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RESEARCH ARTICLE

EFFECT OF DIFFERENT GRAFTING MATERIALS ON ALVEOLAR RIDGE PRESERVATION

Akram Alshirah

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Abstract

Objectives: The purpose of this systematic review was to assess the effect of several grafting materials on alveolar bone resorption after teeth extraction.

Materials & methods: Electronic literature searches in MEDLINE (PubMed) and Cochrane (CENTRAL) were performed, in addition to a manual search through all periodontics and implantology-related journals, for publications in the period from January 1st, 2009, to February 1st, 2021. The primary focus was related to studies comparing alveolar ridge preservation reporting quantitative outcomes of hard tissue changes.

Results: In total,18 randomized controlled studies were included. Mean difference values were calculated with the use of quantitative statistical analysis (RevMan) for split-mouth and parallel study designs. The pooled magnitude of bone resorption was calculated for different dimensions of the alveolar bone process after teeth extraction: for horizontal dimension. Meta-analyses were performed for the use of any graft without membranes compared to empty sockets or specifically for different kinds of grafts (with or without membranes) again compared to empty sockets. Further, a direct comparison was available from studies comparing xenografts either with allografts or alloplasts.

Conclusion: Within the limitation of this systematic review, there is a decrease in alveolar bone resorption after teeth extraction as an impact of bone substitute use, with minimal variations between bone graft materials. Overall, in several outcome parameters, it was noticed that the xenograft materials had the highest amount of bone preservation, and the least magnitude for the alveolar bone reservation was accompanied with the use of alloplastic bone substitutes with a recommendation to make searches about combinations of alloplastic bone substitutes, but confidence intervals were strongly overlapping. Hence, final judgment on any superior graft material cannot be reached from actual available clinical evidence.

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Introduction:-

There is a lifelong catabolic bone remodelling even after healing, (Jahangiri et al. 1998). The alveolar portion of the jawbones begins to atrophy, (Esa klemetti 1996), leading to:

Corresponding Author:- Akram Alshirah

Create a cosmetic problem with Prosthodontics.
• Difficulty in dental implants (Camargo et al. 2000).
• Insufficient support of the dentures (Esa klemetti 1996).
• Impact the bone augmentation procedures, (Jahangiri et al. 1997).

The residual ridge resorption (RRR) is faster in the first 6 months after extraction and continues at a slower rate through lifelong. The RRR rates varied among individuals and in the same person in different periods and different sites(Jahangiri et al. 1998; Krajicek et al.1984).

The RRR process affects the alveolar bone while the basal part remains intact, in another study (Esa klemetti 1996; Cawood et al. 1988 and Qiufei et al. 1997) the basal bone may be affected causing concave mouth floor. However, alveolar ridge preservation (ARP) was incorporated into conventional treatment protocols to minimize such undesirable consequences. ARP is a method for preventing or reducing alveolar ridge resorption after tooth extraction in preparation for prosthodontic rehabilitation, which includes the implantation of a dental implant.

We used to think that delayed implant placement after ARP is useful for bone formation within the extraction socket, but recent data may show the few potential benefits of immediate implantation especially in the aesthetic zone where a high rate of mucosal recession is expected (Hämmerle et al. 2012). Nevertheless, we still do not know the ideal timing of implant placement following ARP so we may need preparation for the preservation of the original alveolar ridge volume after tooth extraction. This will reduce the pain, complications, and enhances soft and hard tissue healing (Khosla et al. 1971).

The “Bone maintenance” term was first used to describe the process of preserving bone after tooth extraction to keep ridge height and width (Ashman et al. 1982; Greenstein et al. 1985; Kentros et al. 1985). However, the term "socket preservation" was created by Cohen (1988) to describe a process that involves ridge preservation and augmentation for prosthetic socket maintenance (Lindhe et al. 1999).

When the alveolar bone reservation is done at the same time as teeth extraction, it provides more control and predictability while preventing site atrophy and esthetic complications. It is one of the most important operations in the modern periodontal paradigm for maintaining health, youth, and beauty. Various idioms were used to describe the same operation, such as "socket preservation", "socket grafting", "alveolar bone grafting", "socket augmentation," "ridge preservation," and "alveolar augmentation," which is defined by the Glossary of Prosthodontic Terms as "any surgical procedure employed to alter the contour of the residual alveolar ridge" (Academy of Prosthodontics 2005). Alveolar ridge preservation (ARP) is the used term in this thesis to avoid misunderstanding. ARP is defined as a treatment used to prevent or minimize alveolar ridge resorption after tooth extraction in preparation for prosthodontic rehabilitation, which may involve dental implant insertion.

The effectiveness of ARP grafting materials and techniques is still debated, with one claiming to work as a panacea in minimizing resorption as well as the width and height of alveolar bone. In the case of ARP, the results of bone graft substitutes and procedures are still questionable (Avila – Ortiz et al. 2019; Mardas et al. 2015). ARP procedures use grafting materials of human, animal, or synthetic origin with or without barrier membranes, and a plethora of research supports the benefits of ARP over spontaneous healing (Macbeth et al. 2017).

Some examples of grafting materials include specific autogenous chips (Araujo et al. 2011; Becker et al. 1994), allografts (Iasella et al. 2003), xenografts (Araujo et al. 2010; Carmagnola et al. 2003), and alloplastic bone graft (Norton et al. 2002). Indeed, non-resorbable and resorbable membranes are described in the literature as options for covering extraction sockets and retaining alveolar ridges. If the membrane is not exposed (e.g, expanded polytetrafluoroethylene (ePTFE), the first one has a bigger bone fill and a better marginal tissue response (Bartee 1998).

When the membrane is not exposed (e.g, expanded polytetrafluoroethylene (ePTFE)), the first one has a bigger bone fill and a good marginal tissue response (Bartee 1998). Resorbable membranes, on the other hand, do not require a second surgery and are associated with considerable improvements in soft tissue healing and little tissue reactivity to membrane exposure (e.g, bovine and porcine collagen matrices) (Iasella et al. 2003).

Resorbable and non-resorbable membranes are expected to preserve the grafting material in place and provide enough space for bone regeneration that keeps the alveolar ridge's structure. The osteoconductive and osteoinductive qualities of bone grafting materials with or without barrier membranes are also exploited. Osteoinduction is the use of grafting materials to stimulate bone development by activating mesenchymal cells to develop into bone-forming cells (Reddi 1981; Urist 1965). Osteoconduction, on the other hand, is the process of promoting the ingrowth of progenitor cells from the recipient site by the use of osteoconductive materials that act as a scaffold for the production of new bone (Buch et al. 1986; Reddi 1987). A bone graft functions as a space-preserving substance, stabilizing the blood clot and preventing volume loss and soft tissue collapse (Friedmann et al. 2002).

In the future, soft-tissue atrophy associated with a narrow strip of keratinized gingiva may obstruct peri-implant disease (De Risi et al. 2017). The dimensions of the keratinized tissue following extraction using various types of ARP procedures and biomaterials are not significantly different from the changes observed during natural socket healing (Mardas et al. 2015); thus, the scientific literature remains divided on the optimal treatment technique and substitute required to minimize alveolar bone changes following tooth extraction.

Background on bone grafts used in selected studies

Autogenous grafts

The golden standard for grafting material is believed to be an autogenous bone substitute. Autogenous bone graft is a bone substitute that is osteoconductive, osteoinductive, and osteogenic. This grafting material is frequently regarded to produce the best and most dependable results. Autogenous bone grafts can be collected from intra- and extra-oral cavity such as edentulous regions, tuberosity, mandibular ramus, and mandibular symphysis, and can also be retrieved in larger quantities from the iliac crest, rib, tibia, and calvarium. There are two types of non-vascularized free autogenous bone grafts: cortical and cancellous autogenous bone grafts, both being composed of approximately one-third of organic and two-thirds of inorganic materials. The inorganic component is often crystalline hydroxyapatite, whereas more than 90% of the organic compounds' composites of collagen type I (Buser 2009).

Allogenous grafts

This is a non-vital replacement that is passed on from one individual to the next of the same species. Fresh frozen, freeze-dried bone allograft (FDBA), and demineralized freeze-dried bone allograft (DFDBA) are the three main kinds of allogenous osseous tissue. The latter works by boosting bone morphogenic proteins BMPs during the demineralization process, including osteoinductive signals besides the osteoconductive properties of the graft. In contrast, FDBA acts only through osteoconduction (Boyan et al. 2006).

Xenogenous grafts

This sort of bone graft is used to transfer tissue between species. For example, a deproteinized cancellous skeletal bone graft is a xenogenous bone graft. Xenogenous bone grafts are usually animal bone minerals or bone-like minerals generated from calcifying corals or algae used in dental operations. The organic component is removed in this situation to avoid an immunogenic reaction and disease transmission (Berglundh et al. 1997).

Alloplastic bone grafts

Alloplastic materials are biocompatible synthetic substances. They are usually regarded as osteoconductive materials (Hoexter et al. 2002). The clinically most commonly used products nowadays comprise alloplastic materials which contain different types of calcium phosphates (CaPs), such as hydroxyapatite (HAP), Biphasic calcium phosphate (BCP), and tricalcium phosphate (TCP). Other types of ceramic alloplastic contain calcium sulfate, bioglass or used in combination with polymers as biocompatible composite.

Plaster of Paris was the first alloplastic bone graft to use. This resorbable highly biocompatible material was used for a long time in the surgery and is made up of the β-hemihydrate form of calcium sulfate ($CaSO_4 \cdot 1/2H_2O$, POP) (Scarano et al. 2007). It has osteoconductive properties.

Polycaprolactone (PCL):

Polymeric graft materials that has been used in medical devices like subdermal contraceptive devices (Capro Nora) and monofilament sutures (Monocryl a) (Darney et al. 1989; Bezwada et al. 1995). It is considered non-toxic and bio-compatible (Pitt et al. 1981). PCL is approved by FDA recently as a bone filler for craniofacial application.

Overall, the most common alloplastic bone graft used is the hydroxyapatite because of its osteoconductive properties, hardness and integration into bone tissue (Prasanna et al. 2013; Buser 2009)

Background on membranes included in selected studies

The used membranes can be resorbable and non-resorbable. Membranes are consisting of synthetic polymers or collagen. They are used in dental surgery to keep clots in place and prevent epithelial migration into a site while another tissue should grow first like bone (Rodella et al. 2011).

Collagen membranes

Collagen membranes are a resorbable, cell occlusive barrier used for dental implant surgery, bone defects, and ridge augmentation. This membrane type is usually consisting of allogeneic or xenogeneic origin. The placement of collagen membranes in the bone defect area prohibits the invading of non-osteogenic cells into the defective area, while simultaneously creating an environment that allows for the protraction and growth of osteoblasts. Collagen membranes also promote platelet aggregation, stabilize blood clots, attract fibroblasts, and facilitate wound healing (Zhang et al. 2009; Taschieri et al. 2011).

Acellular dermal matrix

Acellular dermal matrix (ADM) is defined as a biocompatible material derived from human skin that is obtained through tissue banks. The epidermis and all dermal cells are removed as part of the treatment. The structure of collagen and elastin fibers, as well as the other components of the basement membrane, are retained. In the end, it provides a biocompatible scaffold for the incorporation and migration of epithelial cells, keratinocytes, and fibroblasts. It has also been utilized in guided periodontal surgery, not only because of its biocompatibility, but also because of its capacity to increase the amount of keratinized tissue, strengthen the alveolar ridge, repair tooth recession, augment bone, and treat gingival melanin pigmentation (Wainwright 1995).

Dense polytetrafluoroethylene

This membrane type was developed specifically for the treatment of bone augmentation. When introduced to the mouth, ePTFE is cell occlusive, causes low irritation, and does not bind to tissue (Sonick et al. 2011). This sort of membrane has a limited therapeutic and histological application, because it does not stick to tissues in order to fix the membrane (Strietzel et al. 2006; Al-Hezaimi et al. 2013). However, it was applied in guided tissue regeneration and guided bone regeneration in dental implant surgery as well as in extraction socket preservation (Carbonell et al. 2014; Hoffmann et al. 2008).

Polylactic acid or polylactic-co-glycolic acid

These types of synthetic biodegradable polymers are employed to replace biodegradable medical membranes of natural origin , because they do not cause the infections and immune responses that animal-derived biomaterials do. Polylactide has been extensively researched as a biomedical material in the areas of bone healing materials, tissue engineering, and drug delivery, among other applications (Waksman 2006; Ueki et al. 2011).

Objectives of the study:-

The main aim of this thesis is to investigate the effectiveness of different bone graft substitutes on alveolar ridge reservation. The use of different clinical outcomes that will be compared for alveolar ridge preservation techniques followed tooth extraction using either different types of graft materials with guided membrane or not for a single specific type of graft material versus unassisted and spontaneous empty socket healing. In the case of vertical and horizontal, preservation of bone quantified dimensions will be measured as preliminary focus.

Research question

Does the result of alveolar bone reservation differ according to the type of bone graft with or without guiding membrane in terms of width dimension of alveolar bone after teeth extraction?

Materials and Methods:-

The search strategy in MEDLINE (PubMed) and Cochrane (CENTRAL) was carried out and a manual search through all periodontics and implantology-related journals, from the 1st of January 2009 to the 1st of February, 2021.

This thesis was constructed based on the focused research question according to the PICOS system detailed in chart 1.

Component	Description
Population (P)	Patients in need of tooth extraction
Intervention (I)	Alveolar ridge preservation with or without barrier membrane employing bone grafts (i.e., an osseous autogenous graft, an allogenous graft, a xenogenous graft, and/or an alloplastic bone substitute).
Comparison (C)	Comparison of theeffectiveness of different substances used as bone graft
Outcome (O)	- Evaluate the height and width of the alveolar bone on the basis of: - Baseline: bucco-lingual and palatal socket dimensions are horizontal (bucco-lingual and palatal) and vertical (apico-coronal at two crucial locations like mid-buccal and mid-lingual) after 3 months or more (follow-up). - the findings from the additional two places are found to be vertical alveolar bone levels (at mesial and distal of the socket)
Study Design (S)	randomized control clinical trials in human patients

Table 1:- The PICOS system.

Inclusion criteria:
Exclusively randomized control clinical trials RCTs.

Studies published in the English language.

The minimal period for follow-up is three months with test and control groups in a parallel or split-mouth design with a minimum of a single tooth to be extracted in good and healthy patients with age equal to or more than 18 years old.

It's necessary to apply bone graft substitutes with or without guiding membrane in the procedure of socket preservation. Studies need to include test and control groups on the condition that any extra materials and techniques are excluded that may impact the result of the healing process (e.g., growth factors, platelet-rich plasma, and immediate dental implants).

Either radiological 3D CBCT (cone beam computed tomography) or clinically reflects the standard approach between visits should be used for taking measurements of alveolar bone dimensions after extraction of teeth.

Exclusion criteria
Studies that did not provide a three-dimensional radiographic examination of the ridge dimensions or did not focus on clinical outcomes.

Studies that didn't include randomized studies (i.e. prospective controlled and non-controlled, case series, case reports, and retrospective study designs).

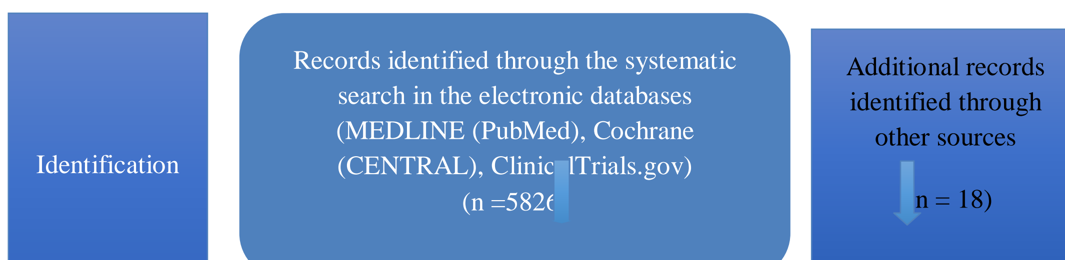
Letters, editorials, Ph. D theses.

Studies without a clear selected topic and not enough information.

Comparative studies that didn't have a control group.

No bone graft was used for socket preservation.

Studies that didn't employ statistical analysis or presentation of quantitative data.



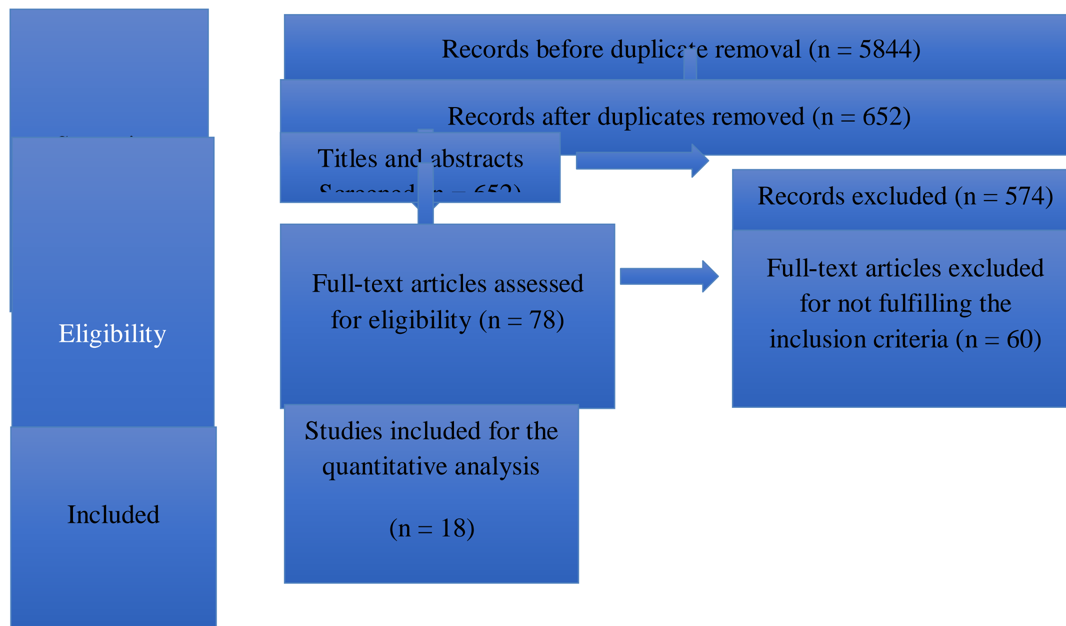


Figure. 1:- Screening process (the selection of the included 18 Studies).

Characteristics of the reviewed studies

The results of RCTs aiming at assessing the effects of different bone replacements on minimizing post-extraction alveolar ridge atrophy were reported in all 18 analysed studies. All the studies that were chosen were published in English. Three studies used a split-mouth approach, while all others used a parallel arm approach. The follow-up lengths for the research ranged from 3 to 8 months. Except for one multi-centre study (Barone et al. 2017), all trials were conducted at a single location. The articles were published between 2009 and 2019. The 18 selected studies comprised a total of 536 participants (ages 18 to 81) and 545 extraction sockets for this quantitative analysis.

Nine of the studies were entirely focused on non-molar extraction sockets, whereas the rest included both molar and non-molar sockets. In one article by Iorio-Siciliano et al. (2017), there was no mention of the type of teeth. All other studies tested the outcome parameters clinically using a custom-made template, with the exception of four studies that used three-dimensional radiography for measurement acquisition. There were no studies that were undertaken in private practices. One study (Barone et al. 2017) was conducted in both institutional and private practice settings, while the others were done only in institutions.

Study	Year	Study design	Follow up period/ mo/w	No. of patients	No. of sockets	Inclusion of molar teeth?	Categorization of bone substitutes	Type of bone substitute	Membrane type	Flap/primary closure	Method of measurement
Imetti et al	2009	Parallel	3	40	22	No	Alloplast	MGCSH	No	No	Clinical
					18		Nothing	Nothing			
Barone et al	2016	Parallel	3	90(total)	30/30/30	Yes	Xenograft	CCPB/CPB	Collagen	No	Clinical
Fernandes et al	2011	Split mouth	6	18	18	No	Allograft	Inorganic bone matrix with synthetic peptide	ADM	No	Clinical

Study	**Year**	**Study design**	**Follow up period/ mo/w**	**No. of patients**	**No. of sockets**	**Inclusion of molar teeth ?**	**Categorization of bone substitutes**	**Type of bone substitute**	**Membrane type**	**Flap/primary closure**	**Method of measurement**
Fernandes et al	2016	Split mouth	6 – 8	16	16	No	Allograft	Mineralized bone graft	ADM	No	NR
Festa et al	2013	Split mouth	6	15/15	15/15	No	Xenograft/ nothing	CCPB/nothing	Soft cortical membrane/ none	Yes/yes	Clinical
Goh et al	2015	Parallel	6	13	6 7	Yes	Alloplast Nothing	PCL Nothing	No	Yes	Clinical
Iorio-Siciliano et al	2017	Parallel	6	10/10	10/10	NR	Xenograft/ nothing	Bovine-derived xenograft collagen/ nothing	Collagen/ none	Yes/yes	Clinical
Iorio siciliano et al	2019	Parallel	6	40(total)	12/13/15	Yes	Xenograft/ Xenograft/ nothing	DBBM-C DBBM Nothing	Collagen/ Collagen/ none	No	Clinical
Jung et al	2013	Parallel	6	40	10/10/10/10	No	Nothing/ Alloplast/ xenograft/ xenograft	Nothing/ □-TCP/ DBBM-C/ DBBM-C	None/ Polylactide /CM/PG	No	CBCT
Kotsakis et al	2014	Parallel	5	10/8/6	12/12/6	Yes	Alloplast/ xenograft/ nothing	Calcium phosphosilicate putty alloplast/ bovine bone mineral/ nothing	None	No	Clinical
Lim et al	2019	Parallel	4	33(total)	11/10/8	Yes	Xenograft	DBBM-C DBBM-C Nothing	Collagen None None	No	CBCT
Mardas et al	2010	Parallel	8	13/14	13/14	No	Xenograft/ alloplast	DBBM/bone ceramic	Collagen	Yes/yes	Clinical
Mayer et al	2016	Parallel	4	36	14	Yes	Alloplast	□-TCP, HAP,	NO	Yes	Clinical

Study	Year	Study design	Follow up period/ mo/w	No. of patients	No. of sockets	Inclusion of molar teeth ?	Categorization of bone substitutes	Type of bone substitute	Membrane type	Flap/primary closure	Method of measurement
								BCS			
					15		Nothing	Nothing			
Mendez et al	2017	Parallel	6	10/10	10/10	No	Allograft/ xenograft	DFDBA/ DBBM	Collagen	Yes/yes	Clinical
Pang et al	2014	Parallel	6	15/15	15/15	Yes	Xenograft /nothing	DBBM/nothing	Collagen/ none	Yes/NR	CBCT
Pelegrine et al	2010	Parallel	6	7/6	15/15	No	Autograft	Bone marrow/ Nothing	None	Yes	Clinical
Poulias et al	2013	Parallel	4	12	12	No	Allograft/Allograft+ Xenograft	Mineralized cancellous particulate	Polylactide	Yes/yes	Clinical
Sun et al	2018	Parallel	4	34(total)	15/16	Yes	Allograft	FDBA	d-PTFE	No	CBCT

Table 2:- Characteristics of selected studies arranged alphabetically.

ADM : acellular dermal matrix , BCS: biphasic calcium sulfate, BLW:horizontal alveolar bone dimensional changes; □-TCP : beta tricalcium-phosphate; CBCT : cone-beam computed tomography; CCPB : cortico-cancellous porcine bone; CM : collagen membrane, CPB : cortical porcine bone ; DBBM : deproteinized bovine bone mineral; DBBM-C : deproteinized bovine bone mineral with 10% collagen , DFDBA: demineralized freeze-dried bone allograft ; DPBM : deproteinized porcine bone mineral , d-PTFE : dense polytetrafluoroethylene ; FDBA : freeze-dried bone allograft ; FST : Facial soft tissue ;HAP: hydroxyapatite; MGCSH: medical-grade calcium sulfate hemihydrate;Mo : months; No : number, NR : not reported, PCL: Polycaprolactone, PG : punch graft, w : weeks

Results:-

Studies comparing bone grafts with or without membranes

Subcategorization into the different applied graft types was possible for the thirteen selected studies using the grafts in combination with membranes, and studies were sorted accordingly. The subchapters that follow are dedicated to the outcomes of changes in alveolar ridge dimensions as well as changes in facial soft tissue. Various subgroup meta-analyses on the type of graft materials were carried out within these chapters. Finally, the results of all of these subgroup analyses will be compared to determine the impact of the various graft types.

Alveolar bone changes in the horizontal dimension

Studies applying allografts

Two studies were included in the meta-analysis for horizontal alveolar bone dimensional alterations (Fernandes et al. 2016; Sun et al. 2018). In all, 47 sockets were treated and analysed. There was a total of 23 experimental sites and 24 control sites in the study. The meta-analysis outcomes found no significant difference between experimental and control locations (P =0.29), with grafts improving alveolar ridge preservation by 1.40 mm (95 % CI = -3.98, 1.19 mm; heterogeneity I2 = 79 %) compared to extraction alone.

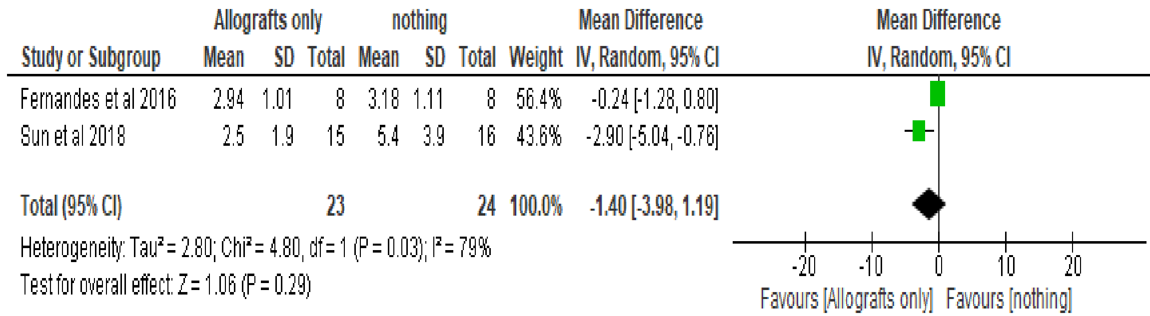


Figure. 2:- Forest plot illustrates the variations in the width alterations of alveolar bone between allograft and empty sockets.

Studies applying xenografts

For the horizontal dimensional changes of alveolar bone, a meta-analysis of 10 groups of 7 studies was carried out (studies of Barone et al. (2016), Fernandes et al. 2011, Festa et al. 2013, Iorio-Siciliano et al. 2017, Iorio- siciliano et al. 2019, Lim et al. 2019, Pang et al. 2014). Three studies used more than one intervention group (studies of Barone et al.(2016), Iorio-Siciliano et al. 2019, Lim et al. 2019). For this outcome variable, a total of 310 sockets were used in the investigations.

A number of 155 experimental locations and 155 control sites were used in this study. A meta-analysis revealed a statistically significant difference (P < 0.00001) between experimental and control locations, favouring alveolar ridge preservation by means of xenografts with a clinical magnitude of 1.53 mm (95 % CI = -2.07, - 0.99 mm; heterogeneity I2 = 81%). However, considerable heterogeneity was observed.

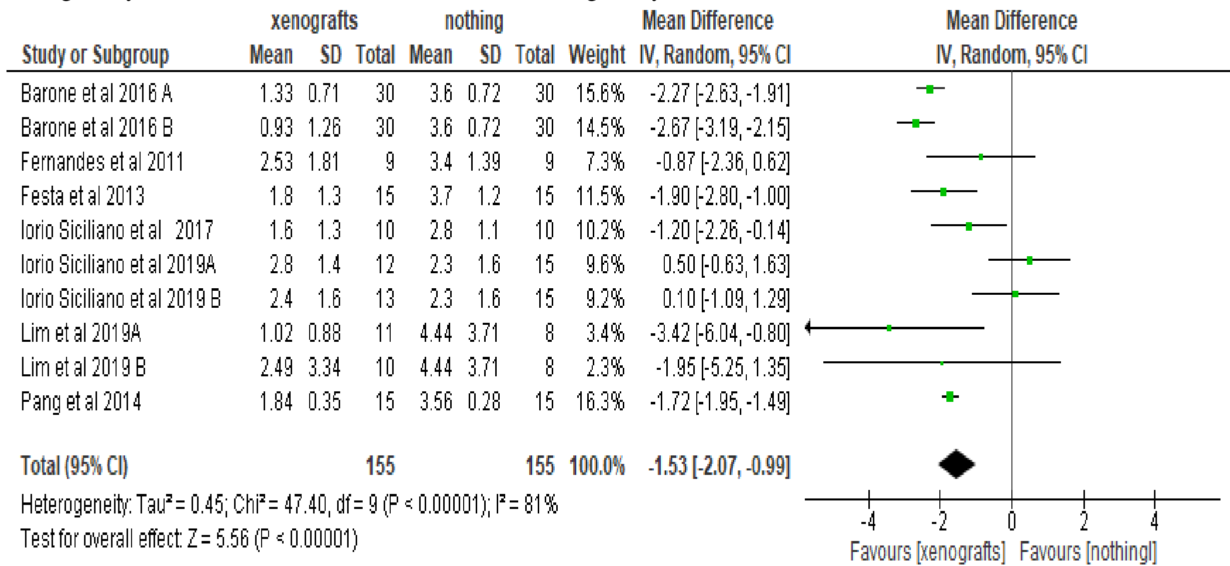


Figure. 3:- Forest plot illustrating the variations in the width alterations of alveolar bone between xenografts and spontaneous healing groups with empty sockets.

Studies applying alloplasts

Three studies were included in the meta-analysis for horizontal dimensional alterations in alveolar bone (Aimetti et al. 2009; Goh et al. 2015; Mayer et al. 2016). There were a total of 82 sockets studied for this outcome variable. The total number of experimental sites was 42, whereas the control sites were 40. There was no significant difference between experimental and control sites (P =0.09), with only a slight tendency to increase alveolar ridge preservation by means of alloplasts with a clinical magnitude of 0.63 mm (95% CI = -1.36, 0.09 mm; heterogeneity I2 = 48%).

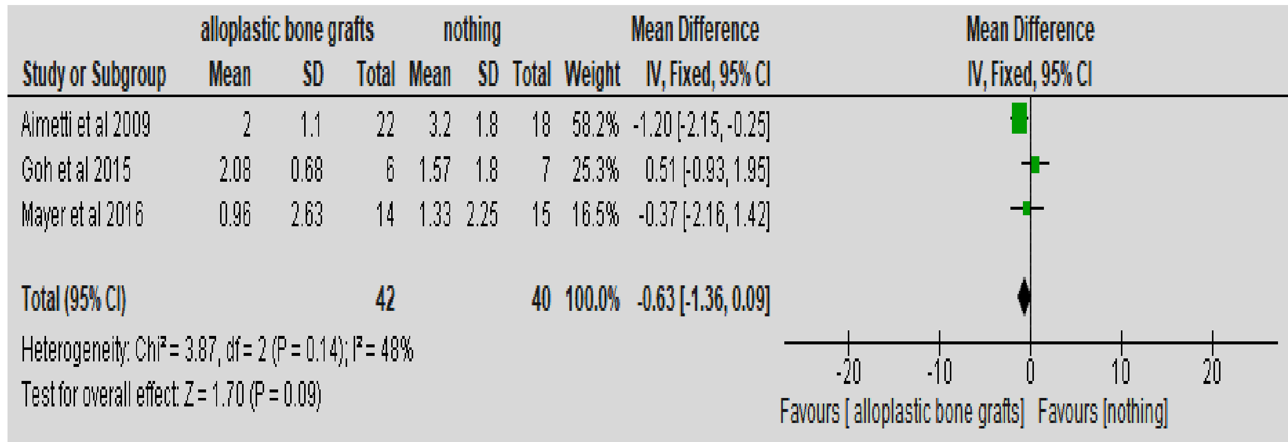


Figure. 4:- Forest plot illustrating the variations in the width alterations of alveolar bone between alloplastic bone graft and control groups with empty sockets.

Studies applying autografts

Pelegrine et al. 2010 reported the use of autogenous bone substitute in its ARP trial, which included a total of 30 treated extraction sockets. The overall number of experimental and control sites was 15, with 15 being experimental and 15 being controlled. The average amount of horizontal ridge resorption was 1.14 ± 0.87 mm, compared to 2.46 ± 0.4 mm in ungrafted sockets. The results of this study were also given using a forest plot for better comparability. This original study likewise found a significant difference (P =0.014) between experimental and control sites, favouring alveolar ridge preservation with an autograft of 1.32 mm clinical value. The relevant 95 percent confidence interval of the differences was calculated using the statistical tools integrated into RevMan (-1.80, - 0.84 mm).

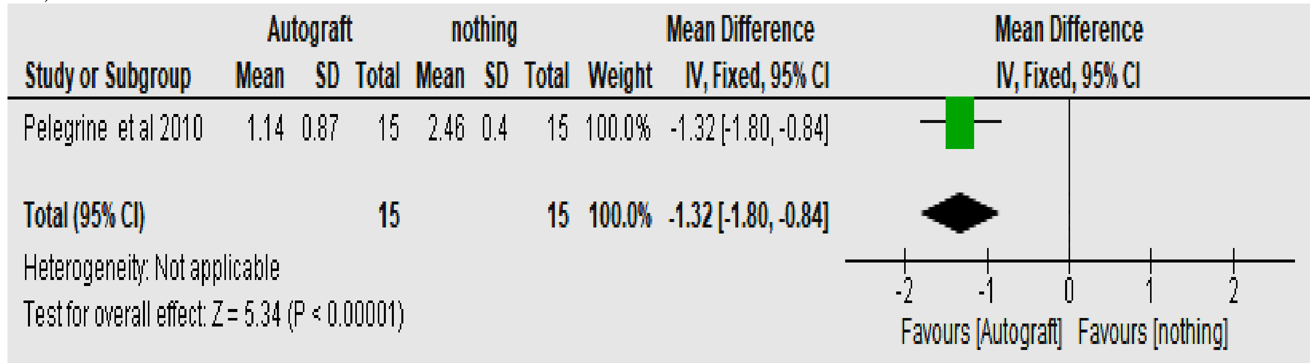


Figure 5:- Use of meta-analysis software to calculate the differences in width alterations of alveolar bone between autogenous bone graft and control group of empty sockets.

Studies comparing allografts with xenografts

Two more studies could be used to conduct a meta-analysis of width alterations in alveolar bone comparing directly two types of different grafts (Mendez et al. 2017; Poulias et al. 2013). There were 32 sockets studied for this outcome variable in total. with 16 being experimental and 16 being controlled.

The two included studies used very different setups as only Mendez et al. 2017 performed a direct comparison while Poulias et al. 2013 compared the application of a sole allograft socket graft with a combination of the same allograft and the xenograft applied only as a buccal overlay.

Meta-analysis resulted thus in a very heterogenous outcome with no significant difference between xenografts and allografts (P =0.96), favouring alveolar ridge preservation employing the xenograft with a clinical magnitude of 0.07 mm (95% CI = -2.38, 2.51 mm; heterogeneity I2 = 91%). In contrast, the study directly comparing the single-use of both materials revealed a tendency for lower resorption for allografts, although also this comparison was not significant.

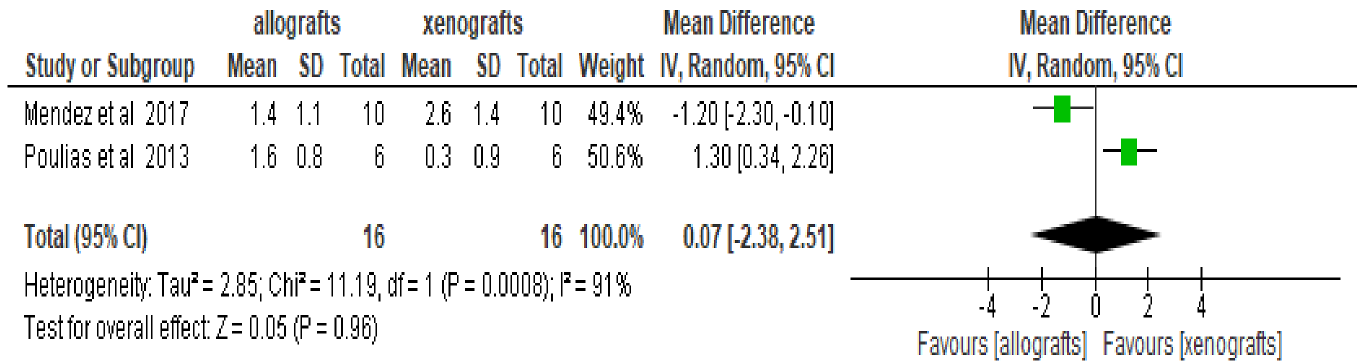


Fig. 6:- Forest plot illustrates the variations in the width alterations of alveolar bone between allografts and xenografts.

Studies comparing alloplasts with xenografts

Another meta-analysis for horizontal dimensional changes of alveolar bone was also possible for three studies (Jung et al. 2013, Kotsakis et al. 2014, Mardas et al. 2010) comparing the outcomes of grafting with alloplastic bone graft vs. the use of xenografts. One study had more than one intervention group qualified for the inclusion in the systematic review (Jung et al. 2013). In total, 91 sockets were included for this outcome variable. The total number of experimental sites was 45, and the total number of control sites was 46. The forest plot of the meta-analysis for horizontal dimensional changes of alveolar bone. Meta-analysis showed no significant difference between alloplastic bone graft and xenografts (P =0.12), with a tendency to better alveolar ridge preservation in xenograft group with a clinical magnitude of 2.03 mm (95% CI = -0.56, 4.61; heterogeneity I2 =

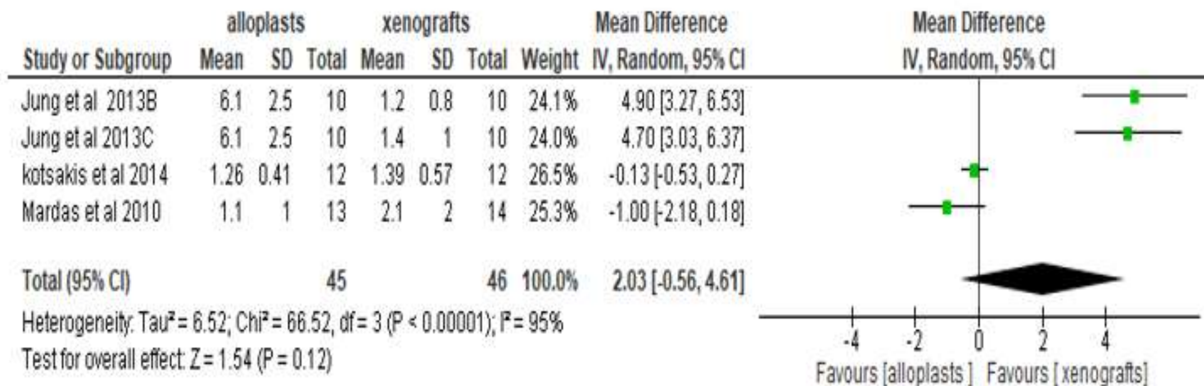


Figure.7:- Forest plot illustrates the variations in the width alterations of alveolar bone between alloplastic bone grafts and xenografts.

Comparison of the different graft types

When the pooled effects of all different graft types were compared in terms of horizontal dimensions of alveolar ridge preservation, the groups of xenografts had the biggest and most significant effect, with a reduction in bone loss of 1.53 mm (-2.07, -0.99 mm). In comparison to unfilled sockets with a similar extent of -1.32 mm, also autografts showed significantly improved bone preservation (- 1.80; -0.84 mm). Even though the pooled effect for allografts was similar with -1.40 mm (-3.98, 1.19 mm), the substantial heterogeneity among the two included studies resulted in non-significantly superior preservation in comparison to the control. Alloplastic bone grafts had a lower and non-significant effect, with just -0.63 mm (-1.36, 0.09 mm).

Graft type	Mean effect (95% CI)
Graft type in comparison to control of empty socket	
Allografts	-1.40 mm (-3.98, 1.19 mm)
Xenografts	-1.53 mm (-2.07, -0.99 mm)
Alloplastic bone graft	-0.63 mm (-1.36, 0.09 mm)
Autografts	-1.32 mm (-1.80; -0.84 mm)

Direct comparison of two graft types	
Xenograft vs. allograft	0.07 mm (-2.38, 2.51 mm)
Xenograft vs. Alloplast	2.03 mm (-0.56, 4.61mm)

Table 3:- Summary of the mean effects for different graft types, in terms of better horizontal ridge preservation.

It should be noted, however, that the confidence intervals of all groups were highly overlapping. This is reflected by the outcome of the direct comparison of xenografts to allografts or alloplastics, finding no substantial benefit of xenografts over allografts or alloplastics. However, in all comparisons, there was a marginal tendency towards lower xenografts, with allografts losing 0.07 mm (-2.38, 2.51 mm) and more bone loss in alloplastic groups 2.03 mm (-0.56, 4.6mm).

Discussion:-

This systematic review seeks to examine the efficacy of various grafting materials that are used after the extraction of the tooth with or without guiding membranes, to keep the alveolar crest intact in vertical and horizontal dimensional states.

This review is based on extracted data from eighteen articles selected from MEDLINE (PubMed) and Cochrane (Central). The studies comparing bone grafts with or without membranes. Meta-analysis, specifically the statistical software embedded in RevMan was used to derive summary measures for different kind of graft types but for studies that could vary in follow-up time, specifically used materials. So, the pooled mean values and respective confidence intervals for different graft types as presented in the respective subchapters in the Results part that allow for the first ranking between these categories.

Studies comparing bone grafts with or without membrane

Changes in the horizontal dimension of alveolar bone

A more specific analysis was performed when available data were pooled from studies, presenting data on patients, irrespective if membranes were used or not. This means that membranes were applied in a variety of studies not on all patients but only in such cases when the actual clinical situation required prevention of ingrowing soft tissue.

However, there it has to be highlighted that there is a certain imbalance in the study setup with respect to membranes, as nearly all xenograft studies included the use of membranes while autograft and alloplast studies consistently did not apply membranes in their patients. A potential distorting impact of membranes on the overall results will be considered, respectively. Nevertheless, a direct comparison was possible in the studies directly comparing xenografts with alloplastic bone graft or allografts, as in these studies all groups were treated identically.

For the thirteen selected studies applying the grafts in combinations with membranes or not, a subcategorization into the different applied graft types was meaningful and studies were sorted accordingly. Pooled data for the subgroups were obtained by means of meta-analyses. This meta-analysis examines the effectiveness of alveolar ridge preservation treatments in reducing post-extraction hard tissue dimensional loss by employing particular types of bone grafts with or without guiding membrane.

Alveolar ridge preservation procedures with xenograft were accompanied with the highest effect in this outcome variable, resulting in a lower amount of bone loss compared to control of empty sockets (with no membranes) with 1.53 mm with nearly a parallel value accompanied with allograft 1.40 mm. The lowest benefit to preserve alveolar ridge compared to empty sockets was found for the use of alloplastic bone graft with values of only 0.63 mm studies (all without the use of membranes in both test and control groups). The obtained value for autograft for the same variable was 1.32 mm.

Although the ability to sustain the alveolar ridge in allografts, xenografts, and autografts was relatively equal for pooled data, only xenografts and autografts exhibited a statistically significant benefit when compared to empty sockets. But as outlined above the specific study characteristics might distort the results as only in the alloplast subgroup, with the seemingly lowest benefit, no membranes were used at all. This impact of membranes is clearly

demonstrated in the different study groups in Lim et al. 2019 who found specifically better ridge preservation with their DBBM when additionally, a membrane was applied.

In a direct comparison of xenografts and allografts (both groups using membranes), no difference in behaviour was found (P =0.96), with a negligible favor of alveolar ridge preservation for the use of xenografts with a clinical magnitude of only 0.07 mm obtained from two studies. Also, the direct comparison of alloplastic bone graft vs. xenografts revealed no significant differences between both materials (P =0.12), again with a clear tendency to better alveolar ridge preservation in xenograft groups with a clinical magnitude of 2.03 mm.

In terms of alloplastic bone grafts, it should be noted that the materials employed were comparatively different in terms of chemical nature and degrading qualities. Individual outcomes were, predictably, quite diverse. As a result, -TCP alone was unable to preserve the alveolar ridge in the horizontal dimension (Jung et al. 2013), whereas combinations with hydroxyapatite HAP and biphasic calcium sulfate provided much better results in Mayer et al. 2016, though the benefits to control were not statistically significant. In contrast, significantly better preservation compared to control and to xenograft (Mardas et al. 2010) was observed for a commercial product by Straumann providing a 1:1 mixture of HAP and -TCP called Straumann Bone Ceramic (SBC). In this study of Mardas et al. 2010, it was noticed after 8 months of follow-up that in the SBC group the creation of new bone in the apical area with woven bone mainly and isolated areas of lamellar bone were observed. The new bone was in immediate contact with SBC particles in the coronal area of the biopsy and dense connective tissue was surrounding the particles of SBC containing multiple forms of collagen fibres, blood vessels, and fibroblast. There was no effective resorption of the particles of SBC.

Regarding the histomorphometric results in DBBM group, similar outcomes were observed. The immediate contact between DBBM particles and woven or lamellar bone was observed in the apical area of biopsy without effective resorption of the DBBM particles, but the biopsy in the coronal area revealed that a dense connective tissue was surrounding the particles of the DBBM.

In the study of Toloue et al. 2012 which compared the use of calcium sulfate CS and FDBA for the variable of total bone formation percentage, it was higher in CS (P= 0.0015) with half amount compared with FDBA and minimal graft remanent in CS compared with a higher percentage in FDBA P=0.0001 for the same variable, while the rate of soft tissue was almost the same in both grafting materials.

The same thing according to this variable was observed in the study of Machti et al. 2018 when compared the use of BCS/HAP and bovine-derived xenograft BDX. The rate of total bone creation was clinically higher in BCS/HAP group with about a double amount compared with BDX and it was near significant (P=0.07), while the residual particles were greater in BDX than BCS/HAP group(P=0.012) with an amount of preeminent was three folds more in BDX compared with BCS/HAP group.

Hence, in this study, it could be shown that a well-composed mixture of alloplast materials can even better performance in terms of the quantitative outcome parameters as well as in the quality of new bone providing direct bone contact to graft material without fibrous layers.

HAP is known for its slow rate of resorption compared with other types of calcium phosphates, while -TCP can be easily resorbed under physiological conditions and promote bone regeneration. A mixture of both can tune the degradation profile to balance resorption with new bone formation.

Due to the small number of included studies in this meta-analysis and the completely different kinds of specifically used alloplastic bone graft the pooled data for this graft type have to be evaluated with caution. More studies in particular investigating newly developed synthetic products might completely change the picture.

When the pooled data including all the studies with or without membranes were compared to the output of other meta-analyses again slightly smaller effects were obtained in contrast to publications that calculated pooled effects over different kind of graft types: with Vignoletti et al. 2012 reporting values of 1.83 mm data pooled from 7 studies, or Avila-Ortiz 2014 with values of 1.89 mm data pooled from 6 studies). Also, Bassir et al. 2018 published similar outcomes with 1.86 mm for all 14 included studies, regardless of the type of bone graft.

However, in contrast, studies reported similar amounts of benefit for the same variable, such as an average of 1.20 mm (95% CI: 0.04, 2.43 mm; data pooled from 4 studies), MacBeth et al. 2017, an average 1.33 mm (95% CI: 0.69, 1.97 mm; data pooled from 13 studies), Willenbacher et al. 2016, and an average 1.52 mm (95% CI: 1.18, 1.86 mm; data pooled from 6 studies) Locca et al. 2017, regardless the type of bone graft.

When directly comparing the values obtained for single graft types Avila-Ortiz et al. (2018) again found higher effects for xenografts than in this thesis with a mean effect of 2.25 mm. Nevertheless, this meta-analysis found similar trends for the other graft types as in this thesis, as lower values were found also for allografts 2.01 mm and alloplastic bone graft 1.25 mm.

In contrast, the pooled data in the publication of Majzoub et al. 2019 were more or less comparable to this thesis with pooled data accounting for improved preservation in xenografts with 1.63 mm, for allografts with 1.58 mm, and again only the lowest values obtained for alloplastic bone graft with 0.73 mm.

It has to be highlighted that the same trends were observed with slightly best ridge preservation in xenografts, somehow markedly lower benefit of alloplastic bone graft, while autograft data were not provided.

Conclusion:-

Aside from the above-mentioned limitations of this study, some summarizing conclusions can be drawn:

Statistically significant differences were identified in horizontal locations with bone grafts exclusively.

The comparison between alveolar ridge preservation with xenograft materials and natural socket healing revealed nearly always a higher rate of reducing bone resorption compared with other materials in horizontal bone dimensional changes, with statistically significant difference to the empty socket.

In general,

We need more research for new alloplastic bone grafts or combination of different material types that serve this topic.

With regards to horizontal bone alterations, alveolar bone resorption was reduced with allograft.
There was no statistically significant difference between xenograft and allograft in alveolar ridge preservation alterations.

But it is important to clarify the very low number of studies in groups used autograft, allograft and alloplastic bone substitutes. So, this should lead to a final conclusion that all these results are very preliminary and to prefer one over the other alone based on summarized data of this analysis would be surely inadequate and other arguments need to be involved.

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