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Evaluation of the Concordance of Cytological Findings Based on the Milan System with Histopathological Findings in Salivary Gland Tumors

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Abstract

Background: The goal of the Milan System for Reporting Salivary Gland Cytopathology (MSRSGC) is to standardize the reporting of salivary gland cytology and guide treatment decisions. Considering the newness of this system and the need for more studies in this regard, the aim of this study was to evaluate the concordance of cytological findings based on the Milan system with histological findings in salivary gland masses.

Aim: evaluating salivary gland tumors' cytological findings of Milan system with histopathological findings**.**

Methods: This diagnostic study was conducted on 94 patients with salivary gland masses were referred to the pathology department of Imam Hossein hospital in 2022. FNA was performed for all patients and cytological classification was done based on the latest classification of the Milan system. Cytological findings were compared with histological findings.

Results: In this study 10.6% were diagnosed as non-neoplastic, 18.1% with AUS, 37.2% benign neoplasm, 20.2% with SUMP, 5.3% suspicious for malignancy, and 8.5% were diagnosed as malignant. In the pathology results, 18.1% of patients were non-neoplastic, 56.4% had benign neoplasm, and 25.5% had malignant mass. The agreement coefficient between the two methods based on the Kappa coefficient was 40%, which indicates a relatively good agreement. The correlation coefficient between the two methods was 0.70.

Conclusion: It is concluded that there is a relatively good agreement between the Milan system in the cytology of salivary gland neoplasms with pathology findings.

Conflicts of Interest: The Authors declare no conflicts of interest.
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Introduction

Salivary gland masses are causes of 3% to 6% of all head and neck masses (1, 2). Currently, a multimodal approach is used for the initial diagnosis of salivary gland masses, which includes imaging studies such as ultrasound and/or MRI for lesion localization followed by fine needle aspiration (FNA) cytology for typing and classification assessment (3, 4). FNA cytology is a sensitive (54-98%) and specific (98-88%) method for diagnosing

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salivary gland masses that allows appropriate preoperative management. However, the heterogeneity of cytomorphological features and the overlapping features between different types of masses lead to disagreement among pathologist for cytological diagnosis (5, 6). In line with the Bethesda system for reporting thyroid and cervical cytopathology, a user-friendly and internationally accepted category-based system for the cytological diagnosis of salivary gland masses has been devised. The Milan System for Reporting Salivary Gland Cytopathology (MSRSGC) includes a six-category diagnostic scheme with risk assessment points of risk for malignancy (ROM) and a brief management plan for each diagnostic category (7-9). MSRSGC has been evaluated by a few authors, demonstrating the usefulness of this system in reporting salivary gland masses (10-12). To date, there are few studies that demonstrate the utility and repeatability of the MSRSGC system. Therefore, a variable ROM has been shown for each of the six categories of MSRSGC (10, 13-15). Considering the need for more studies on the validity of using the Milan system and the importance of accurate classification of patients with salivary gland masses to evaluate their risk of malignancy, in this study we aimed to examine the concordance of cytological findings based on Milan system with histological findings in salivary gland masses.

Methods

This is a diagnostic study that was performed on patients who were referred to pathology ward of Imam Hossein hospital (Tehran-Iran) with a salivary gland mass with clinical suspicion of tumor by an otolaryngologist for performing fine needle aspiration (FNA) during 2022.

All patients with salivary gland masses with clinical suspicious to tumor were referred to the Pathology Department of Imam Hossein Hospital in 2020 and underwent FNA. An expert pathologist performed FNA with a 24-gauge needle and the smears were fixed in both wet and air-dry methods.

If possible, cell block samples were prepared from the clotted and solid part of the sample. The slides were stained with H&E (Hematoxylin & Eosin) and Giemsa methods. The samples were checked for adequacy and the samples with few cells and cystic masses (except mucinous cysts) were excluded from the study. Then, the cytological classification was done based on the latest classification of the Milan system (12) as follows and the percentage of malignant risk was determined in each group. Also, cytological findings were matched with histological findings.

The Milan system for reporting salivary gland cytopathology: implied risk of malignancy and recommended clinical management (12).

Table1. The Milan system for reporting salivary gland cytopathology

Diagnostic category	Risk of malignancy	Management
I. Non-diagnostic	25	Clinical and radiologic correlation/repeat FNAC
II. Non-neoplastic	10	Clinical follow-up and radiological correlation
III. Atypia of undetermined significance (AUS)	20	Repeat FNAC or surgery
IV. Neoplasm		
Neoplasm: Benign	<5	Surgery or clinical follow-up
Neoplasm: Salivary gland neoplasm of uncertain malignant potential (SUMP)	35	Surgery
V. Suspicious for malignancy (SM)	60	Surgery
VI. Malignant	90	Surgery

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The sampling method was available.

Based on the confidence level of 95% and the reported percentage of 14% in the study and using the maximum acceptable error value of 0.07, the sample size was estimated to be 94 people.

Statistical analysis

Frequency and percentage were used to describe the data. Fisher's exact test was used to compare qualitative variables, and kappa agreement coefficient and correlation coefficient were calculated to show the degree of agreement between the two diagnostic methods. All analyzes were done by SPSS 26.0 statistical software. P-value less than 0.05 was considered statistically significant.

Results

Cytology results were assessed for 94 patients. The related results are seen in Table 2.

Table2. Frequency of diagnosis of patients based on cytology

Cytology	N	%
Non-neoplastic	10	10.6
AUS	17	18.1
Benign Neoplasm	35	37.2
SUMP Neoplasm	19	20.2
Suspicious for Malignancy	5	5.3
Malignant	8	8.5

The pathology results of the patients were also evaluated. Seventeen patients (18.1%) were diagnosed as non-neoplastic, 53 patients (56.4%) were diagnosed as benign neoplasm (Fig. 1 benign neoplasm), and 24 patients (25.5%) were diagnosed as malignant. In Table 3, we evaluated and compared cytologic result and pathologic results of masses.

Table3. Evaluation and comparing results of cytology and pathology of masses

		Cytology					
		Non-neoplastic	**AUS**	**Benign Neoplasm**	**SUMP Neoplasm**	**Suspicious for Malignancy**	**Malignant**
Pathology	**Non-neoplastic**	9 (90.0%)	6 (35.3%)	0 (0.0%)	2 (10.5%)	0 (0.0%)	0 (0.0%)
	Benign Neoplasm	1 (10.0%)	7 (41.2%)	35 (100.0%)	10 (52.6%)	0 (0.0%)	0 (0.0%)
	Malignant	0 (0.0%)	4 (23.5%)	0 (0.0%)	7 (36.8%)	5 (100.0%)	8 (100.0%)

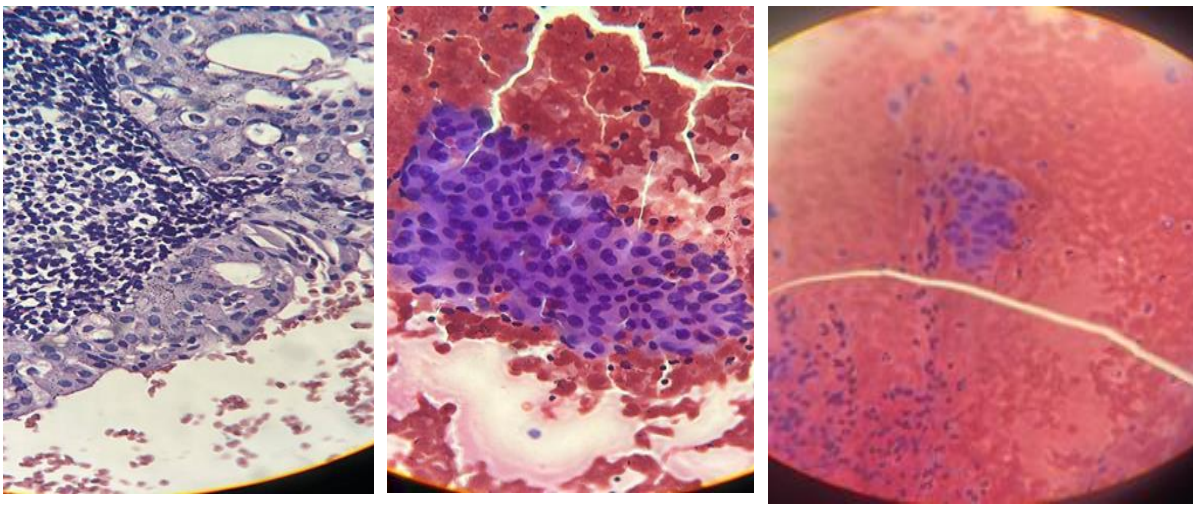

Figure1. Neoplasm (benign).

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Based on the data in Table 3, it can be resulted that there was a relatively good agreement between the two methods. The agreement between the two methods (cytology and histopathology) based on the Kappa agreement coefficient was equal to 40% with a significant P-value less than 0.001, which indicates a relatively good agreement with statistical significance. The correlation coefficient between the two methods was 0.70 (P-value<0.001).

Discussion

In this diagnostic study, which was conducted with the aim of determining the concordance of cytological findings based on the Milan system with histological findings in salivary gland tumors, the cytology results of 94 patients were evaluated. Ten specimens (10.6%) were diagnosed as non-neoplastic, 17 (18.1%) AUS, 35 (37.2%) benign neoplasm, 19 (20.2%) SUMP neoplasm, 5 (5.3%) suspicious for malignancy, and 8 (8.5%) were diagnosis as malignant masses. The pathology results of the patients were also evaluated and it was seen that 17 (18.1%) were diagnosed as non-neoplastic, 53 (56.4%) benign neoplasm, and 24 (25.5%) were diagnosed as malignant. The agreement between the two methods was 40%, which indicates a relatively good agreement. The correlation coefficient between the two methods was 0.70.

In the study of Kala et al., 172 cases were assessed and the distribution of cases in different categories was as follows: non-diagnostic (6.1%), non-neoplastic (38.2%), atypia with uncertain significance (2.7%), benign neoplasm (33.4%), salivary gland neoplasm with unknown potential of malignancy (2.0%), suspected malignancy (2.4%), and malignant (15%). Overall, for MSRSGC, sensitivity was 83.33%, specificity was 98.31%, positive predictive value was 95.74%, and negative predictive value was 92.80%. It was concluded that MSRSGC limits the possibility of false negatives and false positives results (12). Our findings were different from the findings of Kala et al. This difference can be caused by the difference in the sample size of the two studies. Also, genetic and environmental differences are effective on the occurrence of salivary gland masses (16, 17), and this issue can also be one of the factors influencing the difference in the results of two studies, because the current study was conducted on the Iranian population but Kala et al.'s study was conducted on the Indian population. In the current study, it was seen that the correlation coefficient between the two methods of pathology and cytology based on the Milan system was 0.70, which indicates the good agreement of this method with pathology, which confirms the conclusion of Kala et al's study.

In the study by Isgor et al., 85 cases had surgical follow-up and MSRSGC was as follows: non-diagnostic in 7 specimens (8.2%), non-neoplastic in 3 (3.5%), atypia of undetermined significance (AUS) in 9 (10.5%), benign neoplasm in 43 specimens (50.5%), salivary gland neoplasm with unknown malignant potential in 7 specimens (8.2%), suspected malignancy in 10 specimens (11.7%), and malignancy in 6 specimens (7%). The findings of this study were not significantly different from our study and this issue may be due to the close sample size of the two studies (18).

In Torres et al.'s study, 354 FNA samples were evaluated and the results were as following: non-diagnostic (ND) 17.0%, non-neoplastic (NN) 1.4%, atypia of undetermined significance (AUS) 11.0%, benign neoplasm (BN) 49.4%, salivary gland neoplasms with unknown malignant potential (SUMP) 10.7%, suspected malignant (SM) 3.4%, and malignant (M) 7.1%. The diagnostic accuracy for separating benign from malignant neoplasms was 96%. Histological correlation with cytology yielded a false-negative rate of 2.7%, a false-positive rate of 10.5%, a PPV of 89%, an NPV of 97%, a sensitivity of 87%, and a specificity of 98% (19). In the present study, it

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was seen that out of 94 specimens, 10 (10.6%) were diagnosed with non-neoplastic, 17 (18.1%) were diagnosed with AUS, 35 (37.2%) were diagnosed with benign neoplasm, 19 (20.2%) were SUMP, 5 (5.3%) were suspicious for malignancy, and 8 (8.5%) were malignant. The correlation coefficient between the two methods was 0.70. In the current study, the sensitivity and characteristics of other parameters of diagnostic power were not investigated, but the correlation coefficient of the two tests was 0.70, which indicates a suitable correlation between the two tests, and from this point of view, the results were almost similar to Torres et al.'s study and shows the acceptable value of the Milan method for the cytology evaluation of salivary gland neoplasms.

Cormier and Agarwal in 2022 evaluated the utility and performance of MSRSGC, focusing on the cytomorphology of masses diagnosed as atypia of undetermined significance (AUS) and salivary gland neoplasm of undetermined malignant potential (SUMP), and found that sensitivity, specificity, Positive predictive value, and negative predictive value were each 100%. The conclusion was that the sensitivity and specificity of 100% support the compatibility of MSRSGC in the salivary gland cytology reporting system (20). The results of this study were different from the current study, which could be due to the difference in the implementation method; because the current study was performed on patients with all types of salivary gland neoplasm, but the study by Cormier and Agarwal were done on AUS and SUMP types. Although, we did not evaluate the sensitivity and specificity, but we observed that out of 17 patients who had AUS before surgery, 6 (35.3%) were non-neoplastic, 7 (41.2%) had benign neoplasm, and 4 (23.5%) were malignant, and out of 19 patients who were diagnosed with SUMP before surgery, 2 (10.5 %) were non-neoplastic pathology, 10 (52.6%) had benign neoplasm, and 7 (36.8%) had malignant masses. Based on these results, it does not seem that 100% sensitivity and specificity can be imagined for this test. But, further studies should be done for evaluation of diagnostic power of MSRSGC in salivary gland masses.

Conclusion

It is concluded that the Milan system in the cytologic classification of salivary gland neoplasms has a relatively good agreement with the pathology findings, which shows the applicability of this system in studies and in the clinic to evaluate salivary gland masses, especially in forms of malignant masses. Based on our findings, the agreement and correlation between the Milan system and pathology were 40% and 0.70, respectively.

It is suggested that similar studies be conducted with a larger statistical population in the future, and in addition to evaluating the correlation coefficient and agreement, sensitivity, specificity and other parameters related to the diagnostic power of cytology with the Milan system should be evaluated based on pathology.

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Conflicts of Interest

The authors declare no conflicts of interest.

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Ethics

This study was approved by ethical committee of Shahid Beheshti medical university (IR.SBMU.MSP.REC.1400.174).

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