Abstract

Introduction: Infection control compliance in dental schools has been reported as less than ideal and requires improvement. The goal of our study was to evaluate the effectiveness of a centralized educational strategy that used multimedia to improve subject understanding and compliance with infection control guidelines and practices.

Materials and Methods: The training strategy was created to show clinical scenarios and to outline all information relevant to using proper infection control and safety procedures. Pre- and post-intervention observation scores were collected for 59 students, with the scores being used to assess proper use or handling of barriers, personal protective equipment, sharps, handwashing, and disinfection. Scores were summed to form a Total score that was assessed with the non-parametric Wilcoxon-test for paired samples.

Results: For Total scores, 24 of the 59 students (41%) had higher post-video scores whereas only 14 students (24%) had higher pre-intervention scores ($P = 0.04$).

Discussion: This study revealed overall improvements in the infection control practices after an educational intervention, especially for personal protective equipment with 15 positive differences and 6 negative differences, and hand washing scores with 26 positive differences and 16 negative differences.

Conclusions: We consider the higher post-training scores to be clinically important and indicate that didactic intervention is effective in improving IC practices in the school clinic.

Keywords: patient safety; education, dental; teaching methods

1. Introduction

Infection control (IC) practices in all dental health-care settings are fundamental to prevent transmission of infectious agents among patients and dental health-care personnel. Standard Precautions and other infection prevention recommendations contained in Centers for Disease Control and Prevention (CDC)’s Guidelines for Infection Control in Dental Health-Care Settings have been adopted by practicing dentists, dental educators, and state Boards of Dental Examiners (Kohn et al., 2003). Education and training are critical elements of Infection Control Standard Precautions because they help dental health-care professionals make appropriate decisions and comply with recommended practices
IC compliance in dental-school settings has been reported as less than ideal and require improvement (Freire, Pordeus, and Paixao, 2000; Abreu et al., 2009). The current IC training at our school takes place through a slide presentation at the beginning of each academic year; additional lectures within various didactic courses as well as during clinic orientation are also provided. The clinical IC rounds conducted by the Clinical Administration demonstrated that regardless of the current training and availability of reference materials, such as the Clinic Infection Control Manual, students did not consistently follow protocols as strictly as desired. Evaluation presents opportunities to improve the effectiveness of infection-prevention programs (Abreu et al., 2009). For this reason, based upon observations made within the clinic, initial assessments were made to determine which IC protocols were commonly disregarded so that these protocols could be targeted in our training program.

Because of the multiple information sources for IC training, with no assured comprehensive standardization of material, our study responded to the need for centralized IC education and training at our school, and through this study, we sought to give students background information (combined with standardized, fact-based, and complete site-specific procedures) that could be applied in daily practice and would be consistent with the CDC, OSHA, and clinical guidelines. The goal of our study was to evaluate the effectiveness of an inclusive, centralized, impactful training strategy that used audiovisual media to improve understanding and compliance with IC guidelines/practices.

We hypothesized that the use of a didactic training strategy, specific to our dental school clinical environment, would increase student compliance with IC protocols; that is, student perceptions of disease transmission risk, standard precautions, and IC practices in the dental clinic environment would improve with the intervention.

2. Materials and Methods

This study was submitted to the Southern Illinois University Edwardsville Institutional Review Board (IRB) and was evaluated and approved under the expedited review category.

2.1 Literature Review

A systematic review published in 2001 emphasized the need for higher quality studies in the subject area concerning dental IC compliance (Gordon, Burke, Bagg, Marlborough, and McHugh, 2001). A review of the literature has shown that few studies exist that involve observation of clinical IC practices (Anders, Townsend, Davis, and McCall, 2016; Westall & Dickinson, 2017). Some of the studies reviewed relied on self-reporting by subjects to evaluate IC compliance (Abreu et al., 2006; Souza, Namen, Galan Jr, Vieira, and Sedano, 2006). For these reasons, a prospective observational study was chosen for the study design. Additionally, many of the studies that have utilized observation to assess IC compliance in a dental school environment do not evaluate IC based on the current CDC and OSHA standards for clinical dentistry. For example, a study published in 2017 emphasized that dental health care personnel are at high risk of occupational exposure (Westall & Dickinson, 2017). Studies before this did not include a comprehensive evaluation of all areas important to clinical dental IC, especially the use of proper sharps handling procedures (Gordon et al., 2001). Therefore, it was important for the educational intervention to be comprehensive and inclusive of all material outlined in the updated CDC Guidelines, OSHA Guidelines, and the Clinic Infection Control Manual. An instrument was created for observation data to be recorded, including an evaluation of the proper use of personal protective equipment for the patient and student, proper use of operatory barriers, compliance with sharps protocols, handwashing, and disinfection.

Many studies have ultimately shown that dental schools require better training in the subject area concerning dental IC (Abreu et al., 2009; Acosta-Gio et al., 2008). A recent observational study evaluating IC in a dental school environment following incorporation of new online training did not show a significant difference in IC compliance (Anders et al., 2016). However, the benefit of multi-media in education has been well established by Richard Mayer’s work overtime (Brame, 2016). A review of the literature concerning science education, including higher education, has shown that learning is enhanced with the use of educational videos in the classroom (Brame, 2016). The areas of suggested importance when designing an educational video include delivery of an appropriate cognitive load, student engagement to establish relevance of the topic, and providing active learning (Brame, 2016). As active learning is provided within our current curriculum in the form of a mandatory online test, following yearly infection control training, the focus when developing this training strategy was to create an educational video that would ensure delivery of an appropriate cognitive load and engage students by establishing relevance of the clinical scenarios presented (Brame, 2016). It was important to provide a stimulating training strategy with mixed audio-visual media as well as to illustrate how and where the proper procedures would be performed in the clinic, similar to the Khan-Academy style of learning (Brame, 2016). A compilation of video clips showing the procedures, pictures indicating where certain items could be found in the clinic and lists of
important concepts to remember were shown throughout the strategy. Thus, the study was designed around the training strategy that was created, and effectiveness would be evaluated with pre- and post-intervention observation data.

2.2 Study Design

This project was performed in three main phases. In Phase I, prior to the study intervention, subjects were observed for their current clinical IC practices. In Phase II, an intervention video was presented to subjects. This video is a 20-minute, multimedia training video created with a clinical scenario to outline all information relevant to using proper IC/safety procedures at the clinic based on CDC/School guidelines. The video presented visuals of students carrying out proper and improper IC practices in simulated patient encounters and demonstrated systematically the appropriate IC protocols to follow, pre, and post, and during patient treatment. It explored many “what if” situations, as well as infection control in all departments of the clinic and laboratory. At their convenience, subjects were given the opportunity to discuss the main point of the IC practices summarized in the multimedia and ask questions following the intervention. Subjects additionally had the ability to refer to the video via the school’s website, and they were advised to consult the clinical guidelines manual with any additional questions they might have or to gain more in-depth information. In Phase III, post-intervention observations of IC clinical practices were made.

Observations and interventions were performed with 59 subjects. These subjects were third- and fourth-year dental students because these cohorts were involved in clinical activities. Subjects were not informed when observations would be made, and observations were recorded by two calibrated examiners. They observed each study participant for approximately 30 minutes after the initiation of a clinical appointment to examine individual compliance with IC guidelines while providing patient care. Observations occurred once in the fall semester of 2018 and once in the spring semester of 2019, pre- and post-intervention, each over the course of a few weeks. Following a break period, the intervention was shown to all subjects at the same time, in January 2019, and observations began again the following week. Recorded observation data were based upon the school Clinic Manual, as well as the most recent CDC Infection Prevention Practices Guideline and included proper use of personal protective equipment for the patient and student, proper use of operatory barriers, compliance with sharps protocols, handwashing, and disinfection. The observation data were collected in the form of ordinal data, meaning that, each subject began with a perfect score and lost one point for each violation of a guideline. The highest possible score was set at 16, when combining all infection control categories for a total score. Subjects could lose points in any of the infection control categories when improper use was observed. For example, if a subject placed all barriers, complied with the sharps protocol, and performed disinfection properly, but the subject did not wear proper eyewear with side shields and was observed to not perform proper handwashing just once, two points would be deducted from the total score. All observation data were compiled in a spreadsheet that was used for statistical analyses.

2.3 Statistics

Because the data collected for this study are ordinal data, examiner calibration data and pre- and post-training data were analyzed with the non-parametric Wilcoxon test for paired samples (Altman, 1999). As part of this test, the total numbers of positive differences and negative differences for examiner calibration and pre- and post-training were calculated along with the median, 95% confidence interval (CI) for the median, Hodges-Lehmann median difference, and 95% CI for the Hodges-Lehmann median difference. Because this was a preliminary study, no preliminary data was available; therefore, anticipated results were used in a power calculation, which indicated that a sample size of 51 pairs of pre- and post-training cases would have a statistical power of ≥ 80%. For this study, the alpha level was set at 0.05; however, it is pointed out that although some P values are reported, in keeping with a recent admonition made by statisticians/scientists, assessments of differences for this study are based upon the clinical importance of the differences rather than on the P values (Amrhein, Greenland, and McShane, 2019). A sub-goal of the assessments was to determine whether a larger study beyond this preliminary study is warranted. In addition to assessing scores for pre- and post-training, also assessed was the extent to which examiners 1 and 2 could repeat their scores and the extent to which the scores made by the two examiners agreed when the same students were scored. To help in the assessment of results for intra- and inter-examiner calibration, cross tabulations are provided for time 1 versus time 2 scores for examiners 1 and 2, and cross tabulations of scores are also provided for examiner 1 versus examiner 2. These cross tabulations are provided for: (1) Barriers, (2) personal protective equipment (PPE), (3) Sharps, (4) Disinfection and (5) Total (which is the sum of the other 4 categories). Inter-rater agreement (kappa) was calculated for Total. For assessments of pre-and post-training scores, bar plots are provided with the numbers (and percentages) of pre- and post-training scores for each category that was analyzed: (1) Barriers, (2) PPE, (3) Sharps, (4) Handwashing, (5) Disinfection, and (6) Total (which is the sum of the other 5 categories)—also provided for each of these categories are the frequencies (along with probabilities) of the post-intervention score minus the pre-intervention score. For Total scores, in addition to the Wilcoxon test for the differences in pre-and post-training, the exact Agresti-Coull method was used to assess the extent to which the proportions of positive differences exceeded the proportion of negative differences—a power calculation was performed for this assessment. Statistical
analyses were performed with JMP Pro Statistical Software Release 15.0.0 (SAS Institute, Inc., Cary, NC), and MedCalc Statistical Software version 19.1.3 (MedCalc Software bv, Ostend, Belgium; https://www.medcalc.org; 2019).

3. Results

Table 1. Intra- and Inter-examiner calibration*

| Intra-examiner 1 | Intra-examiner 2 | Inter-examiner |
|------------------|------------------|----------------|
| **Barriers T2**  | **Barriers T2**  | **Total**      |
| Count 1          | 5                | 3              |
| Count 2          | 1                | 0              |
| Count 3          | 3                | 1              |
| Total            | 12               | 6              |
| **PPE T2**       | **PPE T2**       | **Total**      |
| Count 1          | 3                | 0              |
| Count 2          | 3                | 1              |
| Count 3          | 1                | 0              |
| Total            | 11               | 5              |
| **Sharps T2**    | **Sharps T2**    | **Total**      |
| Count 1          | 3                | 1              |
| Count 2          | 1                | 0              |
| Count 3          | 0                | 0              |
| Total            | 4                | 1              |
| **Disinf**       | **Disinf**       | **Total**      |
| Count 1          | 3                | 1              |
| Count 2          | 2                | 1              |
| Count 3          | 0                | 0              |
| Total            | 6                | 5              |
| **Total T2**     | **Total T2**     | **Total**      |
| Count 1          | 12               | 3              |
| Count 2          | 4                | 2              |
| Count 3          | 2                | 1              |
| Total            | 17               | 7              |

*Cross tabulations for Time 1 (T1) versus Time 2 (T2) scores for examiners 1 and 2, and cross tabulations of scores for examiner 1 versus examiner 2. These cross tabulations are for: Barriers, Personal Protective Equipment (PPE), Sharps, Disinfection (Disinf), and (5) Total (which is the sum of the other 4 categories).

3.1 Examiner Calibration

For most comparisons of intra-examiner calibration of Examiner 1 and Examiner 2 plus inter-examiner calibration of Examiner 1 and Examiner 2, the median values were the same with the Hodges-Lehmann median differences being 0.0 (0.0 – 0.0, 95% confidence interval). Considering all of the statistical comparisons, the lowest P value was inter-examiner calibration for Total with Examiner 2 having 5 values greater than those for Examiner 1, and Examiner 1 having 1 value greater than that for Examiner 2 (Table 1); however, medians were the same (14.0) and the 95% CIs were nearly the same (Examiner 1 = 12.8 – 14.2 and Examiner 2 = 13.0 – 14.2), with the Wilcoxon test for paired samples having a P value = 0.16. The Hodges-Lehmann median difference was 0.0 (0.0 – 0.5). Inter-rater agreement for Total was assessed with weighted kappa, whose value was 0.74 (95% CI = 0.56 – 0.91), which is considered good agreement (Altman, 1999). The statistical analyses resulted in no concern with the calibration of the observers. Because of space limitations detailed statistical results are not presented for (1) Intra-Examiner Calibration Examiner 1, (2) Intra-Examiner Calibration Examiner 2, and (3) Inter-Examiner Calibration Examiner 1 and 2; however, upon request, these results are available from the lead author. A summary of examiner calibration follows, and this summary does not involve the results of statistical assessments.

For intra-examiner calibration, there were 13 subjects for each examiner and 4 items that were scored for a total of 52 comparisons of first- and second- time scores (that is, 13 x 4 = 52) (Table 1). Examiner 1 had three scores that varied by 1 value; thus, 5.8% (3/52) of Examiner 1’s first- and second- time scores differed by a single score. Prior to completing examiner-calibration assessments, it was decided that if > 5 of the scores differed (6/52 = 11.5%), this would be cause for concern. Examiner 2 had two scores that varied by 1 value; thus, 3.9% (2/52) of Examiner 2’s first-time and second time scores differed by a single score. For inter-examiner calibration, there were 19 subjects and 4 items that were scored for a total of 76 comparisons of the scores for Examiners 1 and 2. Again, prior to completing examiner-calibration assessments, it was decided that if >10 of the scores differed (11/76 = 14.5%), this would be cause for concern. Eight (8/76 10.5%) of the scores for Examiners 1 and 2 differed by a single value. Based upon these results, Examiners 1 and 2 were considered calibrated.
3.2 Observation Data

Total scores are the sums of the scores for all infection control categories, including barriers, PPE, sharps, handwashing, and disinfection. As is shown in Figure 1, the values on the x axis are the students’ scores for each bar plot. The y axis is the probability of a specific score, for each bar plot, out of the total of 59 students. The first number above a bar is the count out of 59, and second number is the probability out of 59—to give an instance, for the bar farthest to the right in L (Post Total Score), the number 12 is the count for the number of totals with a value of 16, and 22% is the percentage (12/59). For L there are 5 different totals for scores (12, 13, 14, 15, and 16) with 16 being the highest total possible. An arrow below a bar points to the highest possible score—for instance, for L, the highest possible score is 16. The counts for the post scores minus the pre scores (and their probabilities) are to the far right of each category. For example, to the right of L for level 1 (a single score value), 14 students (24%) had post scores higher than pre scores by one score value.

3.2.1 Barrier Scores Pre and Post Educational Intervention on Infection

For pre- and post-educational-intervention scores, three groups of students were assessed with sample sizes of 18, 21, and 20 for a total sample size of 59 students, which is the focus of the analyses that are presented. The median pre- and post-scores for Barriers were the same (7.0), as were the 95% confidence intervals (CIs, 6.0 - 7.0), with the Hodges-Lehmann median difference being 0.0 (-0.5 - 0.0). For 14 students, the values for Post were a single value higher than the those for Pre (Figure 1), and for 2 of the students, the values for Post were two values higher than the those for Pre. For 14 students, the values for Pre were a single value higher than the those for Post, and for 2 of the students, the values for Pre were two values higher than the those for Post. For an additional student, the value for Pre was 3 values higher than the value for Post. There was no change for 26 students; thus, for Barriers, the numbers of positive and negative differences were nearly the same, with 16 positive differences and 17 negative differences [Wilcoxon test (paired samples), P = 0.18]. The maximum score for Barriers was 7, and 33 students, 56% (33/59) had Pre scores of 7, and 33 students, 56% (33/59) had Post scores of 7 (Fig. 1).

3.2.2 PPE Scores Pre and Post Educational Intervention on Infection

The median pre- and post-scores for PPE were the same (5.0), as were the 95% confidence intervals (CIs, 5.0 - 5.0), with the Hodges-Lehmann median difference being 0.0 (0.0 - 0.5). For 12 students, the values for Post were a single value higher than the those for Pre, and for 3 of the students, the values for Post were two values higher than the those for Pre. For 6 students, the values for Pre were a single value higher than the those for Post. For PPE there were 15 positive differences and 6 negative differences [Wilcoxon test (paired samples), P = 0.04]. The maximum score for PPE was 5, and 41 students, 69% (41/59) had Pre scores of 5, and 51 students, 86% (51/59) had Post scores of 5.

3.2.3 Sharps Scores Pre and Post Educational Intervention on Infection

The median pre- and post-scores for Sharps were the same (2.0), as were the 95% confidence intervals (2.0 - 2.0), with the Hodges-Lehmann median difference being 0.0 (2.0 - 0.0). For 1 student, the values for Post were a single value higher than those for Pre, and for 2 of the students, the values for Pre were a single value higher than the those for Post. For Sharps there was 1 positive difference and 2 negative differences. Because of the small sample size, no P value could be calculated. The maximum score for Sharps was 2, and 58 students, 98% (58/59) had Pre scores of 2, and 57 students, 97% (57/59) had Post scores of 2.

3.2.4 Handwashing Scores Pre and Post Educational Intervention on Infection

The median Pre-Handwashing score was (0.0), with a 95% CI = 0.0 - 1.0, and the median Post-Handwashing score was (1.0), with a 95% CI = 0.0 - 1.0. The Hodges-Lehmann median difference was 0.0 (95% CI = 0.0 - 0.5). For 26 students, the values for Post were a single value higher than the those for Pre, and for 16 of the students, the values for Pre were a single value higher than the those for Post. For Handwashing, there were 26 positive differences and 16 negative differences [Wilcoxon test (paired samples), P = 0.18]. The maximum score for Handwashing was 1, and 24 students [41% (24/59)] had Pre scores of 1, and 34 students [58% (34/59)] had Post scores of 1.

3.2.5 Disinfection Scores Pre and Post Educational Intervention on Infection

The median pre- and post-scores for Disinfection were the same. (1.0), as were the 95% confidence intervals (CIs, 1.0 - 1.0). The Hodges-Lehmann median difference was 0.0 (95% CI = 0.0 - 0.0). The maximum score for Disinfection was 1, and 100% (59/59) of students had Pre and Post scores of 1; thus, there was no difference between Pre and Post scores for Disinfection.
3.2.6 Total Scores Pre and Post Educational Intervention on Infection

The Total score equals the sum of the scores for (1) Barriers, (2) PPE, (3) Sharps, (4) Handwashing, and (5) Disinfection, with the maximum score being 16. The median Pre- and Post-scores for Total were the same (15.0); however, the 95% confidence intervals for Pre (14.0 – 15.0) were slightly wider than those for Post (15.0 – 15.0), with the Hodges-Lehmann median difference being 0.5 (0.0 – 0.5). As indicated in Fig. 1, 13 (22%, 13/59) of the students had Post scores of 16, whereas only 6 (10%, 6/59) of the students had Pre scores of 16. Twenty-one students (36%, 21/59) had the same Pre and Post Total scores. For 14 students (24%), the values for Post were a single value higher than the those for Pre; for 9
students (15%), the values for Post were two values higher than the those for Pre, and for 1 student (2%), the value for Post was three values higher than the values for Pre. For 12 students (20%), the values for Pre were a single value higher than the those for Post; for 1 student (2%), the value for Pre was two values higher than the value for Post, and for 1 student (2%), the value for Pre was three values higher than the value for Post. For Total, there were 24 differences (41%) for which Post had a larger score than Pre and 14 (24%) differences for which Pre had a larger score than Post [Wilcoxon test (paired samples), \( P = 0.04 \)]. An exact Agresti-Coull calculation of the difference between the proportions of positive differences and negative differences also resulted in a \( P \) value of 0.04 and had a power of 0.83. We consider these differences to be clinically important and support the benefit of educational intervention on IC practices.

4. Discussion

This study supports what we hypothesized and demonstrates improvement in subjects’ compliance and understanding of the IC practices after the educational intervention. We observed positive differences in overall IC practices of subjects after the training multimedia video, which was created to be specific to our dental clinical scenario. We consider the higher scores observed following the incorporation of the multimedia training to be clinically important and indicate that didactic intervention was effective in improving IC practices in the school clinic.

Establishing proper IC understanding and practices is relevant in an educational setting so that this knowledge can be applied in the graduates’ professional careers. A 10-year longitudinal study evaluated attitudes and behavior of dental students concerning IC rules, with the study showing no improvement, and for some parameters, there was a decrease in compliance over the time evaluated (Abreu et al., 2009). The results of our study revealed overall clinically important improvements in the IC practices after an educational intervention, specifically for PPE with 15 of 59 (25%) positive differences and 6 negative differences (10%), and hand-washing scores with 26 of 59 positive differences (44%) and 16 negative differences (27%). The scores for the disinfection parameter showed the same results pre- and post-intervention, with 100% compliance. We did not observe clinically important improvements regarding the proper placement of plastic barriers as well as proper handling of sharps; the median pre- and post-intervention scores were the same for both parameters. Despite being shown proper placement of all the protection barriers, a common item to not be placed was the air-water syringe barrier. According to students’ post-intervention comments, perhaps a reason for inadequate use of the air-water syringe barrier is that students feel they are unable to efficiently work with its placement.

A previous observational study of IC compliance following mandated Ebola virus disease online training, reported that new training did not make a large impact on student IC practices (Anders et al., 2016). However, the present observational study showed improvements in IC practices following the training strategy. Dental Schools should be focused on strategies that may have a positive impact on attitudes and behavior concerning IC practices (Abreu et al., 2009). Didactic resources enhance students’ learning experiences; that is, incorporation of digital multimedia training, specific to the students’ environment has proven to be an impactful teaching strategy for this new generation of learners, as reflected in the results of our study (Brame, 2016). Besides the clinical observations, students were given the opportunity to analyze their own experiences and perceptions of the importance of infection control in the dental clinic before and after the intervention video, to examine their attitudes concerning the intervention video. The results of students’ experiences and perceptions will be reported in a future manuscript.

In our study, the examiners’ calibration protocol prior to data collection allowed standardized data collection and facilitated statistical comparisons of pre- and post- interventions. The didactic educational intervention was effective in improving the overall compliance of the infection-control practices, for total scores; 24 of the 59 students (41%) had higher post- multimedia video scores whereas only 14 students (24%) had higher pre-video scores \( (P = 0.04) \). While it is possible that improvements observed during an observational study may be short-term alterations due to the observations being performed, the scores of subjects showing higher pre-video scores in the present study indicate that this bias did not affect the results of the study (Gordon et al., 2001). Additionally, the previous implementation of weekly IC rounds in the clinic, established prior to the initiation of the study, may have prevented this bias. A study limitation included difficulty in obtaining pre- and post- intervention observation data for all the third- and fourth-year students in the clinic. Patient absences as well as teams’ external clinical rotations outside of the main clinic (where observations were performed and recorded) presented obstacles to observing clinical practices and including all potential subjects in this study.

The advent of the COVID 19 pandemic has created public health concerns throughout the world. The infection-control protocols in dentistry have been modified and are now stricter; additional guidelines have been proposed by the corresponding agencies and adopted in dental practices and dental education institutions. The easier transmission and the ability of the “severe acute respiratory syndrome coronavirus 2” (SARS-CoV-2) to survive outside living organisms (in aerosol or on fomites) is a concern for dental practices (Amato et al., 2020). Additionally, the modifications of infrastructure in clinical environments in dental schools have been imminent, as well as the acquisition of additional
equipment and supplies with subsequent modifications of the clinical protocols. This new reality requires the proper training of students, faculty, and staff, with the utilization of impactful teaching strategies and resources being fundamental to improving infection control practices. We consider that our educational approach was effective in positively changing clinical behaviors related to infection control. A didactic multimedia tool using clinical scenarios to outline relevant information is a dynamic tool that can be used as part of a training program. Similar strategies could be useful and relevant in the training and adoption of the updated clinical protocols in dental school clinics.

5. Conclusion
Overall, IC compliance in the dental clinic improved because of the didactic training. The improvements observed in this study following the intervention are clinically important and support the benefit of a multimedia intervention designed on IC compliance in this setting.

6. Disclosure
The authors do not declare any conflict of interest in connection with this study.

7. Data Availability Statement
The data that support the findings of this study are available from the corresponding author upon reasonable request.

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