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PRISMA—Extracapsular Dissection Versus Superficial Parotidectomy in Treatment of Benign Parotid Tumors

Evidence From 3194 Patients

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Abstract: Benign parotid tumor is one of the most common neoplasms in head and neck region. Its therapeutic methods have been debatable topics over the past 100 years. Recently, some surgeons suggest that extracapsular dissection (ECD) instead of superficial parotidectomy (SP) for treatment of benign parotid tumor. This study aimed to compare ECD with SP in the treatment of benign parotid tumors by a meta-analysis.

We searched Cochrane Library, PubMed, Embase, Ovid, and Web of Science databases on February 14, 2015 for studies that assessed clinical outcomes of SP and ECD as surgical techniques for the management of benign parotid tumors. Outcome data were evaluated by pooled risk ratio (RR) and corresponding 95% confidence interval (CI).

After serious scrutiny, a total of 14 cohort studies with 3194 patients were included in this meta-analysis. The pooled RR revealed that there were no significant difference in tumor recurrence rate between ECD and SP (fixed-effect model: RR = 0.71, 95% CI = 0.40–1.27, $P = 0.249$; random-effect model: RR = 0.67, 95% CI = 0.38–1.23, $P = 0.197$). However, there were significantly lower incidences of transient facial nerve dysfunction (FND), permanent FND, and Frey's syndrome in patients of ECD group compared with SP group.

ECD might be a good choice in treatment of the benign parotid tumor that were mobile, small, located in superficial lobe and without adhesion to facial nerve; ECD should be performed by the experienced surgeons with ability of dissection facial nerve, who should perform SP if tumor is found adhere to facial nerve during an operation; and a multicenter randomized control trial study is necessary to decide the optimal treatment of benign parotid tumor.

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Abbreviations: CEBM = Centre for Evidence-Based Medicine, CI = confidence interval, ECD = extracapsular dissection, FEM = fixed-effect model, FND = facial nerve dysfunction, FS = Frey's syndrome, REM = random-effect model, RR = risk ratio, SP = superficial parotidectomy.

INTRODUCTION

Salivary gland tumors account for 3% to 10% of all head and neck neoplasms.^{1–5} About 80% of them originate in the parotid gland, where about 80% of them are benign.⁶ The guidelines of surgical treatment for benign parotid tumor have been changed on the course of time.

Before the 1940s, the simple surgical technique, enucleation, was a widely used operation because of shortages of understanding of parotid gland and facial nerve anatomy. Around this time, however, some researchers reported the high recurrence rates of enucleation^{7–9} and a new surgical technique, parotidectomy, was reported.^{10–12} After its wide use, the recurrence rates for benign parotid tumor decreased dramatically. Therefore, from that time the parotidectomy and/or superficial parotidectomy (SP) became the golden standard treatment of parotid tumors at most medical centers. However, the complications, such as the facial nerve paralysis, Frey's syndrome (FS), and cosmetic deformities, did arise because of the wide use of parotidectomy and SP. As these postoperative complications must not be ignored, several improvements to this surgical technique have been reported over the past several decades, including extracapsular dissection (ECD).

SP is a technique with the whole removal of superficial lobe, dissection and preservation of branches, and main trunk of facial nerve, and also with a total removal of the parotid neoplasm.^{13,14}

ECD is a technique that involves a total excision of the benign parotid tumor surrounded by healthy parotid gland tissue without planed dissection of the main trunk of facial nerve.^{3,15–18} ECD should be differentiated from enucleation. The latter is a technique which removes the tumor directly at the tumor capsule without any surrounding normal tissue.¹⁷ The main difference between ECD and other types of parotidectomy is that it does not expose the facial nerve trunk when it removes the benign parotid tumor.^{16,17}

With the development of surgical techniques, the enucleation has been abandoned in recent year, and total parotidectomy has only been used in malignant parotid tumor or huge benign parotid tumors. However, as for ECD and SP, which one is the more ideal therapeutic method of benign parotid tumors is one of the most debatable topics in head and neck region. Supporters

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of SP base their evidence on an assumed higher recurrence rate in patients undergoing ECD,^{19,20} and those who support ECD declare that patients with benign parotid gland have better clinical outcomes and similar recurrence rates undergoing ECD compared to SP.^{21–26} Even 3 previous meta-analyses had been reported (data were traced back to 2011), their main results were still conflicting.^{27–29} Owing to existence of debates, many investigations pointing to this topic have emerged in the last 4 years^{16,24,30–32} and might provide a more comprehensive and reasonable conclusion. Based on this condition mentioned above, we performed a systematic review and meta-analysis to further investigate the advantages and disadvantages of ECD and SP.

MATERIALS AND METHODS

Search Strategy

We searched Cochrane Library, PubMed, Embase, Ovid, and Web of Science on February 14, 2015 for papers in English that met the following search strategies: gland, parotid OR glands, parotid OR parotid glands; and neoplasm OR tumors OR tumor OR neoplasia OR benign neoplasms OR neoplasms, benign OR benign neoplasm OR neoplasm, benign; and ECD OR dissections OR SP OR ECD. Retrieved articles were screened by 2 investigators according to the article type, title and abstract. And irrelevant articles were excluded. References in the related articles were also screened to find missed papers by literature retrieval. Then, all relevant articles were estimated by inclusion/exclusion criteria, as performed below.

Inclusion/Exclusion Criteria

Inclusion criteria: studies that compared SP to ECD concerning the recurrences or complications in treatment of benign parotid tumors; the descriptions of surgical procedures of SP and ECD were consistent with the descriptions of the introduction part; the details of surgical procedures were available from the original articles; article types were case-control study, cohort study, or randomized controlled trial (RCT) study; papers were published in English as full paper; risk ratios (RRs) for estimating recurrence rate or/and incidence of complications were provided or were extractable from the original articles to estimate the associations between SP and ECD; and all included patients with benign parotid tumors.

Exclusion criteria: meta-analysis, review, letter, meeting abstract, case series, case reports, editorial, and non-English papers; papers without sufficient information on assessment of association between SP and ECD; when multiple articles were reported by the same group, those shared datasets were excluded except for the articles with the most comprehensive datasets; and the descriptions of surgical procedures were ambiguous.

Data Extraction

The relevant information of all the included studies was independently extracted by 2 authors (SX and X-FS). Controversies between 2 investigators were solved by the other authors or discussion. The following information were extracted from each included study: publication year, first author, study design, number of subjects, outcomes of patients, surgical selection criteria, follow-up time, and other relevant data.

Quality Assessment

Quality assessment of the eligible studies was performed by 2 authors dependently according to Centre for Evidence

Based Medicine (CEBM): Level 1, systematic reviews of RCTs or systematic review of inception cohort studies; Level 2, inception cohort studies or randomized trial or observational study with dramatic effect; Level 3a, systematic reviews of nonrandomized controlled cohort studies; Level 3b, nonrandomized controlled cohort studies or cohort study or control arm of randomized trial; Level 4a, a systematic review of case series, poor quality cohort, poor case-control studies; Level 4b, case series, poor quality cohort, poor case-control study, and historically controlled studies; Level 5, mechanism-based reasoning.³³

Statistical Analysis

Data analyses were performed with STATA 11.0 software (Stata Co., College Station, TX). The RR with its corresponding 95% confidence interval (CI) was used to analyze the association between SP and ECD. The inconsistency index I^2 was used to estimate the variation caused by heterogeneity.³⁴ When $P > 0.10$ and $I^2 < 25\%$, which assumes that inter-study heterogeneity was not obvious. Both the fixed-effect model (FEM) and random-effect model (REM) were performed to estimate the association between ECD and SP. Potential publication bias was detected by Begger's test and Egger's linear regression.³⁵ Sensitivity analysis was used to identify the underlying effect of the individual studies on pooled RR. As a meta-analysis study, ethical approval of this study is not required. This study was reported following the PRISMA guidelines.

RESULTS

Literature Retrieval and Characteristics of Included Studies

A total of 2694 papers were retrieved by literature retrieval. After cutting duplications, 1854 articles were left, of which 1742 papers were dropped out as being unconformity with our topics. A further 5 potentially relevant articles were gained by screening references of the remaining literatures. After more detailed estimations of the 117 papers, 14 met the inclusion/exclusion criteria and were included in this meta-analysis to

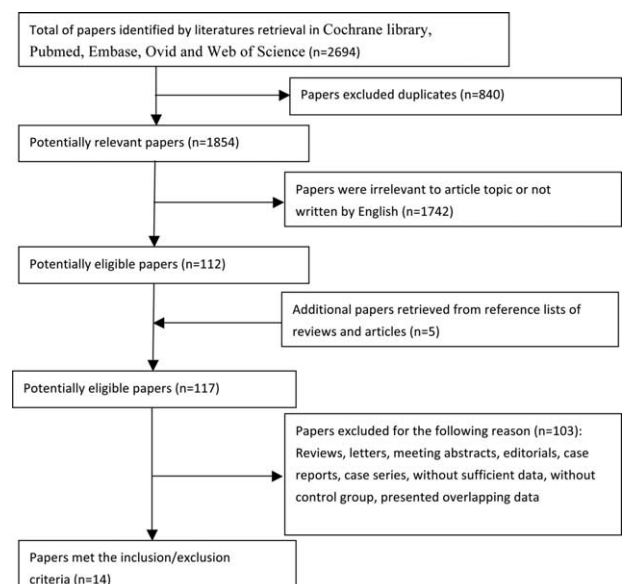


FIGURE 1. Flow diagram of literature retrieval in this study.

TABLE 1. Characteristics of Included Cohort Studies

Year	First Author	Article Types	Country	No. of Subjects	Outcomes	Patients Selection Criteria	Follow-Up Time (Range)	Evidence Level
1979	EN Gleave	RC	United Kingdom	369	R	Favored ECD that included mobility, size large enough to allow for safe manipulation of the nerve and its branches	Unclear	Level 3b
1983	C Martis	RC	Greece	176	R	ECD; small size, up to 2.5 cm in diameter, superficial lobe tumor	Range, 0–2 yr	Level 3b
1992	AJ Prichard	RC	United Kingdom	46	R, T, P, FS	The majority being tumors found in tail of the gland (90%)	Mean 54 mo (>2 yr)	Level 3b
1994	K Natvig	RC	Norway	198	R	Unclear criteria	Mean 18 yr (11–25 yr)	Level 3b
1999	BD Hancock	RC	United Kingdom	101	R, T, P, FS	Mobile and superficial lobe tumor for ECD, otherwise for SP	Mean 10.3 yr (3–21 yr) for ECD; 8.3 yr (3–22) yr for SP	Level 3b
2000	K Marti	RC	Greece	249	R, T, P, FS	Superficial lobe and <2.5 cm in diameter for ECD, unknown for SP	Median 18 yr (6–26 yr)	Level 3b
2003	M McGurk	RC	United Kingdom	630	R, T, P, FS	Tumors <4 cm in diameter. The choice of techniques was made on mobility at surgery after raising the skin flap	Median 12 yr (5–30 yr)	Level 3b
2003	S Ghosh	RC	United Kingdom	71	R	Unclear	Mean 12 yr (5–20 yr)	Level 3b
2011	Y Uyar	PC	Turkey	41	R, T, P, FS	Superficial lobe	Mean 194 mo (117–264 mo)	Level 3b
2012	L Barzan	RC	Italy	349	R, P, FS	Neoplasms with impaired mobility, or deeply located, or with a history of recurrent inflammation	Minimum follow-up, 7 yr	Level 3b
2013	S-S Zhang	RC	China	268	R, T, P	Superficial lobe; ECD was carried out the tumor <2 cm in diameter and located in the tail of the parotid gland	Median 18 mo (6–159 mo)	Level 3b
2013	GD Orabona	RC	Italy	232	R, T, P, FS	ECD was performed in cases of tumor located in the superficial lobe of parotid gland; SP was preferred cases of tumor diameter >3 cm or the case of recurrence	Mean 52.6 mo for SP; 46 mo for ECD (1–108 mo)	Level 3b
2013	H Iro	RC	Germany	144	R	The surgical technique to be performed in an individual case, ECD in cases of a single and mobile tumor located superficially within the lateral lobe of the parotid gland	Mean 7.38 yr (5.05–10.52 yr)	Level 3b
2015	G Huang	RC	China	320	R, T, P, FS	Unclear	Range from 5 to 8 yr	Level 3b

ECD = extracapsular dissection; FS = Frey's syndrome; P = permanent facial nerve dysfunction; PC = prospective cohort; R = recurrence; RC = retrospective cohort; SP = superficial parotidectomy; T = transient facial nerve dysfunction.

TABLE 2. Data Summary From Included Studies

Year	First Author	Recurrence		Transient FND		Permanent FND		Frey's Syndrome	
		ECD	SP	ECD	SP	ECD	SP	ECD	SP
1979	EN Gleave	5/257	2/112						
1983	C Martis	0/98	0/78						
1992	AJ Prichard	0/31	1/15	1/31	2/15	0/31	1/15	0/31	6/15
1994	K Natvig	0/5	5/193						
1999	BD Hancock	0/28	0/73	2/28	6/73	0/28	0/73	0/28	18/73
2000	K Marti	0/139	0/110	6/139	18/110	0/139	0/110	0/139	2/110
2003	M McGurk	8/491	2/139	48/491	45/139	8/491	2/139	25/491	45/139
2003	S Ghosh	1/22	3/49						
2011	Y Uyar	0/21	0/20	0/21	3/20	0/21	0/20	0/21	1/20
2012	L Barzan	7/299	5/50			4/299	3/50	4/299	22/50
2013	S-S Zhang	1/163	0/105	29/163	34/105	3/163	4/105		
2013	GD Orabona	8/176	2/56	7/176	15/56	0/176	5/56	0/176	3/56
2013	H Iro	0/76	1/68						
2015	G Huang	0/79	0/241	6/79	55/241	0/79	2/241	5/79	38/241

ECD = extracapsular dissection; FND = facial nerve dysfunction; SP = superficial parotidectomy.

evaluate the associations between SP and ECD.^{3,16,22–24,30–32,36–41} The literature retrieval process was shown in Figure 1.

The crucial information extracted from each included study was presented in Table 1, including the publication year, first author, country, number of patients, outcomes of patients, surgical selection criteria, and follow-up and other relevant data. Of these 14 studies, 3194 patients (ECD group: 1885 patients; SP group: 1309 patients) were included to analyze the relevance of SP and ECD. And the publication year of eligible studies ranged from 1979 to 2015. As for the types of included articles, there were 13 retrospective cohort studies, 1 prospective cohort study and none of RCT study. Among these included studies, the majority of them were reported from Europe, and the rest were from Asia. The parameters of clinical outcome included recurrence, transient facial nerve dysfunction (transient FND), permanent FND, and FS. All the detailed data were shown in Tables 1 and 2.

The Results of Quality Assessment

All included studies were observational study (cohort study) and the results of quality assessment were shown in

Table 1. Because every included study was supported by the Levels 3b of evidence, some certainties in outcomes of systematic review offered a conditional reliability (the levels of evidence: Level 3a).

Recurrence Rates of ECD Versus SP

The results of meta-analysis with regard to recurrence rate showed that there were no obvious heterogeneities among included studies ($I^2 = 0.0\%$, $P_{(Q-test)} = 0.541$). Both the REM and FEM were performed to pool the RRs and 95% CIs. The overall RRs and the corresponding 95% CIs were 0.67 (0.36–1.23) and 0.71 (0.40–1.27), respectively. (Table 3; Figures 2A and 3A), indicating that ECD leads to a similar recurrence rate with SP.

Incidence of Transient FND of ECD Versus SP

The result of heterogeneity estimation suggested that the similar homogeneity cross all included studies ($I^2 = 24.0\%$, $P_{(Q-test)} = 0.237$). Both the REM and FEM were used to combined RRs and 95% CIs. The meta-analysis results ($RR_{REM} = 0.39$,

TABLE 3. Results of ECD Versus SP in This Meta-Analysis

	Recurrence		Transient FND		Permanent FND		Frey's Syndrome	
	FEM	REM	FEM	REM	FEM	REM	FEM	REM
I^2 , %	0.0	0.0	24.0	24.0	12.5	12.5	46.8	46.8
$P_{(Q-test)}$	0.541	0.541	0.237	0.237	0.335	0.335	0.068	0.068
RR (95% CI)	0.71 (0.40–1.27)	0.67 (0.36–1.23)	0.40 (0.31–0.50)	0.39 (0.28–0.54)	0.35 (0.17–0.69)	0.38 (0.16–0.88)	0.17 (0.12–0.24)	0.15 (0.07–0.30)
P	0.249	0.197	0.000	0.000	0.002	0.024	0.000	0.000
Publication bias								
Begger's test	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000
Egger's test	0.337	0.337	0.904	0.904	0.319	0.319	0.882	0.882

CI = confidence interval; ECD = extracapsular dissection; FEM = fixed-effect model; FND = facial nerve dysfunction; REM = random-effect model; RR = risk ratio; SP = superficial parotidectomy.

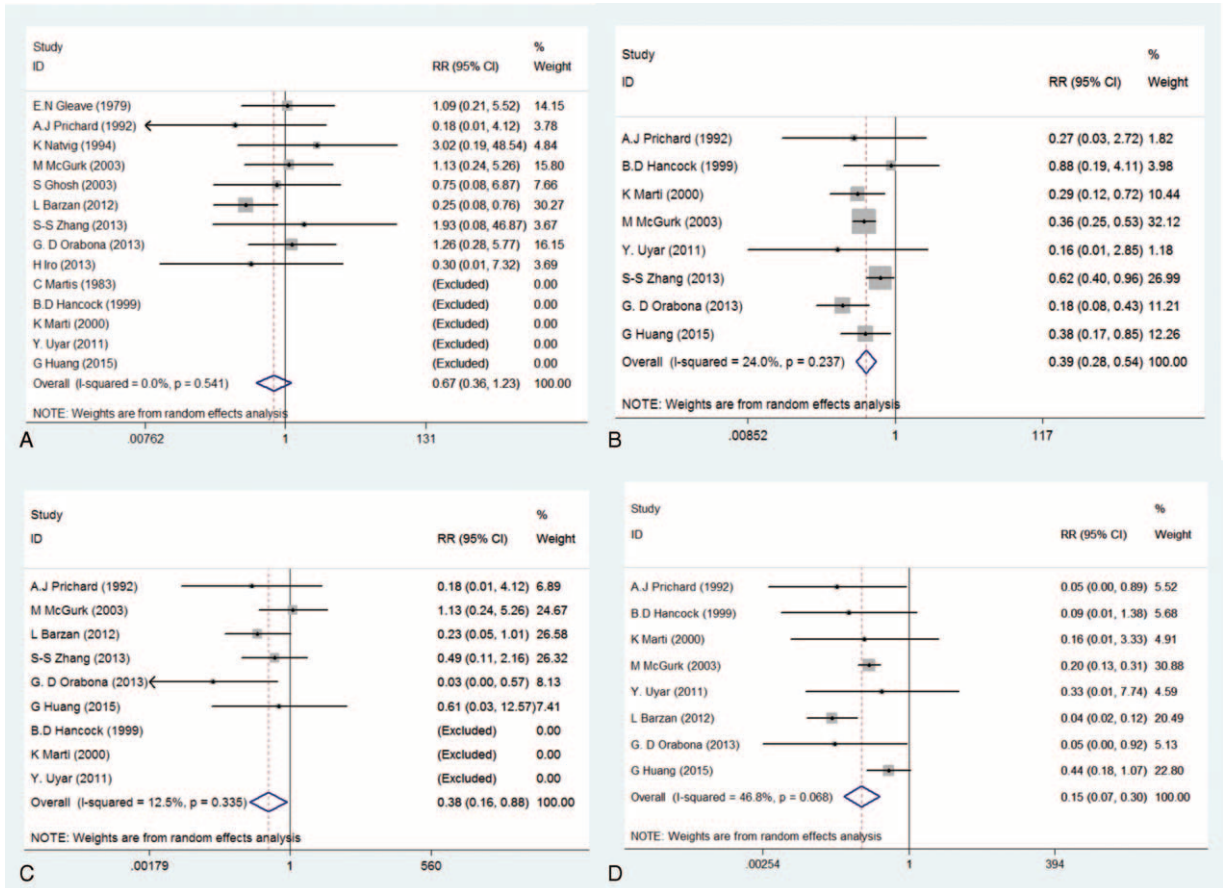


FIGURE 2. Forest plots evaluating clinical outcomes comparing ECD to SP—random-effect model (A: recurrence; B: transient facial nerve dysfunction; C: permanent facial nerve dysfunction; D: Frey’s syndrome). ECD = extracapsular dissection; SP = superficial parotidectomy.

95% $CI_{REM} = 0.28-0.54$, $P = 0.000$; $RR_{FEM} = 0.40$, 95% $CI_{FEM} = 0.31-0.50$, $P = 0.000$) indicated that transient FND has a lower incidence rate with ECD compared with SP (Table 3, Figures 2B and 3B).

Incidence of Permanent FND of ECD Versus SP

Even if fewer heterogeneities existed in these eligible studies ($I^2 = 12.5\%$, $P_{(Q-test)} = 0.335$), both the REM and FEM were carried out to further estimate the incidence of permanent FND. This meta-analysis results ($RR_{REM} = 0.38$, 95% $CI_{REM} = 0.16-0.88$, $P = 0.024$; $RR_{FEM} = 0.35$, 95% $CI_{FEM} = 0.17-0.69$, $P = 0.002$) demonstrated that the incidence of permanent FND was lower in patients with ECD compared with SP (Table 3; Figures 2C and 3C).

Incidence of FS of ECD Versus SP

Owing to moderate heterogeneities in these included studies ($I^2 = 46.8\%$, $P_{(Q-test)} = 0.068$), both the REM and FEM were performed. The results ($RR_{REM} = 0.15$, 95% $CI_{REM} = 0.07-0.30$, $P = 0.000$; $RR_{FEM} = 0.17$, 95% $CI_{FEM} = 0.12-0.24$, $P = 0.000$) suggested that incidence of FS after ECD was significantly lower than that of SP (Table 3; Figures 2D and 3D).

Publication Bias and Sensitivity Analysis

Begger’s and Egger’s tests were calculated to evaluate the possible publication bias. Begger’s and Egger’s tests

demonstrate that no significant publication bias lies in these meta-analyses (the data were shown in Table 3; Figure 4). The sensitivity analyses produced variations only between the lower CIs limits and the upper CIs limits, suggesting that the data from our meta-analyses are robust and credible (Figure 5).

DISCUSSION

All surgical techniques have moved toward less invasive procedures and reduction in surgical complications, including parotid tumor surgery.⁴² Owing to abundant complications, the golden standard, SP, treatment of benign parotid tumor has been questioned for many years. How to reach a good balance between tumor recurrence rates and FND has been debatable for several decades. Although lots of published articles or reviews supported the ECD or partial SP instead of SP,^{17,42,43} dissenters also offered their clinical evidence.¹⁹ The debate continues from the birth of ECD to now, even recent systematic reviews, the main conclusions are still conflicting. Foresta et al²⁹ claimed that the recurrence rate is higher in patients undergoing SP compared with ECD; however, Albergotti et al²⁸ declared that ECD has a similar recurrence rate as SP with few surgical complications. To explore the truth of controversy, we scrutinized these meta-analyses and found that they performed different inclusion/exclusion criteria and included different articles, which might produce their conflicting conclusions.

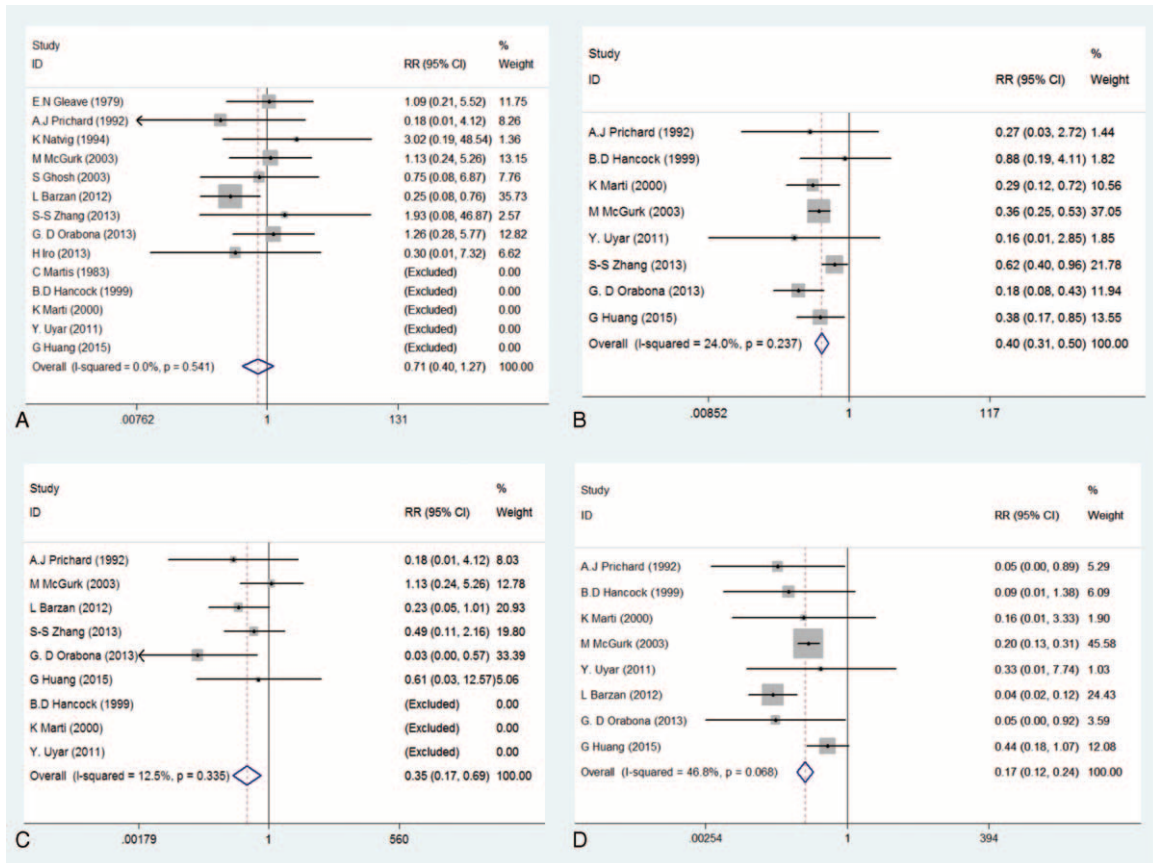


FIGURE 3. Forest plots evaluating clinical outcomes comparing ECD to SP—fixed-effect model (A: recurrence; B: transient facial nerve dysfunction; C: permanent facial nerve dysfunction; D: Frey's syndrome). ECD = extracapsular dissection; SP = superficial parotidectomy.

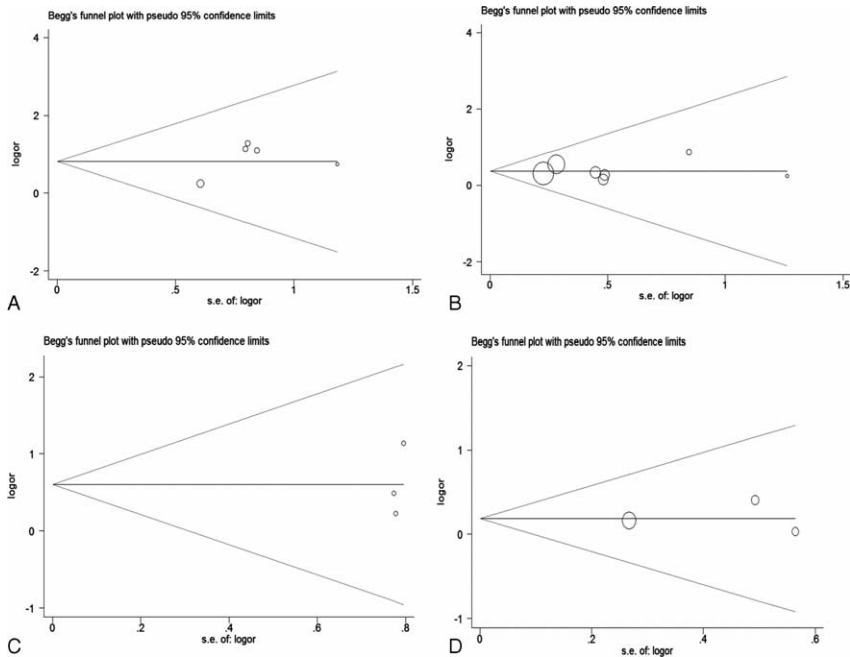


FIGURE 4. Funnel plots evaluating possible publication bias for clinical outcomes comparing ECD to SP (A: recurrence; B: transient facial nerve dysfunction; C: permanent facial nerve dysfunction; D: Frey's syndrome). ECD = extracapsular dissection; SP = superficial parotidectomy.

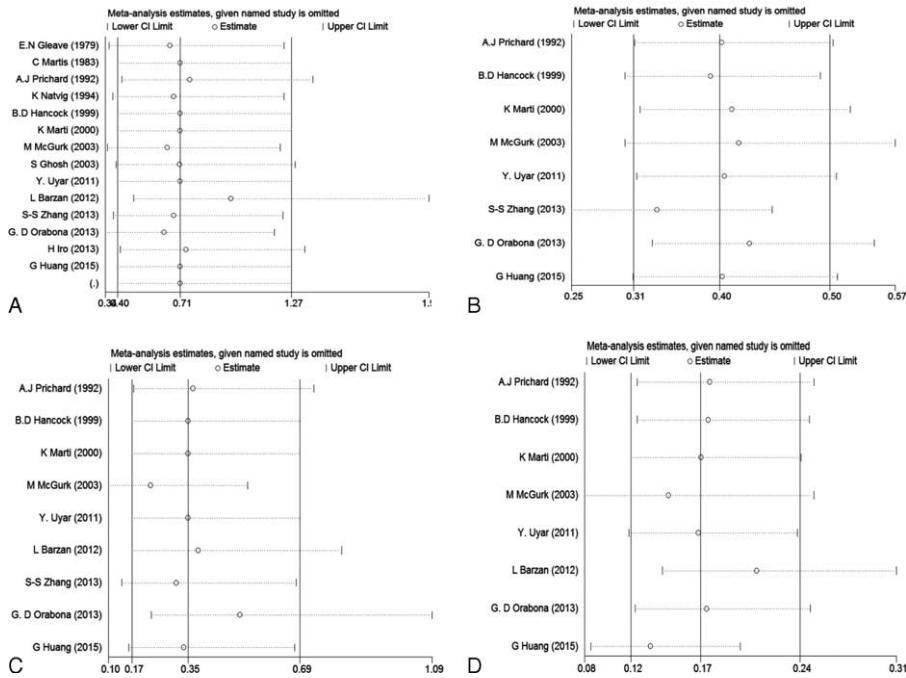


FIGURE 5. Sensitivity analyses of clinical outcomes comparing ECD to SP (A: recurrence; B: transient facial nerve dysfunction; C: permanent facial nerve dysfunction; D: Frey's syndrome). ECD = extracapsular dissection; SP = superficial parotidectomy.

According to the Cochrane handbook, meta-analysis and systematic reviews are considered to be the best available evidence if all good trails are included. However, the best available evidence might not be equal to sufficient evidence.^{44,45} What is more, lower quality of evidence may lead surgeons to make wrong decisions and kill thousands of lives.⁴⁶ Thus, it is necessary to recognize the quality of evidence for all clinicians. With the publication of new evidence, it is necessary to reach more reasonable and comprehensive conclusions by using higher levels of evidence. Thus, next we reported a new meta-analysis with better evidence and more serious quality evaluation, including 14 cohort studies with 3194 patients.

In the process of our literature retrieval, we found that the nomenclature and classification system of parotid surgery were disordered among the different authors, even the same surgical procedures also might be defined as different names. Meanwhile, the same surgical names sometimes might be described as different surgical procedures. This meant that the results of some literatures might confuse one thing with another. For example, some authors mistook enucleation for ECD, which might report high recurrence rates and result in false positive. In order to estimate these surgical techniques with unified standards, our inclusion/exclusion criteria were based on their surgical procedures along with their descriptions of materials and methods. After serious scrutiny, 14 cohort studies were included to analyze this topic. In our meta-analysis, the results showed that ECD leads to a similar recurrence rate and fewer surgical complications compared with SP. Besides, the assessment of evidence quality showed our results were supported by a systematic review of cohort studies (Level 3a in evidence grade), which could be considered as conditionally reliable.

However, several shortages should not be ignored. First, the selection bias of surgical patients. The ECD were performed in most of cases of mobile tumor located in the superficial lobe of parotid, and the diameters are <4cm,²² even 2.5 cm or

2.0 cm.^{32,39} However, the SP was carried out in most of cases with larger, immobile tumor. The tumor sizes are closely related to tumor recurrence and clinical outcomes. Besides, the bigger tumors might be adhesion to facial nerve trunk and its branches, which might result in facial nerve damage during surgery. Thus, the selection bias reduced the application areas of our results. Second, all included studies were retrospective cohort study, and no prospective RCT was reported. The inner limitation of article type might reduce the credibility and robustness of results. Third, different patients have different genotype and genotype difference may influence the tumor susceptibility, such as Mcl-1, Survivin, rs1447295 and rs4430796 polymorphisms, which might influence the tumor prognosis.⁴⁷⁻⁵⁰ Some surgeons lacking ability to dissect facial nerve might also play a significant role on the clinical outcomes. During the surgical procedures of ECD, SP should be performed if surgeons found that tumor adhere to facial nerve. To benefit patients, all surgeons performing ECD must be experienced and capable to perform multiple variation of the parotid operation. Fourth, owing to long clinical course of parotid tumor, the recurrence time of benign parotid tumor is more than 5 years. The follow-up times of several studies included in our meta-analysis are <7 years, even 2 studies^{32,39} <5 years, which might produce false-negative data for the recurrence rate. Thus, it is important to interpret the conclusions with caution.

The goal of evidence-based medicine is to find the best evidence to guide clinical decisions. Good decision needs sufficient and good evidence. Based on these conditions mentioned above, we supported rational recommendation with restricted conditions: ECD might be a good choice in treatment of the benign parotid tumor that were mobile, small, located in superficial lobe and without adhesion to facial nerve; ECD should be performed by the experienced surgeons with ability of dissection facial nerve, who should perform SP if tumor is found adhere to facial nerve during an operation; and a multicenter

RCT study is necessary to decide the optimal treatment of benign parotid tumor.

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