# Autologous Cranioplasty is Associated with Increased Reoperation Rate: A Systematic Review and Meta-Analysis

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**Key words**
- Complication
- Cranioplasty
- Infection
- Material
- Synthetic
- Reoperation
- Resorption

**Abbreviations and Acronyms**
CI: Confidence interval
OR: Odds ratio

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OBJECTIVE: **Consensus regarding selection of synthetic versus autologous flap reimplantation for cranioplasty after decompressive craniectomy has not been reached and the multiple factors considered for each patient make comparative analysis challenging. This study examines the association between choice of material and related complications.**

METHODS: **A systematic literature review and meta-analysis were performed using PubMed for articles reporting delayed cranioplasty after decompressive craniectomy using a cohort design comparing autologous bone and synthetic implants. Extracted data included implant material and incidence of infection, reoperations related to implant, wound complications, and resorption.**

RESULTS: **One randomized controlled trial and 11 cohort studies were included for a total of 1586 implants (950 bone, 636 synthetic). Autologous implants had significantly more reoperations than did synthetic implants ($n$ = 1586 implants; odds ratio [OR], 1.91; 95% confidence interval [CI], 1.40–2.61). Reoperations were most often because of resorption (54%, $n$ = 159/295) followed by infection (41%, $n$ = 121/295). The pooled incidence of resorption in autologous implants was 20% ($n$ = 159/791). Among the other outcomes, there was no significant difference for infections ($n$ = 1586; OR, 1.24; CI, 0.82–1.88) or wound complications ($n$ = 678; OR, 0.56; CI, 0.22–1.45). For the trauma subpopulation, there was no significant difference in infection rate with either material ($n$ = 197; OR, 1.89; CI; 0.59–6.09).**

CONCLUSIONS: **Autologous implants had significantly more reoperations primarily because if the intrinsic risk of resorption (level of evidence 3b).**

## INTRODUCTION

Cranioplasty after decompressive craniectomy is a routine neurosurgical procedure to restore cosmesis, provide cerebral protection, facilitate neurologic rehabilitation, and improve neurologic outcome.[1] Cranioplasty, although considered routine by many, can be associated with significant morbidity.[2-6] The choice of implant material has received considerable attention as a potential modifiable risk factor.[7-9] This choice is typically at the discretion of the operating surgeon or institution. In cases of fragmented or grossly infected bone, the use of synthetic implant seems obvious, but more often the choice is one of cost or convenience.

The purpose of this study was to 1) assess for reported associations between implant material and subsequent complications and 2) catalogue other risk factors for these complications. To answer these questions, a review of the literature and meta-analysis was performed to examine the complications after cranioplasty using either autologous bone or synthetic implants.

## METHODS

### Search

A systematic review of the literature adherent to PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines was performed for published articles reporting on complications related to cranioplasty material.[10] The PubMed/MEDLINE database was searched for articles on cranioplasty procedures that compared both bone versus synthetic materials using the query: "cranioplasty AND (material OR ((autologous OR bone OR allograft) AND (synthetic OR bone-substitute OR polymethylmethacrylate OR PMMA OR titanium OR acrylic OR hydroxyapatite)))." The search was restricted to original clinical studies published between January 2000 and April 2018. From preliminary reading, studies preceding this period tended to use nonstandard techniques or materials no longer in common use, and so the decision was made to exclude older studies. Thorough bibliographic searches of qualifying articles and relevant medical journals were also performed to identify additional articles for inclusion.

### Selection Criteria

Articles reporting on complications after cranioplasty using either autologous bone

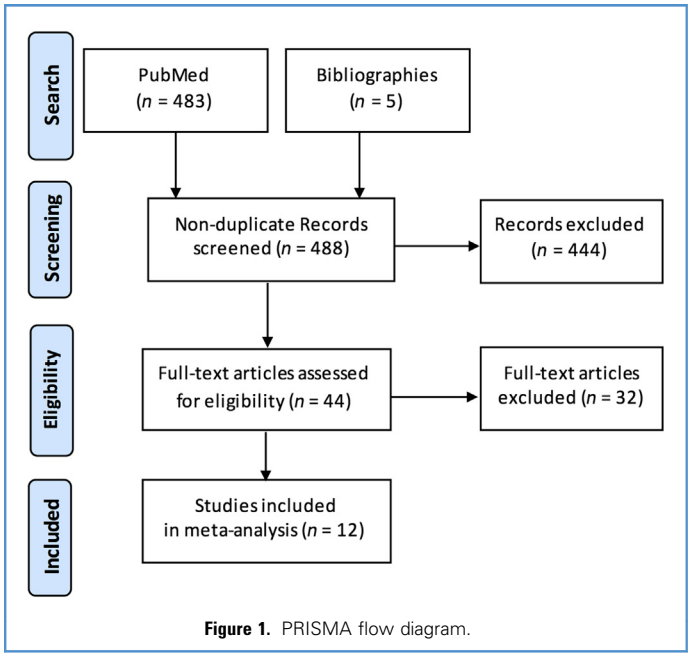


**Figure 1.** PRISMA flow diagram.

or synthetic implant were included in the analyses. With a large body of literature mentioning material choice, only studies specifically designed to compare material choice were included, (e.g., clinical trials and cohort studies). Case series that merely mention material choice were excluded. Further, included studies must have had at least 20 patients with at least 3 months follow-up. Technical notes, letters, and editorials were excluded. Reviews were also excluded; however, referenced articles were thoroughly screened for possible inclusion.[2,7,11] Studies that involved animals, included noncalvarial or maxillofacial procedures, or focused exclusively on the pediatric population were excluded.[12-14] Studies were excluded if more than a quarter of patients underwent nondecompressive single-stage craniectomy (e.g., for resection of meningioma).[15,16] The search results were independently screened by 2 authors (J.M. and Z.M.); disagreements were resolved by consensus. The following studies were excluded: split calvarial or rib grafts,[17-22] comparison only among different synthetic options,[23-27] reporting data not suitable for analysis,[3,28] non-English language,[29] focused only on epidural fluid collections,[30] or a significant portion of patients with previous cranioplasty procedures.

### Data Extraction

The following data were extracted from each article, if reported: number of patients, indication for initial craniectomy, number of autologous bone implants, number of synthetic implants, type of synthetic material, infection, reoperations, wound complications, clinically significant bone resorption (aseptic necrosis), and any risk factors identified. If an implant included primarily bone but was supplemented with allograft, it was considered an autograft.[31] Nondestructive processing of autologous bone was ignored (e.g., autoclave,[31] fat sonication[32]).

### Statistical Analysis

Data were analyzed using Review Manager 5.3.5 (The Cochrane Collaboration). For each complication, odds ratios (OR) and 95% confidence intervals (CI)s were calculated to estimate the odds of each complication for autologous bone implant (i.e., OR <1 indicates bone is associated with decreased complication rate, whereas synthetic material is associated with an increased rate). Odds ratios were pooled using the Mantel-Haenszel method with a fixed-effects model, except where the $\chi^2$ test indicated significant heterogeneity among studies, in which case a random-effects model was used. The $I^2$ metric was used to quantify heterogeneity (0% = no heterogeneity; 100% = maximal heterogeneity).[33] The $\chi^2$ test was used to evaluate significant differences between subgroups. P values $< 0.05$ were considered statistically significant.

### Assessment of Bias

The study quality of individual articles was determined by using the Oxford Center for Evidence-Based Medicine guidelines.[34] Risk of bias was assessed by the Newcastle-Ottawa Scale, which is a 3-category, 9-point scale assessing cohort selection, comparability, and outcome, with a higher score indicating higher quality.[35]

## RESULTS

Literature review results are shown in the PRISMA flow diagram (**Figure 1**). The search identified 483 nonduplicate studies spanning January 1, 2000 to April 30, 2018. Five additional studies were identified from bibliographies.[31,36-39]

The final 12 included studies represented 1586 cranioplasty procedures with a clear preference toward use of a patient's own bone (950 bone, 636 synthetic). **Table 1** lists individual study characteristics. Included were 1 randomized controlled trial (Oxford Center for Evidence-Based Medicine evidence level 1) and 11 cohort studies (level 3b). Indications for initial craniectomy included trauma (most common), ischemic or hemorrhagic stroke, infection, and tumors. **Table 2** summarizes these characteristics across studies.

A variety of synthetic implants were used. Two of the most common were titanium and polymethylmethacrylate. Various other combinations of prefabricated or intraoperative molded implants were made from polyethylene, polyetheretherketone, hydroxyapatite, and various other acrylics and ceramics. Autologous bone implants underwent a variety of handling protocols, most commonly soaking in betadine and frozen storage; however, a few studies autoclaved the bone before reimplantation. One study used a method called Tutoplast processing for autologous bone, which involves a combination of sonication to remove fat, hydrogen peroxide to kill viruses, acetone to dry out prions, and gamma radiation.[32]