Evaluation of the effectiveness of using platelet rich fibrin (PRF) as a sole grafting material and membrane in augmentation of dehiscence and fenestration defects encountered during dental implant surgery

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ABSTRACT

Background: Bone regeneration in dehiscence and fenestration defect can be improved with the use of platelet rich fibrin (PRF) that provides a scaffold for new bone regeneration. This study was conducted to assess the effectiveness of PRF as a graft material and membrane in dehiscence and fenestration defects.

Materials and Methods: This prospective clinical study included patients who received dental implants that demonstrated peri-implant defects which were augmented using Leukocyte- PRF (L-PRF) or Advanced-PRF (A-PRF). Twenty four weeks postoperatively the defect resolution and the density of regenerated bone were assessed by CBCT and re-entry surgery. The assessment also included measurement of primary and secondary implant stability using Periotest® M, success rate and complication rate of the installed implants.

Results: The mean overall intraoperative defect size was 29.44 (± 14.1) mm^2, postoperatively it became 2.07 (± 3.6) mm^2 with a statistically significant difference (p= < 0.0001). There was no significant difference between L-PRF and A-PRF. Defect resolution ranged from 80% to 100% with a mean of 95.7% (± 6.7%). Defects that showed complete resolution were significantly smaller in size (21.2± 7 mm^2) than those that showed partial resolution (44.4± 11 mm^2). The overall mean primary stability recorded was 2.9 (± 1.6) Periotest values (PTV) and overall mean secondary stability was -0.22 (±1.4) (P<0.0001).The overall mean HU of the newly formed peri-implant bone was 385.7 (± 77.4).

Conclusions: PRF as the sole graft material for peri-implant defects results in complete defect resolution in small to moderate defects, larger defects may require the addition of bone substitute to achieve complete defect resolution.

Keywords: bone density; defect resolution; dehiscence, fenestration; implant stability, peri-implant defect. **(Received: 20/11/2018; Accepted: 2/1/2019)**

INTRODUCTION

The dental implants are a reliable and popular treatment of edentulous jaws because of high survival rate and predictability.(1,2) As a general principle for successful implant treatment the implant surface should be covered with at least 1 mm of alveolar bone, placement of dental implants in areas of insufficient bone volume can lead to cortical bone defects such as dehiscence or fenestration that may compromise the survival of implant. A dehiscence is a bone defect involving the cervical portion of the implant whereas fenestration is a bone defect not involving the cervical portion.(3) One of the most popular procedures that has promoted the defect fill with newly formed bone is the Guided bone regeneration (GBR), that allow spaces maintained by barrier membrane to be filled by bone.(1,4)

GBR procedures in dehiscence and fenestration defects can be obtained with resorbable or non-resorbable membranes, in association with a variety of graft materials, such as autogenous bone, allografts, xenografts, and alloplastic materials. (4)
Among these biomaterials, autogenous bone is often selected as the first choice for bone regeneration.(5) Platelet rich fibrin (PRF), first prepared by Choukroun et al. in 2001,(6) is a second generation platelet derivative after platelet rich plasma (PRP). It contains platelets and growth factors in the form of fibrin membranes prepared from the patient's own blood free of any anticoagulant.(7) In the field of dental implants, PRF has been utilized as a clot, mixed with a bone graft, or as a membrane in an effort to enhance and accelerate tissue healing, however variable results have been obtained regarding its benefits.(8) Lee et al. in 2012 (9) demonstrated the ability of PRF alone to successfully repair small to moderately sized peri-implant defects in animal model but they emphasized the need to determine the behavior of PRF in bony defects in humans. There appears to be no clinical studies that use PRF alone in treatment of peri-implant defects,

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therefore, this study was conducted to assess the effectiveness of PRF as a sole grafting material and membrane for augmentation of dehiscence and fenestration defects encountered during implant procedure and the density of the regenerated bone.

MATERIALS AND METHODS

This prospective clinical study included 20 consecutive patients who received (31) dental implants (NucleOSS, Izmir, Turkey) that demonstrated buccal\labial bony defects, in the form of dehiscence or fenestration, with exposed implant surface that were accidentally created during implant placement through either delayed or immediate implant placement protocol.

The bony defects were treated using PRF as the sole graft material to augment the defect. In 10 patients with 15 defects Leukocyte-PRF (L-PRF) was used whereas in the remaining 10 patients with 16 defects Advanced-PRF (A-PRF) was used.

The inclusion criteria for this study were: medically fit patients ≥ 18 years old who developed fenestration or dehiscence defects during immediate or delayed implant placement, with no evidence of local infection at or near the implant zone.

Patients were excluded from this study if they had history of radiotherapy to the head and neck region, chemotherapy or drugs that compromise the healing of bone such as bisphosphonates. Also patients who demonstrated fenestration or dehiscence less than 3 mm in a greatest dimension were excluded from this study.

For dehiscence defects the defect height was measured as the distance from the most apical aspect of the buccal crestal bone to the coronal aspect of the implant body and the defect width was measured as the widest mesio-distal dimension of the buccal bony defect.

The surface area of the defect was calculated according to Zitzmann et al.[10] where the defect was considered as a half ellipse by multiplying length × width × π/4 (where π = 3.14) **Fig.(1)**.

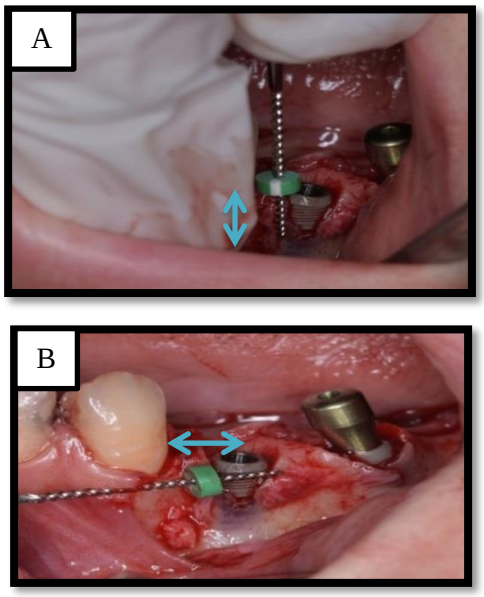

Figure 1: Measurement of (A) Length of the defect and (B) Width of the defect, using reamer with stopper.

For the fenestration defect, the defect was measured at the greatest dimension for the length or width, the surface area calculated as circle (r2× π) where the radius was considered as half of greatest dimension (length or width).[10] **Fig.(2)**

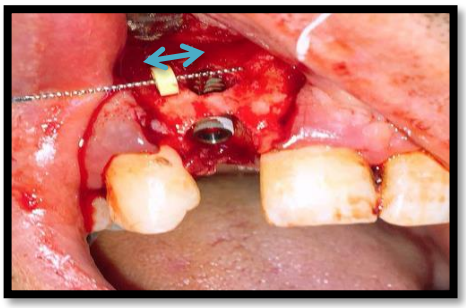

Figure 2: Measurement of fenestration defect at the greatest dimension.

The PRF preparation was as follows: 10 mL of blood was collected from the patient for each implant defect and was immediately centrifuged at 3000 rpm for 10 minutes at the room temperature to prepare L-PRF according to Dohan et al.[11] For preparation of A-PRF the blood was centrifuged at 1300 rpm for 8 minutes.[12] During PRF preparation, the primary implant stability was measured using Periotest® (Medizintechnik Gulden, Germany). The stability was determined as a Periotest value (PTV). Then the obtained PRF clot was divided into two pieces one used to augment the defect and other was compressed

into a membrane used to cover the bony defect **Fig.(3).** The flap was readapted to its position and sutured.

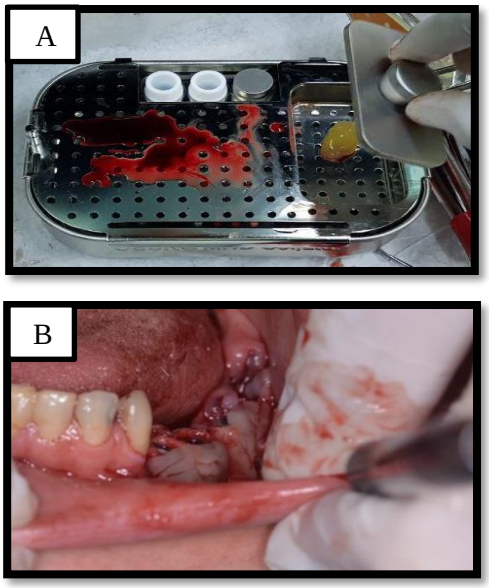

Figure 3 : (A) PRF clot obtained and compressed using PRF Box (B) Defect covering using PRF membrane.

Twenty four weeks after surgery CBCT was taken to assess the bone density of the newly formed bone **Fig.(4).**

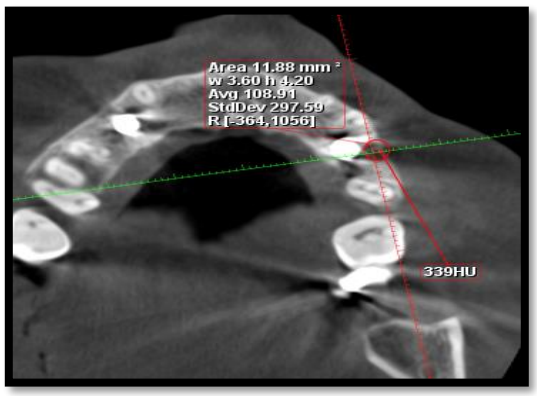

Figure 4 : 24 weeks Postoperative axial view of CBCT showing measurement of bone density in the defect site.

Then defect was examined for defect resolution through re-entry intervention, any residual defect was measured in the same manner **Fig.(5,6).** The healing abutment was then inserted and secondary stability was measured and recorded as described for primary stability.

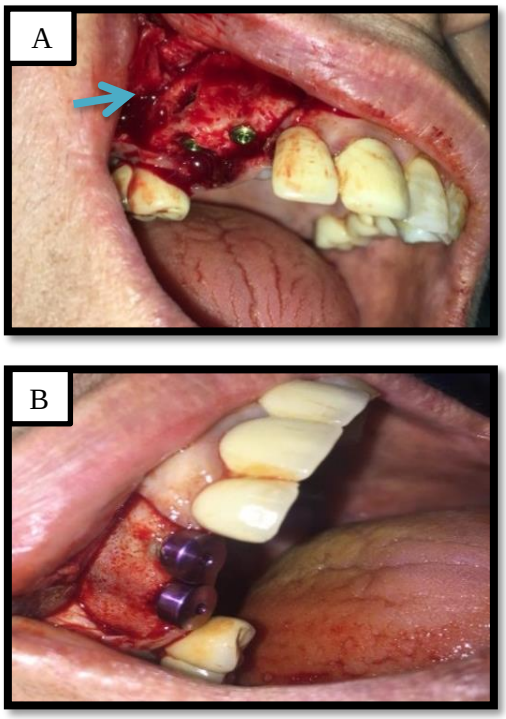

Figure 5: (A) Preoperative clinical view showing fenestration defect (B) Complete defect fill 24 weeks postoperatively.

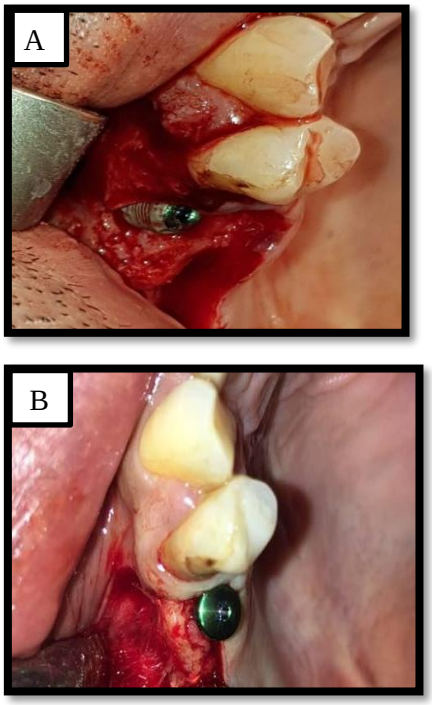

Figure 6: (A) Preoperative clinical view showing dehiscence defect (B) Complete defect fill 24 weeks postoperatively.

The outcome variables were: defect resolution calculated as a percentage of the augmented defect to the original defect by the following formula (residual defect size×100/original defect size), bone density expressed as a Hounsfield Unit (HU) at the augmented defect, and implant stability measured in PTV. This study was approved by the institutional review board and every patient was informed about the procedures and the nature of the study, and those who agreed to participate signed an informed consent. The statistical analysis was performed using GraphPad Prism version 6 for Windows (GraphPad Software, La Jolla, CA, USA). Descriptive analysis included percentages or mean ± standard deviation (SD). The investigated variables were analyzed statistically using the D'Agostino-Pearson omnibus normality test, *t*-test, Mann-Whitney test, Fishers' exact test. The differences were considered significant at $P<0.05$.

RESULTS

Twenty consecutive patients participated in this study, they were 7 males (35%) and 13 females (65%), they ranged in age from 25 to 64 years with a mean age of 43.4 (± 13.4) years. They received 31 dental implants, the dimensions of the used implants are summarized in **Table 1**. Of the 31 implants, 19 (61.3%) were installed conventionally and 12 implants (38.7%) were inserted immediately after tooth extraction. Twenty one implants (67.7%) were inserted in the maxilla and 10 (32.3%) were inserted in the mandible.

Table 1: Dimensions of the implants

	Implant dimension	No. of implants (%)
Length	8 mm	2 (6.5)
	10 mm	17 (54.8)
	12 mm	12 (38.7)
Width	3.5 mm	22 (71)
	4.1 mm	8 (25.8)
	4.8 mm	1 (3.2)

Thirty one peri-implant defects were encountered during installation of the 31 dental implants, these were 25 dehiscence (80.6%) and 6 fenestrations (19.4%). In 10 patients who had 15 defects the augmentation was carried out using L-PRF while in the remaining 10 patients who had 16 defects the augmentation was with A-PRF. The differences in type of the defect, the treatment protocol and the recipient jaws between the two groups were statistically non-significant **Table 2.**

Table 2: The differences between L-PRF and A-PRF group

Variable	L-PRF	A-PRF	P-value
Type of defect			
Dehiscence	13	12	0.65a
Fenestration	2	4	[NS]
Treatment protocol			
Conventional	8	10	0.72a
Immediate	7	6	[NS]
Jaw			
Maxilla	8	13	0.13a
Mandible	7	3	[NS]

a Fishers' Exact test.
[NS] Non-significant.

The mean overall intraoperative defect size was 29.44 (± 14.1) mm^2 (range 11.8-61.2 mm^2). The re-entry after 24 weeks postoperatively revealed that the mean size of the residual defect was 2.07 (± 3.6) mm^2 (range 0-11.8 mm^2). The difference was statistically significant (p= < 0.0001). The differences in intraoperative and postoperative defect sizes between L-PRF and A-PRF are summarized in **Table 3**.

Table 3: The differences in intraoperative and postoperative defect sizes between L-PRF and A-PRF.

Defect size (mean±SD)/mm	L-PRF	A-PRF	P-value
Intraoperatively	33.3 (± 16.3)	25.8 (± 11)	0.1864 **b** [NS]
Postoperatively	3.2 (± 4.5)	1 (± 2.3)	
P-value	**< 0.0001a [S]**	**< 0.0001a [S]**	

a t-test for 2 dependent means.
b t-test for 2 independent means.
[S] Significant.
[NS] Non-significant.

Defect resolution ranged from 80% to 100% with a mean of 95.7% (± 6.7%) and median of 100%. Defects that showed complete resolution (100%) postoperatively had statistically significant smaller defect size intraoperatively than those that showed partial resolution; the other significant difference was in the bone density of regenerated bone which demonstrated statistically higher bone density in defects with complete resolution compared with defects with partial resolution. The overall mean primary stability recorded was 2.9 (± 1.6) PTV and

overall mean secondary stability was -0.22 (±1.4) and the difference was statistically significant (P<0.0001). The mean primary stability of the implants in L-PRF group was 2.65(±1.8) and for A-PRF group was 3.11(±1.47), the secondary stability for L-PRF and A-PRF groups were -0.16 (±1.7) and -0.4 (±1.2), respectively. Within each group the differences between primary and secondary stability were statistically significant (P<0.0001) but the difference between the 2 groups was non-significant (p=0.22). The overall mean HU of the newly formed peri-implant bone measured by CBCT after 6 months was 385.7 (± 77.4). The mean HU of the regenerated bone in defects treated with L-PRF was 398.6 (± 81.5) which was higher than that produced by A-PRF (373.6 ± 73.8), but the difference between the two groups was statistically non-significant (p=0.38). It was also noted that bone density of the newly formed bone in mandibular defects (467.1 ±30.4) was significantly higher than that of maxilla 346.9 (± 60.5) with a level of significance of < 0.0001 **Table 4.**

All implants were successful after 24 weeks and no major complications were recorded during the healing period apart from the postoperative inflammatory response.

Table 4: Comparison between defects that demonstrated complete and partial defect resolution

Variables	Defect resolution		P-value
	Complete	**Partial**	
No. of defects (%)	20 (64.5%)	11(35.5%).	
Mean (± SD) defect size/mm^2	21.2 (± 7)	44.4 (± 11)	p< 0.0001[S]a
Type of PRF (No.)			
L-PRF	7	8	0.066 [NS]b
A- PRF	13	3	
Type of the defect (No.)			
Dehiscence	16	9	1.00[NS]b
Fenestration	4	2	
Treatment protocol (No.)			
Conventional	13	5	0.45[NS]b
Immediate	7	6	
Jaw (No.)			
Maxilla	12	9	0.2617[NS]b
Mandible	8	2	
Bone density/mean (± SD) HU	395.5 (±72.5)	367.8 (±83)	< 0.0001 [S]c
Implant stability/ mean (±SD) PTV			
Primary	2.85 (± 1.7)	2.95 (±1.6)	0.1789[NS]c
Secondary	-0.5 (± 1.6)	0.1 (± 1)	

a t-test for 2 independent means
b Fishers' exact test
c Mann-Whitney test
[S] Significant.
[NS] Non-significant

DISCUSSION

One of the relatively recent advances is the use of bioactive additives such as PRF to regulate inflammation and improve the healing process.[13] In the field of peri-implant defects, PRF can be used in management of peri-implantitis and in peri-implant defects encountered during conventional implant placement or in post-extraction implantation procedures.[7]

Previous animal studies have favored the use of PRF alone or in combination with other materials in treatment of peri-implant defects.[9, 14, 15] Human studies and case reports also demonstrated that the use of PRF in combination with different grafting materials showed favorable results in terms of enhancing new bone regeneration,[1, 16] but there appears to be no human studies that evaluate the use of PRF alone in peri-implant defects.This study achieved a mean overall defect resolution of 95.7% which is a comparable result to that reported by Blanco et al. in 2005 [17] (94.8%) who used non-resorbable membrane with or without bone grafts or decalcified freeze-dried bone allograft and they concluded that implants with peri-implant defects that are treated with GBR had similar survival rates and crestal bone levels compared to implants in native bone. In this study 2 types of PRF were used: L-PRF and A-PRF, the differences in the distribution of the types of defects (dehiscence or fenestration), treatment protocol (conventional or immediate) and the recipient jaw (maxilla or mandible) between the 2 groups were statistically not significant which indicate that these variables were not acting as confounding factors that would affect the primary investigated outcome, namely: the new bone regeneration and defect resolution. In general there was no difference between the 2 types of PRF in terms of the changes between the intra and post-operative (residual) defect sizes and the number of defects that showed complete or partial defect resolution. El Bagdadi et al. in 2017 [18] demonstrated that low speed centrifugation concept affects the growth factor release and platelet distribution in solid PRF-based matrices and they suggested that the A-PRF may be superior to L-PRF in specific clinical applications. In the current study the defects that showed complete resolution in A-PRF group (13/16, 81.3%) were more than the L-PRF group (7/15, 46.7%), but this difference was statistically not significant producing a significance level of (p=0.066) which should be interpreted clinically with caution due to the small sample size. The most important determinant factor of defect resolution in this study was the size of the defect; defects that showed complete resolution postoperatively had significantly smaller defect size intraoperatively (21.2± 7 mm^2), which equals roughly to a 5×5 mm defect, than those that showed partial resolution (44.4± 11 mm^2)which is about 7×8 mm. A possible explanation for this relationship between defect size and defect resolution is that smaller defects provide better support for the PRF membrane preventing it from being compressed into the defect by the overlying soft tissue during healing which may in turn compromise the regeneration of bone. Studies have demonstrated that complex defects require stiff membranes such as titanium mesh or metal supported expanded polytetrafluoroethylene (e-PTFE), whereas for small to moderate defects, resorbable collagen membrane or platelet-rich fibrin (PRF) membranes are preferred.[19] In this study, implant stability was measured using Periotest® which is considered as a reliable method compared to resonance frequency analysis to measure implant stability.[20] With respect to the change in implant stability, this study revealed that there was a significant increase in implant stability after 24 weeks which is reflected by the significant decrease in PTV measurements between primary and secondary stability. PRF has been shown to affect implant stability favorably.[21, 22] The difference between primary and secondary stability in relation to the investigated variables were not significant except in relation to treatment protocol where the difference was significantly higher in immediate implants than those inserted conventionally. In this study the overall mean HU of the newly formed in the peri-implant defect measured by CBCT after 6 months was within the D3 category (350-850 HU) according to CT determination of bone density,[23] the density of the regenerated bone was not affected by the type of PRF used on this study. The treatment protocol and type of defect did not affect the density of the regenerated bone, but the mandibular defects demonstrated significantly higher density than that observed in the maxilla, this result is in keeping with Turkyilmaz et al in 2007 [24] who reported that the bone density around dental implants is superior in the mandible compared to the maxilla. The bone density of regenerated bone demonstrated statistically higher bone density in defects that show complete resolution compared with defects with partial resolution and this may be related to the amount of bone formation. All implants within the time frame of this study were successfully osseointegarted producing a success rate of 100%, Jensen and Terheyden in their review in 2009 [25] demonstrated

that the overall survival rate ranged from 93% to 100% with a median of 95.4%, they also reported that non-resorbable membranes showed slightly better survival rate (96.5%) whereas resorbable membranes showed 95.4% survival rate and they concluded that survival rates of implants placed in augmented bone are comparable to rates of implants placed in native bone. No major complications were observed in this study which can be attributed to the ability of PRF to regulate inflammation and improve the healing process.[13] Many studies have reported peri-implant mucosal inflammatory complications associated with the use of different resorbable and non-resorbable membranes such as suppuration, hyperplasia, pain, redness, wound dehiscence and membrane exposure. [17, 26, 27]

In the conclusion, the use of PRF as the sole graft material for peri-implant defects with simultaneous implant placement results in complete bone fill and defect resolution in defects that are not more than 21 mm^2 in size which equals roughly to a 5×5 mm defect. Larger defects may require the addition of bone substitute to achieve complete defect resolution. The augmentation with PRF alone is associated with high success rate without major complications and the density of the regenerated bone in defects that demonstrated complete resolution was higher than that of defects that showed partial resolution, it was also higher in the mandible than the maxilla.

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المستخلص:

الخلفية: العلاج بالزراعة هو أحد الأساليب الأكثر موثوقية لاستبدال الأسنان المفقودة ويجب تغطية سطح الزرعة بواسطة العظم السنخي كمبدأ عام أثناء تحضير موقع الزرعة ، قد يحدث التوهج أو الانكسار ويهدد بقاء الغرسة. يمكن اعتبار نقص العظم المجاور للزرعة "عيبًا حقيقيًا ، ويمكن تحسين عملية تجديد العظام التي تملأ العيب باستخدام الفايبرين الغني بالصفائح الدموية الذي يوفر سقالة لإعادة تجديد العظام الجديدة.

المواد والطرق العمل : شملت هذه الدراسة السريرية المحتملة 20 مريضا: 7 ذكور و 13 أنثى مع متوسط العمر 43.40 سنة (المدى: 25-64 سنة) الذين تلقوا 31 عملية زراعة أسنان أظهرت 31 عيبا. تم تعزيز هذه العيوب باستخدام الفايبرين الغني بالصفائح الدموية كمواد التطعيم الوحيدة. تم علاج خمسة عشر عيبا في 10 مرضى مع الفايبرين الغني بالصفائح الدموية القياسي و 16 عيبا ، في 10 مرضى الباقين ، تم علاجها مع الفايبرين الغني بالصفائح الدموية المتقدم. بعد 24 أسبوعًا ، تم تقييم حال العيب وكثافة العظم المجدد من قبل الاشعة الثلاثية الابعاد وجراحة إعادة الدخول. شمل التقييم أيضا قياس استقرار الزرعة الأولية والثانوية ، ومعدل النجاح ومعدل مضاعفات الغرسات المثبتة.

النتائج: أظهرت إعادة الدخول بعد 6 أشهر بعد العمل الجراحي أن متوسط حجم العيب الكلي أثناء العملية قد تغير من 29.44 (± 14.1) ملم 2 ليصبح 2.07 (± 3.6) مم 2 وكان الفرق ذو دلالة إحصائية .(p = <0.0001) من 80٪ إلى 100٪ بمتوسط 95.7٪ (± 6.7٪) كان المتوسط العام للثبات الأولي المسجل 2.9 (± 1.6) وكان متوسط الاستقرار الثانوي العام - 0.22 (± 1.4 .. (P <0.0001) (كان المتوسط العام لوحدة العظم المزروع حديثًا هو 385.7 (± 77.4).

الاستنتاجات: ينتج عامل التكاثف (الفايبرين الغني بالصفائح الدموية) باعتباره المادة المطعمة الوحيدة لعيوب المحيط الزائد في ملء العظم الكامل في العيوب التي لا يزيد حجمها عن 21 مم 2 والتي تساوي تقريباً 5 × 5 مم. قد تتطلب العيوب الأكبر إضافة بديل عظمي لتحقيق قرار عيب كامل