Assessing the Usefulness of Salivary Gland Fine Needle Aspiration Cytology as Diagnostic Aid for Salivary gland Malignancy

Sir,

The main goal of any fine needle aspiration cytopathologic (FNAC) exercise is to rule out malignancy and formulate future course of actions. The diagnostic accuracy of FNAC to identify salivary gland (SG) malignancy (SGM) as compared to gold standard histopathology has been debated in systematic review and meta-analysis.[1] In this regard we assessed the probabilistic performance validity of FNAC for SGM and would like to share the interesting results for wider clinical translation.

The uncertainties of diagnostic tests can be explained by the parameters such as sensitivity (Sn), specificity (Sp), positive predictive value (PPV), negative predictive value (NPV), likelihood ratio of a positive and negative tests (LR +ve, LR −ve). Prior to performing FNAC, the dentist is expected to estimate the likelihood of a possible SGM "pretest probability (*P*)". After the FNAC, new additional information is contributed to the likelihood of original working diagnosis, called "post-test probability (*P*')". Bayes theorem provides an excellent aid for this probabilistic approach.[2,3]

To study the accuracy of FNAC for diagnosing SGM, we analyzed collated data from a previous published, exhaustive, systematic review that had employed an extensive search, stringent inclusion and exclusion criteria for this purpose.[4] The collated details of Collela *et al*., were obtained. The diagnostic tests were calculated using formulae.[2,3,5] The PPV and NPV also were identified as a function of Sn, Sp and the *P* by using the formulae.[2]

$$\text{PPV} = \frac{Sn \times p}{Sn \times p + (1-Sp)(1-P)}$$

$$\text{NPV} = \frac{Sp \times (1-P)}{Sp \times (1-P) + (1-Sn) \times P}$$

The PPV and NPV as a function of *P* (in increasing order) were then tabulated by increasing the *P* in the formula. The pre-test odds and post-test odds were calculated as given by the Bayes Theorem using *P*.[2] From this, *P*' was calculated.

Of the 1913 cases considered, FNAC accurately identified SGM in 387 (20.23%) instances and missed in 97 (5.07%) instances. FNAC also identified non-SGM in 1,401 (73.23%) instances and over-diagnosed in 28 (1.46%) instances.[5] The Sn and Sp were calculated as 0.8 and 0.98 respectively. LR +ve was calculated as 40 and LR −ve was calculated as 0.2.

The reported global annual incidence of SGM is 2.6/100,000 (or 0.000026) populations.[6] With this prevalence and using collated data from Colella *et al*., studies the PPV and NPV were derived as 0.1% and 100%. PPV reflects proportion of patients with SGM who were correctly diagnosed while high NPV indicate that a proportion of patients with negative result who were correctly diagnosed. The low prevalence of SGM, the degree of accuracy, trainings of cytopathologist, staining clarity, FNAC procedural accuracy and necrotic element could have contributed to these results.

When the *P* was increased to 50%, PPV% and NPV% was 97.6% and 83.0% respectively. Like all other diagnostic tests, with increasing pre-test probability the reliability of FNAC also increased. We increased the *P* up to 20%, identified the PPV%, NPV%, *P* [Figure 1 and Table 1] and then applied the Bayes theorem to identify the post test odds. From this *P*' was

Table 1: Calculating post-test result (positive and negative) from pretest probability

Pretest probability	Pretest odds	Post-test positive result		Post-test negative result	
		Odds	Probability	Odds	Probability
1	0.01	0.41	0.29	0.002	0.002
3	0.03	1.26	0.56	0.006	0.006
5	0.05	2.15	0.68	0.011	0.01
10	0.11	4.53	0.82	0.022	0.02
20	0.25	10.2	0.91	0.05	0.048
50	1	40.8	0.97	0.2	0.167

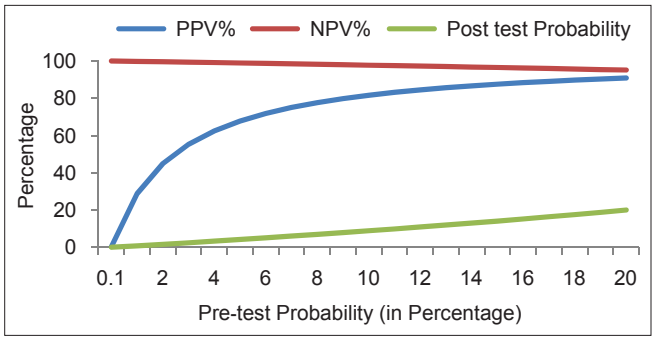

Figure 1: Positive predictive value, negative predictive value and post test probability as a function of pretest probability

calculated and plotted the graph. From the graph, we understood that when *P* was about 2.5%, the PPV% was about 50% and at 20% it was about 90%. On the contrary, the NPV% gradually decreases as the *P* increases. This indicates that FNAC cannot be used as a better screening tool and chance of false diagnosis is always present. On applying Bayes theorem, it was identified that when the *P* was about 10%, the *P*' was 9.91 indicating that the FNAC did not contribute much to the post-test scenario. In other terms, when the *P* was 1 in 10, after performing FNAC, *P*' was 9.91 indicating that the FNAC has not effectively contributed to *P*'. When the *P* was made 50%, indicating a very strong suspicion of SGM, *P*' was calculated to be 83% indicating that even after a negative FNAC, patient still has a 1 in 6 chance of having SGM.

The slowly increasing value of PPV% and falling NPV% in Figure 1 with increase of clinical suspicion (*P*) as well as the fact that with increase of *P*, the non-dramatic change in *P*' level indicates that SGM FNAC need to be reassessed using biopsies. Though the Sn and Sp are derived from several case series selected after careful and stringent criteria's, there are several factors that limit the Sn and Sp.[4] These have been attributed to the fact that SGM have complex morphology, with overlapping features between different pathological entities. This significantly influences the diagnostic precision. Clinically, SG swelling that presents as large swelling are usually pleomorphic adenoma. Paradoxically SGM lesions are often small.[4] Finally, a certain number of SGT have atypical cytological characteristics and capsular infiltration which cannot be assessed using FNAC.

A negative result of an FNAC, though indicates a relatively the absence of the disease at a higher odds, the high NPV% makes FNAC an excellent tool to rule in the disease. However due to a comparatively low PPV, chance of missing malignancy remains high, a trend discussed in literature.[1,4] Understanding the mathematics behind the FNAC testing allows the clinicians effectively, as well as critically appraise the utility of salivary FNAC in clinical practice.

It has been reported that the overall SG FNAC's performance variability is too wide to formulate general guidelines regarding its usefulness for SGM.[1] In addition to many factors, the diagnostic performance occupies an important role. Heterogeneity of accuracy, bias and random variations also appear to influence SG FNAC outcome.[1] Our study could not provide reliable evidence for FNAC as a main diagnostic modality for SGM. However, it may be rendered useful when coupled with advanced technique such as ultrasound guided FNACs and immunocytochemistry. The present study indicates that salivary FNACs are highly beneficial in specialized settings where the pretest probability (*P*) is assessed to be above 10%, this test will be of clinical value. To increase the *P*, careful, detailed history, accuracy imaging modalities, palpatory findings along with an efficient diagnostic algorithm will be helpful. Probabilistic approach has been tried in several cytological studies of pathologies with high degree of effectiveness.[7] To the best of our knowledge probabilistic approach to SG cytology was done for the first time and results presented.

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References

1. Schmidt RL, Hall BJ, Wilson AR, Layfield LJ. A Systematic review and meta-analysis of the diagnostic accuracy of fine-needle aspiration cytology for parotid gland lesions. Am J Clin Pathol 2011;136:45-59.
2. Akobeng AK. Understanding diagnostic tests 2: Likelihood ratios, pre- and post-test probabilities and their use in clinical practice. Acta Pædiatrica 2006;96:487-91.
3. Deeks JJ, Altman DG. Diagnostic tests 4: Likelihood ratios. B Med J 2004;329:168-9.
4. Colella G, Cannavale R, Flamminio F, Foschini MP. Fine-needle aspiration cytology of salivary gland lesions: A Systematic review. J Oral Maxillofac Surg 2010;68:2146-53.
5. Akobeng AK. Understanding diagnostic tests 1: Sensitivity, specificity and predictive values. Acta Paediatrica 2006;96:338-41.
6. Evenson JW, Auclair P, Gnepp DR, El-Naggar. Tumours of the Salivary Glands. In: Barnes L, Eveson JW, Reichart P, Sidransky D, editors. In World Health Organization Classification of Tumours. Pathology and Genetics of Head and Neck Tumours. 1st ed. Lyon: IARC Press; 2005. p. 212-13.

7. MacIntosh RF, Merrimen JL, Barnes PJ. Application of the probablistic approach to reporting breast fine needle aspiration in Males. Acta Cytol 2008;52:530-4.

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