Review

Acellular Dermal Matrix for Mucogingival Surgery: A Meta-Analysis

Ricardo Gapski,* Christopher Allen Parks,* and Hom-Lay Wang†

Background: Many clinical studies revealed the effectiveness of acellular dermal matrix (ADM) in the treatment of mucogingival defects. The purpose of this meta-analysis was to compare the efficacy of ADM-based root coverage (RC) and ADM-based increase in keratinized tissues to other commonly used mucogingival surgeries.

Methods: Meta-analysis was limited to randomized clinical trials (RCT). Articles from January 1, 1990 to October 2004 related to ADM were searched utilizing the MEDLINE database from the National Library of Medicine, the Cochrane Oral Health Group Specialized Trials Registry, and through hand searches of reviews and recent journals. Relevant studies were identified, ranked independently, and mean data from each were weighted accordingly. Selected outcomes were analyzed using a meta-analysis software program. The significant estimates of the treatment effects from different trials were assessed by means of Cochrane's test of heterogeneity.

Results: 1) Few RCT studies were found to compile the data. In summary, selection identified eight RCT that met the inclusion criteria. There were four studies comparing ADM versus a connective tissue graft for root coverage procedures, two studies comparing ADM versus coronally advanced flap (CAF) for root coverage procedures, and two studies comparing ADM to free gingival graft in augmentation of keratinized tissue. 2) There were no statistically significant differences between groups for any of the outcomes measured (recession coverage, keratinized tissue formation, probing depths, and clinical attachment levels). 3) The majority of the analyses demonstrated moderate to high levels of heterogeneity. 4) Considering the heterogeneity values found among the studies, certain trends could be found: a) three out of four studies favored the ADM-RC group for recession coverage; b) a connective tissue graft tended to increase keratinized tissue compared to ADM (0.52-mm difference; $P = 0.11$); c) there were trends of increased clinical attachment gains comparing ADM to CAF procedures (0.56-mm difference; $P = 0.16$).

Conclusions: Differences in study design and lack of data precluded an adequate and complete pooling of data for a more comprehensive analysis. Therefore, considering the trends presented in this study, there is a need for further randomized clinical studies of ADM procedures in comparison to common mucogingival surgical procedures to confirm our findings. It is difficult to draw anything other than tentative conclusions from this meta-analysis of ADM for mucogingival surgery, primarily because of the weakness in the design and reporting of existing trials. *J Periodontol 2005;76:1814-1822.*

KEY WORDS

Alloderm; gingival recession; meta-analysis; tissues.

* Department of Periodontics, School of Dentistry, University of Missouri, Kansas City, MO.
† Department of Periodontics/Prevention/Geriatrics, School of Dentistry, University of Michigan, Ann Arbor, MI.

In recent decades, several surgical procedures have been proposed for the treatment of gingival recession and to increase the width of attached gingiva. These surgical procedures include pedicle soft tissue flaps, autogenous free soft tissue grafts, combination free/pedicle soft tissue grafts for treatment of recession and periosteal retention, denudation procedures, and free gingival grafts for gain in the width of keratinized gingiva (KG).[1-9] Research has demonstrated superior esthetics and predictable outcomes in treating gingival recession in terms of the percentage of root coverage (RC) when a free autogenous connective tissue graft (CTG) is utilized,[10] while a free gingival graft (FGG) remains the chosen method in augmenting the zone of keratinized gingiva.[11,12]

The disadvantages of harvesting free autogenous soft tissue grafts lie in the postoperative discomfort associated with an extra surgical site, as well as the limitations of available donor tissue. Consequently, several non-vital allograft alternatives have been introduced. These include a preserved sclera tissue

Table 1.

Characteristics of Included Studies

Reference	Defect Type	N Subjects	N Defects	Examiner Masked?	Randomization Method Described?	SS at Baseline	Intervention	
							Test	Control
ADM-based root coverage versus CTG								
Aichelmann-Reidy et al.[35]	Miller I-II	22	44	Yes	Yes	No	ADM-RC	CTG
Novaes et al.[41]	Miller I-II	9	30	Unclear	Unclear	No	ADM-RC	CTG
Tal et al.[42]	Miller I-II	7	14	Yes	Yes	No	ADM-RC	CTG
Barros et al.[40]	Miller I-II	14	32	Unclear	Unclear	No	ADM-RC	CTG
ADM-based root coverage versus CAF								
Woodyard et al.[27]	Miller I-II	24	24	Yes	Yes	Unclear	ADM-RC	CAF
Cortes et al.[43]	Miller I	13	26	Unclear	Unclear	No	ADM-RC	CAF
ADM-based augmentation of KG versus FGG								
Wei et al.[29]	NA	12	12	Yes	Unclear	Unclear	ADM-KG	FGG
Harris[34]	NA	30	30	No	Unclear	No	ADM-KG	FGG

SS = statistically significant; NA = not applicable; ADM-KG = acellular dermal matrix for increasing keratinized gingiva.

graft,[13,14] lyophilized homologous dura mater,[15-17] and absorbable and non-absorbable membranes.[18-21]

Recently, an acellular dermal matrix (ADM) allograft‡ was approved as a substitute for autogenous grafts in mucogingival surgeries. The preparation of this dermal allograft involves cell component removal and preservation of the ultrastructural integrity, which if damaged would induce an inflammatory response.[22-24] ADM was originally utilized for use in plastic surgery for the treatment of full-thickness burn wounds.[22] Over the last few years, several studies have evaluated the effect of ADM for mucogingival surgery with promising results.[25-40] Overall, most ADM studies included a small sample size that lacked sufficient statistical power to draw conclusions regarding the efficacy of ADM. Therefore, the aim of this present investigation was to perform a meta-analysis of the available literature to evaluate 1) the efficacy of ADM tissue on percent root coverage and changes in CAL and PD versus coronally advanced flap (CAF) and CTG and 2) the efficacy of ADM in gaining KG versus FGG and CTG. The null hypothesis is that there is no statistical difference in treating patients with ADM as compared to traditional surgical modalities. Hence, the focused question was as follows: In patients with gingival recessions and/or lacking keratinized tissue, is there a benefit in treating the patient with acellular dermal matrix as compared to traditional treatment modalities in regards to relevant clinical parameters?

MATERIALS AND METHODS

Search Strategy

Three data sources were utilized for this review: 1) the MEDLINE database from the National Library of Medicine using the Ovid interface; 2) Cochrane Oral Health Group Specialized Trials Registry (The Cochrane Library); and 3) hand searching of specific journals including the *International Journal of Periodontics & Restorative Dentistry, Journal of Clinical Periodontology, Journal of Periodontology, Journal of Periodontal Research*, and bibliographies of review and investigational papers. No attempt was made to contact researchers in this field to obtain original data or fugitive literature (e.g., unpublished studies). Articles from January 1, 1990 to October 2004 were prescreened using the following key words (italics): *acellular human matrix* OR *acellular dermal matrix allograft* OR *dermal matrix allograft* OR *Alloderm* OR *root coverage* OR *keratinized gingiva* OR *gingival recession* OR *soft tissue* OR *tooth root surgery* OR *grafts* OR *surgical flaps*. Titles and abstracts of studies identified according to the inclusion criteria were then screened independently by the reviewers. Selected full-text studies were subsequently evaluated independently by the same reviewers using the same criteria.

Inclusion Criteria

The following inclusion criteria were applied: 1) published in English; 2) 3 months of duration to ensure

‡ Alloderm, Life Cell Corporation, The Woodlands, TX.

Table 2.

Mean and Standard Deviation From the Included Studies

Reference	Evaluation Time	Groups	Root Coverage			PD		
			BL	End	Δ	BL	End	Δ
Aichelmann-Reidy et al.[35]	6 months	ADM	2.5 ± 0.8	0.8 ± 1.0	1.7 ± 1.2	1.1 ± 1.0	1.3 ± 1.0	0.2 ± 1.0
		CTG	3.0 ± 0.7	0.8 ± 1.1	2.2 ± 1.1	1.1 ± 0.8	1.7 ± 1.2	0.6 ± 1.0
Barros et al.[40]	6 months	ADM	3.9 ± 0.87	0.9 ± 0.64	3.6 ±.6.04	1.6 ± 0.51	1.3 ± 0.45	–0.2 ± 0.54
		CTG	3.4 ± 0.94	1.3 ± 0.7	2.1 ± 0.97	1.6 ± 0.51	1.5 ± 0.50	–0.1 ± 0.66
Novaes et al.[41]	6 months	ADM	3.23 ± 1.08	1.13 ± 1.08	2.10 ± 1.00	1.29 ± 0.57	1.43 ± 0.37	0.13 ± 0.60
		CTG	2.97 ± 0.81	1.13 ± 1.06	1.83 ± 0.83	1.52 ± 0.47	1.43 ± 0.58	–0.09 ± 0.75
Tal et al.[42]	12 months	ADM	5.14 ± 0.9*	0.57 ± 0.6*	4.57 ± 0.9*	1.64 ± 0.2*	1.86 ± 0.5*	0.22 ± 0.3*
		CTG	4.86 ± 0.9*	0.57 ± 0.5*	4.29 ± 0.9*	1.50 ± 0.5*	1.50 ± 0.2*	0.0 ±.4 01*
Cortes et al.[43]	6 months	ADM	3.46 ± 0.85	0.88 ± 0.89	2.58 ± 0.67	1.27 ± 0.44	1.73 ± 0.39	0.46 ± 0.56
		CAF	3.58 ± 0.57	1.08 ± 0.84	2.50 ± 0.64	1.27 ± 0.33	1.85 ± 0.43	0.58 ± 0.57
Woodyard et al.[27]	6 months	ADM	3.46 ± 0.89	0.04 ± 0.14	3.42 ± 0.93	1.42 ± 0.51	1.17 ± 0.39	–0.25 ± 0.62
		CAF	3.27 ± 0.56	1.08 ± 0.90	2.19 ± 0.95	1.67 ± 0.65	1.17 ± 0.39	–0.50 ± 0.90
Harris[34]	3 months	ADM	ND	ND	ND	ND	ND	ND
		FGG	ND	ND	ND	ND	ND	ND
Wei et al.[29]	6 months	ADM	2.52 ± 1.98	2.75 ± 2.02	–0.23 ± 2.8‡	1.26 ± 0.3	1.05 ± 0.15	–0.21 ± 0.3‡
		FGG	1.76 ± 1.49	1.86 ± 1.41	–0.1 ± 1.8‡	1.01 ± 0.03	1.27 ± 0.2	–0.26 ± 0.2‡

* SD values calculated from patient data.
† CAL + SD calculated from given individual patient data.
‡ SD calculated from the square root of the sum of the variances of the measures (assuming the covariance between therapies was zero).
KT = keratinized tissue; BL = baseline; ND = no data could be retrieved.

that the follow-up of the patients were sufficiently long; 3) randomized controlled clinical trials; and 4) studies from January 1, 1990 to October 2004. Multiple reports utilizing the same database or population were identified, and only data from the most recent report was used. Control groups were only included if they were CAF or CTG for root coverage procedures or FGG and CTG for increasing the amount of keratinized tissue. When comparisons were utilized between ADM-based root coverage, only Miller Class I and/or II were included in the analysis. Another inclusion criterion was studies that assessed systemically healthy adult patients. Studies were not excluded on the basis of quality, only whether they fulfilled the inclusion criteria for entry.

Type of Intervention and Outcomes Measured

The intervention of interest was mucogingival surgery for root coverage or augmentation of keratinized tissue. The primary outcomes selected for this analysis were the amount of root coverage and changes in the width of keratinized tissue, while secondary outcomes included changes in clinical attachment levels (CAL) and probing depths (PD).

Validity Assessment

Titles and abstracts were screened for possible relevance by the investigators. For all studies of possible relevance, the full text was retrieved. Two reviewers (CAP and RG) independently extracted data from all primary studies fulfilling eligibility criteria. Any discrepancies in extracted data were resolved by consensus; the K-score for agreement was 0.78. Data extracted included the focus of the study, details of study protocol, demographic data, and reported outcomes. Studies were evaluated for randomization, masking, inclusion of control comparisons, and differences in baseline measurements.

Data Collection and Statistical Analysis

Study grouping was based on therapeutic modalities investigated, outcomes measured, and the quality of studies. For the studies that could be included in the meta-analysis, a weighted treatment effect was calculated, and the results were expressed as weighted mean differences (WMD and 95% confidence intervals [CI]) for continuous outcomes. Some of the studies did not report the standard deviation of the mean difference. In this case, the equation for the SD of

Table 2. (continued)

Mean and Standard Deviation From the Included Studies

CAL			KT		
BL	End	Δ	BL	End	Δ
3.6 ± 0.9 4.1 ± 0.8	2.1 ± 1.0 2.5 ± 1.3	1.5 ± 1.1 1.6 ± 1.1	1.7 ± 0.7 1.8 ± 1.2	2.9 ± 1.2 3.5 ± 1.2	1.2 ± 1.3 1.6 ± 1.9
14.1 ± 1.71 14.3 ± 1.60	12.5 ± 1.39 12.8 ± 1.40	1.6 ± 0.98 1.4 ± 0.96	2.0 ± 1.16 2.2 ± 1.53	3.0 ± 1.12 3.0 ± 1.59	1.0 ± 1.04 0.8 ± 0.75
7.51 ± 1.98 7.55 ± 1.33	6.69 ± 1.42 6.63 ± 1.19	0.81 ± 0.93 0.92 ± 1.23	2.60 ± 0.98 2.46 ± 1.30	3.23 ± 1.45 3.73 ± 1.1	0.63 ± 0.85 1.26 ± 0.88
6.86 ± 0.90† 6.36 ± 1.18†	1.86 ± 0.56† 1.50 ± 0.29†	2.43 ± 0.79† 2.07 ± 0.45†	2.29 ± 0.49* 2.0 ± 0.82*	3.14 ± 0.9* 4.14 ± 0.3*	0.86 ± 0.6* 2.14 ± 0.6*
4.73 ± 0.81 4.85 ± 0.62	2.61 ± 0.74 2.92 ± 0.95	2.11 ± 1.04 1.92 ± 0.93	3.15 ± 0.75 2.73 ± 0.78	3.85 ± 0.75 3.19 ± 0.75	0.69 ± 0.83 0.46 ± 0.63
4.88 ± 0.86 4.94 ± 0.81	1.21 ± 0.40 2.25 ± 1.14	3.67 ± 0.75 2.69 ± 1.32	1.79 ± 1.27 1.54 ± 1.16	2.6 ± 1.02 1.88 ± 0.93	0.81 ± 0.96 0.33 ± 1.05
ND ND	ND ND	ND ND	0.6 ± 0.87 0.8 ± 0.59	4.7 ± 1.92 4.8 ± 1.16	4.1 ± 1.79 4.1 ± 1.25
ND ND	ND ND	ND ND	0.68 ± 0.26 0.57 ± 0.41	3.25 ± 0.89 6.15 ± 0.49	2.59 ± 0.92 5.57 ± 0.44

* SD values calculated from patient data.
† CAL + SD calculated from given individual patient data.
‡ SD calculated from the square root of the sum of the variances of the measures (assuming the covariance between therapies was zero).
KT = keratinized tissue; BL = baseline; ND = no data could be retrieved.

the difference was calculated from the square root of the sum of the variances of the measures, minus the covariance of the measurements. In determining the standard deviation of the difference between groups, the conservative assumption was made that the covariance between therapies was zero. Then, primary and secondary outcomes were analyzed.§ The significant estimates of the treatment effects from different trials were assessed by means of Cochrane's test of heterogeneity.

RESULTS

Details of Included Studies

The initial application of described search strategies resulted in the identification of 105 publications. Further screening by the primary reviewer identified 40 articles appropriate for full review by both reviewers. Of these 40 articles, eight studies were selected based on the criteria for inclusion. The most common reason for study exclusion was the lack of a control group, lack of randomization, or lack of outcome measured. In summary, four studies were eligible for comparisons between ADM-based root coverage and CTG,[35,40-42] two for comparisons between ADM-based root coverage and CAF[27,43] and two for comparisons between ADM-based augmentation of KG and FGG.[29,34] For all these subgroups, the groups were treated equally apart from the experimental therapy. The characteristics of the included studies are shown in Tables 1 and 2.

Quality Assessment of Studies

The evaluation of the quality of the included studies was impaired due to the failure of many reports to provide sufficient information allowing for accurate assessment. Four of the eight studies reported masked examiners,[27,29,35,42] while three studies did not report information regarding masking.[40,41,43] One study was unmasked.[34] Only randomized studies were included for the analysis. Methods of randomization for these studies varied. Five of the eight studies failed to report the method of randomization,[27,29,34,40,41] while three studies presented appropriate randomization mechanisms.[27,35,42] Among all

§ Revman Metaview, Cochrane Collaboration, Oxford, U.K.

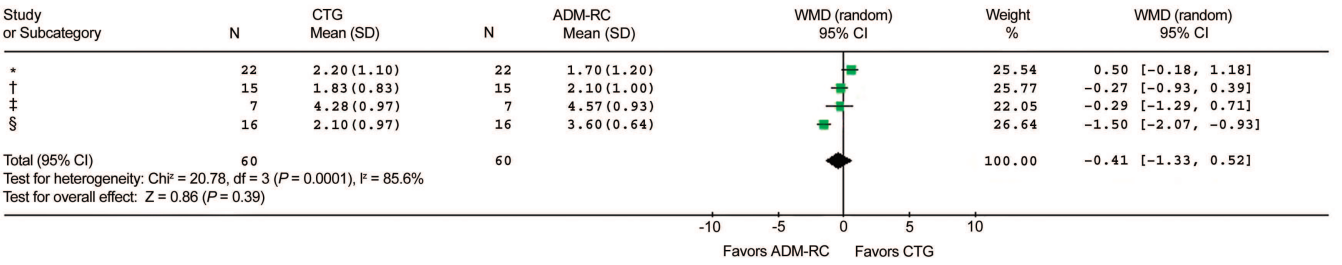

Figure 1.
*Meta-analysis of recession coverage comparing ADM versus connective tissue grafting procedures. *Aichelmann-Reidy et al.[35]; †Novaes et al.[41]; ‡Tal et al.[42]; §Barros et al.[40]*

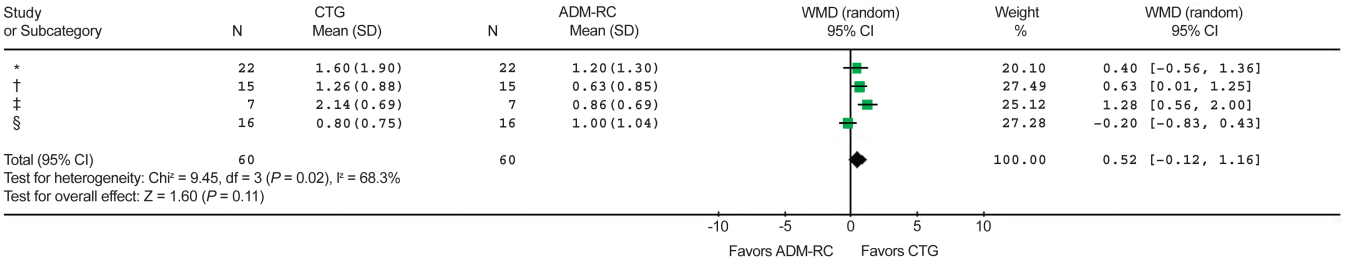

Figure 2.
*Meta-analysis of keratinized tissue augmentation comparing ADM versus connective tissue grafting procedures. *Aichelmann-Reidy et al.[35]; †Novaes et al.[41]; ‡Tal et al.[42]; §Barros et al.[40]*

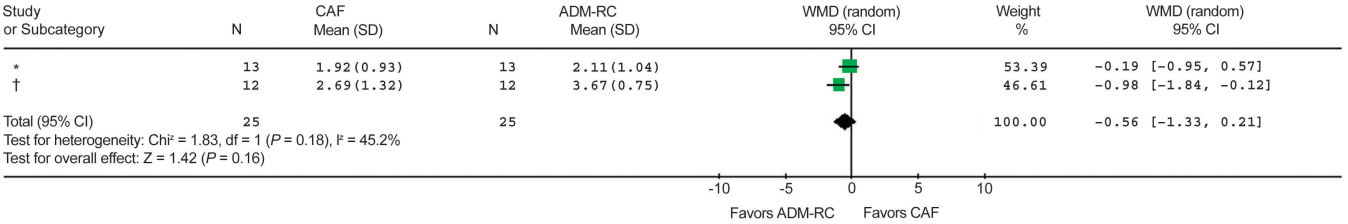

Figure 3.
*Meta-analysis of clinical attachment levels comparing ADM versus coronally advanced flap procedures. *Cortes et al.[43]; †Woodyard et al.[27]*

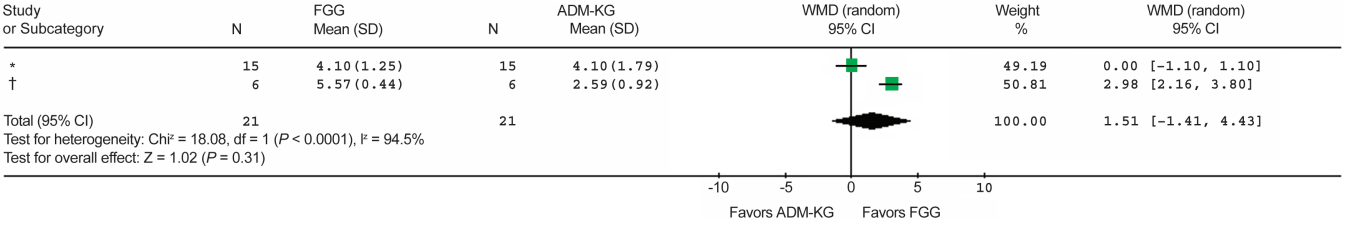

Figure 4.
*Meta-analysis of keratinized tissue augmentation comparing ADM versus free gingival grafting procedures. *Harris[34]; †Wei et al.[29]*

the included studies, two did not report comparisons between groups at baseline,[27,29] while the remaining investigations found no statistically significant (NS) differences between groups at baseline for any of the studied parameters.[27,29,34,35,40-43]

ADM-Based Root Coverage Versus Connective Tissue Graft

The results of four studies that compared ADM versus CTG totalized 60 sites for the ADM group and 60 sites for the CTG group. The combined data indicated no statistically significant differences between groups in terms of recession coverage (0.41 mm favoring ADM-RC; test for overall effect, $P = 0.39$ and 95% CI [–1.33, 0.52]; chi-square for heterogeneity, 20.78 [df = 3], $P = 0.0001$, and $I^2 = 85.6\%$). Considering the high heterogeneity values among the studies, it is interesting to note that three out of four studies favored the ADM-RC group (Fig. 1). Changes in probing depths were minimal for all studies, with a mean increase of 0.02 mm (not significant; test for overall effect, $P = 0.89$ and 95% CI [–0.28, 0.24]; chi-square for heterogeneity, 3.78 [df = 3], $P = 0.29$, and $I^2 = 20.6\%$), and may be reflective of the shallow mean probing depths at baseline. In addition, CTG groups had trends of increased keratinized tissue compared to the ADM-RC group. The differences were not statistically significant by random effect meta-analysis (0.52 mm favoring CTG; test for overall effect, $P = 0.11$ and 95% CI [–0.12, 1.16]; chi-square for heterogeneity, 9.45 [df = 3], $P = 0.02$, and $I^2 = 20.6\%$) (Fig. 2). Reports of clinical attachment levels were not analyzed due to possible errors in CAL calculations found in two out of the four studies.[40,41]

ADM-Based Root Coverage Versus Coronally Advanced Flap

The results of four studies that compared ADM-RC versus CAF totaled 25 sites for the ADM group and 25 sites for the CTG group. The results revealed no statistically significant differences between groups in terms of recession coverage (0.62 mm favoring ADM-RC; test for overall effect, $P = 0.28$ and 95% CI [–0.74, 0.51]; chi-square for heterogeneity, 6.20 [df = 1], $P = 0.01$, and $I^2 = 83.6\%$), probing depths (0.00 mm; test for overall effect, $P = 0.99$ and 95% CI [–0.36, 0.35]; chi-square for heterogeneity, 0.92 [df = 1], $P = 0.34$, and $I^2 = 0\%$), or clinical attachment levels (0.56 mm favoring ADM-RC; test for overall effect, $P = 0.16$ and 95% CI [–1.33, 0.21]; chi-square for heterogeneity, 1.83 [df = 1], $P = 0.18$, and $I^2 = 45.2\%$) (Fig. 3). In addition, two out of two studies favored ADM-RC in augmentation of keratinized tissue (0.31-mm difference), but the results were not statistically significant (test for overall effect, $P = 0.19$ and 95% CI [–0.78, 0.15]; chi-square for heterogeneity 0.25 [df = 1], $P = 0.62$, and $I^2 = 0\%$).

ADM-Based Increase in Keratinized Tissue Versus Free Gingival Graft

The results of two randomized clinical trials[29,34] that compared ADM versus FGG for an increase in KG are summarized in Figure 4. One study did not report PD and CAL changes[34]; therefore, only KG changes were included in this analysis. There were a total of 21 grafts for the ADM group and 21 grafts for the FGG group. The results demonstrated no statistically significant differences between groups and high levels of heterogeneity among studies (1.51 mm favoring FGG; test for overall effect, $P = 0.31$ and 95% CI [–1.41, 4.43]; chi-square for heterogeneity, 18.08 [df = 1], $P < 0.0001$, and $I^2 = 94.5\%$).

DISCUSSION

Acellular dermal matrix allograft is processed from human donor skin obtained from approved tissue banks. The donor tissue is prepared by removing the epidermis and cellular components of the skin.[24] The remaining dermal layer is washed in detergent solutions to inactivate viruses and reduce rejection. The remaining acellular collagen matrix is then cryoprotected and rapidly freeze-dried in a proprietary process to preserve the biochemical and structural integrity. ADM became widely utilized in the grafting of burn patients during the 1990s.[23] The medical community has expanded its use to include tympanic membrane reconstruction,[44] nasal reconstruction,[45] treatment of dermal atrophy,[46] repair of fistulae,[47] and facial esthetic plastic surgery applications.[48,49] Shulman[50] was the first author to document the use of ADM in dentistry. Intraorally, ADM has since been utilized in a wide range of dental applications such as soft tissue augmentation,[51] augmentation of keratinized gingiva,[29] as a barrier membrane,[52] as a soft tissue grafting material to cover amalgam tattoos, and for root coverage procedures. The focused question of this meta-analysis was as follows: In patients with gingival recessions and/or lacking keratinized tissue, is there a benefit in treating the patient with acellular dermal matrix as compared to traditional treatment modalities in regards to relevant clinical parameters?

This meta-analysis did not demonstrate differences between ADM versus CTG and ADM versus CAF for recession coverage. In fact, the analysis for recession coverage between ADM and CTG indicated statistical heterogeneity, whereas a glance at the forest plot (Fig. 1) demonstrated that three out of four studies had outcomes that favored acellular dermal matrix procedures. It must be emphasized that the studies included in the analysis were short-term in nature (≤12 months). It has been recently demonstrated that ADM-based root coverage has broken down over the long-term

(4 years) as compared to short-term results (4 months).[26] This study has found a statistical superiority of connective tissue graft compared to ADM at 4 years but not at 4 months. The selected publications utilized in this meta-analysis have not reached the possible breakdown effect of ADM yet, reporting comparable results to CTG. More importantly, due to the small number of studies included in this meta-analysis, the validity of drawing conclusions about the efficacy of ADM for root coverage in comparison to other common mucogingival surgeries from the available data is questionable. It also remains difficult to speculate how the inclusion of more randomized studies and longer-term data would affect the results. Researchers should consider extended data rather than the standard 6 to 12 months performed in mucogingival surgery to investigate the possible instability of ADM.

With regards to augmentation of KG, the result obtained from this meta-analysis showed trends of more keratinized tissue formation in CTG compared to ADM (not significant). Similar but smaller trends were also noted between ADM and FGG. Histological characteristics of ADM and its healing process may explain the lack of keratinization. Karring et al.[53] suggested that the genotype of underlying connective tissue would determine the characterization of the epithelium. In this investigation, the autogenous connective tissue originated from the keratinized gingiva and was placed onto non-keratinized alveolar mucosa, which subsequently gained the keratinized features of the gingiva[53]; based on the results of this study, that could be speculated as a possible mechanism for the lack of KG seen in ADM-treated sites. Histological data has demonstrated an inflammatory response within the grafted tissue that resembles a foreign body reaction.[30] Furthermore, the resultant tissue types of ADM were similar to ''scar'' tissue.[30] Therefore, the transplantation of a non-vital graft originating from a genetically different individual and genetically different epithelium (dermis) may lack the inherent ability to direct differentiation of the surface oral epithelium. The process of remodeling to generate the scar-like tissue may also lead to wound contracture. One study found that ADM showed significantly greater shrinkage than FGG treated sites 6 months after graft placement (71% versus 16%).[29] Further randomized clinical trials are necessary to unravel this possible phenomenon.

The purpose of a meta-analysis is to help understand and quantify sources of variability in results across studies. It is important to note that a bias may be introduced in the selection of articles in any meta-analysis. The predetermined inclusion and exclusion criteria of this study resulted in the utilization of a small percentage of the total number of studies available (eight out of 40). The most common reason for exclusion among studies was the lack of randomization and lack of data required for analysis. Many other studies were also mainly descriptive in nature and did not report the parameters required based on the inclusion criteria. It is also unknown how many studies were excluded for being reported in other languages and how they would impact the data. Even considering all the including and excluding factors, it must be emphasized that the majority of the analyses demonstrated moderate to high statistical heterogeneity values, indicating that there are sufficient differences between the studies that were compiled for this analysis. Therefore, this means that differences between treatment groups or trends toward one therapy should be interpreted with extreme caution. This limits the applicability of this study, and the clinical significance of these findings may be limited at best. There are a number of suggestions that may be made as a result of this review, the majority of which are based on the quality of reporting of clinical trials. Researchers may consider: 1) performing randomized controlled trials involving ADM comparing to other mucogingival procedures, 2) stating the method of randomization, 3) calculating a sample size, 4) stating clear inclusion and exclusion criteria of patients, 5) attempting to make studies single-masked, and 6) utilizing longer-term data (more than 12 months).

CONCLUSIONS

Within the limitations of this study, ADM-based mucogingival surgery can be used successfully to repair gingival recession defects and to increase keratinized gingiva. Despite all the trends presented in this study, differences in study design and lack of data precluded an adequate and complete pooling of data for a more comprehensive analysis. In summary, it is difficult to draw anything other than tentative conclusions from this systematic review of ADM for mucogingival surgery, primarily because of weaknesses in the design and reporting of existing trials.

ACKNOWLEDGMENTS

The authors would like to thank Dr. Philip Feil, the chair of Dental Public Health and Behavioral Science of the University of Missouri, Kansas City, and Dr. Daniel Tira for their review of the statistical methods.

REFERENCES

1. Björn H. Free transplantation of gingiva propria. *Swed Dent J* 1963;22:648-689.
2. Cohen DW, Ross SE. The double papillae repositioned flap in periodontal therapy. *J Periodontol* 1968;39: 65-70.

3. Edel A. Clinical evaluation of free connective tissue grafts used to increase the width of keratinised gingiva. *J Clin Periodontol* 1974;1:185-196.
4. Grupe HE, Warren RF. Repair of gingival defects by a sliding flap operation. *J Periodontol* 1956;27: 92-95.
5. Pennel BM, Higgason JD, Towner JD, et al. Oblique rotated flap. *J Periodontol* 1965;36:305-309.
6. Langer B, Langer L. Subepithelial connective tissue graft technique for root coverage. *J Periodontol* 1985; 56:715-720.
7. Karring T, Cumming BR, Oliver RC, et al. The origin of granulation tissue and its impact on postoperative results of mucogingival surgery. *J Periodontol* 1975; 46:577-585.
8. Ramfjord SF, Costich ER. Healing after exposure of periosteum on the alveolar process. *J Periodontol* 1968;39:199-207.
9. Costich ER, Ramfjord SP. Healing after partial denudation of the alveolar process. *J Periodontol* 1968; 39:127-134.
10. Clauser C, Nieri M, Franceschi D, et al. Evidence-based mucogingival therapy. Part 2: Ordinary and individual patient data meta-analyses of surgical treatment of recession using complete root coverage as the outcome variable. *J Periodontol* 2003;74:741-756.
11. Ouhayoun JP, Sawaf MH, Gofflaux JC, et al. Re-epithelialization of a palatal connective tissue graft transplanted in a non-keratinized alveolar mucosa: A histological and biochemical study in humans. *J Periodontal Res* 1988;23:127-133.
12. Hill MW, Mackenzie IC. The influence of differing connective tissue substrates on the maintenance of adult stratified squamous epithelia. *Cell Tissue Res* 1984; 237:473-478.
13. Klingsberg J. Preserved sclera in periodontal surgery. *J Periodontol* 1972;43:634-639.
14. Klingsberg J. Periodontal scleral grafts and combined grafts of sclera and bone: Two-year appraisal. *J Periodontol* 1974;45:262-272.
15. Bartolucci EG. A clinical evaluation of freeze-dried homologous dura mater as a periodontal free graft material. Study in humans. *J Periodontol* 1981;52: 354-361.
16. Nayot C, Beagrie GS. An assessment of the biocompatibility of "Lyodura" in the oral mucosa of the hamster. *J Periodontol* 1978;49:181-188.
17. Martis C, Lazaridis N, Karabouta I, et al. Free transplantation of lyophilized dura for vestibuloplasty: A clinical and histological study. *J Oral Surg* 1979;37: 646-649.
18. Harris RJ. A comparison of 2 root coverage techniques: Guided tissue regeneration with a bioabsorbable matrix style membrane versus a connective tissue graft combined with a coronally positioned pedicle graft without vertical incisions. Results of a series of consecutive cases. *J Periodontol* 1998;69:1426-1434.
19. Harris RJ. A comparative study of root coverage obtained with guided tissue regeneration utilizing a bioabsorbable membrane versus the connective tissue with partial-thickness double pedicle graft. *J Periodontol* 1997;68:779-790.
20. Pini Prato G, Clauser C, Cortellini P, et al. Guided tissue regeneration versus mucogingival surgery in the treatment of human buccal recessions. A 4-year follow-up study. *J Periodontol* 1996;67:1216-1223.
21. Tinti C, Vincenzi G, Cortellini P, et al. Guided tissue regeneration in the treatment of human facial recession. A 12-case report. *J Periodontol* 1992;63:554-560.
22. Wainwright DJ. Use of an acellular allograft dermal matrix (AlloDerm) in the management of full-thickness burns. *Burns* 1995;21:243-248.
23. Wainwright D, Madden M, Luterman A, et al. Clinical evaluation of an acellular allograft dermal matrix in full-thickness burns. *J Burn Care Rehabil* 1996;17: 124-136.
24. Rhee PH, Friedman CD, Ridge JA, et al. The use of processed allograft dermal matrix for intraoral resurfacing: An alternative to split-thickness skin grafts. *Arch Otolaryngol Head Neck Surg* 1998;124:1201-1204.
25. Harris RJ. Gingival augmentation with an acellular dermal matrix: Human histologic evaluation of a case–placement of the graft on periosteum. *Int J Periodontics Restorative Dent* 2004;24:378-385.
26. Harris RJ. A short-term and long-term comparison of root coverage with an acellular dermal matrix and a subepithelial graft. *J Periodontol* 2004;75:734-743.
27. Woodyard JG, Greenwell H, Hill M, et al. The clinical effect of acellular dermal matrix on gingival thickness and root coverage compared to coronally positioned flap alone. *J Periodontol* 2004;75:44-56.
28. Paolantonio M, Dolci M, Esposito P, et al. Subpedicle acellular dermal matrix graft and autogenous connective tissue graft in the treatment of gingival recessions: A comparative 1-year clinical study. *J Periodontol* 2002;73:1299-1307.
29. Wei PC, Laurell L, Geivelis M, et al. Acellular dermal matrix allografts to achieve increased attached gingiva. Part 1. A clinical study. *J Periodontol* 2000;71: 1297-1305.
30. Wei PC, Laurell L, Lingen MW, et al. Acellular dermal matrix allografts to achieve increased attached gingiva. Part 2. A histological comparative study. *J Periodontol* 2002;73:257-265.
31. Harris RJ. Cellular dermal matrix used for root coverage: 18-month follow-up observation. *Int J Periodontics Restorative Dent* 2002;22:156-163.
32. Henderson RD, Greenwell H, Drisko C, et al. Predictable multiple site root coverage using an acellular dermal matrix allograft. *J Periodontol* 2001;72:571-582.
33. Novaes AB Jr., Souza SL. Acellular dermal matrix graft as a membrane for guided bone regeneration: A case report. *Implant Dent* 2001;10:192-196.
34. Harris RJ. Clinical evaluation of 3 techniques to augment keratinized tissue without root coverage. *J Periodontol* 2001;72:932-938.
35. Aichelmann-Reidy ME, Yukna RA, Evans GH, et al. Clinical evaluation of acellular allograft dermis for the treatment of human gingival recession. *J Periodontol* 2001;72:998-1005.
36. Harris RJ. A comparative study of root coverage obtained with an acellular dermal matrix versus a connective tissue graft: Results of 107 recession defects in 50 consecutively treated patients. *Int J Periodontics Restorative Dent* 2000;20:51-59.
37. Haeri A, Parsell D. Creeping attachment: Autogenous graft vs dermal matrix allograft. *Compend Contin Educ Dent.* 2000;21:725-729; quiz 30.

38. Tal H. Subgingival acellular dermal matrix allograft for the treatment of gingival recession: A case report. *J Periodontol* 1999;70:1118-1124.
39. Harris RJ. Root coverage with a connective tissue with partial thickness double pedicle graft and an acellular dermal matrix graft: A clinical and histological evaluation of a case report. *J Periodontol* 1998;69:1305-1311.
40. Barros RM, Novaes AB Jr., Grisi MFM, et al. A 6-month comparative clinical study of a conventional and a new surgical approach for root coverage with acellular dermal matrix. *J Periodontol* 2004;75:1350-1356.
41. Novaes AB Jr, Grisi DC, Molina GO, et al. Comparative 6-month clinical study of a subepithelial connective tissue graft and acellular dermal matrix graft for the treatment of gingival recession. *J Periodontol* 2001; 72:1477-1484.
42. Tal H, Moses O, Zohar R, et al. Root coverage of advanced gingival recession: A comparative study between acellular dermal matrix allograft and subepithelial connective tissue grafts. *J Periodontol* 2002; 73:1405-1411.
43. Cortes Ade Q, Martins AG, Nociti FH Jr., et al. Coronally positioned flap with or without acellular dermal matrix graft in the treatment of Class I gingival recessions: A randomized controlled clinical study. *J Periodontol* 2004;75:1137-1144.
44. Benecke JE Jr. Tympanic membrane grafting with alloderm. *Laryngoscope* 2001;111:1525-1527.
45. Kridel RW, Foda H, Lunde KC. Septal perforation repair with acellular human dermal allograft. *Arch Otolaryngol Head Neck Surg* 1998;124:73-78.
46. Fisher E, Frodel JL. Facial suspension with acellular human dermal allograft. *Arch Facial Plast Surg* 1999; 1:195-199.
47. Girard S, Sideman M, Spain DA. A novel approach to the problem of intestinal fistulization arising in patients managed with open peritoneal cavities. *Am J Surg* 2002;184:166-167.
48. Castor SA, To WC, Papay FA. Lip augmentation with AlloDerm acellular allogenic dermal graft and fat autograft: A comparison with autologous fat injection alone. *Aesthetic Plast Surg* 1999;23:218-223.
49. Gryskiewicz JM. Alloderm lip augmentation. *Plast Reconstr Surg* 2000;106:953-954.
50. Shulman J. Clinical evaluation of an acellular dermal allograft for increasing the zone of attached gingiva. *Pract Periodontics Aesthet Dent* 1996;8:201-208.
51. Fowler EB, Breault LG. Ridge augmentation with a folded acellular dermal matrix allograft: A case report. *J Contemp Dent Pract* 2001;2:31-40.
52. Novaes Junior AB, Papalexiou V, Luczyszyn SM, et al. Immediate implant in extraction socket with acellular dermal matrix graft and bioactive glass: A case report. *Implant Dent* 2002;11:343-348.
53. Karring T, Lang NP, Löe H. The role of gingival connective tissue in determining epithelial differentiation. *J Periodontal Res* 1975;10:1-11.

Correspondence: Dr. Ricardo Gapski, Department of Periodontics, School of Dentistry, University of Missouri, Kansas City, 650 East 25th St., Room 3101, Kansas City, MO 64108. Fax: 816/235-5472; e-mail: gapskir@umkc.edu.

Accepted for publication April 11, 2005.