

# Reconstructive Peri-implant Site Development throughout an Implant Life Cycle. A Retrospective Study

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## Abstract

**Purpose:** Regenerative hard or soft tissue augmentation procedures (ReP) are crucial in dental implant therapy. This study evaluates the frequency, timing, and financial implication of these procedures before and after implant placement, alongside the influence of systemic conditions on the need for additional interventions. **Materials and Methods:** This cohort included patients who received implants with or without ReP at the University of Michigan Graduate School of Dentistry from 2011-2023. Data on demographics and systemic health conditions were collected and analyzed using univariable and multivariable logistic regression. **Results:** 4,803 patients (10,247 implants) were included—48.9% of the patients and 21.7% of the implants received at least one ReP. Ancillary ReP was needed for 14.7% of the implants. The most common of these was alveolar ridge augmentation (ARA) simultaneous with

implant placement (42.1%) and alveolar ridge preservation (ARP) (26.4). Diabetics showed significantly higher odds of repeating procedures pre-implant (OR=5.47; p=0.016) and required more frequent hard tissue augmentations post-implant (OR=3.58; p=0.006). Cost analysis revealed that ReP constituted 12.9% of the total implant procedure cost. Notably, the mandibular anterior area was the most likely to undergo ReP (OR=2.08; p=0.001). Conclusions: One of every two patients received a ReP. Almost half of these patients received ARA (simultaneous or staged), and 1/4 received ARP. Diabetic patients exhibited significantly higher odds of requiring hard tissue augmentation pre-IP and post-IP. Trends showed a shift towards soft tissue augmentation over hard tissue procedures for managing peri-implant deficiencies. *Int J Oral Maxillofac Implants 2025;40:xxx-xxx. doi: 10.11607/jomi.11162*

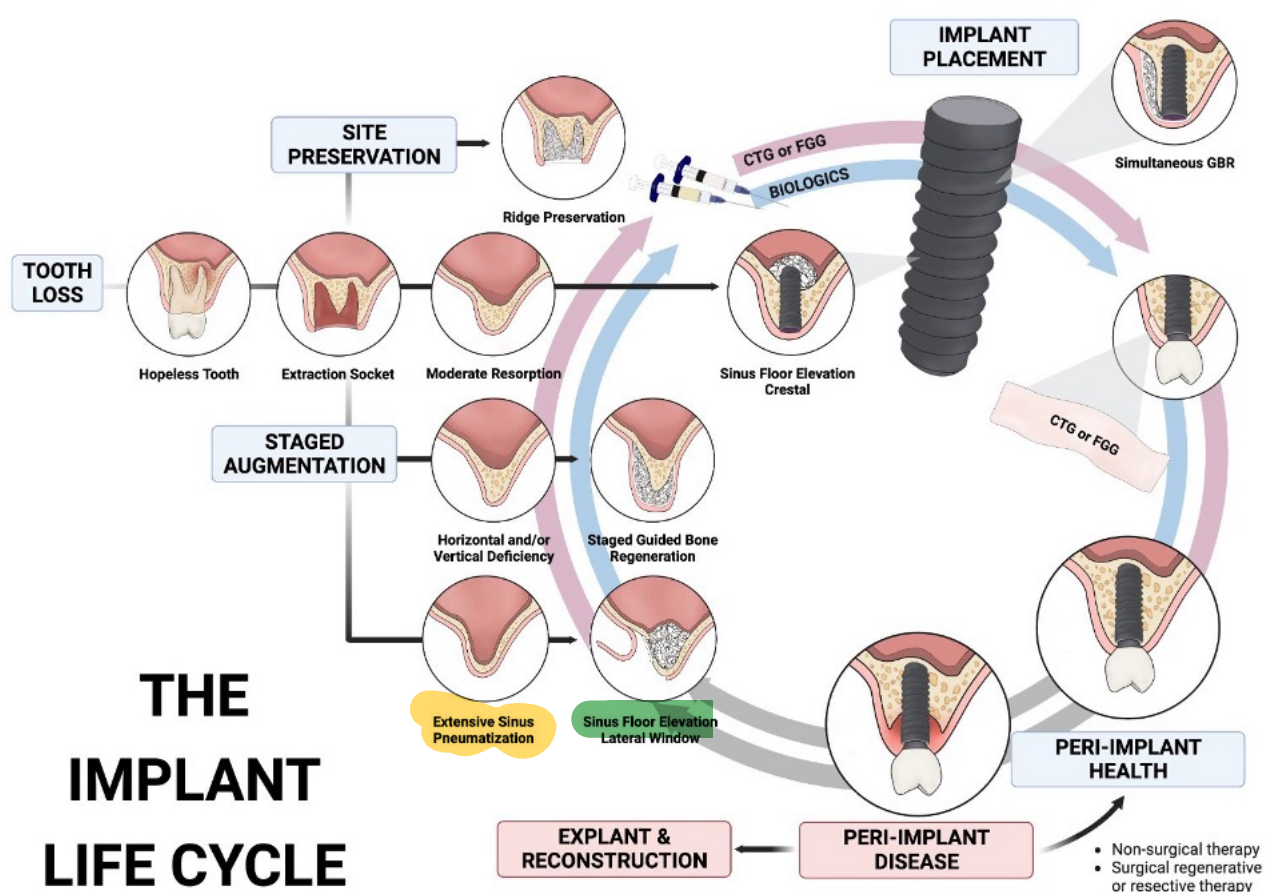
*Keywords (MeSH): Dental Implants; Regeneration; Alveolar Ridge Augmentation; Costs and Cost Analysis; Prevalence*

## Introduction

Emerging trends in proper case selection and risk assessment before implant placement have been a focal point for clinicians and researchers alike.<sup>1</sup> Understanding the financial aspects of these risks can guide targeted strategies for the public, policymakers, educators, and professional organizations regarding the prevention, diagnosis, and management of dental implant procedures.<sup>2,3</sup>

Deficiencies in peri-implant tissues may result from anatomy, sinus pneumatization, systemic conditions, ridge resorption, trauma, infectious diseases, mechanical influences, insufficient keratinized mucosa, and implant malposition. Failing to reconstruct tissue deficits can compromise implant success, stability, and longevity.<sup>4,5</sup> Moreover, mucosal margin recession, soft tissue volume, and ridge deficiencies worsen over time when single, immediately restored implants are placed, potentially causing additional aesthetic issues.

Various hard and soft tissue regenerative procedures (ReP) that can be performed at different stages of an implant's life cycle to facilitate dental implant placement or maintain its condition. (Fig 1) Pre-implant site preparation (pre-IP) typically involves post-extraction hard tissue augmentation, including techniques like alveolar ridge preservation (ARP),<sup>6</sup> simultaneous and staged alveolar ridge augmentation (ARA),<sup>7</sup> and sinus floor elevation (SFE),<sup>8</sup> which may be required in cases of significant bone loss and sinus pneumatization. Similarly, pre-IP may include soft tissue augmentation procedures like phenotype modification.<sup>9,10</sup>



This peer-reviewed, accepted manuscript will undergo final editing and production prior to print publication.  
Any blinded information will be available then.

**Fig 1** The figure illustrates "The Implant Life Cycle," starting with tooth loss, proceeding to an extraction socket, and then sequelae of moderate bone resorption transitioning to site preservation techniques such as ridge preservation or staged augmentation phases, including sinus floor elevation techniques. The cycle further explains the simultaneous and post-implant augmentations phase in implant placement, followed by the maintenance of peri-implant health, which can involve non-surgical or surgical therapy, and addressing the management of the peri-implant disease or failure, circling back to site development. Abbreviations: CTG: Connective tissue graft, FGG: Free gingival graft.

Additionally, post-implant site preparation (post-IP) involves additional regenerative procedures to maintain peri-implant health.<sup>11</sup> Unfortunately, peri-implantitis might still develop, requiring additional or repeated corrective regenerative interventions.<sup>12,13</sup> Progression to implant failure may occur, pivoting back to considering reconstructive procedures for site development.<sup>14</sup>

The patient's systemic conditions and overall health status influence the implant's success and survival, thereby aiding clinicians in identifying higher-risk patients to avoid potential complications during the healing process and after maturation for long-term stability.<sup>15,16</sup> While few studies have linked specific systemic diseases (i.e., history of radiotherapy, chemotherapy, Crohn's disease, smoking, and diabetes) to EIL, these findings require further confirmation.<sup>19–21</sup>

Recent studies indicate that re-grafting and supplementary surgical procedures are frequently required at the time of implant placement.<sup>22</sup> From the patient's perspective, the added costs of ancillary regenerative procedures and re-grafting substantially elevate the initial expenditure.<sup>23</sup> This added financial burden may significantly impact the treatment plan and influence the patient's treatment choice.

Therefore, the present study aimed primarily to evaluate the frequency and timing of regenerative hard and soft tissue augmentation procedures performed before (pre-IP) and after implant placement (post-IP) and the financial burden of these procedures as a part of the implant placement procedure.

Secondarily, the impact of systemic conditions on the need for additional implant-related regenerative procedures (ReP) throughout the implant life was analyzed.

## MATERIALS AND METHODS

### *Patient Population*

This retrospective cohort study is based on dental records from the University of Michigan School of Dentistry. The records were selected electronically based on patient treatment codes from 11/2012 (when all dental records became digital) to 06/2023. Periodontics residents or faculty members performed all treatments in the Departments of Periodontics or Prosthodontics at the University of Michigan School of Dentistry. The study protocol was approved by the ethics committee of the University of Michigan Medical School Institutional Review Board (IRBMED). The study eResearch ID is HUM00228878, and the IRB acceptance date was 2/24/2023. The study was conducted following the Helsinki Declaration and complies with the STROBE guidelines.

### *Data Collection Process*

The electronic health records (EHR) of all patients who received an implant between 01/2011 and 06/2023 were extracted based on the selected criteria. The EHR was manually screened twice by examiners (DM and MHAS). Implant placement at the University of Michigan School of Dentistry was the starting point of data collection. Data was collected on any regenerative procedure performed before or at the time of implant placement and after implant placement until the last documented date of implant presence. All related EHR information from the year before and the year following each procedure until prosthetic restoration was collected for complete anamnestic data.

## *Inclusion and Exclusion Criteria*

### *Inclusion criteria*

Patients who received dental implants with or without regenerative procedures at the University of Michigan School of Dentistry, Department of Prosthodontics and Periodontics.

At least one year of follow-up after implant placement.

Availability of multiple updated EHR data for patients placing more than one implant (in case medical history changed at the time of another implant placement).

### *Exclusion criteria*

Implants that were placed at a facility other than the University of Michigan.

Implants not restored at the University of Michigan.

Implants not followed for one-year follow-up after implant restoration.

## *Case Definitions and Extracted Parameters*

The following parameters were extracted:

1) Age, 2) gender, 3) implant location, 4) hard or soft tissue augmentation before, simultaneously, or following implant installation, 5) date of each procedure in relation to implant placement, 6) smoking status (current, former, non-smoker) at the time of implant installation, 7) diabetic status (type II), 8) arthritis status, 9) history of periodontitis, and 10) cost of the procedure.

## *Case definitions*

Smoking: It was diagnosed as a current, former, and non-smoker based on three separate self-reported questionnaires.

Diabetes Mellitus (Type 2) and arthritis: The medical questionnaire provided at the time of patient admission diagnosed diabetes and arthritis. The questionnaire recorded the physician-diagnosed status of either condition.

Periodontitis: It was confirmed if a periodontitis diagnosis was entered in the EHR (regardless of the classification) or if the patient received any type of active or supportive periodontal therapy.

Early implant Loss: Implant failure within one year of implant placement or 3 months after implant restoration was considered an early failure.

ReP Re-do: Any regenerative procedure that was done more than once in the same fashion for the same implant site due to the failure of the initial procedure.

Example: A lateral window SFA that was redone before due to the procedure failing for any reason.

Ancillary ReP: A supplemental regenerative procedure was performed due to incomplete ridge regeneration.

Example: A transcrestal SFA was performed at the time of implant placement for a site that previously received a lateral window SFA.

## *The effect of systemic conditions on ReP*

The effect of systemic conditions on ReP was studied through multiple surrogates, which all indicate the need for more ReP in some way:

A) ReP Re-do. Surrogate for failed procedures.

B) Rep Post-IP. Surrogate for the need for additional ReP after implant placement.

C) **Ancillary** ReP. Surrogate for the need for additional ReP before implant placement.

### *Primary Outcomes*

The primary outcomes assessed in this study included the frequency and timing of regenerative hard and soft tissue augmentation procedures performed both pre-IP and post-IP, as well as the cost associated with these procedures as part of the overall implant placement process. Additionally, the study evaluated the impact of systemic conditions such as smoking, diabetes, and periodontitis on **the need for additional implant-related regenerative procedures (ReP) throughout the implant's lifecycle.**

### *Statistical Analysis*

Descriptive statistics were calculated for patient- and implant-related characteristics. All primary outcomes were described at the implant level because medical history changes over time. Univariable random effects logistic regression analyses assessed the impact of predictors (age, gender, implant region, regenerative procedures, timing of each procedure, smoking status (Never/Former/Current), and history of periodontitis) on the primary outcome. Parameters significant at the 0.10 level were considered for the final multivariable model, while age and gender were considered **confounders.** Statistical analysis used SPSS Version 24.0 (SPSS Inc.), with p-values <.05 considered statistically significant.



Results

Sample Demographic

Out of 6158 patients initially screened, 4,803 patients were included. Most excluded patients (1200) had their implants placed and/or restored outside the University of Michigan. The remaining 155 patients had no/incomplete EHR data.

A total of 10,247 dental implants of 4,803 patients, 2802 males (58.3%) and 2001 females (41.7%) were assessed. The mean age of included patients was 63.5 ± 5.7 years, ranging from 19–93 years. Among these, 437 patients had type 2 diabetes (9.1%), 1153 patients were former smokers (24.0%), 663 patients were current smokers (13.8%), 873 patients had rheumatoid arthritis (18.1%), and 1374 patients had a history of periodontitis (28.6%) (Table 1).

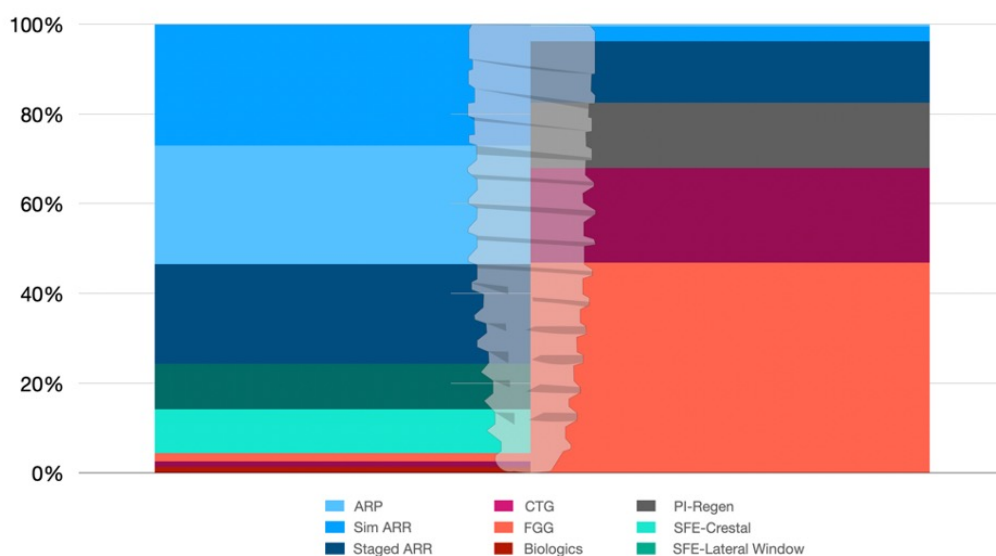
Table 1 Patient Demographics.

Description	Total	Percentage
Patients Included	4,803	-
Gender Distribution		
- Males	2,802	58.30%
- Females	2,001	41.70%
Mean Age of Patients	63.5 years	-
- Age Range	19–93 years	-
Type 2 Diabetes	437	9.10%
Former Smokers	1,153	24.00%
Current Smokers	663	13.80%
Rheumatoid Arthritis	873	18.10%
History of Periodontitis	1,374	28.60%

## *Prevalence of Regenerative Procedures*

### *Prevalence of overall, pre-IP and post-IP procedures*

The analysis revealed 48.9% of the patients and 21.7% of the implants received at least one ReP. For the pre-IP procedures, 1,823 implants (17.8%) underwent ReP before implant placement (pre-IP), and 257 implants (14.1%) underwent multiple pre-IP regenerative procedures. 1,782 implants of the pre-IP ReP were hard tissue augmentation (97.7%). (Fig 2). The most common of these was ARA simultaneous with implant placement (42.1%), ARP (26.4%), staged ARA (22.3%), and lateral window SFA (10.1%) (Fig 3).



**Fig 2** Prevalence of regenerative interventions done pre-IP compared to post-IP. Most pre-IP interventions were hard tissue augmentations, while most post-IP interventions were soft tissue procedures.

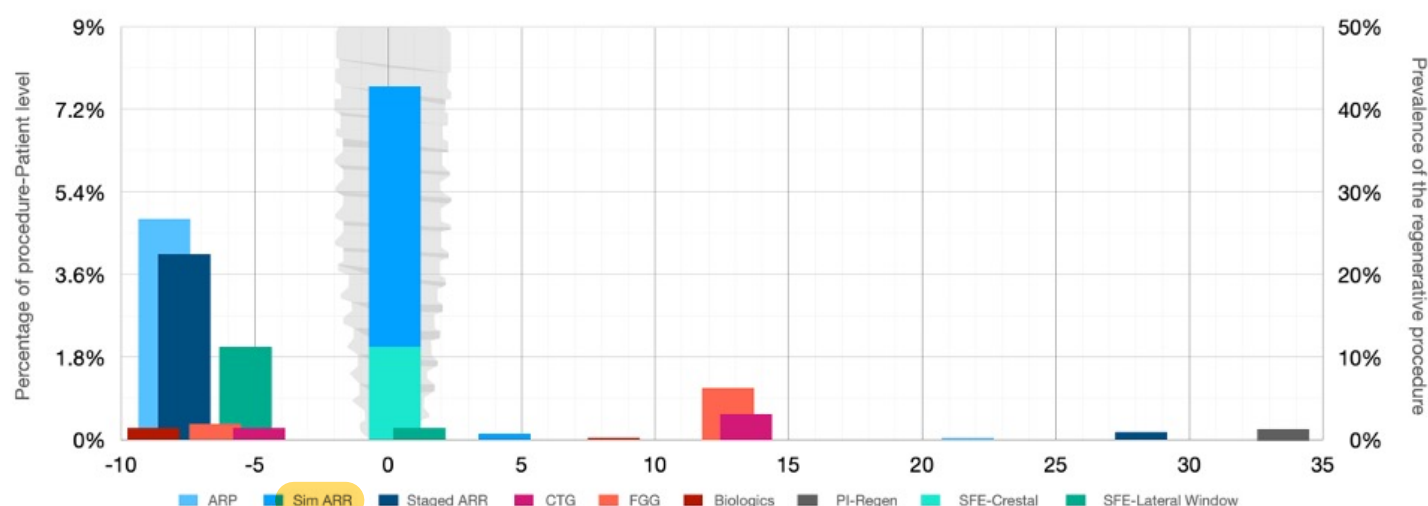


Fig 3 The Bar Graph shows the incidence of regenerative procedures on two metrics: the patient-level analysis of the percentage of regenerative procedures on the left vertical axis and the overall prevalence of the procedures as regenerative treatment options on the right vertical axis. The x-axis represents the timing (in months) of the regenerative procedures performed.

For the post-IP procedures, 213 implants (2.1%) underwent ReP post-IP, and 12 implants (0.12%) had multiple post-IP regenerative procedures. In contrast to pre-IP, most post-IP procedures were soft tissue grafting 145 implants (68% of post-IP ReP). (Fig 2).

### *Prevalence re-dos and ancillary ReP*

Procedure redo pre-IP (implants receiving the same treatment more than once before implant placement) at the implant level was a very low percentage of the total ReP (20 procedures, 1.1%).

However, ancillary ReP at the implant level (supplemental regenerative procedures that were done due to inadequate results) was much higher, with 257 ancillary pre-IP ReP (14.1%) and 12 ancillary post-IP Rep (5.6%), for a total of 14.7% ancillary ReP.

### *Effect of systemic conditions on re-dos and ancillary ReP*

Patients who currently or formerly smoked and those diagnosed with diabetes or periodontitis had a higher likelihood of repeating the same procedure pre-IP (ReP Re-do) (Table 2; Supplementary Fig 1).

This association was only significant for subjects with diabetes (OR=5.47; p=0.016).

Smokers and patients with rheumatoid arthritis, diabetes, or periodontitis were more likely to undergo hard tissue augmentation post-IP (Table 2). Again, this association was significant only for diabetics (OR=3.58; p=0.006). No differences were found in the prevalence of soft tissue augmentation post-IP between patients with and without the studied systemic conditions.

Smokers and patients with rheumatoid arthritis or periodontitis had a higher chance of undergoing hard tissue augmentation post-IP (Ancillary ReP) (Table 2). However, none of these associations reached statistical significance.

### *Early Implant Loss*

Only 113 implants (1.1%) experienced EIL. No statistically significant difference in EIL was found between implants that received ReP (19 implants, 1%) and those that didn't (94 implants, 1.1%).

No effect of any systemic conditions was found to be correlated to EIL. Current smokers had increased odds for EIL but without statistical significance (OR: 6.27, CI: -2.6-15.1; p=0.166).

ReP had no effect on EIL. 33% of EIL were in implants without any ReP, followed by staged ARA (28.30%), followed by Simultaneous ARA (18.4%), and ARP (17.92%). Lateral SFE made up 5.19%, and crestal SFE made up 4.72% of EIL. There was no statistical difference between EIL rates in augmented versus non-augmented sites. (p=0.92)

## *Cost Analysis*

The cost minimization analysis demonstrated that pre-IP procedures comprise 11.7% of “the cost of the implant procedure.” Post-IP procedures make up 1.2%. Combined, pre- and post-IP procedures accounted for 12.9% of the total implant procedure cost.

## *Trends Based on the Location of the Rep*

Based on the site analysis, the mandibular anterior area had the highest overall ReP performed (OR: 2.08; CI: 1.35 - 3.19;  $p=0.001$ ).

For soft tissue augmentation procedures, the likelihood of performing a connective tissue graft (CTG) was greater in the maxillary anterior region (OR = 3.92; CI: 1.47-10.4;  $p=0.006$ ), while the probability of performing a free gingival graft (FGG) was higher in the mandibular anterior region (OR=10.7; CI 3.57-31.9;  $p<0.001$ ) (Table 3).

For hard tissue augmentation procedures, no differences were found based on the implant site, except for peri-implant regenerative procedures, which had a lower chance of being performed in the mandibular anterior area (OR=0.1; CI: 0.01-0.84;  $p=<0.0034$ ) (Table 3).

## *Chronological Trends of Regenerative Procedures*

The graphical representation in (Fig 4) represents trends observed in reconstructive procedures over 11 years (2012-2023). Pre-IP trends demonstrated an increased trend for performing simultaneous ARA compared to staged ARA and transcrestal SFA compared to lateral window SFE. A limited increase in CTG cases was observed in the last few years compared to FGG.

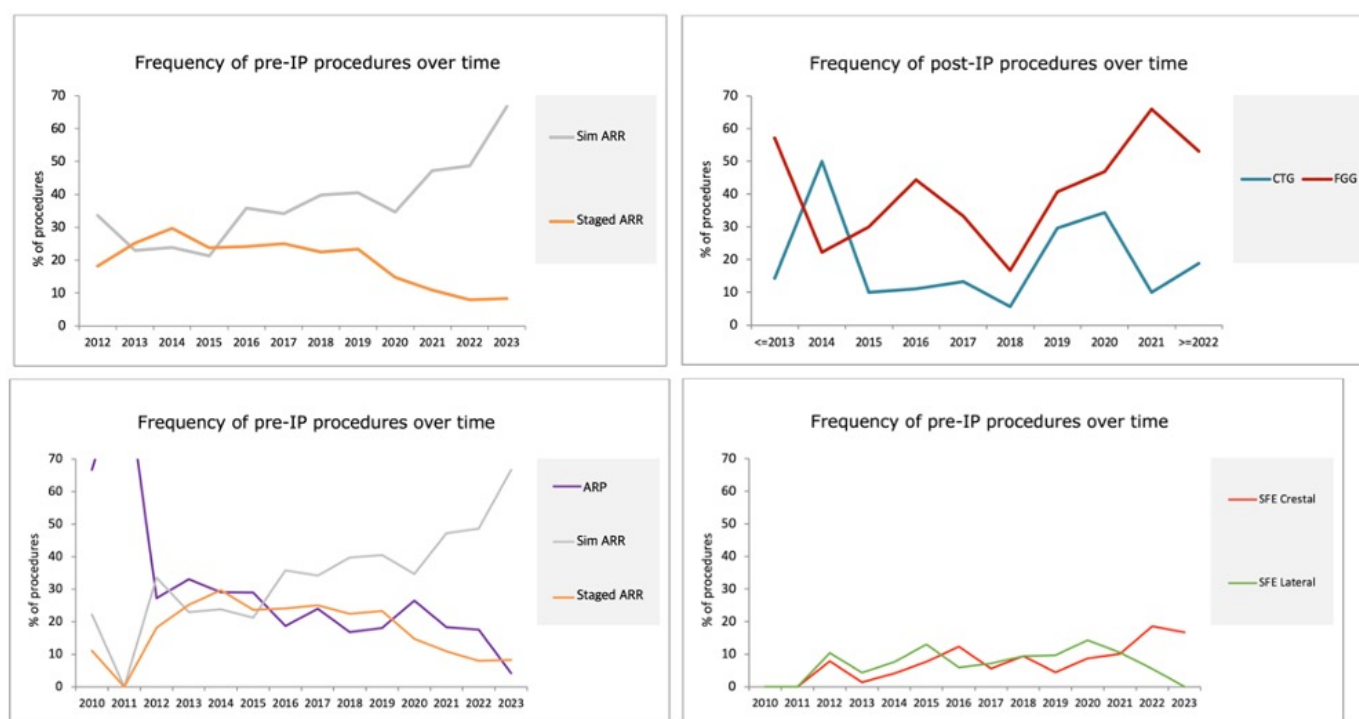


Fig 4 Trends in reconstructive procedures over 11 years depict an increase in simultaneous ridge augmentation over staged ridge augmentation pre-IP and a notable positive trend for free gingival grafts post-IP.

Conversely, post-IP trends demonstrated a higher tendency to perform in CTG than FGG over the last 11 years.

### Timing Of Regenerative Procedures

For the pre-IP ReP, the hard tissue reconstruction procedures included ARP (8.7 months pre-IP), followed by staged ARA (7.73 months) and lateral window SFA (5.73 months). FGG and CTG were performed at 6.98- and 5.24-months pre-IP for soft tissue reconstruction, respectively (Fig 3).

For post-IP ReP, the hard tissue reconstruction procedure involved regenerative treatment for peri-implantitis (33.5 months post-IP), followed by staged ARA (27.75 months). FGG and CTG were

conducted at very close intervals for soft tissue post-IP reconstruction, with means of 12.42 months and 12.82 months post-IP, respectively.

## Discussion

The analysis of the current implant lifecycle shows a substantial number of implants underwent ReP, mainly before implant placement. Systemic conditions like diabetes increased the need for ReP. There was minimal EIL, and although current smokers showed a higher risk of EIL, it was not statistically significant. ReP accounted for 12.9% of the total implant procedure cost. The mandibular anterior region had the highest rate of ReP. During the observation period, there was a trend toward increased simultaneous versus staged ARA, and transcrestal versus lateral window SF utilization pre-IP. In contrast, CTG was utilized more than FGG post-IP over time.

Common challenges drive the need for peri-implant site development procedures at implant sites, such as bony defects and insufficient soft tissue, which can jeopardize implant success.<sup>(24)</sup> Hard tissue and contour augmentation are essential for establishing a strong anatomical basis and ensuring stable soft tissue, thus supporting aesthetic outcomes. Additionally, soft tissue augmentation addresses complications like volume deficiency and recession, which can lead to aesthetic issues, such as long crowns or black triangles, impacting patient perceptions.

Accordingly, Data shows that 48.9% of patients and 21.7% of implants received at least one regenerative procedure (ReP), and 17.8% of implants underwent regenerative procedures pre-IP, consistent with the literature indicating the need for implant site development procedures.<sup>25,26</sup>

The relationship between diabetes and implant-related complications is complex, with evidence both supporting and challenging the hypothesized association. Research conducted by Al Ansari et al.,<sup>27</sup> Annibali et al.,<sup>28</sup> and Fiorellini et al.<sup>29</sup> suggest that diabetes might be a significant risk factor for implant

failure. In contrast, studies by Chrcanovic et al.<sup>30</sup> Eskow et al.<sup>31</sup> and Moraschini et al.<sup>32</sup> have demonstrated that diabetes can have varying effects on implant outcomes, influenced by glycemic control levels and individual patient responses. The present study contributes to this discourse by revealing an increased likelihood of regenerative procedures in diabetic patients, particularly when repeated hard tissue augmentation is necessary. Complementing these findings, the review by Buser et al.<sup>4</sup> emphasizes the necessity of prioritizing patient-centered approaches when it comes to implant placement. Such approaches focus on achieving minimal surgical interventions and reducing pain and complications throughout the healing phase, ultimately leading to more effective treatment outcomes. This study highlights that diabetic patients often need regenerative procedures, especially for repeated hard tissue augmentation. This stems from challenges such as slower healing times that delay recovery and hinder implant effectiveness, higher infection rates requiring additional interventions, and compromised bone density reducing structural support for implants. These factors necessitate multiple augmentations for successful long-term integration and function. Thus, diabetes underscores these patients' critical need for continuous regenerative interventions.

Another patient-level covariate commonly discussed in the literature is smoking, which has shown a strong association with implant failure<sup>33</sup> and marginal bone loss (MBL), especially in heavy smokers.<sup>34,35</sup> However, the link between smoking and peri-implantitis remains uncertain.<sup>36</sup> While some studies suggest that smoking increases the risk of developing peri-implantitis,<sup>37,38</sup> others found no substantial evidence.<sup>39</sup> In the context of reconstructive procedures, a review by Chambrone et al.<sup>40</sup> reported that smoking can significantly increase the risk of implant loss after sinus lift procedures. One possible explanation could be the impairment of blood flow, tissue oxygenation, and inflammatory responses, which can affect the implant site's regenerative capacity and reduce bone-to-implant contact



and implant stability.<sup>41</sup> However, the present study found no significant association between smoking and the prevalence of regenerative procedures and repeated augmentation.

In the last decade, regenerative procedures have shifted to emphasize soft tissue management rather than complex hard tissue augmentations. Most interventions involve soft tissue grafts following implant placement. CTG tends to be more common in the maxillary anterior region, while FGG is more frequently utilized in the mandibular anterior region, per the current findings, as it enhances keratinized tissue width, which is crucial for plaque control, reducing inflammation and ensuring long-term peri-implant health. Based on the RCTs,<sup>42–45</sup> soft tissue grafting procedures can result in more favorable peri-implant health. Utilizing CTG, with or without bone grafting, can help reduce horizontal changes of the alveolar ridge and maintain tissue contour due to increased soft tissue thickness. Additionally, systematic reviews by Thoma et al.<sup>46</sup> and Fickl et al.<sup>47</sup> provide evidence supporting the utilization of these procedures, as the changes in the marginal bone level were similar for soft or hard tissue augmentation. Moreover, a recent review by Rocuzzo et al.<sup>48</sup> highlights that these interventions aim to establish an optimal peri-implant soft tissue seal and allow optimal healing after a reconstructive procedure.

Different cut-off points have been proposed to define early implant failures (EIL). In most publications, this is before the abutment connection.<sup>19,49</sup> For practical considerations, some authors considered the first annual checkup or failures between 3-12 months from loading as an early loss.<sup>50,51</sup> The present study chose  $\leq 3$  Months following the final restoration. An additional year was added from the time of implant placement, as there are instances where the ReP may fail, resulting in the simultaneous implant being lost before the final restoration is completed.<sup>52</sup>

This study found that regenerative procedures comprise 12.9% of the total implant cost, with pre-IP alone at 11.7%. Smokers and patients with a history of periodontitis were associated with

underutilization of regenerative procedures, given their risk profiles indicated by the fact that these patients incurred lower costs compared to other covariates. This underutilization suggests a potential disconnect between the costs incurred and the expected clinical outcomes for these patient groups. Another aspect discussed by Barootchi et al.<sup>53</sup> emphasizes the importance of balancing clinical efficacy with economic considerations, particularly in selecting combinations of bone graft materials and barrier membranes for alveolar ridge preservation. Notably, their cost-effectiveness analysis has revealed that higher costs do not necessarily lead to better outcomes, and comprehensive analysis is required to guide treatment decisions. It is also important to acknowledge that financial costs associated with these procedures can vary significantly across countries due to differences in healthcare systems, economic conditions, and accessibility of materials, necessitating country-specific cost-effectiveness evaluations.

The current study had limitations in interpreting its findings. The retrospective design based on patient charts may have introduced information bias. Procedures were performed by clinicians with varying experience levels, and collected data began at implant placement rather than tooth extraction. This could lead to inconsistencies in treatment application and outcomes, making it difficult to standardize the results.

Additionally, this study did not account for assessing periimplantitis, making it difficult to determine causality or the nature of the relationship. Decisions regarding redo procedures were left to the clinicians' discretion, introducing subjectivity that complicates objective assessments of the procedures' effectiveness.

Patients who smoked or had arthritis were offered fewer ARA procedures, resulting in no statistical significance in the findings about these patients. Hence, as presented in the prior literature, this study lacked data on less-treated conditions, which could have affected the ability to assess complications or outcomes for these patients. To address these limitations in future research, it would be beneficial to

design a prospective clinical study, standardize treatment protocols across clinicians, and include a larger, more diverse patient population to minimize bias and improve the ability to draw definite conclusions.

## Conclusions

This study highlights the substantial prevalence of ReP associated with dental implant therapy, particularly pre-IP procedures. Nearly half of the patients and over one-fifth of implants required at least one ReP. Hard tissue augmentation accounted for most pre-IP procedures, with ARP and ARA being the most common. Certain systemic conditions, notably diabetes, demonstrated a significant association with the need for ReP, exhibiting higher odds of needing hard tissue augmentation pre-IP, post-IP, and repeated augmentations. Interestingly, temporal trends were revealed in selected therapy, with a shift towards soft tissue augmentation procedures over complex hard tissue augmentation procedures. Overall, regenerative procedures accounted for 12.9% of the total cost of implant therapy, with pre-IP procedures contributing 11.7%. These implications make careful patient selection and risk stratification crucial for optimizing treatment outcomes and resource allocation.

## Supplemental Figures and Tables

Supplemental figures will be available in the final version of this article. Tables 2 and 3 are too large to be included in this format and will also be available in the final version.

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Data Availability: The data supporting this study's findings are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

Ethics Statement: The study protocol was approved by the ethics committee of the University of Michigan Medical School Institutional Review Board (IRBMED). The study eResearch ID is HUM00228878, and the IRB acceptance date was 2/24/2023.

Author's contribution (CRediT):

MHAS: Conceptualization

MHAS, SS: Methodology

DM, MHAS: Investigation and Data Curation

KK: Formal Analysis and Writing – Original Draft

JL: Visualization

HLW, MHAS, SS: Supervision and Writing – Review & Editing

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This peer-reviewed, accepted manuscript will undergo final editing and production prior to print publication.  
Any blinded information will be available then.

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