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Review article

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Selection of bone graft material and proper timing of periodontal surgery for orthodontic patients: A systematic review

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ABSTRACT

Introduction: Bone loss progression due to periodontitis can lead to pathologic tooth migration, ultimately compromising the overall structure and function of the oral cavity. In pathologic tooth migration, a periodontal–orthodontic interdisciplinary approach is necessary. The combination of a bone graft and orthodontic treatment has shown promising results for periodontal regeneration. The treatment sequence and selection of a bone graft define the success of the therapy.

Objective: This study aims to discuss the protocol of the interdisciplinary approach to regenerative periodontal surgery in cases of intrabony defects requiring orthodontic treatment.

Material & methods: Literature searches were conducted on four online databases (PubMed, Wiley, ScienceDirect, and Google Scholar). The keywords used were (intrabony defect OR vertical bone defect) AND (bone graft OR periodontal regeneration) AND (orthodontic). Out of 1656 studies that were retrieved initially, 14 full-text articles were checked for eligibility assessment. Finally, a total of seven studies met all of the requirements for inclusion in this study. This study includes two randomized controlled trials (RCTs), which are considered the highest level of evidence, however it is important to note that the overall evidence base is heterogeneous, inclusive of various study designs.

Discussion: Periodontal tissue damage must be addressed before considering orthodontic therapy, including cases with intrabony defects. On the basis of the seven studies, orthodontic therapy can be initiated as early as four weeks after surgery or as late as one year after periodontal surgery. Different types of bone graft materials, such as autografts, allografts, xenografts, and alloplasts, are used in the included studies. Three out of seven studies used autogenous graft combined with xenograft or enamel matrix derivative as the graft material as it is osteoconductive, osteogenic, and osteoinductive. Regular periodontal tissue maintenance therapy should be performed every 2–6 months, before, during, and after orthodontic treatment.

Conclusion: Making a proper diagnosis and treatment sequence is key to the success of a periodontal–orthodontic treatment. In addition, identifying the appropriate timing between periodontal surgery and orthodontic movement, selecting the most suitable bone graft material, and ensuring regular maintenance of periodontal tissue are important considerations.

1. Introduction

Periodontitis is an inflammatory disease dominated by bacterial infections in periodontal tissue. This disease involves damage to the periodontal ligaments, alveolar bones, gums, and cementum [1]. In 2018, The World Workshop consensus formulated the latest classification of periodontal diseases by classifying periodontitis by their staging and grading. Staging classifies periodontal disease according to the severity of damage and the complexity of treatment required, with stage I being the least severe periodontal tissue

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damage and stage IV being the most severe periodontal tissue damage [2]. The determination of the staging category is based on various factors, including the assessment of adhesion loss, percentage of bone loss, probing depth, presence of angular bone damage, involvement of furcation, tooth mobility, and loss of periodontal attachment [2,3]. The objective of grading is to categorize diseases according to the extent of harm, likelihood of subsequent harm, prediction of unfavorable treatment outcomes, and association to the patient's overall systemic condition. The grading system divides periodontitis to three groups, with grade A representing a lower level of risk and grade C indicating a higher level of risk [3].

Along with the latest periodontal disease classification, there is also a new clinical practice guideline containing steps 1–4, to facilitate preventive and therapeutic interventions more suitable to the stage and grade of the cases [4,5]. Several clinical manifestations of stage IV periodontitis include vertical bone loss, significant clinical attachment loss, extensive tooth loss resulting from periodontitis, bite collapse, and pathological tooth migration [6]. As a result, patients in stage IV need to complete steps 1–3 and step 4 (supportive periodontal treatment) in order to get control of their periodontal status. Patients with severe tooth malposition then require an interdisciplinary approach with a combination of periodontal and orthodontic treatment to address both the functional and aesthetic aspects of the oral cavity [1,3,4]. Treating stage IV periodontitis is more than just focusing on the survival of a single tooth, but it is equally important to maintain the overall dentition [4].

There are two types of bone loss based on their pattern: horizontal and vertical. Horizontal bone loss is said to be more common in periodontitis patients, but in reality, the combination of horizontal and vertical bone loss happens more often. Intrabony defects, especially vertical bone defects with multiple osseous walls, can be treated effectively with a bone graft procedure [7]. Previous studies have shown the significance of periodontal–orthodontic intervention, particularly the utilization of periodontal regenerative surgery in conjunction with orthodontic appliances, for the successful management of periodontal infection control, bone reconstruction, and tooth repositioning to achieve optimal alignment [1,8].

During the tooth movement process, the periodontal ligament (PDL) experiences compression on the pressure side. This compression stimulates cellular processes that lead to bone resorption and remodeling. This phenomenon is similar to tooth periodontal regenerative treatment. Bone graft particles are absorbed, and the reestablishment of periodontal tissue is demonstrated [1]. Ideally, orthodontic tooth movement should not be initiated until the bone graft particle is fully resorbed. Thus, the consideration for starting orthodontic tooth movement is dependent on the specific bone graft material used [9].

2. Objective

The purpose of this review is to discuss the protocol of the interdisciplinary approach of regenerative periodontal surgery and orthodontic treatment in the case of intrabony defects. The study explored in detail the appropriate timing between regenerative surgery and orthodontic treatment, the selection of a bone graft material for periodontal regenerative therapy, and its maintenance therapy.

3. Methods

Prior to this study, the protocol was registered and approved by Prospective Register of Systematic Reviews (PROSPERO) under the code CRD42023445327. Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) was performed to find articles to be reviewed in this paper. A focus question was made according to the following PICO questions: populations: patients with intrabony defects of the periodontal tissue who require regenerative periodontal surgical therapy, followed by orthodontic treatment; interventions: bone graft procedure and orthodontic treatment; comparison: different types of bone graft; and outcome: periodontal regeneration.

3.1. Research question

In patients with intrabony defects, what is the ideal protocol of regenerative surgery to facilitate optimal periodontal tissue regeneration during orthodontic treatment?

3.2. Research strategies

The literature search was conducted using the online databases Google Scholar, PubMed, Wiley, and ScienceDirect. The keywords used in this search were (intrabony defect OR vertical bone defect) AND (bone graft OR periodontal regeneration) AND (orthodontic). A total of seven studies were identified and considered to meet the necessary criteria for inclusion in the present study.

3.3. Inclusion and exlusion criteria

The inclusion criteria taken into account for this systematic review were as follows: cases of intrabony defects that require regenerative periodontal surgical therapy, which was then followed by orthodontic treatment. Moreover, this study only included original studies, such as retrospective study, randomized clinical trials and case reports, so that the information can be more relevant to not only academicians, but also to clinicians. To adjust for the most recent 2017 World Workshop consensus, the studies included only covered periods between 2018 and 2023 in English language.

Reviews and commentaries were excluded. Cases related to implant placement were excluded. Furthermore, studies without







human subjects were excluded.

4. Results

The complete selection process of the studies involved is shown in the PRISMA diagram in Fig. 1. Electronic searches on four databases using selected keywords and Boolean operators found 1656 titles: 10 studies from PubMed, 116 studies from Wiley, 120 studies from Science Direct, and 1410 Google Scholar. All of the articles were then filtered based on their title and abstract to assess their eligibility based on already-established criteria. Seven articles were then excluded after an evaluation of full-text articles. Two articles were excluded because there were insufficient details regarding orthodontic treatment [10,11], two articles were excluded because there were excluded because the full-text paper was not published in English [15], the last article was excluded because it was a systematic review [16]. Finally, a total of seven studies were identified and considered to meet the necessary criteria for inclusion in the present study.



D7: Bias in the selection of the reported result





Q8: Does the case report provide takeaway lessons?

Fig. 4. Case report quality assessment.

This study included 83 patients with chronic or aggressive periodontitis who had pathologic tooth migration requiring orthodontic treatment. The time interval between regenerative periodontal surgery and orthodontic treatment discussed in the included studies ranged from as early as four months to as late as 1 year. On the basis of the seven studies included, there were three studies using autografts [1,17,18], two studies using alloplasts [19,20], one study using a xenograft [8], and one using an allograft as its regenerative material [21]. Furthermore, the frequency of periodontal maintenance therapy in all studies varied between two and 6 months, with the exception of one study that did not specify the frequency detail [21].

4.1. Risk of bias

Risk of Bias was analyzed by three authors independently (FAD, BS, and DAS), and final decisions were made based on the discussion with the investigator. Two RCTs were evaluated using the RoB-2 method: one raised some concerns, and the other had a low risk of bias (Fig. 2) [22]. After being evaluated by the ROBINS-I method, one retrospective study revealed a high risk of bias (Fig. 3) [23]. Joanna Brigs Institute critical appraisal tools were used to assess the methodological quality of the case report and case series. All case reports and case series were defined as having a high risk of bias (Figs. 4 and 5) [24].



Q7: Was there clear reporting of the clinical information of the participants?

Q8: Were the outcomes or follow-up results of cases clearly reported?

Q9: Was there clear reporting of the presenting site(s)/clinic(s) demographic information?

Q10: Was statistical analysis appropriate?

Fig. 5. Case series quality assessment.



Fig. 6. Schematic of orthodontic tooth movement after bone graft implantation. Illustrated/Modified by Deandra, F A.

5. Discussion

5.1. Time interval between bone graft procedure and orthodontic tooth movement

The timing to start orthodontic treatment after regenerative periodontal surgery plays a crucial role in determining the overall effectiveness of this interdisciplinary therapy. Orthodontic treatment can only be conducted once inflammation has been effectively controlled. Failure to control inflammation prior to orthodontic intervention may result in the exacerbation of periodontal tissue damage caused by orthodontic tooth movement [1,4].

The retrospective study conducted by Tu et al. (2022) found that 41 teeth that underwent regenerative surgery in conjunction with orthodontic treatment exhibited favorable enhancements in periodontal tissue. Orthodontic interventions carried out within a period of \leq 8 weeks after periodontal regenerative surgery showed improvement in clinical attachment loss (CAL) better than when the intervention was performed \geq 6 months after the regenerative operation, although the difference was statistically insignificant [1]. The faster improvement can be due to the orthodontic force that has a positive effect on the turnover rate of bone grafts, which can accelerate the bone formation process. In addition, orthodontic movement is believed to be beneficial in promoting the proliferation of PDL cells as well as the differentiation of those cells into osteoblasts [1,9]. Similar to the study by Tu et al. (2022), a randomized clinical trial by Jepsen et al. (2021) showed that the orthodontic tooth movement performed four weeks after periodontal regenerative surgery demonstrated comparable efficacy in periodontal tissue regeneration when compared to the same procedure performed six months later [8].

Histologically, osteoid mineralization starts at 18–21 days following bone graft implantation. Subsequently, the full maturation of the bone is expected to occur approximately 100 days after [25]. Hence, the initiation of orthodontic tooth movement three months postsurgery would involve tooth movement within an immature bone (Fig. 6). One significant disadvantage of orthodontic tooth movement in an immature bone is the possibility of severe root resorption along the way [26]. This phenomenon may occur because of the influence of growth factors and cytokines on bone remodeling, which can lead to both bone resorption and the resorption of neighboring roots [25]. In an agreement to the theory above, case reports by Kumar et al. and Rodríguez-Pulido et al. initiated

Table 1

Summary of included studies.

| No | Author | Year | Study | Population | Type of bone graft | Type of surgery | Orthodontic treatment | Maintenance |
|----|---------------------------------------|------|--------------------------|--|---|---|--|------------------------------------|
| 1. | Tu et al. | 2022 | Retrospective study | 21 adult patients, 23–66 year old | Autograft or Xenograft (DBBM) + EMD | Mucoperiosteal Flap | 8–24 weeks after surgery | Every 3 months |
| 2. | Israel Rodríguez- Pulido et al. | 2018 | Case report | 40 year old female patients | Autograft + EMD | Mucoperiosteal Flap | 3 months after surgery | Every 3 months |
| 3. | Attia et al. | 2019 | RCT | 15 adult patients | Alloplast + laser therapy | Mucoperiosteal Flap | Immediately after surgery | N/A |
| 4. | Kumar et al. | 2018 | Case report | A 17 year old female patient | Allograft (DFDBA) + PRF membrane | Mucoperiosteal Flap | 3 months after surgery | Every 8–12 weeks to 6 months |
| 5. | Bouziane et al. | 2018 | Series of case report | A 19 year old woman patient | Alloplast (β- <i>TCP</i>) | Mucoperiosteal Flap | 1 year after surgery | N/A |
| 6. | França et al. | 2018 | Case report | A 9 year old female patient | Autograft + Xenograft (Bovine) | Flap | 1 year after surgery | Every 3 months |
| 7. | Jepsen et al. | 2021 | RCT | 43 adult patients | Xenograft (DBBMc, Bio Oss® Collagen) | Mucoperiosteal flap with minimally invasive microsurgical approaches using papilla preservation flaps | 4 weeks (early) or 6 months (late) after surgery | Every 2 months |

orthodontic tooth movement three months post-regenerative periodontal surgery [18,21]. Furthermore, França et al. and Bouziane et al. started the orthodontic phase one year postsurgery [17,19] This condition may be proposed so that the orthodontic treatment does not impede the healing process of the periodontal tissue, and to reach the end-point of regenerative therapy (6–12 months) [27, 28].

In conclusion, tooth movement using an orthodontic appliance is best performed after the bone graft material is fully resorbed as the nonresorbed material may potentially interfere tooth movement [9]. The authors argue that the ideal time to do tooth movement postregenerative surgery is more than three months. Tooth movements performed prior to the three-month period could risk to accelerated tooth displacement and an increased likelihood of root resorption [25].

5.2. Bone graft material selection

On the basis of the components' origin, bone graft materials are classified into four types, namely: autografts (same individual origin), allografts (same species origin), xenografts (different species origin), and alloplasts (bone graft synthetic) [9,29]. The distinct components of bone graft materials contribute to their distinctive characteristics and properties. The successful outcome of bone graft implementation is demonstrated by the ability of the implanted material to integrate with the surrounding tissue, achieve sufficient vascularization, and develop the expected morphology [30]. The bone grafts used should possess the ability to provide not only stability in alveolar bone reconstruction enhancing the volume of the alveolar ridge but also tooth movement facilitation through an orthodontic appliance [9].

The entire study reviewed in this paper used the mucoperiosteal flap technique together with the addition of the bone graft material, with or without a combination of growth factors, as a periodontal regenerative therapy on intrabony defects that will subsequently use an orthodontic appliance [1,8,17–20]. Rodríguez-Pulido et al. utilized an autograft in conjunction with an enamel matrix derivative (EMD), França et al. used a combination of an autograph and a xenograft, and Kumar et al. utilized an autograft, a membrane, and platelet-rich fibrin (PRF) as regenerative materials [30,31]. Attia et al. used laser diodes to stimulate the regeneration of periodontal tissue in their study (Table 1) [20].

Bone graft materials applied in dentistry are chemicals that are surgically implanted to stimulate the development of new bone tissue via osteoconduction, osteoinduction, and osteogenic mechanisms. The term "osteoconductive" refers to the property of a bone graft material to serve as a scaffold, facilitating the infiltration of osteogenic cells from the surrounding bone edges. Additionally, osteoconductive phase enables the formation of a new bone on the surface of the grafting material [9,30,31]. Osteoinduction is a process in which the bone graft material stimulates mesenchymal stem cells that are not differentiated in the surrounding tissue to then transform into osteogenic cells. The osteogenic process involves the generation of new bone tissue through the differentiation of progenitor cells within the bone graft material, leading to the formation of osteoblasts and subsequent bone formation [9,30,31].

5.3. Autograft

Case reports by Tu et al., Rodríguez-Pulido et al., and França et al. utilized autografts as their regenerative material [1,17,18]. An

autograft is a viable option due to its ability to possess osteogenic, osteoinductive, and osteoconductive properties [9,30,31]. As it comes from the same individual, an autograft carries a low risk of inflammation, no risk of disease transmission, and no risk of rejection from the host body [30]. The autograft resorption rate is approximately 3–6 months, making it a very ideal regenerative material to use for intrabony defects [32].

Autografts can be classified into two different types: cortical and cancellous. A cancellous bone graft has greater porosity compared to the cortical one, resulting in an earlier onset of revascularization typically observed within a five-day period following implantation [9,33]. Nevertheless, an autograft does have certain limitations that should be considered, such as the potential for infection in the donor site, a longer treatment time, and the limited availability of the graft material [9,34]. To address these limitations, autografts are commonly used in combination with other types of bone grafts [34].

5.4. Allograft

An allograft refers to a graft material derived from the same species with the host, which is created to overcome the limitations associated with autografts. A freeze-dried bone allograft (FDBA) and a demineralized freeze-dried bone allograft (DFDBA) are the most widely developed types of allografts. Both of these allograft materials possess osteoconductive properties, and DFDBA is believed to possess osteoinductive capabilities because it contains bone morphogenic protein (BMP) [31,33]. Primarily, the distinction stems from the differences in the manufacturing processes of the two materials. During the manufacturing process of DFDBA, an acid solution is applied to mineralize the bone, thereby eliminating its inorganic components and exposing the bone morphogenetic protein (BMP) [35]. The osteogenic capability of FDBA can be enhanced by combining it with an autograft. Moreover, the use of DFDBA can be in conjunction with FDBA or an autograft [33].

The case report by Kumar et al. (2018) demonstrated the efficacy of treating one wall defect in tooth 36 using DFDBA and PRF as the graft materials, followed by an orthodontic appliance. The rapid resorption rate of DFDBA allows the initiation of orthodontic tooth movement as early as 2.5 months following regenerative surgery [17,33]. However, FDBA has a slower resorption rate, so it would be best to use it in an augmentation procedure [9,31]. Unfortunately, the long process of making allograft raises concerns in reducing their mechanical strength [9].

5.5. Xenograft

A xenograft implies a type of bone graft material derived from species other than the recipient, including porcine, bovine, and coral sources [9,31,36]. Xenografts demonstrate a noteworthy capacity for osteoconduction [34]. The inorganic component of xenografts has the potential to serve as an essential calcium source, thereby facilitating the generation of new bone tissue. The use of xenografts carries some risk of disease transmission despite being heated to eliminate the majority of the organic components [32].

The xenograft that has been extensively studied in the field of periodontology is deproteinized bovine bone material (DBBM). This type of bone graft exhibits a significantly low resorption rate, and in some cases, it may even be considered nonresorbable [34]. On the basis of this particular characteristic, it can be suggested that DBBM demonstrates compatibility for application in bone augmentation procedures surrounding implant sites, sinus augmentation, and cases with intrabony defects where periodontal pathogens are known to increase the resorption rate of the bone graft material [33,34].

Theoretically, the slow absorption rate of xenografts raises a concern that its use may impede tooth movement by an orthodontic appliance [9,37]. However, this theory lacks scientific proof as study by Jepsen et al. (2021) showed that the utilization of xenografts does not cause any hindrance to orthodontic tooth movement [6,8].

Jepsen et al. conducted a randomized clinical trial aimed at examining the outcomes for intrabony defects in cases that were given orthodontic interference at 4 weeks or 6 months after regenerative surgery. This study used a xenograft (DBBM) as a regenerative material. The results of this study indicated that an interdisciplinary approach involving periodontology and orthodontics provided satisfactory results for periodontal tissue repair and there was no statistically significant difference in CAL values between teeth that were moved 4 weeks or 6 months after surgery. The results of this study can be interpreted that the use of xenografts does not inhibit tooth movement using an orthodontic appliance despite having a slow rate of resorption [8].

Moreover, a retrospective study conducted by Tietmann et al. (2021) using 10-years period of data confirms that the combination of regenerative surgery using DBBM and orthodontic tooth movement has a favorable results, with a decreased mean of probing depth by 3 mm at 4 years follow up [6] and even a stable long-term results with an increase in the frequency of sites with probing depth \leq 4 mm from 33 % at baseline to 90 % at 10 years of follow-up [38].

5.6. Alloplast

Researchers started to develop synthetic bone formations to overcome the drawbacks of natural bone grafts. The most studied synthetic bone grafts, referred to as alloplasts, are hydroxyapatite (HA) and β -tricalcium phosphate (β -TCP), both of which show osteoconductive ability [33]. A higher calcium/phosphate (Ca/P) ratio in HA results in a slower transformation of the bone graft into a native bone. Conversely, a lower Ca/P ratio in β -TCP leads to increased resorbability and faster degradation [9,34]. Thus, β -TCP is ideal to use for the periodontal–orthodontic approach. The majority of the β -TCP particles will be absorbed 4 weeks following regenerative periodontal surgery, so orthodontic tooth movement can be performed after. β -TCP also has an interconnected porous architecture that facilitates the acceleration of vascularization and bone formation while simultaneously reducing mechanical pressure [9]. Furthermore, the serial case report presented by Bouziane et al. showed that β -TCP has been used in the periodontal–orthodontic approach,



Fig. 7. Flowchart of the interdisciplinary periodontal–orthodontic treatment. Illustrated by Deandra, F A.

resulting in 50 % new bone formations based on four months of radiographic evaluation [19].

5.7. Periodontal maintenance therapy

The goal of orthodontic treatment may differ from that for healthy periodontal patients because tooth movements become limited in adult patients with an advance stage of periodontitis [39]. The main focus is to achieve the proper overbite, overjet, close contacts between teeth, and posterior occlusal support with balanced contacts because establishing an ideal class I molar relationship is not always manageable [25].

In cases of pathologic migration involving intrabony defects, orthodontic treatment can be started once periodontal tissue damage has been resolved and optimal oral hygiene has been achieved. The tooth movement produced by the orthodontic forces will only accelerate the damage to the inflammation of the untreated periodontal tissue [1]. Orthodontic tooth movement might start at least three months after the completion of active periodontal therapy. Before utilizing an orthodontic appliance, some parameters, such as full mouth bleeding score for <20 %, full mouth plaque score <20 %, and no pathological sites (no probing depth >4 mm), must be obtained (Fig. 7) [4,40].

A complete periodontal tissue examination should be conducted every two to six months, with the majority of the clinicians recalling their patients every three months, depending on the existing periodontal risk factors and tooth movement to be performed [1, 8,17–21]. The periodontal maintenance therapy agenda covers many aspects, including the following: 1) regular tooth cleaning performed by the dentist at three-month intervals, 2) re-evaluation of probing depth, clinical attachment level, and bleeding on probing at intervals of 6–12 months, and 3) throughout the active period of dental intrusion, the procedure of scaling root planning is consistently carried out periodically.

If there is any periodontal inflammation detected, active orthodontic forces should be interrupted, and reinitiate again only if the periodontal stability/health has been established along with the improvement of the patient's oral hygiene. It is crucial to advise patients on altering their home oral hygiene practices after the insertion of an orthodontic appliance as plaque removal is more challenging when there are fixed orthodontic appliances present [4]. Consequently, if the patient fails to practice good oral hygiene habits, it becomes crucial to adjust the orthodontic treatment right away [21,41]. Patients should get their periodontal health regularly examined after completing orthodontic treatment, in addition to having their fixed passive retainers examined [4].

5.8. Study limitations

As the authors primarily focused on qualitative data, this study's limitation is the absence of quantitative findings. Further research is needed to evaluate the follow-up data regarding periodontal status improvement in quantitative measurement.

6. Conclusion

The interdisciplinary approach of periodontal regenerative therapy and orthodontic treatment in cases of intrabony defects provides satisfactory results both clinically and radiographically. The appropriate timing to start orthodontic treatment depends heavily on the resorption rate of the bone graft material used. Ideally, tooth movement is performed when the bone graft material has been fully resorbed. This paper argues that three months are expected to be enough to give stability to the periodontal tissue before orthodontic tooth movement is initiated. There is no justification for delaying orthodontic treatment as the evidence from a previous study stated that initiating orthodontic treatment early has comparable results to postponing the treatment for up to six months after periodontal regenerative surgery. However, evidence suggesting early initiations remains limited, and future research is warranted to strengthen the evidence. Autografts, allografts, xenografts, and alloplasts, used individually or in combination, have shown success in the interdisciplinary periodontal–orthodontic approach. However, because of its characteristic, an autograft is still the gold standard of bone graft materials for periodontal regenerative surgery. Periodic periodontal maintenance and examination should be continued throughout the whole orthodontic treatment, at least every three months. In addition, to adequate maintenance therapy and patient motivation, the success of treatment is determined by the patient's commitment to maintaining oral hygiene. Finally, it is pertinent to highlight that the findings of this study are recommendations and may be adjusted based on the judgment and observation of the clinician.

Data availability statement

Data will be made available on request.

CRediT authorship contribution statement

Fathia Agzarine Deandra: Writing - original draft, Visualization, Methodology, Investigation, Conceptualization. Benso Sulijaya: Writing - review & editing, Methodology, Investigation. Dewi Ayuningtyas Sudjatmika: Writing - review & editing, Investigation. Nadhia Anindhita Harsas: Writing - review & editing, Validation, Supervision, Methodology, Investigation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

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