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Article

# Contributions of Clinical Simulation to Group Cohesion: A Quasi-Experimental Study

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## Abstract

(1) Background: The increasing complexity of today's healthcare system requires the formation of highly cohesive work teams that guarantee safe and high-quality care. Clinical simulation has become established as a pedagogical strategy capable of promoting the collaborative skills of teams of students and healthcare professionals. The objective of this study was to analyze the influence of learning through clinical simulation on promoting group cohesion in nursing student teams; (2) Methods: A quasi-experimental study with a pre-post design without a control group was conducted with final-year nursing students using the short Spanish version of the Group Environment Questionnaire, validated for nursing students. This questionnaire was completed twice by the participating students, before and after clinical simulation practices; (3) Results: Clinical simulation sessions significantly increased group cohesion in most items and in all dimensions with a large effect size greater than 0.5. The dimension Group Integration-Task (GI-T) showed the greatest improvement after clinical simulation practices; (4) Conclusions: Clinical simulation has significantly increased all dimensions of group cohesion among nursing students. Clinical simulation primarily enhances collaboration and commitment among nursing students to achieve common goals. Due to its impact on group cohesion, clinical simulation should be used systematically to improve the efficiency and quality of student and healthcare professional teams.

**Keywords:** group cohesion; simulated learning environment; nursing

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## 1. Introduction

High levels of technology development and the need for continuity of care are the determining factors in healthcare today. This increase in healthcare complexity means that individual work is no longer sufficient to meet all needs and requires healthcare professionals to work as a team in order to provide efficient, high-quality care to patients (Braš et al., 2022; Salihović et al., 2024). Teamwork allows for more efficient use of available healthcare resources, while simultaneously reducing stress and increasing satisfaction among healthcare professionals (Anselmann et al., 2023; Schmutz et al., 2019; Wang et al., 2023).

To work effectively as a team, healthcare professionals need to develop a set of non-technical skills, including effective communication, coordination, complementarity, trust, and commitment. These non-technical skills are essential for strengthening the cohesion of the healthcare team, enabling the achievement of common goals within a work environment characterized by excessive workload and high emotional involvement from both patients and professionals (Anselmann et al., 2023; Stahel et al., 2022; Zeng et al., 2022).

Group cohesion refers to the process that keeps a healthcare team united as it works toward achieving common care goals. Adequate cohesion within healthcare teams ensures comprehensive patient care and also promotes the emotional well-being of healthcare professionals. Two aspects can be distinguished within group cohesion: task cohesion, or commitment to achieving common goals, and social cohesion, or the degree of interaction among team members. Addressing these two aspects, both as a group and individually, will give rise to the four dimensions that make up group cohesion: Group Integration-Task (GI-T) or degree of group union to achieve common objectives, Group Integration-Social (GI-S) or degree of group union to develop social relations within the group, Individual Attractions to Group-Task (ATG-T) or individual motivations towards common objectives, and Individual Attractions to Group-Social (ATG-S) or individual motivations towards social relations within the group (Borrego et al., 2012; Carron et al., 1985; Gu & Xue, 2022; Mehdi, 2023; Sghari et al., 2019).

The Group Environment Questionnaire (GEQ) allows for the assessment of these four dimensions of group cohesion (Carron et al., 1985; Eys et al., 2007). Among the various adaptations and validations of the original questionnaire for the Spanish language and context (Checa & Bohórquez, 2020; Leo et al., 2015) is the short version validated for nursing students undergoing clinical simulation training (García-Álvarez et al., 2025). This version has shown acceptable values for internal consistency, homogeneity, and test-retest reliability, both for the questionnaire as a whole and for its individual dimensions. Exploratory and confirmatory factor analyses of this version have confirmed that it adequately fits the original four-dimensional model of group cohesion (García-Álvarez et al., 2025). Therefore, the short Spanish version of the Group Environment Questionnaire (GEQ) can be considered a valid and reliable instrument for analyzing group cohesion in nursing student teams undergoing training in simulated learning environments (García-Álvarez et al., 2025).

Clinical simulation has amply demonstrated its ability to develop non-technical skills considered essential for improving teamwork and fostering group cohesion among teams of students and healthcare professionals. Clinical simulation promotes situational awareness, efficient use of available resources, strengthened decision-making processes, and effective information transfer. In addition, clinical simulation also leads to increased trust and mutual respect, greater commitment and collaboration, appropriate distribution of leadership, and substantial improvement in stress management (Allard et al., 2020; Flynn et al., 2022; Griffin et al., 2020; Innocenti et al., 2022; Peddle, 2019; Lee & Lee, 2022; Lynch, 2020; Ounounou et al., 2019; Wu, 2025).

Analyzing the influence of clinical simulation on group cohesion using this questionnaire would allow for the development of intervention programs specifically designed to strengthen group cohesion within healthcare teams. Increased group cohesion among healthcare teams would improve the efficiency and quality of patient care. In addition, it would reduce stress and increase the job satisfaction of healthcare professionals.

The objective of this study was to analyze the influence of learning through clinical simulation on promoting group cohesion in nursing student teams.

## 2. Materials and Methods

### 2.1. Ethics Statement

This study was conducted in accordance with the ethical principles established by the Declaration of Helsinki (World Medical Association, 2013) and with the approval of the Ethics Committee of the Catholic University of Murcia (UCAM).

All participating students were fully informed about the characteristics of the study, emphasizing the voluntary nature of their participation and their right to withdraw at any time. Written informed consent was obtained from all participants, and confidentiality was ensured by the absence of any identifying information.

## 2.2. Study Design

To analyze the changes in group cohesion produced by clinical simulation sessions, a quasi-experimental study with a pre-post design without a control group was conducted, following the TREND (Transparent Reporting of Evaluations with Non-Randomized Designs) checklist for non-randomized intervention studies (Des Jarlais et al., 2004).

## 2.3. Subjects and Scope of Study

The study participants were fourth-year nursing students from the Catholic University of San Antonio of Murcia, Spain (UCAM) and the University of Murcia, Spain (UMU) who had participated in clinical simulation sessions between October 2023 and July 2024. These students were selected for this study because they had prior experience in training in simulated environments. This prior experience reduced the variability among the participating students and allowed the observed results to be attributed with a high probability to the intervention performed.

## 2.4. Sample Selection

The inclusion criteria were: being a fourth-year nursing degree student at participating universities, having completed all clinical simulation sessions, and wanting to participate voluntarily in the study.

The sample was selected using non-probability convenience sampling based on the groups assigned by the Nursing Practice Unit of each of the participating universities.

## 2.5. Measurement Instrument and Data Collection

To collect the information, each participant completed the same questionnaire twice: once before beginning the clinical simulation sessions and again after finishing them. The initial questionnaire included a section with sociodemographic data and another with the short Spanish version of the Group Environment Questionnaire (GEQ), validated for nursing students participating in clinical simulation practices (García-Álvarez et al., 2025). The final questionnaire included only the GEQ. The GEQ consists of 12 items with a five-point Likert-type response format, ranging from strongly disagree (1) to strongly agree (5). Items 1, 3 and 5 assessed the dimension Individual Attractions to Group-Social (ATG-S), items 2, 4 and 6 analyzed the dimension Individual Attractions to Group-Task (ATG-T), items 7, 9 and 11 assessed the dimension Group Integration-Social (GI-S) and items 8, 10 and 12 analyzed the dimension Group Integration-Task (GI-T) (Table 1) (García-Álvarez et al., 2025).

The variables analyzed were: university of origin, age, gender, region of origin, previous academic qualification, work activity, scores of the questionnaire items, scores of the questionnaire dimensions, and total questionnaire score.

## 2.6. Data Analysis

The information was collected in a database that was later analyzed using the SPSS v26® statistical software for Windows (Armonk, NY, USA: IBM Corp.).

**Table 1.** Spanish short version of the Group Environment Questionnaire (GEQ) for nursing students.

Number	Item
1	I like to participate in extracurricular activities with the other members of my group (dinners, excursions...)
2	I am happy with my contributions to the work of the group
3	I have good friends in this group
4	In this group I can perform to the best of my ability
5	Group members are one of the most important social groups to which I belong
6	I like the style of work of this group
7	Group members like to party together

- 8 Group members join forces to achieve the objectives during the preparation and conduct of the simulation sessions
- 9 Group members would like to get together a few times after the clinical simulation is over
- 10 All members take responsibility for a poor group performance
- 11 Our group members would like to meet in situations other than preparing and conducting simulation sessions
- 12 If there is a problem during the preparation of the simulation sessions, all members join forces to overcome it

Note: García-Álvarez et al., 2025.

For dichotomous or polytomous qualitative variables, frequencies and percentages were calculated. For quantitative variables, the mean was calculated as a measure of central tendency and the standard deviation as a measure of dispersion, verifying their normality using the Kolmogorov-Smirnov test. For ordinal qualitative variables, the median was calculated as a measure of central tendency and the interquartile range (IQR) as a measure of dispersion (Kaliyadan & Kulkarni, 2019; Mishra et al., 2018). Inferential statistical analysis was also performed using appropriate tests based on the characteristics of the variables analyzed (Table 2) (Patel, 2021a; Patel, 2021b).

**Table 2.** Inferential statistics of sociodemographic data.

Variables	Statistical test
Age and university	Mann-Whitney U
Age and gender	Mann-Whitney U
Age and region of origin	Kruskal-Wallis
Age and previous academic qualification	Mann-Whitney U
Age and work activity	Mann-Whitney U
Gender and university	Chi-square
Gender and region of origin	Chi-square
Gender and previous academic qualification	Chi-square
Gender and work activity	Chi-square
Region of origin and university	Chi-square
Region of origin and previous academic qualification	Chi-square
Region of origin and work activity	Chi-square
University and previous academic qualification	Chi-square
University and work activity	Chi-square
Work activity and previous academic qualification	Chi-square

To assess the influence of clinical simulation on group cohesion, variations in item and dimension scores were analyzed between the two administrations of the GEQ questionnaire, before and after clinical simulation practices. The Wilcoxon test was used for statistical analysis, relating a dichotomous qualitative independent variable (before and after clinical simulation) to ordinal qualitative dependent variables (item and dimension scores) in a paired sample (Fritz et al., 2012; Stewart et al., 2016).

To calculate the effect size of clinical simulation practices on group cohesion, the biserial correlation coefficient  $r [r=Z/\sqrt{N}]$  were used, employing the Z value from the Wilcoxon test to analyze pre-post clinical simulation differences. Values below 0.3 were considered small effects, values between 0.3 and 0.49 were considered medium effects, values between 0.5 and 0.69 were considered large effects, and values equal to or greater than 0.7 were considered very large effects (Lafferty et al., 2016).

### 3. Results

The study sample consisted of 188 students from UCAM and 123 students from UMU. Most of the students were between 21 and 22 years old (63.65%), were female (78.14%), and came from the

region where the universities were located, the Region of Murcia (Spain) (71.06%). A significant percentage of the students did not have a previous degree (81.68%) and were not working (91.00%).

Statistically significant associations were found between age and gender ( $p=0.001$ ), previous academic qualification ( $p=0.000$ ), and work activity ( $p=0.000$ ). Significant associations were also observed between region of origin and university ( $p=0.000$ ), and between work activity and previous academic qualification ( $p=0.000$ ).

Following the clinical simulation sessions, group cohesion improved, as indicated by the increased median for most items and all dimensions of the second questionnaire completed after the simulation practices. The decrease in the IQR values for the dimensions of the second questionnaire suggests a high degree of consensus among the participants' responses, due to their clustering around the median (Table 3 and Table 4).

**Table 3.** Descriptive statistics of the questionnaire items.

Initial questionnaire	Item 1	Item 2	Item 3	Item 4	Item 5	Item 6	Item 7	Item 8	Item 9	Item 10	Item 11	Item 12
Median	4	4	4	4	3	4	3	4	4	4	4	3
IQR	1	1	1	1	1	1	1	1	1	1	1	1
Final questionnaire	Item 1	Item 2	Item 3	Item 4	Item 5	Item 6	Item 7	Item 8	Item 9	Item 10	Item 11	Item 12
Median	5	4	5	5	4	5	4	5	4	5	4	5
IQR	1	1	1	1	1	1	1	1	1	1	1	1

**Table 4.** Descriptive statistics of the questionnaire dimensions.

	ATG_S1	ATG_T1	GI_S1	GI_T1	ATG_S2	ATG_T2	GI_S2	GI_T2
Median	11	12	11	11	13	13	13	14
IQR	3	4	3	4	2	2	2	2

Note: initial questionnaire (1), final questionnaire (2).

The improvement in scores for most items and all dimensions of group cohesion after clinical simulation practices was statistically significant. The effect size achieved was moderate or large for individual items and large for all dimensions and for the total group cohesion score. The total group cohesion score and the GI-T dimension were the variables that showed the greatest improvement after the clinical simulation exercises (Table 5 and Table 6).

**Table 5.** Influence of clinical simulation on group cohesion - items.

	Z	Bilateral significance	Size of effect
Item 1_1 - Item 1_2	-9.935*	0.000	0.563
Item 2_1 - Item 2_2	-7.365*	0.000	0.418
Item 3_1 - Item 3_2	-11.393*	0.000	0.646
Item 4_1 - Item 4_2	-8.006*	0.000	0.454
Item 5_1 - Item 5_2	-4.483*	0.000	0.254
Item 6_1 - Item 6_2	-9.800*	0.000	0.556
Item 7_1 - Item 7_2	-6.401*	0.000	0.363
Item 8_1 - Item 8_2	-10.208*	0.000	0.579
Item 9_1 - Item 9_2	-7.059*	0.000	0.400
Item 10_1 - Item 10_2	-8.117*	0.000	0.460
Item 11_1 - Item 11_2	-6.954*	0.000	0.394
Item 12_1 - Item 12_2	-10.337*	0.000	0.586

Note. Statistical tests used: Wilcoxon test (Z and bilateral significance), biserial correlation coefficient r (effect size). \* Negative ranks: final questionnaire score (2) > initial questionnaire score (1).

**Table 6.** Influence of clinical simulation on group cohesion - Dimensions and total score.

	Z	Bilateral significance	Size of effect
ATG-S_1 – ATG-S_2	-10.549*	0.000	0.598

ATG-T_1 – ATG-T_2	-9.599*	0.000	0.544
GI-S_1 – GI-S_2	-9.805*	0.000	0.556
GI-T_1 – GI-T_2	-11.099*	0.000	0.629
Total score_1 – Total score_2	-12.046*	0.000	0.683

Note. Statistical tests used: Wilcoxon test (Z and bilateral significance), biserial correlation coefficient r (effect size). \* Negative ranks: final questionnaire score (2) > initial questionnaire score (1).

#### 4. Discussion

The superior scores on the items and dimensions of the second questionnaire indicate that clinical simulation has been an effective learning tool for increasing group cohesion among nursing students. The effect size achieved by clinical simulation practices was large for all four dimensions of group cohesion analyzed by the GEQ questionnaire for nursing students.

The results obtained in this research coincide with previous studies that have also observed that carrying out simulation activities in sports or educational contexts has favored the formation of work teams by increasing group cohesion, supporting the use of simulation as an effective strategy to promote team cohesion in different training areas (Lafferty et al., 2016; Mathieu et al., 2015; Stewart et al., 2016).

The group cohesion dimension GI-T showed the greatest improvement after the clinical simulation sessions. This result indicates that this learning tool has increased the bonds between team members to achieve common goals. Participating together in the same situations and with shared learning objectives has promoted communication, collaboration, coordination, and commitment. These non-technical skills are essential for achieving common objectives and are recognized for their ability to increase group cohesion. Clinical simulation is a shared experience carried out through teamwork, which helps to increase the sense of belonging to the team. This learning tool allows team members to face challenges, successes, and failures together. All these non-technical skills fostered by clinical simulation strengthen the emotional and professional bond between team members, thus promoting group cohesion (Fritz et al., 2012; Stewart et al., 2016; Lafferty et al., 2016; Mathieu et al., 2015; Mende et al., 2020; Power et al., 2022; Roqueta-Vall-Llosera et al., 2024; Fornander et al., 2024; Roh et al., 2024).

The improvement in the ATG-S dimension following clinical simulation sessions has highlighted its ability to foster a strong desire among members to belong to the work team, an interest that goes beyond mere commitment to achieving common goals. The increase in this dimension suggests that clinical simulation not only reinforces formal cohesion within the group but also enhances the sense of collective identity, interpersonal trust, and the perception of mutual support. Clinical simulation has enabled participants not only to work together more effectively but also to develop a deeper sense of belonging. Strengthening this sense of belonging will increase motivation, team stability, and the willingness to collaborate proactively in real or simulated healthcare settings (Cheng et al., 2020; Benchadlia et al., 2023; Mabry et al., 2020; Melo & Cole, 2024; Roh et al., 2024).

The increase in the GI-S dimension has highlighted the team members' commitment to establishing interpersonal connections outside of clinical simulation practices. This result suggests that the shared experiences during simulation have not only strengthened collaboration within the training environment but have also fostered the creation of stronger and more lasting personal relationships. These bonds established outside of academic activities can contribute to improving the climate of trust, open communication, and mutual support, factors that will allow for a much more cohesive and effective work dynamic when team members face future simulated or real clinical situations (Cheng et al., 2020; Benchadlia et al., 2023; Mabry et al., 2020; Melo & Cole, 2024; Roh et al., 2024).

The improvement, lastly, in the ATG-T dimension indicated that clinical simulation promotes the prioritization of group objectives over individual interests. This result suggests that clinical simulation has been a collective experience capable of ensuring that the team's competencies as a whole exceeded the mere sum of its members' individual competencies, placing the collective above

the individual in order to strengthen group cohesion (Cheng et al., 2020; Benchadlia et al., 2023; Mabry et al., 2020; Melo & Cole, 2024; Roh et al., 2024).

Clinical simulation has been shown to promote effective communication within work teams. This type of communication is characterized by the exchange of clear, concise, and easily interpretable messages to avoid any possible confusion. By training these communication skills in a safe and controlled environment, students learn to express their ideas precisely, listen actively, and validate the information received. Effective communication improves the quality of interactions among team members, facilitating the development of stronger mutual trust and increasing their satisfaction (Peng et al., 2019; Robson et al., 2023).

Clinical simulation also provides an excellent opportunity to learn how to address potential conflicts that may arise within a team, helping to improve trust and interpersonal relationships among its members. By recreating complex situations in a safe environment, participants can practice conflict management strategies, such as assertive communication, active listening, and collaborative problem-solving, without the risks associated with a real clinical setting. This training promotes the early identification of tensions, the collaborative resolution of disagreements, and the strengthening of mutual respect. As a result, teams acquire a greater capacity to face challenges, maintain cohesion, and work more harmoniously in demanding contexts such as the healthcare setting (Barr et al., 2020; Benchadlia et al., 2023; Cheng et al., 2020; Gunasingha et al., 2023; Johnston & Pierce, 2023; Mabry et al., 2020; Melo & Cole, 2024).

Clinical simulation is primarily based on collaborative learning and group reflection. These characteristics enable clinical simulation to foster a culture of mutual support within an inclusive environment, where each team member feels valued regardless of their hierarchical level or experience. The opportunity to share perceptions, emotions, and analysis during debriefing encourages all participants to recognize themselves as active members of the improvement process, thus reinforcing equal participation and respectful listening. This inclusive environment allows errors made during clinical simulation practice to be viewed as opportunities for improvement rather than sources of blame. By addressing failures from a growth perspective, participants develop greater openness to feedback and a more proactive attitude toward self-reflection and continuous improvement. This constructive view of mistakes strengthens the sense of collective achievement, motivates the team to work better in the future, and ultimately promotes group cohesion by consolidating the idea that progress is the result of shared effort and not isolated individual performances (Cust et al., 2022; Power et al., 2022).

In short, clinical simulation increases group cohesion by providing a safe and inclusive space where team members can practice critical skills, face common challenges, and reflect together on any present or future tasks. This protected learning environment allows participants to experiment, make decisions, and manage complex situations without the risk inherent in real practice, promoting greater openness to collaborate, communicate, and learn together. Clinical simulation can improve both the technical and non-technical skills of team members, strengthening interpersonal bonds between them and building more effective, resilient, and cohesive teams. It also promotes understanding of professional roles, increases the ability to anticipate the needs of the group, and fosters a culture of support and shared responsibility. The recurring practice of simulated scenarios improves group work dynamics and promotes team success in real clinical settings, as the lessons learned are naturally transferred to healthcare practice. Clinical simulation allows for the formation of teams that are more confident, coordinated, and better prepared to deal with high-pressure situations more effectively.

The selection of participating students through non-randomized convenience sampling and their affiliation with two different universities in the same geographic area may limit the external validity of this study, as the results obtained could be heavily influenced by the specific characteristics of the region where they are located. This implies that the findings may not be directly applicable to nursing students from other universities, regions, or different cultural contexts. To allow for a more robust generalization of the results, it would be advisable to conduct further studies with a more

diverse and representative sample, selected through random sampling at universities in different regions. This would also allow for an assessment of whether the effects of clinical simulation on group cohesion persist across different educational settings, strengthening the external validity and practical applicability of the conclusions.

Due to the characteristics of the university educational context in which this research was conducted, it was not possible to establish a control group. All students were part of the same educational program where clinical simulation practices are mandatory and universal, making it impossible to exclude a number of students to establish a control group. The pre-post quasi-experimental design without a control group is quite common in educational settings where the intervention, as in this case with clinical simulation practices, is an integral part of the students' curriculum. The lack of a control group may be a limitation as it prevents the results obtained in improving group cohesion from being attributed with complete certainty to clinical simulation practices. However, considering that during the study period the students only participated in clinical and simulated practice, and that the two key elements on which group cohesion is based (common goals and shared leadership) were present exclusively in the simulated practices, it would be highly probable to attribute the improvement in group cohesion to clinical simulation. It would be advisable to conduct future studies that include a control group of nursing students who do not perform clinical simulation practices in order to determine the true influence of this learning tool on improving group cohesion in these teams.

Conducting this study with nursing students rather than practicing professionals could affect the generalizability of the results, as academic activity can differ significantly from professional practice, which is influenced by patient care pressure, case complexity, responsibility, and the dynamics of multidisciplinary teams. Therefore, it would be advisable to conduct future studies assessing group cohesion in real healthcare settings, where teams include physicians, nurses, technicians, and other professionals with varying levels of experience and responsibility. Analyzing group cohesion among the different professionals comprising healthcare teams would allow researchers to identify how interpersonal relationships and collaboration influence teamwork effectiveness, decision-making, and care coordination. Likewise, such studies could provide more direct evidence on the impact of group cohesion on the quality of healthcare, patient safety, and the satisfaction of both healthcare professionals and users, thus providing valuable information for designing interventions aimed at strengthening clinical teams.

Furthermore, qualitative studies would be beneficial to explore in greater detail the individual perceptions, emotions, and experiences that contribute to group cohesion within healthcare teams. This type of research would make it possible to understand not only observable behaviors but also of the subjective factors that influence team dynamics, such as motivation, trust, communication, conflict management, and the perception of peer support. A broader understanding of these interpersonal relationships would enable the identification of specific patterns, barriers, and facilitators of cohesion, as well as the particularities of different roles within the team. In addition, the findings of qualitative studies could guide the implementation of more precise and context-specific intervention strategies, such as teamwork training programs, collaborative simulation activities, mentoring, or group reflection exercises, with the aim of strengthening group cohesion and, ultimately, improving both team efficiency and the quality of healthcare.

## 5. Conclusions

Clinical simulation has significantly increased group cohesion in teams of final-year nursing students in all dimensions analyzed by the short Spanish version of the Group Environment Questionnaire (GEQ) for nursing students.

Group Integration-Task (GI-T) was the group cohesion dimension that showed the greatest improvement after the clinical simulation sessions. This result highlights the significant influence of this learning tool in enhancing collaboration and commitment among nursing students in achieving common goals.

Since clinical simulation has proven capable of increasing group cohesion in nursing student teams, its regular use in healthcare settings should be considered to improve the efficiency and quality of student and healthcare professional teams.

**Author Contributions:** J.M.G.-Á. and A.G.-S.: conceptualization, investigation, data curation, writing, original draft preparation, introduction, discussion, and conclusion; J.L.D.-A.: conceptualization, introduction, methodology, project administration, writing, editing, and supervision; J.M.G.-Á. and A.G.-S.: results and editing; J.L.D.-A.: results and editing; J.M.G.-Á. and A.G.-S.: conceptualization, investigation, and results. All authors have read and agreed to the published version of the manuscript.

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**Institutional Review Board Statement:** The study was performed in accordance with the guidelines of the Declaration of Helsinki and has been approved by the Ethics Committee of the Catholic University of Murcia (UCAM), Spain (Reference number: CE012310 / Date of approval: January 26, 2023).

**Informed Consent Statement:** Informed consent was obtained from all subjects involved in the study.

**Data Availability Statement:** The data used to support the findings of this study are available from the corresponding author upon request.

**Conflicts of Interest:** The authors declare no conflicts of interest.

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