Porous and nonporous orbital implants for treating the anophthalmic socket: A meta-analysis of case series studies

Silvana Schellini, Eliane Jorge, Roberta Sousa, John Burroughs & Regina El-Dib

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**ABSTRACT**

**Purpose:** To assess the efficacy and safety of porous and nonporous implants for management of the anophthalmic socket.

**Methods:** Case series meta-analysis was conducted with no language restriction, including studies from: PUBMED, EMBASE and LILACS. Study eligibility criteria were case series design with more than 20 cases reported, use of porous and/or nonporous orbital implants, anophthalmic socket and, treatment success defined as no implant exposure or extrusion. Complications rates from each included study were quantified. Proportional meta-analysis was performed on both outcomes with a random-effects model and the 95% confidential intervals were calculated.

**Results:** A total of 35 case series studies with a total of 3,805 patients were included in the meta-analysis. There are no studies comparing porous and nonporous implants in the anophthalmic socket treatment. There was no statistically significant difference between porous polyethylene (PP) and hydroxyapatite (HA) on implant exposure: 0.026 (0.012–0.045) vs 0.054 (0.041–0.070), respectively and, neither on implant extrusion: 0.0042 (0.0008–0.010) vs 0.018 (0.004–0.042), respectively. However, there was a significant difference supporting the use of PP when compared to bioceramic implant: 0.026 (0.012–0.045) vs. 0.12 (0.06–0.20), respectively, on implant exposure.

**Conclusion:** PP implants showed lower chance of exposure than bioceramic implant for anophthalmic socket reconstruction, although we cannot rule out the possibility of heterogeneity bias due to the nature and level of evidence of the included studies. Clinical trials are necessary to expand the knowledge of porous and nonporous orbital implants in the anophthalmic socket management.

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**INTRODUCTION**

The loss of an eye or its content may lead to orbital and even facial asymmetry if the lost volume is not replaced. Orbital implants are used to replace the lost volume and to enable the use of an aesthetic ocular prosthesis with good mobility.1 Currently, there are several types of orbital implants that can be used. The ideal material is not yet known, but it must be biocompatible, non-allergenic, non-carcinogenic and inexpensive.2

The first implants were manufactured with smooth-surfaced material, nonporous and non-integrated, in an attempt to prevent the inflammatory response that might cause extrusion of the implant from the cavity. Until 1941, the most often used material to replace orbital volume was glass, followed by polymethylmethacrylate (PMMA) after the Second World War.2,3 Indeed, PMMA is the most often used nonporous implant material because, in addition to its low price, it is accessible, available in several sizes, easily placed, and not associated to local irritation, allergy or cancer.4

The most modern implants, called porous or integrated implants, are the natural hydroxyapatite (HA), bioceramics and high density porous polyethylene (PP). These implants have similar clinical behavior, good integration and low rates of rejection or intolerance reactions.5 Several publications have documented the benefits of porous ocular implants.4,5 However, despite advances in new materials, orbital implants are far from being devoid of important complications such as extrusion, infection, inflammation and exposure of the implant.6

A systematic review showed there are no studies comparing porous and nonporous implants in the anophthalmic socket repair and only one randomized controlled trial comparing two porous materials (bioceramic versus hydroxyapatite spheres) with a very small sample size.7,8

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**CONTACT** Silvana Schellini, SARTIOLI@FMB.UNESP.BR, Department of Ophthalmology, Faculdade de Medicina de Botucatu/UNESP, Campus Universitario, Botucatu 18619-970, Brazil.

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A case series study including non-randomized studies is an alternative method to ascertain more knowledge regarding orbital implants used to treat the anophthalmic cavity until higher-quality primary studies are conducted. Thus, the present study was done, assessing through a meta-analysis of the available case series studies with porous and nonporous orbital implants, to evaluate the efficacy and complication rates of the orbital implants in the anophthalmic socket treatment.

**Methods**

**Literature search and studies selection**

A review of case series studies with a proportional meta-analysis of anophthalmic socket reconstruction was performed according to an alternative methodology to summarize the available evidence. There was no language restriction. Studies were obtained from the following sources: US National Library of Medicine (PUBMED; 1966–2011), Excerpta Medica database (EMBASE; 1980–2011) and Literatura Latino-Americana e do Caribe em Ciências da Saúde (LILACS; 1982–2011) to identify all case series regarding porous and/or nonporous implants in the anophthalmic socket management.

A comprehensive search strategy for anophthalmic socket and orbital implant was performed, along with MeSH and text words, including an exhaustive list of synonyms (see the Appendix). The search strategy was adapted for each database in order to achieve more sensitivity.

The following study eligibility criteria were used: (a) case series studies with more than 20 reported patients; (b) use of nonporous (i.e., smooth surface composed by acrylic or silicone) and/or porous (i.e., synthetic or natural HA, PP or bioceramic) orbital implants with or without a peg system; (c) patients with anophthalmic socket (patients that had received an implant as a secondary or exchange procedures were also considered); (d) studies that specified a measure of treatment success, regardless of the follow-up length, and/or the complications rates and the implant exposure.

Treatment success was defined as no implant exposure or extrusion. Implant removal and implant exposure needing implant removal was considered as implant extrusion. When the authors included implant extrusion along with other complications it was not computed as treatment success. There was no minimum duration of follow-up required for inclusion in the study.

The operative and postoperative complications rates were quantified and classified as implant exposures, exposure requiring implant removal, conjunctival dehiscence or thinning, malposition of the implant, granulation tissue overgrowth, and prosthesis removal indication and orbital cellulitis from each included study when it was available. Studies that aimed to evaluate motility peg system complications were excluded from this review.

**Data collection**

Two reviewers screened independently the titles identified by the literature search, extracted the data, and analyzed the results. Discrepancies in the results were resolved by discussion. A standard form was used to extract the following information: authors and year of publication, number of participants/cases, mean age of patients, type of implants (porous or nonporous orbital implants), technique (evisceration, enucleation or secondary), duration of patient follow-up and the outcomes of interest. The mean age and mean follow-up calculated in this study were based on the mean age and follow-up from each case series included in this review.

**Statistical analysis**

Treatment success and complications rates were treated as dichotomous variables with their respective 95% confidential intervals (CI). Statistical heterogeneity was assessed using the I^2 statistic and assume influential when the I^2 was greater than 50%. This illustrates the percentage of the variability in effect estimates resulting from clinical and/or methodological heterogeneity rather than sampling error. Because of the clear differences among the included studies and several uncontrolled variables, we used a random-effect model to perform a proportional meta-analysis. The software used to plot the studies into a meta-analysis was StatsDirect.

Forest plots are presented to summarize the data. Each horizontal line on a forest plot represents a case series included in the meta-analysis. The effect estimate is marked with a solid black square. The size of the square represents the weight that the corresponding study employs in the meta-analysis. The pooled estimate is marked with an unfilled lozenge at the bottom of the forest plot.

The statistically significant difference between both interventions studied was defined if their combined 95% CIs did not overlap. We considered p < 0.05 as statistically significant for the calculation of heterogeneity.
Results

The search was performed up to July 2011 and identified 892 titles. After a title and then abstract screening, we obtained full paper copies of 73 studies on porous and nonporous orbital implants that were potentially eligible for inclusion in the review. However most of these studies were animal studies, reviews, less than 20 cases reports, or did not evaluate a relevant clinical outcome. Thus, a total of 35 case series studies (13 HA, 14 PP, 3 bioceramic, 2 PMMA, 2 silicone, and 1 nylon implant) met all inclusion criteria and were included in the meta-analysis (Figure 1).²⁻⁴,⁶⁻⁸,¹⁴⁻³⁹ We computed as different study when there was more than one implant reported at the same publication.

There were a total of 3,805 patients with 1,785 cases in the HA group compared with 1,195 and 486 patients in the PP and bioceramic groups, respective. Of the HA case series, 526 enucleations and 464 eviscerations were performed, and 336 implants were secondarily placed (there was no information about the technique in 459 patients). Of the PP case series, 526 patients were performed by enucleation, 248 by evisceration, and 202 were performed secondarily. The mean follow-up was 20 months in the HA group and 23.3 months in the PP group. The mean age was 41.1 years in HA and 40.8 years in PP while the bioceramic group was 39.5 years (Table 1).

The pooled proportion of implant extrusion was 0.018 [95% confidential interval (CI) 0.004–0.042) in HA implant from nine studies with a total of 1,621 cases. There was a statistical significance regarding heterogeneity (I² value) of 0.817 showing the inconsistency of clinical and methodological aspects between the included studies in the meta-analysis (P < 0.0001) (Figure 2).

The pooled proportion of implant extrusion was 0.004 [95% CI 0.0008 to 0.0103) in PP implant from six studies with a total of 698 cases. There was no statistical significance in regard to heterogeneity (I² value = 0%) (P = 0.537) between the studies included in the meta-analysis (Figure 3).

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**Figure 1.** PRISMA flowchart from systematic review evolving anophthalmic socket case series studies.
Table 1. Demographics characteristics of patients undergoing orbital implants: comparison of nonporous and porous studies.

<table>
<thead>
<tr>
<th>Study</th>
<th>HA</th>
<th>PP</th>
<th>Bioceramic</th>
<th>PMMA</th>
<th>Silicone (Oertli)</th>
<th>Nylon implant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total case series</td>
<td>13*</td>
<td>14#</td>
<td>3c</td>
<td>2d</td>
<td>2e</td>
<td>1f</td>
</tr>
<tr>
<td>Number of patients/cases</td>
<td>1,785</td>
<td>1,195</td>
<td>486</td>
<td>90</td>
<td>156</td>
<td>93</td>
</tr>
<tr>
<td>Technique</td>
<td>Enucleation</td>
<td>526</td>
<td>526</td>
<td>202</td>
<td>17</td>
<td>48</td>
</tr>
<tr>
<td></td>
<td>Evisceration</td>
<td>464</td>
<td>248</td>
<td>161</td>
<td>3</td>
<td>59</td>
</tr>
<tr>
<td></td>
<td>Secondary</td>
<td>336</td>
<td>202</td>
<td>123</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Not reported</td>
<td>459</td>
<td>219</td>
<td>0</td>
<td>0</td>
<td>78</td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>41.1* (29.5–53.8)</td>
<td>40.8* (2.0–53.5)</td>
<td>39.5 (34.0–46.0)</td>
<td>53.8* (NA)</td>
<td>47.3 (41.1–53.5)</td>
<td>31.2 (NA)</td>
</tr>
<tr>
<td>Mean follow-up (months)</td>
<td>20.0 (6.0–50.0)</td>
<td>23.3* (6.0–42.0)</td>
<td>24.9 (9.0–35.8)</td>
<td>17.1* (NAA)</td>
<td>15.6 (7.5–23.7)</td>
<td>36.9 (NA)</td>
</tr>
</tbody>
</table>

NA = not applicable. Values in parentheses are range from each study’s age mean. *Two studies did not report the mean age. ¥Three studies did not report the mean follow-up. ¥Two studies did not report the mean follow-up. ¥Two studies did not report the mean follow-up. ¥Two studies did not report the mean follow-up. ¥Only reported by Perry 2004 study.

Figure 2. Proportional meta-analysis of case series studies regarding the occurrence of implant extrusion in hydroxyapatite implant.

Figure 3. Proportional meta-analysis of case series studies regarding the occurrence of implant extrusion in porous polyethylene implant.
The pooled proportion of implant exposure was 0.054 [95% CI 0.041 to 0.070) in HA implant from eight studies with a total of 1,565 cases. There was no statistical significance in regard to heterogeneity (I² value = 17.2%) (P = 0.293) (Figure 4).

The pooled proportion of implant exposure was 0.026 [95% CI 0.0121 to 0.0450) in PP implant from 10 studies with a total of 943 cases. There was a statistical significance in regard to heterogeneity for this outcome (I² value = 51.2 %) (P = 0.030) (Figure 5).

The pooled proportion of implant exposure was 0.12 [95% CI 0.06 to 0.20) in bioceramic implant from three studies with a total of 486 cases. There was a statistical significance in regard to heterogeneity for this outcome (I² value = 71.9%) (P = 0.028) (Figure 6).

The pooled proportion of complications rate was 0.064 [95% CI 0.024–0.121) in HA implant from 11 studies with a total of 1,289 cases. There was a statistical significance in regard to heterogeneity for this outcome (I² value = 87.3 %) (P < 0.0001) (Figure 7).

The pooled proportion of complications rate was 0.067 [95% CI 0.034 to 0.110) in PP from 13 studies with a total of 1,159 cases. There was a statistical significance in regard to heterogeneity for this outcome (I² value = 82.3%) (P < 0.0001) (Figure 8).

There was no statistically significant difference in regard to implant extrusion and complication rates between HA and PP as their CIs overlapped each other (Figures 2, 3, 7 and 8). However, there was a statistically significant difference supporting the use of PP when compared to bioceramic implant on implant exposure (0.026 vs. 0.12, respectively).

**Discussion**

Because Perry had a new proposition to replace volume in the anophthalmic cavity using HA, a wide dissemination of porous or integrated implants concept occurred. Many other new materials such as synthetic hydroxyapatite, PP and bioceramic were described for this purpose in a very short period of time. Our study showed very clearly the focus of the latest research is on porous implants.

Nevertheless, a protocol of a Cochrane systematic review about the new options to be employed in the anophthalmic cavity treatment was published and during the search process it was verified that only one randomized trial met the inclusion criteria. Unfortunately, it was not able to draw any conclusions on the efficacy and safety of integrated versus non-integrated implants in the reconstruction of the ophthalmic cavity due to insufficient evidence.

Another way to know more about this topic is including non-randomized studies as an alternative method, through a proportional meta-analyses including all available case series studies with regards to porous and/or nonporous implants used for anophthalmic socket. This is the first study about anophthalmic socket to summarize the evidence using this new approach, as an alternative to reviews that often conclude absence of clinical trials.

Some criteria, in this study, were followed to reach efficient conclusions: only case series studies about porous and/or nonporous orbital implants with 20 patients or more; studies about biomaterials in anophthalmic socket; studies evaluating clinical efficacy defined as no implant extrusion; and studies with a
minimal follow-up were included. These criteria were adopted by the authors to ensure consistency but it should be observed that exclusion on the basis of sample size alone may have introduced bias.

Even though it would be helpful to have a meta-analysis comparing porous versus nonporous implants, it was not possible to perform this analysis because there were few studies about nonporous implants identified in the literature. Furthermore, studies about bioceramic implants did not report implant extrusion either complications rate. Therefore, we could not perform a meta-analysis for implant extrusion. We were also not able to perform a meta-analysis for silicone and PMMA implants as there were only two included case series for each procedure.

Motility was not considered in this review as there were also few studies presenting its results as a dichotomous data. There was no statistically significant difference with regards implant extrusion and complication rates between HA and PP as their CIs overlapped each other. However, there was a statistically significant difference favoring PP compared to
bioceramic on implant exposure (0.026 vs. 0.12), although no statistical significance difference was found comparing HA versus both PP and bioceramic on implant exposure (0.054 vs. 0.026 and 0.12, respectively). Our analysis showed that there is significant heterogeneity in HA complication rate outcome ($I^2$ value = 87.3%).

Reasons for this heterogeneity, besides the nature of the case series study, could be both clinical and methodological.

It is also necessary to consider that surgical technique may be as important as implant selection in reducing the risk of implant exposure following enucleation or evisceration surgery.\textsuperscript{18,19}
PP and HA implants did not present a statistically significant difference in regard to implant extrusions as well as complications rates in the anophthalmic socket reconstruction. This means either a lack of statistical power or the same efficacy, however further well-conducted high-quality primary studies are needed. Only randomized controlled trials will be able to establish whether clinical efficacy for patients with anophthalmic socket can be improved using porous or nonporous materials.

**Conclusions**

Implications for clinical practice: There are evidence supporting the use of PP implant compared to bioceramic implant on the reduction of implant exposure rates, although we cannot rule out the possibility of heterogeneity bias due to the nature and level of evidence of the included studies.

Our research data suggests the need for high-quality primary studies comparing porous (integrated) versus nonporous (non-integrated) orbital implants for the treatment of anophthalmic socket with longer follow-up and larger sample size to evaluate adverse events.

**References**


Appendix

Table A1. Summary of the bibliographic search strategies for type of clinical situation and intervention of interest.

<table>
<thead>
<tr>
<th>Search History</th>
</tr>
</thead>
</table>
| (Anophthalmos OR Anophthalmia OR Anophthalmias OR (anophthalmic socket) OR (anophthalmic sockets) OR (eye socket reconstruction)) AND ((anophthalmic socket implants) OR (anophthalmic socket implant) OR (Orbital implant) OR (Orbital implants) OR (non-integrated orbital implant) OR (non-integrated orbital implants) OR (integrated orbital implant) OR (integrated orbital implants) OR (anophthalmic socket reconstruction) OR (Nonintegrated sphere) OR (Nonintegrated spheres) OR (Integrated sphere) OR (Integrated spheres) OR BioEye OR Durapatite OR Hydroxylapatite OR (Hydroxylapatite Orbital Implant) OR (natural hydroxyapatite) OR Hydroxyapatite OR (porous integrated materials) OR Bio-Eye OR (Synthetic hydroxyapatites) OR (Synthetic hydroxyapatite) OR (Calcium Hydroxyapatite) OR Interpore-500 OR (Interpore 500) OR Intermay200 OR Alveograf OR Calcite OR Ossspan OR Osteogen OR Periograf OR (Ossein-Hydroxyapatite Compound) OR (Ossein Hydroxyapatite Compound) OR Interpore-200 OR (Interpore 200) OR Interpore200 OR Osprovit OR Polyethylene OR Polythene OR Medpor OR (porous polyethylene) OR (porous polyethylene orbital implant) OR (wrapped materials) OR (wrapped material) OR (Low-Density Polyethylene) OR (Low Density Polyethylene) OR LDPE OR (High-Density Polyethylene) OR (High Density Polyethylene) OR HDPE OR (Polymethyl Methacrylate) OR Polymethylmethacrylate OR PMMA OR Acron OR (CMW Bone Cement) OR Implast OR (Kallocryl K) OR Lucite OR (Methyl Acrylic Plastic) OR (Palacos R) OR Plexiglas OR (Acrylic Bone Cement) OR Plexiglass OR (Isostatic Poly methyl Methacrylate) OR (Simplex Opague Poly methyl Methacrylate) OR (Ammonium Salt Poly methyl Methacrylate Surgical Simplex Bone Cement) OR (Surgical Simplex P Poly methyl Methacrylate) OR (Syndiostatic Poly methyl Methacrylate) OR Sol OR Supercryl OR Palavit OR Perspex OR Silicone OR silicones OR (solid non-integrated materials) OR (anophthalmic Reconstructive Surgical Procedures))
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