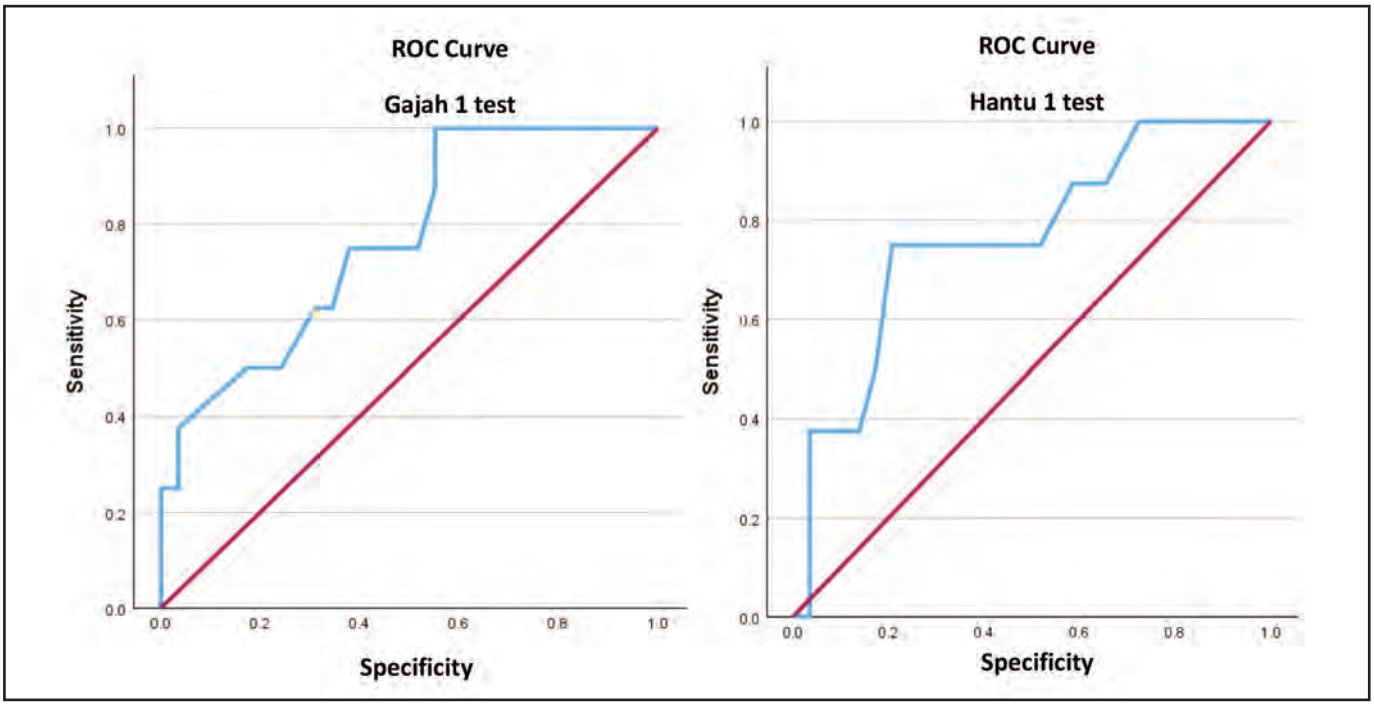

Fig. 1: ROC curve for Gajah 1 test and Hantu 1 test based on resonance disorder

The inclusion criteria for this study were NPC patients aged 18–60 years who had completed definitive radiation therapy with no residual mass in the nasopharynx and at least three months since the last radiation session. Exclusion criteria included: (1) patients with other malignancies, (2) those with progressive or degenerative nerve disorders, (3) acute nerve injuries, (4) tracheostomies, (5) anatomical abnormalities in the nasal cavity or throat unrelated to radiation, (6) a history of severe bilateral hearing loss, (7) prior nasopharyngectomy, and (8) acute infections or allergies in the nose or sinuses during the examination. All participants provided written informed consent for the study.

Study procedure and outcomes

The study subjects underwent clinical evaluations, including age, gender, clinical symptoms (ear, nose, throat, and neck), NPC treatment history, and resonance disorders assessed by an experienced speech and language therapist. Flexible laryngoscopy (Olympus Visera OTV-S7 videoscope, 3 mm diameter, Maxenon Xi 300 light source) was used to examine

nasal and throat structures and evaluate VP function. An Otorhinolaryngology consultant with over 15 years of experience reviewed and validated the nasopharyngoscopy videos for velopharyngeal function.

Nasometry was performed using the Pentax Model 6500, which involved placing a computer-based device with a headset and microphone on the nose and mouth. Patients read Indonesian passages, including the Sengau test, Gajah 1 test, and Hantu 1 test, to calculate the average nasalance score by comparing acoustic energy in the nasal and oral cavities. The Gajah 1 test corresponds to zoo passages, the Hantu 1 test to rainbow passages, and the Sengau test to nasal sentences. A speech and language therapist with over 20 years of experience evaluated and validated resonance disorders using perceptual speech assessments and nasometry.

Statistical analysis

Descriptive data were presented as frequencies and proportions for categorical variables and as mean ± standard deviation (SD) for continuous variables. Associations between age, gender, treatment type, time since last radiation, and radiation doses to the pharyngeal constrictor muscle (PCM) and soft palate with resonance disorders and velopharyngeal dysfunction were analyzed using Fisher's exact test, Mann-Whitney test, or Independent t-test. Sensitivity, specificity, and the area under the curve (AUC) were calculated, and a receiver operating characteristic (ROC) curve was plotted when a correlation between nasalance score and resonance disorder was identified.

Ethics approval

The study protocol has been approved by the Health Research Ethics Committee, Faculty of Medicine Universitas Indonesia and Dr. Cipto Mangunkusumo National General Hospital.

RESULTS

Characteristics of study population

A total of 37 post-radiation NPC patients were assessed at the Ear, Nose, Throat, and Head and Neck Surgery Outpatient Clinic during this study. We evaluated age, sex, treatment type, tumor size, and time since the last radiation. Normality tests were conducted on numerical variables, including age, radiation doses to the pharyngeal constrictor muscles and soft palate, time since the last radiation, and results from the Gajah 1, Hantu 1, and Sengau tests. Variables that showed a normal distribution included the Gajah 1 test, Sengau test, and PCM radiation dose. The distribution of the study population is presented in Table I.

Resonance Disorder and Velopharyngeal Dysfunction

Gender and radiation dose to the pharyngeal constrictor muscle were found to significantly contribute to resonance disorder, with p-values of 0.035 and 0.037, respectively. The distribution of treatment modalities related to resonance disorder is shown in Table II. Velopharyngeal dysfunction with hypernasality was observed, with 3 subjects having a coronal closure pattern, 2 having a sagittal pattern, and 2 having a circular pattern. One subject had a normal velopharyngeal closure pattern.

Velopharyngeal dysfunction was observed in 13 (35.1%) of the study subjects. No significant association was found between age, sex, radiation dose to the pharyngeal constrictor muscle, radiation dose to the soft palate, or time since the last radiation and velopharyngeal dysfunction (Table III).

Nasalance score of study population

The nasalance scores for each test type in patients with normal resonance and hypernasality are shown in Table IV. In the subsequent analysis, the Gajah 1 and Hantu 1 tests were included for determining the nasalance cut-off scores and confidence intervals, as only these two tests demonstrated statistically significant differences between normal and hypernasal perceptual speech groups.

The cut-off point for the Gajah 1 test nasalance score, distinguishing normal resonance from hypernasality, is 16.5%, with a sensitivity of 62.5% (95% CI: 30.6%–86.3%) and a specificity of 69% (95% CI: 50.8%–82.8%). Similarly, the cut-off point for the Hantu 1 test nasalance score is 42.5%, with a sensitivity of 75% (95% CI: 40.9%–92.9%) and a specificity of 79.3% (95% CI: 61.6%–90.1%).

DISCUSSION

This study found that the prevalence of NPC was higher in males (67.8%) than in females (32.2%). According to Global Cancer Statistics10 and Beyene et al.[11], males are 2-3 times more at risk than females. Adham et al.[12] reported that from 1995 to 2005, the male-to-female ratio of NPC patients at Cipto Mangunkusumo General Hospital was more than 2.4:1. The higher incidence of NPC in men is likely due to biological or lifestyle factors, such as smoking and exposure to carcinogens. The median age in this study was 42.97 years, with the 45-60 age group being the most affected. Yu et al.[13] noted that NPC incidence increases with age, possibly due to genetic factors and early Epstein-Barr virus (EBV) infection. Long-term environmental factors may impair the immune control of EBV over time, leading to the development of NPC. Velopharyngeal dysfunction occurred in 35.1% of subjects, with 5 having a coronal pattern, 4 a sagittal pattern, and 4 a circular pattern. Sun-Yung Bak et al.[8] noted that head and neck cancer treatments not only affect tumor cells but also normal cells. Wang et al.[14] highlighted that collagen deposition causes hypovascularity, leading to fibrosis and making these areas more vulnerable to physical damage, ischemia, and eventual loss of function, atrophy, or necrosis. In velopharyngeal function, radiation can cause soft palate dyskinesia, including muscle atrophy and sclerosis, as well as hard palate osteonecrosis and perforation. These side effects may develop later due to hypovascularity and hypocellularity from radiation exposure, resulting in fibrosis and scar tissue that interfere with VP movement when opening and closing the nasopharynx.

Resonance disorder, specifically hypernasality, was found in 8 subjects. Kraaijenga et al.[6] reported resonance abnormalities in 64% of 22 post-radiation head and neck cancer patients. Radiation can cause resonance disorders by affecting the laryngeal tissue, leading to edema during treatment and fibrosis afterward. An inadequate VP closure

during speech, with a velopharyngeal gap greater than 0.1 mm, can cause hypernasality. Warren et al.[15] noted that inadequate VP closure leads to hypernasality, which also reduces oral muscle mobility, affecting both speech and swallowing functions. Gender and radiation dose to the PCM were found to be significantly associated with resonance disorders in post-radiation NPC patients. Although no studies have focused on the impact of gender on speech resonance in these patients, a study by Pearsell et al.[16] found that gender influences speech perception in individuals with normal hearing and cognition. The pharyngeal constrictor muscle helps close the velopharynx during speech by moving anteromedially, along with the superoposterior movement of the velum. Radiation-induced fibrosis in this muscle can affect VP function.

Jordan HN et al.[17] suggests sex differences in velopharyngeal closure patterns with the increased velar length observed in males compared with females. Kumar et al18 found significant increases in the nasalance values during the menstruation phase. The findings indicate that hormonal and other related changes occurring during menstruation leads to a significant change in the resonance characteristics of voice.

Late-onset side effects after radiation in head and neck cancer patients are influenced by various factors. Kraaijenga et al.6 conducted a study to assess voice, speech, and quality of life in head and neck cancer patients 10 years after chemoradiation. The study found that voice and speech dysfunction were common problems in this population. Jacobi et al.[1] reviewed the literature and found that voice and speech often decreased during chemoradiation but improved within 1 to 2 months, continuing to improve for up to a year or more after therapy. However, voice and speech assessments did not return to normal levels, either before or after treatment.

Larger or more advanced tumors are associated with greater toxicity compared to early-stage tumors due to higher radiation doses and broader radiation exposure.[19] Stelzle et al.[20] found that tumor size was linked to speech intelligibility, though it is important to consider that tumor removal may lead to fibrosis, which is worsened by radiotherapy. Radiation doses above 40 Gy in NPC can damage the oral, pharyngeal, or glandular tissues in the mucous and submucous layers. Jacobi et al.[21] stated that radiation to the base of the tongue and velopharynx can alter speech by affecting the strength, movement, and balance between the muscles, which impacts articulation after treatment. According to Kraaijenga et al.[6], radiotherapy for non-laryngeal cancers can affect voice and speech due to changes in the anatomy of the vocal tract, such as scar tissue, edema, and fibrosis in surrounding structures, leading to less clear speech and poor articulation. This can affect daily activities and social interactions, leading to functional and psychosocial issues and a reduced quality of life. Patients receiving Intensity-Modulated Radiotherapy (IMRT) generally experience fewer voice and speech problems than those who receive conventional radiotherapy.[6,8]

Chemotherapy helps tumors and surrounding tissues more sensitive to radiation, which can worsen radiation-related side effects. Morton et al.[22] reported that speech impairment worsened in head and neck cancer patients undergoing multimodal treatment. Chemotherapy is known to cause cytotoxicity, leading to conditions like xerostomia and oral mucositis, which can affect speech function.[23,24]

Individual factors can cause variations in nasalance scores. In this study, the mean nasalance scores for post-radiation NPC patients were as follows: 14% (7% - 22%) for the Gajah 1 test, 39.8% ± 4.5 for the Hantu 1 test, and 62.4% ± 6.9 for the Sengau test. NPC patients with hypernasality had higher mean nasalance scores than those with normal resonance across all three tests. Nasometry is used to assess the impact of therapy or procedures on speech and helps differentiate between hypernasal and hyponasal speech, as well as determining the severity of hypernasality.[25] In post-radiation head and neck cancer, radiation can cause edema and muscle fibrosis in the oral and nasal structures, influencing resonance and nasalance scores. The study found that the Hantu 1 test had higher sensitivity 75% (95% CI: 40.9%–92.9%) and specificity 79.3% (95% CI: 61.6%–90.1%) than the Gajah 1 test with sensitivity 62.5% (95% CI: 30.6%–86.3%) and specificity 69% (95% CI: 50.8%–82.8%). However, this study did not assess nasalance scores and resonance before radiation, which could be a potential bias affecting the results.

CONCLUSION

Radiotherapy is the primary treatment for NPC because it is a radiosensitive cancer. However, while effective, radiation can have side effects that impact resonance speech and velopharyngeal function in head and neck cancer patients. These side effects may develop gradually, requiring long-term follow-up for post-radiation NPC patients. Nasalance scores serve as a valuable quantitative tool for identifying individuals at risk of hypernasality, enabling timely and targeted interventions. High nasalance scores, particularly in high-risk groups, can act as early indicators of velopharyngeal dysfunction. By identifying high-risk patients early, clinicians can implement preventative measures or interventions at the beginning of the treatment course, reducing the long-term impact of velopharyngeal dysfunction and enhancing overall communication outcomes.

This study had a few limitations. Hypernasality may be influenced by various factors, including hormonal levels, psychological conditions, and detailed anatomical variations. Furthermore, the current study offers only a cross-sectional perspective, without investigating longitudinal changes in hypernasality or nasalance scores. Cultural and linguistic differences in speech patterns may also impact both the perception and measurement of hypernasality. As initial resonance characteristics prior to radiation were not captured, drawing conclusions about radiation-induced changes remains challenging. To comprehensively evaluate the effects of radiation on all functional aspects of voice and speech, a prospective study incorporating pre- and post-radiation resonance assessments, followed by longitudinal evaluations, is warranted.

CONFLICT OF INTEREST

The authors have no conflicts of interest.

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