

## Original Article

# Pleomorphic adenoma parotid surgery, how much margin we can reach to be safe?

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## ABSTRACT

**Background:** The extent of surgery in cases of parotid gland pleomorphic adenoma (PA) remains challenging. This study aims to evaluate the importance of surgical margins in ensuring safe surgery for patients with PA.

**Materials and Methods:** This prospective study was conducted to evaluate the risk of local recurrence based on surgical margins in patients with parotid PA who underwent superficial or total parotidectomy between May 2019 and November 2021 at a tertiary referral hospital in Tehran, Iran. Patients were followed for at least 2 years. Data were analyzed using SPSS version 23. The normality of data distribution was assessed using the Kolmogorov–Smirnov test. Quantitative and qualitative variables were analyzed with the independent *t*-test and Chi-square test, respectively. A *P* < 0.05 was considered statistically significant.

**Results:** Fifty-seven cases were included in the study. The mean age was 40.7 years, with 37 of 57 (64.9%) patients being female. Of these, 35 of 57 (61.4%) underwent superficial parotidectomy. All tumors were resected with negative margins, with an average safe margin of 0.58 cm (range: 0–3.7 cm). The greatest margin was found at the anterior side (average: 0.76 cm), whereas the smallest margin was at the vertical side (average: 0.39 cm). Postoperative radiotherapy was not administered to patients with close surgical margins. No recurrence was observed after a 2-year follow-up.

**Conclusion:** In the surgical resection of parotid PA, negative margins are sufficient, and there is no need to obtain additional safe margins to reduce the risk of recurrence. Therefore, extracapsular dissection (which carries higher morbidities) can be replaced by superficial parotidectomy with negative margins (which carries lower morbidities).

**Key Words:** Adenoma, head and neck neoplasms, parotid gland, salivary gland neoplasms, surgery

Received: 21-Jul-2024  
Revised: 08-Nov-2024  
Accepted: 15-Dec-2024  
Published: 20-Feb-2025

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DOI: 10.4103/drj.drj\_336\_24

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**How to cite this article:** Mohebbi S, Zahedi M, Basir Shabestari S, Ahmadi A, Kazemipour S, Kadkhoda-Mohammadi M. Pleomorphic adenoma parotid surgery, how much margin we can reach to be safe? Dent Res J 2025;22:6.

## INTRODUCTION

The prevalence of head-and-neck cancers in the general population ranges from 0.4 to 13.5 cases/100,000 people.<sup>[1]</sup> Salivary gland tumors account for 2%–4% of cervical tumors.<sup>[2]</sup> The parotid gland is the most common site for salivary gland tumors, accounting for about 60%–75% of all salivary gland neoplasms.<sup>[3]</sup> Pleomorphic adenoma (PA) is the most common benign tumor of the salivary glands, representing 45%–75% of all such tumors.<sup>[4,5]</sup> PA was first described by Almeslet.<sup>[6]</sup> More than 85% of cases involve large salivary glands, though it is also seen in small salivary glands (10%) and in the submandibular gland (5%).<sup>[3,7]</sup> Women are more frequently affected (2:1 ratio), with the peak incidence occurring between the third and fifth decades of life.<sup>[8]</sup>

PA is a localized, pleomorphic tumor of epithelial origin, typically comprising a mixture of mucoid, myxoid, and chondroid tissue.<sup>[9]</sup> The adenomas usually appear in the superficial lobe of the parotid gland but can occasionally penetrate deeper into the glandular tissues and involve the parapharyngeal space.<sup>[10]</sup> PA often manifests as a slow-growing, asymptomatic swelling, typically without facial nerve involvement.<sup>[11,12]</sup> Although most commonly found in the parotid gland, it can also occur in the hard palate, soft palate, upper lip, tongue, chin, and floor of the mouth.<sup>[13]</sup> The etiology of PA remains unclear, though studies suggest possible links to the SV40 virus,<sup>[14,15]</sup> tobacco use, genetic predisposition, and chemical exposure.<sup>[9]</sup> Chromosomal variants on chromosomes 8q12 or 12q15 have also been associated with PA.<sup>[6,16]</sup>

PA predominantly affects young- and middle-aged individuals, particularly between 30 and 60 years of age.<sup>[6]</sup> Women are more commonly affected, with tumors typically located in the superficial lobe of the parotid gland, often causing swelling at the mandibular angle.<sup>[17]</sup> Cystic degeneration of the tumor surface may sometimes be palpable.<sup>[18]</sup> PA is usually asymptomatic, with rare occurrences of pain or facial nerve involvement. Malignant transformation of PA is extremely rare.<sup>[19]</sup> Diagnosis is confirmed by computed tomography scan or magnetic resonance imaging (MRI), with MRI being preferred for detecting tumor margins. Needle biopsy is essential to distinguish between benign and malignant tissues.<sup>[20-22]</sup> Concerns exist about tumor extension into surrounding tissues, which may increase the risk of recurrence.<sup>[23]</sup> Surgical excision remains the

primary treatment,<sup>[24]</sup> with enucleation of the mass posing a higher risk of recurrence.<sup>[6,25]</sup> Superficial parotidectomy is typically performed for tumors in the superficial lobe, preserving the facial nerve.<sup>[26]</sup> Total parotidectomy is required when the tumor extends into or originates from the deep lobe.<sup>[19,27]</sup> Partial superficial parotidectomy is appropriate for tumors under 4 cm in size or low-grade malignant tumors that are mobile and confined to the superficial lobe.<sup>[19]</sup> Tumor mobility, capsule thickness, and size must be considered when planning surgery.<sup>[7,19,28]</sup> This study aims to assess the importance of tumor margins in achieving a good surgical outcome in parotid PAs. We also evaluated patient demographics and tumor characteristics.

## MATERIALS AND METHODS

This prospective study was conducted on patients with parotid PA who underwent surgery at the Ear, Nose, and Throat (ENT) and Head and Neck Research Center, Iran University of Medical Sciences, Tehran, between October 2019 and October 2021. The study was approved by the Ethics Committee of Iran University of Medical Sciences (IR.IUMS.FMD.REC.1399.239). The principles of the Helsinki Declaration were fully observed, and the objectives of the study were explained to the patients. Patients under 18 years of age and those who had previously undergone surgery for a parotid tumor or malignancy were excluded.

Following surgery (total parotidectomy or superficial parotidectomy), the resected mass was sent for pathological assessment. In cases involving the superficial mass, an additional sample was taken from the SMAS, and in cases involving the deep lobe, biopsies were taken from the parotid gland remnant or masseter. The pathology specimens included sufficient salivary gland tissue along with healthy tissue, and all parts were marked to identify their anatomical directions for the pathologist. The pathologist was instructed to examine the entire capsule in all directions (anterior, posterior, superior, inferior, and vertical margins).

Due to the presence of the facial nerve in the deep or superficial regions, only one axis was analyzed for the vertical side. Patient information such as tumor type, lobe involvement (superficial or deep), and margin status was recorded. Patients were followed by phone and in person; for patients with long follow-up periods or those who were unavailable, phone follow-ups were used.

Data were analyzed using SPSS version 23 (IBM Corp. Armonk, NY). The normality of data distribution was tested using the Kolmogorov–Smirnov test. Quantitative variables were analyzed using the independent *t*-test, and qualitative variables were compared using the Chi-square test. A *P* < 0.05 was considered statistically significant.

## RESULTS

A total of 134 patients with parotid masses underwent surgical resection at the ENT and Head and Neck Research Center, Iran University of Medical Sciences. Of these, 16 were malignant, and 118 were benign tumors [Table 1]. Fifty-seven cases of parotid PA were included in the study. The prevalence of parotid PA was 48.3% among all benign lesions and 42.5% among all parotid lesions studied [Table 1].

The mean age of patients was  $40.75 \pm 13.68$  years, with ages ranging from 21 to 72 years. Lymph node involvement was noted in 15 cases (26.3%), with 11 cases (16.3%) involving one lymph node, 2 cases (3.5%) involving two lymph nodes, and 2 cases (3.5%) involving three lymph nodes. All lymph nodes were reactive, and no pathological lymph nodes were identified [Table 2].

There were no significant differences in age, tumor location, or lymph node involvement between men and women. However, more males underwent superficial parotidectomy (70.3%) than total parotidectomy (50%), though this difference was not statistically significant (*P* = 0.061) [Table 3].

The mean anterior, posterior, inferior, superior, and vertical margins were 0.76 cm, 0.64 cm, 0.61 cm, 0.48 cm, and 0.39 cm, respectively (*P* = 0.57). The largest margin was obtained at the anterior axis (3.5 cm), whereas the smallest margin was at the vertical axis (0 cm) [Table 4]. All margins were negative. One case showed focal involvement of the capsule due to rupture during surgery, but this case did not experience recurrence during follow-up. All patients were followed for an average of 24 months (range: 16–30 months), and no recurrence was observed.

## DISCUSSION

The epidemiology of parotid PA in this study aligns with that of other studies in terms of age and gender distribution, with women being affected more often

**Table 1: Type of pathology of surgical specimens**

Malignant	Frequency	Benign	Frequency
MEC	5	PA	57
ACC	3	Wartin	17
SCC	3	Sialadenitis	13
Small cell carcinoma	2	Normal salivary	8
Metastasis	1	Simple cyst	8
Lymphoma	1	Hemangioma	5
Adenocarcinoma	1	Basal cell adenoma	5
		Lipoma	3
		Oncocytoma	2
Total	16		118

ACC: Adenoid cystic carcinoma; MEC: Mucoepidermoid carcinoma; SCC: Squamous cell carcinoma; PA: Pleomorphic adenoma

**Table 2: Demographic characteristics**

Variable	Value, n (%)
Gender	
Male	20 (35.1)
Female	37 (64.9)
Surgery type	
Superficial parotidectomy	35 (61.4)
Total parotidectomy	22 (38.6)
Involvement side	
Right	31 (54.4)
Left	26 (45.6)
Lymph node involvement	
Present	15 (26.3)
Absent	42 (73.7)

**Table 3: Comparison of underlying characteristics of patients by gender**

Variable	Male, n (%)	Female, n (%)	<i>P</i>
Age	41.86±14.23	38.70±12.71	0.410 <sup>a</sup>
Type of surgery			
Superficial parotidectomy	26 (70.3)	9 (45)	0.061 <sup>b</sup>
Total parotidectomy	26 (29.7)	11 (55)	
Involvement side			
Right	26 (51.4)	12 (60)	0.532 <sup>b</sup>
Left	26 (48.6)	8 (40)	
Lymphadenopathy	26 (27)	5 (25)	0.889 <sup>b</sup>

<sup>a</sup>Using independent *t*-test; <sup>b</sup>Using Chi-square test

than men, and the peak incidence occurring in the third to fifth decades of life.<sup>[29,30]</sup> The prevalence in our series was estimated to be 48.3% among all benign lesions and 42.5% among all suspected parotid lesions. As mentioned earlier, the tumor is most prevalent in women in the third to fifth decades, which is in line with our findings. In fact, although this tumor can be identified at various ages, the most common age range is the third to sixth decades of life, particularly between 43 and 46 years.<sup>[31-33]</sup> These studies have also confirmed a higher prevalence of the disease in

**Table 4: The margins in the overall cohort**

Seial number	Anterior	Posterior	Inferior	Superior	Vertical	Seial number	Anterior	Posterior	Inferior	Superior	Vertical
1	10	8	7	8	2	30	10	10	5	5	0
2	20	15	18	10	10	31	6	4	6	7	0
3	1	2	3	7	8	32	10	5	5	5	0
4	7	6	2	3	2	33	10	5	5	5	4
5	2	4	3	5	2	34	10	5	10	10	3
6	1	1	1	1	11	35	5	5	5	5	5
7	2	3	1	1	1	36	3	2	7	8	2
8	1	1	1	2	1	37	5	5	3	2	3
9	7	8	1	1	1	38	2	3	1	1	1
10	7	8	4	7	1	39	9	8	4	4	2
11	10	7	7	8	10	40	10	10	1	1	0
12	10	7	6	6	2	41	5	15	5	5	1
13	10	5	4	2	1	42	7	8	2	3	4
14	1	1	1	1	1	43	15	10	10	5	10
15	4	2	2	3	1	44	3	4	4	6	3
16	10	10	1	1	1	45	10	10	7	8	3
17	5	5	2	4	0	46	15	15	9	8	10
18	5	4	2	4	20	47	3	2	4	2	1
19	5	5	3	3	0	48	35	15	20	20	15
20	10	10	5	5	2	49	10	10	7	8	3
21	20	20	10	10	10	50	3	2	2	4	1
22	4	3	4	6	10	51	3	3	2	3	2
23	2	4	6	4	3	52	1	1	1	1	1
24	15	15	7	8	10	53	8	3	5	5	5
25	7	3	8	7	15	54	3	3	2	1	0
26	10	5	3	4	4	55	10	4	8	8	8
27	4	3	4	5	2	56	10	10	5	5	0
28	3	3	2	4	1	57	2	3	4	4	2
29	15	15	7	8	5						

All data are in millimeters

women compared to men, with equal distribution on both sides. Lymph node involvement is also seen in about a quarter of all samples. Studies have shown that the main involvement of the parotid gland in this tumor occurs in 70%–80% of cases in the superficial lobe, and therefore, superficial parotidectomy is the primary treatment for these patients.<sup>[34-36]</sup> In our data, 60% of patients underwent superficial parotidectomy. According to a study by Riad *et al.*, prospective data were collected on 180 parotidectomies, with the resected margin ranging from 0 to 26 mm, with an average of 5.8 mm. They reported that tumor recurrence was inversely related to the safe margin, with a mean of 1.3 mm in recurrent tumors and 0.6 mm in nonrecurrent tumors. In addition, the safe margin was inversely related to tumor size.<sup>[33]</sup>

Despite no intention to obtain a fixed margin around the tumor, all our cases had negative margins. The range of resected margins was between 0 and 37 mm, with an average of 5.8 mm. The greatest margin was achieved in the anterior axis, and the smallest margin

was in the vertical axis. One factor often cited as very important in surgical outcomes and tumor recurrence is the positive margin of the tumor. However, in our study, none of the samples had a positive margin, so it was not possible to evaluate the effect of this parameter. In a study by Wong *et al.*, if there was a tumor at the margin, recurrence occurred in 17.6% of cases. However, in cases where tumors were marginally removed (margin <1 mm), recurrence occurred in only 1.8% of cases.<sup>[37]</sup>

Although we did not emphasize the margin, we did not encounter any problems even with a zero margin. In some parts of the parotid gland, due to the mass's location and the presence of the facial nerve and other structures, no extra margin can be achieved. In other words, focal exposure of the capsule in different areas is inevitable. This means that extracapsular dissection could be an acceptable option in experienced hands. According to a comprehensive meta-analysis, data on recurrence rates and times based on the type of surgical treatment are limited.<sup>[32]</sup> The lowest

recurrence rates are reported for total parotidectomy and extracapsular dissection.<sup>[38]</sup>

As mentioned earlier, in masses located in the superficial lobe of the parotid gland, superficial parotidectomy is considered, with preservation of the facial nerve.<sup>[17,39,40]</sup> Total parotidectomy is required when the tumor progresses to or originates in the deep lobe. Regarding outcomes after treatment, despite differences in approaches and margins, the prognosis remains excellent. Studies have also shown that surgical treatment generally yields an acceptable outcome, and cases of tumor recurrence are rarely reported.<sup>[19,41]</sup> Factors associated with tumor recurrence include incomplete tumor capsule removal, tumor nodular proliferation, the presence of separate satellite nodules, tumor injury during surgery, high mesenchymal content, female sex, young age, and enucleation versus parotidectomy.<sup>[33,42]</sup> Therefore, when assessing the outcome of surgery and tracking tumor recurrence, it is important to evaluate the positivity of margins and traces of tumor tissue at the margins. However, some studies prefer radiotherapy for recurrent PA but question the use of adjuvant radiotherapy for close margins.

## CONCLUSION

Finally, it can be concluded that, according to our study, half of all benign parotid lesions are parotid PAs. The prevalence of this lesion in women is twice as high as in men, and its peak age in our series is 30–40 years. We can also conclude that extracapsular dissection may be an acceptable option, and its evaluation is possible by performing long-term follow-up on patients who have undergone this method.

## Acknowledgments

This article is part of a thesis proposal for medical graduation as a specialist (M Z). The authors would like to express their gratitude to the authorities of Rasool Akram Medical Complex Clinical Research Development Center (RCRDC) for their kind cooperation.

## Financial support and sponsorship

This study was funded by Iran University of Medical Sciences.

## Conflicts of interest

The authors of this manuscript declare that they have no conflicts of interest, real or perceived, financial or non-financial in this article.

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