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Research Article

Role of Sonoelastography in Differentiating Benign and Malignant Salivary Gland Tumors: A Systematic Review and Meta Analysis

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Abstract

Objective: The goal of this systematic review is to determine the diagnostic accuracy of sonoelastography in evaluating salivary gland tumors.

Data sources: A highly sensitive search for sonoelastography and salivary gland tumors was performed through MEDLINE, Cochrane Library, ACP Journal Club, EMBASE, Health Technology assessment, and ISI web of knowledge for studies published prior to January 2013.

A manual search was performed to include additional studies from references of the retrieved articles.

Review methods: Two independent reviewers evaluated articles for eligibility. They extracted data from included studies.

The quality of included studies was evaluated by use of Quality Assessment of Diagnostic Accuracy Studies (QUADAS) questionnaire which consists of 14, four option questions (yes, no, unclear, Not Applicable (N/A)).

Forest plots for pooled estimates and summery of ROC plots for different cut-offs were produced.

Results: The literature review and manual search yielded 15 articles, 6 of which eligible to be included. A total of 348 individuals with total number of 366 salivary gland masses were evaluated. Eighty seven were malignant while, 269 were benign. Three hundred and twenty two were located in parotid gland and forty four were in sub-mandibular gland.

The summary sensitivity and specificity for the differentiation of benign and malignant salivary gland masses were 0.63 and 0.59.The summary Diagnostic OR (D OR), positive and negative LRs were 3.18, 1.63 and 0.61. The Area Under the Curve (AUC) was 0.68 (SE=0.03).

Conclusion: Sono-elastography had moderate accuracy in differentiating benign from malignant salivary gland tumors.

Keywords: Sonoelastography; Salivary gland tumors

Introduction

Salivary gland tumors count near 3% of all head and neck tumors [1] which could locate in major or minor salivary glands. The incidence rate of these tumors has been reported between 1 to 5 cases per 100000 person [1,2].

The initial imaging modality applied for salivary gland masses is sonography as it is cost-effective, non invasive and easy to apply [3].

By means of B-mode and color Doppler evaluation, echogenicity, structure, size, contour, calcification and vascularity could be examined, although previous studies demonstrated that the accuracy of these parameters for differentiating benign and malignant lesions are not satisfactory [4-6].

Elastography is a new sonographic modality which provides data regarding tissue stiffness. It provides tissue elasticity estimation by means of local compression.

Under external forces, soft tissues move more than harder ones and reflecting that malignant tissues are firmer than surrounding benign counterparts [7].

Series of previous studies had evaluated accuracy of sonoelastography in differentiating benign and malignant salivary gland tumors. Its sensitivity and specificity had been reported ranging from 41% to 75% and 47% to 91%, respectively [3,7-11].

The goal of this study was to perform a meta-analysis of published information to evaluate the overall accuracy of sonoelastography for differentiation of benign and malignant salivary gland tumors.

Materials and Methods

We searched MEDLINE, Cochrane Library, EMBASE,ACP Journal Club, Health Technology Assessment, and ISI web of

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Table 1: Characteristics of the included studies.

Author	Publication year	Mean age	Total number of patients	Male/female	Total number of masses	Malignant /Benign	Parotid/ submandibular	Method of classification
Bhatia	2010	60	61	48/13	65	6/59	57/8	Scoring system (1-4)
Dumitriu	2011	50	66	37/29	74	18/56	63/11	Scoring system (1-4)
Yerli	2012	49	46	N/A	36	8/28	30/6	Scoring system (1-4)
Wierzbicka	2012	54	43	16/27	43	10/33	43/0	Scoring system (1-5) and strain ratio
Celebi	2012	47	75	36/39	81	32/49	81/0	Scoring system (1-4)
Dumitriu	2010	50	57	N/A	57	13/44	48/9	Strain ratio

Table 2: Quality assessment of included studies.

Author	Q1 Spectm composion	Q2 Selecton criteria	Q3 Appropriate reference standard	Q4 Disease Progression bias	Q5 Partial verification bias	Q6 Differential verification bias	Q7 Incorpo-ration bias	Q8 Test execution details	Q9 Reference execution details	Q10 Test review bias	Q11 Diagnostic review bias	Q12 Clinical review bias	Q13 Intermediate results	Q14 Withdrawals
Bhatia	Yes s	yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Un clear	Un clear
Dumitru	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Un clear	Un clear	Un clear	Un clear
Yerli	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Un clear	Un clear	Yes	Un clear	Un clear
Wierzbicka	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Un clear	Un clear	Yes	Un clear	Un clear
Celebi	Yes	Yes	Yes	Un clear	Un clear	Yes	Yes	Yes	Yes	Un clear	Un clear	Yes	Un clear	Un clear
Dumitru	Yes	Yes	Yes	Un clear	Un clear	Yes	Yes	Yes	Yes	Un clear	Un clear	Yes	Un clear	Un clear

Table 3: Summary estimates of sonoelastography.

	(95%CI)
Sensitivity	0.63 (0.52-0.73)
Specificity	0.59(0.53-0.65)
Diagnostic OR (DOR)	3.18(1.86-5.44)
Positive LR	1.63(1.33-2.01)
Negative LR	0.61(0.47-0.79)

knowledge for studies published prior to December 10th, 2012 by using these search terms: "elastography", "sonoelastography", "real-time tissue elastography", "elasticity", "elastogram", "elasticity imaging techniques", "salivary gland", "neoplasm", " tumor", "carcinoma".

A manual search was performed to include additional studies from references of the retrieved articles. Two independent reviewers evaluated articles for eligibility. The criteria for eligibility were:

1. Studies evaluated diagnostic accuracy of sonoelastography in differentiating malignant and benign salivary gland tumors. Systematic review articles, narrative review articles, letter to editors and editorial articles were excluded.

2. Using appropriate reference standard test such as Fine-Needle Aspiration (FNA), histological assessment of specimens obtained by surgery or dissection.

3. Diagnostic measures on sonoelstographic evaluation results such as sensitivity, specificity, positive and negative predictive values.

Data extraction and quality assessment

Two independent reviewers extracted data from included studies. Extracted data included: first author name, study publication year, country, number of patients, number of malignant and benign salivary masses, mean patient age in each study, number of male and female patients, classification method, number of parotid or submandibular masses.

The quality of included studies was evaluated by means of Quality Assessment of Diagnostic Accuracy Studies (QUADAS) questionnaire which consists of 14, four option questions (yes, no, unclear, Not Applicable (N/A)). The same two independent reviewers evaluated the quality of studies and in discord cases, disagreement solved by consensus of reviewers.

Statistical analysis and data synthesis

Accuracy of sonoelastography method was assessed by pooled estimates of sensitivity, specificity, positive and negative predictive values, and diagnostic odds ratio. In case of homogenity, fixed-effect model applied for pooled estimate calculation and if significant heterogeneity was present, the random-effect model was used .The Cochran *Q* test was estimated to detect the heterogeneity among studies. Inconsistency (I^2) was calculated to describe the percentage of the variability attributable to heterogeneity.

Summary Receiver Operating Characteristic (SROC) curves were constructed, by means of Moses-Shapiro-Littenberg method and the Area Under the Curve (AUC) was calculated. *P* Value of <0.05 was considered significant.

Results

The chart describes the fellow of study selection in this systematic review. The literature and manual search yielded 15 articles, of which, 6 were eligible to include in this study which were published between 2010 and 2012. The studies were conducted in Poland (N=1), Romania (N=2), Turkey (N=2) and China Union (N=1).

A total of 348 individuals with total number of 366 salivary gland masses were evaluated. Eighty seven were malignant while, 269 were benign. Three hundred and twenty two were located in parotid gland and forty four were in sub-mandibular gland.

In five studies, only qualitative scoring system (in four articles scoring 1-4) was used. In one study only strain ratios applied for

classification and in remaining one study, both strain ratio and elasticity scoring system (1-5) were applied.

Four studies used 1-4 scoring system while one used 1-5 and one strain ratio.

The characteristics of included articles are listed in (Table 1).

Quality assessment of included studies

Quality of included studies was evaluated by means of QUADAS questionnaire and information is present in (Table 2).

The summary sensitivity and specificity for the differentiation of benign and malignant salivary gland masses were 0.63 and 0.59. The summary Diagnostic OR (D OR), positive and negative LRs were 3.18, 1.63 and 0.61 (Table 3).

Test of heterogeneity

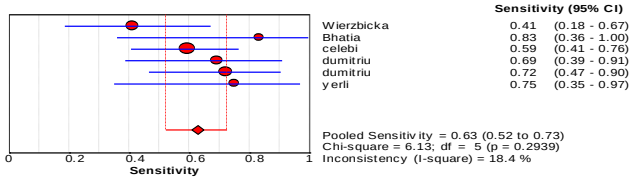
All measurements showed homogeneity (I^2<50%) in differentiating benign and malignant salivary gland masses except specificity (I^2> 50%).

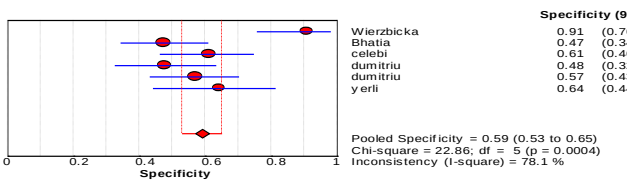
Discussion

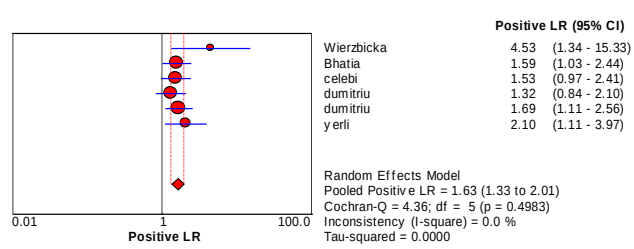
This is the first systematic review evaluating diagnostic accuracy of sonoelastography in differentiating benign and malignant salivary gland tumors.

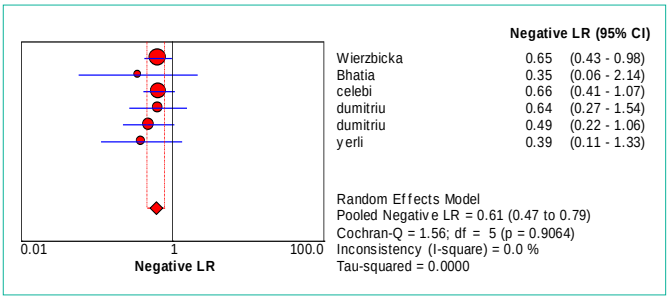
The results of current study demonstrated that sonoelastography has modest accuracy in differentiating benign and malignant salivary gland tumors. The pooled sensitivity was 63% and pooled specificity was 59%. The summary diagnostic OR was 3.18 which could be indicative that the odds of obtaining a test positive result in malignant rather than benign tumors is three.

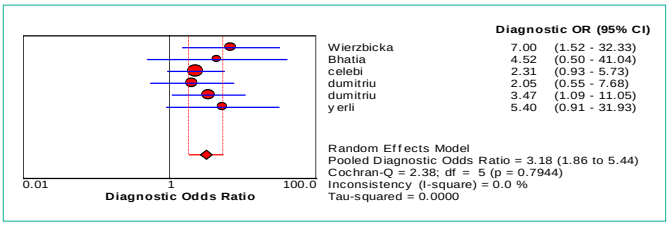
Salivary gland tumors form a wide group of masses which could locate in major or minor salivary glands. It is crucial to determine if

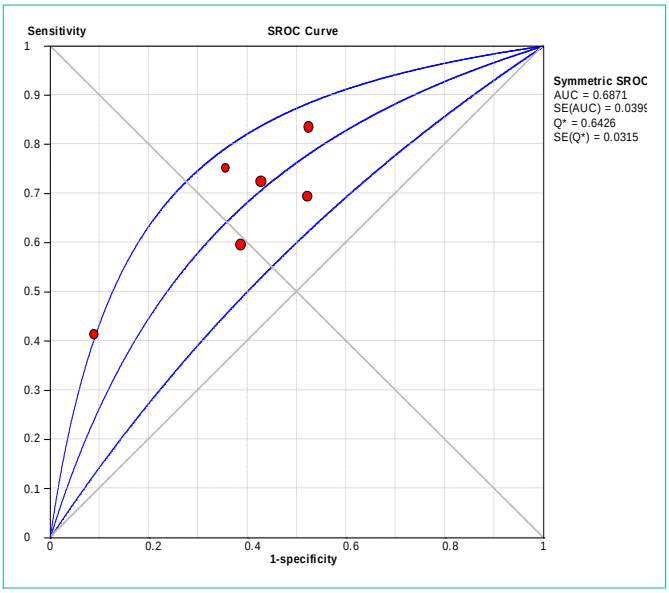












the pathology of the salivary gland mass is benign or malignant as lateral parotidectomy or extra capsular dissection could be applied for benign masses and total or radical parotidectomy along with neck dissection could be planned for malignant masses [12,13].

Salivary glands are superficial and most current imaging techniques such as B-mode sonography, Magnetic Resonance Imaging (MRI), And Computed Tomography (CT) is used as the imaging techniques in evaluating salivary gland masses. Although these modalities are used widely, they could not differentiate benign and malignant pathologies properly due to morphological overlaps between benign and malignant masses [14-16]. B-mode sonography is a time and cost-effective, easy to apply, and radiation free method which needs no contrast agent administration. However, most characteristics of benign masses overlap with malignant masses such as margin and echogenity [17].

Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) provide more information about the relationship surrounding tissues of the tumor or bony structures, but these modalities are time consuming, expensive and unavailable in all settings. Alternatively,

pre-operative cytological evaluation has been considered as the gold standard for evaluating salivary gland masses but its false negative and positive results is notable [18,19].

Palpation is a subjective method which gives information about the degree of firmness of the tumor as the malignant tumors are firmer than benign tumors.

By introducing sonoelastography in 1987 by Krouskop et al. evaluation of the elasticity features of the tissue and examination of changes in tissue hardness in response to external forces will be possible [20].

Nowadays, it is widely used for distinguishing benign and malignant pathologies in different tissues such as breast, thyroid, prostate, liver and lymph nodes [21-25].

In previous systematic reviews, summary sensitivities of sonoelastography in differentiating benign and malignant breast, thyroid, prostate and lymph nodes were 0.83, 0.92, 0.62, 0.74 and summary specificities were as follow: 0.84, 0.79, 0.9 and 0.9 [26-29].

We found that summary sensitivity and specificity of sonoelastography in differentiating benign and malignant parotid tumors were lower than the diagnostic accuracy of this method for pathologies of masses in other tissues. As sonography is operator dependent and elastography is a new method, its application in evaluating superficial glands such as tumors located in salivary glands. Maybe, more experience and precise definition of elastography method and application should be introduced to radiologist.

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