PSP versus ECD

Search and select
A systematic review of the literature was performed to answer the following question:
What are the (un)beneficial effects of a extracapsular dissection (ECD) on tumor recurrence and facial nerve injury in patients with a benign parotid tumor when compared to partial superficial parotidectomy?

P: patients with benign parotid tumor;
I: extracapsular dissection (ECD);
C: partial superficial parotidectomy (PSP);
O: tumor recurrency, facial nerve injury.

Relevant outcome measures
The guideline development group considered tumor recurrence as a critical outcome measure for decision making; and facial nerve injury as an important outcome measure for decision making.

A priori, the working group did not define the outcome measures listed above but used the definitions used in the studies. The working group defined OR<0.9 and OR>1.1 as a minimal clinically (patient) important differences for tumor recurrency and facial nerve injury.

Search and select (Methods)
The databases Medline (via OVID) and Embase (via Embase.com), were searched with relevant search terms until February 10, 2023. The detailed search strategy is depicted under the tab Methods. The systematic literature search resulted in 120 hits. The systematic review was selected based on the following criteria:

- Minimum of two databases searched;
- Detailed search strategy with search date;
- In- and exclusion criteria;
- Evidence table for included studies;
- Risk of bias assessment per study;
- Intervention and Comparison according to the PICO;
- Study population according to the PICO.

Eleven systematic reviews were initially selected based on title and abstract screening. After reading the full text, ten systematic reviews were excluded (see the table with reasons for exclusion under the tab Methods), and one systematic review was included.

Results
One systematic review is included in the analysis of the literature. Important study characteristics and results are summarized in the evidence table. The assessment of the risk of bias is summarized in the risk of bias table.

Summary of literature
Description of studies
Mashrah (2021) performed a systematic review and meta-analysis with the aims of investigated whether the extent of surgical resection of benign parotid tumors increase the risk of postoperative complications and what the best surgical intervention is for treatment of benign parotid tumors that can provide an acceptable balance between the tumor recurrence and

other postoperative complications. A comprehensive search on PubMeD, Embase, Scopus, and Cochrane library was conducted to identify the studies.
The outcome measures were; the incidence rates of tumor recurrence, temporary facial nerve weakness (TFW), permanent facial nerve paralysis (PFP), Frey Syndrome (FS), sialocele, and salivary fistula following a particular parotid surgery. 44 studies were included in this systematic review.

Six studies in the systematic review reported the comparison of interest (i.e. ECD versus PSP) (Zheng, 2018; Ciuman, 2012; Park, 2018; Ruohoalho, 2017; Iro, 2012; Witt, 2002). Regarding the outcome of interest in the present analysis, two studies in the systematic review reported **tumor recurrence** (Zheng, 2018; Iro, 2012). **Temporary facial weakness** was reported in three studies (Zheng, 2018; Ruohaolho, 2017; Witt, 2002). For the outcome **permanent facial nerve paralysis**, it is unclear which studies are included by the author in the pooled analysis. Regarding the outcome **Frey's syndrome**, three studies are included (Zheng, 2018; Ciuman, 2012; Witt, 2002). **Sialocele** was reported in two studies (Zheng, 2018; Ruohoalho, 2017). None of the studies reported on **salivary fistula**.

Results
Tumor recurrence
Mashrah (2021) performed a meta-analysis with two studies (192 participants) and reported an overall OR of 6.443 (95% CI: 0.655-63.406, I^2: 0%), with the point estimate favoring ECD.

Temporary facial weakness
Mashrah (2021) performed a meta-analysis with three studies (338 participants) and reported an overall OR of 2.265 (95% CI: 0.548-9.335, I^2: 63%), with the point estimate favoring ECD.

Permanent facial nerve paralysis
Mashrah (2021) performed a meta-analysis with three studies (392 participants) and reported an overall OR of 1.063 (95% CI: 0.248-4.563, I^2: 0%), with the point estimate favoring ECD.

Frey's syndrome
Mashrah (2021) performed a meta-analysis with three studies (338 participants) and reported an overall OR of 6.35 (95% CI: 1.19-33.73, I^2: 18%), with the point estimate favoring ECD.

Sialocele
Mashrah (2021) performed a meta-analysis with two studies (257 participants) and reported an overall OR of 3.066 (95% CI: 0.310-11.934, I^2: 0%), with the point estimate favoring ECD.

Salivary fistula
Not reported.

Level of evidence of the literature
The level of evidence regarding the outcome measure *tumor recurrence* started as low, as data was retrieved from observational studies. The level of evidence was downgraded by 3 levels because of study limitations (risk of bias, -1) and absence of events (imprecision, -2). The level of evidence for this outcome is *very low*.

The level of evidence regarding the outcome measure *temporary facial weakness* started as low, as data was retrieved from observational studies. The level of evidence was downgraded by 3 levels because of study limitations (risk of bias, -1) and absence of events (imprecision, -2). The level of evidence for this outcome is *very low*.

The level of evidence regarding the outcome measure *permanent facial nerve paralysis* started as low, as data was retrieved from observational studies. The level of evidence was downgraded by 3 levels because of study limitations (risk of bias, -1) and absence of events (imprecision, -2). The level of evidence for this outcome is *very low*.
The level of evidence regarding the outcome measure *Frey's syndrome* started as low, as data was retrieved from observational studies. The level of evidence was downgraded by 3 levels because of study limitations (risk of bias, -1) and absence of events (imprecision, -2). The level of evidence for this outcome is *very low*.

The level of evidence regarding the outcome measure *sialocele* started as low, as data was retrieved from observational studies. The level of evidence was downgraded by 3 levels because of study limitations (risk of bias, -1) and absence of events (imprecision, -2). The level of evidence for this outcome is *very low*.

The level of evidence regarding the outcome measure *salivary fistula* could not be graded since none of the included studies reported this outcome.

Conclusions

Very low GRADE	The evidence is very uncertain about the effect of extracapsular dissection (ECD) on **tumor recurrence** in patients with a benign parotid tumor, when compared to partial superficial parotidectomy (PSP). *Source:* Mashrah, 2021

Very low GRADE	The evidence is very uncertain about the effect of extracapsular dissection (ECD) on t**emporary facial weakness** in patients with a benign parotid tumor, when compared to partial superficial parotidectomy (PSP). *Source:* Mashrah, 2021

Very low GRADE	The evidence is very uncertain about the effect of extracapsular dissection (ECD) on **permanent facial nerve paralysis** in patients with a benign parotid tumor, when compared to partial superficial parotidectomy (PSP). *Source:* Mashrah, 2021

Very low GRADE	The evidence is very uncertain about the effect of extracapsular dissection (ECD) on **Frey's syndrome** in patients with a benign parotid tumor, when compared to partial superficial parotidectomy (PSP). *Source:* Mashrah, 2021

Very low GRADE	The evidence is very uncertain about the effect of extracapsular dissection (ECD) on **sialocele** in patients with a benign parotid tumor, when compared to partial superficial parotidectomy (PSP). *Source:* Mashrah, 2021

- GRADE	No evidence was found regarding the effect of extracapsulair dissection (ECD) on **salivary fistula**, in patients with a benign parotid tumor, when compared to partial superficial parotidectomy (PSP).

	Source: -

Overwegingen – van bewijs naar aanbeveling

Voor- en nadelen van de interventie en de kwaliteit van het bewijs
Voor de cruciale uitkomstmaat (tumor recurrence) en de belangrijke uitkomstmaat (facial nerve injury zijn uitkomsten gerapporteerd door de systematic review van Mashrah (2021).

Zes studies in de systematic review bekeken de vergelijking ECD versus PSP. Twee studies uit de systematisch review van Mashrah (2021) rapporteerden tumorrecidief (Zheng, 2018; Iro, 2012). Drie studies rapporteerden tijdelijke gezichtszwakte (Zheng, 2018; Ruohaolho, 2017; Witt, 2002). Voor de uitkomstmaat permanente verlamming van de aangezichtszenuw werden er drie studies geïncludeerd, maar voor deze uitkomstmaat was het onduidelijke welke individuele studies deze uitkomstmaat rapporteerde. Drie studies rapporteerden Frey's syndrome (Zheng, 2018; Ciuman, 2012; Witt, 2002) en twee studies rapporteerden sialocèle (Zheng, 2018; Ruohoalho, 2017). Geen enkele studie rapporteerde de uitkomstmaat speekselfistel.

De overall bewijskracht is **zeer laag.** Dit gezien de beperkingen in de onderzoeksopzet (observationele studies), het geringe aantal of afwezigheid van 'events' (imprecisie).

De studie van Mashrah (2021) had als doel om te bekijken of 1) de omvang van de operatie van een benigne speekselkliertumor van invloed is op de postoperatieve complicaties en 2) wat de beste chirurgische interventie is voor de behandeling van goedaardige speekselkliertumoren met het best aanvaardbare evenwicht tussen de tumorrecidiefkans en de postoperatieve complicaties. Hiervoor werd een uitgebreide literatuuronderzoek verricht in PubMed, Embase, Scopus en de Cochrane database. De uitkomsten van interesse waren; tumorrecidief, zenuwzwakte (permanent/tijdelijk), Frey's syndroom, sialocèle en speekselfistel. Een Bayesiaanse netwerk meta-analyse (NMA) werd uitgevoerd, met een random-effect mode. In totaal werden er 44 studies geïncludeerd (1 RCT en 43 observationele studies) met in totaal 7841 patiënten waarbij er gekeken werd naar vijf verschillende chirurgische ingrepen, namelijk; enucleatie, extracapsulaire dissectie (ECD), partiële superficiële parotidectomie (PSP), partiële parotidectomie (SP) en totale parotidectomie (TP).

De tumorrecidiefpercentages bij enucleatie, ECD, PSP, SP en TP was respectievelijk 14,3%, 3,6%, 3,7%, 2,8% en 1,4%. Enucleatie vertoonde de hoogste tumorrecidief in vergelijking met ECD, SPS, SP en TP, maar er lijkt geen verschil te zitten in de keuze tussen ECD, PSP, SP en TP. Daarnaast was er wel een verhoogde incidentie van tijdelijke zenuwzwakte en Frey's syndrome met de toename van de omvang van de parotidectomie. De huidige NMA toonde aan dat het risico op TFW en FS toeneemt met de toename van de omvang van de parotidectomie en dat ECD en PSP beschouwd kunnen worden als de behandeling van keuze voor goedaardige parotis tumoren, omdat beide een acceptabele balans bieden tussen de incidentie van tumorrecidief en gezichtszenuwdysfunctie. Daarnaast wordt opgemerkt dat ECD in verband wordt gebracht met verminderde morbiditeit, maar dat deze techniek alleen gebruikt zou moeten worden voor specifieke parotistumoren en door een ervaren chirurg.

Een mogelijke oorzaak voor de verschillen in de literatuur is de indicatie voor de toepassing van de techniek. De grootte en met name de lokalisatie van de laesie zijn hierin de meest bepalende parameters. De ESGS stelde recent daarom een chirurgische benadering voor gebaseerd op de lokalisatie van de laesie. Een andere belangrijke parameter lijkt de ervaring van de chirurg, waarbij de ECD is voorbehouden aan de ervaren chirurg die bekend is met alle technieken en zorgvuldig overweegt of de laesie via ECD veilig kan worden verwijderd, zonder kapselruptuur en facialis letsel.

Er lijkt dus plaats te zijn voor de ECD voor de resectie van oppervlakkig gelegen benigne speekselkliertumoren, echter moet verder prospectief onderzoek laten zien of de ECD ook superieur is ten opzichte van de PSP in selecte gevallen.

Literatuur

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Evidence table for systematic review of RCTs and observational studies (intervention studies)

Research question: What are the (un)beneficial effects of a extrasapsular dissection (ECD) on tumor recurrence and facial nerve injury in patients with a benign parotid tumor when compared to partial superficial parotidectomy?

Study reference	Study characteristics	Patient characteristics	Intervention (I)	Comparison / control (C)	Follow-up	Outcome measures and effect size	Comments
Mashrah, 2021 NB: study characteristics and results are extracted from the SR (unless stated otherwise) NB2: only the studies with the PSP and ECD comparison are included in this table.	SR and meta-analysis of retrospective (RS) and prospective (PS) cohort studies *Literature search up to October 2020.* **A**: Zheng, 2018 (RS) **B**: Ciuman, 2012 (RS) **C**: Park, 2018 (RS) **D**: Witt, 2002 (RS) **E**: Ruohoalho, 2017 (RS) F: Iro, 2012 (RS) <u>Study design</u>: prospective / retrospective cohort studies <u>Setting and Country</u>: <u>Source of funding and conflicts of interest:</u> [commercial / non-commercial / industrial co-authorship]	Inclusion criteria SR: • RCTs and non-RCTs with at least 10 participants in each comparator. • Studies that compared at least two surgical interventions for the treatment of benign parotid tumors. • Reporting at least one of the following outcomes: tumor recurrence, TFW, PFP, FS, sialocele, or salivary fistula Exclusion criteria SR: • Studies including malignant tumors • Animal studies, case reviews, and review articles *44 studies were included*	Describe intervention: Extracapsular dissection (ECD)	Describe control: Partial superficial parotidectomy (PSP)	<u>End-point of follow-up</u>: **A**: 3 years **B**: 3 years, 8 months and 16 days **C**: > 2 years **D**: 8 to 9 years **E**: 1 year F: 7.38 years (mean) <u>For how many participants were no complete outcome data available?</u> **A:** Not reported for subgroups **B**: Not reported for subgroups **C**: Not reported for subgroups **D**: Not reported for subgroups **E**: Not reported for subgroups F: Not reported for subgroups	<u>Outcome measure-1</u> **Tumor recurrence** Studies A and F are included for this pooled effect: 192 participants Total number of participants: Pooled effect for PSP versus ECD: OR (95% CI): 6.443 (0.655, 63.405), heterogeneity: 0% p-value = 0.110 [favoring ECD] The study by Witt (2002) reported 0 event in both groups and were excluded from the meta-analysis <u>Outcome measure-2</u> **Temporary facial weakness** Studies A, B and D are included for this pooled effect: 338 participants	<u>Risk of bias (high, some concerns or low):</u> Tool used by authors: The classification of the risk of bias potential for each study was based on five criteria: (1) random selection, (2) definition of inclusion and exclusion criteria, (3) report of losses to follow-up, (4) validated measurements, and (5) statistical analysis. A study that met all the above-mentioned criteria was classified as having a low risk of bias; a study that did not meet one of these criteria was classified as having a moderate risk of bias. When two or more criteria were not met, the study was considered to have a high risk of bias **A**: Some concerns **B**: High **C**: High **D**: High **E**: Some concerns **F**: Some concerns Remarks:

		<u>Important patient characteristics at baseline</u>: <u>N, mean age (SD)</u> **A**: I=91, 49 (17) C=92, 49 (16) **B**: I=20, NR C=95, NR **C**: I=12, NR C=15, NR Mean age whole group: 49 **D:** I=20, 44.4 C=20, 45.7 **E:** I=17, NR C=57, NR Mean age whole group, 54.3 F: I=76 C=18 Mean age whole group, 51.35 <u>*Sex, ratio M;F:*</u> **A**: I: 49:43 / C: 49:42 **B**: NR for subgroups Whole group: 102:94 **C**: I: 8:4 / C: 4:11 **D:**				Pooled effect for PSP versus ECD: OR (95% CI): 2.265 (0.548, 9.355), heterogeneity: 63% p-value = 0.259 [favoring ECD] <u>Outcome measure-3</u> **Permanent facial nerve paralysis** Unclear which studies are included for this pooled analysis. Pooled effect: 392 participants Pooled effect for PSP versus ECD: OR (95% CI): 1.063 (0.248, 4.563), heterogeneity: 0% p-value = 0.935 [favoring ECD] <u>Outcome measure-4</u> **Frey syndrome** Studies A, B and D are included for this pooled effect: 338 participants Pooled effect for PSP versus ECD: OR (95% CI): 6.35 (1.19, 33.73), heterogeneity: 18% p-value = 0.030 [favoring ECD]	• Masrah (2021) claims that the study by Iro (2012) investigates the ECD, PP, TP, and PSP techniques. However, the study by Iro (2012) evaluates the clinical follow-up of a pleomorphic adenoma with the ECD, PP, TP, and SP techniques. • Schapher (2020) combines all the different surgical techniques (PSP, SP, TP) and makes a comparison between ECD and all other surgical techniques, without stratification. Therefore, this study could not be used to answer our clinical question. [see supplementary file from Masrah, 2021] • Not clear for all outcomes which individual studies are included in the pooled effect Author's conclusion: Within the limitations of the current NMA, it seems that no significant difference between ECD, PSP, SP, and TP was found concerning tumor recurrence. Although

		I: 8:12 / C: 8:12 **E**: NR for subgroups Whole group: 59:73 F: NR for subgroups Whole group: 29:47 Groups comparable at baseline? Probably no				<u>Outcome measure-5</u> Sialocele: Studies A and E are included for this pooled effect: 257 participants Pooled effect for PSP versus ECD: OR (95% CI): 3.066 (0.310, 11.934), heterogeneity: 0% p-value = 0.483 [favoring ECD] <u>Outcome measure-6</u> Salivary fistula: Not reported	ECD was associated with reduced morbidity without oncological compromise, it should only be used for specific parotid tumors through an experienced surgeon. The incidence of TFW and Frey's syndrome appears to be increased with an increased extent of parotid surgery, whereas the incidence of PFP, salivary fistula, and sialocele seems to have no relation with the extent of parotid surgery.

Table of excluded studies (search strategy)

Author and year	Reason for exclusion
Witt 2002	No systematic review
Witt 2009	No systematic review
Zbären 2013	No systematic review
Foresta 2014	Wrong comparison
Colella 2015	Overlap with included systematic review (Mashrah 2021)
Xie 2015	Wrong comparison
Mehta 2015	Wrong comparison
Jia 2017	Article in Chinese
Lin 2019	No systematic review
Martin 2020	Wrong comparison