The Use of Tissue Sealant in Parotidectomy – a Systematic Review and Meta-Analysis

Djamila Rojoa[1], Firas Raheman[2], Rosanna Wright[1], and Samit Ghosh[1]

[1]Royal Oldham Hospital
[2]Leicester Royal Infirmary

July 16, 2020

Abstract

Background: Drains are used post-parotidectomy to reduce seroma and haematoma formation. Tissue derived thrombin sealant can enable a drainless procedure, allowing for an earlier discharge, less discomfort and a more cost-efficient method. We aimed to assess whether tissue sealant improves wound-related outcomes in parotidectomy. Method: A systematic literature review was performed using a standardised published methodology and custom database search strategy. A fixed-effect meta-analysis of the combined complications was conducted. Results: Thirteen studies were identified relating to parotidectomies using tissue sealants. Our analysis showed a statistically significant reduction in the complication rates with tissue sealant use, including haematoma and seroma (Odds Ratio 0.59 [0.36, 0.95], 95% CI, I2 =23%, P =0.03). Conclusion: The use of drains post-parotidectomy is superseded by tissue sealant due to the shorter admission time and the lower risk of post-operative complications.

The Use of Tissue Sealant in Parotidectomy – a Systematic Review and Meta-Analysis

ABSTRACT

Background : Drains are used post-parotidectomy to reduce seroma and haematoma formation. Tissue derived thrombin sealant can enable a drainless procedure, allowing for an earlier discharge, less discomfort and a more cost-efficient method. We aimed to assess whether tissue sealant improves wound-related outcomes in parotidectomy.

Method : A systematic literature review was performed using a standardised published methodology and custom database search strategy. A fixed-effect meta-analysis of the combined complications was conducted.

Results : Thirteen studies were identified relating to parotidectomies using tissue sealants. Our analysis showed a statistically significant reduction in the complication rates with tissue sealant use, including haematoma and seroma (Odds Ratio 0.59 [0.36, 0.95], 95% CI, I^2 =23%, P =0.03).

Conclusion : The use of drains post-parotidectomy is superseded by tissue sealant due to the shorter admission time and the lower risk of post-operative complications.

KEYWORDS

Drainless, parotidectomy, tissue sealant, ARTISS, TISSEEL, fibrin, parotid surgery

INTRODUCTION

Parotidectomy is one of the head and neck soft-tissue surgeries where biological glue is increasingly being used to achieve haemostasis and prevent fluid collection (1). Convention dictates insertion of a percutaneous drain post-surgery to close "dead space" and allow blood and fluid to drain (2) but requires an overnight stay and has been associated with complications such as pain, infection, fistula formation, drain obstruction, discomfort and psychological impact (3,4). Moreover, there is no firm evidence that drains improve patient outcome (5). Most patients are reluctant to be discharged with a drain, and hence stay in until the drain is removed.

Fibrin sealants encourage haemostasis by initiating the final stage of the anticoagulation pathway and mechanically bringing tissue surfaces together (6). The apposition of the skin flap to closes" dead space" thus preventing seroma and haematoma formation.

Therefore, fibrin sealant obviates the need for percutaneous drains, potentially allowing for outpatient parotidectomies or a shorter hospital stay (1). Until now, there has been no systematic review specific to parotidectomy that examined the efficacy and safety of drainless parotidectomies with fibrin sealants. Our aim was to assess the benefits and post-operative outcomes of fibrin sealants in parotidectomy surgery as compared to post-operative percutaneous drain use without fibrin sealants (conventional). We also intend to evaluate the safety and efficacy of drainless parotidectomies with the use of tissue sealants.

METHODS

Design

We prespecified the review objectives, inclusion criteria and methods of analysis in a study protocol. We reported the review according to the Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) of diagnostic test accuracy studies (7).

Criteria for considering studies for this review

Types of studies

We included retrospective observational, cohort or cross-sectional and prospective studies as well as conference abstracts which assessed the use of fibrin sealants in parotidectomy with or without drains.

Participants

We considered patients of any age and gender who had undergone parotidectomy with or without drains. We considered any type tissue sealants used for closure of parotidectomy flaps and included the use of pressure bandages in some studies.

Conventional procedure

Percutaneous drains are traditionally placed after parotid surgery. In many centres this occurs when drain output is less than 30 mls/day or on post-operative day 3 (8). J.Jiang et al. (9) suggested that the optimum timing is when the output is less than 20 mls in 24 hours. This aims to reduce postoperative haematoma and seroma formation (9).

Intervention

The use of fibrin sealant in parotidectomy enables the avoidance of post-operative drains. Sealants also aid the formation of blood clots due to the thrombin and fibrinogen components, reducing haematoma and seroma formation and risk of infection (1). They expedite discharge from hospital, thus increasing the cost-effectiveness of the procedure. The studies included in our analysis have assess the efficacy of two types of fibrin sealants: TISSEEL and ARTISS.

Outcome parameters

In our included studies, the primary dichotomous outcome was complications including seroma, sialocele and haematoma formation, post-operative infection, sepsis, flap necrosis, facial nerve weakness and facial fistula. The secondary continuous outcomes were the length of hospital stay (LoS) and drain output.

Search methods for identification of studies

A literature search of electronic information sources (Medline, EMBASE, CINAHL) using the online search engine: NICE Healthcare Database Advanced Searches (hdas.nice.org.uk) was performed by two independent authors (DMR and FJR). The search was done in June 2020 over a three-week period and without applying any language restriction. The terms included were: drainless parotidectomy, parotidectomy and parotid surgery, combined with tissue sealant, TISSEEL, ARTISS and drainless, as shown in Appendix 1. Requests were put into local resources for full texts.

Data collection and analysis

Selection of studies

Eligibility assessment of identified studies was performed by two review authors (DMR and FJR) independently. We screened the titles and abstracts of the studies identified during electronic searches. Relevant studies meeting the inclusion criteria for the review were selected and the full-text articles were retrieved.

Data extraction

Data extraction was undertaken by both review authors (DMR and FJR). The following data were extracted from the full texts of the selected articles:

1. Author, date
2. Type of study
3. Number of participants
4. Type of surgery
5. The use of drain
6. Type of sealant used
7. Control
8. Outcomes in terms of hospital in-stay and complications
9. Information about the quality assessment using the Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) tool

Statistical analysis and data synthesis

A table of 'event', the number of complications encountered in parotidectomies with fibrin sealants versus those without, was constructed. We generated forest plots to show the variation of the results together with their 95% CI. A fixed-effect meta-analysis of the combined complications was conducted using RevMan 5.3 (Cochrane collaboration, Copenhagen, Denmark, and funnel plots were obtained using Stata 16 (Stata-corp, college station, Texas, USA). All studies were considered to have been conducted under similar conditions with similar interventions and subjects. Hence, we assumed the only difference between studies was their ability to detect the outcomes of interest.

The secondary continuous outcomes were the length of in-hospital stay and drain output. Due to the methodological heterogeneity in the included studies, a narrative analysis of the results was performed.

Assessment of reporting bias

Despite the small number of studies included, funnel plots were constructed to determine whether publication bias was a factor due to the inclusion of grey literature in our analysis.

RESULTS AND ANALYSIS

In our literature search on MEDLINE for "drainless or tissue sealant", 38,910 results were obtained and for "parotidectomy", 4,259 reports were found. Combination of both terms yielded 15 papers. During a similar search on EMBASE, 48,928 results were obtained for "drainless or tissue sealant" and 3,242 results were obtained for "parotidectomy". Combination of both results retrieved 17 papers. Using PubMed, 50,802 results were generated for "drainless or tissue sealant" and 4,528,258 results for "parotidectomy", giving a combined result of 15,828. Our final comprehensive search identified 15,860 studies. 15,847 were irrelevant and discarded, and the remaining 13 studies were selected for our review based on the inclusion criteria. The search process performed in June 2020 is detailed in the PRISMA flow diagram as shown in Figure 1.

Characteristics of included studies

A total of 642 patients were included in our analysis. Of the 13 selected papers, 8 studies were performed prospectively (10–16) and 6 were done retrospectively (4,8,17–20). 4 of the studies had no control and only assessed the outcomes of fibrin use in parotidectomies (12–14,17) while the remaining 9 compared the Fibrin-use with the conventional method (4,8,10,11,15,16,18–20). In the study of M.J. Patel et al. (8), they assessed 3 sets of data, the use of haemostatic agent (AHA) was not analysed in this paper since we decided to assess fibrin sealants only in drainless cases. Table 1. summarises the main characteristics of the studies.

Methodological quality of included studies

The inclusion of grey literature (unpublished studies in the form of conference abstracts or letters, which might not have been peer-reviewed) minimises publication bias. The argument for the inclusion of grey literature is to fully take into consideration all existing evidences. These studies often include a smaller sample but excluding them can lead to the exaggeration of statistically significant results, publication bias and skewing the effect size estimates (21,22). Hence Conn et al (22) encourage the inclusion of grey literature with assessment of heterogeneity. However, due to a lack of methodology details, the papers have been highlighted as high risk as shown in Figure 3. Some papers have not commented on whether participants and outcome assessors have been blinded while others have not expanded the selection process (as detailed in Appendix 2). Figure 3. provides a summary of the quality of the studies.

Findings

Table 1. summarizes how the primary and secondary outcomes post-parotidectomy with tissue sealant compare to conventional methods. It provides a numerical comparison of the length of stay, drain output and complication rates for both.

Figure 2. shows the post-operative complications for procedures using fibrin glue compared to conventional ones. Complications rates varied from 2.6% (8) to 61.5% (18) with fibrin use and from 2.3% (8) to 66.7% (18) with conventional surgery. The most common complication was seroma formation, reported by 6 studies (4,8,11,15,16,20), followed by haematoma, reported by 3 studies (10,16,17,19,20). Other complications reported were salivary leak, salivary fistula, facial paralysis, facial nerve weakness, sialocele, flap necrosis and sepsis. (4,8,10,16,19,20)

A fixed-effect meta-analysis was carried out over different formulations of fibrin sealants to assess its effectiveness on post-parotidectomy outcomes in terms of complications, as shown in the forest plot (Figure 3).

The meta-analysis favors the use of tissue sealant over the conventional method, with p=0.03 (OR=0.59, 95% CI 0.36 to 0.95). Due to the variation in the secondary dichotomous outcomes as mentioned above, as well as the disparities in methodologies used, mainly in the grey literature (non-peer reviewed literature) a subgroup meta-analysis were performed, excluding the latter. A similar statistically significant result (p=0.03) favoring the use of fibrin sealant (OR=0.57, 95% CI 0.34 to 0.96), as shown in Figure 3. Both between- and within-studies heterogeneity contributed to variance in our analysis (I^2=23%, Cochran's Q=10.43). However, upon filtering out grey literature we note an unchanged variance (Cochran's Q=10.35) supporting its inclusion in our study, as shown in Figure 4.

DISCUSSION

Our meta-analysis favours the use of fibrin sealant over parotidectomy with drain, since it is associated with a statistically significant reduction in complications. The randomised-controlled trial by Maharaj et al. (15) has reported similar results with a lower incidence of haematoma and seroma formations with fibrin sealant use. Chua et al. (10) and Heffernan et al. (11) have shown a relatively lower rate of complications, with 8.5% and 4.8% respectively with the use of fibrin sealant, compared to 11.4% and 6.9% respectively in conventional parotidectomies. Other complication included including salivary leak, salivary fistula, facial paralysis, sepsis and flap necrosis, reported in the studies by Cunniffe et al. (4) and Depondt et al. (19). The former had an equal number of complications with both fibrin sealant uses and conventional surgery. Similarly, only 1 seroma formation was reported by Patel et al. (8) in both groups.

Complications rates have varied in studies that only reviewed the use of fibrin sealant. Trujillo et al. (13) and Conboy et al. (14) had a 0% complication rate in a sample size of 10 and 21 patients respectively. Poolovadoo et al. (17) reported 1 post-operative haematoma and 1 decline in respiratory function (6.5% incidence rate). These are relatively low incidences which might not be fibrin sealant related. Chorney et al.'s (20) study, with one of the largest series of patients, found no statistical significance in wound complications between the sealant and non-sealant groups, when other factors such as tissue volume removed, smoking history, diabetes or anticoagulant use, were accounted for Chudek et al. (16) also demonstrated a reduced incidence of seromas and haematoma in the fibrin sealant group, supporting the use of fibrin sealant as a safe alternative, enabling the omission of surgical drains whilst also reducing patient discomfort and anxiety associated with these (4).

Al-Qahtani et al. (12) had 2 incidences of facial nerve weaknesses with full recovery, out of 10 surgeries performed with fibrin sealant. Albeit this is a comparatively higher incidence, the sample size is too small to conclude. Similarly, Too et al. (18) have reported a higher number of complications with fibrin sealant, compared to conventional surgery. However, not all complications were ARTISS-related, and their sample size was small as well.

One argument for fluid collection leading to seroma and haematoma formation could be due to uneven distribution of the fibrin glue along the parotid bed and lack of manipulation and compression, leading to less adherence. (4) Improved surgical techniques with more widespread use of fibrin sealants in parotidectomies could help further reduce the incidence of fluid collection in these procedures.

Most studies have shown a comparative or lower incidence rate of post-parotidectomy complications with fibrin sealant. Hence, fibrin sealant can be considered as a safe alternative, enabling the omission of surgical drains whilst also reducing patient discomfort and anxiety associated with these (4).

Considering drain output volume, a meta-analysis on fibrin sealant use by Bajwa et al. (1) in Head and Neck surgery has shown a statistically significant reduction in wound drainage volume with fibrin sealant. A similar result was reported by Maharaj et al. (15), C. Heffernan et al. (11) and Trujillo et al. (13) with the latter reporting a p value of <0.005. Hence, fibrin sealants can enable drainless surgeries, overcoming the pain, distress and discomfort caused by surgical drains (1).

Cost-effectiveness of a procedure is a crucial part to consider. Length of in-hospital stay is an important contributory factor. Fibrin sealants enables a drainless procedure, hence most patients can be discharged on the same day. Chua et al. (10) and Patel et al. (8) found a statistically significant reduction in length of hospital stay. The former study showed a mean length of hospital stay of 1.1 days versus 2.8 days while latter had a length of 1.2 days versus 2.8 days for drainless and conventional parotidectomy respectively. Nausea control was the main reason for overnight stay in both studies.

In the study by Depondt et al. (19), all patients who had surgery with fibrin sealant were discharged by day 2, whilst those who underwent conventional surgery were only discharged after day 3, due to complications and drain care.

Social aspect can also be a barrier to discharge as shown by Poolovadoo et al. (17), who reported 4 overnight

in-hospital stays out of 31 patients, 1 of which was due to lack of support at home. Cunniffe et al. (4) stated that 9 out of 17 patients required an overnight stay due to a late afternoon finish, in the group with fibrin sealant use, with an average length of stay of 0.52 days compared to 1.64 days in those who had conventional surgery.

The overwhelming majority of patient who underwent parotidectomy with a post-operative drain had 2 or more days of in-hospital stay. Cost-wise, although as mentioned by Cunniffe et al. (4), fibrin sealant (ARTISS in this case) costs £165.75 compared to £30 for a drain per patient, an overnight hospital stay cost was £241 on a surgical ward in 2018/19 (23), hence the reduction in Los in hospital greatly outweighs the price difference.

CONCLUSION

Overall, the use of fibrin sealant has been shown to result in a statistically significant reduction in the incidence of complications post-parotidectomy. It also decreases the total drain volume. It can be used as a drainless approach, facilitating recovery and offering better comfort to patients. Furthermore, patients are candidates for same day discharges, reducing the length of in-hospital stay, saving on costs and resources. Although larger studies comparing the use of fibrin sealant without drain to the use of post-parotidectomy drains are required, our analysis has showed fibrin sealant offers significant advantages over traditional parotidectomies with drain insertion, with comparable safety.

REFERENCES

1. Bajwa MS, Tudur-Smith C, Shaw RJ, Schache AG. Fibrin sealants in soft tissue surgery of the head and neck: A systematic review and meta-analysis of randomised controlled trials. Clinical Otolaryngology. 2017;42(6):1141–52.
2. Hey SY, Flach S, Shahsavari S, Manickavasagam J. Drainless parotidectomy and the same day discharge with routine use of topical haemostatic agent and Balaclava bandage. Clinical Otolaryngology [Internet]. 2019 [cited 2019 Jul 6]
3. Findik UY, Topcu SY, Vatansever O. Effects of Drains on Pain, Comfort and Anxiety in Patients Undergone Surgery. 2013;6(3):9.
4. Cunniffe HA, Wong BLK, Hilger AW, Burgan OT. Drain-free parotidectomy: a pilot study using ARTISS fibrin sealant. European Archives of Oto-Rhino-Laryngology. 2019;276(7):2025–9.
5. Systematic review and meta-analysis of wound drains after thyroid surgery. - PubMed - NCBI [Internet]. [cited 2019 Jul 6].
6. Jain R, Wairkar S. Recent developments and clinical applications of surgical glues: An overview. International Journal of Biological Macromolecules. 2019;137:95–106.
7. McInnes MDF, Moher D, Thombs BD, McGrath TA, Bossuyt PM, the PRISMA-DTA Group, et al. Preferred Reporting Items for a Systematic Review and Meta-analysis of Diagnostic Test Accuracy Studies: The PRISMA-DTA Statement. JAMA. 2018 23;319(4):388–96.
8. Patel MJ, Garg R, Rice DH. Benefits of Fibrin Sealants in Parotidectomy: Is Underflap Suction Drainage Necessary?: The Laryngoscope. 2006;116(9):1708–9.
9. Jiang J, Jia M, Cai Z, Yuan R, Wang K, Zhang K, et al. [The effect evaluation of suction drainage to prevent fistula after superficial parotidectomy]. Shanghai Kou Qiang Yi Xue. 2014;23(6):759–62.
10. Chua DYK. Drainless Parotidectomies versus Conventional Parotidectomies: Randomised Control Study on Efficacy and Safety [Internet]. [cited 2019 Aug 7].
11. Heffernan C. ARTISS® IN PAROTID SURGERY: ARE SUCTION DRAINSSTILL REQUIRED? [Internet]. 2015 [cited 2019 Aug 7].
12. AL-Qahtani K. Initial experience with hemostatic fibrin glue as adjuvant during drainless parotidectomy. The Saudi Dental Journal. 2011;23(2):67–71.
13. Trujillo MM. Biological glues based on fibrin for use in parotid tumour surgery. Transfusion Alternatives in Transfusion Medicine. 2009;11:19-40.
14. Conboy P, ChB M, Brown DH, ChB M. Use of Tissue Sealant for Day Surgery Parotidectomy. Journal of Otolaryngology - Head & Neck Surgery. 2008;37(2):208-11.

15. Maharaj M, Diamond C, Williams D, Seikaly H, Harris J. Tisseel to Reduce Postparotidectomy Wound Drainage: Randomized, Prospective, Controlled Trial. The Journal of Otolaryngology. 2006;35(01):36.
16. Chudek DA, Wilkie MD, Hampton T, Siau R, Panarese A. The effect of fibrin sealant tissue glue in reducing post-operative collections following parotidectomy. European Archives of Oto-Rhino-Laryngology. 2020;277(7):2055–9.
17. Poolovadoo Y, Aggarwal R, Loughran S. The use of ARTISS^{TM} in performing parotidectomies as day case surgery: A single-centre review of 31 cases. Clinical Otolaryngology. 2019;23;13386.
18. Too L, Nugent M. Early experience with ARTISS in parotidectomy. International Journal of Oral and Maxillofacial Surgery. 2015;44:e297–8.
19. Depondt J, Koka VN, Nasser T, Portier F, Guedon C, Barry B, et al. Use of Fibrin Glue in Parotidectomy Closure. The Laryngoscope. 1996;106(6):784–7.
20. Chorney SR, Ryan JT. Fibrin sealant and parotidectomy wound complications in 100 patients. European Archives of Oto-Rhino-Laryngology. 2019;276(9):2621–4.
21. McAuley L, Pham B, Tugwell P, Moher D. Does the inclusion of grey literature influence estimates of intervention effectiveness reported in meta-analyses? The Lancet. 2000;356(9237):1228–31.
22. Conn VS, Valentine JC, Cooper HM, Rantz MJ. Grey literature in meta-analyses. Nursing Research. 2003;52(4):256–61.
23. National tariff payment system | NHS Improvement [Internet]. Improvement.nhs.uk. [cited 12 July 2020].

FIGURE LEGENDS

Figure 1. Shows the PRISMA diagram for the search strategy

Figure 2. Shows the complications rates between the sealant and non-sealant groups

Figure 3. Shows the forest plots and methodological quality analysis for the included studies

Figure 4. Shows the funnel plots for the included studies

Table 1. Shows the characteristics of included studies

Key points

1. Fibrin sealant is favoured by many of our studies due to the benefits it offers over conventional post-operative drains.
2. It enables a shorter length of in-hospital stay, reducing drain-related discomfort and improving patient care.
3. It has a comparable complication profile, and a statistically significant reduction in complication rates compared to the use of post-parotidectomy drains due to its adhesive properties.
4. It enables earlier discharges, hence reducing the cost of parotidectomy surgeries.
5. Larger trials are required to evaluate the advantages of fibrin sealant over post-operative drain use and the related complications in order to ascertain its benefits.

Figure 1. shows the studies selection using the PRISMA diagram

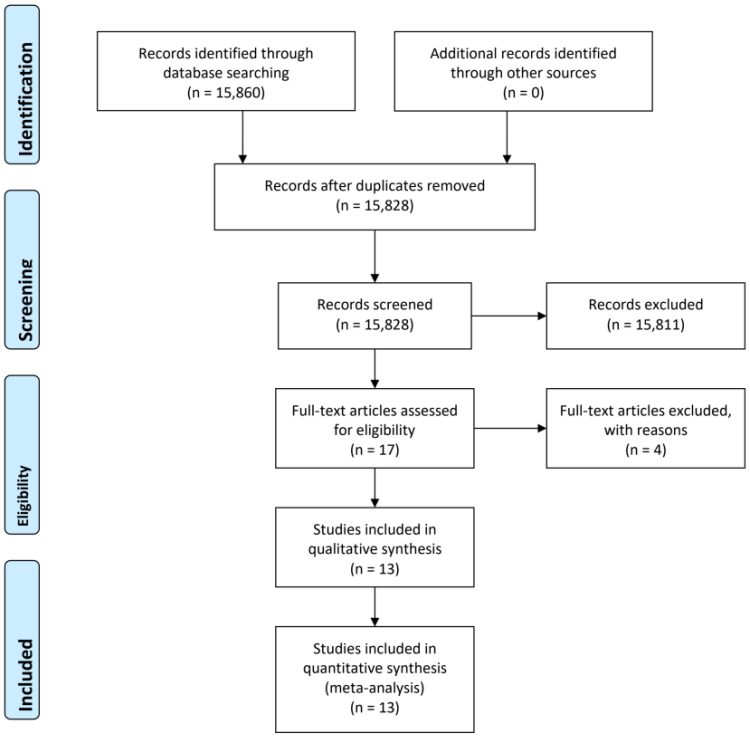
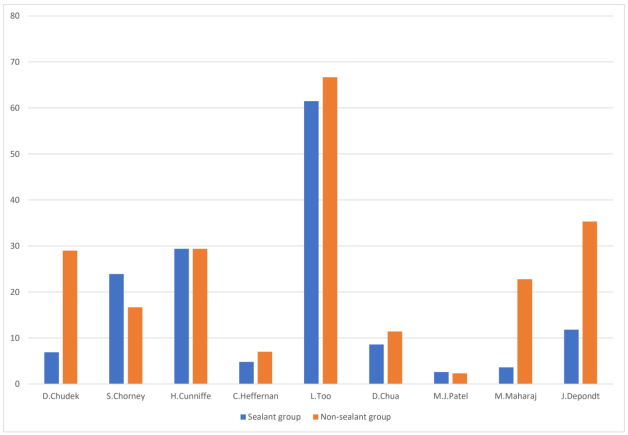


Figure 2. shows the percentage complications of parotidectomies using fibrin sealants compared to conventional ones.



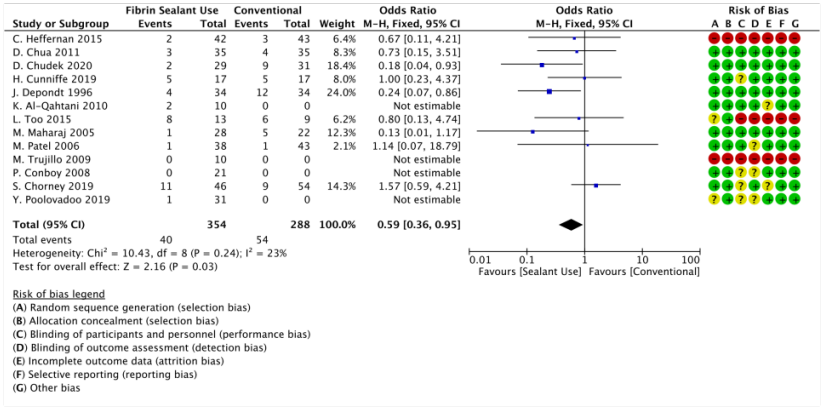


Figure 3a. Shows the forest plot and methodological quality analysis of all included studies

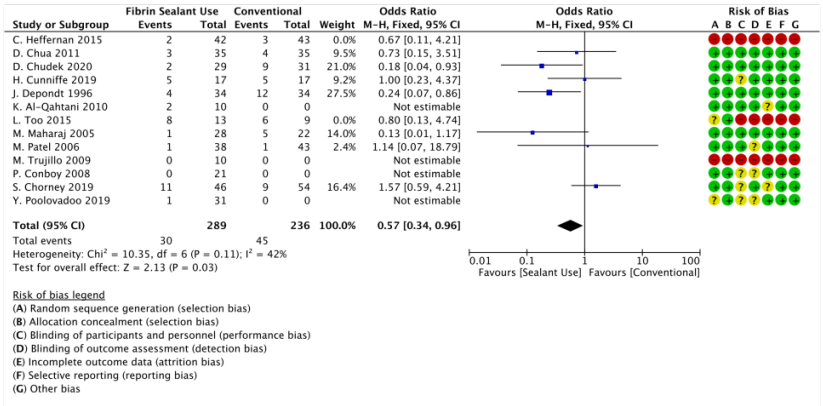


Figure 3b. Shows the forest plot and methodological quality analysis excluding grey literature

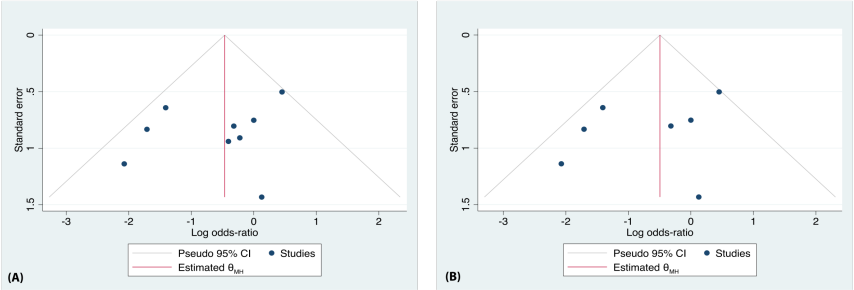


Figure 4. Shows the funnel plot to assess publication bias (A) in all included studies and (B) where grey literature was exlcuded. The horizontal axis represents the log odds-ration against the vertical Standard Error (SE) of log odds-ratio.

Hosted file

Table 1. shows characteristics of included studies.docx available at https://authorea.com/users/342313/articles/469114-the-use-of-tissue-sealant-in-parotidectomy-a-systematic-review-and-meta-analysis