Contents lists available at ScienceDirect

Journal of Clinical Neuroscience

Review article

Impact of cement cranioplasty on cerebrospinal fluid leaks after retrosigmoid craniotomy – A systematic review and meta-analysis

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ABSTRACT

Background: Cerebrospinal fluid (CSF) leaks and related complications (CLRC) are common after retrosigmoid approaches for cerebellopontine angle (CPA) surgeries. Bone cement cranioplasty (CCP) may provide additional sealing benefits over reconstruction without cement (RWC) in reducing these complications. This study aimed to compare the outcomes of CCP versus RWC in CPA surgery.

Methods: A systematic review and *meta*-analysis following PRISMA guidelines was conducted using three databases (PubMed, Scopus, Web of Science). Studies were included comparing CCP and RWC in retrosigmoid craniotomies/craniectomies for CPA pathologies. Primary outcomes were pseudo meningocele, external CSF leaks, and CLRC, while secondary outcomes included wound infection rates and rates of reoperation for wound problems. **Results:** Five retrospective studies were analyzed with 1,838 patients (931 CCP, 907 RWC). CCP significantly reduced the rates of pseudo meningocele (OR 0.264, CI 0.150–0.463), wound CSF leaks (OR 0.105, CI 0.028–0.399) and CLRC (OR 0.248, CI 0.078–0.794). In the CCP group, there were fewer wound infections (OR 0.310, CI 0.114–0.790) and lower reoperation rates (OR 0.189, CI 0.050–0.708).

Conclusions: Cement cranioplasty is associated with a lower incidence of CSF leaks and related complications compared to RWC following retrosigmoid approaches for CPA pathology. CCP also reduces reoperations and wound infections. These findings support using CCP as an effective technique for lowering postoperative complications of retrosigmoid approaches.

1. Introduction

Cerebrospinal fluid (CSF) leaks and related complications (CLRC) represent one of the most relevant issues in post-operative course of patients undergoing retrosigmoid craniotomies for treatment of cerebellopontine angle (CPA) pathologies [1–3]. The importance of a watertight dural closure and the role of additional dural sealing techniques have been extensively discussed in the literature [4,5]. Bone cement (either calcium phosphate or acrylic-based) has also been widely adopted as an additional aid in reconstruction [6–8], improving esthetic outcomes, sealing bony gaps and exposed air cells, and potentially reducing the incidence of external CSF leaks and their complications [5,9–11].

Here, we systematically reviewed all the available studies comparing cement cranioplasty (CCP) and reconstruction without cement (RWC) after retrosigmoid approaches to evaluate if the sealing effect provided by CCP can provide additional benefits as compared to other non-sealing reconstruction methods (such as autologous bone flap replacement, reconstruction with titanium mesh, etc.) [2,12,13].

2. Materials and methods

2.1. Study design and review Question

The study design followed the 2020 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [14]. The review questions were formulated using the population, intervention, comparison, and outcome (PICO) scheme as follows: among the patients that undergo a retrosigmoid craniotomy/craniectomy for cerebellopontine angle (CPA) pathologies (population), do the patients receiving cement cranioplasty (CCP, intervention) experience a different rate of CSF leaks and related complications (CLRC) (outcome) when compared to patients receiving reconstruction without cement (RWC, comparison)?

CSF leaks were distinguished in pseudo meningocele, cutaneous CSF fistula or CSF rhinorrhea/otorrhea. CLRC was defined as CSF leak-associated meningitis, tension pneumocephalus, or subdural hematomas [15].

We also included other parameters, such as wound infections and surgical revision/permanent CSF shunting, as secondary outcomes in our analysis.

2.2. Literature search

Three medical databases (PubMed, Scopus, and Web of Science) were screened for eligible scientific reports. We used the following search string: *"(retrosigmoid OR cerebellopontine OR CPA) AND (CSF OR "cerebrospinal fluid" OR leak* OR fistula)"*. The keywords *"cement"* and related terminology (calcium phosphate, resin, etc.) were purposefully omitted from the string as they significantly restricted the search output; we opted for a string that granted the highest possible sensitivity. The last search was conducted in September 2024. To identify relevant reports, two reviewers (A.B. and F.Z.) independently searched the databases, eliminated duplicated articles, and screened pertinent papers' abstracts and reference lists (Fig. 1). Papers corresponding to the inclusion criteria underwent full-text review. Results of the search were compared, and disagreements were resolved by consensus with a third senior author (C.L.S.).

2.3. Inclusion and exclusion criteria

Studies were included if they met the following criteria: 1) Comparative, prospective, or retrospective studies on CCP vs. RWC in patients status post retrosigmoid craniotomy/craniectomy for the
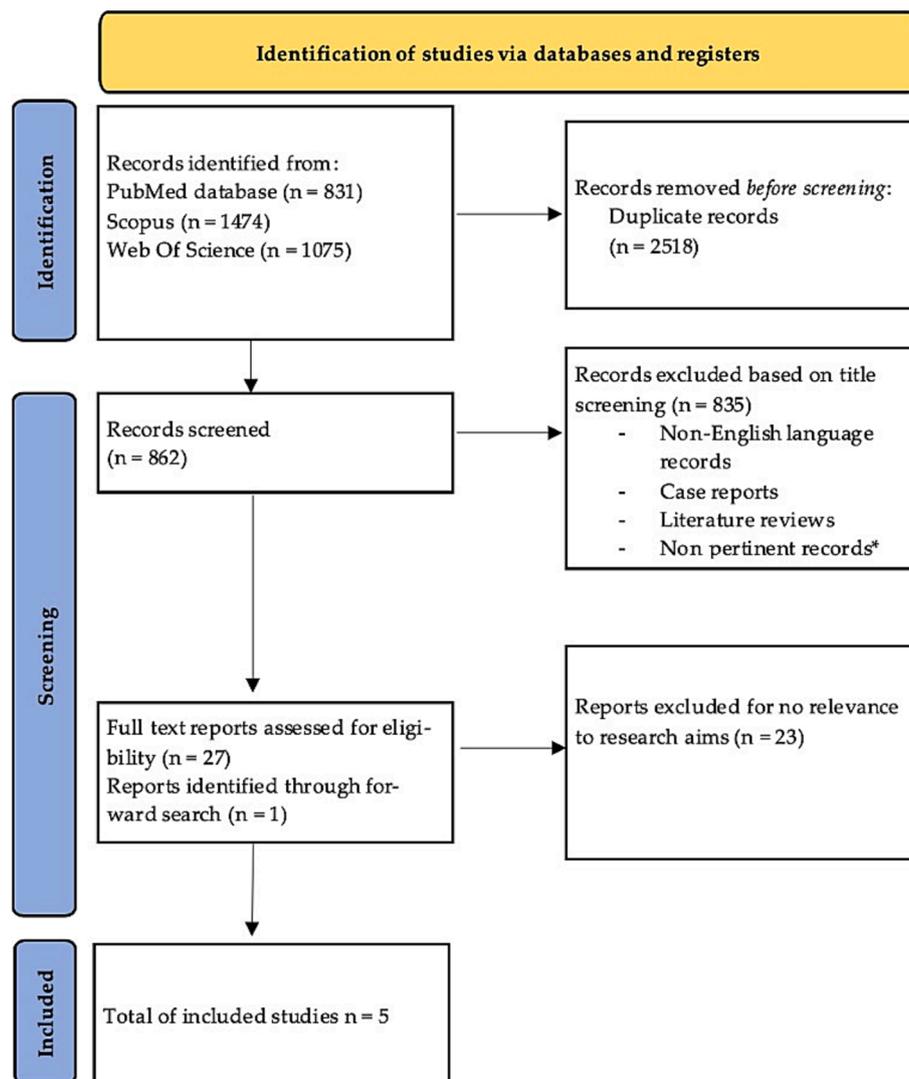

Fig. 1. PRISMA flowchart detailing the process of our literature search. *Ex-vivo studies; studies conducted on non-human animals; studies dealing with cranial approaches other than retrosigmoid; studies dealing with cement repair of the internal acoustic meatus; studies dealing with the use of cement as a secondary repair method for CSF leaks; studies in which cement was not employed.

treatment of CPA pathologies; 2) Bone cement was used for partial or total reconstruction of the bony defect and/or for sealing of mastoid air cells opened during the craniectomy; 3) Reporting at least one outcome measurement related to postoperative CSF leak or CLRC; 4) Describing a study population of more than ten patients.

The exclusion criteria were: 1) Papers written in languages other than English; 2) Studies dealing with other approaches to CPA pathology (trans labyrinthine, middle fossa approaches, etc.); 3) Studies dealing with secondary repair of postoperative CSF leaks or primary repair of spontaneous CSF leaks; 4) Studies where cement was only used to reconstruct the internal acoustic canal (IAC) after IAC drilling; 5) Studies on non-human animals or ex-vivo/laboratory studies; 6) Studies using bone substitutes with biophysical properties different from those of semiliquid bone cement (e.g., demineralized bone matrix).

2.4. Risk of bias assessment

Three authors (AB, FZ, and DP) independently assessed the risk of bias for each included study using the Risk of Bias In Non-randomized Studies – of Interventions (ROBINS-I) tool.

2.5. Considered variables

The following demographic and clinical outcome variables were collected for *meta*-analysis purposes:

- Demographic data (age and sex);
- Preoperative and postoperative clinical data (BMI, pathology, % of CPA angle schwannomas, history of previous surgery at the same site, length of follow-up);
- Technical/surgical features (craniotomy vs. craniectomy, type of cement used, type of reconstruction, frequency of IAC opening, IAC reconstruction techniques, intraoperative opening of mastoid air cells);
- Postoperative outcome data, i.e. development of postoperative pseudomeningocele, wound CSF leaks, CSF rhinorrea/otorrhea, CLRC (meningitis, pneumocephalus, subdural hematomas), need for further surgery (wound revision, permanent CSF shunting) and wound infection rates.

2.6. Statistical analysis

Data derived from the single studies were statistically pooled according to a bivariate random-effects model (DerSimonian–Laird method). Pooled data are presented with 95 % confidence intervals (95 %CI). Two-arm *meta*-analysis Odds Ratio (OR) metrics were used to assess the association between treatment groups (cement Vs. non-cement) and the following post-operative outcomes: pseudo meningocele; external CSF leaks (wound leaks + CSF rhinorrhea/otorrhea); CLRC; wound infection; intracranial infection; reoperation, namely wound revision or ventricular shunting. Heterogeneity was calculated by the I-squared index (I^2), representing percentage variation across studies due to heterogeneity rather than chance. Statistical analyses were performed using OpenMetaAnalyst software (https://www.cebm.brown.edu/openmeta/).

P values < 0.05 were considered statistically significant.

3. Results

The search through all databases yielded 3380 results. After the removal of duplicates, 862 papers were identified for title screening. After excluding 835 nonrelevant records, 27 records were screened, and 1 further record was identified through forward search of bibliographies. The high rate of paper exclusion based on title screening is explained by the breadth of the search strategy (see the "methods" section). Ultimately, five studies were included in the analysis. All

included studies were retrospective and were published between 2015 and 2022. They presented 1838 patients (931 for the CCP group and 907 for the RWC group). Demographics and the adopted reconstruction methods are reported in Table 1.

The overall risk of bias, evaluated with the ROBINS-I tool, was deemed to be moderate for all the included papers (Table 2).

3.1. Demographics

The global average age (weighted) of patients was 54.7 years, 55.42 in the CCP group and 53.91 years in the RWC group. This difference was not significant (t = 0.68, p = 0.644). Four series reported aggregated sex data; global sex distribution across these papers was 32 % males and 68 % females [9,10,17]. Only three series reported sex distribution across intervention groups; in these papers, there were 31 % males and 69 % females in the CCP group and 32 % males and 68 % females in the RWC group [9,17]. This difference was not significant (chi squared = 1.66, p = 0.20). Two studies reported BMI data. Mean BMI (weighted) was 27.9 in the CCP group and 27.4 in the RWC group. The difference was not statistically significant (p = 1).

3.2. Pathologies treated

Most patients in our analysis (n = 1782, 97 %) were treated for neurovascular conflicts of the cerebellopontine angle; only a minority were treated for CPA tumors (n = 56; 3 %). Across the two groups, tumor patients were 18 in the CCP group (1.9 %) and 38 in the RWC group (4.1 %). This difference was significant (chi-squared = 7.62; p = 0.0058).

3.3. Techniques

In all studies except for two [5,16], the typical diameter of the craniotomy/craniectomy is reported, ranging from 2 to 3 cm. In all included studies, bone cement (either calcium phosphate or poly-methylmethacrylate) was used to perform a total cement cranioplasty, completely sealing any bony gaps/defects. In some studies, cranioplasty with autologous bone flap and titanium miniplates was performed, and then cement was spread on top and around to evenly seal any gaps [10,17]. In other studies, cement was used to completely fill a craniectomy defect [5,9,16,17]. In all studies, watertight dural closure was attempted regardless of the intervention. When watertight dural closure was not achievable by reapproximating the dural edges, dural substitutes/patches [5,9,16,17] or muscle plugs [10] were utilized to obtain a watertight sealing. In all studies except two [9,16] adhesive matrices were put on top of the autologous dura to reinforce the sealing effect. Only in one study, watertight closure was not always attempted when the dural margins could not be sutured [9].

3.4. Primary outcomes

The analysis of the included studies revealed a significantly lower incidence of CSF leaks in the CCP group; in particular, there were lower rates of pseudo meningocele (1.71 % in the CCP group vs 6.06 % in the RWC group, OR 0.264, CI 0.150 – 0.463, p < 0.01), wound CSF leaks (0.15 % in the CCP group vs 4.16 % in the RWC group, OR 0.105, CI 0.028–0.399, p < 0.01) and CLRC (0.21 % in the CCP group vs 1.65 in the RWC group, OR 0.248, CI 0.078–0.794, p = 0.01). Heterogeneity among studies was low as concerns pseudo meningocele, wound CSF leaks and CLRC (I^2 = 0 % for all these parameters).

3.5. Secondary outcomes

We observed a significant difference between groups as regards wound infection rates, with fewer infections in the CCP group (0.54 % in the CCP group vs 2.53 in the RWC group, OR 0.301, CI 0.114 – 0.790, p = 0.01). Heterogeneity regarding this parameter was low (I^2 = 0 %). The

Table 1
Summary of the included studies.

Author, year	Group	Pts	Mean Age (y)	Male %	Pathology	Material	Dural closure	Reconstruction	FU (mos)
Eseonu 2015 [5]	CCP	105	52.5	NR	NVC	Calcium Phosphate	Nylon + duramatrix + duragen	Total cement cranioplasty	2.29
	RWC	116	51.2	NR	NVC	Medpor Plate		Medpor cranioplasty	2.35
Foster 2016 [16]	CCP	336	56.9	35	Mixed	Calcium Phosphate	Nylon ± animal pericardium ± fibrin glue	Total Cement cranioplasy	26.6
	RWC	336	53.7	31	Mixed	Titanium Mesh		Titanium-Polyethylene Mesh	16.5
Ou 2019[10]	CCP	136	58.5	92	Mixed	PMMA	Vycril + muscle + collagen matrix	Total cement cranioplasty	12
	RWC	107	58	NR	Mixed	Autologous bone flap		Autologous bone flap	13
Wolfson 2020 [9]	CCP	288	56.8	74	NVC	Calcium Phosphate or PMMA	Suture + dural substitute	Total cement cranioplasty	NR
	RWC	259	55	74	NVC	Autologous Bone		Autologous bone	NR
Shi 2022 [17]	CCP	66	50.9	26	NVC	Calcium Phosphate	Absorbable suture + epidural dural substitute	Total cement cranioplasty	NR
	RWC	89	53.3	40	NVC	Titanium Mesh		Titanium Mesh	NR
Total	**CCP**	**595**	**54.67**	**100**	–	–	–	–	**7.14**
	RWC	**571**	**54.37**	**114**	–	–	–	–	**7.67**

Abbreviations: CCP = cement cranioplasty; NVC = CPA neurovascular conflict; PMMA = polymethyl methacrylate; RWC = reconstruction without cement.

Table 2
Results of the Risk of Bias assessment with the ROBINS-I tool.

Author et al. (Year)	Confounding	Selection of participants into the study	Classification of interventions	Deviations from intended interventions	Missing data	Measurement of the outcome	Selection of the reported result	Overall
Shi et al. (2022)	Moderate	Moderate	Moderate	Low	Moderate	Low	Low	Moderate
Wolfson et al. (2020)	Moderate	Low	Low	Low	Low	Moderate	Low	Moderate
Ou et al. (2019)	Moderate	Moderate	Low	Low	Low	Moderate	Low	Moderate
Eseonu et al. (2015)	Moderate	Low	Low	Low	Low	Moderate	Moderate	Moderate
Foster et al. (2016)	Moderate	Low	Low	Low	Low	Moderate	Moderate	Moderate

CCP group also had significantly lower reoperation rates (0.54 in the CCP group vs 2.53 in the RWC group, OR 0.189, CI 0.050–0.708, p = 0.01) as compared to the RWC group. Heterogeneity was low regarding this parameter (I^2 = 18.19 %).

Primary and secondary outcomes are reported in Table 3. Fig. 2 resumes the statistical analysis of the outcomes.

3.6. Subgroup analysis

To account from potential biases arising from clustering heterogeneous reconstruction techniques in the group "RWC" (namely, medpor/titanium cranioplasty vs autologous bone flap replacement) we performed a subgroup analysis of the studies that compared CCP with autologous bone flap replacement only. [9,10] Of note, we still observed

a statistically significant difference between CCP and RWC groups in terms of pseudomeningocele rates (OR = 0.29, 95 % CI 0.16–0.53, p < 0.01), CLRC (OR = 0.13, 95 % CI 0.03–0.56, p < 0.01), and reoperation rates (OR = 0.12, 95 % CI 0.04–0.38, p < 0.01). There was no statistically significant difference in wound infection rates. Wound CSF leak rates could not be studied in this subgroup analysis as they were not clearly described in the study from Wolfson and colleagues [9].
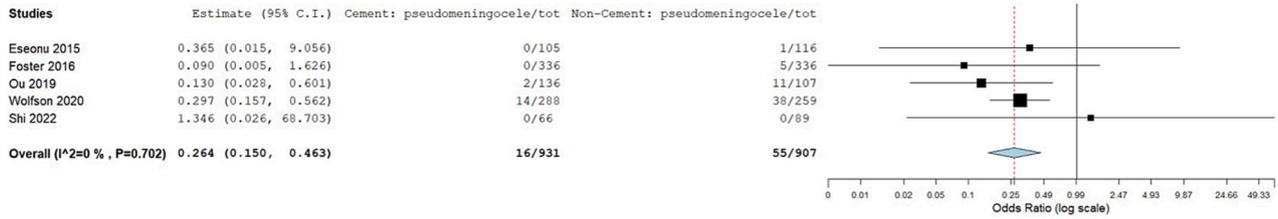
Similarly, to account for heterogeneity in dural closure protocols, we performed another subgroup analysis excluding the only study where watertight dural closure was not performed in 100 % of cases. [9] In the CCP group, there were lower rates of pseudomeningocele (OR = 0.15, 95 % CI 0.04–0.51, p < 0.01), wound CSF leak (OR = 0.11, 95 % CI 0.02–0.63, p = 0.01), and wound infections (OR = 0.28, 95 % CI 0.08–0.98, p = 0.05).

Table 3
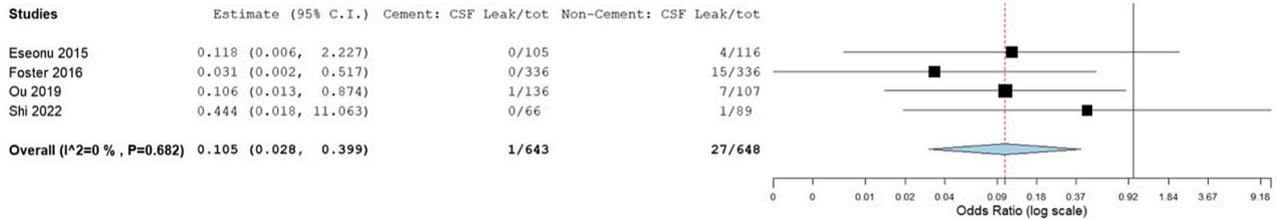Outcome comparison between the two groups.

Complication type	CCP (N = 595)	% tot pts	RWC (N = 571)	% tot pts	Odds Ratio	Odds Ratio 95 % CI	p-value	I^2
Pseudomeningocele	16/931	1.71	55/907	6.06	0.264	0.150 – 0.463	**<0.01**	0 %
Wound CSF leaks	1/643*	0.15	27/648*	4.16	0.105	0.028——0.399	**<0.01**	0 %
CLRC	2/931	0.21	15/907	1.65	0.248	0.078——0.794	**0.01**	0 %
CSF Rhinorrhea	2/643*	0.31	2/643	0.31	0.922	0.208——4.089	0.9	0 %
Intracranial Infection	1/931	0.10	8/907	0.88	0.407	0.097——1.712	0.2	0 %
Wound Infection	5/931	0.54	23/907	2.53	0.301	0.114 – 0.790	**0.01**	0 %
Revision surgery or Shunt	4/595§	0.67	26/571§	0.46	0.189	0.050——0.708	**0.01**	18.19 %

Abbreviations. CLRC = CSF leak related complications (CSF leak-related meningitis, pneumocephalus, subdural hematoma); CCP = cement cranioplasty; RWC = reconstruction without cement; *incidence reported in 4 out of 5 studies (missing in Shi et al., 2022 [16]); §incidence reported in 3 out of 5 studies (missing in [16 17]).
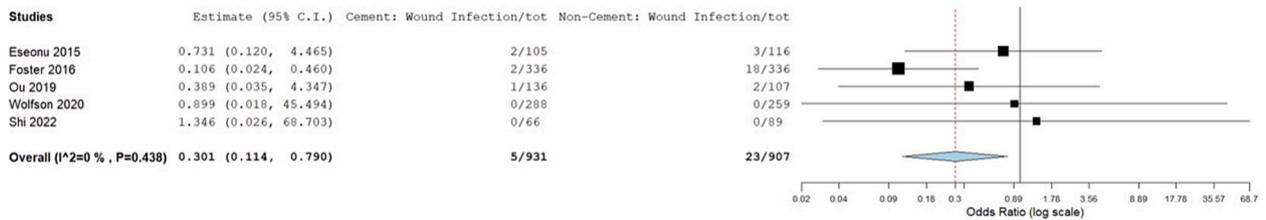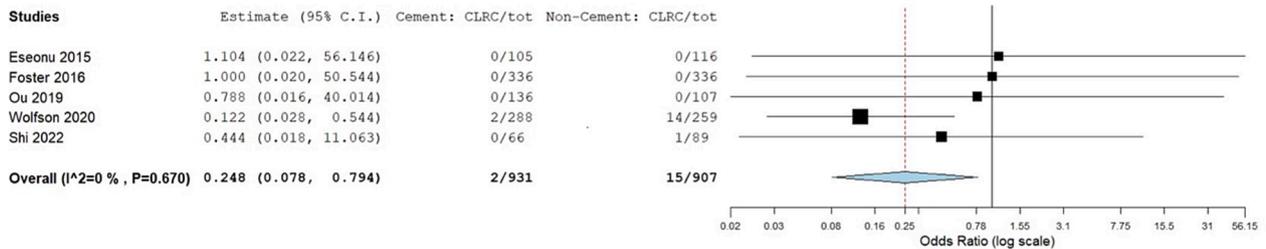
PSEUDOMENINGOCELE

Studies	Estimate (95% C.I.)	Cement: pseudomeningocele/tot	Non-Cement: pseudomeningocele/tot
Eseonu 2015	0.365 (0.015, 9.056)	0/105	1/116
Foster 2016	0.090 (0.005, 1.626)	0/336	5/336
Ou 2019	0.130 (0.028, 0.601)	2/136	11/107
Wolfson 2020	0.297 (0.157, 0.562)	14/288	38/259
Shi 2022	1.346 (0.026, 68.703)	0/66	0/89
Overall (I^2=0 % , P=0.702)	0.264 (0.150, 0.463)	16/931	55/907

WOUND CSF LEAK

Studies	Estimate (95% C.I.)	Cement: CSF Leak/tot	Non-Cement: CSF Leak/tot
Eseonu 2015	0.118 (0.006, 2.227)	0/105	4/116
Foster 2016	0.031 (0.002, 0.517)	0/336	15/336
Ou 2019	0.106 (0.013, 0.874)	1/136	7/107
Shi 2022	0.444 (0.018, 11.063)	0/66	1/89
Overall (I^2=0 % , P=0.682)	0.105 (0.028, 0.399)	1/643	27/648

WOUND INFECTION

Studies	Estimate (95% C.I.)	Cement: Wound Infection/tot	Non-Cement: Wound Infection/tot
Eseonu 2015	0.731 (0.120, 4.465)	2/105	3/116
Foster 2016	0.106 (0.024, 0.460)	2/336	18/336
Ou 2019	0.389 (0.035, 4.347)	1/136	2/107
Wolfson 2020	0.899 (0.018, 45.494)	0/288	0/259
Shi 2022	1.346 (0.026, 68.703)	0/66	0/89
Overall (I^2=0 % , P=0.438)	0.301 (0.114, 0.790)	5/931	23/907

CLRC

Studies	Estimate (95% C.I.)	Cement: CLRC/tot	Non-Cement: CLRC/tot
Eseonu 2015	1.104 (0.022, 56.146)	0/105	0/116
Foster 2016	1.000 (0.020, 50.544)	0/336	0/336
Ou 2019	0.788 (0.016, 40.014)	0/136	0/107
Wolfson 2020	0.122 (0.028, 0.544)	2/288	14/259
Shi 2022	0.444 (0.018, 11.063)	0/66	1/89
Overall (I^2=0 % , P=0.670)	0.248 (0.078, 0.794)	2/931	15/907

REOPERATION

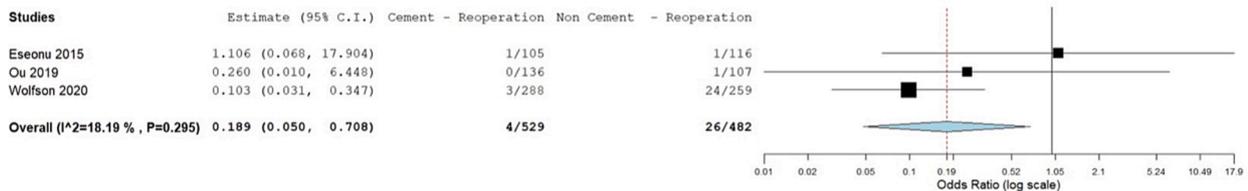| Studies	Estimate (95% C.I.)	Cement – Reoperation	Non Cement – Reoperation
Eseonu 2015	1.106 (0.068, 17.904)	1/105	1/116
Ou 2019	0.260 (0.010, 6.448)	0/136	1/107
Wolfson 2020	0.103 (0.031, 0.347)	3/288	24/259
Overall (I^2=18.19 % , P=0.295)	0.189 (0.050, 0.708)	4/529	26/482

Fig. 2. Illustrative diagrams of the statistical analysis (only the statistically significant results are shown).

4. Discussion

The retrosigmoid approach represents the neurosurgeon's workhorse to access CPA pathology and is one of the most common used approaches in day-to-day neurosurgical practice. As for every posterior fossa approach, a meticulous closure technique is mandatory to minimize CSF leaks and their complications, which can have a severe impact on a patient's quality of life and can produce morbidity, mortality, and excess costs [18,19].

Cranioplasty with bone cement is among the techniques employed to enhance the quality of the reconstruction in retrosigmoid approaches. In this context, authors have described the use of bone cement to improve aesthetic outcomes [11], as filling the gaps generated by the craniotomy/craniectomy could prevent visible skin retraction caused by traction from epidural scar tissue. Moreover, creating a complete barrier between muscle layers and the dura could prevent the formation of adhesions, which have been associated with postoperative headaches [8,11,17,20,21].

Besides these advantages, CCP could also theoretically reinforce the watertightness of the closure by providing additional sealing [21–23]. This could help addressing cerebrospinal fluid leaks and related complications, which are one of the major concerns in patients treated for posterior fossa pathologies. The hypothesized mechanisms for this include: the formation of a plug through the adhesion of cement to the craniotomy margins, providing a further barrier and thus increasing the pressure gradient required to produce a CSF leak [5,16]; the outward pressure on the dural reconstruction generated by cement, eliminating dead space and enhancing the adherence of any epidural matrices or reinforcing seals (e.g., fibrin glue); [10] the sealing of mastoid air cells by cement, closing another possible pathway of CSF leak.

However, the use of bone cement in reconstruction could produce additional costs and prolong the operative time. Additionally, cement as a foreign body could theoretically be associated with rejection reactions, impaired wound healing and increased infection rates [11,24–27].

The aim of this study was to *meta*-analyze the available papers in the literature to evaluate if the evidence supporting this practice based on postoperative appearance of CSF leaks, CSF leak-related complications, and wound infections [28,29].

The results of our *meta*-analysis support a total reconstruction with bone cement as a measure to reduce the incidence of CSF leaks and related postoperative complications. Moreover, patients treated with CCP developed fewer wound infections and underwent less reoperations related to wound problems (e.g., wound revision, CSF shunting).

Interestingly, most of the patients in our analysis were affected by CPA neurovascular conflicts (i.e., conflicts between cranial nerves and vessels in the cerebellopontine angle). Only 56 patients were affected by CPA tumors (18 in the cement and 38 in the non-cemented groups) [10]. Even if the difference between groups is statistically significant (chi squared = 7.62, p = 0,005), tumors represent only 3 % of the total cases included. We believe that the significant homogeneity of pathologies treated among studies reinforces the conclusions of our analysis. Treating neurovascular conflicts, in fact, does not mandatorily require drilling the posterior wall of the internal acoustic canal [23,30]. A confounding factor is thus removed, as the opening of mastoid air cells during this procedure can be an independent source of CSF leak, which is, of course, not affected by cement reconstruction of the cranial vault [5,31,32].

In all included papers, the technique employed was total cement cranioplasty, i.e., complete sealing of all bone defects (with or without replacement of the autologous bone flap). This was obtained by evenly spreading PMMA or calcium phosphate cement, filling all gaps. We were not able to identify in the literature any comparative studies dealing with usage of bone cement other than total cranioplasty (for example, focal sealing of mastoid air cells opened during the craniotomy/craniectomy). Total cement cranioplasty could reduce the incidence of CSF leaks through two mechanisms: by closing/reducing the communication

between the epidural and subcutaneous spaces and by providing additional sealing of opened mastoid air cells [33].

As regards the latter, however, since the included studies were all retrospective, the opening of air cells during craniotomy was not consistently reported and could not be analyzed as an independent factor. Our analysis thus does not allow us to conclude the impact of CCP on CSF rhinorrhea and otorrhea. The incidence of these complications is reported for both groups (CCP and RWC) in four studies; three of them report zero cases in both cohorts and one study reports 2 cases in each cohort. The difference is not statistically significant (0.208–4.089, p = 0.9). Of note, this analysis is very partial as the fifth included study does not report the separate incidence for the two cohorts, but states that there were globally 25 cases of CSF rhinorrhea/otorrhea distributed between the CCP and RWC groups [10,17]. We thus believe that no solid conclusions can be drawn with respect to the impact of CCP on this complication.

We opted to include only comparative studies in our analysis to minimize potential biases that could arise from comparing heterogeneous, non-comparative series addressing CCP and RWC, respectively. In particular, among the studies, two were single-surgeon series, and the other three were single-institution, multi-surgeon series [5,9,10,16,17].

In all studies, dura was closed in a watertight fashion whenever feasible. In four studies, when primary watertight closure could not be achieved, dural substitutes or muscle plugs were used to close the gaps, and epidural collagen matrices with or without fibrin glue were always employed for additional sealing [5,10,17]. In one study only, additional measures to obtain a watertight dural seal were not always employed [9]. This heterogeneity in dural closure methods could lead to a bias, as watertightness of dural closure is generally maintained to be an important element in preventing CSF leaks in posterior fossa surgery. To account for this possible bias, we performed a subgroup analysis excluding this latter study [9]. In this analysis, the CCP group still had a significantly lower incidence of pseudomeningocele, wound CSF leaks and wound infections. However, since it is difficult to retrospectively assess the actual "watertightness" of dural closure, it is impossible to completely eliminate this bias from a *meta*-analysis of retrospective studies, and the only way to solve this problem would be to conduct a prospective study.

Another possible confounding factor is represented by the size of craniotomies. Same as for dural closures, the retrospective nature of the studies prevented authors from reporting accurate statistics in this respect. However, as previously mentioned, all studies except for two [5,16] report in their "methods" the typical size of the craniotomies performed, which in all cases ranged between 2 and 3 cm. This information does not eliminate the possibility of biases but does indicate a certain level of homogeneity among studies in this regard.

A further bias could derive from the heterogeneity of reconstruction techniques that have been grouped in the RWC group. Reconstruction with heterologous materials (such as titanium meshes or polyethylene-titanium plates) could potentially be associated with more complications and/or different CSF leak rates as compared to autologous bone flap replacement. For this reason, we performed a subgroup analysis comparing CCP to reconstruction with autologous bone flap. Of note, the analysis confirmed the reduction in rates of postoperative pseudomeningocele, CLRC and reoperation rates with CCP (see paragraph 3.6). The difference in wound infection rates did not reach statistical significance (there were only three total cases of infections, one in the CCP group and two in the autologous bone flap group).

As a final consideration, the costs associated with the reconstruction techniques were reported in only one study, which indicated that CCP was not more expensive than reconstruction using titanium mesh [16]. Costs of titanium-polyethylene plates, as reported by a separate study, seem to be similar [34]. Unfortunately, direct cost comparisons among other reconstructive methods (especially autologous bone flap replacement with miniplates) remain unavailable.

The main limitation of this study is the small number of included

papers; however, the number of patients included was considerable, with similar numerosity in both groups. Another area for improvement is related to the heterogeneity of reconstructive techniques adopted in the RWC group; none of the adopted techniques, however, provided a sealing effect. Also, the incidence of opening of superficial mastoid air cells during the craniotomy was never reported in the included studies, and no solid conclusions can be draw regarding the impact of CCP on CSF rhinorrhea/otorrhea. Finally, bias due to the heterogeneity of the dural closure methods and craniotomy sizes (and their impact on CSF leaks) cannot be completely excluded.

5. Conclusions

When there are no additional sources for potential CSF leaks (such as drilling of the IAC), total cement cranioplasty is associated with - significantly lower rates of pseudo meningocele, wound CSF leaks, and CSF leak-related complications as compared to simple bone flap replacement or other non-sealing reconstructive techniques. CCP is also associated with fewer wound infections and lower reoperation rates as compared to other types of reconstruction.

6. Declarations

Autorship: All Authors have read the manuscript and agreed on its publication in the present form.

Funding: No funding was received for the present work.

Ethics. Due to the nature of this study, no approval from the institutional board review was necessary.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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