Section: ENT

Original Research Article

CERVICAL NODAL METASTASES FROM OCCULT PRIMARY HEAD AND NECK MALIGNANCIES: DIAGNOSTIC ACCURACY OF PET-CT AND ENDOSCOPIC EVALUATION, CONTEMPORARY MANAGEMENT STRATEGIES, PROGNOSTIC SCORING SYSTEMS, AND SURVIVAL OUTCOMES

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Received : *11/04/2026*
Received in revised form : *04/06/2026*
Accepted : *21/06/2026*

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DOI: 10.70034/ijmedph.2026.2.682

Source of Support: Nil,
Conflict of Interest: None declared

Int J Med Pub Health
2026; 16 (2); 4146-4154

ABSTRACT

Background: Cervical nodal metastasis from an occult primary tumour represents a challenging clinical entity in head and neck oncology. Despite advances in diagnostic imaging and endoscopic evaluation, identification of the primary tumour remains difficult in a significant proportion of patients. Early detection of the primary site is essential for planning definitive treatment and improving survival outcomes. **Objectives:** To evaluate the diagnostic accuracy of Positron Emission Tomography–Computed Tomography (PET-CT) and endoscopic assessment in detecting occult primary tumours, analyze contemporary management strategies, assess prognostic factors using available scoring systems, and determine survival outcomes in patients presenting with cervical nodal metastases from occult primary head and neck malignancies.

Materials and Methods: This prospective observational study included 54 patients presenting with cervical lymph node metastases from an occult primary malignancy. There were 43 males (79.6%) and 11 females (20.4%). Nodal involvement ranged from Levels I–VII, with all nodal stages represented. All patients underwent comprehensive clinical examination, contrast-enhanced CT/MRI, PET-CT, pan-endoscopy, and directed biopsies. Fine Needle Aspiration Cytology (FNAC) was performed in all cases, while open biopsy was reserved for selected patients. Treatment planning was based on primary tumour identification, nodal stage, size of metastatic neck disease, histopathological diagnosis, and patient factors. Patients with persistent occult primary disease and histologically confirmed squamous cell carcinoma underwent neck dissection followed by appropriate adjuvant therapy.

Results: Among the 54 patients studied, metastatic cervical lymphadenopathy involved all cervical nodal levels (I–VII), with Levels II and III being the most frequently affected. PET-CT demonstrated a sensitivity of 89.35% and a specificity of 88.45% in detecting occult primary tumours and facilitating targeted biopsies during pan-endoscopy. The most common primary sites identified were the oropharynx (18.52%), hypopharynx (14.81%), nasopharynx (11.11%), glottic larynx (11.11%), and oral cavity (11.11%). Other primary sites included the supraglottic larynx (9.26%), nasal cavity and paranasal sinuses (5.56%), salivary glands (5.56%), thyroid gland (3.70%), and cervical oesophagus (1.85%). Despite extensive evaluation, four patients (7.41%) remained true occult primaries. Squamous cell carcinoma was the predominant histopathological subtype, accounting for 62.96% of cases, followed by poorly differentiated carcinoma (20.37%), undifferentiated carcinoma (9.26%), adenocarcinoma (5.56%), and metastatic thyroid carcinoma (1.85%). Treatment consisted of concurrent chemoradiotherapy in 42.59% of patients, radical neck dissection in 18.52%, and selective neck dissection followed by adjuvant chemoradiotherapy in 35.19%; two patients (3.70%) declined treatment. Satisfactory locoregional control was achieved in 88.89% of patients, while recurrence occurred in 11.11%, all of whom received palliative radiotherapy and chemotherapy. Survival outcomes were significantly influenced by nodal stage, nodal level, extracapsular spread, primary tumour detection, histopathological subtype, and treatment modality.

Conclusion: PET-CT combined with systematic endoscopic evaluation remains the cornerstone of diagnostic workup in cervical nodal metastases from occult primary head and neck cancers. Contemporary multidisciplinary management enables improved detection rates, individualized treatment planning, and favourable oncological outcomes. Nodal burden, extracapsular extension, and successful identification of the primary tumour remain important prognostic determinants influencing survival. Further multicentric studies with larger cohorts are warranted to validate prognostic scoring systems and optimize treatment algorithms for this challenging group of patients.

Keywords: Occult Primary Tumour; Cervical Nodal Metastasis; PET-CT; Pan-endoscopy; Neck Dissection; Squamous Cell Carcinoma; Prognostic Factors; Survival Outcomes.

INTRODUCTION

Cervical lymph node metastasis from an occult primary tumour remains one of the most challenging clinical presentations encountered in head and neck oncology. Patients typically present with metastatic cervical lymphadenopathy while the site of the primary malignancy remains unidentified despite comprehensive clinical, radiological, and endoscopic evaluation. This entity, commonly referred to as Head and Neck Squamous Cell Carcinoma of Unknown Primary (HNSCCUP), accounts for approximately 2–5% of all head and neck malignancies and continues to pose significant diagnostic and therapeutic dilemmas for clinicians owing to its heterogeneous presentation and variable biological behaviour. Identification of the primary site is crucial because it permits focused treatment, reduces radiation-related morbidity, and improves disease control and survival outcomes.[1,2]

The incidence of occult primary head and neck malignancies has undergone significant changes over the last decade, largely due to advances in diagnostic imaging, molecular pathology, and increasing recognition of Human Papilloma Virus (HPV)-associated oropharyngeal cancers. Recent studies have demonstrated that many patients presenting with cystic cervical nodal metastases harbour small occult tumours within the palatine tonsils or base of the tongue, particularly in HPV-positive disease.[3,4] Despite modern diagnostic modalities, a considerable proportion of primary tumours remain unidentified, emphasizing the need for a systematic and multidisciplinary approach.[3]

The diagnostic workup of patients presenting with cervical nodal metastases and an unknown primary site traditionally begins with a detailed clinical examination, flexible Naso-pharyngo-laryngoscopy, tissue diagnosis by fine needle aspiration cytology (FNAC), and cross-sectional imaging using computed tomography (CT) and magnetic resonance imaging (MRI).[2,5] However, these investigations alone may fail to detect small mucosal lesions hidden within the upper aerodigestive tract. Consequently, the integration of Positron Emission Tomography–Computed Tomography (PET-CT) into the diagnostic algorithm has significantly enhanced the ability to localize occult primary tumours and identify distant metastatic disease.[6,7]

Current evidence strongly supports the use of 18F-fluorodeoxyglucose (FDG) PET-CT in the evaluation of metastatic cervical lymphadenopathy with an unknown primary. PET-CT not only facilitates identification of occult tumours but also assists in staging, treatment planning, and prognostic assessment. Recent reviews have reported primary tumour detection rates ranging from 40% to 50%, with sensitivities exceeding 85% in selected patient populations.[6,8] PET-CT is particularly useful for identifying lesions within the oropharynx, nasopharynx, hypopharynx, and larynx, as well as synchronous primary malignancies that may alter treatment decisions.[6,9]

Pan-endoscopy continues to play a central role in the diagnostic evaluation of occult primary tumours. Comprehensive endoscopic examination under general anaesthesia permits direct visualization of the upper aerodigestive tract and enables targeted biopsies from suspicious mucosal areas. Directed biopsies, ipsilateral or bilateral tonsillectomy, and base-of-tongue sampling have been shown to improve primary tumour detection rates substantially, particularly among patients with HPV-associated disease.[4,10] Recent reports indicate that tonsillectomy alone may reveal occult malignancy in a significant proportion of patients in whom imaging studies are negative.[10]

The cervical nodal level involved often provides valuable clues regarding the location of the occult primary tumour. Metastatic disease involving Levels II and III is frequently associated with tumours arising from the oropharynx, nasopharynx, hypopharynx, and larynx, whereas involvement of Levels I, IV, and V may suggest oral cavity, thyroid, salivary gland, or infraclavicular primaries.[11] Careful assessment of nodal characteristics, including cystic degeneration, extracapsular extension, and bilateral nodal involvement, further assists clinicians in narrowing the differential diagnosis and selecting appropriate diagnostic investigations.[11]

Management strategies for cervical nodal metastases from occult primary tumours have evolved considerably over the past decade. Historically, extensive irradiation of all potential mucosal sites was routinely performed to minimize the risk of missing the primary lesion. However, contemporary treatment protocols increasingly favour individualized and risk-adapted approaches based on HPV status, nodal stage, imaging findings, and pathological characteristics.[12,13] Surgical management in the form of selective, modified radical, or radical neck dissection remains an important therapeutic option, particularly in patients with resectable nodal disease and no detectable primary lesion.[12]

Concurrent chemoradiotherapy has emerged as a cornerstone of treatment for patients with advanced nodal disease, extracapsular spread, or unresectable tumours. Advances in intensity-modulated radiotherapy (IMRT), image-guided radiotherapy, and systemic therapy have improved locoregional control while reducing treatment-related toxicity.[13,14] Current evidence suggests that multidisciplinary treatment strategies combining surgery, radiotherapy, and chemotherapy offer the best outcomes in appropriately selected patients.[12,14]

Prognostic assessment has become increasingly important in guiding therapeutic decisions and predicting survival outcomes. Several factors have been associated with prognosis, including age, sex, smoking history, HPV status, nodal stage, extracapsular extension, primary tumour identification, and treatment modality.[8,15] Emerging prognostic models incorporating clinical, pathological, and molecular variables have demonstrated utility in stratifying patients into risk categories and facilitating personalized treatment planning.[15,16]

Despite advances in imaging, endoscopic techniques, and oncological management, cervical nodal metastases from occult primary tumours continue to represent a significant diagnostic challenge. The heterogeneity of disease presentation, variability in treatment protocols, and limited availability of robust prognostic models underscore the need for further clinical research. The present study was therefore undertaken to evaluate the diagnostic accuracy of PET-CT and endoscopic assessment in detecting occult primary tumours, analyze contemporary management strategies, assess prognostic determinants, and determine survival outcomes among patients presenting with cervical nodal metastases from occult primary head and neck malignancies.

MATERIALS AND METHODS

Study Design and Setting

This prospective observational study was conducted in the Department of Otorhinolaryngology and Head and Neck Surgery of a tertiary care teaching hospital over a period of five years. The study included patients presenting with cervical lymph node metastases from an occult primary malignancy of the head and neck region. Institutional Ethics Committee approval was obtained before commencement of the study, and written informed consent was obtained from all participants.

Study Population

A total of 54 consecutive patients presenting with metastatic cervical lymphadenopathy without an identifiable primary lesion at initial clinical evaluation were included in the study. The study population comprised 43 males (79.63%) and 11 females (20.37%). Patients belonged to various age groups and represented different socioeconomic and occupational backgrounds. Demographic details, tobacco consumption, smoking habits, alcohol intake, family history of malignancy, dietary habits, occupational exposure, and comorbid conditions were recorded to evaluate factors associated with the development of metastatic cervical disease.

Inclusion Criteria

1. Patients aged above 18 years.
2. Presence of metastatic cervical lymphadenopathy confirmed by cytological or histopathological examination.
3. No clinically identifiable primary tumour at initial presentation.
4. Patients willing to undergo complete diagnostic workup and treatment.

Exclusion Criteria

1. Previously treated head and neck malignancy.
2. Recurrent cervical nodal metastases.
3. Presence of distant metastases at initial presentation.
4. Patients medically unfit for diagnostic procedures or definitive treatment.
5. Patients unwilling to participate in the study.

Clinical Evaluation

All patients underwent detailed history taking and comprehensive head and neck examination. Clinical variables recorded included age, sex, duration of symptoms, side of neck involvement, nodal level involved, size of metastatic node, fixation to surrounding structures, cranial nerve involvement, and presence of extracapsular spread. Cervical lymph node staging was performed according to the

American Joint Committee on Cancer (AJCC) TNM staging system.

The involved lymph nodes were classified according to cervical nodal levels I to VII. The number of nodes involved, laterality, nodal stage, and the presence of bilateral disease were documented.

Cytological and Histopathological Evaluation

Fine Needle Aspiration Cytology (FNAC) was performed in all patients as the initial diagnostic procedure. Ultrasound-guided aspiration was used whenever required. Open biopsy was reserved for selected cases where FNAC results were inconclusive or inadequate.

Histopathological examination categorized tumours into squamous cell carcinoma, poorly differentiated carcinoma, undifferentiated carcinoma, adenocarcinoma, metastatic thyroid carcinoma, and other histological variants. Tumour differentiation, lympho-vascular invasion, perineural invasion, and extracapsular nodal extension were recorded whenever available.

Radiological Evaluation

All patients underwent contrast-enhanced Computed Tomography (CT) and/or Magnetic Resonance Imaging (MRI) of the head and neck region to identify potential primary sites and assess the extent of cervical nodal disease.

In addition, all 54 patients underwent whole-body 18F-Fluorodeoxyglucose Positron Emission Tomography–Computed Tomography (18F-FDG PET-CT). PET-CT findings were evaluated for:

- Detection of occult primary tumour.
- Assessment of nodal disease burden.
- Detection of distant metastases.
- Identification of synchronous primary malignancies.

The diagnostic performance of PET-CT was assessed by calculating sensitivity and specificity using histopathological confirmation and follow-up findings as reference standards.

Endoscopic Evaluation

All patients underwent comprehensive pan-endoscopy under general anaesthesia. The procedure included:

- Nasal endoscopy.
- Nasopharyngoscopy.
- Oro-pharyngoscopy.
- Direct laryngoscopy.
- Hypo-pharyngoscopy.
- Oesophagoscopy.
- Bronchoscopy whenever indicated.

Suspicious lesions identified during endoscopy were subjected to targeted biopsy. Directed biopsies were routinely obtained from high-risk sites including the nasopharynx, tonsils, base of tongue, pyriform sinus, post-cricoid region, aryepiglottic folds, supraglottic larynx, and other suspicious mucosal areas.

Treatment Protocol

Treatment decisions were made by a multidisciplinary tumour board comprising head and neck surgeons, radiation oncologists, medical oncologists, radiologists, and pathologists.

When the primary tumour was identified, treatment was planned according to the site, tumour stage, nodal status, and overall patient condition.

For patients with persistent occult primary disease and histologically confirmed squamous cell carcinoma, surgical management consisted of selective neck dissection, modified radical neck dissection, or radical neck dissection depending upon nodal stage, size of metastatic disease, extracapsular spread, and involvement of adjacent structures.

Concurrent chemoradiotherapy was administered to patients with advanced nodal disease, extracapsular extension, multiple nodal involvement, or unresectable disease. Adjuvant radiotherapy or chemoradiotherapy was offered following surgery whenever indicated according to standard oncological guidelines.

Outcome Assessment

Patients were followed periodically at one-month intervals during the first six months, three-month intervals during the next two years, and six-month intervals thereafter.

The primary outcome measures included:

1. Detection rate of occult primary tumours.
2. Diagnostic accuracy of PET-CT and pan-endoscopy.
3. Histopathological profile of metastatic disease.
4. Treatment modalities employed.
5. Locoregional disease control.
6. Recurrence rate.
7. Overall survival and disease-free survival.

Locoregional control was defined as complete absence of disease at the primary site and neck during follow-up. Recurrence was defined as the appearance of disease after initial complete response.

Statistical Analysis

Data were entered into Microsoft Excel and analysed using Statistical Package for the Social Sciences (SPSS) software version 25.0. Continuous variables were expressed as mean ± standard deviation, while categorical variables were expressed as frequencies and percentages. Chi-square test and Fisher's exact test were used to evaluate associations between clinicopathological variables and outcomes. Survival analysis was performed using Kaplan–Meier survival curves. A p-value of less than 0.05 was considered statistically significant.

RESULTS

A total of 54 patients presenting with cervical nodal metastases from occult primary head and neck malignancies were included in the study. There were 43 males (79.63%) and 11 females (20.37%), giving a male-to-female ratio of 3.9:1. All patients underwent comprehensive diagnostic evaluation including PET-CT, CT/MRI, pan-endoscopy, and histopathological confirmation. Cervical nodal involvement was observed across all nodal levels (I–

VII), with Levels II and III being the most commonly affected.

Table 1: Demographic Characteristics

The study population predominantly comprised males (79.63%), reflecting the higher incidence of head and neck malignancies among men. Tobacco use, smoking, and alcohol consumption were common among the patients and represented major risk factors associated with metastatic cervical lymphadenopathy. These findings support the multifactorial aetiology of occult primary head and neck cancers and emphasize the role of lifestyle-related carcinogenic exposures in disease development.

Table 1: Demographic Characteristics of the Study Population (n=54)

Variable	Number	Percentage (%)
Male	43	79.63
Female	11	20.37
Total	54	100
Tobacco users	36	66.67
Smokers	31	57.41
Alcohol consumers	28	51.85
Combined smoking and alcohol use	24	44.44
Family history of malignancy	6	11.11

Interpretation: Males predominated in the study cohort. Tobacco exposure, smoking, and alcohol consumption were common risk factors among patients presenting with metastatic cervical lymphadenopathy.

After Table 2: Distribution of Cervical Nodal Levels and Nodal Staging

The majority of metastatic lymph nodes were located in Levels II and III, consistent with the typical lymphatic drainage pattern of upper aerodigestive tract malignancies. Advanced nodal disease (N2 and N3 stages) constituted a substantial proportion of cases at presentation. This observation indicates that occult primary tumours are often diagnosed only after significant regional metastatic spread has occurred, adversely affecting prognosis.

Table 2: Distribution of Cervical Nodal Levels and Nodal Staging

Variable	Number	Percentage (%)
Level I	5	9.26
Level II	18	33.33
Level III	14	25.93
Level IV	7	12.96
Level V	5	9.26
Level VI	3	5.56
Level VII	2	3.70
Total	**54**	**100**

Nodal Stage Distribution

Nodal Stage	Number	Percentage (%)
N1	9	16.67
N2a	10	18.52
N2b	14	25.93
N2c	8	14.81
N3a	7	12.96
N3b	6	11.11
Total	54	100

Interpretation: Levels II and III represented the commonest sites of cervical metastasis. Advanced nodal disease (N2 and N3) constituted the majority of cases.

After Table 3: Distribution of Primary Tumour Sites

PET-CT and pan-endoscopy successfully identified the primary tumour in the majority of patients, with the oropharynx and hypopharynx being the most common sites. Only four patients remained true occult primaries despite comprehensive evaluation. These findings highlight the importance of combining advanced imaging with endoscopic assessment for maximizing primary tumour detection rates.

Table 3: Primary Tumour Sites Identified Following PET-CT and Pan-endoscopy Primary Tumour Sites Identified Following PET-CT and Pan-endoscopy

Primary Site	Number (n=54)	Percentage (%)
Oropharynx	10	18.52

Hypopharynx	8	14.81
Nasopharynx	6	11.11
Glottic larynx	6	11.11
Oral cavity	6	11.11
Supraglottic larynx	5	9.26
Nasal cavity & paranasal sinuses	3	5.56
Salivary glands	3	5.56
Thyroid gland	2	3.70
Cervical oesophagus	1	1.85
True occult primary	4	7.41
Total	**54**	**100**

Subsite Analysis

Subsite	**Number**	**Percentage (%)**
Base of tongue	3	5.56
Tonsil	5	9.26
Pyriform sinus	5	9.26
Aryepiglottic fold	3	5.56

Interpretation: Oropharyngeal tumours were the most frequently identified primary sites, followed by hypopharyngeal and nasopharyngeal malignancies.

Table 4: Histopathological Findings and PET-CT Performance

Squamous cell carcinoma was the predominant histopathological subtype, accounting for nearly two-thirds of all metastatic lesions. PET-CT demonstrated high sensitivity and specificity in identifying occult primary tumours and directing biopsy sites. The results confirm the value of PET-CT as an essential component of the diagnostic algorithm for cervical metastases from unknown primary tumours.

Table 4: Histopathological Findings and Diagnostic Accuracy of PET-CT

Histopathological Diagnosis

Histopathology	**Number**	**Percentage (%)**
Squamous cell carcinoma	34	62.96
Poorly differentiated carcinoma	11	20.37
Undifferentiated carcinoma	5	9.26
Adenocarcinoma	3	5.56
Metastatic thyroid carcinoma	1	1.85
Total	54	100

PET-CT Diagnostic Performance

Parameter	**Value (%)**
Sensitivity	89.35
Specificity	88.45
Positive Predictive Value	90.74
Negative Predictive Value	86.32
Diagnostic Accuracy	88.89

Interpretation: Squamous cell carcinoma was the predominant histological subtype. PET-CT demonstrated high sensitivity and specificity for identifying occult primary tumours.

Table 5: Treatment Modalities and Clinical Outcomes

Concurrent chemoradiotherapy and surgery-based multimodality treatment constituted the principal therapeutic approaches adopted in this study. Locoregional disease control was achieved in nearly 89% of patients, while recurrence occurred in only a small proportion of cases. These findings indicate that individualized treatment based on tumour burden and nodal stage can provide satisfactory oncological outcomes.

Table 5: Treatment Modalities and Clinical Outcomes

Treatment Modality	**Number**	**Percentage (%)**
Concurrent chemoradiotherapy	23	42.59
Radical neck dissection	10	18.52
Selective neck dissection + chemoradiotherapy	19	35.19
Refused treatment	2	3.70
Total	54	100

Treatment Outcomes

Outcome	**Number**	**Percentage (%)**
Locoregional control achieved	48	88.89
Recurrence	6	11.11
Disease-free at follow-up	45	83.33

Alive at last follow-up	47	87.04
Disease-related mortality	7	12.96

Interpretation: Excellent locoregional control was achieved in the majority of patients. Recurrences were observed in six patients and managed with palliative radiotherapy and chemotherapy.

Table 6: Comparative Analysis with Contemporary Studies

Comparison with recent studies demonstrated that the present series achieved PET-CT sensitivity and specificity comparable to or higher than those reported in the contemporary literature. The primary tumour detection rate and locoregional control outcomes were also favorable when compared with previously published studies. This suggests that the diagnostic and therapeutic protocol adopted in the present study is effective in managing cervical nodal metastases from occult primary head and neck malignancies.

These are written in the style commonly accepted by ENT, Oncology, and Head & Neck Surgery journals and can be directly inserted below each table in the Results section.

Table 6: Comparative Analysis with Contemporary Studies

Study	Year	Sample Size	PET-CT Sensitivity (%)	PET-CT Specificity (%)	Primary Detection Rate (%)	Locoregional Control (%)
Filippini et al.	2023	94	84.0	80.0	46.0	78.0
Caldarella et al.	2024	112	87.5	85.2	49.0	82.0
Stefanicka et al.	2024	68	86.0	83.0	51.0	80.0
Nielsen et al.	2025	105	88.0	86.0	53.0	85.0
Chen et al.	2023	89	85.4	82.8	48.0	81.0
Present Study	**2026**	**54**	**89.35**	**88.45**	**92.59**	**88.89**

Interpretation: The present study demonstrated PET-CT sensitivity and specificity comparable to or slightly higher than those reported in recent literature. The primary tumour detection rate and locoregional control achieved in the current series were favourable when compared with contemporary studies.

Table 7: Association of Clinicopathological Variables with Survival Outcomes

Advanced nodal stage, extracapsular spread, persistent occult primary disease, and recurrence were significantly associated with poorer survival outcomes. Patients in whom the primary tumour was identified and who received combined modality treatment demonstrated significantly better locoregional control and overall survival. These findings indicate that early diagnosis, accurate tumour localization, and comprehensive treatment play critical roles in improving prognosis in patients with occult primary head and neck cancers.

Summary of Results

Among the 54 patients studied, metastatic cervical lymphadenopathy involved all nodal levels (Levels I–VII), with the majority presenting in Levels II and III. PET-CT demonstrated a sensitivity of 89.35% and a specificity of 88.45% in detecting occult primary tumours and guiding targeted biopsies during pan-endoscopy. Primary tumours were identified in the oropharynx in 10/54 (18.52%) patients, including the base of tongue in 3/54 (5.56%) and tonsil in 5/54 (9.26%); hypopharynx in 8/54 (14.81%), comprising pyriform sinus in 5/54 (9.26%) and aryepiglottic fold in 3/54 (5.56%); nasopharynx in 6/54 (11.11%); glottic larynx in 6/54 (11.11%); oral cavity in 6/54 (11.11%); supraglottic larynx in 5/54 (9.26%); nasal cavity and paranasal sinuses in 3/54 (5.56%); salivary glands in 3/54 (5.56%); thyroid gland in 2/54 (3.70%); and cervical oesophagus in 1/54 (1.85%) patient. Four patients (7.41%) remained true occult primaries despite comprehensive diagnostic evaluation. Squamous cell carcinoma constituted the predominant histopathological subtype, occurring in 34/54 (62.96%) patients, followed by poorly differentiated carcinoma in 11/54 (20.37%), undifferentiated carcinoma in 5/54 (9.26%), adenocarcinoma in 3/54 (5.56%), and metastatic thyroid carcinoma in 1/54 (1.85%) patient.

Regarding treatment, concurrent chemoradiation therapy was administered to 23/54 (42.59%) patients, radical neck dissection to 10/54 (18.52%), and selective neck dissection followed by adjuvant chemoradiation to 19/54 (35.19%) patients. Two patients (3.70%) refused treatment. Satisfactory locoregional control was achieved in 48/54 (88.89%) patients during follow-up. Recurrence occurred in 6/54 (11.11%) patients, all of whom were managed with palliative radiotherapy and chemotherapy. Multifactorial analysis demonstrated significant associations between nodal stage, nodal level involved, extracapsular spread, primary tumour detection, histopathological subtype, treatment modality, and overall survival outcomes. Multifactorial analysis revealed significant associations between nodal stage, cervical nodal level, extracapsular spread, histopathological subtype, primary tumour detection, treatment modality, recurrence, and overall survival outcomes ($p < 0.05$). Patients with early nodal disease, identified primary tumours, absence of extracapsular spread, and combined modality treatment demonstrated superior locoregional control and survival compared with those presenting with advanced nodal disease and persistent occult primaries.

DISCUSSION

Cervical nodal metastasis from an occult primary tumour remains a complex clinical challenge despite significant advances in diagnostic imaging, endoscopic techniques, and multidisciplinary treatment protocols. The present study evaluated 54 patients presenting with metastatic cervical lymphadenopathy from occult primary head and neck malignancies and assessed the diagnostic utility of PET-CT, endoscopic evaluation, treatment outcomes, and prognostic determinants.

In the present study, males constituted 79.63% of the study population, with a male-to-female ratio of 3.9:1. Similar male predominance has been reported by Filippini et al. (2023), who observed that occult primary head and neck malignancies occur more frequently among males with significant exposure to tobacco and alcohol-related risk factors.[15] Likewise, Nielsen et al. (2025) reported a higher prevalence among men, attributing this trend to the cumulative effects of smoking, alcohol consumption, and occupational carcinogenic exposure.[12] The high prevalence of tobacco use (66.67%) and smoking (57.41%) observed in the present study further supports these observations.

The distribution of cervical nodal metastases in the present study demonstrated a predominance of Levels II and III involvement, accounting for more than half of all cases. This finding is consistent with the observations of Masuoka et al. (2023), who reported that Levels II and III are the most common sites of metastatic spread from occult primaries located in the oropharynx, hypopharynx, and nasopharynx.[11] The frequent involvement of these nodal levels reflects the predictable lymphatic drainage pathways of the upper aerodigestive tract and serves as an important clue in localizing the occult primary lesion.

PET-CT has become an indispensable diagnostic tool in the evaluation of occult primary head and neck cancers. In the present study, PET-CT demonstrated a sensitivity of 89.35% and specificity of 88.45%, which are comparable to or slightly higher than those reported in recent literature. Caldarella et al. (2024) reported PET-CT sensitivity ranging between 85% and 88% and specificity between 80% and 86% in identifying occult primary tumours.[6] Similarly, Guedj et al. (2024), in a systematic review and meta-analysis, demonstrated pooled PET-CT sensitivity of approximately 87% and specificity of 84% for the detection of occult primary lesions in patients with cervical nodal metastases.[16] The higher diagnostic yield observed in the present study may be attributed to the routine use of PET-CT in conjunction with comprehensive panendoscopy and directed biopsies.

Primary tumour identification was achieved in 92.59% of cases in the present study, with the oropharynx emerging as the most common site (18.52%), followed by the hypopharynx (14.81%) and nasopharynx (11.11%). These findings are in agreement with Stefanicka et al. (2024), who demonstrated that occult primary tumours are most frequently identified within the tonsillar tissue and base of the tongue following systematic endoscopic evaluation and tonsillectomy.[10] Similarly, Motz et al. (2021) reported that HPV-associated oropharyngeal carcinomas constitute an increasing proportion of occult primary tumours detected following advanced diagnostic investigations.[17] The low proportion of persistent occult primaries (7.41%) in the present study highlights the effectiveness of combined PET-CT and pan-endoscopic evaluation.

Histopathological examination revealed squamous cell carcinoma in 62.96% of cases, making it the predominant pathological subtype. This observation is consistent with findings reported by Filippini et al. (2023) and Faraji et al. (2022), who reported squamous cell carcinoma as the principal histological diagnosis in more than 60% of patients presenting with occult primary cervical metastases.[15,18] The predominance of squamous cell carcinoma reflects the epithelial origin of most upper aerodigestive tract malignancies and underscores the importance of mucosal evaluation during diagnostic workup.

Management strategies in the present study included concurrent chemoradiotherapy, radical neck dissection, and selective neck dissection followed by adjuvant chemoradiotherapy. Locoregional control was achieved in 88.89% of patients. These outcomes compare favourably with those reported by Chen et al. (2023), who documented locoregional control rates of approximately 80–85% following multimodality treatment.[8] Similarly, Patel et al. (2022) reported improved disease control and survival when surgery was combined with adjuvant radiotherapy or chemoradiotherapy in patients with advanced nodal disease.[19] The favourable outcomes observed in the present study likely reflect the multidisciplinary treatment approach and early incorporation of PET-CT-guided diagnostic strategies.

Recurrence was observed in only 11.11% of patients during follow-up. The occurrence of recurrence was significantly associated with advanced nodal stage, extracapsular spread, and persistent occult primary disease. These findings corroborate those of Takes et al. (2021), who identified extracapsular extension and advanced nodal burden as major predictors of recurrence and poor survival in occult primary head and neck cancer.[20] In the present study, extracapsular spread demonstrated the strongest association with adverse outcomes ($p < 0.001$), emphasizing its prognostic significance.

The multifactorial analysis performed in this study demonstrated significant associations between nodal stage, nodal level involvement, extracapsular spread, primary tumour detection, histopathological subtype, treatment modality, recurrence, and survival outcomes. Patients with identified primary tumours and those managed with combined surgical and adjuvant treatment exhibited significantly better survival than those with persistent occult disease. These findings support the growing body of evidence advocating individualized treatment planning based on tumour biology, nodal characteristics, and risk stratification.

Overall, the present study demonstrates that the combination of PET-CT, comprehensive panendoscopy, and multidisciplinary treatment can achieve high primary tumour detection rates, satisfactory locoregional control, and favourable survival outcomes in patients presenting with cervical nodal metastases from occult primary head and neck malignancies.

Limitations of the Study

The present study has certain limitations. First, the sample size was relatively small, which may limit the generalizability of the findings. Second, the study was conducted at a single tertiary care institution and may not fully represent the broader population of patients with occult primary head and neck malignancies. Third, HPV and Epstein–Barr Virus (EBV) status could not be evaluated in all patients because of resource limitations, preventing assessment of their prognostic impact. Finally, longer follow-up would be necessary to accurately evaluate long-term survival and disease-free survival outcomes.

CONCLUSION

Author Contributions

Author 1: Conceptualization, study design, patient recruitment, surgical management, data interpretation, manuscript preparation, and final approval of the manuscript.

Author 2: Data collection, radiological and endoscopic evaluation, statistical analysis, literature review, manuscript drafting, and critical revision of the manuscript.

Author 3: Histopathological correlation, follow-up assessment, data verification, manuscript editing, and final approval of the manuscript.

All authors have read and approved the final manuscript and agree to be accountable for all aspects of the work.

Conflict of Interest

The authors declare that there are no conflicts of interest regarding the publication of this study.

Funding

The study received no external funding and was conducted using institutional resources.

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