Bone augmentation with TiMesh. autologous bone *versus* autologous bone and bone substitutes. A systematic review

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Summary

***Aim of the study*. Reconstruction of segmental defects and the atrophic maxilla and mandible is performed using various techniques. Bone substitutes have received a wealth of reports in the literature demonstrating a long-term success when used in alveolar bone augmentation procedures.**
***Materials and methods.* We reviewed articles comparing TiMesh GBR technique with different percentage of bone: autogenous bone alone (AB); anorganic bovine bone alone (ABB); 50:50 or 70:30. From an initial pool of 122, we selected 14 studies. ANOVA followed by Tukey HSD test was used for statistical analysis.**
***Results*. We present a table analysing fundamental parameters to value a successful GBR therapy. Autogenous bone remains the gold standard in GBR technique with TiMesh; however, the combination between AB/ABB in relation 50:50 and 70:30 allows reducing surgical cost exploiting properties of eterologous bone.**
***Conclusion.* The use of autologous bone is associated with a height and width gain of bone, which are greater compared to other techniques, with a lower exposure of the mesh and a lower bone resorption. The use of heterologous graft leads to a lower bone earn and to percentage of resorption greater than autologous graft but does not differ from the gain and resorption of the bone of AB/ABB in percentage 50:50 and 70:30.**

Key words: GBR technique, TiMesh, alveolar ridge augmentation, anorganic bovine bone, bone substitute.

Introduction

The atrophy of the alveolar ridge is a physiological event leading to a state of partial or total edentulous jaw bones. Periodontitis, endodontic failures, root fractures and periapical infections represent the main cause of losing teeth (1). To restore the proper amount of alveolar bone volume, the guided bone regeneration (GBR) by Boyne and James (2) was introduced in 1989. This method allows simultaneous implant or delayed placement otherwise precluded (3-10). Clinical and histological data support the use of this approach (11-13).
However, GBR seems to be a highly sensitive technique and applying it to a large community of operators remains challenging (5-7,10,14-16). Moreover, in the literature there is a debate regarding two aspects: type of barrier (membranes versus titanium mesh) and type of graft used (17,18). Graft materials such as autologous, homologous, heterologous and synthetic bone are used singly or in combination. Autologous bone (AB) graft was considered the "gold standard" due to its high biocompatibility, osteoinductive, osteoconductive and osteogenic ability, but the limited availability of intraoral sites and the high morbidity associated to extra-oral donor site has hampered its use. Biomaterials alternative to autologous bone as alloplastic substitutes have been developed: hydroxyapatite (HA), natural coral (1) and calcium carbonate; allogeneic substitutes; demineralized freeze-dried bone allograft and heterologous bone from bovine, swin or equine. In particular, the anorganic bovine bone (ABB) has received attention in the literature, since it yielded a long-term success in ridge augmentation technique. ABB has fundamental characteristics of biocompatibility and osteoconductivity and produces a good scaffold for new bone formation (19,20). It is widely used for vertical and horizontal augmentation (21-23), sinus lift procedure (9), and socket preservation (24).
Previous studies introduced the use of ABB in bone regeneration with TiMesh either alone or in combination with autologous bone (25-28). However, only few studies have performed histological analysis on regenerated bone (25,26,29,30). In particular, we found

that only two studies (27,31) compared the ability of bone regeneration with AB 100% *versus* a combination of AB and ABB in different percentage.

Materials and methods

Source of material, inclusion and exclusion criteria

A systematic review of the major online databases (MEDLINE, PUBMED and SCIENCE DIRECT) and a manual search of the most relevant articles from journals with Impact Factor was carried out covering the period between 1974 and 2013. Several dental journals were searched manually, in particular those specialised in periodontal and oral- maxillofacial surgery. We focused our review on articles that compared GBR technique with several kind of bone: autogenous bone (100%); mixture of autogenous and heterologous bone (50:50); mixture of autogenous and heterologous bone (70:30); heterologous bone (100%). The keywords used for the literature screening were: "ridge" AND "augmentation" AND "titanium mesh" AND "mandibular" OR "maxilla" AND "autogenous bone" AND "bone substitute." The search was carried out by two independent observers (AE and PJ) according to the following criteria.
The inclusion criteria were:

- English articles
- Alveolar ridge defects requiring vertical and/or lateral augmentation with TiMesh prior to or at implant placement (non-space - maintaining dehiscence - type defects)
- Reports describing the following parameters: number of patients in correlation with the surgical site of each patient, type of bone used, width and height of bone gained; mesh exposition, time of mesh removal; percentage of bone absorption under TiMesh, placed number of implants, implant success and survival
- Regeneration with TiMesh on human bone not tested in animals

The exclusion criteria were:

- Use of different barriers (membranes) in addition to TiMesh (35)
- Use of bone grafts with non-defined percentages (35)
- Case reports or case series with less than four patients
- GBR with growth factor (the test group 33)
- Paper with insufficient data for statistical analysis
- Incomplete radiographic examination in the reviewed articles
- Articles with follow-up shorter than 4 months.

Populations in the review

One study (32) performed bone regeneration with TiMesh and different grafting materials (eterologous, allogenic and autogenous bone) without reporting the percentage composition; averages of height and weight bone gained mesh exposition; time of mesh removing; percentage of bone absorption under Ti-mesh; number of implants placed, implants success and survival were not reported. The data of two papers could not be used because in one study (33) a growth factor was added to the test group; in the other one in the control group an autogenous bone graft block was used (34). Another report (35) was not included because of bone augmentation with TiMesh without reporting how the population was divided; moreover a resorbable membrane was introduced to cover the mesh.

Outcome measures and determinants

The studies included in the review had to report: number of patients in correlation with the surgical site of each patient; type of bone used; width and height of bone gained; mesh exposition; time of mesh removing; percentage of bone absorption under TiMesh; number of implants placed; implants success and implants survival. The data needed for analysis were retrieved from tables, figures or text; sometimes calculations were needed.
The initial search identified a total of 122 articles. From a careful consideration of the titles and abstracts 36 articles were selected. The next step was a thorough evaluation of the text of these papers by the same two observers. Only 14 articles had the previously described requirements fulfilling the aim of this study (Tab. 1).

Statistical analysis

Statistical analysis was performed with SPPSS and Excel using analysis of variance (ANOVA) followed by multiple comparisons by HSD Tukey test. The level of significance was set at $p < 0.05$.

Results

The selected articles allowed acquiring significant data on the efficacy of different bone grafts in combination with titanium mesh. We have divided values according to the quality of the bone graft into four groups: autogenous bone graft only (AB 100%); mixture of autograft and allograft in equal parts (AB/ABB 50:50); mixture in different proportions (AB/ABB 70:30); heterologous bone graft only (ABB 100%). For each group we statistically evaluated four parameters (Tabs. 2, 3): average of transversal bone earned in mm (ABW); average of vertical bone earned in mm (ABH); percentage of exposure of the mesh (ME); percentage of bone resorption (BR).
The overall results on the difference in effectiveness of different bone grafts (tested with ANOVA) are reported in Table 4.
To specifically test the differences between the subgroups, multiple comparisons were performed by HSD Tukey post hoc test. We divided the results of the analysis according to the four parameters.

Table 1. Articles included in the paper.

Reference	PS(TS)/SS	Type of bone (%)	ABW (mm)	ABH (mm)	ME (%)	MR & IP (months)	BR (%)	Impl (n°)	Success (%)	Surv (%)	Follow-up
Von Arx et al. 1996	20(20)/20	AB (100)	ID	ID	50	4.7	10	28	ID	ID	ID
Malchiodi et al. 1998	25(25)/25	AB (100)	5.65	ID	0	8 (IP time zero)	ID	120	100 (8 month)	97.5	
Maiorana et al. 2001	14(14)/23	AB/ABB (50/50)	ID	ID	14.2	5	ID	59	98.3	100 (48 month)	5 months
Artzi et al. 2003	10(10)/10	ABB (100)	ID	5.2 (9 month)	20	9	18.8 ± 7.98	20	100	100 (24 month)	24 months
Rocuzzo et al. 2004	18(18)/18	AB (100)	ID	4.8	17.3	4.6	ID	37	100	100	6 months
Proussaefs and Lozada 2006	17(17)/17	AB/ABB (50/50)	3.88 (6 month)	2.59 (6 month)	35.3	8.47	15.11 (6 month)	41	ID	ID	
Corinaldesi 2007	6(12)/6 (control group)	AB (100)	ID	4.17	0	8.6±0.51	ID	17	100	100	12 months
	6(12)/6 (test group)	AB/ABB (70/30)	ID	4	0	8.6±0.51	ID	18	100	100	12 months
Rocuzzo et al. 2007	12**(23)/12 (control group)	AB (100)* (no Ti-mesh)	ID	5.5	NO MESH	4.7	34.5	ID	ID	ID	
	12**(23)/12 (test group)	AB (100) (with Ti-mesh)	ID	5.7	33.3	4.6	13.5	ID	ID	ID	
Louis et al. 2008	44(44)/45	AB (100)	ID	13.7	52.27	6.9	ID	174	ID	100 (17 months)	
Pieri et al. 2008	16(16)/19	AB/ABB (70/30)	4.16 ± 0.59	3.71 ± 1.24	5.3	8-9	ID	44	100	100 (24 months)	
Corinaldesi 2009	13(24)/13 11(24)/14	AB (100) AB (100)	ID ID	5.4 ± 1.81 4.5 ± 1.16	23 7	0 8-9	ID ID	20 36	96.4%. 96.4%.	100 100	
Torres et al. 2010	15(30)/21 (control group)	ABB (100)	3.7 ± 0.6 (6 months)	3.1 ± 0.8 (6 months)	28.5	6	22.6	46	97.3	100	
	15(30)/22 (test group)	ABB (100) + PrP	4.1 ± 0.6 (6 months)	3.5 ± 0.7 (6 months)	0	6	14.3	51	100	100	
Miyamoto et al. 2011	41(41)/50	AB (100)	4.3 ± 2.0	8.1 ± 4.8	36	6	8	87	98	92.8	
Khamees et al. 2012	8(16)/16 (control group)	AB(100)	3.44 ± 0.54	ID	4	ID	43.62	59	ID	ID	
	8(16)/16 (test group)	AB/ABB (50/50)	2.88 ±0.57	ID		ID	36.65		ID	ID	

Note. TS, total specimen; PS, partial specimen; SS, surgical site; ID, insufficient data; ABW, average bone weight gained; ABH, average bone height gained; ME, bone exposure; AB, autologous bone; ABB, bovine bone; MR and IP, time of mesh removed and implant placed; BR, bone resorption under Ti-mesh; Impl, implant number; Surv, implant survival; Success, implant success; * bone block graft; **1 patient subdued with both treatment (control/test)

Table 2. Descriptive statistics.

		ABW	ABH	ME	BR
N	Valid	164	231	331	162
	Missing	167	100	0	169
Mean		4,1468	6,8837	0,2478	0,1828
Median		4,1600	5,4000	0,2300	0,1300
Mode		4,30	8,10	0,36	0,08
Std. Deviation		0,77038	3,78541	0,18100	0,12012
Percentiles	25	3,7000	4,0000	0,0530	0,0800
	50	4,1600	5,4000	0,2300	0,1300
	75	4,3000	8,1000	0,3600	0,2260

Table 3. Descriptive statistics stratified by groups.

		ABW	ABH	ME	BR
AB 100%	N	91	168	229	108
	Mean	4,5197	8,2531	0,2846	0,1522
	Std.Deviation	0,7674	3,5675	0,1903	0,1233
	Std. Error Mean	0,0805	0,2752	0,0126	0,0119
AB/ABB 50/50	N	33	17	56	33
	Mean	3,3952	2,5900	0,1763	0,2556
	Std.Deviation	0,5075	0,0000	0,1238	0,1093
	Std. Error Mean	0,0884	0,0000	0,0126	0,0191
AB/ABB 70/30	N	19	25	25	-
	Mean	4,16	3,7796	0,0403	-
	Std.Deviation	0,0000	0,1264	0,0231	-
	Std. Error Mean	0,0000	0,0253	0,0046	-
ABB 100%	N	21	21	21	21
	Mean	3,7000	3,1000	0,2850	0,2260
	Std.Deviation	0,0000	0,0000	0,0000	0,0000
	Std. Error Mean	0,0000	0,0000	0,0000	0,0000

Table 4. Results overview of the ANOVA test.

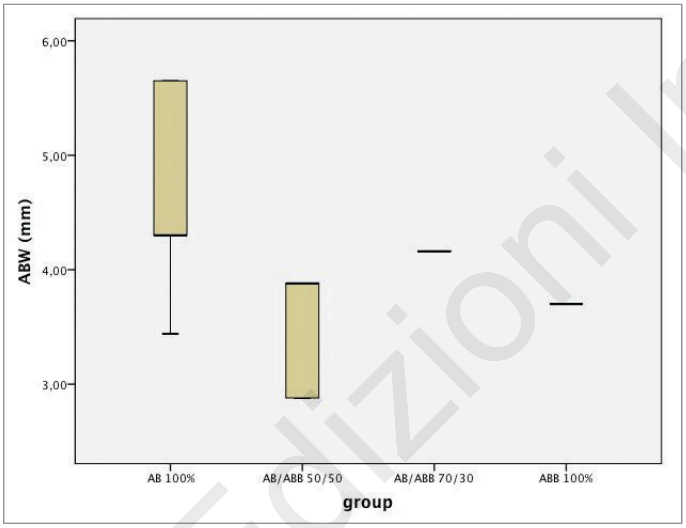
		ANOVA				
		Sum of Squares	df	Mean Square	F	Sig.
ABW	Between Groups	35,492	3	11,831	30,906	< 0,01
	Within Groups	61,247	160	0,383		
	Total	96,739	163			
ABH	Between Groups	1169,981	3	389,994	41,645	< 0,01
	Within Groups	2125,765	227	9,365		
	Total	3295,746	230			
ME	Between Groups	1,701	3	0,567	20,357	< 0,01
	Within Groups	9,110	327	0,028		
	Total	10,812	330			
BR	Between Groups	0,315	2	0,157	12,462	< 0,01
	Within Groups	2,008	159	0,013		
	Total	2,323	161			

Average of bone width gained (ABW)

The highest bone gain was obtained with the use of autologous bone (AB 100%, average: 4.52; sd: 0.77). We observed a statistically significant difference between autologous bone and heterologous (ABB 100%) and the mixture 50:50. The mixture of autologous and heterologous bone in 70:30 ratio to tended to provide better results than the single bone allograft, but the lack of studies in the literature did not allow reaching a significant difference compared to the other groups (mean 4.16, sd: 0.0). The groups AB/ABB 50:50 and ABB 100% showed no significant differences and they were characterised by low bone earning (Tab. 5, Graph. 1).

Table 5. Results of Tukey HSD test for ABW.

Multiple Comparisons TEST TUKEY HSD						
Dependent Variable: ABW						
(I) group	(J) group	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
					Lower Bound	Upper Bound
AB 100%	AB/ABB 50/50	1,12452*	0,12572	< 0,01	0,7981	1,4509
	AB/ABB 70/30	0,35967	0,15606	0,101	-0,0455	0,7648
	ABB 100%	,81967*	0,14978	< 0,01	0,4308	1,2085
AB/ABB 50/50	AB 100%	-1,12452*	0,12572	< 0,01	-1,4509	-0,7981
	AB/ABB 70/30	-,76485*	0,17818	< 0,01	-1,2274	-0,3023
	ABB 100%	-0,30485	0,17271	0,294	-0,7532	0,1435
AB/ABB 70/30	AB 100%	-0,35967	0,15606	0,101	-0,7648	0,0455
	AB/ABB 50/50	,76485*	0,17818	< 0,01	0,3023	1,2274
	ABB 100%	0,46000	0,19590	0,092	-0,0486	0,9686
ABB100%	AB 100%	-,81967*	0,14978	< 0,01	-1,2085	-0,4308
	AB/ABB 50/50	0,30485	0,17271	0,294	-0,1435	0,7532
	AB/ABB 70/30	-0,46000	0,19590	0,092	-0,9686	0,0486



Graphic 1. Box Plot for ABW.

Average of bone height gained (ABH)

In this case, only the use of autologous bone was associated with a marrow gain bigger than with all other types of grafts. Even in this case, the group AB/ABB 70:30 seemed to lead to a similar gain to AB 100%, but the lack of sufficient data did not allow reaching a statistical difference compared to heterologous and autologous bone mixed. There were no significant differences comparing AB/ABB 70/30, AB/ABB 50/50 and ABB 100% (Tab. 6, Graph. 2).

Mesh exposition (ME)

The data revealed a bigger exposure of the mesh in groups AB 100% and ABB 100%, with a significant difference when compared to both other groups.

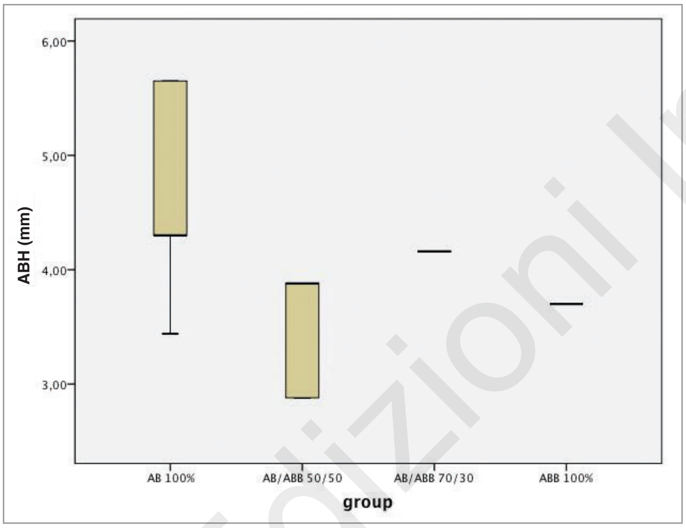
It must be noted the prevalence of studies that used autologous bone alone compared to others, which produced a large variance in the first group (mean: 0.28; sd: 0.19) (Tab. 7, Graph. 3).

Bone resorption

At the removal of the titanium mesh, which occurred after 4 to 6 months, the use of autologous bone led to a percentage of bone resorption lower than the other groups (mean 0.15; sd : 0.12). No data were available concerning the use of AB/ABB 70:30 (Tab. 8, Graph. 4).
Finally, the use of autologous bone was associated with a height and width gain of bone greater than other techniques, with a lower exposure of the mesh and a lower bone resorption.

Table 6. Results of Tukey HSD test for ABH.

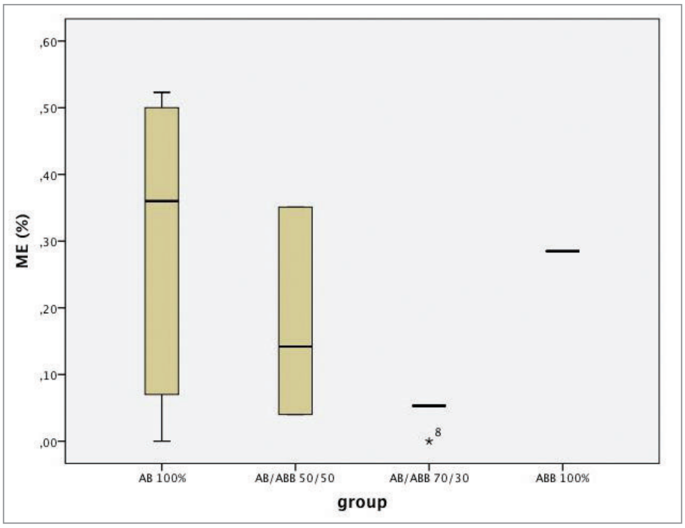
Multiple Comparisons						
Dependent Variable: ABH						
(I) group	(J) group	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
					Lower	Upper
AB 100%	AB/ABB 50/50	5,66310*	0,77885	< 0,01	3,6473	7,6789
	AB/ABB 70/30	4,47350*	0,65599	< 0,01	2,7757	6,1713
	ABB 100%	5,15310*	0,70829	< 0,01	3,3199	6,9863
AB/ABB 50/50	AB 100%	-5,66310*	0,77885	< 0,01	-7,6789	-3,6473
	AB/ABB 70/30	-1,18960	0,96200	0,604	-3,6794	1,3002
	ABB 100%	-0,51000	0,99840	0,956	-3,0940	2,0740
AB/ABB 70/30	AB 100%	-4,47350*	0,65599	< 0,01	-6,1713	-2,7757
	AB/ABB 50/50	1,18960	0,96200	0,604	-1,3002	3,6794
	ABB 100%	0,67960	0,90582	0,876	-1,6648	3,0240
ABB100%	AB 100%	-5,15310*	0,70829	< 0,01	-6,9863	-3,3199
	AB/ABB 50/50	0,51000	0,99840	0,956	-2,0740	3,0940
	AB/ABB 70/30	-0,67960	0,90582	0,876	-3,0240	1,6648



Graphic 2. Box Plot for ABH.

Table 7. Results of Tukey HSD test for ME.

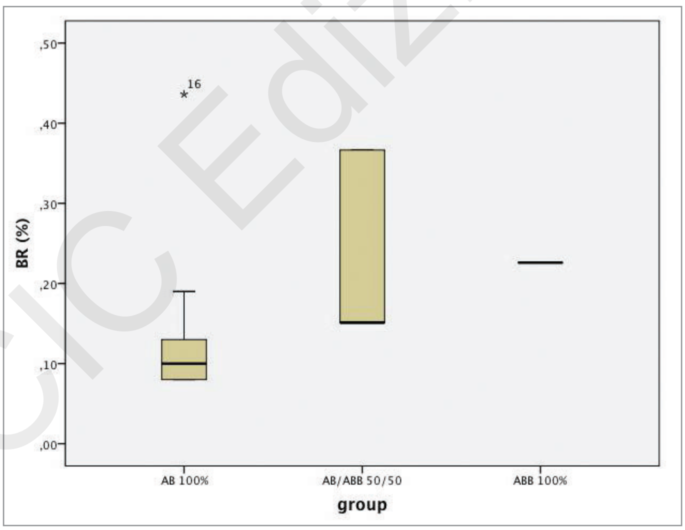
Multiple Comparisons						
Dependent Variable: ME						
(I) group	(J) group	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
					Lower	Upper
AB 100%	AB/ABB 50/50	,10826*	0,02488	< 0,01	0,0440	0,1725
	AB/ABB 70/30	,24428*	0,03516	< 0,01	0,1535	0,3351
	ABB 100%	-0,00044	0,03806	1,000	-0,0987	0,0978
AB/ABB 50/50	AB 100%	-,10826*	0,02488	< 0,01	-0,1725	-0,0440
	AB/ABB 70/30	,13602*	0,04015	0,004	0,0323	0,2397
	ABB 100%	-0,10870	0,04271	0,055	-0,2190	0,0016
AB/ABB 70/30	AB 100%	-,24428*	0,03516	< 0,01	-0,3351	-0,1535
	AB/ABB 50/50	-,13602*	0,04015	0,004	-0,2397	-0,0323
	ABB 100%	-,24472*	0,04941	< 0,01	-0,3723	-0,1171
ABB100%	AB 100%	0,00044	0,03806	1,000	-0,0978	0,0987
	AB/ABB 50/50	0,10870	0,04271	0,055	-0,0016	0,2190
	AB/ABB 70/30	,24472*	0,04941	< 0,01	0,1171	0,3723



Graphic 3. Box Plot for ME.

Table 8. Results of Tukey HSD test for BR.

Multiple Comparisons TEST TUKEY HSD						
Dependent Variable: BR						
(I) group	(J) group	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
					Lower	Upper
AB 100%	AB/ABB 50/50	-,10332*	0,02235	< 0,01	-0,1562	-0,0504
	ABB 100%	-,07379*	0,02680	0,018	-0,1372	-0,0104
AB/ABB 50/50	AB 100%	,10332*	0,02235	< 0,01	0,0504	0,1562
	ABB 100%	0,02954	0,03137	0,615	-0,0447	0,1038
ABB 100%	AB 100%	,07379*	0,02680	0,018	0,0104	0,1372
	AB/ABB 50/50	-0,02954	0,03137	0,615	-0,1038	0,0447



Graphic 4. Box Plot for BR.

The use of heterologous graft led to a lower bone earned and a greater percentage of resorption than autologous graft but did not differ from the gain and resorption of the bone of grafts of mixed quality.

Discussion

Initial studies with GBR TiMesh technique using autologous bone (Boyne) had shown satisfactory re-

sults (Tab. 1). However, the use of autologous bone is limited by its related mobility and limited availability of intraoral bone harvesting. Recent studies (25,28, 36,37) proposed the combination of autologous bone with ABB (in different percentages) to reduce the need to withdraw the autogenous bone from the patient (33). Maiorana et al. (25) found that after two weeks from AB/ABB 50:50 graft, osteoid cells surround the particles of ABB, resulting in the formation of initial immature bone. The process continues and a new line of osteoblasts appears on the primary mineral structure, bringing a connection to the particles of ABB. After six weeks, the new bone tissue leads to a stabilization (39). The histological samples taken six months before implant placement show that the ABB particles are surrounded and interconnected by newly formed bone, which continues to reshape (40-42).
After one year at least 91% of the surface of ABB was covered with new bone (38). The positive results encouraged related clinical trials on the potential of ABB 100% in the GBR with Ti-Mesh. Torres et al. (33) showed that ABB is a predictable material, with a low incidence of complications, able to achieve similar results to autologous bone. Then, the use of ABB graft was related to a high dimensional stability during the two years of follow-up. This is due to the combination of biocompatibility, osteoconduction and low resorption *in vivo* (43,44). There are controversial opinions regarding the use of ABB as onlay graft. Skoglund et al. (45) and Proussaef et al. (36,37) provided histological evidence in humans regarding the potential for ABB used as onlay graft in combination with intramembranous bone graft. On the contrary, Pinholt et al. (46) and Young et al. (47), found no bone formation around the particles of ABB when it was used as a onlay graft.

Conclusion

When ABB is associated with an autologous graft, as shown by several studies (9,26,28, 29,38), formation of new bone is observed. ABB acts as a scaffold for new bone formation. From our review we found that the autologous 100% bone graft is still related to a height and width gain of bone greater than the others, together with a lower exposure of the mesh and a lower bone resorption. The 100% anorganic bovine bone is confirmed being a valid substitute due to its osteoconductive properties. However, these surveys found a bone gain and a percentage of resorption greater than autologous graft. As shown in the literature, the values of the parameters evaluated in the bone autograft and allograft AB/ABB 50:50 and AB/ABB 70:30 do not deviate from the bone gain and bone resorption compared to autologous bone (100%). The osteogenic potential that characterizes AB seems to improve bone formation around the particles of ABB. Due to its intrinsic properties (osteosynthesis, osteoinductivity and osteoconductivity), autogenous bone graft material remains the *gold standard* in the regeneration of horizontal or vertical bone with TiMesh (48-51), but the increased morbidity associated with the donor site have reduced its usage. Further studies with the same parameters are needed to evaluate the role of allograft materials used alone or with different percentages of autologous bone (38).

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