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Strength Exercises With Blood Flow Restriction Promotes Hypotensive and Hypoglycemic Effects in Women With Mellitus Type 2 Diabetes?: Randomized Crossover Study

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ABSTRACT

The aim of this study was to investigate the effects of blood flow restriction (BFR) strength exercises on blood pressure (BP) and blood glucose (BG) in diabetic women. Ten women with type II diabetes (Age = 56.9 ± 7.4 years old; BMI = 27.2 ± 4.2 kg/m^2; Diagnostic time = 10.6 ± 4.1 years) participated in this study. On three non-consecutive days, participants were randomly assigned to 1 of 3 training conditions: (i) Low-load exercise [LL; ~ 20% of 1 maximum repetition (1RM)]; (ii) LL-BFR exercise [~ 20% of 1RM/50% of arterial occlusion pressure (AOP)]; (iii) High load exercise (HL; ~ 65% of 1RM). Systolic BP (SBP), diastolic BP (DBP) and mean (MBP) values were assessed before, immediately, 15, 30, 45 and 60 min after the interventions. BG concentrations were analyzed before, immediately and 60 min after the interventions. SBP significantly reduced 60 min after LL exercise ($p = 0.002$), but it was not significantly reduced at any point after LL-BFR or HL exercise. DBP decreased significantly 45 min after LL exercise ($p = 0.028$) and 60 min after LL and LL-BFR exercise ($p = 0.004$ and $p = 0.002$, respectively). We verified a condition effect for the BG percentage variation, however post-hoc analyzes revealed only a difference tendency between LL and LL-BFR exercises (3.5% and -10%, respectively; $p = 0.053$). It is concluded that the LL and LL-BFR exercise protocols resulted in a post-exercise hypotensive effect, and the BFR protocol, apparently, presents superiority in BG reduction.

Keywords: *Kaatsu training; vascular occlusion; resistance training; blood pressure; blood glucose.*

1. Introduction

The new estimates of diabetes prevalence present that there will be approximately 592 million people with diabetes across the world by the year 2035 (1). *Diabetes* mellitus is a group of metabolic *diseases*, characterized by chronic hyperglycemia (2) which is related to an increased risk for cardiovascular diseases development (3). Generally, diabetic individuals have higher blood pressure (BP) values compared to their non-diabetic peers (4). Based on research evidences, BP reduction and glycemic control have been associated with a reduced risk for diabetes-related complications (5, 6).

In this sense, regular physical exercise should be encouraged in the diabetes mellitus management (7), considering that this intervention type has the capacity to reduce BP values (8) and improve blood glucose (BG) (9) in diabetic individuals. Recently, blood flow restriction (BFR) physical training has been recommended for hypertensive people (10, 11) and has been suggested as a possible training strategy for diabetic people (12).

The training strategy that associates low-load physical exercise with BFR, artificially generated by pneumatic cuff tightening or elastic band in the proximal region of the exercised limb, has the capacity to increase GLUT4 concentrations (i.e., glucose transporter) (13) and may have a more pronounced hypotensive effect than traditional training (14).

Currently, the literature does not provide studies that have evaluated the BFR training effect on the cardiovascular and glycemic responses of diabetic individuals (15). As such, it is not known whether the use of this technique actually reflects any additional benefit for this population or if use is safe. We consider it pertinent to analyze this type of outcome, especially because diabetics may have a post-exercise hypotensive effect different from their non-diabetic peers (16) or even generate a hyperglycemic or hypoglycemic effect. Therefore, the aim of this study was to analyze the hypotensive and hypoglycemic effect of BFR strength exercise (SE) in type II diabetes women.

2. Methods and Materials

2.1. Subjects

A total of 10 untrained women with type 2 diabetes mellitus participated in this study. The participant's characteristics are described in Table 1. The participants were recruited through the research propagation in local gyms and social networks. The following inclusion criteria were adopted: (i) not being part of systematic physical training programs for at least six months; (ii) not having osteomioarticular lesions in the lower limbs in the last six months; (iii) not have an existing medical condition that contraindicated physical activity (assessed by the PAR-Q); (iv) age 18-60 years. Participants using insulin, metformin, diuretics, beta-blockers during the research period were excluded. All participants received information about the risks and benefits of the research and provided a written consent to participate in the study. This study was conducted in accordance with the Helsinki Declaration and was approved by the Ethics Committee on Human Research at the local institution (Nº. 3.520.337).

Table 1

Subject characteristics.

Variables	Mean ± SD
Age (years)	56.9 ± 7.4
Body mass (kg)	62.9 ± 11.7
Height (cm)	149.0 ± 3.8
BMI (kg/m^2)	27.2 ± 4.2
T2DM Diagnostic Time (years)	10.6 ± 4.1
1RM knee extension (kg)	28.2 ± 6.2
BFR (mmHg)	190.0 ± 21.6

SD = Standard Deviation; n = 10; BMI = body mass index; T2DM = type 2 diabetes mellitus; 1RM = one repetition maximum; BFR = blood flow restriction.

2.2. Experimental Design

The study was a randomized, crossover clinical trial that aimed to analyze the acute effect of BRF strength exercise on BP and BG of type II diabetes women. Participants made four visits to a local gym (Campestre Club, Campina Grande-PB, Brazil). A 3-5 days washout was established between visits. On visit 1, the participants answered an anamnesis form and the Physical Activity Readiness Questionnaire (PAR-Q). Subsequently, the participants underwent an anthropometric assessment (body mass and height), measurement of the foot dorsal artery pressure (AOP) and predictive test of 1 maximum repetition (1RM) of knee extension (KE). Visits 2, 3 and 4 were randomized to: (i) High-load exercise (HL; 65% of 1RM); (ii) Low load exercise (LL; 20% of 1RM); (iii) Low load exercise with blood flow restriction (LL + BFR; 20% 1RM). Randomization was achieved by a draw. The experimental

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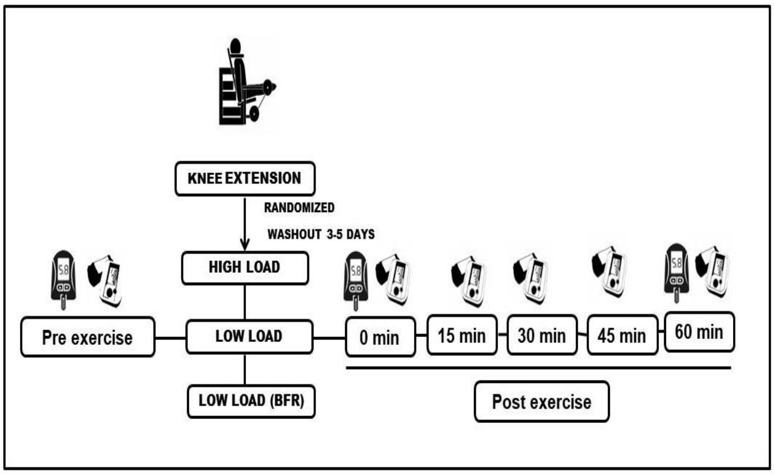
sessions were carried out at the same day time (3 p.m. – 6 p.m.), aiming to control the daytime variation of hemodynamic measurements. BG was measured before, immediately after and 60 min after the experimental sessions. Individuals with BG values above 250 mg/dL without ketoacidosis symptoms were allowed to perform the experimental protocol. BP values were measured before, immediately after, 15, 30, 45 and 60 min after the experimental sessions. During the study, participants were asked to abstain themselves from exhaustive exercise, avoid caffeine and alcohol intake in the 24 hours before and after the tests, and to sleep at least 6 hours the night before the exercise session. In addition, they were also instructed to maintain the same eating habits throughout the study period. During all exercise sessions, individuals were asked not to perform a Valsalva maneuver (Figure 1).

Figure 1

Experimental sessions design.



2.3. *Procedures*

2.3.1. *BFR Evaluation*

After 5 minutes of rest, a pressure (mmHg) was obtained to restrict the posterior tibial artery blood flow by means of a portable vascular doppler (MedPej®, DF-7001 VN, Ribeirão Preto, São Paulo - Brazil). The probe was fixed above the tibial artery, in order to capture the auscultatory pulse. A pneumatic tourniquet (Dimensions: width 100 mm; length 540 mm - Riester®) was attached below the inguinal fold and inflated until the pulse was completely eliminated (AOP) (17). Considering that the body position has an effect on the absolute pressure levels (11), the measurement was performed while the participants remained seated (position adopted in the exercise).

2.3.2. *1RM Predictive Test*

The 1RM values for knee extension were determined using a submaximal test. Initially, the participants performed a warm-up consisting of 10 repetitions with 40-60% of the 1RM estimate. After 1 minute, the participants performed a warm-up consisting of 5 repetitions with 60-80% of the 1RM estimate. After a new 1-minute interval, we adjusted the load, and asked the participant to perform as many repetitions as possible. The load and the number of repetitions were recorded and used to predict the values of 1RM using the Brizycki equation (18): 1-RM = 100 × load / [102.78 - (2.78 × reps)].

2.4. *Physiological measures*

2.4.1. *Blood pressure*

Blood pressure was assessed at rest and immediately, 15, 30, 45 and 60 minutes after the experimental session tested. To perform the measurements, the participants were seated, with the back supported on a chair, legs aligned with the hips and the feet in contact with the ground. All evaluations were performed using oscillometric method (OMROM®; model HEM-705CP 705CP). The systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean blood pressure (MBP) [(SBP + 2 DBP) ÷ 3] measurement were recorded for further analysis.

2.4.2. Blood glucose

Blood glucose was assessed using a portable glucose meter (Accu-Chek®; Active). A 7μl blood sample was taken from the tip of the participant's index finger and was immediately deposited in specific reagent strips inserted in the equipment before, immediately and 60 minutes after the experimental session. To mitigate chances of infections, the finger was previously sterilized with alcohol.

2.5. Experimental sessions

The experimental sessions consisted of three bilateral KE series. In the LH exercise protocol, three sets of 10 repetitions were performed, interspersed with 90 seconds of passive recovery, adopting a 65% overload of the predicted 1RM. In the LL exercise protocol, three sets of 15 repetitions were performed, interspersed with 30 seconds of passive recovery, adopting a 20% intensity of predicted the 1RM. Finally, in the LL + BFR exercise protocol, the same conditions were replicated, but a tourniquet was fixed in the thigh proximal region and inflated to a 50% AOP pressure. The pressure was maintained throughout the exercise (continuous BFR). An execution rhythm of 1.5s for the eccentric phase and 1.5s for the concentric phase was established for all exercise protocols tested.

2.6. Statistical Analysis

The data normality and sphericity were verified using the Shapiro-wilk and Mauchly's tests, respectively. All variables assumed normality, so we used two-way repeated measures to analyze the condition and time effects on the analyzed hemodynamic measures ([3] condition x [6] time) and blood glucose ([3] condition x [3] time). The percentage change was calculated for blood glucose values (pre-exercise and 60 minutes after), using the following equation: [(Post - Pre)/Pre*100)]. One-way Repeated Measure ANOVA was used to analyze this variable. Bonferroni Post-hoc analysis was further used to locate the source of the significant differences. The level of significance was set at $p \leq 0.05$. All statistical analyzes were performed using the SPSS statistical software package version 20.0 (SPSS Inc., Chicago, IL).

3. Findings

All participants were able to complete all research stages and no serious side effects could be observed during or after performing the proposed exercise protocols.

3.1. Blood pressure

There was no significant interaction between conditions and time for SBP (F = 1,065; p = 0.383), DBP (F = 0.658; p = 0.625) and MBP (F = 0.662; p = 0.602). There was no main effect of the SBP condition (F = 0.745; p = 0.484), DBP (F = 0.483; p = 0.622) and MBP (F = 0.551; p = 0.583). In contrast, there was a major time effect for the three analyzed measures [SBP (F = 37,018; p <0.001), DBP (F = 21,194; p <0.001) and MBP (F = 34,898; p <0.001)]. SBP increased significantly immediately after all the exercise protocols tested [HL (p <0.001; ES = 2.8); LL (p = 0.007; ES = 2.3); LL + BFR (p <0.001; ES = 2.8)]. Regarding baseline values, SBP remained significantly elevated for up to 15 minutes after the end of the HL (p = 0.044) and LL + BFR exercise protocols (p = 0.004). SBP significantly reduced 60 minutes after the LL exercise protocol (p = 0.021; ES = 1.9) (Figure 2).

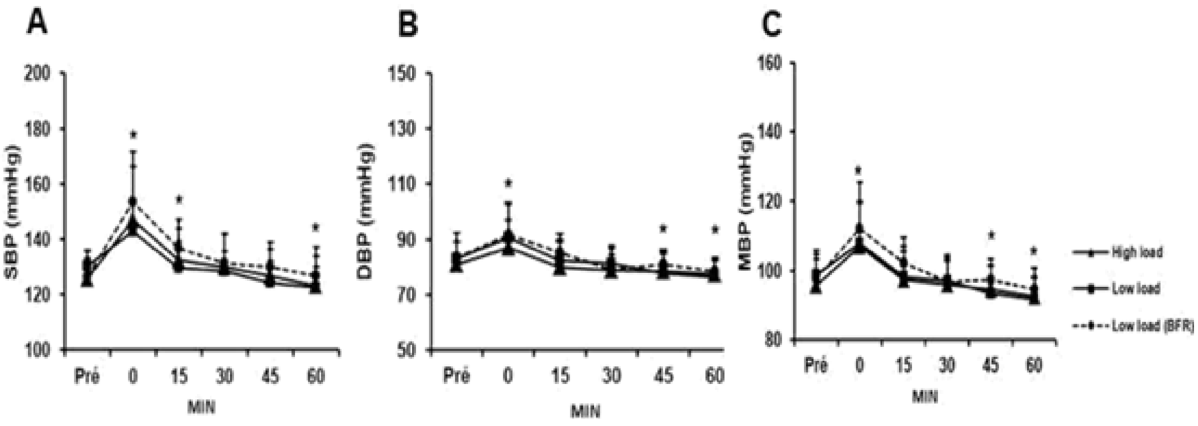
DBP increased significantly immediately after all the exercise protocols tested [HL (p <0.001; ES = 0.72), LL (p = 0.004, ES = 1.2) and LL + BFR (p = 0.003; ES = 0.91)]. Regarding baseline values, DBP significantly decreased 45 minutes after the LL exercise protocol (p = 0.028; ES = 0.8) and 60 minutes after the end of the LL exercise protocol (p = 0.004; ES = 1.0) and LL + BFR (p = 0.021; ES = 0.59) (Figure 2).

MBP increased significantly immediately after all the tested exercise protocols [HL (p <0.001; ES = 1.4), LL (p = 0.002; ES = 2.1) and LL + BFR (p <0.001; ES = 1.8)]. Regarding baseline values, MBP significantly reduced 45 (p = 0.015; ES = 1.2) and 60 (p = 0.001; ES = 1.5) minutes after the LL exercise protocol (Figure 2).

MBP increased significantly immediately after all the tested exercise protocols [HL (p <0.001; ES = 1.4), LL (p = 0.002; ES = 2.1) and LL + BFR (p <0.001; ES = 1.8)]. Regarding baseline values, MBP significantly reduced 45 (p = 0.015; ES = 1.2) and 60 (p = 0.001; ES = 1.5) minutes after the LL exercise protocol (Figure 2).

Figure 2

Exercise protocols effect on SBP (A), DBP (B) and MBP (C).



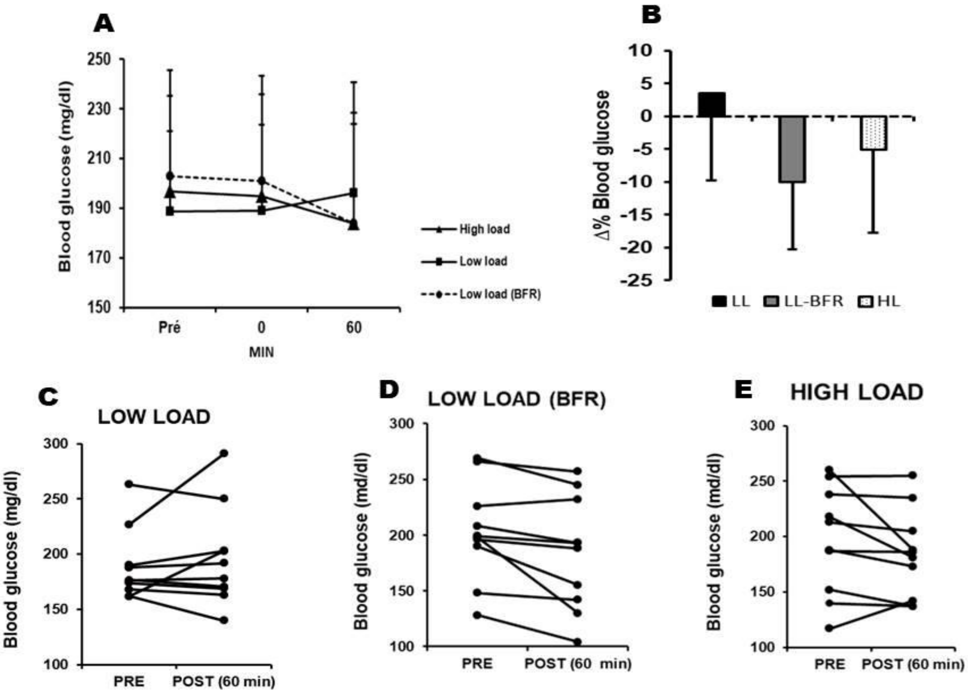
* = time main effect

3.2. Blood glucose

There was no significant interaction between conditions and time for blood glucose (F = 2,925; η² = 0.178; p = 0.054). There was no main effect of the condition (F = 0.036; η² = 0.003; p = 0.964) or time (F = 2,919; η² = 0.098; p = 0.087). We verified a condition effect for the percentage changes in blood glucose (F = 3,824; η² = 0.298; p = 0.041), but the post-hoc analyzes revealed only a tendency for a difference between LL exercise and LL-BFR (p = 0.053) (Figure 3).

Figure 3

Exercise protocol effects on blood glycemia.



4. Discussion

The study analyzed the acute effects of BFR strength exercises on BP and BG in untrained women with type II diabetes mellitus. To the best of our knowledge, this is the first documented attempt to analyse such kind of response in diabetic women. Our main findings were: (i) SBP, DBP and MBP increased significantly immediately after all the protocols tested, with no differences between conditions; (ii) Regarding baseline values, SBP remained elevated for up to 15 min after the LL-BFR and HL protocols; (iii) Only the LL and LL-BFR resistance exercise protocols promoted post-exercise hypotensive effect (HPE); (iv) Glycemia did not significantly decrease in any of the tested protocols, but there was a strong trend in the percentage change in BG between LL and LL + BFR (3.5% vs -10%, respectively; p = 0.053).

BP levels increased shortly after the end (i.e., 0-2 min post) of the resistance exercise with and without BFR as were previously noted (10, 11, 19, 20). In part, this increase can be justified by an activity enhancement of the pressure reflex of the exercise due to the mechanical and metabolic stimuli provided by exercises (21). Interestingly, when compared to baseline values, SBP remained elevated for up to 15 minutes after HL and LL-BFR exercise. This answer differs from the results presented in previous studies (10, 11, 20). We speculate that this divergence is due to the samples investigated in the study in question. The aforementioned studies analyzed samples composed of healthy and trained individuals, while our study included a sample composed of diabetic and sedentary women. Diabetic individuals may have dysfunctions in the autonomic nervous system (22) and, therefore, post-exercise parasympathetic activity may be impaired (23).

In addition, it has been speculated that endothelial dysfunction would compromise the hypotensive effect of physical exercise in diabetic patients (16). In our study, we were able to evidence a reduction in SBP 60 min after LL exercise protocols, but not after HL or LL-BFR exercise protocols. Both exercise protocols increased SBP for up to 15 min post-exercise, therefore, we cannot exclude the possibility that periods above 60 min were necessary for our sample to experience a significant decrease in SBP after such exercise protocols.

Regarding DBP values, only the LL and LL-BFR exercise protocols were able to reduce this measure. Similarly, Maior et al. (10) showed no reduction in BPD after an HL exercise session (~80% of 1RM), in contrast to the LL-BFR exercise session (~40% of 1RM). Maior et al. (10) analyzed a single exercise (elbow flexion) and applied long recovery intervals [i.e., ≥ 60 seconds (24)]. It is possible that the low volume of exercises associated with long inter-set recovery intervals limited metabolic stress and, as a result, HPE was mitigated after the LH exercise sessions tested in our study and in the study conducted by Maior et al. (10). Supporting our theory, Veloso et al. (25) found that a RT session performed with a 60-second recovery interval induced HPE in DBP of longer duration and magnitude, when compared to RT sessions with a recovery interval of 120 and 180s.

According to our theory, the LL exercise would have presented a significant metabolic stress, being even greater than the HL exercise, which contrasts with the results presented by Poton & Polito (26). Some factors could justify this possible divergence. For example, in our study, for LL sessions, we established inter-set recovery periods of 30 s, while Poton & Polito (26) adopted periods of 45s. In the HL sessions, we used a 90s recovery period, while Poton & Polito (26) established 60s periods. In addition, the intensity (% 1RM) applied in our study was lower (65% 1RM vs. 80% 1RM). Finally, we opted for a bilateral exercise protocol, while Poton & Polito (26) used a unilateral exercise protocol. Previously, it was found that the use of a bilateral protocol is able to promote a greater increase in the enzyme lactate dehydrogenase (LDH) levels, compared to a unilateral protocol (27).

Besides the hemodynamic responses, our study analyzed the effect of LL-BFR exercise on BG. We observed a trend (p = 0.053) for difference between percentage changes in BG caused by LL and LL + BFR exercise (3.5% vs -10%, respectively). Together, hypoxia and muscle contraction seem to maximize glucose uptake (28). The hypoxia condition appears to increase glucose uptake by increasing GLUT4 transporters (29). This metabolic adaptation was observed after a training program with BFR (13). Christiansen et al. (13)0 found that six weeks of intermittent cycling with BFR (3 sessions/week) significantly increased GLUT4 concentrations (~ 28%; p = 0.02; d = 0.8), a response that was not observed in the control condition (i.e., cycling without BFR). Increases in GLUT4 concentrations were positively associated with an increased glucose uptake ($r2 = 0.23–0.35$; $p \leq 0.003$).

In addition, a previous study found that muscle glycogen concentrations increase to a greater extent after BFR training, when compared to training without BFR (30). The authors speculate that the GLUT4 transient translocation to the sarcolemma, responsible for post-exercise glucose uptake, is related to this adaptation. In the present study, a 10% percentage reduction was found 60 min after the LL-BFR exercise, an aspect that was not evidenced in the LL exercise. It is possible that our findings are explained by a sharp increase in GLUT4 concentrations due to the hypoxia condition that was artificially established.

5. Conclusion

The LL and LL-BFR exercise protocols resulted in a post-exercise hypotensive effect, with the BFR protocol apparently showing superiority in reducing BG. These findings are of particular interest, given that glycemic control and BP reduction are associated with reducing the risk of disease-related complications. We add that diabetes is associated with a series of orthopedic complications, so a training strategy that has the potential to promote favorable physiological responses, regardless of high mechanical stress, may be feasible for this group. Additionally, the volunteers did not report any serious side effects, such as syncope, clinical symptoms of rhabidomyolysis (i.e., excessive late muscle pain and change in urine color), venous thrombosis and retinal vascular occlusion after performing the BFR exercise. These findings provide evidence that the application of BFR training can be a safe option for untrained diabetic women, if there is a control of the variables inherent to the training technique. We suggest that future studies analyze the chronic effect of this intervention type on diabetic people health.

6. Limitations and Suggestions

The present study has some limitations that need to be emphasized. Firstly, the sample size was small. Hence, more studies with larger sample size should be conducted to verify these results in order to generalize to other diabetic patients. We note that, in a previous study (13), this sample size was sufficient to verify a significant effect of glucose uptake after a BFR training program. Our BP and BG measurements were limited to 60 min post-exercise. This period was used in a significant number of studies that evaluated the hypotensive effect of BFR exercise (10, 11, 20). We believe it is necessary to conduct new clinical trials that monitor BP values for up to 24 hours post-exercise. We did not assess factors associated with BP reduction (e.g., release of vasodilating agents, change in stroke volume, metabolic concentration) or BG (e.g., GLUT4 concentrations) post-exercise. Our results are specific to untrained women with type II diabetes; therefore, they cannot be extrapolated to other populations.

Authors' Contributions

G.R.N: devised the project and wrote the manuscript. A.W.S.R; A.B.A.M; N.J.B.A.F; V.S.Q; M.G.A; E.S.B.S and L.A.C.C: conceived and planned the experiments. F. B. G: performed the numerical calculations and supervised the project; M.T. and K.I: verified the numerical results and revised the manuscript.

Transparency Statement

The authors are willing to share their data, analytics methods, and study materials with other researchers. The material will be available upon reasonable request.

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Declaration of Interest

All authors declare that they have no conflict of interest and therefore have nothing to declare.

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Ethics Considerations

This study was conducted in accordance with the Helsinki Declaration and was approved by the Ethics Committee on Human Research at the local institution (Nº. 3.520.337).

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