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(RESEARCH ARTICLE)

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Parotid gland tumors, staging, diagnostic and therapeutic approaches: A comparison between two countries

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Abstract

BACKGROUND: Epidemiological studies on parotid gland tumors are often limited to single institutions, lacking comprehensive statistical analysis. In Albania, the only study on the disease, conducted nine years ago, did not address correlations with risk factors, treatment, or post-surgical rehabilitation. Additionally, no studies compare the management of parotid tumors in different countries, which hinders the evaluation of various approaches.

AIM: This study compares two multicenter experiences regarding the diagnosis, treatment, and follow-up of parotid gland tumors using consistent statistical data.

METHODS: Data was collected from 2016 to 2023 at five healthcare institutions in Tirana, Albania, and Rome, Italy, including patient demographics, lesion characteristics, histology, and surgical procedures, adhering to European Association of Salivary Glands (ESGS) guidelines.

RESULTS: The study included 100 patients from each country. The average age was 59.2 years for Italians and 63.9 years for Albanians. In Italy, 88% of lesions were benign, while 12% were malignant. In Albania, 63% were benign, and 37% were malignant, with 16% of malignant cases originating from benign tumors (e.g., pleomorphic adenoma). Common benign tumors in both groups were pleomorphic adenoma and Warthin's tumor, while malignant tumors included squamous cell carcinoma and adenocarcinoma. Surgical procedures mainly involved parotidectomy I-II for benign tumors and parotidectomy I-IV for malignant tumors.

CONCLUSIONS: Early diagnosis and awareness of parotid gland tumors in Albania are crucial for improving treatment outcomes and minimizing complications. Efforts should focus on achieving tumor-free excision margins with minimal surgery.

Keywords: Parotid; Salivary Glands; Tumor; Pleomorphic Adenoma; Warthin; Parotidectomy

1. Introduction

Salivary gland tumors are rare entities, accounting for approximately 3-6% of all head and neck neoplasms, with an incidence rate ranging from 0.4 to 13.5 per 100,000 inhabitants per year1.

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Generally, parotid glands are affected in 70% of cases, submandibular glands in 10%, and sublingual glands in less than 1%. The remaining 20% are tumors of the small salivary glands, mostly originating in the upper aerodigestive tract, such as the palate and lips.1,2,3

The majority of parotid gland tumors are benign, while malignant forms are relatively rare. The risk of malignancy increases with the smaller size of the gland, so malignant lesions are more common in small salivary glands.2,3

Typically, patients are over 40 years old, and both genders are equally affected. Salivary glands have several histological subtypes. The 5th edition of WHO classification of Head and Neck tumors of 2022 listed 22 different primary neoplasms.2

Numerous studies on the epidemiology of salivary gland tumors highlight that prevalence, incidence, gender distribution, age, anatomical location, and survival rates vary significantly across different regions of the world.3

Many other studies report that the most common histological types of tumors affecting the parotid gland include pleomorphic adenoma, Warthin's tumor, mucoepidermoid carcinoma, and adenoid cystic carcinoma.4 Ad-hoc investigations in countries like the United States and Japan have shown a notable increase in the incidence of parotid gland tumors compared to other salivary gland neoplasms.4

The study by Boci et al.5 analyzed the surgical variations and treatment outcomes of parotid gland tumors in patients who underwent parotidectomy between 2004 and 2015 at Tirana University Hospital Center (TUHC). This study found that the average age of patients with parotid gland disorders requiring surgery was 41 years and identified pleomorphic adenoma as the most prevalent pathology affecting the parotid gland5. However specific details regarding surgical techniques and variations were not provided there.

Our study aims to investigate whether there is a similar trend in the increasing rate of parotid gland tumors within our population. Additionally, it seeks to evaluate the incidence, follow-up outcomes, and surgical approaches to the treatment of parotid gland tumors in Albania.

To analyze this data properly, it is crucial to compare and identify differences in the diagnostic and treatment protocols for these tumors with those of neighboring countries, such as Italy and Greece. To date, no such comparative study has been conducted

It is worth reminding that two major systems are commonly used for analyzing parotid tumors, whether benign or malignant: the TNM system and the ESGS classification. The ESGS Classification divides the parotid gland into five anatomical levels for describing the location of the tumor and helping to identify the most appropriate surgical approach.

- Level I: Superior lateral parotid gland (superficial portion).
- Level II: Inferior lateral parotid gland.
- Level III: Deep inferior parotid gland.
- Level IV: Superior deep parotid gland.
- Level V: Accessory parotid tissue or glands.

Meanwhile, TNM staging follows the AJCC (American Joint Committee on Cancer) guidelines. The TNM system stages the tumors based on size, regional lymph node involvement, and distant metastasis; it is more focused on the oncologic management of the patient.

This article provides a comprehensive analysis of parotid gland tumors, focusing on their epidemiology, staging, diagnostic approaches, and surgical treatment, with a comparative assessment of cases from Italian and Albanian medical centers over 7 years. This comparison will provide valuable insights and facilitate the adoption of new techniques to improve treatment outcomes for parotid gland tumors in our countries.

2. Materials and methods

This retrospective study, aimed to analyze data from patients treated for suspected primary neoplastic lesions of the parotid gland, across several medical centers in Italy and Albania, from January 2016 to December 2023. Data was

collected from the TUHC and the Departments of Otolaryngology and Head and Neck Surgery at four major health institutions in Central Italy.

Each center contributed data on patients who underwent surgery for parotid tumors during the specified period. Information collected included patient demographics, histology of the tumors (classified as benign or malignant), fine-needle aspiration cytology (FNAC) reports, types of surgical procedures performed, postoperative complications, and histopathological findings of the excised masses.

All data were sourced directly from the clinical databases and medical records of the participating hospitals. Throughout the data collection and presentation process, strict measures were implemented to ensure the protection of sensitive patient information and maintain confidentiality. Exclusion criteria for the study included secondary neoplasms of the parotid gland arising from primary tumors located in other anatomical sites.

The study included a total of 250 patients, all suspected of having malignancy in the parotid gland. Based on histological evaluation, only patients with confirmed parotid gland tumors were

included in further analysis. Therefore, the Italian and Albanian samples consisted solely of 200 patients who met this criterion.

The subjects were categorized based on gender, incidence by decade, laterality, tumor size, histology, and the type of surgical procedures used, under the new classification proposed by the European Salivary Gland Society (ESGS). The staging of the tumors was also part of the initial evaluation of the subjects, but it was not analyzed in depth in this study.

2.1. Statistical Analysis

Data from 200 selected cases was collected and analyzed using the Excel-incorporated Tool-Pack (Microsoft Corp., Redmond, WA, USA) to estimate descriptive statistics. Levene's and T-test statistical methods were used and calculated to compare results. All estimates are within the standards of professional ethics and are part of routine hospital procedures.

3. Results

Of the 200 patients included in the study (100 from Italy and 100 from Albania), there were notable differences in gender distribution between the two samples.

In the Italian sample, 55 (55%) patients were male and 45 (45%) were female, indicating a slight male predominance with a female-to-male (F:M) ratio of 1:1.3. Conversely, in the Albanian sample, 64 (64%) patients were male and 36 (36%) were female, demonstrating a more pronounced male predominance with an F:M ratio of 1:1.8.

The average age of patients was 59.2 years (57.9, SD 16,7) in the Italian cohort (age range: 8–94 years) and 63.9 years (64.3 SD 13.3) in the Albanian cohort (age range: 23–89 years). It was noted that the mean age difference was not statistically significant (t=.015, df =198, $p<0.05$)

Table 1 Age/Incidence Descriptive Statistic

Descriptive Statistics					
	N	**Minimum**	**Maximum**	**Mean**	**Std. Deviation**
Italian	100	8	94	57.86	16.727
Albanian	100	23	89	64.33	13.317
Valid N (listwise)	100				

Table 2 Age difference/Incidence descriptive analysis

Independent Samples Test										
		Levene's Test for Equality of Variances		**t-test for Equality of Means**						
		F	**Sig.**	**t**	**df**	**Sig. (2-tailed)**	**Mean Difference**	**Std. Error Difference**	**95% Confidence Interval of the Difference**	
									Lower	**Upper**
Age	Equal variances assumed	6.06	0.015	-3.026	198	0.003	-6.47	2.138	-10.686	-2.254
	Equal variances not assumed			-3.026	188.528	0.003	-6.47	2.138	-10.688	-2.252

As illustrated in Figure 1 and 2, the peak incidence of parotid tumors in both samples occurred during the sixth and seventh decades of life. Notably, the Italian sample exhibited a higher incidence of diagnosis at relatively younger ages compared to the Albanian sample.

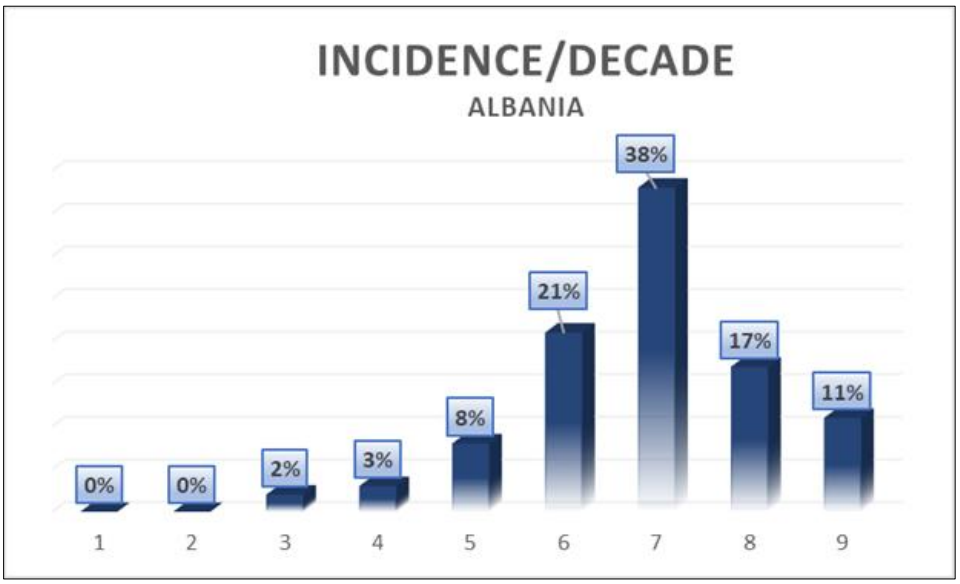

Figure 1 Evaluation of Albanian incidence according to decades of age

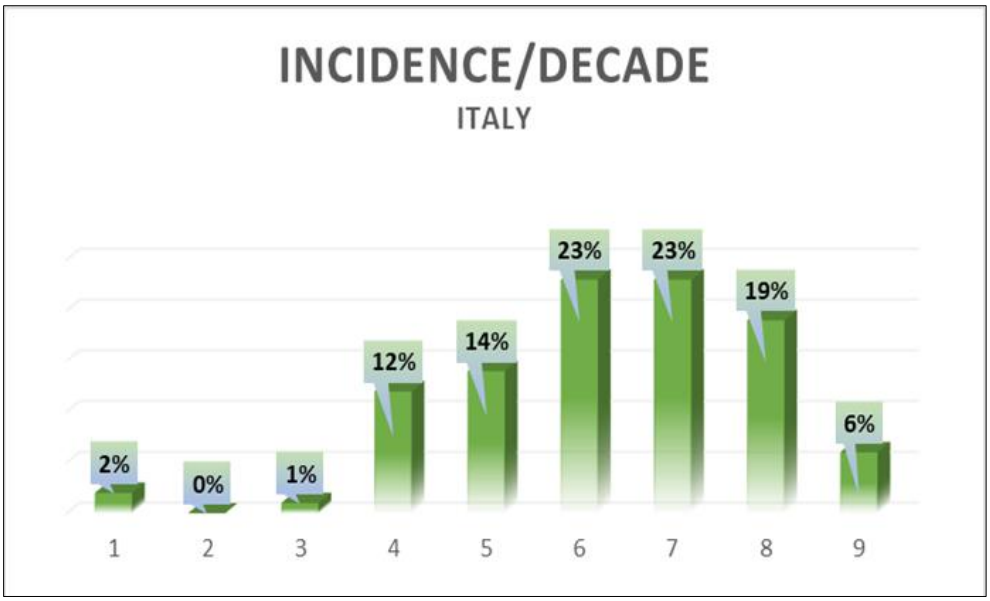

Figure 2 Evaluation of Italian incidence according to decades of age

In the Italian cohort, the right side was affected in 56% of cases, while the left side was involved in 44%. Conversely, in the Albanian cohort, 59% of cases involved the left side, and 41% affected the right side.

The average size of neoplasms (measured as the largest diameter) was 2.4 cm ± in the Italian sample and 3.8 cm ± in the Albanian sample. As shown in Figure 3 and 4, most tumors in the Italian cohort measured 2–3 cm at the time of diagnosis. In contrast, the majority of tumors in the Albanian cohort were larger, measuring 3–4 cm, followed by 4–5 cm.

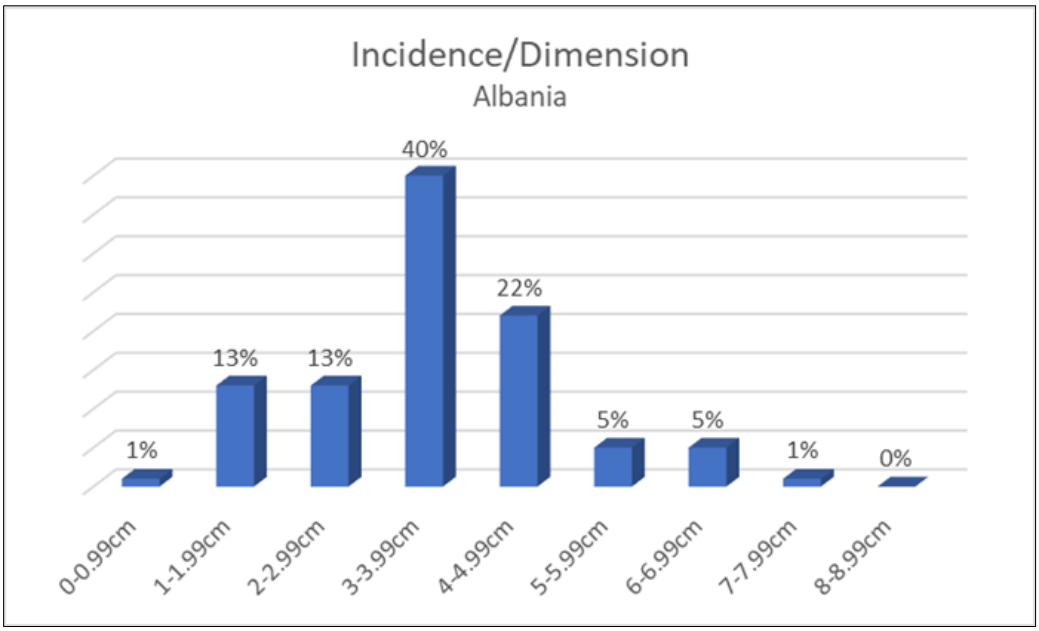

Figure 3 Evaluation of Albanian incidence according to neoplasm dimensions

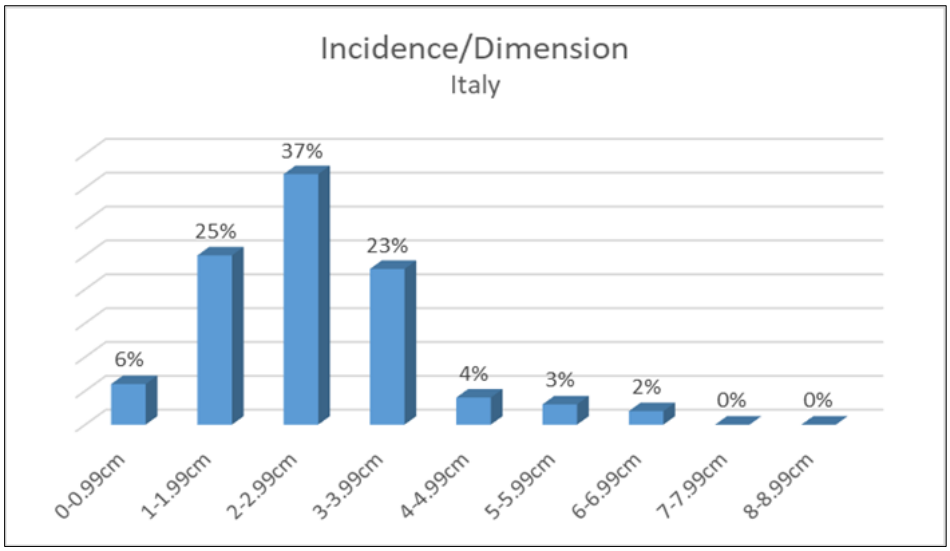

Figure 4 Evaluation of Italian incidence according to neoplasm dimensions

In terms of histology, 88% of tumors in the Italian sample were benign, and only 12% were malignant. In the Albanian sample, however, 63% of tumors were benign, while 37% were malignant. Of the malignant cases in the Albanian group, 16% had developed from an initially benign lesion (e.g., pleomorphic adenoma).

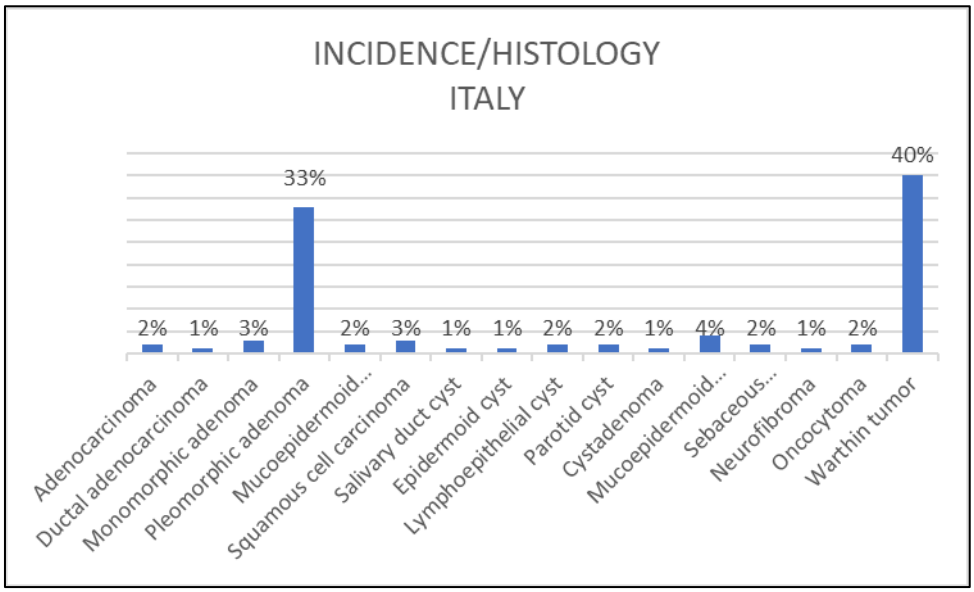

Figure 5 Evaluation of Italian incidence according to tumour histological type

The most common benign tumors in the Italian cohort were Warthin's tumor and pleomorphic adenoma**.** Among malignant tumors, the most frequent histotypes were mucoepidermoid carcinoma, squamous cell carcinoma **and** adenocarcinoma in that order as stated in Figure 5.

In the Albanian sample, the most frequent benign tumors were pleomorphic adenoma **and** Warthin's tumor**,** while the most common malignant tumors were adenocarcinoma**,** squamous cell carcinoma**, and** myoepithelial carcinoma as reflected in Figure 6.

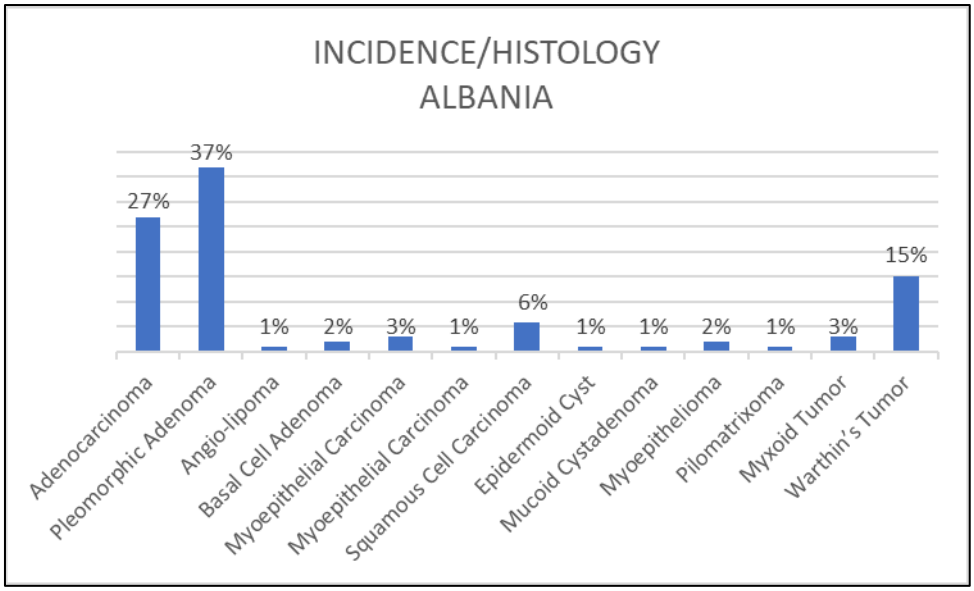

Figure 6 Evaluation of Albanian incidence according to tumour histological type

In the Italian sample, the average age of patients with benign lesions was 56.9 years, compared to 64.24 years for malignant cases. In the Albanian sample, the average age was 60.8 years for benign lesions and 70.2 years for malignant cases. The age difference for malignant cases was not statistically significant ($t = 1.307$, $df = 47$, $p < 0.05$) (Table3,4). Similarly, the age difference for benign cases was not statistically significant ($t = 0.176$, $df = 149$, $p < 0.05$)(Table5,6)

Table 3 Age/Malignancy descriptive analysis

Group Statistics					
	Nationality	N	Mean	Std. Deviation	Std. Error Mean
Age	Italian	12	64.25	22.046	6.364
	Albanian	37	70.22	9.903	1.628

Table 4 Age difference/ Malignancy descriptive analysis

Independent Samples Test										
		Levene's Test for Equality of Variances		**t-test for Equality of Means**						
		F	**Sig.**	**t**	**df**	**Sig. (2-tailed)**	**Mean Difference**	**Std. Error Difference**	**95% Confidence Interval of the Difference**	
									Lower	**Upper**
Age	Equal variances assumed	8.205	0.006	-1.307	47	0.198	-5.966	4.565	-15.151	3.218
	Equal variances not assumed			-0.908	12.47	0.381	-5.966	6.569	-20.219	8.287

3.1. Benign

Table 5 Age/benign descriptive analysis

Group Statistics					
	Nationality	**N**	**Mean**	**Std. Deviation**	**Std. Error Mean**
Age	Italian	88	56.99	15.828	1.687
	Albanian	63	60.87	13.907	1.752

Table 6 Age difference/ benign descriptive analysis

Independent Samples Test										
		Levene's Test for Equality of Variances		**t-test for Equality of Means**						
		F	**Sig.**	**t**	**df**	**Sig. (2-tailed)**	**Mean Difference**	**Std. Error Difference**	**95% Confidence Interval of the Difference**	
									Lower	**Upper**
Age	Equal variances assumed	1.847	0.176	-1.563	149	0.12	-3.884	2.485	-8.795	1.026
	Equal variances not assumed			-1.597	142.798	0.113	-3.884	2.432	-8.693	0.924

Overall, 15 different primary histological tumor types were identified in the Italian sample.

3.1.1. Benign Tumors

The most prevalent benign tumors in this sample were **Warthin's tumor** (40%) and **pleomorphic adenoma** (33%). Less common benign forms included:

- **Cystic lesions (4%)**
- **Monomorphic adenoma** (2%)
- **Oncocytoma** (2%)
- **Neurofibroma** (1%)

3.1.2. Malignant Tumors

The most frequent malignant histotypes were:

- **Mucoepidermoid carcinoma** (6%)
- **Squamous cell carcinoma** (3%)

Other less common malignant tumors included:

- **Carcinoma ex pleomorphic adenoma** (2% of Carcinoma lesions%)
- **Adenocarcinoma** (2%)

In the Albanian sample, 12 histological types were identified. The most common benign forms were pleomorphic adenoma (37%) and Warthin's tumor (15%), followed cystic adenoma (2%), and others.

On the other hand, malignant lesions were primarily represented by adenocarcinoma (27%), with 16% developing from a pre-existing benign condition (e.g., pleomorphic adenoma). Squamous cell carcinoma (6%) and myoepithelial carcinoma (4%) were also observed. Further details are presented in Graphic 6.

The general diagnostic protocol used in Italian hospital centers involved a clinical and ultrasound assessment, followed by a preoperative evaluation through ultrasound-guided fine-needle aspiration (US-FNA) and radiological imaging (CT and/or MRI) to determine the most appropriate surgical approach.

In contrast, the diagnostic workup for Albanian patients was based on clinical evaluation, followed by CT and/or MRI imaging, and concluded with a histopathological examination of the excised mass after surgery.

In both groups, the surgical approach was determined based on the size and location of the tumor within the gland. The procedures included superficial parotidectomy, partial superficial parotidectomy, deep lobe parotidectomy, superficial parotidectomy extended to the deep inferior lobe, extracapsular dissection, and total parotidectomy with either preservation or resection of the facial nerve in cases of malignant tumor infiltration.

For malignant lesions, surgical treatment was planned after clinical evaluation of the primary tumor (T) and cervical lymph nodes (N). The primary approach consisted of total parotidectomy, with or without facial nerve preservation, and, when necessary, extension to extra glandular structures and adequate neck dissection.

The study also analyzed the collected data according to the 2016 ESGS classification.

3.1.3. Italian Sample

Table 7 indicates that the most common tumor size range was 2–2.99 cm, accounting for 37% of cases. Across all size categories, the most frequently performed surgical procedure was superficial parotidectomy (also referred to as parotidectomy I-II, according to the ESGS classification).

Table 8 outlines the histological characteristics of the tumors, showing that Warthin's tumor was the most common type, representing 40% of all lesions. The primary treatment for this tumor was parotidectomy I-II, performed in 75% of cases with this type of tumor. The second most common procedure was total parotidectomy, classified as parotidectomy I-IV (13% of cases), followed by deep inferior lobe parotidectomy, also known as parotidectomy III-IV (3%).

Table 7 Types of ESGS according to tumor dimensions in Italy

Table I.—ESGS types according tuo dimensiions

Dimensiions	0-0.99cm	1-1.99 cm	2-2.99 cm	3-3.99 cm	4-4.99 cm	>5 cm
%	3.5%	25.6%	36.8%	19.4%	10%	4.7%
ESGS type	70.6% (I-II)	57.6% (I-II)	57.2% (I-II)	48.4% (I-II)	32.6% (I-II)	39.1% (I-II)
	17.6% (I-IV)	13.6% (I-IV)	11.7% (I-IV)	20% (I-IV)	28.6% (I-IV)	26.1%(I-IV)
5.8% (I-II-III) and 5.8% (II)		11.2% (I-II-III) and 11.2% (II)	13.9% (I-II-III)	14.7% (I-II-III)	18.4% (I-II-III)	13% (II)

Table 8 Types of ESGS according to histology in Italy

TabIe II.—ESGS types according to histology

Histology	Tumor Warthin	Pleomorphic Adenoma	Malign Tumors
%	40%	33%	12%
ESGS types	51.8% (I-II)	63.4% (I-II)	41.2% (I-IV)
	18.6% (II)	12.9% (I-IV)	27.9% (I-II)
	15% (I-II-III)	12.9% (I-II-III)	11.7% (I-II-III)

Pleomorphic adenoma, accounting for 33% of all tumors, was treated with parotidectomy I-II in 77 % of cases, parotidectomy I-IV in 6% of cases, and parotidectomy I-II-III in another 9% of adenomas.

Malignant tumors, representing 12% of all cases, were primarily managed with total parotidectomy (46.2%). In some patients, a portion of the gland was preserved, with surgical approaches including

superficial parotidectomy (27.9%) or parotidectomy I-II-III (15.3%). In another 11.7% of cases, facial nerve sacrifice was necessary, requiring total facial resection parotidectomy, classified as parotidectomy I-IV (VII). Additionally, some

cases required total extended parotidectomy with facial nerve resection, along with skin, muscle, and masseter removal, defined as parotidectomy I-IV (VII, S, MM).

3.1.4. Albanian Sample

At the time of diagnosis, the average size of parotid gland neoplasms ranged from 3–4 cm, followed by 4–5 cm. Due to the lesion size, the most common surgical procedure was superficial parotidectomy (I-II), followed by superficial parotidectomy extended to the deep lobe (I-II-III). The study also observed a tendency toward more extensive surgical interventions in cases involving deep lobe or malignant tumors, often requiring facial nerve sacrifice.

For benign lesions, the most frequently performed procedure was parotidectomy I-II, followed by I-II-III. In malignant cases, total parotidectomy with facial nerve sacrifice (I-IV VII) was the most commonly used approach.

Table 9 presents the correlation between tumor size and the surgical procedures performed according to ESGS classification.

Table 10 illustrates the histological characteristics of tumors and their respective surgical procedures based on the ESGS classification. The collected data indicate a greater tendency toward radical surgery in the Albanian sample compared to the Italian model, particularly in malignant cases. Pleomorphic adenoma was the most prevalent benign tumor, with superficial parotidectomy (I-II) being the most frequently performed procedure, followed by superficial parotidectomy extended to the deep lobe (I-II-III).

Table 9 Types of ESGS according to dimensions in Albania

Table III. —ESGS types according to dimensions

Dimensions	0-0.99 cm	1-1.99 cm	2-2.99 cm	3-3.99 cm	4-4.99 cm	>5 cm
%	1%	13%	13%	40%	22%	II%
ESGS	100% (I-II)	67% (I-II)	56% (I-II-III)	56% (I-II-III)	40% (I-II-III)	32% (I-II-III)
		33 (I-IV)	22% (I-IV)	19% (I-IV)	27% (I-IV)	27%(I-IV)
			22% (I-IV VII)	25% (I-IV VII)	33% (I-IV VII)	41% (I-IV VII)

Table 10 Types of ESGS according to histology in Albania

Table IV.— *ESGS types according to histology*

Histology	Warthin	Pleomorphic adenoma	Malign tumors
%	15%	37%	37%
ESGS types	52 % (I-II)	43 % (I-II)	
	23 % (I-II-III)	28 % (I-II-III)	8 % (I-II-III)
	13 % (I-IV)	17 % (I-IV)	34 % (I-IV)
	12 % (I-IV VII)	13 % (I-IV VII)	58 % (I-IV VII)

A similar trend was observed in Warthin's tumor cases. However, for malignant tumors, total parotidectomy and total parotidectomy with facial nerve sacrifice were the most commonly performed surgeries.

4. Discussion

Most available epidemiological studies on parotid tumors are limited, often based on data from a single institution without detailed statistical analysis. This is likely due to the rarity of these histological varieties.

In Albania, there is also a lack of comprehensive studies with concrete data on the correlation between the disease and risk factors, treatment, or post-surgical rehabilitation. Over the past few decades, only one study5 has been published that sheds light on parotid gland tumors, but it lacks comparative data with neighboring countries, limiting the scope of the analysis.

Furthermore, no studies have yet correlated, compared, or evaluated the experiences of two different countries based on the same criteria, even though each country follows different protocols.

In 2016, the European Salivary Gland Society (ESGS) proposed a new classification for parotid gland surgery based on the anatomical division of the salivary glands into five levels: Level I (superior lateral), Level II (inferior lateral), Level III (deep inferior), Level IV (superior deep), and Level V (accessory). This European proposal focuses on two main surgical procedures: extracapsular dissection (ECD) and parotidectomy.

In our study, we observed a slight male predominance in the Italian sample, which was more pronounced in the Albanian sample. This finding aligns with other epidemiological reports on

salivary gland tumors. Further analysis of the sample subgroup following a T test form confirmed that there was no significant gender difference between benign and malignant lesions.6

The average age was 59.2 years for Italian patients and 63.9 years for Albanian patients. Malignant tumors tended to appear later in life, with a 6–8-year age difference. These findings are consistent with other studies, such as that of Venkatesh, who found that parotid malignant lesions are more common between the fourth and seventh decades of life, with an average age of 56 years, compared to benign forms, which typically occur in younger patients.7

In most cases, parotid tumors are benign, comprising 88% of neoplasms in the Italian sample compared to 63% benign and 37% malignant in the Albanian sample. In the Albanian sample, 16% of malignant forms developed from an initially benign tumor, indicating that delayed diagnosis and treatment may influence prognosis. These findings align with the most recent literature, which reports that 70–80% of parotid tumors are benign.13

The Italian data showed a higher prevalence of Warthin tumors compared to pleomorphic adenomas, although previous reports have indicated that pleomorphic adenoma is the most common benign tumor of the parotid gland, accounting for over two-thirds of cases. However, recent studies, mainly conducted in Central Europe, have reported an increasing incidence of Warthin tumors, likely due to smoking14. In contrast, the Albanian sample showed that pleomorphic adenoma was the most prevalent benign tumor, consistent with the epidemiological literature. The same conclusion was drawn by the previous study in Albania5. However, there has also been an increase in the incidence of Warthin tumors, reflecting a growing trend observed in European countries, including Albania6.

Another aspect analyzed in this study is the classification of surgical approaches. The 2016 classification of surgical approaches by the European Salivary Gland Society (ESGS)15 is regarded as clear, simple, and comprehensive by institutions that have already integrated it into clinical practice, facilitating potential multicentric communication. Therefore, we adopted this international classification for our multicentric study. Based on the above, parotidectomy I-II was the most frequently performed procedure for managing benign tumors in both the Italian and Albanian samples, particularly for Warthin tumors and pleomorphic adenomas. Benign tumors are typically treated with superficial parotidectomy (parotidectomy I-II, based on ESGS) or with extracapsular dissection (ECD) in selected cases. Malignant lesions were managed with total parotidectomy, with or without facial nerve preservation. Comparing the two samples, we observed that the Albanian approach showed a greater tendency to sacrifice the facial nerve during surgical procedures compared to the Italian sample. This probably ensured the complete excision of suspicious areas. Also, the literature widely supports the recommendation for partial or total parotidectomy for malignant tumors, with excision of peri-neural and connective tissue if there is evidence of infiltration16.

To conclude, we believe that multi-institutional data collection is crucial for improving the management of head and neck tumors, especially salivary gland tumors, which have a wide variety of histological types. Applying these standardized criteria will enhance the understanding of epidemiological data, helping clinicians provide better medical care for patients with parotid neoplasms

This study is an important step towards further research on these tumors and will undoubtedly serve as a valuable source of information, raising awareness for early diagnosis and treatment and improving healthcare outcomes for affected patients

5. Conclusion

Warthin tumor and pleomorphic adenoma appear to be the most common benign tumors in both Albanian and Italian populations, while the prevalence of malignant tumors differs between the two groups. Further studies are necessary to identify the risk factors associated with these malignant lesions. The age at diagnosis for malignant lesions is lower in the Italian cohort, highlighting the need for improved early detection in the Albanian population. Earlier diagnosis would help reduce the extent of surgery and improve facial nerve preservation. Ongoing research is essential to monitor changes in the epidemiology of parotid gland tumors in similar geographic areas.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict-of-interest to be disclosed.

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