

NECK MASSES IN AGED PATIENTS: ETIOLOGY AND SEMIOLOGICAL FEATURES ASSOCIATED WITH MALIGNANCY

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Abstract Introduction: The purposes of our study were to describe the distribution of diagnoses in a series of 273 patients over 65 years of age who presented for neck masses and to identify semiological features associated with malignancy. **Methods:** Neck masses were categorized as congenital lesions (n = 7, 3%, 95% CI: 1%- 5%), inflammatory masses (n = 67, 25%, 95% CI: 19%- 30%), benign neoplasms (n = 77, 28%, 95% CI: 23%- 34%), and malignant neoplasms (n = 87, 32%, 95% CI: 26%- 38%). **Results:** A group of patients had discontinued care and, consequently, a definitive diagnosis could not be reached (n = 35, 12%). Age (OR 1.06, 95% CI 1.00-1.12), male sex (OR 2.35, 95% CI 1.11-4.96), prior history of cancer (OR 2.66, 95% CI 1.02-6.92), mass fixation to skin or deep tissues (OR 4.87, 95% CI 2.20-10.76), and the involvement of multiple cervical lymph node levels (OR 4.15, 95% CI 1.64-10.51) were identified as semiological features associated with malignancy. **Conclusion:** In the case of a neck mass in an elderly patient, its neoplastic origin should be strongly suspected.

Key words: neck mass, aged, diagnosis, neoplasia, malignancy

Resumen Masas cervicales en adultos mayores: Etiología y características semiológicas asociadas a malignidad

Introducción: El objetivo de nuestro estudio fue describir la distribución de diagnósticos en una serie de 273 pacientes mayores de 65 años que consultaron por masas cervicales e identificar características semiológicas asociadas a malignidad. **Métodos:** Las masas cervicales fueron categorizadas como lesiones congénitas (n = 7, 3%, 95% CI: 1%- 5%), masas de origen inflamatorio (n = 67, 25%, 95% CI: 19%-30%), neoplasias benignas (n = 77, 28%, 95% CI: 23%- 34%) y neoplasias malignas (n = 87, 32%, 95% CI: 26%-38%). **Resultados:** Un grupo de pacientes discontinuó el tratamiento y en consecuencia no fue posible alcanzar un diagnóstico definitivo (n = 35, 12%). La edad (OR 1.06, 95% CI 1.00-1.12), el sexo masculino (OR 2.35, 95% CI 1.11-4.96), los antecedentes de cáncer (OR 2.66, 95% CI 1.02-6.92), la fijación de la masa a los planos profundos o a piel (OR 4.87, 95% CI 2.20-10.76) y la afectación de más de un nivel ganglionar del cuello (OR 4.15, 95% CI 1.64-10.51) fueron identificados como características semiológicas asociadas a malignidad. **Conclusión:** En presencia de una masa cervical en un paciente adulto mayor debe existir una fuerte sospecha de origen neoplásico.

Palabras clave: masa cervical, adultos mayores, diagnóstico, malignidad,

KEY POINTS

- The diagnosis of a neck mass is usually a challenge, with age being the main clinical factor to be considered. Neck masses have been extensively studied in children, adolescents, and adults, but studies clearly addressing this issue in aged patients are still scarce.
- In this study, we describe the distribution of diagnoses in a series of 273 aged patients and evaluate nine different semiological features and their association with malignancy. Malignant (38%) and benign neoplasm (34%) were the most common diagnoses, followed by inflammatory (30%) and congenital lesions (5%). Age, male sex, history of cancer, mass fixation, and mass involvement with multiple cervical lymph node levels were identified as semiological features associated with malignancy.

Neck masses are a common reason for consultation among adult patients¹. These are defined as abnormal lesions (congenital or acquired) that are visible, palpable, or evident through diagnostic imaging studies¹. The diagnosis of a neck mass is usually a challenge, and age is the main clinical factor to be considered². An asymptomatic mass in the neck of an adult patient is often the first manifestation of a malignant disease¹. Neck masses have been extensively studied in children, adolescents, and adults, but studies clearly addressing this issue in aged patients remain scarce^{3,4}. In this context, the aims of our study were to describe the distribution of diagnoses in patients over 65 years of age who presented for neck masses and to identify semiological features associated with malignancy.

Materials and methods

We conducted a descriptive retrospective study including 273 consecutive patients with neck masses. In an electronic database, we identified patients over 65 years of age who presented to the maxillofacial surgery department of Dr. César Milstein Hospital between January 2008 and December 2018 and whose chief complaint was a neck mass. The Dr. César Milstein Hospital is a tertiary teaching hospital that exclusively provides care to patients covered by government health insurance for retirees and pensioners (The National Institute of Social Services for Retirees and Pensioners, INSSJP) and, consequently, the vast majority of patients who attend are over 65 years of age. Patients with previously diagnosed malignant tumors of the aero digestive tract and patients with thyroid disease were excluded.

The following variables were retrospectively recorded: age, sex, history of cancer, history of tobacco smoking, presence of pain, location and size of the mass, bilaterality, whether or not the mass was fixed to either the deep tissues or the skin, and the final diagnosis. Continuous variables were recorded as the mean and standard deviation (SD) or the median and interquartile range (IQR), according to the distribution of the

data. Categorical variables were recorded as proportions. The location of the mass was determined by clinical examination and recorded as a nominal categorical variable; the categories were established according to the classification system published by the American Society for Head and Neck Surgery and the American Academy of Otorhinolaryngology and Head and Neck Surgery in 2002⁵. The diagnosis was recorded as a categorical variable. The following categories were evaluated: benign neoplasms, malignant neoplasms, congenital pathology, and inflammatory pathology. Neoplastic processes and congenital lesions were diagnosed through fine-needle aspiration cytology or open biopsy and histopathological evaluation. When lymphoproliferative disorders were inferred from clinical examination or imaging studies, a flow cytometry test was routinely used. Inflammatory conditions were diagnosed on the basis of clinical or imaging signs of infection or inflammatory pathology. These conditions were diagnosed and managed following standard procedures. The diagnostic algorithm is outlined in Figure 1.

To identify semiological features associated with malignancy, a multiple logistic regression model was performed. The following variables were evaluated in the crude analysis: age, sex, history of cancer, history of tobacco smoking, pain, mass size, bilaterality, mass fixation to either the deep tissues or the skin, and mass involvement with multiple cervical lymph node levels. The variables that reached statistical significance in the crude analysis were included in the final multivariable model. Using the estimation of Peduzzi et al⁶ and considering a total of 65 malignancy events, a maximum of 6 variables were included in the model, given a fixed sample size. For the analysis of the secondary objective, we used a complete case analysis ($n = 181$). For the analysis, we used the Stata statistical package (StataCorp. 2013. Stata Statistical Software: Release 13. College Station, TX: StataCorp LP).

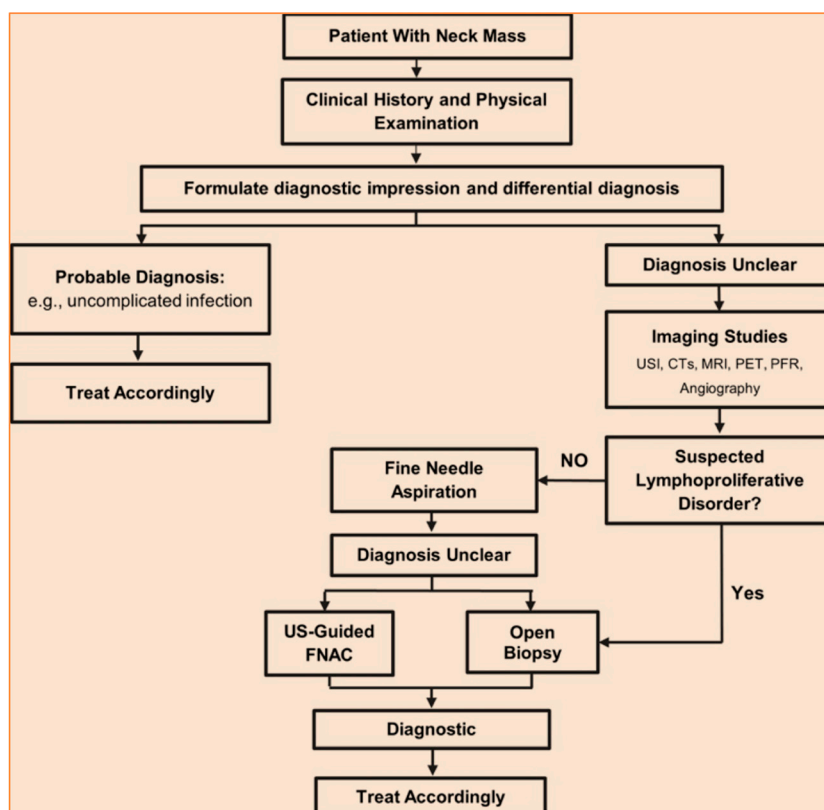
Our study was approved by the Dr. César Milstein Hospital Institutional Review Board (Register Number 1562) and was conducted in accordance with ethical principles for medical research in humans as established in the 2013 version of the Declaration of Helsinki of the World Medical Association.

Results

Two hundred eighty-nine patients were assessed for inclusion. Sixteen patients were excluded. The flowchart of patients included is shown in Figure 2. The clinical and demographic characteristics of the patients included are presented in Table 1. Neck masses were categorized as congenital lesions ($n = 7$, 3%, 95% CI: 1%-5%), inflammatory masses ($n = 67$, 25%, 95% CI: 19%-30%), benign neoplasms ($n = 77$, 28%, 95% CI: 23%-34%), and malignant neoplasms ($n = 87$, 32%, 95% CI: 26%-38%). In a subset of the patients, it was not possible to reach a definitive diagnosis because they had discontinued care ($n = 35$, 12%). The distribution of the diagnoses within each group is presented in Table 2.

In the logistic regression analysis for the identification of semiological features associated with malignancy, the following variables were statistically significant: age, male sex, history of cancer, mass fixation to either the deep tissues or the skin, and the involvement of the mass with multiple cervical lymph node levels. Table 3 shows the

Fig. 1.– Diagnostic algorithm



USI: ultrasound imaging; CTs: computed tomography scan; MRI: magnetic resonance imaging; PET: positron emission tomography; PFR: plain film radiography; FNAC: fine-needle aspiration cytology

Fig. 2. Flowchart of patients included and excluded

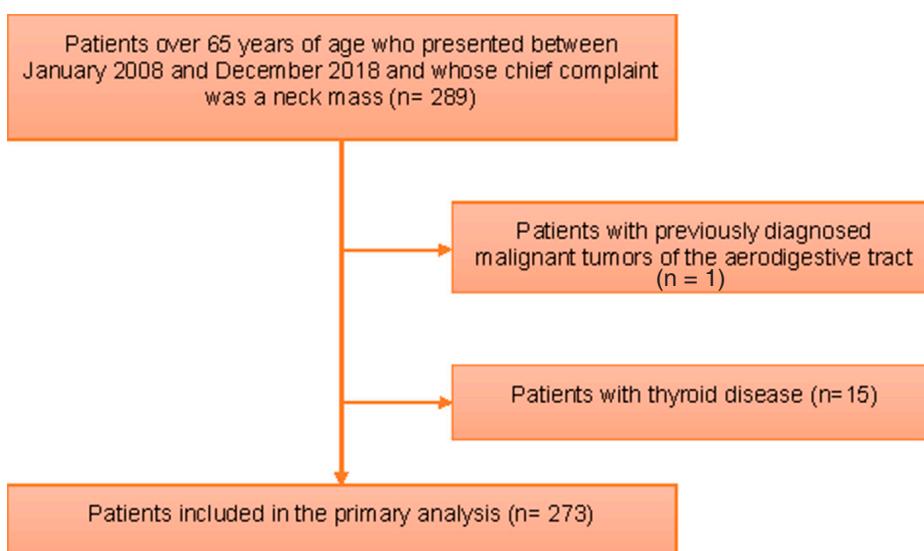


TABLE 1.– *Clinical and demographic characteristics of the patients included (N = 273)*

Variable	Value
Age, median (IQR)	72 (69-78)
Female sex, n (%)	165 (60)
Prior history of malignancy, n (%)	53 (19)
Tobacco smoking history, n (%)	151 (55)
Pain, n (%)	96 (35)
Size of the mass in mm, median (IQR)	35 (20-60)
Bilaterality, n (%)	24 (9)
Mass fixation to deep tissues or skin, n (%)*	80 (36)
Involvement of multiple cervical lymph node levels, n (%)	68 (25)

IQR: Interquartile range; mm: millimeters

*Total sample size for the evaluation of this variable: 221

TABLE 2.– *Distribution of diagnoses within each group (N = 273)*

Definitive diagnosis	n	%
Malignant neoplasms (32%)		
Cervical lymph node metastases from carcinomas	33	38
Lymphomas	32	37
Malignant tumors of salivary glands	21	24
Cervical lymph node metastases from melanomas	1	1
Total	87	100
Benign neoplasms (28%)		
Benign tumors of salivary glands	66	86
Lipomas	6	8
Hemangiomas	5	6
Total	77	100
Inflammatory masses (25%)		
Sialadenitis	29	43
Infection	24	36
Nonspecific lymphadenitis	14	21
Total	67	100
Congenital lesions (3%)		
Epidermoid cyst	5	72
Thyroglossal duct cyst	1	14
Branchial cleft cyst	1	14
Total	7	100
Patients without a definitive diagnosis (12%)		
Total	35	100

TABLE 3.– Crude and adjusted analysis of the clinical predictive factors evaluated for malignancy (N = 181)

Variable	Crude OR (95% CI)	p value	Adjusted OR (95% CI)	p value
Age	1.05 (1.006-1.10)	0.027	1.059 (1.00-1.12)	0.041
Male sex	2.08 (1.12-3.87)	0.020	2.35 (1.11-4.96)	0.025
Prior history of malignancy	2.39 (1.12-5.10)	0.024	2.66 (1.02-6.92)	0.045
Size of the mass	1.015 (1.00-1.025)	0.005	1.00 (0.99-1.017)	0.410
Fixation of the mass to deep tissues or skin	6.84 (3.46-13.52)	< 0.001	4.87 (2.20-10.76)	< 0.001
Involvement of multiple cervical lymph node levels	6.78 (3.07-14.99)	< 0.001	4.15 (1.64-10.51)	0.003

crude and adjusted analysis of the evaluated semiological features associated with malignancy (n = 181).

Discussion

In the present study, we evaluated 273 aged patients whose chief complaint was a cervical mass. Malignant neoplasms were the most frequent diagnoses, followed by benign neoplasms and inflammatory and congenital lesions.

Although the scientific literature has consistently pointed out that malignant lesions are more common than any other etiology of neck masses in patients over 40 years of age, the proportions of malignant tumors reported in this age group vary widely between 16% and 80%^{2, 7-9}. This variability may be explained by differences in the characteristics of the patients included, the diagnostic criteria used, or the setting in which the studies were carried out. In the present study, we report the distribution of diagnoses in a cohort consisting exclusively of patients over 65 years of age. In agreement with other researchers, we found that lymphomas and cervical lymph node metastases from carcinomas were the most frequently occurring malignant lesions⁸. We also found a high proportion of benign neoplasms, which may be related to the high prevalence of benign salivary gland tumors in our cohort. Inflammatory masses ranked third in frequency in our study, and sialadenitis –a condition frequently affecting aged patients¹⁰– was the most common inflammatory lesion. The low frequency observed for congenital lesions coincides with results reported by other authors for patients over 40 years of age².

Clinical risk factors for malignancy described in the literature include age over 40 years, male sex, mass fixation, mass size, B symptoms, ulceration of the skin, and prior history of cancer and smoking, among others^{1, 7, 11, 12}. In our study we evaluated the influence of nine different semiological features. Age, male sex, prior history of cancer, mass fixation to either the deep tissues or the skin, and the involvement of the mass with multiple cervical lymph node levels were identified as associated features with malignant neoplasms.

Our study has some limitations. Since it was carried out in a tertiary teaching hospital, results are probably affected by underlying referral bias. Missing data for the secondary analysis may be regarded as an additional limitation, as thirty-three percent of patients had at least one missing data point. Since we assumed that the missing data were missing at random, we decided to use a complete case analysis approach. Conversely, our study has several strengths. The patients included may appropriately represent the population of aged patients. Semiological features associated with malignancy were specifically addressed in a large sample of patients through a robust regression method, which allowed for adjustment for potentially confounding factors. Overall and despite study limitations, our results are consistent with the literature and are supported by clear biological plausibility, as the association of increased risk of malignancy and aging has been extensively demonstrated^{1, 3, 7-9, 13, 14}.

When evaluating a neck mass in an elderly patient, a neoplastic origin should be strongly suspected. The suspicion of malignancy increases in the presence of advanced age, male sex, prior history of cancer, mass fixation to the surrounding tissues, and mass involvement with multiple cervical lymph node levels.

Conflict of interest: Victoria de la Paz Sáenz works as Value-based Healthcare Manager in *Productos Roche Argentina* and receives a full-time salary from the company. The remaining authors none to declare.

References

1. Pynnonen MA, Gillespie MB, Roman B, et al. Clinical practice guideline: evaluation of the neck mass in adults. Executive summary. *Otolaryngol Head Neck Surg* 2017; 157: 355-71.
2. Balıkcı HH, Gurdal MM, Ozkul MH, et al. Neck masses: diagnostic analysis of 630 cases in Turkish population. *Eur Arch Otorhinolaryngol* 2013; 270: 2953-8.
3. Rosenberg TL, Brown JJ, Jefferson GD. Evaluating the adult patient with a neck mass. *Med Clin North Am* 2010; 94: 1017-29.
4. Meier JD, Grimmer JF. Evaluation and management of neck masses in children. *Am Fam Physician* 2014; 89: 353-8.

5. Robbins KT, Clayman G, Levine PA, et al. Neck dissection classification update: revisions proposed by the American head and neck society and the American academy of otolaryngology-head and neck surgery. *Arch Otolaryngol Head Neck Surg* 2002; 128: 751-8.
6. Peduzzi P, Concato J, Kemper E, Holford TR, Feinstein AR. A simulation study of the number of events per variable in logistic regression analysis. *J Clin Epidemiol* 1996; 49: 1373-9.
7. Bhattacharyya N. Predictive factors for neoplasia and malignancy in a neck mass. *Arch Otolaryngol Head Neck Surg* 1999; 125: 303-7.
8. McGuirt WF. The neck mass. *Med Clin North Am* 1999; 83: 219-34.
9. Lee J, Fernandes R. Neck masses: evaluation and diagnostic approach. *Oral Maxillofac Surg Clin North Am* 2008; 20: 321-37.
10. Rahman K, Kreicher K, Kost K, Parham K. Sialadenitis in the old-old and its risk factors. *Ear Nose Throat J* 2021; 100: 475S-6S.
11. Celenk F, Gulsen S, Baysal E, Aytac I, Kul S, Kanlikama M. Predictive factors for malignancy in patients with persistent cervical lymphadenopathy. *Eur Arch Otorhinolaryngol* 2016; 273: 251-6.
12. Ozkiriş M, Kala M. Histopathological examination of patients operated on for a neck mass: 4-year follow-up results. *Turk Patoloji Derg* 2011; 27: 134-7.
13. U.S. Cancer Statistics Working Group. US cancer statistics: 1999–2009 incidence and mortality web-based report. Atlanta GA: USDHHS, CDC; 2013. In: www.cdc.gov/uscs; accessed April 2022.
14. Laconi E, Marongiu F, DeGregori J. Cancer as a disease of old age: changing mutational and microenvironmental landscapes. *Br J Cancer* 2020; 122: 943-52.