Vol. 128 No. 4 October 2019

The diagnostic role of ultrasonography, computed tomography, magnetic resonance imaging, positron emission tomography/computed tomography, and real-time elastography in the differentiation of benign and malignant salivary gland tumors: a meta-analysis

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Objective. The objective of this study was to assess the diagnostic properties of ultrasonography, computed tomography (CT), magnetic resonance imaging (MRI), positron emission tomography/computed tomography (PET/CT), and real-time elastography (RTE) in distinguishing between benign and malignant salivary gland tumors.

Study Design. English databases were searched for eligible studies. Diagnostic accuracy parameters, including sensitivity, specificity, diagnostic odds ratio (DOR), and summary receiver operating characteristic curves (SROC) were calculated. Meta-regression and subgroup analyses were performed to identify the source of heterogeneity.

Results. In total, 38 studies were included. Pooled sensitivities for ultrasonography, CT, MRI, PET/CT, and RTE were 0.66, 0.70, 0.80, 0.81, and 0.80, respectively. Pooled specificities were 0.92, 0.73, 0.90, 0.89, and 0.70, respectively. The DORs were 23, 6, 38, 20, and 10, respectively. The areas under the curve (AUC) of SROC for US, CT, MRI, PET/CT, and RTE were 0.91, 0.77, 0.92, 0.88, and 0.82, respectively.

Conclusion. Based on the results of the meta-analysis, MRI may be the first choice for the differential diagnosis of benign and malignant salivary gland tumors for its relatively high diagnostic value. PET/CT tends to have greater accuracy than CT. Ultrasonography and RTE may help achieve better diagnostic outcomes if they are used in conjunction. (Oral Surg Oral Med Oral Pathol Oral Radiol 2019;128:431−443)

Salivary gland tumors are relatively rare neoplasms, comprising approximately 5% of all head and neck tumors and 0.5% of all malignancies.[1,2] Approximately 70% of salivary gland neoplasms are characterized as benign and are mostly located in the parotid, submandibular, and sublingual glands. The rest are malignant tumors that threaten the survival and quality of life of patients.

Differentiating benign salivary gland tumors from malignant lesions becomes clinically essential for preoperative treatment planning because treatment options depend on the histologic type of the tumor.[3] Although superficial tumors are easy to detect, it is difficult to identify tumors located deep in the tissue or at an early stage. Fine-needle aspiration cytology is still regarded as the most definitive tool for discriminating between benign and malignant tumors in clinical practice.[4] However, this invasive procedure might cause pain, hemorrhage, and complications such as intensifying the spread of the tumor cells, which limit its clinical uses.[5] When fine-needle aspiration cytology is unavailable, imaging techniques become a useful option.

Ultrasonography, computed tomography (CT), and magnetic resonance imaging (MRI) are commonly used in the clinical diagnosis of salivary gland tumors. Numerous studies have been performed, and the common characteristics of benign and malignant salivary gland tumors on ultrasonography, CT, and MRI have been summarized and established to aid in the identification of salivary gland tumors.[6,7] Previous analyses have suggested that ultrasonography, CT, and MRI are feasible methods in diagnosing salivary gland tumors clinically, with 70% to 90% accuracy.[8] However, ultrasonography, CT, and MRI have some limitations, and with the development of different imaging modalities, several other techniques have attracted increased attention.

As relatively novel imaging modalities, positron emission tomography/computed tomography (PET/CT) and real-time elastography (RTE) have been recommended in recent years and show promising effectiveness for differentiating benign and malignant salivary gland lesions. Park et al. suggested that PET/CT has higher diagnostic value in

Statement of Clinical Relevance

We assessed the diagnostic performance of ultrasonography, computed tomography, magnetic resonance imaging, computed tomography/positron emission tomography, and real-time elastography in distinguishing between benign and malignant salivary gland tumors. Our findings may help improve the diagnosis and prognosis for patients with salivary gland malignancies.

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Received for publication Mar 12, 2019; returned for revision Jun 16, 2019; accepted for publication Jun 22, 2019.

2212-4403/$-see front matter
https://doi.org/10.1016/j.oooo.2019.06.014

detecting salivary gland tumors compared with conventional CT.[9] Research suggests that RTE could provide additional information that is not detected with conventional ultrasonography, and RTE could be used as an adjunct to ultrasonography for evaluation of salivary gland lesions.[10] However, controversy still exists regarding the most desirable imaging modality. Although some clinicians and pathologists strongly suggest one particular technique, others recommend that certain imaging techniques should be used together.

The primary objective of the present meta-analysis was to assess the diagnostic properties of ultrasonography, CT, MRI, PET/CT, and RTE in distinguishing between benign and malignant salivary gland tumors by synthesizing all available published studies. The secondary objective was to identify the most ideal imaging modality or the best combination of modalities for the diagnosis of salivary gland tumors.

MATERIALS AND METHODS

This meta-analysis was conducted in accordance with the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement.

Search strategy

Studies in the English language literature investigating the diagnosis accuracy of ultrasonography, CT, MRI, PET/CT, and RTE in discriminating between benign and malignant salivary gland tumors were the focus of this meta-analysis. The PubMed, ScienceDirect, and Web of Science databases were searched to find relevant publications up to January 2019, with the keywords “ultrasound,” “computed tomography,” “magnetic resonance imaging,” “positron emission computed tomography,” “real-time elastography,” “salivary gland,” “accuracy,” and “diagnosis,” as well as their abbreviations and synonyms and all the possible combinations. To ensure a more complete literature search, references of the retrieved articles were also reviewed to cover all relevant studies.

Study selection

Inclusion criteria were as follows: (1) use of ultrasonography, CT, MRI, PET/CT, or RTE to differentiate benign from malignant salivary gland tumors; (2) comparison of the diagnostic results of the imaging modalities with a reference standard; and (3) provision of sufficient data for constructing 2×2 contingency tables. Citations that did not meet the aforementioned criteria, review studies, case reports, comments, unpublished materials, and studies published in abstract form were excluded. For multiple reports with the same cohort of patients, only the one with the most complete data was included. The corresponding author was contacted for detailed information in cases of an eligible study with insufficient data.

Data abstraction and quality assessment

Data extraction of each included study was performed independently by 2 authors, who used a standardized form. Disagreements were resolved through discussion. Extracted information included first author, publication year, study design, sample size, patient demographic characteristics (age, gender, type of disease), reference standards, and imaging interpretation method (blinded or not). Diagnostic accuracy data for ultrasonography, CT, MRI, PET/CT, and RTE, and the number of true-positive (TP), true-negative (TN), false-positive (FP), and false-negative (FN) responses were recorded or calculated.

The same 2 authors also evaluated the quality of the included studies in the data abstraction process. The quality assessment of diagnostic accuracy study form (QUADAS-2) was used as the guideline.[11] By judging 4 domains (patient selection, index test, reference standard, and flow and timing), each study was ranked as having high, unclear, or low risk of bias.

Statistical analysis

Diagnostic values of ultrasonography, CT, MRI, PET/CT, and RTE in differentiating benign and malignant salivary gland lesions were determined by calculating pooled sensitivity, specificity, and diagnostic odds ratio (DOR) with 95% confidence intervals (CI). Summary receiver operating characteristic curves (SROCs) were generated to estimate the effect of sensitivity and specificity. The area under the curve (AUC) of the SROC was calculated to reveal the performance of determined groups. An AUC figure closer to 1 represents a better test result.

Heterogeneity of each study group was tested using the χ^2 test and the inconsistency index (I^2). An I^2 greater than 50% and P value of the χ^2 test less than .05 confirmed the existence of significant heterogeneity, and a random effect model was chosen to pool the data. Otherwise, a fixed-effect model was used. As a possible source of heterogeneity in diagnostic accuracy analysis, threshold effect was also assessed. Spearman correlation coefficients between the logit of sensitivity and the logit of [1 − specificity] were calculated to express the threshold effect.[12] A strong positive correlation between sensitivity and [1 −specificity] ($P < .05$) represented the presence of a threshold effect. A meta-regression analysis and a subgroup analysis were also conducted to determine if certain variance could affect the heterogeneity and overall diagnostic effect. Kruskal-Wallis, least significant difference, and Scheffe tests were used for comparing the diagnostic accuracy of ultrasonography, CT, MRI, PET/CT, and RTE studies. Publication bias was analyzed by using the Deeks funnel plot and an asymmetry test.

Statistical analysis was performed by using Stata, version 15.0 (Stata Corporation, College Station, TX) and Meta-DiSc 1.4 (Unit of Clinical Biostatistics, Madrid, Spain) software. Risk of bias assessment was conducted by using Review Manage 5.3 software (The Nordic Cochrane Centre, The Cochrane Collaboration).

RESULTS

Literature evaluation

Initially, the databases identified a total of 5796 potential publications for review. Many of these articles were excluded on the basis of titles and abstracts. Only 115 articles were identified for full-text review and data extraction. After excluding the studies that were not within the field of interest of this meta-analysis, articles that did not provide sufficient data for the calculation of diagnostic accuracy, and duplicate reports, 38 studies were included in the analysis. Supplemental Figure S1 demonstrates the flowchart of the literature selection process.

Study characteristics

Table I presents the relevant data of the included publications. With regard to the 38 eligible trials,[4,9,13−48] 7 studies described diagnostic performance of ultrasonography,[15,18,19,22,26,33,36] 6 of CT,[23,24,28,30,32,35] 15 of MRI,[23,28,35,37−48] 9 of PET/CT,[9,20,24,25,29−32,34] and 7 of RTE.[4,13,14,16,17,21,27] In all, 2753 salivary gland tumors were analyzed, and the reports of ultrasonography, CT, MRI, PET/CT, and RTE imaging modalities included 573, 397, 900, 417, and 584 patients, respectively. Histopathologic findings, cytologic diagnoses, or clinical follow-up data were applied as the reference standard. Detailed information regarding study design, sample size, age, gender, reference standard, blinded status, and imaging modality used in each study is provided in Table I.

Quality assessment

According to the results of the QUADAS-2 items, high risk of bias was mostly observed in the "index test" category because many studies did not provide the interpretation method of the imaging results and did not prespecify a threshold. Unclear risk of bias was mostly observed in the "reference standard" category because the majority of trials did not clarify whether the reference standard results were interpreted without knowledge of the results of the index tests. Detailed information of the included studies and the results of the distribution are presented in Supplemental Figure S2.

Diagnostic accuracy of ultrasonography

The pooled sensitivity of the 7 studies that applied ultrasonography in differentiating benign and malignant salivary gland tumors was 0.66 (95% CI, 0.43−0.83) and the pooled specificity was 0.92 (95% CI 0.84−0.96) (Figure 1A). The DOR was 23 (95% CI 6−94). The AUC of SROC was 0.91 (95% CI 0.88−0.93). (Figure 1B) Threshold analysis revealed a Spearman correlation coefficient of 0.45 ($P = .21$), which confirmed the absence of threshold effect in this group of studies. Because relatively high I^2 values were observed in both sensitivity (71.65%) and specificity (87.30%), a subgroup analysis, separating studies according to study design (prospective or retrospective) and interpretation method (blinded or not), was performed. Similar sensitivity and specificity values were found in the 4 subgroups compared with the overall effect (Table II).

Diagnostic accuracy of CT

With regard to the diagnostic quality of CT in differentiating benign and malignant salivary gland tumors, pooled sensitivity was 0.70 (95% CI 0.44−0.87) and the pooled specificity was 0.73 (95% CI 0.38−0.92) (Figure 2A). The DOR was 6 (95% CI 1−46). The AUC was 0.77 (95% CI 0.73−0.80) (Figure 2B). A threshold effect (Spearman correlation coefficient: 0.26; $P = .07$) did not exist in this group of studies. Meta-regression and subgroup analyses revealed that study design and interpretation method had no significant effect on the diagnostic accuracy of CT or the heterogeneity among studies (see Table II).

Diagnostic accuracy of MRI

The application of MRI in discriminating between benign and malignant salivary gland tumors presented a pooled sensitivity of 0.80 (95% CI 0.67−0.89) and a pooled specificity of 0.90 (95% CI 0.83−0.95) (Figure 3A). The DOR was 38 (95% CI 13−108). The AUC was 0.92 (95% CI 0.90−0.94) (Figure 3B). A threshold effect was not detected in this group of studies; the Spearman correlation coefficient was 0.34 ($P = .12$). Significant heterogeneity in sensitivity (72.54%) and specificity (90.18%) necessitated further investigation of the source of the heterogeneity. Meta-regression and subgroup analyses revealed that the study design and the interpretation method significantly affected the results of sensitivity and specificity. Use of a prospective design and single-blinded index text interpretation method resulted in a significantly lower sensitivity ($P \leq .03$) and specificity ($P \leq .02$) compared with a retrospective design and unblinded or unknown interpretation (see Table II).

Table I. Characteristics of the included studies

Author	*Year*	*Study design*	*Sample size*	*Age*	*Male/Female*	*Reference standard*	*Blinded*	*Imaging modality*
Bhatia et al.[4]	2010	Prospective	61	60.5 ± 17.6	48/13	Histopathologic findings	Single-blinded	RTE
Celebi et al.[13]	2013	Prospective	81	10−83	42/39	Cytologic or histopathologic findings	Single-blinded	RTE
Cortcu et al.[14]	2017	Prospective	39	52 ± 14	22/17	Histopathologic findings	Not reported	RTE
Davachi et al.[15]	2014	Prospective	22	46.59 ± 13.97	8/14	Histopathologic or surgical findings	Single-blinded	Ultrasonography
Dumitriu et al.[16]	2010	Prospective	67	50.6 (18−78)	43/24	Histopathologic findings	Not reported	RTE
Dumitriu et al.[17]	2011	Prospective	74	50.8 ± 2.07	37/29	Histopathologic or surgical findings	Single-blinded	RTE
Edia et al.[37]	2007	Cohort study	31	63 ± 11	13/18	Histopathologic findings	Not reported	MRI
Gerwel et al.[18]	2015	Prospective	51	22−79	31/20	Histopathologic findings	Not reported	Ultrasonography
Higashino et al.[19]	2012	Retrospective	154	53.9 (12−85)	87:67	Histopathologic findings	Not reported	Ultrasonography
Inohara et al.[38]	2008	Retrospective	81	–	-	Cytologic diagnoses with histopathologic findings	Single-blinded	MRI
Jeong et al.[20]	2007	Retrospective	33	31−83	22/11	Histopathologic findings; clinical and radiologic follow-up	Single-blinded	PET/CT
Karaman et al.[21]	2018	Prospective	60	48.8 ± 20.48	30/30	Histopathologic findings	Single-blinded	RTE
Khalife et al.[22]	2016	Cross-sectional	28	18−92	17/11	Histopathologic findings	Not reported	Ultrasonography
Kim et al.[23]	1998	Retrospective	136	–	-	Histopathologic findings	Single-blinded	CT; MRI
Kim et al.[24]	2012	Retrospective	18	39−73	14/4	Histopathologic findings	Unblinded	CT; PET/CT
Kim et al.[25]	2013	Prospective	54	16−80	39/15	Histopathologic findings	Not reported	PET/CT
Klintworth et al.[26]	2012	Retrospective	57	53.3 (14−93)	27/30	Histopathologic findings	Unblinded	Ultrasonography
Kurabayashi et al.[39]	2002	Retrospective	30	43.1 (9−69)	14/16	Histopathologic findings and clinical follow-up	Single-blinded	MRI
Lam et al.[40]	2015	Retrospective	98	53 (17−82)	36/62	Histopathologic findings	Single-blinded	MRI
Mansour et al.[27]	2015	Prospective	202	58.6 ± 14.7	-	Histopathologic findings	Not reported	RTE
Milad et al.[41]	2017	Prospective	46	49.8 ± 11.3	15/31	Clinical and histologic findings	Single-blinded	MRI
Motoori et al.[28]	2005	Retrospective	33	60.8 (16−91)	26/7	Histopathologic findings	Single-blinded	CT; MRI
Pair et al.[42]	2004	Retrospective	181	54 (13−80)	83/98	Histopathologic findings	Single-blinded	MRI
Park et al.[29]	2012	Retrospective	67	61.1 ± 12.8	47/20	Histopathologic findings	Not reported	PET/CT
Park et al.[30]	2013	Retrospective	66	49.8 ± 14.9	39/27	Histopathologic findings	Not reported	CT; PET/CT
Park et al.[9]	2017	Prospective	67	55 (49−64)	37/30	Histopathologic findings	Double-blinded	PET/CT
Razfar et al.[31]	2010	Retrospective	55	59 (29−87)	36/19	Clinicopathologic information	Not reported	PET/CT
Roh JL et al.[32]	2007	Retrospective	34	53.5 ± 13.9	25/9	Histopathologic findings	Single-blinded	CT; PET/CT
Rzepakowska et al.[33]	2017	Prospective	72	57.6 (20−83)	28/44	Histopathologic findings	Single-blinded	Ultrasonography
Sharma et al.[34]	2013	Retrospective	30	43.8 ± 16.8	20/10	Histopathologic findings and clinical follow-up	Single-blinded	PET/CT
Takashima et al.[43]	1999	Prospective	26	14−81	17/9	Histopathologic findings	Double-blinded	MRI
Takashima et al.[44]	2001	Prospective	72	53 (3 mo−81)	35/37	Histopathologic findings and radiologic follow-up	Single-blinded	MRI
Vogl et al.[35]	2017	Retrospective	110	–	-	Histopathologic findings	Single-blinded	CT; MRI
Wu et al.[36]	2012	Retrospective	189	42.3 (1.5−76)	91/98	Histopathologic findings	Single-blinded	Ultrasonography
Yabuuchi et al.[45]	2003	Retrospective	29	27−77	13-16	Histopathologic findings	Double-blinded	MRI
Yabuuchi et al.[46]	2008	Retrospective	47	61 (12−82)	23/24	Histopathologic findings	Single-blinded	MRI
Yuan et al.[47]	2016	Retrospective	207	48.4 ± 17.0	111/96	Histopathologic findings	Single-blinded	MRI
Zheng et al.[48]	2018	Retrospective	45	62.3 (15−79)	27/18	Histopathologic findings	Single-blinded	MRI

CT, computed tomography; *MRI,* magnetic resonance imaging; *PET/CT,* positron emission tomography/computed tomography; *RTE,* real-time elastography.

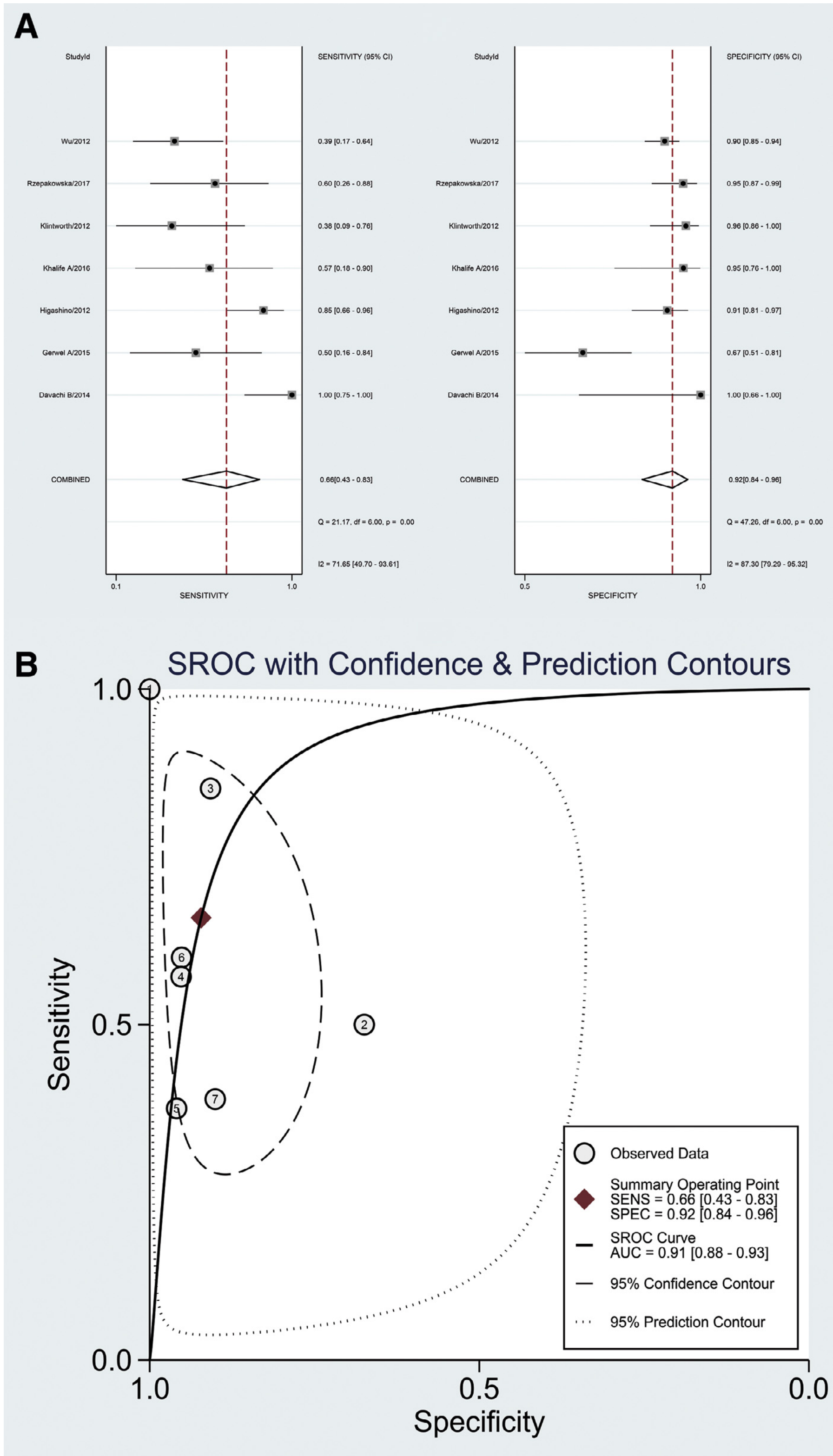

Fig. 1. Diagnostic accuracy of ultrasonography in differentiating between benign and malignant salivary gland tumors. **A**, Pooled sensitivity and specificity of ultrasonography. **B**, Summary receiver operating characteristic curve of ultrasonography.

Table II. Results of meta-regression and subgroup analyses

Imaging modality	*Category*	*Studies*	*Sensitivity*	*P value*	*Specificity*	*P value*
Ultrasonography	Study Design					
	Prospective	5	0.70 (0.47−0.92)	.53	0.94 (0.89−0.99)	.75
	Retrospective	2	0.55 (0.14−0.97)		0.85 (0.71−0.99)	
	Blind					
	Yes	2	0.49 (0.14−0.84)	.24	0.93 (0.85−1.00)	.74
	No	5	0.73 (0.54−0.92)		0.91 (0.84−0.99)	
Computed tomography	Study Design					
	Prospective	5	0.66 (0.41−0.91)	.68	0.68 (0.35−1.00)	.65
	Retrospective	1	0.80 (0.44−1.00)		0.90 (0.61−1.00)	
	Blind					
	Yes	5	0.77 (0.59−0.95)	.15	0.65 (0.32−0.97)	.30
	No	1	0.43 (−0.05−0.91)		0.94 (0.78−1.00)	
Magnetic resonance imaging	Study Design					
	Prospective	8	0.70 (0.53−0.86)	**.02**	0.86 (0.77−0.95)	**.01**
	Retrospective	7	0.89 (0.76−0.99)		0.94 (0.88−0.99)	
	Blind					
	Yes	11	0.74 (0.62−0.87)	**.03**	0.87 (0.79−0.94)	**.02**
	No	4	0.91 (0.81−1.00)		0.96 (0.91−1.00)	
Positron emission tomography/ Computed tomography	Study Design					
	Prospective	5	0.82 (0.73−0.91)	.25	0.80 (0.60−1.00)	.16
	Retrospective	4	0.78 (0.66−0.90)		0.94 (0.87−1.00)	
	Blind					
	Yes	5	0.81 (0.71−0.91)	.14	0.89 (0.72−1.00)	.77
	No	4	0.81 (0.70−0.93)		0.89 (0.73−1.00)	
Real-time elastography	Blind					
	Yes	3	0.79 (0.58−0.99)	.70	0.62 (0.44−0.79)	.09
	No	4	0.81 (0.63−0.99)		0.76 (0.63−0.88)	

Diagnostic accuracy of PET/CT

For calculation of the diagnostic performance of PET/CT, the pooled sensitivity was 0.81 (95% CI 0.72−0.88) and the pooled specificity was 0.89 (95% CI 0.71−0.96) (Figure 4A). The DOR was 20 (95% CI 6−71). The AUC of SROC was 0.88 (95% CI 0.85−0.91) (Figure 4B). The assessment of the Spearman correlation coefficient (0.21; $P = .04$) indicated that the threshold effect was significant. Meta-regression and subgroup analyses based on study design and blinded method revealed no strong association between the 2 variances with PET/CT accuracy and heterogeneity (see Table II).

Diagnostic accuracy of RTE

In the accuracy evaluation for RTE, the pooled sensitivity was 0.80 (95% CI 0.64−0.90) and the pooled specificity was 0.70 (95% CI 0.57−0.81) (Figure 5A). The DOR was 10 (95% CI 3−32). The AUC was 0.82 (95% CI 0.78−0.85) (Figure 5B). The existence of a threshold effect was disproven because the Spearman correlation coefficient (0.62) did not reach statistical significance ($P = .39$). Meta-regression and subgroup analyses revealed that the diagnostic accuracy of RTE was not affected by the imaging interpretation method (see Table II).

Comparison of diagnostic accuracy among the 5 imaging modalities

Results of the Kruskal-Wallis test showed that there were no significant differences among the 5 groups with regard to sensitivity, specificity, DOR, or SROC ($P > .05$). The least significant difference and Scheffe tests produced similar results, except that a significant difference was observed in DOR between MRI and CT ($P = .035$). The pooled DOR of MRI was higher than that of CT for differentiating benign and malignant salivary gland tumors.

Publication bias

According to the Deeks funnel plot asymmetry test, no publication bias was detected among the studies in the ultrasonography ($P = .87$), CT ($P = .84$), MRI ($P = .22$), PET/CT ($P = .69$), or RTE ($P = .98$) groups.

DISCUSSION

In the differentiation of benign and malignant salivary gland tumors, fine-needle aspiration biopsy is still the most commonly used diagnostic procedure. However, the accuracy of this method cannot reach 100%, and the performance can be affected by unusual locations of lesions or patients' unwillingness to undergo this procedure.[49] In such circumstances, imaging examinations become important. It is, therefore, crucial to

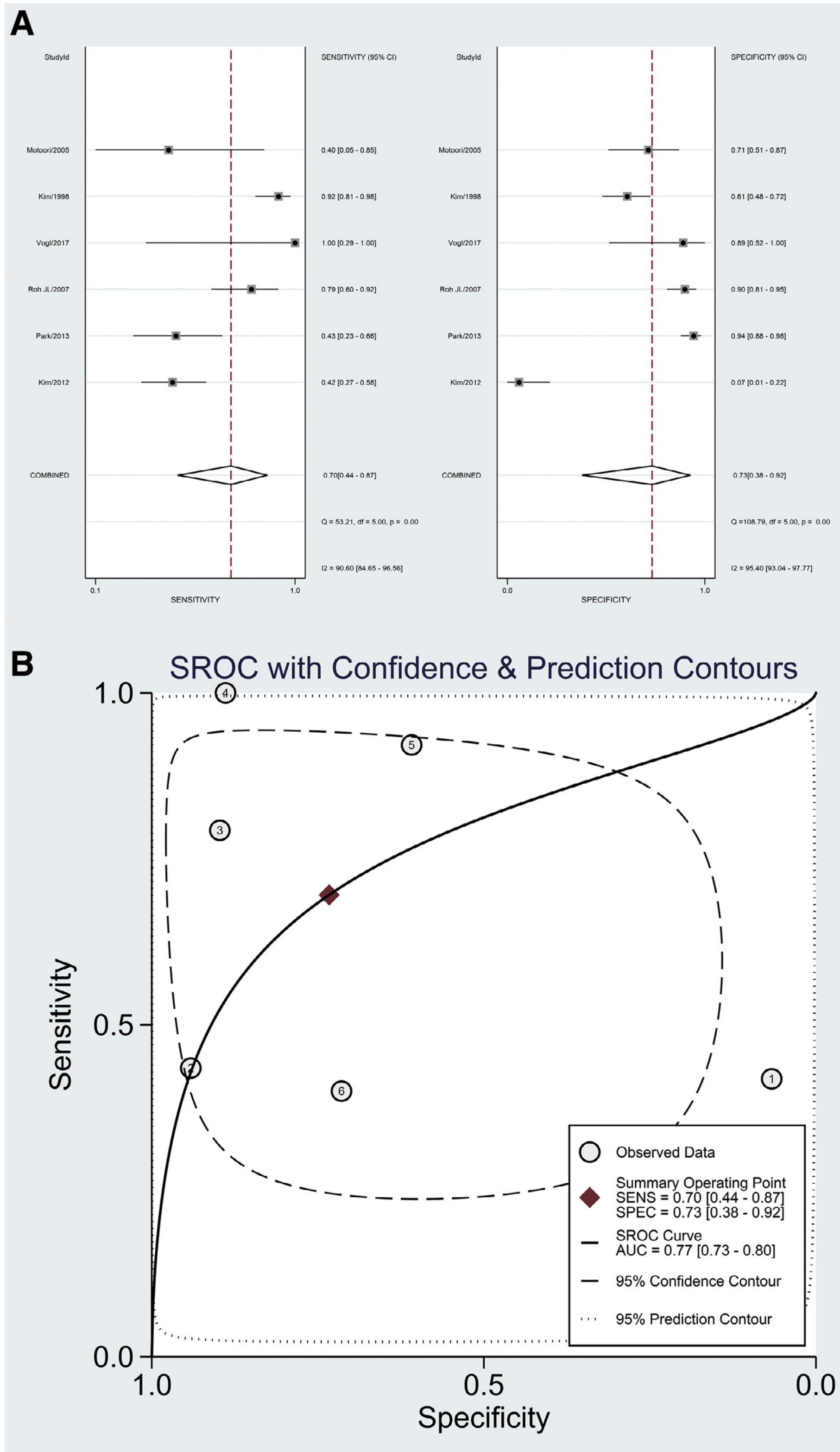

Fig. 2. Diagnostic accuracy of computed tomography (CT) in differentiating between benign and malignant salivary gland tumors. **A**, Pooled sensitivity and specificity of CT. **B**, Summary receiver operating characteristic curve of CT.

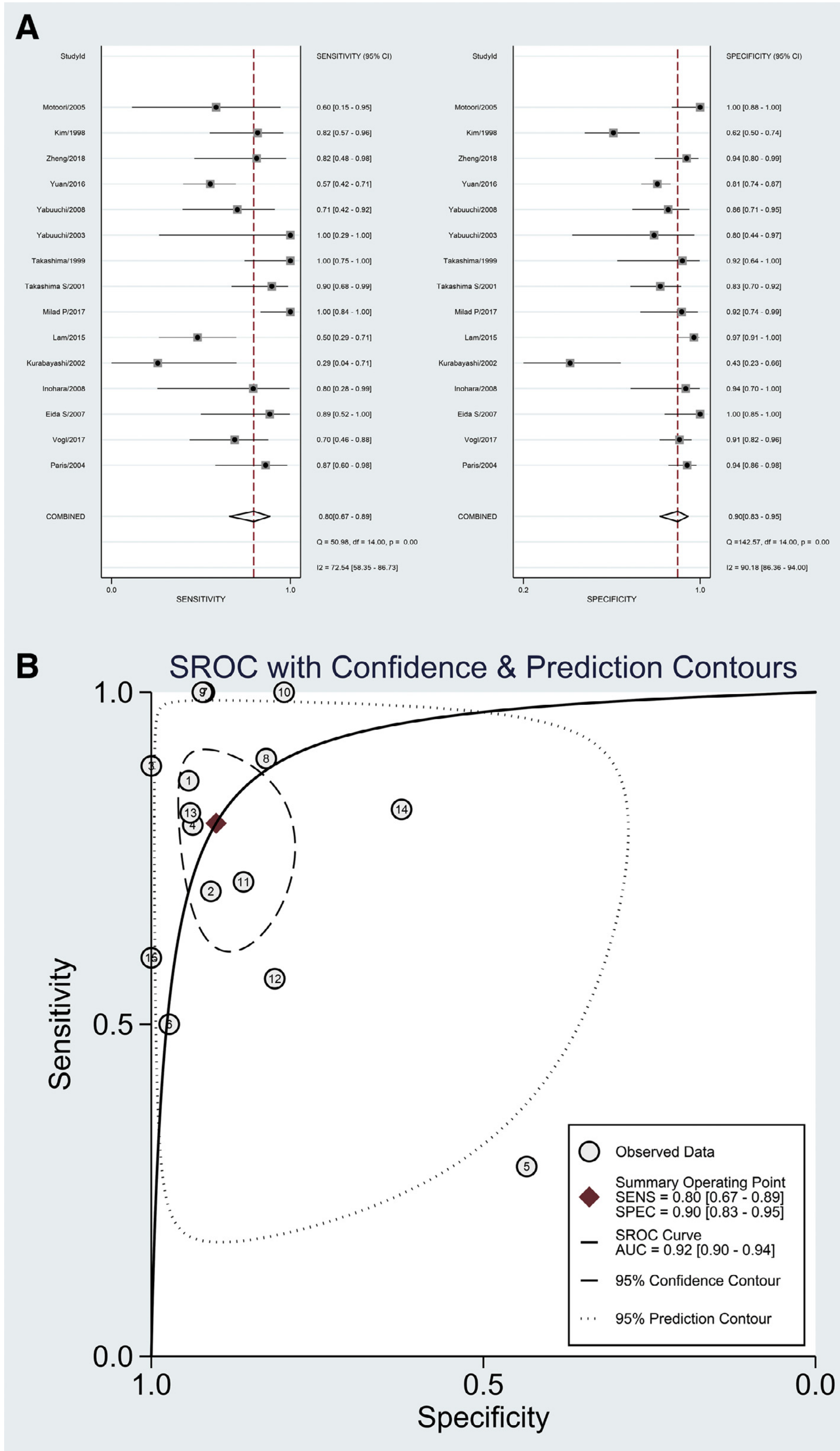

Fig. 3. Diagnostic accuracy of magnetic resonance imaging (MRI) in differentiating between benign and malignant salivary gland tumors. **A**, Pooled sensitivity and specificity of MRI. **B**, Summary receiver operating characteristic curve of MRI.

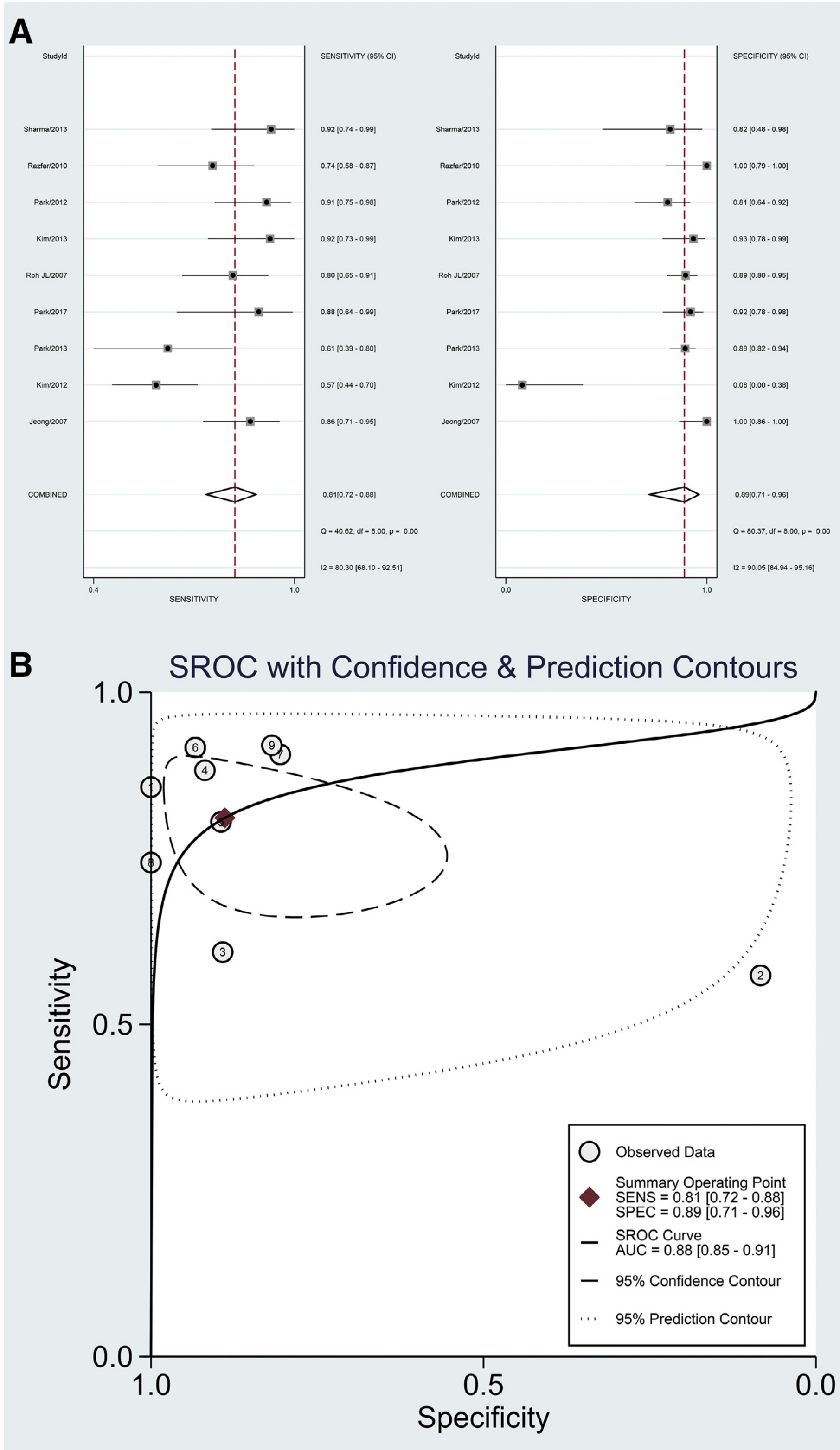

Fig. 4. Diagnostic accuracy of positron emission tomography/computed tomography (PET/CT) in differentiating between benign and malignant salivary gland tumors. **A**, Pooled sensitivity and specificity of PET/CT. **B**, Summary receiver operating characteristic curve of PET/CT.

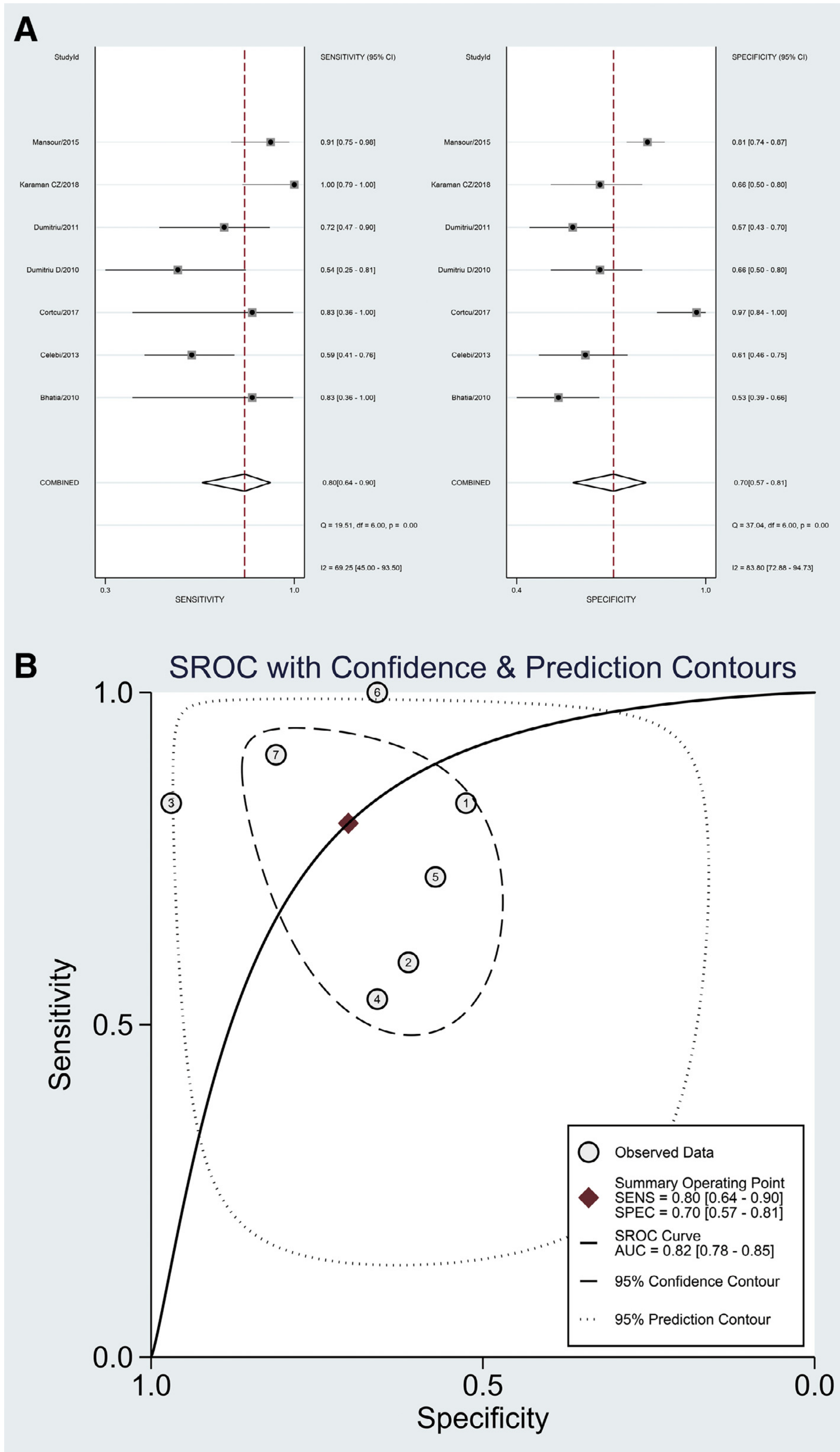

Fig. 5. Diagnostic accuracy of real-time elastrography (RTE) in differentiating between benign and malignant salivary gland tumors. **A**, Pooled sensitivity and specificity of RTE. **B**, Summary receiver operating characteristic curve of RTE.

identify a preferable and predictive diagnostic imaging method. Thus, this meta-analysis was performed to assess the diagnostic performance of ultrasonography, CT, MRI, PET/CT, and RTE in distinguishing between benign and malignant lesions.

Diagnostic accuracy was compared among the 5 imaging techniques, and no significant differences were found. However, MRI seemed to present the best diagnostic performance among the evaluated modalities, with a relatively high sensitivity, specificity, DOR, and AUC. MRI is the modality of choice in the clinical diagnosis of salivary gland tumors, with its superb low-density contrast and anatomic resolution, multiplanar facilities, and avoidance of radiation exposure and interfering factors.[38,44] It is superior in differentiating soft tissues and detecting deep tissue extension, perineural spread, and facial nerve and marrow infiltration/edema. MRI is optimal in monitoring signal changes and extracapsular spread in regional lymph nodes.[50] MRI has been used mandatorily to assess complete tumor extent, local invasion, and perineural spread when tumors are located in deep tissues or when they are suspected to have a high risk of malignancy. Several studies have argued that the ability of MRI in predicting salivary gland malignancy is limited.[51,52] However, our meta-analysis showed great potential for MRI in discriminating between benign and malignant salivary gland tumors.

As indicated by the results of the analysis, ultrasonography also achieved a relatively high AUC (0.91); that is, ultrasonography may lead to better diagnostic performance. Ultrasonography, with its high accessibility, cost-effectiveness, and wide acceptance by patients, is regarded as a basic examination in the assessment of salivary gland tumors. In ultrasonography evaluation, malignant lesions are depicted with ill-defined tumor margins, inhomogeneous echostructure, increased vascularity, and pathologic local lymph nodes.[53] However, researchers have also argued that these characteristics may not be sufficient to distinguish between malignant tumors and benign lesions because well-defined tumors with smooth outlines can also represent low-grade malignant salivary gland neoplasms, and lesions located in the deep lobes and deeper structures are difficult to assess with ultrasonography.[54] The results of our meta-analysis seem to further confirm the limitations of ultrasonography evaluation. A high specificity was detected (0.92), whereas the sensitivity (0.66) was the lowest among the 5 modalities, which means that ultrasonography may successfully identify patients with benign lesions but would misclassify malignant tumors as benign. Thus, other imaging modalities with higher sensitivity, such as CT, MRI, PET/CT, and RTE are needed.

In the evaluation of neck lesions, CT is widely used because of its anatomic resolution, soft tissue contrast, and detailed display characteristics.[55] CT possesses the ability to gauge the extent and invasion of tumors, thus providing additional information for accurate diagnosis.[56] Also, CT is a better diagnostic technique in the case of bone infiltration, inflammation, and vascular damage.[50] However, the time, the cost, and some patients' reluctance to accept radiation exposure and the injection of a contrast agent hamper the use of CT. In recent years, many studies have focused on the diagnostic performance of PET/CT. Previous research has suggested that the combination of functional PET and anatomic CT data was superior to CT data alone in the assessment of malignancies.[57,58] Additionally, as a whole-body imaging technique, PET/CT has the extra advantage of detecting subclinical metastatic diseases or a second cancer located in another part of the body, and this is useful for therapeutic management and greater success of therapy.[59] The findings of our meta-analysis seem to further confirm that PET/CT may be a better technique in the diagnosis of malignant salivary gland tumors. PET/CT showed higher sensitivity and specificity compared with CT in this investigation. Although statistical significance was not achieved, PET/CT appeared to have a higher DOR and AUC compared with CT alone, suggesting that when CT and PET/CT are both available, PET/CT should be used as the first choice. However, in this analysis, a threshold effect was found in the PET/CT studies—that is, the diagnostic performance of PET/CT in detecting malignant salivary gland tumors still needs further investigation.

As a novel noninvasive imaging modality, RTE has been widely applied in assessing breast and prostate malignancies.[60,61] The use of RTE in discriminating between malignant and benign salivary gland tumors was not reported until 2010. The accuracy of this relatively new technique is still controversial. Thus, this study included the analysis of RTE to validate its performance for evaluation of salivary gland malignancies. Meta-analysis findings showed that RTE had high sensitivity but low specificity—that is, RTE is more effective in the identification of malignant salivary gland tumors than of benign lesions. This result is in contrast to that of ultrasonography, which had the poorest sensitivity among the 5 imaging techniques but showed high specificity. Accordingly, instead of using RTE or ultrasonography alone, the combined use of these 2 techniques may lead to a more accurate diagnosis.

This study has some limitations, which should be taken into consideration while interpreting its findings. High heterogeneity among the included studies was a major problem. Although meta-regression and subgroup analyses ruled out the influence of some factors on the study results, there were still other variances, such as patient demographic characteristics, specific devices used in evaluation, and cutoff values, which need to be considered. Moreover, the small number of eligible studies and the inconsistent information provided from some trials hampered the performance of a correlative analysis. Meta-regression and subgroup analyses results in the MRI group showed that the study design and the interpretation method of the index test significantly influenced diagnostic accuracy. Studies with a less rigorous design might have introduced bias and exaggerated the diagnostic performance of the imaging modality. Thus, future prospective multicenter trials with a more rigorous study design and a larger sample size is required to verify our results. The comparison of diagnostic accuracy among the 5 imaging techniques was indirect. To decide which imaging technique is most accurate, a more rigorous investigation should be conducted with use of different imaging modalities on the same cohort of patients.

CONCLUSIONS

The results of the current meta-analysis indicated that there is no statistically significant difference among the 5 imaging modalities in the differential diagnosis of benign and malignant salivary gland tumors. However, MRI stands out as the most highly recommended modality because of its high sensitivity, specificity, and AUC. With regard to ultrasonography, CT, PET/CT, and RTE, each technique has its own advantages and weaknesses. Thus, the use of the imaging techniques in combination may enhance the strength and reduce the deficiency of each, resulting in a more accurate diagnosis.

FUNDING

This research is supported by Beijing Municipal Administration of Hospitals Incubating Program (code: PX2019057).

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SUPPLEMENTARY MATERIALS

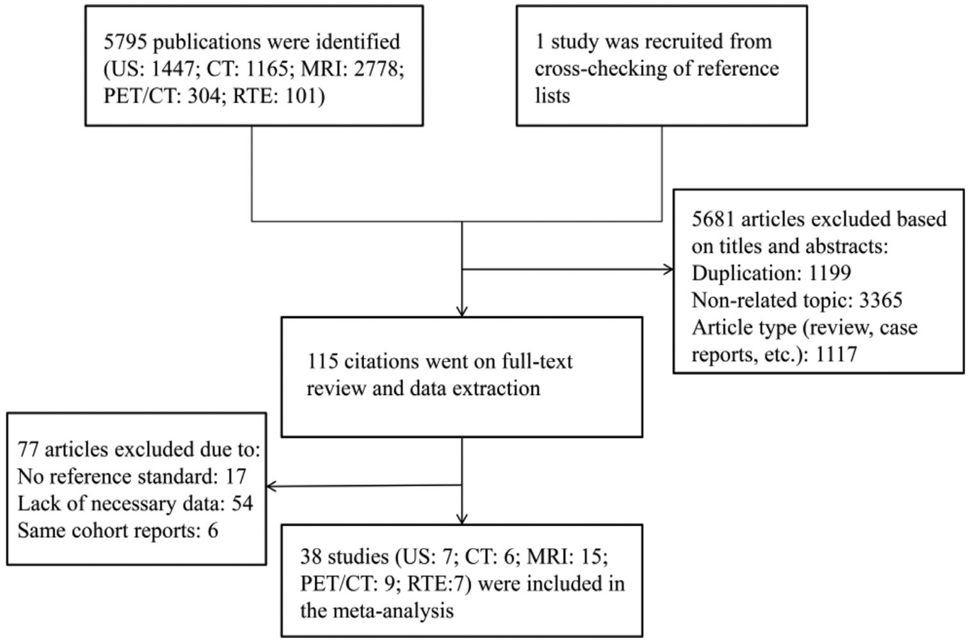

Figure S1. Flowchart of literature search and study selection.

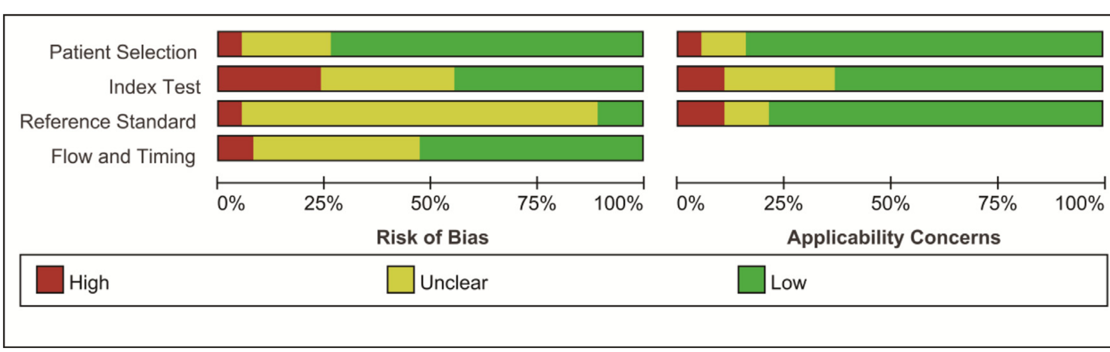

Figure S2. Risk of bias and applicability concerns graph of the 38 included studies (*red*: high; *yellow*: unclear; *green*: low).