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DES de Chirurgie générale

par

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META-ANALYSE : EVALUATION CLINIQUE DE L'EFFICACITE DES MATERIAUX UTILISES EN RECONSTRUCTION PRIMAIRE POUR LES FRACTURES DU PLANCHER ORBITAIRE

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SOMMAIRE

ABREVIATION LIST

CODB: Castor Oil Derived Biopolymer (Poliquil®)

ICB: Iliac Crest Bone

IRM: Inferior Rectus Muscle

NMA: Network Meta-Analysis

OFF: Orbital Floor Fractures

PDS: PolyDioxanone Sheet

PDS/PG: PDS/Polyglactin (Ethisorb®)

P(L/DL)LA 70/30: Polymer with L-lactic acid 70 and DL-Lactic Acid 30

PP: Porous Polyethylene (Medpor®)

PPC: Periosteum Polymer Complex

PSI: Personal Specific Implant

SUCRA: Surface Under the Cumulative RAnking curve

ABSTRACT

BACKGROUND: Orbital floor fractures (OFF) are common facial trauma, representing around 15% of all the fractures of the facial skeleton in Europe. There are no general recommendations regarding the type of material to use for surgical repair of OFF. The aim of this network meta-analysis (NMA) was to compare the clinical results obtained after primary reconstruction of OFF using different materials.

METHODS: PubMed, Cochrane and Google Scholar databases were screened from January 1989 to September 2019. Eligible studies were the ones evaluating two or more materials and reporting the following clinical parameters: diplopia and/or enophthalmos and/or other complications (infection, hemorrhage, extrusion). Two independent investigators participated to the literature analysis. Extracted data were analyzed using a NMA.

RESULTS: Nine studies enrolling 946 patients presenting with an OFF were finally included in this work. Patients were mostly men in 75% of cases with a mean age of 31.5 years. After the surgical procedure, 105 patients presented a diplopia (11%), while 43 patients suffered from enophthalmos (4.5%). A 0.74% complication rate was found. The NMA reported a better result obtained with polydioxanone, P(L/DL)LA, porous polyethylene and titanium mesh than with autologous bone grafts for the correction of the postoperative diplopia and enophthalmos.

CONCLUSION: The current evidence does not support recommendation for the choice of the material usable in repair of OFF. The biopolymer materials, resorbable or not, and titanium mesh allow a better correction of postoperative diplopia and enophthalmos.

INTRODUCTION

Orbital floor fractures (OFF) are common facial trauma, representing around 15% of all the fractures of the facial skeleton in Europe (Boffano et al. 2014). Patients are mostly men (75%) aged from 20 to 49 years. Etiologies of OFF are mainly represented by violent assault (37.1%), then falls (21.5%), sports (14.3%) and traffic accidents (13.9%) (Boffano et al. 2014). Clinically, these fractures may result in binocular diplopia, enophthalmos, and extraocular motility impairment (Bartoli et al. 2015). Diplopia and oculomotor disturbances are the result of modifications in the soft-tissue position. It can be due to herniation/incarceration of the inferior rectus muscle (IRM) in the fractured floor, or secondary to muscle fibrosis (Dietz et al. 2001), or to a different eye-ball level of both eyes (Converse et Smith 1957). Enophthalmos is the consequence of the increase of the orbital volume and the prolapse of the intra-orbital soft-tissue contents in the maxillary sinus (Pfeiffer 1943).

The surgical repair of OFF aims to restore a normal anatomy and volume of the orbit, an appropriate position of the orbital content and a functional vision. In this way, diplopia, enophthalmos and extraocular movements can be significantly restored and improved by surgical repair (Shin et al. 2013). The materials used for primary repair should restore the eye level and thus the visual axis after liberating the IRM, and reestablish a normal volume to the orbit (Ellis et Tan 2003). A lot of materials are available: alloplastic materials resorbable or not, metal implant, autologous bone graft or cartilaginous graft (Totir et al. 2014). The ideal material should be stable, easy to conform to substance loss, biocompatible, radio-opaque to control its position by postoperative imaging, readily available and low-cost (Dubois et al. 2016). None of them reunite all these qualities (Rinna et al. 2005). Autologous grafts are cost-effective but they increase morbidity and surgical time and are associated with variable resorption. Allogeneic materials are easier to manage and easily available but could be expensive. Secondary displacements, extrusion or infection could occur with permanent materials. Resorbable materials avoid risks of long-term complications but lose their mechanical properties with time.

Despite the frequency of OFF, there is no recommendation for the type of material to choose for their surgical repair. Through the use of a network meta-analysis (NMA), the objective of this study was to compare the clinical results regarding diplopia and enophthalmos obtained after primary reconstruction of OFF using different materials.

MATERIALS AND METHODS

RESEARCH STRATEGY

The selection process of this meta-analysis was adapted from the items of the check-list PRISMA-NMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses – Network Meta Analyses) (Hutton et al. 2015).

A systematic research of the literature was done on PubMed, Cochrane Library and Google Scholar using the terms (orbit*[MESH] AND (fracture*[MESH] OR defect*[MESH] OR trapdoor [MESH] OR blowout [MESH]) AND (reconstruction [MESH] OR repair [MESH] OR material [MESH] OR graft [MESH] OR implant*[MESH]) from the 1st January of 1989 to 20st September of 2019. A first reading allowed to select the relevant titles, a second reading the abstracts and a final reading the entire articles that could be included. The eligibility assessment of the studies was performed separately by two reviewers. If they disagreed on their choices, a third reader would decide. The criteria for inclusion in the study were: comparative study between two or more materials, primary time to repair an orbital floor fracture, on living subjects, with clinical evaluation of diplopia and/or enophthalmos at three months post-operative or more, English or French languages. The exclusion criteria were: non-comparative studies, in vivo studies, cadaveric studies, animal studies, lack of clinical data evaluating diplopia or enophthalmos, literature reviews. No authors were contacted to collect the missing data.

The main test criteria were: diplopia at more than 3 months post-operatively and defined by a double vision hindering daily life, and clinical enophthalmos greater than 2mm. A secondary criterion was the frequency of post-operative complications defined as hemorrhage, infection or extrusion of equipment.

STATISTICAL ANALYSIS

The NMA was performed using Stata software (Stata Corp LP, College Station, TX). Diplopia, enophthalmos and other complications were treated as separated variables. To realize NMA, three assumptions had to be verified: Similarity, transitivity and consistency. Similarity was qualitatively defined if the included studies had been realized with similar methodological conditions (similar patients, similar designs). Transitivity was qualitatively defined if the inferred comparisons (in particular between treatments never tested together) had any sense. Consistency was a statistical phase to define if the comparisons between treatments could be established. A test of consistency could then be provided and the NMA could be realized by assuming the consistency.

A linear model allowed to aggregate the results of all the included studies in order to estimate the odds ratios between each pair of treatments on each criterion. These odds ratios were directly estimated from studies comparing this couple of treatment, or indirectly inferred from all the studies by using transitivity principle (if A can be compared to B, and B can be compared to C, then A can be compared to C).

From the obtained results, to order all the 10 treatments, we simulated data bases on the estimated results, as if we had realized a randomized study with all the 10 treatments. We simulated 10000 such randomized studies and for each of them, we ordered the 10 treatments from the first one (the treatment creating the more complications), to the last one (the treatment creating the less complications). Then the orders of each treatment could be represented on a graph representing in abscise the rows, and in ordinate the proportions of randomized studies were each treatment had been classified on the first row (first point), or on the two first row (second point), or on the three first rows (third point) and so on… the Surface Under the Cumulative RAnking curve (SUCRA) allowed to ordinate all the treatments from the estimated best one (treatment with the lower SUCRA) to the estimated worst one (treatment with the larger SUCRA).

The methodological quality of studies was assessed with a score designed according Jüni *et al.* (Jüni, Altman, et Egger 2001):

- Prospective design: 1 point; retrospective: 0 point.

- Multicentric study: 1 point; monocentric study: 0 point.

- Randomized study: 1 point, non-randomized: 0 point.

- The groups comparability in term of age, sex and fracture area, unknown: 0 point; data shown but reporting mild differences: 1 point; data shown demonstrating comparable groups: 2 points.

- Evaluation of the main criteria with an objective method: 2 points if used for diplopia and enophthalmos; 1 point if used for only one parameter; 0 if unknown or subjective method.

The total quality score ranged from 0 to 7 points and was assessed by one of the investigators.

RESULTS

REVIEW PROCEDURE

The literature analysis identified 1177 articles (Pubmed: 890; Cochrane Library: 78; Google Scholar: 209). After a title reading, 1020 articles were excluded, and 157 abstracts were selected for complementary analysis. At the end of the selection 45 full articles were retained. After full text analysis, ten articles were selected according the inclusion and exclusion criteria. One article compared two materials exclusively to each other (no comparison with materials from other studies), and could not be included in the final statistical analysis (Fig. 1). Nine articles were finally included in the NMA (Annex 1, fig. 1).

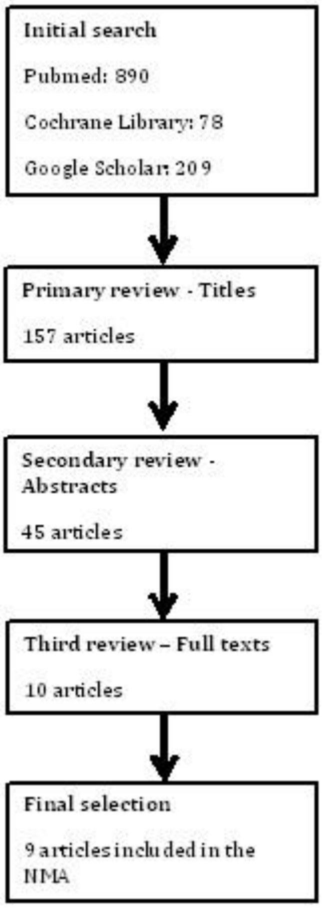


Fig 1: Flow-chart, process of studies selection.

EPIDEMIOLOGIC DATA

The selected studies included 946 patients, 75% of patients were men with a mean age of 31.5 years. The fracture area was unknown in most of studies and heterogeneous, some authors describing as large fracture (more than $2cm^2$ (Al-Sukhun et Lindqvist 2006) or more than 50% of the orbital floor (Han et Chi 2011)), others as limited (inferior to $2cm^2$ (Jank et al. 2003; Dietz et al. 2001)) (Table 1).

Methodological quality of the studies was heterogeneous with a quality score ranging from 1 (Siddique et Mathog 2002) to 7 (Dietz et al. 2001) (Annex 1).

Among the selected comparative studies, ten materials were used for primary OFF repair (Table 2). Porous polyethylene (PP) was the must studied material (254 patients), followed by autogenous grafts from calvaria and iliac crest bone (ICB) (38 patients and 101 patients, respectively). Durapatch was studied in one series including 120 patients. The alloplastic materials were used in 373 patients: Polydioaxone (PDS) in 95 patients, Polydioxanone with Polyglactin (PDS/PG) in 136 patients, polymer with L-lactic acid and DL-lactic acid (P(L/DL)LA) in 121 patients, Castor Oil-Derived Biopolymer (CODB) in 21 patients. Titanium mesh represented 40 patients. Periosteum polymer complex (PPC) was a mixed material combining autogenous periosteum and alloplastic permanent material and was studied in 20 patients.

Studies	Materials	Number of patients	Age	Ratio (%) men/women	Size of the fracture, method for measurement
Al-Sukhun, 2006	ICB P[L/DL]LA 70/30	24 15 Total: 39	37 41	62.5 / 37.5 60 / 40	Fracture area >2cm². Measurement method unknown.
Asamura, 2010	PPC ICB	20 18 Total: 38	37	71 / 29	Type of fracture unknown. Per-operative evaluation with sterile gum and measure using an imaging apparatus after surgery
Dietz, 2001	Titanium PDS	14 14 Total: 28	27 33	Unknown	Dislocation of bone >3mm. Maximum defects: 13.3mm (PDS) 13.9mm (titanium). Per-operative estimation.
Han, 2011	PP P[L/DL]LA	225 106 Total: 331	33.9 25.5	79 / 21 84.9 / 15.5	Fracture >50% of the floor area on the CT scan. Measurements method unknown.
Jank, 2003	PDS/PG PDS Durapatch	136 81 120 Total: 337	35.8	82 / 18	Fracture <2x2cm. Measurement method unknown.
Khalid, 2012	Calvaria ICB	29 29 Total: 58	30.31 29.6	79.3 / 20.7 86.2 / 13.8	Unknown.
Marano, 2016	Titanium PP CODB	26 17 21 Total: 64	Unknown	Unknown	Fracture area >1cm². Measurement method unknown.
Siddique, 2002	Calvaria ICB	9 16 Total: 25	32.1 29.5	71 / 29 60 / 40	Unknown.
Wajih, 2011	PP ICB	12 14 Total: 26	24.5 24.5	84.6 / 15.4	Unknown.

Table 1. Epidemiological characteristics of patients of the included studies. ICB, iliac crest bone; P[L/DL]LA, polymer with L-lactic acid and DL-lactic acid; PPC, periosteum polymer complex; PDS, polydioxanone; PP, porous polyethylene; CT, computed tomography; PDS/PG, polydioxanone and polyglactin; CODB, castor-oil derived biopolymer.

	Titanium mesh				**Porous Polyethylene**				**CODB**				**P[L/DL]LA 70/30**				**Calvaria**			
Studies	N	D	E	C	N	D	E	C	N	D	E	C	N	D	E	C	N	D	E	C
Al-Sukhun, 2006													15	1	1	0				
Asamura, 2010																				
Dietz, 2001	14	0	0																	
Han, 2011					225	25		1					106	12		0				
Jank, 2003																				
Khalid, 2012																	29	2		
Marano, 2016	26	1	3	4	17	1	2	1	21	0	1	0								
Siddique, 2002																	9		5	
Wajih, 2011					12	3	4													
TOTAL	**40**	1	3	4	**254**	29	6	2	**21**	0	1	0	**121**	13	1	0	**38**	2	5	0

	PPC				**Iliac crest bone**				**Polyglactin/PDS**				**PDS**				**Durapatch**			
Studies	N	D	E	C	N	D	E	C	N	D	E	C	N	D	E	C	N	D	E	C
Al-Sukhun, 2006					24	0	1	1												
Asamura, 2010	20	2	0	0	18	2	0	0												
Dietz, 2001													14	0	2					
Han, 2011																				
Jank, 2003									136	18	7	0	81	12	3		120	20	5	
Khalid, 2012					29	5														
Marano, 2016																				
Siddique, 2002					16		6													
Wajih, 2011					14	1	3													
TOTAL	**20**	2	0	0	**101**	8	10	1	**136**	18	7	0	**95**	12	5	0	**120**	20	5	0

Table 2. Clinical data extracted from the studies for the NMA; N, number of patients in the group; D, number of patients with postoperative diplopia; E, number of patients with postoperative enophtalmos; C, number of patients with postoperative complication. CODB, Castor Oil Derived Biopolymer; PPC, Periosteum Polymer Complex; PDS, Polydioxanone.

NETWORK GEOMETRY

Interactions between the selected studies are represented in figure 2. Each node represents one material. The node size is proportional to the number of articles dealing with the considered material and to the number of materials with which it was compared. The thickness of the edge between materials is proportional to the number of studies comparing the two materials.

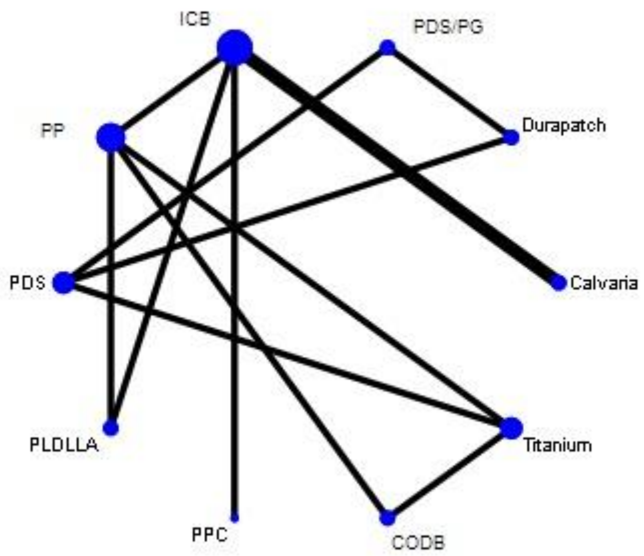


Figure 2. Schematic representation of the interactions existing between the articles included in the NMA. CODB: Castor Oil Derived Biopolymer; ICB: Iliac Crest Bone; PDS, polydioxanone; PDS/PG, polydioxanone and polyglactin ; PP, porous polyethylene; P[L/DL]LA, polymer with L-lactic acid and DL-lactic acid; PPC, Periosteum polymer complex.

The ICB and PP were the most studied materials and were compared to four others whereas calvaria and PPC were compared to only one other material but the comparison used for calvaria was evaluated in two different studies.

The construction of a network between materials allowed us to construct a statistical analysis between all the materials through a NMA.

DIPLOPIA

A postoperative diplopia was found in 105 patients (11%) all the materials considered. The NMA allowed to compare all the materials between them, representing 45 possible comparisons. When analyzed separately none of the materials studied revealed a superiority compared to others, as evidenced by the forest-plot diagram (Fig. 3).

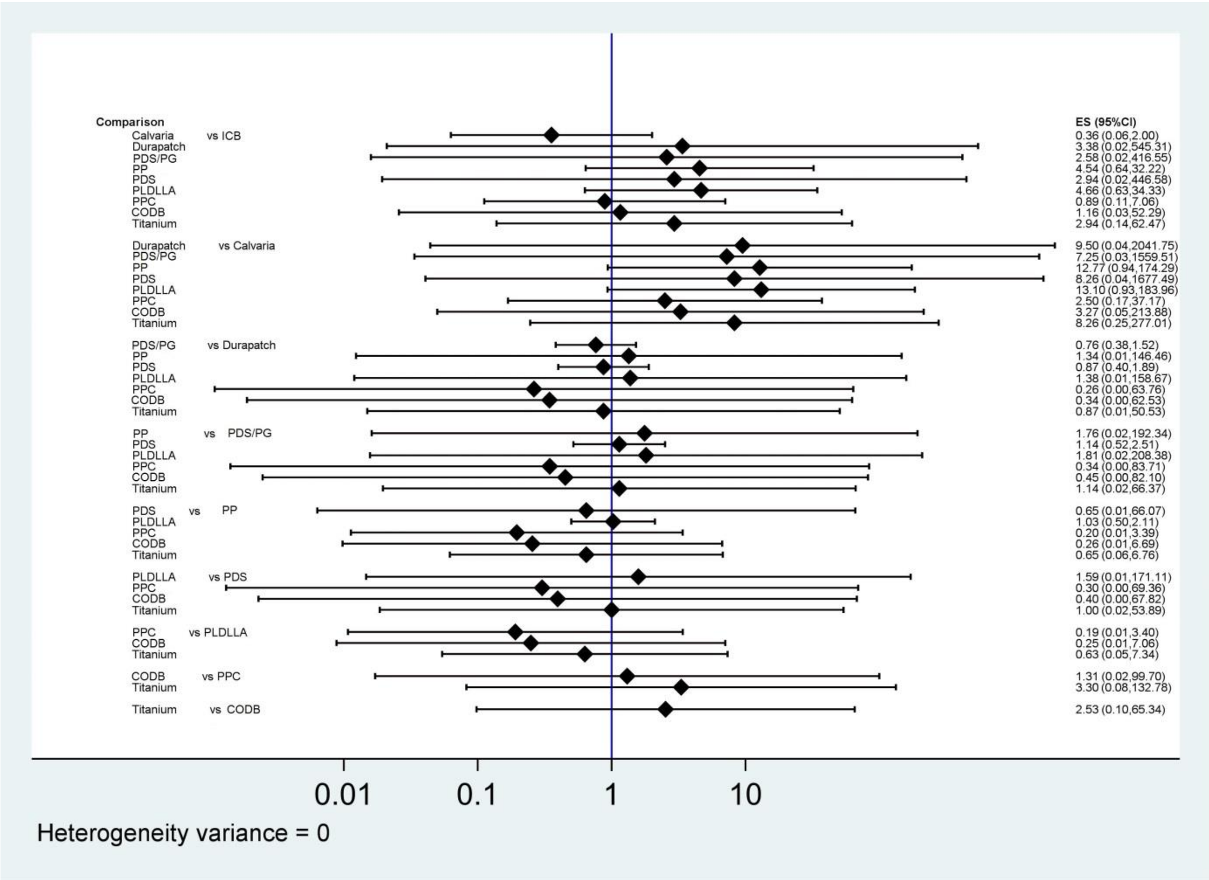


Figure 3: Forest-plot representing the 45 possible comparisons between materials regarding the postoperative diplopia. ICB: Iliac Crest Bone; PDS/PG, polydioxanone and polyglactin ; PP, porous polyethylene ; PDS, polydioxanone;; P[L/DL]LA, polymer with L-lactic acid and DL-lactic acid; PPC, Periosteum polymer complex ; CODB: Castor Oil Derived Biopolymer.

The cumulative ranking or SUCRA revealed that P(L/DL)LA and PP were the materials with the lowest SUCRA thus suggesting better results on postoperative diplopia than durapatch, titanium and PDS (Fig. 4). Calvaria represented the poorer material regarding the occurrence of a post-operative diplopia.

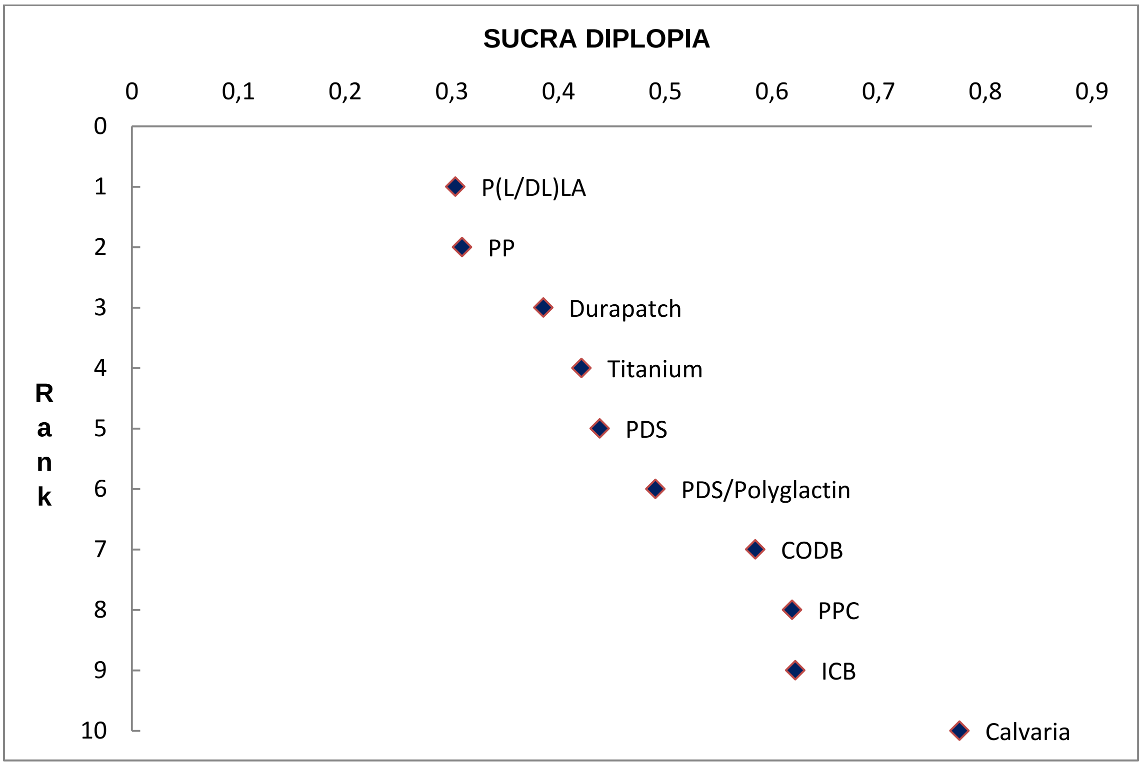


Figure 4 . Ranking plots for diplopia. The rank is inversevely proportionnal to the SUCRA. P[L/DL]LA, polymer with L-lactic acid and DL-lactic acid; PP, porous polyethylene; PDS, polydioxanone; PDS/PG, polydioxanone and polyglactin; CODB: Castor Oil Derived Biopolymer; PPC, Periosteum polymer complex; ICB: Iliac Crest Bone.

ENOPHTHALMOS

A postoperative enophthalmos was revealed in 43 patients (4.5%) all the materials considered. None of the materials studied revealed a superiority compared to others, as evidenced by the forest-plot diagram (Fig. 5).

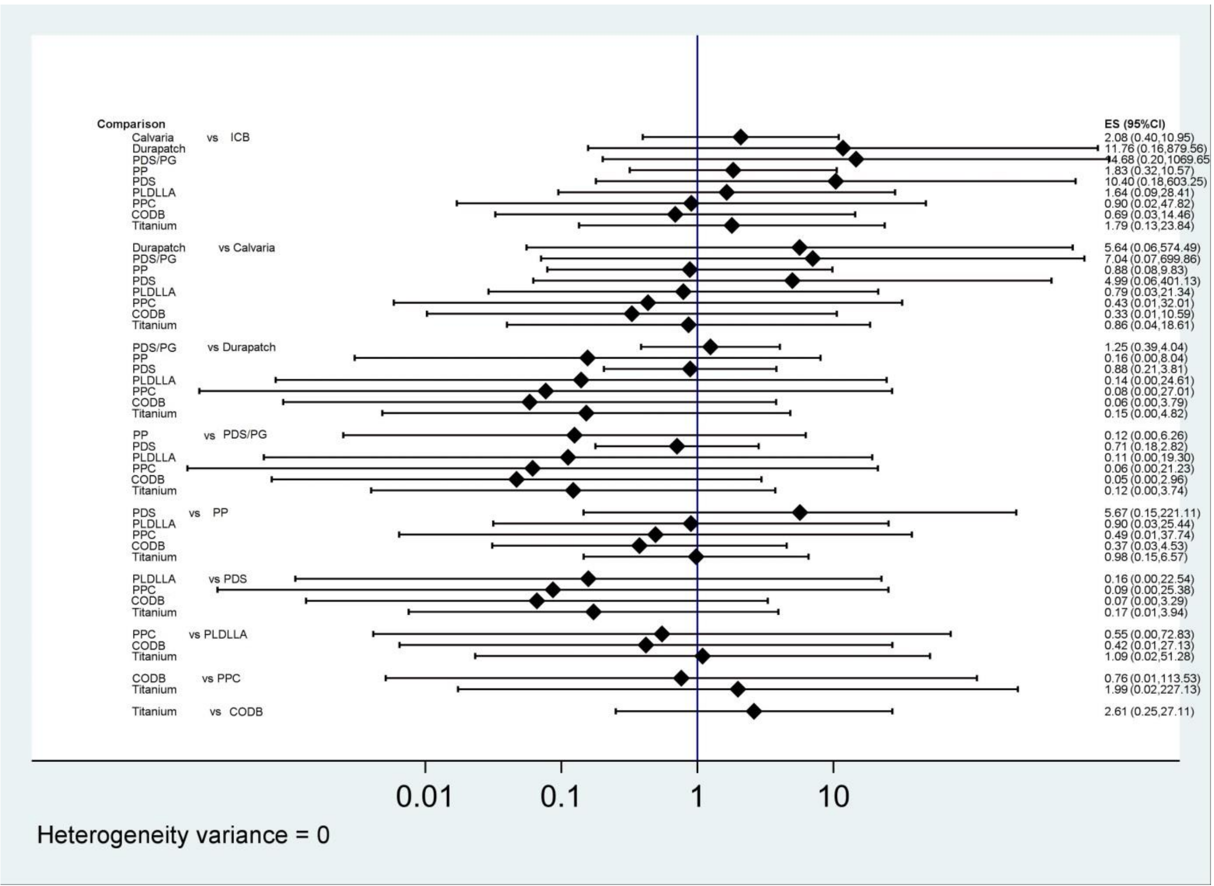


Figure 5. Forest-plot representing the 45 possible comparisons between materials regarding enopthalmos. ICB: Iliac Crest Bone; PDS/PG, polydioxanone and polyglactin ; PP, porous polyethylene ; PDS, polydioxanone;; P[L/DL]LA, polymer with L-lactic acid and DL-lactic acid; PPC, Periosteum polymer complex ; CODB: Castor Oil Derived Biopolymer.

The analysis of cumulative ranking or SUCRA suggested that PDS/PG, PDS and durapatch were the materials with the best results in term of postoperative enophthalmos (Fig. 6). While ICB and CODB represented poor materials regarding enophthalmos.

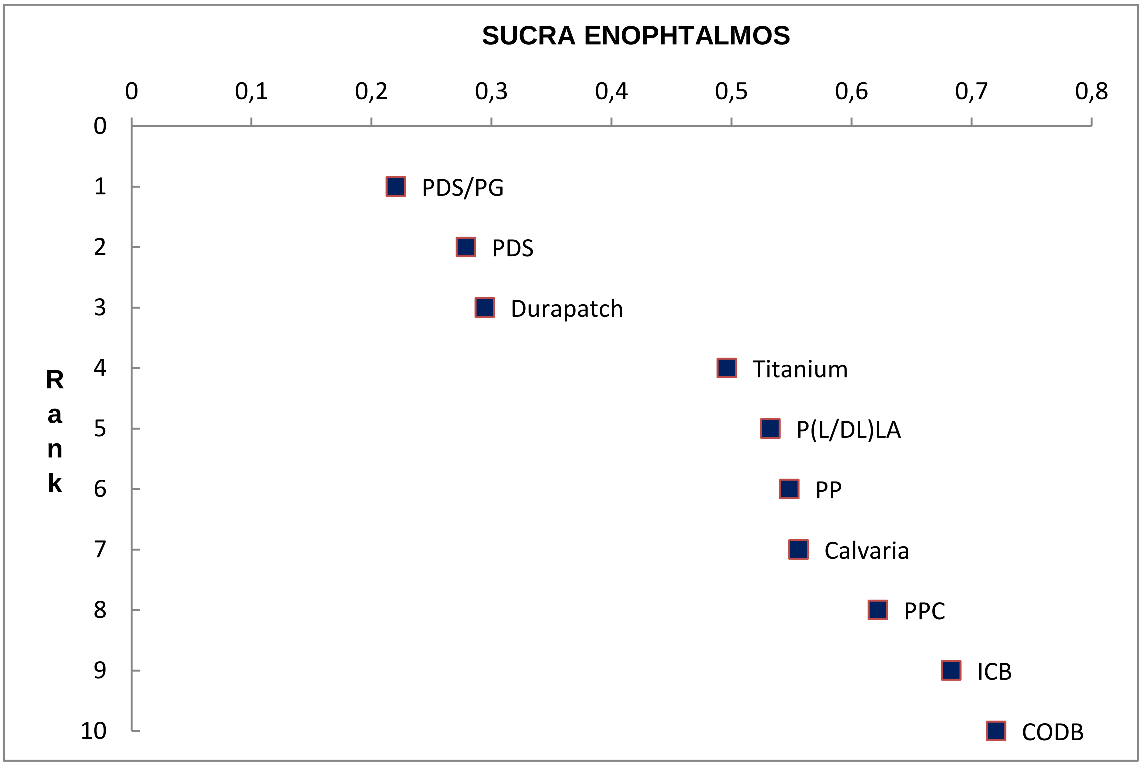


Figure 6. Ranking plots for enopthalmos. The rank is inversevely proportionnal to the SUCRA. PDS/PG, polydioxanone and polyglactin; PDS, polydioxanone; P[L/DL]LA, polymer with L-lactic acid and DL-lactic acid, PP, porous polyethylene; PPC, Periosteum polymer complex; ICB: Iliac Crest Bone; CODB: Castor Oil Derived Biopolymer.

Postoperative diplopia and enophthalmos were analyzed as covariables showing a better correction of these two clinical parameters when using durapatch, PDS, PP, PL(DL/LA) and titanium for the primary repair of OFF while poorer outcomes were observed when using PPC, calvaria, ICB and CODB with no statistical significance.

COMPLICATIONS

Other complications defined as hemorrhage, infection or extrusion of the material were found in 7 patients (0.74%) all materials combined. When analyzed separately none of the materials studied presented a higher risk of complications than the other, as seen in the forest-plot diagram (Fig.7).

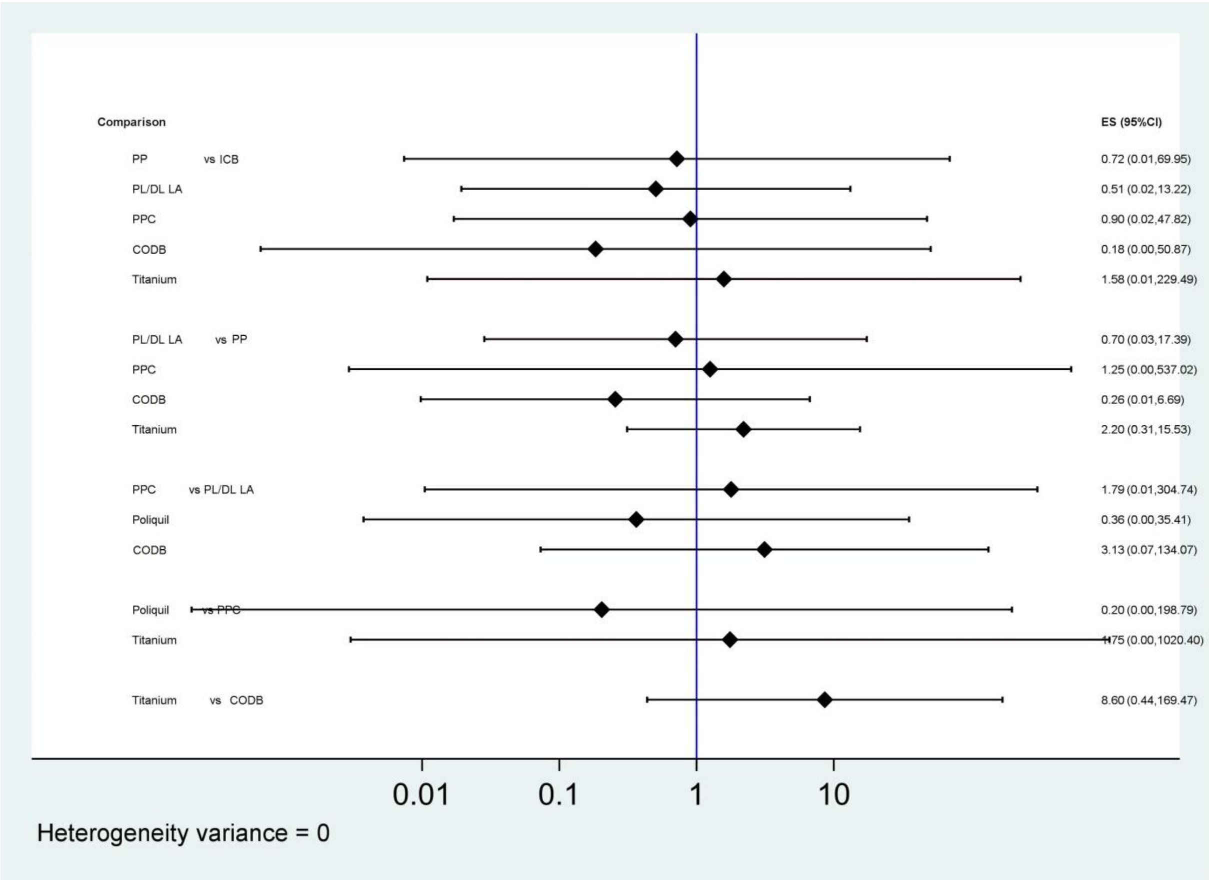


Figure 7.Forest-plot of the 15 possible comparisons between materials regarding other post-operative complications. PP, porous polyethylene ; ICB: Iliac Crest Bone; P[L/DL]LA, polymer with L-lactic acid and DL-lactic acid; PPC, Periosteum polymer complex ; CODB: Castor Oil Derived Biopolymer.

The cumulative ranking or SUCRA (Fig.8) showed that titanium was less responsible of complications than the other materials. CODB was the material with the highest SUCRA thus the higher risk of complications.

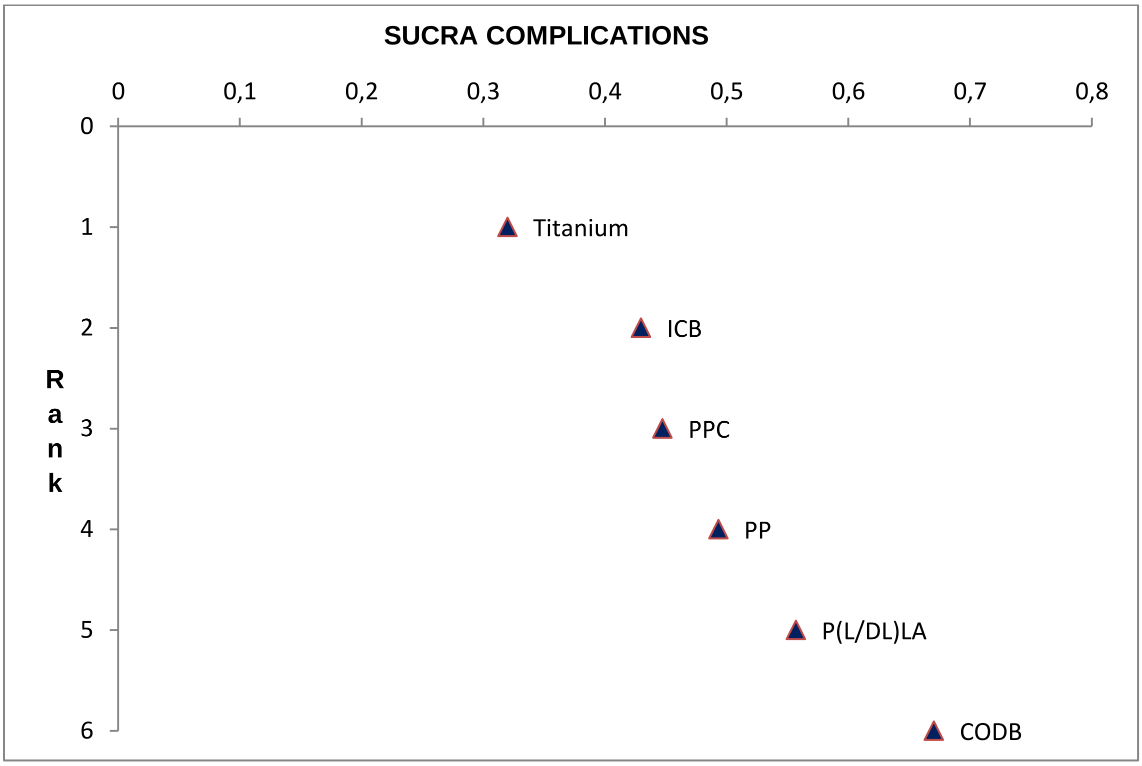


Figure 8. Ranking plots for complications. The rank is inversevely proportionnal to the SUCRA. CODB: Castor Oil Derived Biopolymer; ICB: Iliac Crest Bone; PP, porous polyethylene; P[L/DL]LA, polymer with L-lactic acid and DL-lactic acid; PPC, Periosteum polymer complex.

DISCUSSION

OFF represent a very common injury in maxillofacial traumatology. These fractures can vary from a simple fracture which does not need any surgical intervention, to complicated surgical fracture with displaced bony fragments (Wajih, Shaharuddin, et Razak 2011). Various materials have been described for the primary bony repair (Dubois et al. 2016). Among these materials, autogenous implants include all the material that could be harvested from the individual himself, including bone (calvaria, iliac crest) or cartilage (septum, concha). Bone graft allows to restore the orbital contour and increases the orbital volume, other advantages are represented by resistance to infection and incorporation in new bone by the host (Al-Sukhun et Lindqvist 2006). Inconvenients include the difficulty to sculpt and breakable properties (Vehmeijer et al. 2016), an increased operative time, and the donor-site morbidity (Bratton et Durairaj 2011). Cartilage grafts can be harvested from nasal septum and concha, and are reserved for small defects (Bayat et al. 2010). Alloplastic implants are mainly represented by titanium mesh, PP and PDS (Aldekhayel et al. 2014; Gunarajah et Samman 2013); they regroup all synthetic materials and could be resorbable or not. Resorbable materials avoid long-term complications such as secondary displacement or extrusion of the graft. Furthermore they do not necessitate removal procedure (Kontio et al. 2005). Their degradation may modify their mechanical properties and they could be not enough resistant to support the globe content in blow-out fractures. Resorption would create an inflammatory process leading to a foreign-body reaction (Kontio et al. 2005). Allogeneic implants refer to tissue from individuals of the same species but genetically different. It includes dura patch which couldn't be used anymore because of cases of Creutzfeldt-Jakob disease (Ae et al. 2018). Furthermore, allogeneic implants increase the risk of immunologic reaction (Marano et Tincani 2016). The ideal material should be stable, easy to conform to substance loss, biocompatible, if possible radiopaque to control its position by postoperative imaging, readily available and low-cost (Dubois et al. 2016). This ideal material doesn't exist for the time being and there is no consensus regarding the best material to use for the primary repair of OFF. The selected studies compared ten different materials for the primary repair of OFF (Fig. 9). Advantages and inconvenients of the different materials are listed in Table 3.

To classify the materials for the repair of OFF according to their efficiency and their safe use, indirect comparisons could be done. In this context, NMA is the most suitable statistical method to represent the entire hierarchy of a therapeutic field (Haute Autorité de Santé 2009). We conducted a NMA focusing on the clinical postoperative issues (diplopia, enophthalmos and potential surgical complications).

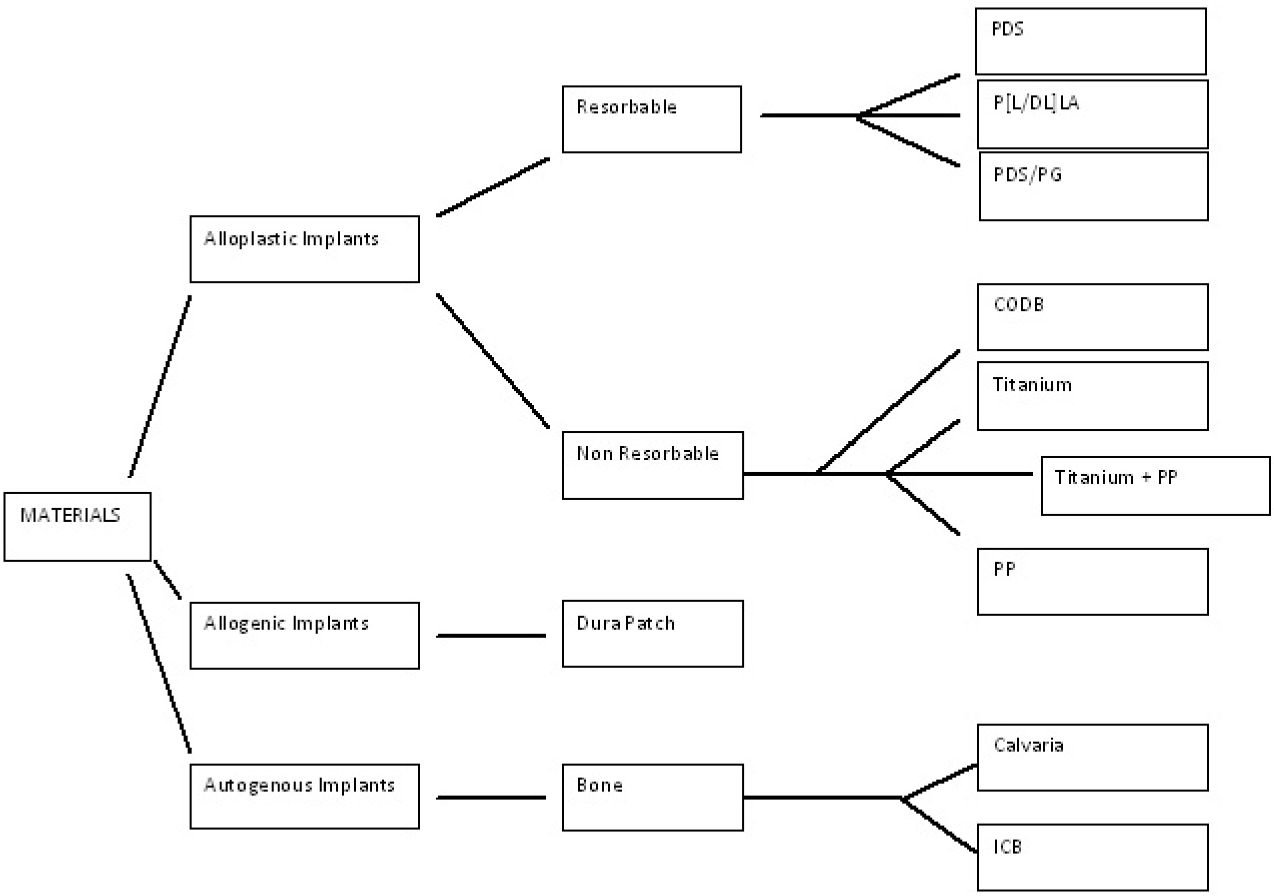


Figure 9. Classification of the materials compared in the selected studies.

MATERIALS	ADVANTAGES	INCONVENIENTS
Polydioxanone	Easy to handle (Dietz et al. 2001). Exists with different thickness : 0.15, 0.25mm, 0.5mm or 1mm.	Reabsorbed within 6 months, stiffness decreases by 50% in 4-5 weeks leading to a premature loss of its mechanical properties before the healing process has been finished (Han et Chi 2011). Too poor mechanically to be recommend for large orbital floor fracture (Kontio et al. 2005).
[P(L/DL)LA] 70/30	New bone growth observed along the plate. MRI studies: no abnormal tissue, foreign body or reactions in the orbital region (Al-Sukhun et Lindqvist 2006). Resorption is slow enough to tolerate the pressure of the orbital content (Kontio et al. 2005). Easy to contour (Al-Sukhun et al. 2006).	Few studies available.
Polydioxanone/Polyglactin (Ethisorb®)	No inflammatory reactions, no adhesions to the surrounding tissue (Jank et al. 2003).	Recommended only for defects that do not exceed 1.5x2.5cm or 2.5cm^2 (Blake et al. 2011).
Titanium mesh	Widely tested, bio-compatible, can be fixed with screws (Dietz et al. 2001). Can restore the shape of the orbit in 3 dimension (Marano et Tincani 2016). Easy to conform (Ellis et Tan 2003) and radiopaque allowing a control of the position.	Difficult to remove because of osteointegration, (Marano et Tincani 2016). Possible foreign-body sensation (Holtmann et al. 2016).
Porous Polyethylene Porous Polyethylene	Easy to work, can be carved to obtain a precise three-dimensional construct. Biocompatible, have a long-term stability and no	Porosity increases the ability of bacterial adhesion thus the risk of infection (Toribio et al. 2018).

	surrounding soft tissue reaction (Han et Chi 2011). Good tensile strength and sufficient flexibility (Marano et Tincani 2016).	
Castor Oil Derived Biopolymer	Can be conformed to the orbit by increasing the temperature of the implant. Osteoconductive properties (Marano et Tincani 2016).	High degree of brittleness, no possible fixation with a screw, lack of porousness questioning its ability to be integrated (Marano et Tincani 2016).
Iliac crest bone	Represents a large amount of bone, can be trimmed to provide the good curvature (Siddique et Mathog 2002). Can be harvested simultaneously with orbital exploration (Al-Sukhun et Lindqvist 2006).	May resorb unpredictably (Al-Sukhun et Lindqvist 2006), dyesthesia, chronic pain, visible scar, hematoma, seroma, infection (Banwart, Asher, et Hassanein 1995).
Calvaria	Naturally curved, invisible scar, volume maintaining better than ICB (Siddique et Mathog 2002).	Difficult to mould (Muhammad Usman Khalid, Riaz Ahmed Warraich, Khalid Mahmood Akhtar 2012).
Periosteum-polymer Complex	Easy to conform, easy to use, and allows osteoconductivity (Asamura et al. 2010).	Needs another operated site to harvest periosteum, increasing operating time (Asamura et al. 2010).
Dura-patch		Could not be used anymore because of cases of Creutzfeldt-Jakob disease (Ae et al. 2018).

Table 3. List of the advantages and inconvenients of the different materials presented in the studies.

Various materials can be combined with each other to increase their benefits and overcome their disadvantages. For example, the association between PP and titanium (Kim et al. 2012) could provide a good structural support for large fractures, while keeping malleability, and maintain contour once shaped thanks to a rapid host integration via fibrovascular ingrowth (Garibaldi et al. 2007).

Few comparative studies were found in the literature analysis including few total numbers of patients. This is a pity regarding the occurrence of OFF and the possibility to perform large studies. This can be explained by the difficulty to obtain a long-time follow-up in traumatology as patients stop to visit when they become asymptomatic (Dietz et al. 2001). Furthermore, we focused on the monitoring of the postoperative clinical parameters, whereas some others studies focused on the radiographic monitoring of the orbital volume (Ellis et Tan 2003). Furthermore, the nine studies included in this NMA presented a lack of homogeneity regarding the methods, as evidenced by the variation of the methodological score from 1 (Siddique et Mathog 2002) to 7 (Dietz et al. 2001) depending on the quality of the design of the study (randomization, multicentric studies, clear definition of the evaluation criterion) (Annex1, Table 1). The measurement methods for the evaluation of diplopia and enophthalmos differed widely according to the authors. Diplopia is usually defined by a functional splitting of an object always in the same direction in binocular vision; it could be evaluated with an oral questionnaire (Marano et Tincani 2016) or with an objective ophthalmologic examination: Goldmann perimetry (Dietz et al. 2001; Wajih, Shaharuddin, et Razak 2011), Harms tangent screen test (Dietz et al. 2001). Most of the studies evaluated the enophthalmos using a Hertel's exophtalmometer, representing a non-invasive tool but raising the question of its accuracy (Nightingale et Shakib 2019). The study of oculomotor disturbance could be of interest in this NMA, but this parameter was finally rejected because of the variability in assessment methods (Laurentjoye et al. 2014). Others clinical and radiographic parameters including the size and the location of the fracture, the operative timing and the placement of the implant are known to influence the postoperative results (Kim et al. 2012), and were not objectively assessed in our study.

Patients included in the analysis were mostly men (75%), with a mean age of 31.5 years, which is in agreement with the literature analysis (Boffano et al. 2014; Shin et al. 2013). A postoperative diplopia was observed in 11.1% of cases, while enophthalmos and postoperative complications were assessed in 4.5% and 0.74% of cases respectively. While the literature analysis report variable results from 1.6% (Shin et al. 2013) to 37% (Biesman et al. 1996) regarding the diplopia, 0.4% (Shin et al. 2013) to 4% (Gunarajah et Samman 2013) for enophthalmos and a 0.5-1.8% rate of complications (Gosau et al. 2011; Xu 2019). Our study suggested that durapatch, PDS, PP, PL(DL/LA) and titanium represented good materials for the primary repair of OFF regarding the occurrence of postoperative diplopia and enophthalmos. Dura patch could not be used anymore because of the risk of Creutzfeldt-Jakob disease (Ae et al. 2018). These results have to be interpreted cautiously because of the lack of precision and homogeneity among studies with regard of the fractured surface of orbital floor, and four studies not reporting on their measurement method. PDS, PDS/PG and dura-patch have been mainly described for a fractured area less than $2cm^2$ (Jank et al. 2003; Dietz et al. 2001), whereas P(L/DL)LA, PP and ICB are usually applied in fracture over than $2cm^2$ or more than 50% of the floor area (Al-Sukhun et Lindqvist 2006; Han et Chi 2011). When deciding which material is the most suitable for an orbital floor reconstruction, four variables should be taken into account: the size of the orbital floor defect, the mechanical properties of the material, the thickness of the device, and the pressure load of the orbital content on the material (van Leeuwen et al. 2012). The rigidity of the material is an important parameter for large fracture to bridge the osseous defects without sagging (Ellis et Tan 2003). When using a resorbable polymer the tissue formed at the site of the defect should be strong enough to support the pressure load of the orbital content; the speed of resorption also needs to be adapted to the bone healing process (Al-Sukhun et Lindqvist 2006). The size of the OFF appears as a key component for the surgery indication and for the choice of the material (Gunarajah et Samman 2013). There is no consensus on the method used to evaluate the fractured area on CT-scan (Schouman et al. 2012). Jaquiery *et al.* proposed a classification allowing a semi-quantitative analysis of the importance of the fractured floor surface on a two-dimensional clover diagram (Jaquiéry et al. 2007) (Fig. 10). This classification could be used by authors to constitute homogenous groups of patients to study and compare the efficiency of materials within same categories. In the light of this classification and of the results obtained with the NMA, we recommend the use of resorbable materials (PDS and PL(DL/LA)) for categories 1 and 2, with an increased resistance in large fractures (PL(DL/LA). Whereas materials with a good tensile strength and with a possible fixation (PP, titanium) are privileged for the surgical treatment of categories 3, 4 and 5 (Fig. 11). Various software have also been developed to bring a more accurate and easy method for the fracture measurement on CT-scan (Ploder et al. 2002), but do not categorize the fractures to elaborate a treatment plan.

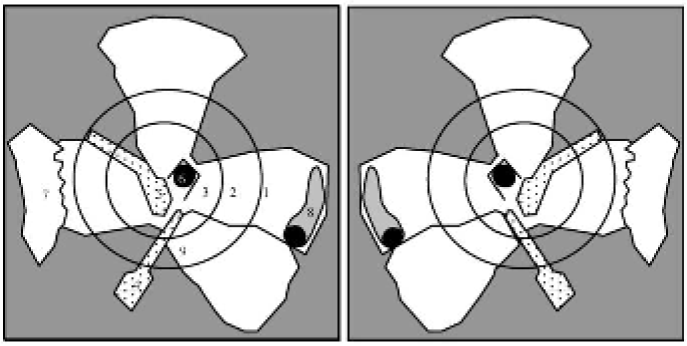
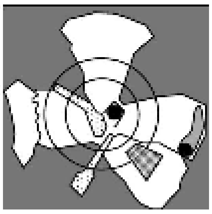
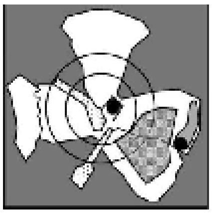


Fig. 1. Left and right orbital sketch: (1) orbital floor, anterior third. (2) orbital floor, middle third, (3) orbital floor, dorsal third, (4) infraorbital fissure, (5) supraorbital fissure, (6) optical nerve. (7) lateral wall, (8) nasal–lachrymal duct, (9) medial border of the infraorbital fissure.



Category I

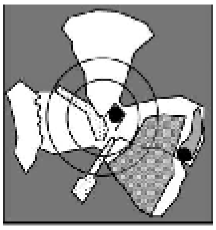
Isolated defect of the orbital floor or the medial wall, 1–2 cm² within zones 1 and 2.



Category II

Defect of the orbital floor and/or of the medial wall, >2 cm², within zones 1 and 2.

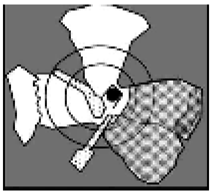
Bony ledge preserved at the medial margin of the infraorbital fissure.



Category III

Defect of the orbital floor and/or of the medial wall, >2 cm², within zones 1 and 2.

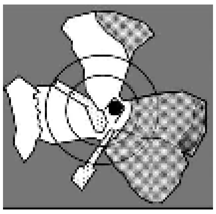
Missing bony ledge medial to the infraorbital fissure.



Category IV

Defect of the entire orbital floor and the medial wall, extending into the posterior third (zone 3).

Missing bony ledge medial to the infraorbital fissure.



Category V

Same as IV, defect extending into the orbital roof.

Figure 10. Jaquiery classification for semi-quantitative evaluation of OFF.

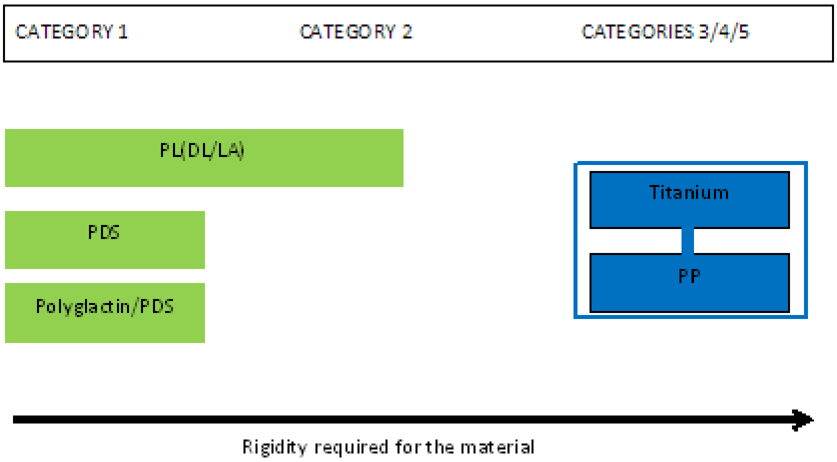


Figure 11. Decision chart for the treatment of OFF according to the Jaquiery Classification.

The shape of the implant needs also to be considered. Personalized Specific Implants (PSI) have widely been developed in the past decade, they allow to fit perfectly to the substance loss. These implants are particularly suitable in case of defect of the orbital floor and the medial wall. PSI necessitates an accurate evaluation of the substance loss from the 3D virtual printing mold (Vehmeijer et al. 2016) or with the use of prefabricated titanium implants. Furthermore, the use of such device does not resolve the issue of the adequate material but add the question of the shape above the material's one. Longitudinal comparative randomized studies built on a validated classification of fractures are needed to assess the superiority of a material for the primary bone repair of OFF.

CONCLUSION

The current evidence does not support recommendation for the choice of material to repair the orbital floor fracture. P(L/DL)LA, PP and titanium seem to represent the best options whatever the substance loss regarding postoperative diplopia and enophthalmos. More comparative and randomized studies are needed to determine the best material for orbit reconstruction.

ANNEX 1 - LIST OF THE STUDIES INCLUDED IN THE NMA, METHODOLOGICAL SCORE

- ✓ Al-Sukhun, Jehad, et Christian Lindqvist. 2006. « A Comparative Study of 2 Implants Used to Repair Inferior Orbital Wall Bony Defects: Autogenous Bone Graft Versus Bioresorbable Poly-L/DL-Lactide [P(L/DL)LA 70/30] Plate ». *Journal of Oral and Maxillofacial Surgery* 64 (7): 1038-48. https://doi.org/10.1016/j.joms.2006.03.010.

- ✓ Asamura, Shinichi, Yoshito Ikada, Kazuhide Matsunaga, Mitsuhiro Wada, et Noritaka Isogai. 2010. « Treatment of Orbital Floor Fracture Using a Periosteum–Polymer Complex ». *Journal of Cranio-Maxillofacial Surgery* 38 (3): 197-203. https://doi.org/10.1016/j.jcms.2009.06.011.

  Dietz, A., C. M. Ziegler, A. Dacho, F. Althof, C. Conradt, G. Kolling, H. von Boehmer, et H. Steffen. 2001. « Effectiveness of a New Perforated 0.15 Mm Poly-p-Dioxanon-Foil versus Titanium-Dynamic Mesh in Reconstruction of the Orbital Floor ». *Journal of Cranio-Maxillo-Facial Surgery: Official Publication of the European Association for Cranio-Maxillo-Facial Surgery* 29 (2): 82-88. https://doi.org/10.1054/jcms.2000.0188.

- ✓ Han, Dae Heon, et Mijung Chi. 2011. « Comparison of the Outcomes of Blowout Fracture Repair According to the Orbital Implant »: *Journal of Craniofacial Surgery* 22 (4): 1422-25. https://doi.org/10.1097/SCS.0b013e31821cc2b5.

- ✓ Jank, Siegfried, Rüdiger Emshoff, Barbara Schuchter, Heinrich Strobl, Iris Brandlmaier, et Burghard Norer. 2003. « Orbital Floor Reconstruction with Flexible Ethisorb Patches: A Retrospective Long-Term Follow-up Study ». *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology* 95 (1): 16-22. https://doi.org/10.1067/moe.2003.11.

- ✓ Marano, Renato, et Alfio Jose Tincani. 2016. « Is There an Ideal Implant for Orbital Reconstructions? Prospective 64-Case Study ». *Journal of Cranio-Maxillofacial Surgery* 44 (10): 1682-88. https://doi.org/10.1016/j.jcms.2016.08.006.

- ✓ Muhammad Usman Khalid, Riaz Ahmed Warraich, Khalid Mahmood Akhtar. 2012. « Comparison of Outcomes of Membranous With Endochondral Bone Graft in Orbital Floor Reconstruction ». *A.P.M.C Vol: 6 No. 2*.

- ✓ Siddique, Shoab A., et Robert H. Mathog. 2002. « A Comparison of Parietal and Iliac Crest Bone Grafts for Orbital Reconstruction ». *Journal of Oral and Maxillofacial Surgery* 60 (1): 44-50. https://doi.org/10.1053/joms.2002.29072.

- ✓ Wajih, Wahid Abdullah Salem, Bakiah Shaharuddin, et Noor Hayati Abdul Razak. 2011. « Hospital Universiti Sains Malaysia Experience in Orbital Floor Reconstruction: Autogenous Graft Versus Medpor ». *Journal of Oral and Maxillofacial Surgery* 69 (6): 1740-44. https://doi.org/10.1016/j.joms.2010.07.053.

Methodological score (Jüni *et al.)Table 1*

Studies	*Design (pro- or retrospective study)*	*Mono- or multicentric study*	*Randomized or non-randomized study*	*Comparability between the groups*	*Objective evaluation of the main criteria*	*SCORE*
Al-Sukhun, 2006	1	0	0	2	1	**5**
Asamura, 2010	1	0	1	0	1	**3**
Dietz, 2001	1	1	1	2	2	**7**
Han, 2011	0	0	1	2	1	**4**
Jank, 2003	0	0	0	1	1	**2**
Khalid, 2012	1	0	1	1	0	**3**
Marano, 2016	1	0	1	0	0	**2**
Siddique, 2002	0	0	0	0	1	**1**
Wajih, 2011	0	0	0	0	2	**2**

ANNEX 2 - STATISTICAL ANALYSIS OF DIPLOPIA

Diplopia was absent in the publication from Siddique et al., thus this study could not be included in the NMA. The figure 1 presents the comparisons made between 10 materials in 8 articles regarding the postoperative diplopia.

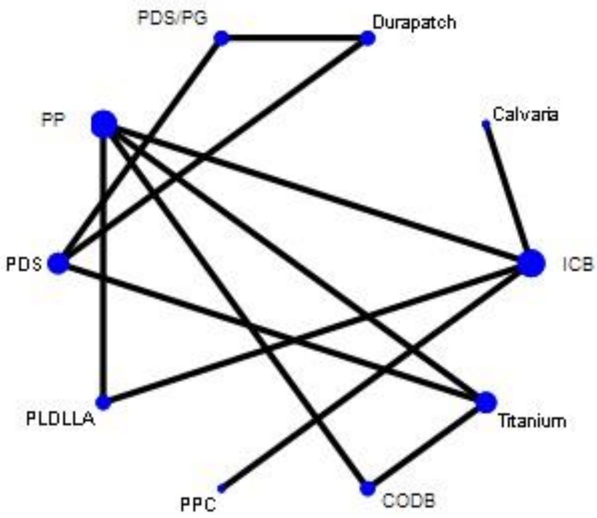


Figure 1. Network geometry of diplopia. Inconsistency test: p=0.95. CODB: Castor Oil Derived Biopolymer; ICB: Iliac Crest Bone; PDS, polydioxanone; PDS/PG, polydioxanone and polyglactin ; PP, porous polyethylene; P[L/DL]LA, polymer with L-lactic acid and DL-lactic acid; PPC, Periosteum polymer complex.

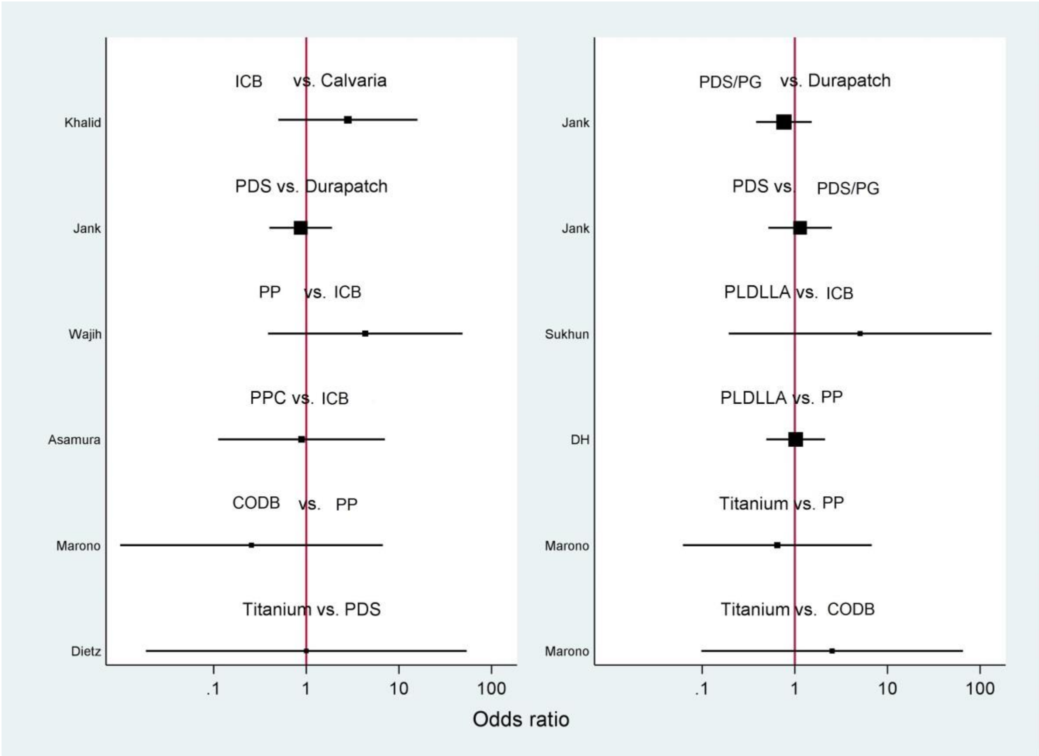


Figure 2. Forest-plot of the selected comparative studies, presenting Odds ratio for postoperative diplopia. ICB: Iliac Crest Bone; PDS, polydioxanone; PDS/PG, polydioxanone and polyglactin ; PP, porous polyethylene; P[L/DL]LA, polymer with L-lactic acid and DL-lactic acid; PPC, Periosteum polymer complex CODB: Castor Oil Derived Biopolymer.

The NMA allowed to simulate 10 000 randomized trials with the 10 materials according the odds ratios established previously. This simulation gave for each treatment the number of times it arrived first, second, etc until ten. The cumulative ranking was given by the SUCRA. The SUCRA could be between 0 and 1. The more it was closed to 1, the more the material caused diplopia when compared to another one (Table 1). SUCRA is also represented by a curve (Fig. 3).

	ICB	calvaria	DP	PDS/PG	PP	PDS	PLDLLA	PPC	CODB	Titanium
Best	2.2	44.7	2.3	10.5	0.1	4.6	0.1	14.2	19.6	1.7
2nd	17.3	21.0	6.8	10.1	0.4	8.3	0.3	19.6	11.9	4.4
3rd	28.3	8.8	10.8	9.0	1.1	10.5	1.5	16.0	8.5	5.4
4th	13.3	805	8.1	10.3	5.3	9.3	6.4	11.8	16.7	10.4
5th	9.3	6.8	8.4	8.7	12.8	9.5	12.3	8.3	7.8	16.1
6th	10.9	5.0	8.8	7.7	16.2	9.1	14.1	8.5	7.6	12.2
7th	10.5	2.7	8.2	7.8	12.1	8.0	13.1	7.6	9.4	20.7
8th	5.2	1.3	10.6	18.1	13.6	15.7	12.2	5.4	5.9	12.0
9th	2.0	0.6	14.7	12.1	23.9	14.5	19.7	2.7	3.6	6.4
Worst	1.0	0.7	21.4	5.6	14.6	10.6	20.4	5.9	9.1	10.8
Mean rank	4.3	2.5	6.6	5.5	7.4	6.1	7.5	4.2	4.6	6.3
SUCRA	0.619	0.7759	0.3859	0.4908	0.3098	0.43865	0.3035	0.6221	0.58455	0.4217

Table 1. Ranking probabilites, cumulative rankograms for all treatments based on the SUCRA for the criteria diplopia. ICB = Iliac Crest Bone; DP = DuraPatch; PDS/PG = PDS/Polyglactin (Ethisorb) ; PP : Porous Polyethylene, PDS = PolyDioxanone Sheet ; PLDLLA = Polymer with L-lactic acid 70 and DL-Lactic Acid 30 ; PPC = Periosteum Polymer Complex ; CODB = Castor Oil Derived Biopolymer ; SUCRA = Surface Under the Cumulative RAnking curve.

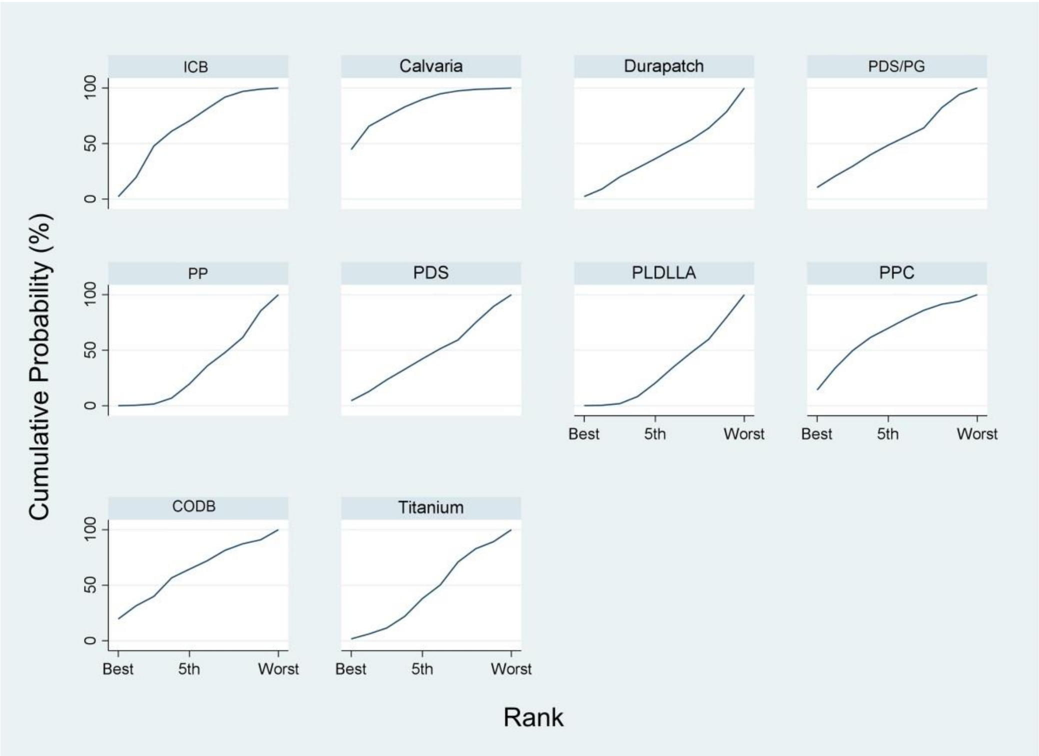


Figure 3. SUCRA for diplopia. The more the area under the curve is close to 1, the worse is the material regarding diplopia. ICB: Iliac Crest Bone; PDS/PG, polydioxanone and polyglactin; PP, porous polyethylene; PDS, polydioxanone; P[L/DL]LA, polymer with L-lactic acid and DL-lactic acid; PPC, Periosteum polymer complex CODB: Castor Oil Derived Biopolymer.

ANNEX 3 - STATISTICAL ANALYSIS OF ENOPHTHALMOS

This criterion was absent in the studies of Han and Khalid, thus this study could not be included in the NMA for this criterion. The figure 1 presents the comparisons made between 10 materials in 7 articles regarding the postoperative enophthalmos.

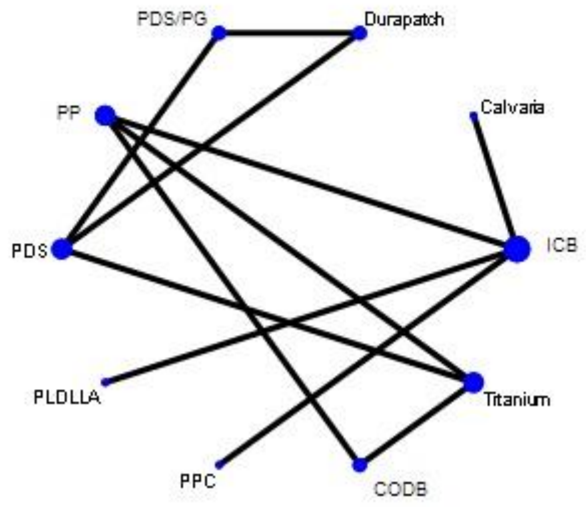


Figure 1. Network geometry of enophthalmos. Inconsistency test: p=0.27. CODB: Castor Oil Derived Biopolymer; ICB: Iliac Crest Bone; PDS, polydioxanone; PDS/PG, polydioxanone and polyglactin ; PP, porous polyethylene; P[L/DL]LA, polymer with L-lactic acid and DL-lactic acid; PPC, Periosteum polymer complex.

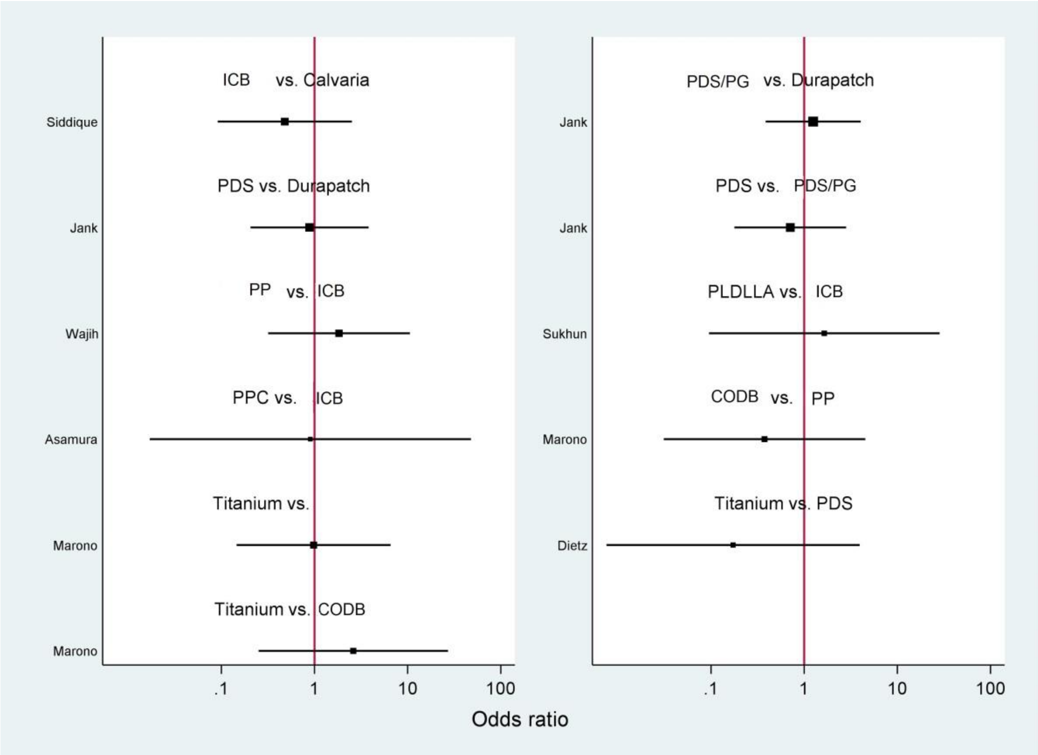


Figure 2. Forest-plot of the selected comparative studies, presenting Odds ratio for postoperative enophthalmos. ICB: Iliac Crest Bone; PDS/PG, polydioxanone and polyglactin; PP, porous polyethylene; PDS, polydioxanone; P[L/DL]LA, polymer with L-lactic acid and DL-lactic acid; PPC, Periosteum polymer complex CODB: Castor Oil Derived Biopolymer.

Then 10 000 randomized trials were simulated with the 10 materials according to the odds ratio established previously (Table 1). The cumulative ranking is given by the SUCRA (Fig. 3), from 0 to 1.

	ICB	calvaria	DP	PDS/PG	PP	PDS	PLDLLA	PPC	CODB	Titanium
Best	8.1	3.9	1.9	0.8	1.5	1.4	14.3	32.1	31.9	4.1
2nd	21.8	7.8	2.7	2.0	5.8	2.3	13.5	12.8	19.7	11.6
3rd	25.5	10.9	3.6	2.5	12.2	3.5	10.0	8.0	11.7	12.1
4th	18.2	13.8	3.6	3.4	17.9	3.6	9.5	6.7	10.5	13.1
5th	11.2	13.9	4.4	3.3	21.5	4.6	9.5	6.7	9.2	15.7
6th	6.5	15.7	4.9	4.0	18.9	6.4	10.7	6.9	7.6	18.3
7th	4.4	13.4	9.1	6.6	11.4	10.4	11.9	9.5	5.2	18.1
8th	2.9	5.8	24.0	15.2	4.6	34.4	4.8	3.3	1.6	3.4
9th	1.2	7.3	27.3	26.9	4.0	19.6	5.9	4.3	1.5	2.1
Worst	0.2	7.6	18.4	35.3	2.1	13.8	10.1	9.7	1.3	1.5
Mean rank	3.6	5.5	7.7	8.3	5.2	7.5	5.0	4.1	3.1	4.9
SUCRA	0.68315	0.4961	0.2787	0.2203	0.5324	0.2946	0.54815	0.62195	0.72045	0.55585

Table 1. Ranking probabilites, cumulative rankograms for all treatments based on the SUCRA for the criterion enophthalmos. ICB = Iliac Crest Bone; DP = DuraPatch; PDS/PG = PDS/Polyglactin (Ethisorb) ; PP : Porous Polyethylene, PDS = PolyDioxanone Sheet ; PLDLLA = Polymer with L-lactic acid 70 and DL-Lactic Acid 30 ; PPC = Periosteum Polymer Complex ; CODB = Castor Oil Derived Biopolymer ; SUCRA = Surface Under the Cumulative RAnking curve.

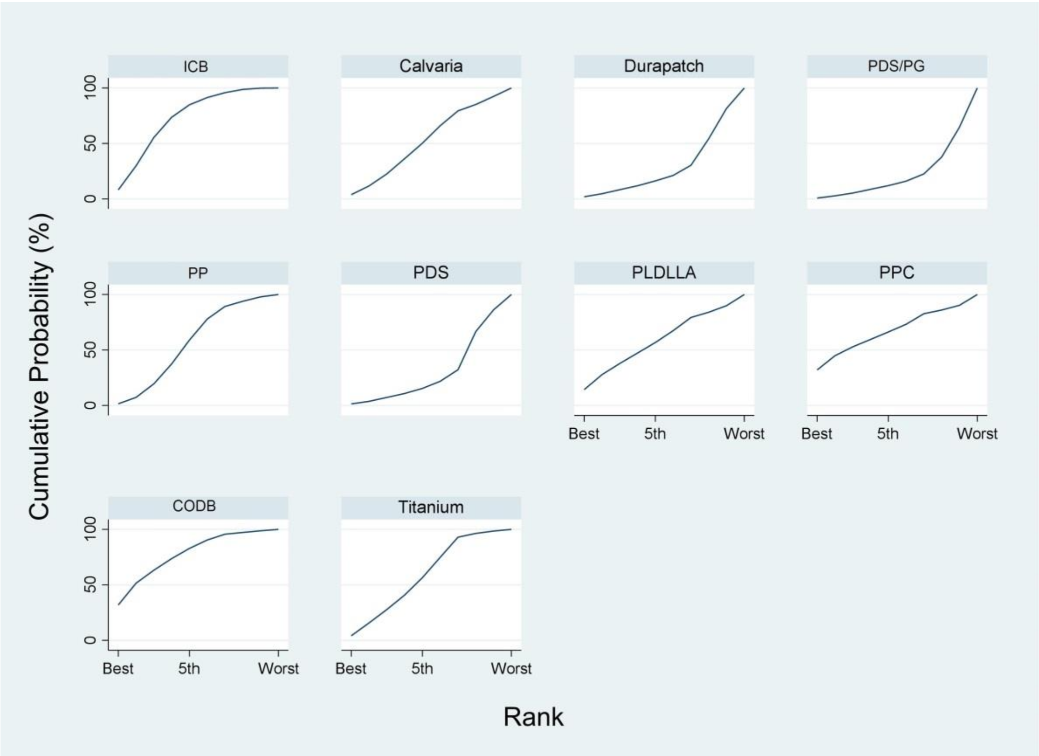


Figure 3. SUCRA for enophthalmos. The more the area under the curve is close to 1, the worse is the material regarding enophthalmos. ICB: Iliac Crest Bone; PDS/PG, polydioxanone and polyglactin; PP, porous polyethylene; PDS, polydioxanone; P[L/DL]LA, polymer with L-lactic acid and DL-lactic acid; PPC, Periosteum polymer complex ; CODB: Castor Oil Derived Biopolymer.

ANNEX 4 - STATISTICAL ANALYSIS OF POSTOPERATIVE COMPLICATIONS

Only four articles described this criterion: Al-Sukhun, Asamura, Han and Marano ones including 6 materials. The figure 1 represents the comparisons made in the analyzed articles.

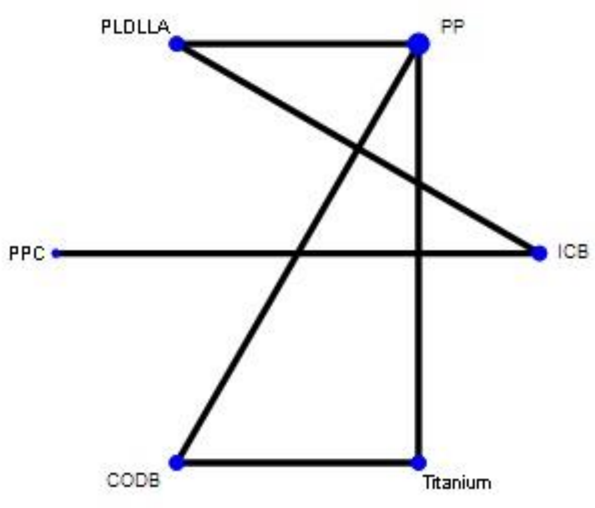


Figure 1. Network geometry of complications. Inconsistency test: p=0.16.

CODB: Castor Oil Derived Biopolymer; ICB: Iliac Crest Bone; PP, porous polyethylene; P[L/DL]LA, polymer with L-lactic acid and DL-lactic acid; PPC, Periosteum polymer complex.

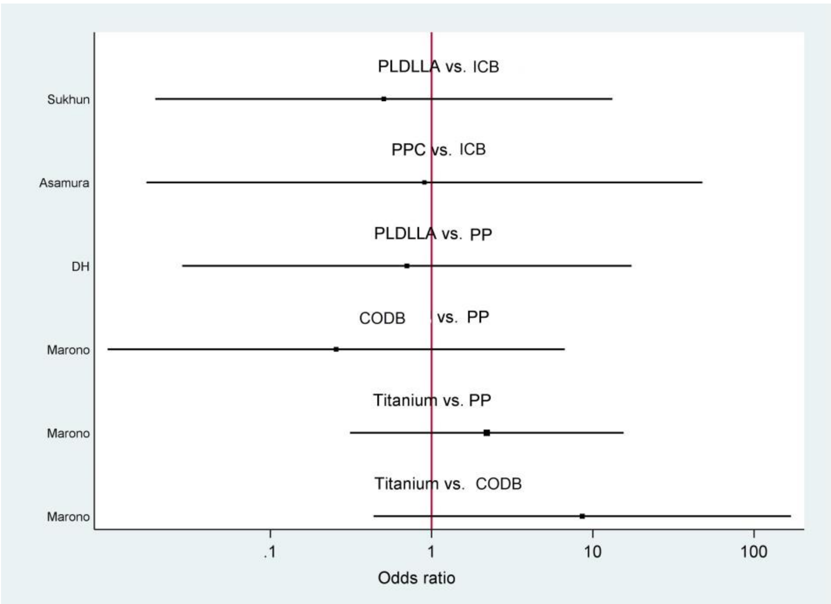


Figure 2. Forest-plot of the selected comparative studies, presenting Odds ratio for postoperative complications. ICB: Iliac Crest Bone; PP, porous polyethylene; P[L/DL]LA, polymer with L-lactic acid and DL-lactic acid; PPC, Periosteum polymer complex; CODB: Castor Oil Derived Biopolymer.

Then 10 000 randomized trials were simulated with the 6 materials according to the odds ratios established previously (table 1). The cumulative ranking is given by the SUCRA (Fig. 3), from 0 to 1.

	ICB	PP	PLDLLA	PPC	CODB	Titanium
Best	8.2	5.4	14.8	21.5	49.1	1.0
2nd	17.2	21.7	22.2	14.2	16.4	8.3
3rd	16.0	23.0	24.0	9.9	11.6	15.6
4th	14.5	21.7	23.1	10.6	11.8	18.3
5th	25.1	22.4	10.5	13.9	7.3	20.8
Worst	19.0	5.8	5.5	29.9	3.8	36.0
Mean Rank	3.9	3.5	3.1	3.7	2.2	4.6
SUCRA	0.42967	0.493167	0.55691	0.44725	0.6704	0.31983

Table 1. Ranking probabilites, cumulative rankograms for all treatments based on the SUCRA for the criterion postoperative complications. ICB = Iliac Crest Bone; PP : Porous Polyethylene; PLDLLA = Polymer with L-lactic acid 70 and DL-Lactic Acid 30 ; PPC = Periosteum Polymer Complex ; CODB = Castor Oil Derived Biopolymer ; SUCRA = Surface Under the Cumulative RAnking curve.

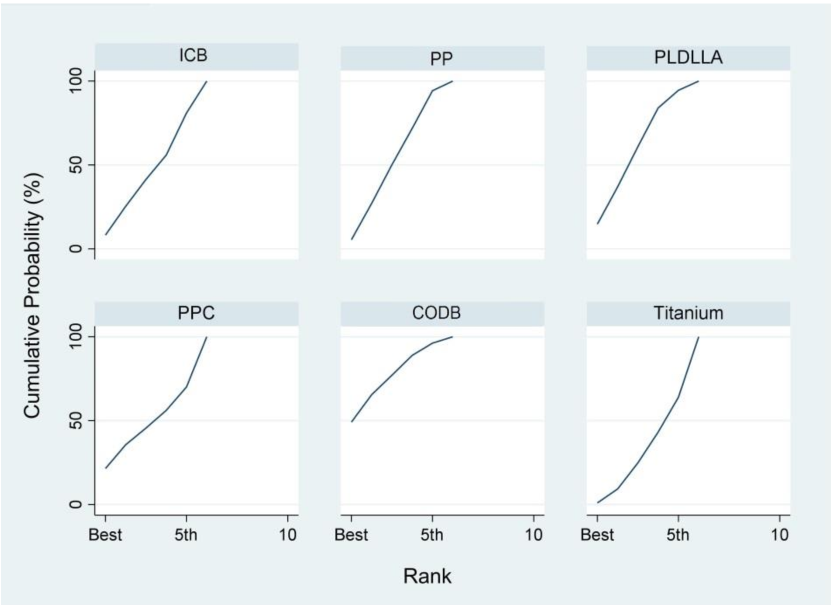


Figure 3. SUCRA for complications. The more the area under the curve is close to 1, the more complication was encountered with the material. ICB = Iliac Crest Bone; PP : Porous Polyethylene; PLDLLA = Polymer with L-lactic acid 70 and DL-Lactic Acid 30 ; PPC = Periosteum Polymer Complex ; CODB = Castor Oil Derived Biopolymer.

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Vu, le Président du Jury,
(tampon et signature)

Titre Prénom NOM

Vu, le Directeur de Thèse,
(tampon et signature)

Titre Prénom NOM

Vu, le Doyen de la Faculté,

Professeur Pascale JOLLIET

NOM : BOURRY PRENOM : Maëva

Titre de Thèse : META-ANALYSE : EVALUATION DE L'EFFICACITE CLINIQUE DES MATERIAUX UTILISES POUR LA RECONSTRUCTION PRIMAIRE DES FRACTURES DU PLANCHER ORBITAIRE

INTRODUCTION : Les fractures du plancher orbitaire (FPO) sont fréquentes représentant 15% de l'ensemble des fractures faciales en Europe. Il n'existe pas de recommandation pour le choix du matériau utilisé pour la réparation chirurgicale de ces fractures. L'objectif de cette méta-analyse en réseau est de comparer les résultats cliniques (diplopie et enophtalmie) des différents matériaux utilisés pour la reconstruction primaire des FPO.

METHODE : Une revue de la littérature a été réalisée à partir des bases de données PubMed, Cochrane Library et Google Scholar entre 1989 et 2019. Les articles inclus comparaient au moins deux matériaux selon les critères de diplopie et/ou d'énophtalmie et/ou de complications postopératoires. L'analyse a été menée par deux investigateurs. Les données ont été extraites et analysées selon une méta-analyse en réseau.

RESULTATS : Neuf études incluant 946 patients avec une fracture du plancher d'orbite ont été analysées. Les patients étaient majoritairement des hommes (75%) avec un âge moyen de 31.5 ans. Après intervention, 105 patients présentaient une diplopie (11%), 43 une enophtalmie (4.5%), tandis que 7 patients présentaient d'autres complications (0.74%). La méta-analyse en réseau a mis en évidence la supériorité des biomatériaux PDS, P(L/DL)LA, PP ainsi que des grilles en titane pour la correction de la diplopie et de l'énophtalmie postopératoires par rapport aux greffes autologues.

CONCLUSION : Les preuves actuelles ne permettent pas d'établir des recommandations pour le choix des matériaux utilisés en reconstruction orbitaire. Les matériaux polymères résorbables ou non ainsi que les grilles titane semblent plus efficace pour la correction de la diplopie et de l'énophtalmie dans les FPO.

MOTS-CLES

FRACTURE, PLANCHER ORBITAIRE, RECONSTRUCTION, MATERIAUX, META-ANALYSE, DIPLOPIE, ENOPHTALMIE