

Tumour Recurrence and Facial Nerve Injury Rates After Surgery of Pleomorphic Adenoma Through 5-Year Follow-Up: A Retrospective Single-Centre Study

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Abstract

According to the guidelines for the treatment of pleomorphic adenoma of parotid gland patients should undergo superficial parotidectomy. The aim of our study was to compare facial nerve injury rates and tumour recurrence rates after superficial parotidectomy vs. tumour extirpation as an alternative procedure of treatment.

Study was conducted as a retrospective analysis of the data from patients, who underwent different surgeries of pleomorphic adenoma removal in our university centre between 2005 till 2017 and were followed up for 5 years after the procedure. The major independent variables were superficial parotidectomy or extirpation, and the main outcome parameter was diagnosis of facial nerve injury or tumour recurrence.

Overall 161 cases of surgical removal of pleomorphic adenomas were analysed. Mean age of patients was 47.9±19.5 years. The male-to-female ratio was 1:1.04 with no significant differences between genders. Adenoma pleomorphic as diagnosis was mostly found at parotid gland; in 111 (68.9%) of all cases. Superficial parotidectomy was performed in 32 (19.9%), surgical extirpation in 112 (69.6%) cases. Recurrence of tumour occurred in 7 (4.3%) patients with no detectable risk factors. Facial nerve injury as facial paralysis was diagnosed in 4 (2.5%) cases, of which all patients had undergone total parotidectomy. One transformation of pleomorphic adenoma in a malignant carcinoma ex pleomorphic adenoma was detected.

According to the surgical procedures, only total parotidectomy was detected as a risk factor for facial nerve injury. However, these findings should be interpreted with caution, since we have only detected facial nerve injury in 4 and tumour recurrences in 7 cases.

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Introduction

Pleomorphic adenomas (PAs) are the most common benign tumours of the salivary glands comprising 85% of all salivary gland neoplasms and 60% of the benign tumours of the parotid gland. They are most frequently located in the superficial parotid lobe lateral to the facial nerve.¹⁻⁵ PAs are less common in the minor salivary glands, and rarely occur at others sites of the head and neck region (intraosseous,

lacrimal gland, chest). Tumours range in size from a few millimeters to several centimeters and are capable of reaching giant proportions in the major salivary glands, especially at the parotid.⁶

The surgical treatment of a PA has been the subject of many discussions, mainly because of the risks of facial nerve injury and tumour recurrence.^{7,8} The two conventional goals of parotid surgery for benign tumours are the removal of the lesion with a clear margin and preservation of the facial nerve branches.⁹ Therefore, the effective treatment for PA is surgical excision of the tumour by local excision with 0.5 to 1 cm margins.⁶ Through the years, the surgical technique of PA excision has shifted from simple enucleation with high recurrence rates to superficial or total parotidectomy with less recurrences,^{10,11} which are otherwise often related to the incomplete excision, intra-operative

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tumour spillage or capsule rupture with the dissemination of tumour cells.¹²⁻¹⁴ However, even with avoidance of these, the reported incidence of recurrence is up to 5%.^{6,7} According to other reports from literature, additional risk factors for tumour recurrence include age, gender, tumour location and histological tumour characteristics.¹⁵⁻¹⁷

Although superficial parotidectomy (SP) as the procedure is associated with complications including facial nerve injuries and Frey syndrome, it is still currently the golden standard of treatment for benign parotid tumours.¹⁸ Superficial or total parotidectomy involve the resection of a considerable amount of normal parotid tissue with dissection of the facial nerve, causing facial nerve injury and the loss of parotid function.⁷ Thus, SP ensures lower incidence of tumour recurrence than enucleation, but it can cause facial nerve dysfunction that can appear as paralysis (complete loss of function) or paresis (partial loss of function).^{1,19}

This observations in order to avoid the risks and preserve part of the superficial lobe of the parotid gland, led to adoption of less invasive surgical techniques, such as partial parotidectomy and extracapsular dissection (ED).^{7,20-23} This involves the removal of less parotid tissue and dissection of fewer facial nerve branches, resulting in fewer complications and a recurrence rate comparable to SP.^{12,22-25}

We hypothesized that a minimally invasive surgical technique, such as surgical tumour extirpation, would result in lower recurrence rate comparable with that of SP. The aim of our study was to investigate and compare tumour recurrence rates and facial nerve injury rates after surgical removal of PA according to the treatment procedure, namely SP vs. tumour extirpation. We want to answer an important question; is it worth to perform SP, when tumour extirpation method is possibly more useful and less damaging for facial nerve, and there is no difference in recurrence rates after 5 years of follow-up between the two methods.

Materials and methods

Study design

Study was conducted as a retrospective analysis of cohort of patients from our tertiary Department of Maxillofacial Surgery in Clinical University Centre of Kosovo from year 2005 till

2017, 12 years of data timeline, on patients undergoing different surgical procedures (SP, total parotidectomy, surgical extirpation or surgical excision) with dissection of the facial nerve for PA located in the area of the salivary glands. The research has been conducted in full accordance with the Declaration of Helsinki on medical protocols and ethics. Institutional ethical review board of Medical faculty in Prishtina approved the study. Patients did not need to give the consent of participation, since data were obtained from our archive database.

Data collection

We included patients of all ages (children and adults), who underwent surgery for PAs, and were followed up for 5 years. Preoperatively, the diagnosis of PA was established in all cases by histology. All surgical procedures met two conditions: removal of the superficial lobe and dissection of the facial nerve. The following pre-operative demographic and clinical data were included: age and sex of patients, location of the tumour and type of the surgical procedure. Postoperative complications such as facial paralysis and tumour recurrence were prospectively recorded by one of the authors in follow-up visits through 5 years.

Outcome parameters

The primary outcome variable was the occurrence of postoperative complication such as facial nerve injury, which was diagnosed as facial paralysis. The secondary outcome variable was tumour recurrence through 5 years of follow-up. Demographic characteristics (age and gender), clinical history, preoperative and postoperative histopathologic findings were obtained from retrospective analysis of the medical records.

Statistical analysis

The collected data were analysed by Statistical Package of Social Sciences SPSS 21 (IBM, New York, USA). Age as the descriptive variable was expressed as mean \pm standard deviation and as was normally distributed compared by the use of the independent t-test. Qualitative variables were compared by Pearson's chi square test according to the type of variable. The major independent variables were

SP and surgical extirpation, and the main outcome parameters were diagnosis of facial nerve injury and tumour recurrence. Odds ratios as predictive values for tumour recurrence were calculated by logistic regression. Statistical significance for all tests was set at $p < 0.05$.

Results

From 2005 till 2017 we have surgically treated 161 cases of PAs from different salivary glands. All cases were analysed through 5 years of follow-up after surgical removal of the tumour.

Study has included 79 men and 82 women, with the male-to-female ratio 1:1.04. The mean age of patients was 47.9 ± 19.5 years. Distribution of cancers by anatomical regions/locations was different and is presented in Table 1. The most frequently tumours were found at parotid gland in 111 (68.9%) cases and followed by palate region in 36 (22.4%) cases.

According to the surgical procedures, most common procedure was surgical extirpation in 112 (69.6%) of cases, followed by SP in 32 (19.9%) of cases and then surgical excision. Total parotidectomy was performed in only 4 cases.

Recurrence of tumour was detected in 7 cases: Facial nerve injury was diagnosed as facial paralysis was detected in 4 patients (Table 1).

Analyses according to the gender showed no statistical differences between males and females (Table 2). Men were older, facial nerve injury was detected in 3 male patients and only 1 female, but the differences were not statistically significant. Distribution of tumour recurrences was approximately equal for both genders.

Logistic regression for evaluation of risk factors for tumour recurrence showed no statistical significance for all tested parameters (Table 3). However, when taking into consideration all tested parameters, patients with tumour recurrence were older when compared to mean age of patients with no tumour recurrences. Total parotidectomy showed 25% tumour recurrence rates, which was higher compared to other techniques, but there was no statistically significant difference among techniques.

Patients with facial nerve injuries were older, when compared to the mean age of patients with no facial paralysis, but the difference was not statistically confirmed (Table

4). Moreover, all patients with facial paralysis underwent total parotidectomy, which might have contributed to facial paralysis as surgical procedure. When comparing SP vs. surgical extirpation, no difference was observed between the two methods, also due to the reason that no nerve injuries were detected in these patients.

| N=161 | |
|---------------------------|-----------------|
| Gender | |
| M/F | 79/82 |
| Age [years] | 47.9 ± 19.5 |
| Salivary gland | |
| Buccal | 1 (0.6%) |
| Labial | 1 (0.6%) |
| Parotid | 111 (68.9%) |
| Submandibular | 11 (6.8%) |
| (Sub)lingual | 1 (0.6%) |
| Palate | 36 (22.4%) |
| Operation | |
| Superficial parotidectomy | 32 (19.9%) |
| Total parotidectomy | 4 (2.5%) |
| Surgical extirpation | 112 (69.6%) |
| Surgical excision | 13 (8.1%) |
| Tumour recurrence | 7 (4.3%) |
| Facial nerve injury | 4 (2.5%) |

Table 1. Basic characteristics of patients with PA

| | Male (N=79) | Female (N=82) | p-value |
|---------------------------|-----------------|------------------|---------|
| Age [years] | 50.6 ± 23.5 | 45.3 ± 14.2 | 0.090 |
| Salivary gland | | | 0.145 |
| Buccal | 1 (1.6%) | 0 | |
| Labial | 0 | 1 (0.9%) | |
| Parotid | 59 (72.3%) | 52 (53.5%) | |
| Submandibular | 7 (10.9%) | 4 (11.4%) | |
| (Sub)lingual | 0 (2.3%) | 1 (3.5%) | |
| Palate | 12 (12.5%) | 24 (30.7%) | |
| Operation | | | 0.093 |
| Superficial parotidectomy | 13 (17.2%) | 19 (23.2%) | |
| Total parotidectomy | 3 (7.8%) | 1 (18.4%) | |
| Surgical extirpation | 60 (60.9%) | 52 (57.0%) | |
| Surgical excision | 3 (14.1%) | 10 (4.4%) | |
| Tumour recurrence | 3 (5.5%) | 4 (7.9%) | 0.737 |
| Facial nerve injury | 3 (3.9%) | 1 (0.9%) | 0.372 |

Table 2. Characteristics of patients according to the gender.

| | Tumour recurrence | | Recurrence rates | B value | OR (95% CI) | p-value |
|---------------------------|-------------------|-----------|------------------|-----------|----------------------|---------|
| | No (N=154) | Yes (N=7) | | | | |
| Age | 47.4±19.5 | 58.9±15.2 | / | 0.018 | 1.018 (0.993-1.043) | 0.158 |
| Gender M/F | 76/78 | 3/4 | 3.8%/4.9% | -0.262 | 0.770 (0.167-3.554) | 0.737 |
| Salivary gland | | | | -0.352 | 0.703 (0.261-1.895) | 0.487 |
| Buccal | 1 (0.6%) | 0 | / | / | | |
| Labial | 1 (0.6%) | 0 | / | / | | |
| Parotid | 105 (68.2%) | 6 (85.7%) | 5.4% | / | | |
| Submandibular | 11 (7.1%) | 0 | / | / | | |
| Palate | 35 (22.7%) | 1 (14.3%) | 2.8% | / | | |
| (Sub)lingual | 1 (0.6%) | 0 | / | / | | |
| Operation | | | | -0.227 | 0.758 (0.347-1.655) | 0.486 |
| Superficial parotidectomy | 30 (19.5%) | 2 (28.6%) | 6.3% | Reference | | |
| Total parotidectomy | 3 (1.9%) | 1 (14.3%) | 25.0% | -0.223 | 0.800 (0.066-9.669) | 0.861 |
| Surgical extirpation | 109 (70.8%) | 3 (42.9%) | 2.7% | 1.386 | 4.000 (0.190-84.199) | 0.373 |
| Surgical excision | 12 (7.8%) | 1 (14.3%) | 7.7% | -1.108 | 0.330 (0.032-3.430) | 0.354 |

Table 3. Risk factors for the recurrence of tumours.

Case of carcinoma ex pleomorphic adenoma

Among 161 patients one case of transformation of pleomorphic adenoma in malignant carcinoma ex pleomorphic adenoma was encountered. Salivary gland PA was diagnosed in 2006 in a 67-year old male patient. The tumour was found at parotid salivary gland and was removed by total parotidectomy with neck dissection. After 5 years of follow-up no tumour recurrence was observed, but histologic examination confirmed carcinoma ex adenoma pleomorpha but with no metastases. Patients suffered of injury of facial nerve branches with facial paralysis.

Discussion

Although surgical excision is the treatment of choice for benign parotid tumours, the major concerns are complications such as facial nerve injury and tumour recurrence. Several previous studies have compared various aspects of surgical methods for the excision of parotid tumours^{1, 26}, but the aim of current study was to compare complication rates such as recurrence rates and facial nerve injury rates in patients, who underwent different surgical procedures of PA removal, namely we wanted to compare SP vs. surgical extirpation. In our centre

we hypothesized that a minimally invasive surgical technique, such as surgical tumour extirpation, would result in lower recurrence rates comparable with that of SP. Thus we questioned ourselves is it worth to perform SP, when tumour extirpation method is possibly more useful and less damaging for facial nerve and there is no difference in recurrence rates after 5 years of follow-up between the two methods. According to the surgical procedures, most frequent procedure was surgical extirpation in 112 (69.6%) of cases, followed by SP in 32 (19.9%) of cases and then surgical excision. Total parotidectomy was performed in only 4 cases. In a study of 161 patients, who underwent different surgical procedures, 7 cases (4.3%) of tumour recurrences and 4 cases (2.5%) of facial nerve injuries, diagnosed as facial paralysis, have been detected.

In our study the rates of tumour recurrences for SP (6.3%), surgical extirpation (2.7%) and other two groups were not significantly different (p=0.486). We would like to point out that 25% of all total parotidectomies showed tumour recurrence through 5 years of follow-up and only 2.7% with tumour extirpation. However, interpretation of these results should be taken with extreme caution, since the sample sizes in groups were very small and not comparable. In the past, the correlation between surgical technique and recurrence rates led to a

change of primary treatment from tumour enucleation to parotidectomy. However, the total reported recurrence rates, as also shown by our analysis, are still as high as 5% despite presumed adequate resection.¹⁶ While SP is the surgical treatment of golden standard for PA, the extent of surgical resection is in question because on one hand complete extirpation of tumour is desired; however, the risk of facial nerve injury increases with total parotidectomy. Moreover, in such case partial SP could contribute to preservation of facial nerve branches, but to the other hand might enable the tumour recurrence due to incomplete resection.¹²⁻¹⁴ Transient or permanent facial nerve paralysis is reported up to 90 and 40%, respectively and is often attributed to the initial superficial or total parotidectomy.¹⁶

Furthermore, facial nerve injury was reported as the main factor affecting patients' post-operative quality of life.²⁷ We performed SP in 19.9% of patients. In our series the overall postoperative facial nerve injury rate was 2.5% but none with SP. All cases underwent total parotidectomy. For instance in another study, Witt²² observed facial nerve dysfunction in 26% of cases after SP. By contrast, this author found permanent facial paralysis in 1.9% of patients after SP. The statistical data collected in the study are in agreement with those reported in the literature and confirm lower incidence of facial nerve injuries, but we did not find significantly more rates after SP than after surgical extirpation. Different rates could result from surgical manipulation that causes a nerve injury, and are proportional to the length of time the nerve is exposed during the surgery. Cristofaro et al.⁹ showed permanent facial nerve injury rates in 2.2% after SP, and Papadogeorgakis² reported 4% rate after SP.

Several previous studies have compared SP and partial SP procedures. Kilvuz et al.¹⁸ found that the overall complication rate in the partial SP group (12.2%) was significantly lower than in the SP group (21.6%; $p=0.031$). These findings indicate that partial SP is a less morbid procedure and is associated with fewer complications with a recurrence rate comparable with that of SP. Furthermore, similar was found in another study by Zhang et al.²⁸ Thus they concluded that partial SP should be the surgical treatment of choice for primary benign parotid gland tumours smaller than 2 cm located in the

superficial lobe. The same was also observed by Papadogeorgakis et al.² who concluded that partial PS was an organ-preserving procedure with a similar recurrence rate to that of SP. The author found the procedure to be simpler, less time-consuming, and more cost-effective than SP, with a lower risk of facial nerve injury because fewer nerve branches were dissected.

PAs most frequently occur in patients between the ages of 40 and 50 years, and in women than in men.¹⁻³ Studies in the literature indicate that minor salivary gland tumours are more common in females with male-to-female ratio ranging from 1:1.2 to 1:1.5.²⁹ Our findings showed that patients' characteristics did not contribute significantly to recurrence rates. Although the percentage of appearance of facial nerve injury was 2.5%, in the literature this varies from 10% to 70% for transient involvement, and from 0 to 19% for definitive involvement.^{1,30-33} Although the majority of tumours were located in the parotid gland area (68.9%), we did not find a statistical relationship between tumour recurrence and dysfunction of the facial nerves. Our results suggest that the location of tumour was not a risk factor that could worsen treatment outcomes. According to previous studies, several other factors have been associated with a higher incidence of facial nerve injuries^{1,22,30,34-38} extent and type of surgical procedure (higher incidence in total parotidectomy and greater resection of glandular tissue), age, surgery duration, tumour histopathology, tumour size (greater incidence in larger tumours), location (higher incidence in deep lobe tumours) and previous parotid surgery (higher incidence in cases of recurrent disease. Unfortunately, we did not find any of these associations (age, gender, location), or have not tested them at all (histopathology, surgery duration, tumour size).

Some previous data report an overall malignant transformation rate of around 4% over 15 years of follow-up (0–23%).^{16,17} This number cannot be ignored and should be taken into consideration when planning surgery. The risk of malignant transformation increases with time and with the number of recurrences. In the current analysis of 161 cases, only one case of malignant transformation was detected contributing to rate of 0.6%. Low percent in our study could be due to a low number of cases or short follow-up period.

Among the main limitations of our study, we must mention the lack of a control group and the relatively small group sample sizes, since it was a single centre study, so the results should be interpreted with extreme caution. Finally, in future studies, other procedures for treatment of pleomorphic adenoma, such as extracapsular dissection or partial parotidectomy, could be considered for comparisons and, we should follow-up our patients for at least 10-15 years, to evaluate the rates with greater confidence. The main limitation of our study is that it was a single centre study; thus the findings may not be generalizable to other institutions and should be interpreted with caution. Moreover, we did not include several tumour and surgical procedure characteristics.

Conclusions

In our centre relatively low rates of tumour recurrences and facial nerve injuries were detected. Total parotidectomy was detected as the only potential risk factor for facial nerve injury. With surgical extirpation as non-radical procedure no cases with facial nerve injuries and 3 cases of tumour recurrences were discovered, on the other hand also with SP no cases of facial nerve injuries were discovered and the cases with recurrences were not so high after 5 years of follow-up. So our initial question; should we apply more radical surgical procedure like SP (with higher risk of injury of facial nerve branches but less risk for recurrence), or should we use surgical extirpation (with low risk of facial nerve injury but higher risk for recurrence) as a technique of choice? According to our results, there were no differences between the techniques, but we would suggest extirpation as much simpler, less time-consuming, and more cost-effective procedure than SP, that is more organ-preserving procedure with a lower risk of facial nerve injury. However, these findings should be interpreted with caution, since we have only detected facial nerve injury in 4 and tumour recurrences in 7 cases through our follow-up period of 5 years; thus the long-term effects and benefits of techniques remain largely unknown. Studies with longer follow-up periods are necessary to fully understand the long-term outcomes.

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Declaration of Interest

All authors declare that they have no conflict of interest.

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