A systematic literature review to compare clinical outcomes of different surgical techniques for second branchial cyst removal.

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Abstract

Aims: During the last two decades, new treatment methods have been developed for the surgical removal of second branchial cysts which result in less visible scars. The aim of this systematic review is to assess which surgical technique for second branchial arch cyst removal results in the lowest complication and recurrence rates with the highest scar satisfaction. Methods: Two authors systematically reviewed literature in the Cochrane, PubMed and EMBASE databases (search date: 1975 to December 23th, 2019) to identify studies comparing surgical outcomes of second branchial arch cyst removal. Authors appraised selected studies on directness of evidence and risk of bias. Results are reported according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. Results: Out of the 2101 retrieved articles, four articles were included in the current review including a total of 140 operated cysts. Only two studies included pre-operatively infected cysts. Follow up ranged from 3 to 24 months. Complication rates ranged between 0 to 27.3% (conventional: [0-10.4%]; endoscopic/retro auricular: [0-27.3%]). None of the patients presented with postoperative recurrence. Significantly higher scar satisfaction was found in adult patients who underwent endoscopic or retro-auricular hairline incision cyst removal. Conclusion: No recurrence of disease occurred during (at least) 3 months of follow up using either conventional surgery or endoscopic/retro auricular techniques. Although more (temporary) complications occur using endoscopic and retro-auricular techniques, patients report a significantly higher scar satisfaction 3 to 6 months after surgery in comparison to the conventional technique. Future studies are needed to support these findings.

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Level of Evidence: Level IIA

5 key points :

- Branchial cysts are the most common branchial anomalies in adults and early and complete surgical excision is the recommended treatment

- More (temporary) complications occur using endoscopic and retro-auricular techniques [0-27.3%] than through application of the conventional technique [0-10.4%].
- Retroauricular and endoscopic surgery results in significantly higher scar satisfaction in uninfected branchial cysts 3 to 6 months after surgery in comparison to the conventional technique
- No disease recurrence was reported during (at least) 3 months of follow up using either conventional surgery or endoscopic/retro auricular techniques
- Since follow up was short, recurrence rates could be underreported and scar judgment could be affected. Therefore, no evidence based treatment advice can be provided and future prospective studies with long-term follow up (> five years) are indicated.

Abstract: Aims : During the last two decades, new treatment methods have been developed for the surgical removal of second branchial cysts which result in less visible scars. The aim of this systematic review is to assess which surgical technique for second branchial arch cyst removal results in the lowest complication and recurrence rates with the highest scar satisfaction.**Methods:** Two authors systematically reviewed literature in the Cochrane, PubMed and EMBASE databases (search date: 1975 to December 23th, 2019) to identify studies comparing surgical outcomes of second branchial arch cyst removal. Authors appraised selected studies on directness of evidence and risk of bias. Results are reported according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.

Results: Out of the 2101 retrieved articles, four articles were included in the current review including a total of 140 operated cysts. Only two studies included pre-operatively infected cysts. Follow up ranged from 3 to 24 months. Complication rates ranged between 0 to 27.3% (conventional: [0-10.4%]; endoscopic/retro auricular: [0-27.3%]). None of the patients presented with postoperative recurrence. Significantly higher scar satisfaction was found in adult patients who underwent endoscopic or retro-auricular hairline incision cyst removal.

Conclusion: No recurrence of disease occurred during (at least) 3 months of follow up using either conventional surgery or endoscopic/retro auricular techniques. Although more (temporary) complications occur using endoscopic and retro-auricular techniques, patients report a significantly higher scar satisfaction 3 to 6 months after surgery in comparison to the conventional technique. Future studies are needed to support these findings.

INTRODUCTION

Second branchial cysts (SBCs) are the most common second branchial arch anomalies (SBAAs) in adults whereas sinuses, fistulas and cartilaginous remnants are in children (1–3). The branchial arches consist of clefts and pouches and are the embryological precursors of the face, neck and pharynx. In total, six pairs of branchial arches form on either side of the pharyngeal foregut. Incomplete obliteration of these arches can lead to formation of branchial anomalies, of which the SBAA represent up to 95% of the cases (2). The second branchial arch forms part of the hyoid and surrounding structures of the head and neck, while the second branchial pouch shapes the palatine tonsil and the supratonsillair fossa (1). Therefore SBAAs can occur anywhere along the course of the second branchial arch tract that extends from the skin overlying the supraclavicular fossa up to the pharynx at the level of the tonsillar fossa (2).

In adults, when encountering an unilateral swelling of the neck, a cystic metastasis of head and neck cancer should always be excluded before SBC diagnosis can be confirmed (4,5). Since SBCs are prone to recurrent infections and do not dissolve spontaneously, early and complete surgical excision is the recommended treatment (1,6). Different surgical techniques for SBC removal have been proposed. Traditionally, conventional surgery using a large cervical incision was used to ensure complete removal (7). However, the large cervical incision results in a prominent scar. In an attempt to reduce visible scars, newer techniques have been developed, such as endoscopic surgery (6,8–10) and the use of a retro-auricular hairline incision (RAHI) (11–13). RAHI can be performed either as an open procedure using a 'facelift' incision or as an endoscopic technique. To provide insight in the optimal surgical management of patients presenting with a SBC, this systematic review evaluates which surgical technique (conventional, endoscopic or RAHI) for SBC removal results in

the lowest recurrence and complication rates with the highest scar satisfaction.

METHOD

Identify relevant studies and study selection A systematic literature search was conducted on the 23th of December 2019, in the PubMed, Cochrane and EMBASE databases to identify articles comparing outcome data from different surgical techniques for SBC removal (syntax provided in Appendix 1). No restriction regarding publication data and language were applied. This study is reported according to the Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) statement (14).

Study selection Two authors (S.M., R.M.) independently screened the retrieved articles on title and abstract using pre-defined inclusion and exclusion criteria (Fig. 1). The selected articles were read in full-text by the aforementioned two authors. Only studies comparing different surgical techniques in one cohort of patients were selected. The reference lists of the selected articles were reviewed for a cross-reference check to select relevant studies that were not identified in the initial search. All authors were involved in the discussion leading to final article inclusion. Disagreement between authors was solved by discussion.

Data extraction Data from all included studies was independently extracted by the authors. The predefined included data contained: year of publication, number of included patients (total and patients with SBC specifically), occurrence of bilateral anomalies, pre-operative SBC infection, gender, age at surgery, pre-operative imaging with: computed tomography, magnetic resonance imaging or ultrasound, operation technique, operating time, incision type and length, follow up duration, recurrence and complication rates, and scar satisfaction.

Quality assessment Four authors (S.M., H.B., E.v.d.V. and M.v.d.A.) critically appraised selected articles regarding directness of evidence (DoE) and risk of bias (RoB) (Table 1). We assessed the DoE using three criteria: 1) domain: studies comparing surgical techniques for SBC removal 2) determinant: clear description of the selected surgical technique and 3) surgical outcome: report on recurrence and complication rates. To perform RoB assessment on the selected studies, authors applied an appraisal tool derived from the Cochrane risk of bias Tool (15) . Each criterion was rated satisfactory (*), partly satisfactory (*), or unsatisfactory (-) (explanatory legend of Table 1). Overall DoE was rated as high (H), moderate (M) or low (L). Only studies with a high directness of evidence were selected for final inclusion. No studies were excluded based on RoB, adhering to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system (16).

Data synthesis Pooling of data was considered in case of homogeneity between studies (if I^2 was $<50\%$)(17).

RESULTS An overview of the study selection process and reasons for exclusion is presented in figure 1. (flowchart). Four articles had a high DoE and were included for final selection. This resulted in the inclusion of the treatment of 140 cysts. No patients with bilateral cysts were included. These four studies (6,9,10,12) contained two randomized controlled trails (RCTs) and two prospective trials. For an overview of the included surgical techniques see Figure 2 and the description in Appendix 2. Two authors (9,10) were contacted to provide additional information regarding the applied incision type, however, no additional information was provided. The inclusion dates of the patient cohorts of Chen *et al.* 2012 (10) and Chen *et al.* 2014 (9) did not overlap and therefore, both studies were included in the current review. Meta-analysis was not performed in this review due to heterogeneity regarding: baseline characteristics, study design and applied surgical techniques.

Data extraction: Table 2 shows the data extraction of four included studies that directly compared outcomes between conventional surgery and modern removal techniques in patients presenting with unilateral SBCs. All patients from these studies underwent pre-operative imaging using CT-scan or ultrasound scanning and pre-operative fine needle cytology to confirm the diagnosis (data not shown). Chen *et al.* (10) compared SBC removal results between conventional, curvilinear, cervical incisions along a natural skin crease (3-4 cm below the lower border of the mandible) to the endoscopic RAHI technique. Adult patients were randomly assigned between both techniques (Table 2). None of the included patients suffered from a pre-operative

SBC infection. No recurrence occurred during a follow up of at least six months. There was no significant difference in operating time between both techniques; however, there was a significantly ($p = < .001$) higher scar satisfaction rate in the RAHI group. Scar satisfaction was measured six months postoperatively using a visual analog scale ranging from 0-10. Chen *et al.* (9) compared SBC removal using a curvilinear cervical incision along a natural skin crease (4-5 cm below the lower border of the mandible) to an endoscopic approach of the lateral neck using two randomly assigned patient groups. Twenty adult patients were assigned to the conventional cervical incision, whereas 21 patients were assigned to the endoscopic lateral neck approach. None of the included patients suffered from a pre-operative SBC infection. No recurrence occurred during a follow up of at least six months. Although no significant difference in operating time was reported between both groups, incision length and scar satisfaction did significantly ($p < .05$) differ in favor of the endoscopic technique. Scar satisfaction was measured six months postoperatively using a visual analog scale ranging from 0-10. Ahn *et al* . (12) compared SBC removal outcomes between a conventional approach (by making a curvilinear incision directly over the anomaly) and an open RAHI approach in a prospective case control study. Thirteen adult patients were operated by the open RAHI approach while 17 adult patients underwent a (conventional) cervical incision. Ahn *et al.* reported a pre-operative SBC infection rate of 30.8% in the patients who were operated using the open RAHI technique. No recurrence occurred during a follow up of three months. Of the patients who underwent conventional surgery, 11.8% suffered from a postoperative hematoma or seroma, compared to 7.7% of the patients who underwent open RAHI surgery (*non-significant difference*). Only patients of the open RAHI group suffered from postoperative neurological damage that spontaneously resolved (23.1%). The retro-auricular approach entailed significantly longer operating time ($p = .019$), however, resulted in significantly higher scar satisfaction ($p= < .001$). Scar satisfaction was measured three months postoperatively using a visual analog scale ranging from 0-10. Iaremenko *et al.* (6) compared SBC removal outcomes between a conventional approach (by making a skin incision 2.0-2.5 centimeter below the lower border of the mandible) and an endoscopic occipital approach using a controlled study design. The latter technique is comparable to the endoscopic RAHI technique of Chen *et al.* (10) from a surgical perspective. Twenty-two adult patients were operated by the occipital endoscopic approach, while 22 adult patients underwent a (conventional) cervical incision. No recurrence occurred during a follow up of six months. Of the conventional group, 4.5% developed a hematoma and 4.5% developed temporary neurological damage. In the occipital approach group 27.3% reported temporary pain and difficulty at sideward arm raise. The endoscopic approach resulted in a significantly higher scar satisfaction ($p = .05$), but took significantly longer operating time ($p = .05$). Scar satisfaction was measured six months postoperatively using the criteria 'emotional component' of the 'Attitude to health' questionnaire. Since no recurrence was reported in any of the included studies, no data regarding revision surgery were retrieved.

DISCUSSION Summary of findings: In this systematic literature review, we compared the clinical outcome (complication and recurrence rates and scar satisfaction) of SBC removal between conventional surgery and less invasive removal techniques (endoscopic surgery or open/endoscopic RAHI). Only four studies (6,9,10,12) were identified that compared the conventional technique with newer techniques within one patient cohort. All of these included studies are of low quality due to: short follow up periods, small patient groups and a study design prone to bias due to both selection criteria (e.g. no inclusion of pre-operatively infected cysts) and lack of blinding. Since evidence is scarce, it remains difficult to provide evidence-based surgical treatment advice. Results demonstrate that surgical treatment of SBC results in a complication rate ranging between 0 to 27.3%. The most reported complications were temporary earlobe hypoesthesia in patients who underwent endoscopic or (endoscopic) RAHI surgery (most likely due to perioperative greater auricular nerve manipulation), temporary pain and difficulty of sideward arm raise (most likely resulting from spinal accessory nerve manipulation). No permanent neurological damage was reported. Surgical treatment provides a definitive treatment with no reported recurrence using either one of the techniques. Studies that compared both techniques within the same adult patient cohort demonstrated that both the (endoscopic) RAHI approach as well as other endoscopic techniques resulted in higher scar satisfaction. Therefore, available evidence demonstrates that application of less invasive SBC removal techniques to treat uninfected second branchial cleft cysts results in relatively higher, temporary complication rates, however, with a significantly higher scar satisfaction. An interesting result, since the operating area is in a prominently

visible location in a patient population containing young adults.

Two included studies (9,10) excluded patients presenting with fistulas and sinuses, pre-operatively infected SBCs and patients who underwent prior neck surgery or radiotherapy. Only Ahn *et al.* reported on open RAHI treatment of patients with pre-operatively infected SBCs. Although 30.8% of these patients suffered from a pre-operative infection, no relatively higher complication rate was reported for this population compared to the cervical incision group. Iaremenko *et al.* did not report whether any pre-operatively infected SBC were included in their study cohort.

Comparison with other studies and techniques: This is the first literature review reporting on the clinical outcome of SBC removal comparing different surgical techniques. Cohort studies(9,11,13) investigating either open RAHI or endoscopic RAHI found similar results: absence of recurrence in combination with low complication rates, with an average follow up of (at least) 6, 14.5 and 42 months respectively. The only reported complications in open RAHI surgery were temporary hypoesthesia of the earlobe and hypertrophic scars.

In previous studies, conventional second branchial arch anomaly removal techniques have been studied intensively. Appendix 3 shows an overview of these studies that were identified through the same literature search. This Appendix also includes patients presenting with fistulas and sinuses (mostly children). Precise data regarding the distribution of (included) cysts, sinuses and fistulas, side of the anomalies, description of the used surgical technique or duration of follow up is lacking in most studies (Appendix 3). Only retrospective studies were identified with a complication rate ranging between 0 and 32% and a recurrence rate ranging between 0 and 4.9%. These recurrence rates were reported when follow up lasted till four or even ten years (18,19). Therefore, the follow-up of the included studies in this review (ranging between 3-24 months) could be too short to identify recurrence following surgery. Long-term recurrence rates are of major importance because recurrence of disease will cause high morbidity and can make revision surgery complex. Furthermore, this short follow up could also affect the reported scar satisfaction since three to six months after surgery the final scar result may not be visible yet.

Multiple authors (20–22) refer to Deane *et al.* (23) regarding recurrence percentages: Deane *et al* described the results of a retrospective study (performed between 1954 and 1975) including 274 patients with branchial cleft remnants below the mandible. The surgical technique is described as a local excision of the lesion (plus tract when necessary). The reported recurrence rate was 2.7% in patients without a prior infection, 14% in patients with a pre-operative infection and 21.2% in patients who underwent revision surgery. The average follow up duration was 12.4 years (1-22 years). No distinction between second, third and fourth branchial anomalies was made.

Quality of evidence and potential biases The overall quality of the included studies was low (IIb -IV regarding the *Oxford Centre for Evidence-Based Medicine guidelines*): only two studies used a RCT to compare the clinical outcome between surgical techniques. In these RCTs, selection bias could not be ruled out since lack of blinding. The quality of evidence regarding SBAA removal was mostly affected by small patient cohorts resulting in Type II error (i.e., failing to reject a false null hypothesis), short follow up, unclear inclusion criteria and selective reporting.

Conclusion

This literature review compares the clinical outcome of SBC removal between conventional surgery and endoscopic surgery or open/endoscopic RAHI. Surgical treatment of uninfected SBCs provides a definitive solution with no reported recurrence using either one of the techniques during relatively short follow up (range: [3 to 24 months]). Endoscopic or (endoscopic) RAHI surgery results in significantly higher scar satisfaction in comparison with the conventional technique in adults, however, causes more temporary complications (0 – 27.3%). Since follow up was short, recurrence rates could be underreported and scar satisfaction could be affected by not (yet) judging the final scar result. Large prospective studies with long-term follow up (> five years) are currently lacking and will be essential to confirm whether newer techniques (endoscopic surgery or open/endoscopic RAHI) indeed result in higher scar satisfaction and less recurrence on the long-term.

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Appendix 1: Search syntax:

Pubmed:

1. (((second[Title/Abstract]) OR 2nd[Title/Abstract]) 2.(((pharyng*[Title/Abstract]) OR branch*[Title/Abstract]) OR viscer*[Title/Abstract]) OR branchial region[MeSH Major Topic] 3.((((cleft*[Title/Abstract]) OR groov*[Title/Abstract]) OR pouch*[Title/Abstract]) OR regio*[Title/Abstract]) OR arch*[Title/Abstract] 4.((((((((((((anomal*[Title/Abstract]) OR malform*[Title/Abstract]) OR defec*[Title/Abstract]) OR deform*[Title/Abstract]) OR cyst*[Title/Abstract]) OR tract*[Title/Abstract]) OR fistu*[Title/Abstract]) OR pit*[Title/Abstract]) OR pouch*[Title/Abstract]) OR leas*[Title/Abstract]) OR lesi*[Title/Abstract]) OR mass*[Title/Abstract]) OR sinus*[Title/Abstract]) OR congenital abnormalities[MeSH Major Topic]

5.(((((((((treat*[Title/Abstract]) OR procedur*[Title/Abstract]) OR oper*[Title/Abstract]) OR surg*[Title/Abstract]) OR therap*[Title/Abstract]) OR excis*[Title/Abstract]) OR manag*[Title/Abstract]) OR surgical procedures, Operative[MeSH Major Topic]) OR Surgery[MeSH Subheading] 1 AND 2 AND 3 AND 4 AND 5

Embase:

1.second*:ab,ti OR 2nd:ab,ti 2. pharyng*:ab,ti OR branch*:ab,ti OR viscer*:ab,ti OR 'branchial arch'/exp 3. cleft*:ab,ti OR groov*:ab,ti OR pouch*:ab,ti OR regio*:ab,ti OR arch*:ab,ti 4. anomal*:ab,ti OR malform*:ab,ti OR defec*:ab,ti OR deform*:ab,ti OR cyst*:ab,ti OR tract*:ab,ti OR fistu*:ab,ti OR pit*:ab,ti OR leas*:ab,ti OR lesi*:ab,ti OR mass*:ab,ti OR sinus*:ab,ti OR 'congenital disorder'/exp 5. treat*:ab,ti OR procedur*:ab,ti OR oper*:ab,ti OR surg*:ab,ti OR therap*:ab,ti OR excis*:ab,ti OR manag*:ab,ti OR 'surgery'/exp

1 AND 2 AND 3 AND 4 AND 5

Cochrane:

1. Second or 2nd:ti,ab,kw
2. Pharyng* or branch* or viscer*:ti,ab,kw (Word variations have been searched)
3. Cleft* or groov* or pouch* or Regio* or arch*:ti,ab,kw (word variations have been searched)
4. Anomal* or malform* or defec* or deform* or cyst* or tract* or fistu* or pit* or pouch* or leas* or lesi* or mass* or sinus*: ti,ab,kw (word variations have been searched)
5. Treat* or procedur* or oper* or surg* or therap* or excis* or manag*:ti,ab,kw (Word variations have been searched)

1 AND 2 AND 3 AND 4 AND 5

Table 1: Critical Appraisal of Topic

	Directness of evidence	Directness of evidence	Directness of evidence	Directness of evidence	Directness of evidence	Risk of Bias	Risk of Bias	Risk of Bias	Risk of Bias	Risk of Bias	Risk of Bias

Study (et al), year	Study design	Sample size(n)	Sample size(n)	domain determinant	out-come	DoE total	DoE total	Patient selection	Allocation concealment	Blinding	Incomplete outcome	Follo up
L. Chen, 2012	RCT	25	25			H	H	-		-		*
J. Chen, 2014	RCT	41	41			H	H	-		-		*
Ahn, 2017	PT	30	30			H	H		-	-		-
Iaremenko 2018	PT	44	44			H	H	-	-	-		*

Legend: NA= not applicable. PT= prospective trial. RCT = randomized controlled trail RCS = retrospective case study. Symbols: satisfactory (*), partly satisfactory (*), or unsatisfactory (-). Inclusion: high Directness of Evidence.

Explanatory Legend of table 1: Critical appraisal of studies reporting on surgical treatment of 2nd branchial arch cysts

Assessed Study Aspect:

DIRECTNESS OF EVIDENCE: Domain: -2nd branchial cyst only or 2nd branchial cysts reported separately - also other branchial arch anomalies included -

Determinant: - clear description of surgical technique - unclear description of surgical technique * - no description of surgical technique -

Outcome: - recurrence rate clearly mentioned - no recurrence rate mentioned -

RISK OF BIAS:1.Patient selection: - Clear inclusion and exclusion criteria - Unclear inclusion and exclusion criteria -

2. Allocation concealment: - type of treatment is randomly assigned - treatment is not randomly assigned - - Not applicable NA

3. Blinding: - the two treatment groups were blinded for the researchers - the two treatment groups were not blinded for the researchers - - Not applicable NA

4. Incomplete outcome: - <10% loss to follow up - >10% loss to follow up or unclear -

5. Follow up: - > 1 year - > 6 months * - unclear -

6. Selective reporting: - clear definition and description of complications - unclear or no definition and description of complications -

DIRECTNESS OF EVIDENCE: = 1 point * = 0,5 point - = 0 points RISK OF BIAS: - = 1 point * = 0,5 point = 0 points

Table 2: Results of the included studies selected from the systematic review.

Study	Chen, 2012 (10)	Chen, 2012 (10)	Chen, 2014 (9)
Incision type	Cervical incision	Endoscopic RAHI	Cervical incision
Patients	12	13	20
Sex (male/female)	5/7	6/7	9/11

Study	Chen, 2012 (10)	Chen, 2012 (10)	Chen, 2014 (9)
Age (years)	31.7 (median±2.9)	26.0 (median±11.9)	32 (median±11)
Follow up (months)	median 16 (6-24)	median 16(6-24)	16 (6-24)
Scar satisfaction:	6.2 ± 0.8*	9.2 ± 0.6*	6.4 ± 0.5*
Incision length (in centimeters)	NR	NR	6.4 ± 0.5
Operating time (in minutes)	49.6 ± 6.9	54.6 ± 6.3	94 ± 21
Complications:	Complications:	Complications:	Complications:
Recurrence:	**0%**	**0%**	**0%**
Seroma / hematoma	0%	0%	0%
Infection	0%	0%	0%
Temporary hypoesthesia of the earlobe	0%	7.7%	0%
Temporary pain and difficulty at sideward raising of the arm	NR	NR	NR

Abbreviations: RAHI= Retro Auricular hairline incision NR= not reported

*Scar satisfaction was measured using a visual analog scale ranging from 0-10 six months after surgery **Scar satisfaction was measured using a visual analog scale ranging from 0-10 three months after surgery *** Scar satisfaction was measured using the questionnaire "Attitude to health" by R.A. Berezovskaya. Six months after surgery. The criteria "emotional component" was selected for evaluation of subjective satisfaction with incision scar.

Figure 1: Flow-chart demonstrating the selection of articles from the literature describing surgical second branchial cyst removal.

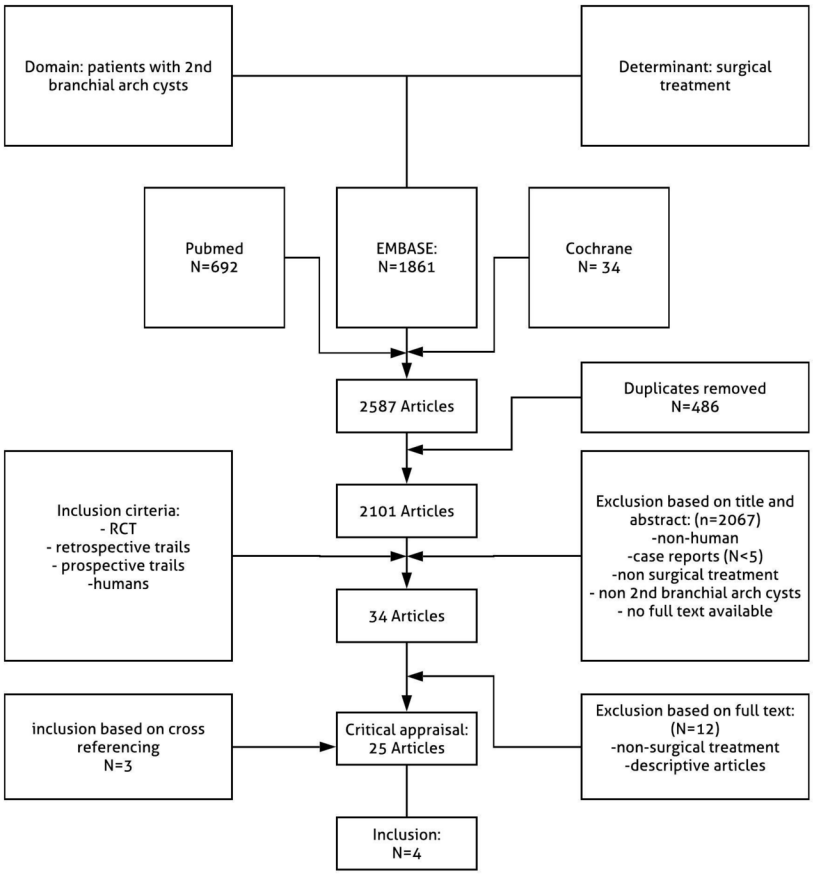
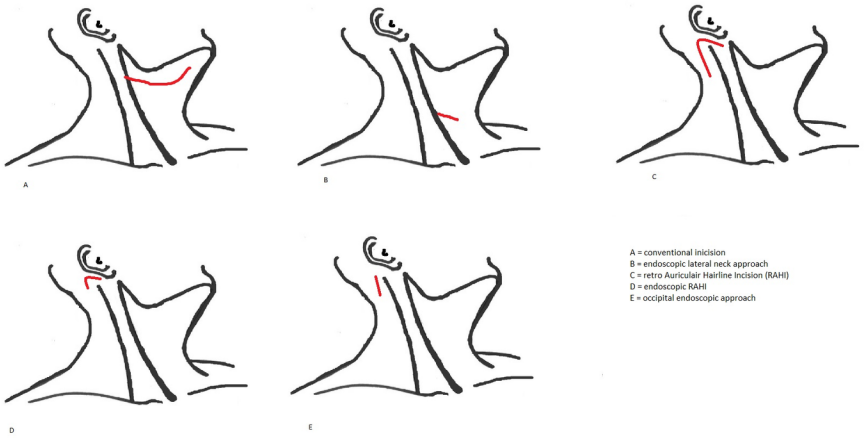


Figure 2: overview of used surgical techniques.



Appendix 2: overview of surgical techniques.

Conventional approach: (Iaremenko (6)): An incision is made in the upper third part of the lateral neck, along a skin crease. Usally 2,0-2.5 below the lower border of the mandibule. Incision is made trough

the subcutaneous tissue, the fascia superficialis, platysma muscle. External jugular vein is transected and ligated. Fascia media and fascia profunda are dissected. Cyst fluid aspiration is performed if required. Cyst is removed in total. The wound is closed layer by layer using biodegradable sutures. Drainage tube is placed. The wound is covered with a tight aseptic dressing.

Retro auricular hairline approach (Chen 2009 (11)): Retro auricular incision was made through the skin, subcutaneous tissue, and platysma

muscle. The incision was made along the post auricular sulcus and hairline, starting from the lower end of the post auricular sulcus, moving upward to the middle or upper third of the sulcus, and then smoothly angulating downward to 0.5 to 1 cm under the hairline. Careful attention to the overlying sternocleidomastoid muscle prevented injury to the great auricular nerve. The skin flap

was elevated just above the sternocleidomastoid muscle onto the carotid triangle. The cysts were exposed anterior and deep to the sternocleidomastoid muscle at the level of the carotid bifurcation. Dull dissection was used to free the attachments of the cysts. The cysts were then completely removed after aspirating luminal contents. All of the cysts were separated easily from the surrounding

normal tissues and removed completely using this approach without tumor spillage. The retro auricular skin flap was repositioned and sutured.

Endoscopic lateral neck approach (Chen 2014(9)): A lateral neck incision was made in the skin, subcutaneous tissue, and platysma muscle. The incision was made along the skin line below the lower bound of the cyst. The working space was created by elevating the skin flap with self-designed custom-made retractors to establish a stable operative space. The wound margin was protected by two applications to avoid injury from the ultrasonic scalpel. Dissection using the ultrasonic scalpel was performed to free the attachments of the cyst. When we separated the cyst, we took care to avoid impairing the common carotid artery, internal jugular vein, vagus nerve, hypoglossal nerve, and accessory nerve. The cyst was completely removed. For very large cysts (longest diameter

of 7 cm) decompression was often performed by fluid aspiration and needle pricking.. The wound was closed by a subcuticular suture with 4-0 Dexon, and a small ventricular drainage tube was inserted.

Endoscopic RAHI: (Chen 2012 (10)): A retroauricular incision was made through the skin, subcutaneous tissue, and platysma muscle. The incision was made along the postauricular sulcus and hairline, starting from the lower end of the postauricular sulcus, moving upward to the middle or upper third of the sulcus, and then smoothly angulating downward to 0.5 cm above

the hairline. The skin flap was dissected under platysma with the help of the 4-mm-diameter endoscope. During this step, careful attention to the overlying sternocleidomastoid muscle prevented injury to the great auricular nerve and external jugular vein. The working space was then produced by elevating the skin flap just above the sternocleidomastoid muscle onto the carotid triangle. The cyst was exposed anterior and deep to the sternocleidomastoid muscle at the level of the carotid bifurcation after carful dissection of the accessory nerve and posterior belly of digastric muscle. Then, dissection using the ultrasonic scalpel was carried out to free the attachments of the cyst, and the cyst was completely removed. In very large cysts (longest diameter 8 cm), decompression was often performed by fluid aspiration and needle-pricking. Finally, the wound was closed by subcuticular suture with 4-0 Dexon, and a small Hemovac was placed for drainage.

Occipital endoscopic approach: (Iaremenko (6))

An incision was performed in the occipital hairline region from occipital bone condylar fossa and going along the hairline 1.2 ± 0.3 cm under it. Layer by layer incision of skin and subcutaneous tissue was done. Fascia dissection was performed by means of unipolar and bipolar laparoscopic tools; a "tunnel" was formed under control of a rigid endoscope; "tunnel" vector was directed along the inferior border of the mandible. Anterior border of sternocleidomastoid muscle was visualized; fascia dissection under internal border of sternocleidomastoid muscle was performed, and the muscle was elevated by means of a retractor. Neurovascular bundle

fascia was dissected and exposed the cyst fascia with an anterior-inferior adjoining swollen lymphatic node. In larger cysts, the cyst fascia exposed under the internal border of sternocleidomastoid muscle. In all the cases, aspiration of cyst fluid was performed. The fascia was clamped with forceps and excised by means of ultrasound unipolar and bipolar laparoscopic tools. Tube drainage was inserted into the wound on vacuum. The wound was closed layer by layer with biodegradable synthetic loop sutures. The skin incision was closed with polypropylene loop sutures. The wound was covered with tight aseptic dressing.

Appendix 3 : Studies using conventional surgery for removal of second branchial arch anomalies (including cysts, fistulas and sinus).

Study (et al), year (reference)	Study design	Used surgical technique	Patients with 2nd arch anomaly (total)	Cyst-fistula-sinus total	Side (L-R-B) / Sex (M-F)	Age at surgery (in years) (SD or range)	Follow-up (in months)	Recurrence	Co
Queizan, 1985(1)	RCS	Fistula: elliptical incision Cyst: cervical, transversal incision	48 (52)	11-19-13(17 remnants)	B: 7/ (27-25)	1-7y	NR	2%	NR
Doi, 1988 (2)	RCS	'surgical excision'	44 (58)	7-20-12-39	NR / (32-26)*	Fistula <5 cyst >9	NR	2.3%	0%
Ford, 1992 (3)	RCS	68/98 conventional 30/98 stepladder	98 (106)	90-2-?-98 **	40%-60%-6 / (45-53)	<13y	NR	3%	NR
Perez, 1994(4)	RCS	'cystectomy'	19 (32)	19-0-0-19	NR /(11-21)	23.9	4 years	6.3%	9.4 wo inf
Atlan, 1997 (5)	RCS	'Local excision'	17 (20)	NA	NR / (11-6)	2-60m	NR	NR	11. hy tro sca
Agaton, 1996(6)	RCS	Wide, transverse cervicotomy	137(183)	113-24-0-137	(58-123-2) / (43-98)	Cyst mean 23,6 fistula mean 24,6	24	4.9%	2.9 ter ne cal da 6.6 inf 11. he
Karabulut, 2005 (7)	RCS	Stepladder incision	14 (14)	?-?-13-14	(6-R-3)/ (6—8)	1,5-16 (5.3)	6 years	0%	0%

Rattan, 2006 (8)	RCS	32/52 surgical excision 20/52 surgical excision and fistulogram 10/52 stepladder	52 (52)	0-52-0-52	(12-29-11)/ (38-14)	1-13 (4.5)	NR	4%	32 me spi
Schroeder, 2007(9)	RCS	Lateral cervicotomy	51 (67)	14-14-23-51	NA/NA	Cyst: 4.9[?] Sinus: 4.5[?] fistula: 2.8[?]	48	3.9%	1.9 ter net cal da 1.5 he 10. inf
Mitroi, 2008 (10)	RCS	Lateral cervicotomy	23(23)	10-0-13-23	NR / (11-12)	NR	1-5 years	0%	0%
Papadogeorgakis, 2009 (11)	RCS	Lateral cervicotomy	18(18)	18-0-0-18	11-7 / (10-8)	27.8 (21-62)	1-7y	0%	11. ser
Bajaj, 2011(12)	RCS	55/62 elliptical incision 7/62 stepladder	62 (80)	NA	16-34-12 / (30-32)	1-14	6 weeks	1.6%	1.6 ser
Maddalozzo, 2012(13)	RCS	Elliptical incision (4cm)	208(232)	?-28-?-232	0-25-3 / (11-17)	6-131 months	2 years	0%	0%
Zeifullah, 2012 (14)	RCS	Wide horizontal incision / stepladder	11 (26)	11-2-0-13***	7-3-1 / (5-7)	19,6 (4-44)	NR	0%	25 hy tro sca
Erikci, 2014 (15)	RCS	'surgical resection'	24(179)	8-16-0-24	11/10/4	0-14	4-120m	0%	0%
Kajosaari, 2014 (16)	RCS	'surgical excision'	68(68)	0-68-0-68	(13-49-6) / (39-29)	0-16	NR	0%	2.9 sil re- 1.5 dis sca

Prasad, 2014 (17)	RCS	'surgical excision'	17 (34)	8-9-0-17	NR / (9-8)	NR	NR	NR	5.9 wo inf 5.9 wo gap 5.9 rol def
Spinnelli, 2015 (18)	RCS	Transverse cervical incision	39(50)	11-27-1-39	NR / (21-29)	Cyst 9.5 Fistula 5.1 Sinus 3.7	1-10 years	4%	0%
Kalra, 2017 (19)	RCS	'surgical excision'	94 (94)	8-48-38-94	(24-62-8)/(70-24)	3m-14y	NR	2.1%	4.2 wo inf

Adult studies marked in **bold** , pediatric studies in*italic* . Abbreviations: NR = not reported L = left R = Right B = Bilateral M = male F = Female Symbols: ~ RCS = retrospective cohort study *all patients (also including other than 2nd branchial anomalies) ** 90 patients had cleft sinus or cyst, 6 had cleft cartilage remnant. ***= (1 cyst and fistela bilateral) [?]= average in only 19/32 patients the perioperative diagnosis of 2nd branchial cyst was made. Recurrence and complications were calculated for 32 patients.

Critical Appraisal of Topic of studies in Appendix 3

Study (et al), year	Study design	Sample size(n)	Directness of evidence Sample size(n)	Directness of evidence domain	Directness of evidence determinant	Directness of evidence out-come	Directness of evidence DoE total	Risk of Bias DoE total	Risk of Bias Patient selection	Risk of Bias Allocation concealment	Risk of Bias Blinding	Risk of Bias Incomplete outcome	Risk of Bias Follo up
Schroeder, 2007	RCS	51	51				H	H		NA	NA		
Queizan, 1985	RCS	48	48	-			M	M	-	NA	NA	-	-
Ford, 1992	RCS	98	98	-			M	M		NA	NA	-	-
Perez , 1994	RCS	32	32		-		M	M	-	NA	NA		
Karabulut, 2005	RCS	14	14	-			M	M		NA	NA		-
Mitroi et al, 2008	RCS	23	23		-		M	M	-	NA	NA		
Roh, 2008	PT	12	12				M	M		NA	NA		*
W. Chen, 2009	RCS	8	8				M	M	-	NA	NA		

Papadogeorgakis, 2009	RCS	18	18				M	M		NA	NA			
Bajaj, 2011	RCS	62	62	-			M	M		NA	NA			-
Maddalozzo, 2012	RCS	28	28	-			M	M		NA	NA			*
Erikci, 2014	RCS	24	24	-	-		M	M		NA	NA	-		
Prasad, 2014	RCS	17	17			-	M	M		NA	NA	-	-	
Spinelli, 2016	RCS	39	39		-		M	M		NA	NA			
Teng, 2016	RCS	25	25	-			M	M		NA	**NA**	-	-	
Kalra, 2017	RCS	94	94		*		M	M	-	NA	NA	-	-	
Doi, 1988	RCS	44	44		-	-	L	L		NA	NA	-	-	
Choi, 1995	RCS	21	21		-	-	L	L		NA	NA	-	-	
Agaton, 1996	RCS	137	137	-	*		L	L		NA	NA	-		
Atlan , 1997	RCS	17	17	-	-	-	L	L	-	NA	NA	-	-	
Rattan, 2006	RCS	52	52	-			L	L		NA	NA	-	-	
Al-Khateeb, 2007	RCS	47	47		-	-	L	L	-	NA	NA	-	-	
Zaifullah, 2013	RCS	11	11	-	-		L	L		NA	NA	-	-	
Al-Mufarrej, 2017	RCS	316	316	-	-	-	L	L		NA	NA	-	-	
Li, 2018	RCS	13	13	-	*		L	L		NA	NA			*

Legend: NA= not applicable. PT= prospective trial. RCT = randomized controlled trail RCS = retrospective case study. Symbols: satisfactory (*), partly satisfactory (*), or unsatisfactory (-). Inclusion: high Directness of Evidence.

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