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ORIGINAL RESEARCH

Ambulatory blood pressure monitoring in prepubertal idiopathic dilated cardiomyopathy children

Aline Cristina Tavares,[I,II] Edimar Alcides Bocchi,[I] Iram Soares Teixeira-Neto,[I] Guilherme Veiga Guimarães[I]

[I]Instituto do Coração (InCor), Hospital das Clınicas da Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil [II]Hospital Sírio Libanês (HSL), São Paulo, Brazil

BACKGROUND AND OBJECTIVES: Ambulatory blood pressure monitoring is recommended for several diseases in childhood; however, there are no reports about its use in the monitoring of children with dilated cardiomyopathy so far. We evaluated the pattern of ambulatory blood pressure monitoring in children with dilated cardiomyopathy and correlated it to height, weight, and body mass index.

METHODS: Prepubertal children with dilated cardiomyopathy were assessed by ambulatory blood pressure monitoring. Data were collected for systolic and diastolic blood pressure. Means, for 24 hours, daytime, and nighttime, dipping pattern and levels above the normal expected values were computed.

RESULTS: Children with cardiomyopathy have the same blood pressure as normal kids. Weight was moderately but significantly correlated to nighttime systolic blood pressure. Children with left ventricular ejection fraction $<50\%$ have 6% less diastolic blood pressure dipping. These same children were also receiving higher doses of carvedilol and captopril.

CONCLUSIONS: Children with idiopathic dilated cardiomyopathy have the same blood pressure values and blood pressure dipping patterns on ambulatory blood pressure monitoring as normal healthy children are expected to have. Children with low left ventricular ejection pressure have lower dipping pattern.

KEYWORDS: ambulatory blood pressure monitoring; children; cardiomyopathy.

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INTRODUCTION

Accuracy and reliability are two crucial reasons why ambulatory blood pressure monitoring (ABPM) in children is preferred over office blood pressure (BP) monitoring.[1–3] Together with the "exact" value of BP, ABPM is regarded as the gold standard for circadian BP variation, for monitoring nocturnal BP and for determining whether the patient is a dipper or non-dipper,[2] which says whether or not nocturnal lowering of BP exists[1,2] and may help identify those at risk of organ-damage.[3] Dippers also have significantly lower all-cause mortality than non-dippers.[4]

In children, ABPM is recommended for patients with morphological changes of the aorta or the renal artery, renal diseases,[2,5] risk of hypertension,[6,7,8] diabetes, solid organ transplantation, and obstructive sleep apnea.[9] But there are no recommendations for ABPM evaluation in children with morphological or functional cardiac alterations as there are in adults.[10]

The dilatation of one or both ventricles in dilated cardiomyopathy, which is the most common cause of pediatric heart transplantation,[11] may result in alterations in standard systemic pressure.[12,13] Nonetheless, there are no ABPM values for the above-cited population. Performing ABPM in children with idiopathic dilated cardiomyopathy may overcome this challenge and categorize subgroups more precisely and distinguish dippers from non-dippers. Identifying these factors may be helpful for the development of clinical guidelines and better screening of pediatric populations.

METHODS

Participants

Prepubertal children with idiopathic dilated cardiomyopathy were recruited from a pediatric outpatient clinic at the University Hospital of the University of São Paulo between February 2011 and November 2011.

The Tanner-Whitehouse scale was used to analyze children's maturation. Only children with stages 1 to 3 were included. This evaluation is based on the development

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of secondary sexual characteristics such as breast development and menarche in girls, and standards for the penis in boys and pubic hair development in both sexes.[14]

Children with any previous cardiovascular events, surgery, renal failure, pulmonary disease, and insulin dependent diabetes were excluded.

Ethics statement

This study was approved by the local institutional ethics committee. Written informed consent was obtained from either parents or guardians. Verbal consent from each child was also taken into consideration.

Clinical assessments

All children were assessed with both office BP and ABPM. Data on each child were collected during a 2-day follow-up visit to the clinic.

Office Blood Pressure

Office blood pressure measurement was performed according to recommended guidelines. After a 5-minute rest period, BP was measured 3 times with patients in the sitting position using the auscultatory method (Heidji – mercury sphygmomanometer, São Paulo, Brazil) taken at intervals of 1 minute, on the same arm, between 9 A.M. and 10 A.M., by a staff professional. The mean among the 3 readings was considered as the office BP value.[15,16]

Ambulatory blood pressure monitoring (ABPM)

A BP cuff was placed on the nondominant arm with proper cuff size, according to the child's maximum upper arm circumference (cm), as previously recommended. And then, the cuff was connected to an oscillometric portable automatic monitor (Spacelabs model 90207, Spacelabs Medical Inc., Redmond, WA) that records BP readings.

ABPM began at the same time of the day (between 09:00 A.M. and 10:00 A.M.). Subjects were instructed to perform their habitual daily activities, not to exercise, and to relax and straighten the arm during the recording interval for daytime ABPM.

The device was set to measure and record readings every 15 minutes during the daytime (based on the time patients got out of bed) and every 20 minutes during nighttime (based on the time patients went to bed, according to parents' information).

The 24-hour ABP readings were downloaded using a Spacelabs ABP Local Report Generator. For analysis, ABPM data were collected for systolic and diastolic blood pressure, separately. ABPM data were also classified by mean, 24 hours, daytime, and nighttime. The 24-hour ABP data from each child were only accepted with >75% of the measurements successfully taken. Levels above normal expected values were also taken into consideration when analyzing data.[17,18]

All children were instructed to maintain the same treatment and the same habitual routine during the collection of ABPM data.

Dipping pattern was calculated as dip = (1 − BP sleep/BP awake) and expressed in percentage. Non-dippers are defined by a systolic or diastolic nocturnal drop of less than 10%.[1,3,19,20,21]

Outcomes

Accepted values for arterial BP were taken under consideration according to the sex, age, and height from *'The fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents'*.[22]

Based on the results of both office BP and ABPM, and the correspondence from the published values for children,[22] the BP status was classified as i) normotension; ii) white-coat hypertension; iii) masked or nocturnal hypertension; iv) prehypertensive; v) hypertensive stage 1, or vi) hypertensive stage 2.[22,23,24]

Statistical analyses

Descriptive statistics were used to describe the characteristics of the subjects. Data are presented as mean ± standard deviation.

Statistical analyzes were performed with SPSS 12.0 for Windows software (SPSS Inc., Chicago, IL, USA). The level of significance was set at $P < .05$.

The Shapiro-Wilk Test was used to test the normality of the data of the population. Either Pearson or Spearman correlation was performed whenever data were considered normal or not within Gaussian distribution, respectively.

Correlations were performed to observe the role of height, weight, and body mass index (BMI) on BP (office, 24-hour mean, daytime and nighttime means on ABPM). Correlation values within the $0.1 \leq 0.5$ range were considered as weakly correlated; values of $0.5 \leq 0.8$ were considered as moderately correlated; values of $0.8 \leq 1$ were considered as strongly correlated.[25]

RESULTS

Participants

There were 18 prepubertal children with idiopathic cardiomyopathy in the mentioned outpatient pediatric clinic. Because 1 declined to participate and 4 had clinical decompensations, 13 participants were recruited.

Baseline characteristics of the study population are given in Table 1. BMI range varied from severely underweight to normal healthy weight. No child was found to be obese.[26]

The mean period of time children used the device for AMBP exceeded 24 hours (24.8 hours and 23.4 minutes), showing that no children had the evaluation for less than the recommended time. The number of valid ABPM readings was 91% for total analysis. There were 53 valid readings for daytime (86%), and 24 valid readings for nighttime (96%).

Table 1 - Sample characteristics. AAS: acidumacetylsalicylicum. BMI: body mass index; LVEF: left ventricular ejection fraction; F: female; M: male; n: number.

	Total (n = 13)
Age (years)	9.3 ± 1.9
Sex (F-M)	5–8
Weigh (kg)	33.8 ± 8.1
Height (m)	1.39 ± 0.13
BMI (kg/m^2)	17.2 ± 2.9
LVEF (%)	48.8 ± 16.6
Medication mg (n)	
–carvedilol	22.4 ± 28.4 (7)
–captopril	12.5 ± 16.3 (6)
–spironolactone	9.6 ± 19.2 (4)
–furosemide	0.4 ± 1.0 (2)
–digoxin	11.5 ± 30.0 (2)
–AAS	12.5 ± 31.1 (2)

Office systolic blood pressure was weakly correlated to its equivalent in ABPM in all measurements: 24-hour mean ($r = 0.48$); daytime ($r = 0.51$); nighttime ($r = 0.52$) with $P < .001$.

Office diastolic pressure was not correlated to its equivalent in ABPM 24-hour mean ($r = 0.04$); daytime ($r = 0.01$); nighttime ($r = 0.11$) with $P < .001$.

For systolic ambulatory pressure, the 24-hour mean (103.5 ± 7.9) was 4 mm Hg lower than the daytime mean (107.1 ± 8.8), and 6 mm Hg higher than the nighttime mean (97.2 ± 7.8).

For diastolic ambulatory pressure, the 24-hour mean (64.8 ± 5.8) was 4 mm Hg lower than the daytime mean (68.8 ± 6.7), and at 7 mm Hg higher than the nighttime mean (57.0 ± 5.3).

Both the systolic and the diastolic dipping patterns were present and corresponded to 9% and 16% of the nocturnal BP, respectively.

Only one child (8% of the sample) did not belong to the group with normal BP because of a high systolic measurement. This child was therefore considered to have prehypertension, with mean systolic pressure of 125 mm Hg and 30% above values considered normal in 24 hours.

No child fell within the groups with hypertension stage 1 or stage 2.

There was no significant correlation between office BP, mean 24-hour and daytime mean with height ($r = 0.28$; $P = .35$). Only systolic nighttime mean was moderately significantly correlated to height ($r = 0.6$; $P = .01$) (Figure 1).

Weight was moderately but significantly correlated to nighttime systolic BP ($r = 0.52$; $P = .02$). Diastolic blood pressure was not correlated to weight in any of the measurements.

There was no significant correlation between systolic and diastolic pressures (office BP and ABPM values) with BMI ($r = 0.32$; $P = .3$).

Children with left ventricular ejection fraction $<50\%$ (seven out of the total sample) have 6% less diastolic pressure dipping. Those exact same children were also the ones who received higher doses of carvedilol and captopril.

DISCUSSION

To the best of our knowledge, this is a pioneering study reporting values of ABPM in children with idiopathic dilated cardiomyopathy. The main finding is that this population has the expected normal values for BP and dipping patterns.

First of all, the low correlation between office BP and ABPM values only reaffirms that office BP does not represent real daytime BP. ABPM has advantages over office BP. Only ABPM has the ability to reveal nocturnal pressure values, helping to diagnose white-coat hypertension.[27,28,29] Only ABPM can clarify the influence of activities and the diurnal cycle on arterial pressure.[30] Office BP is fraught with potential sources of error, because it depends on the individual, on the brands of the devices used and on the observer.[31]

Our high percentage of valid measurements probably happened because we chose three times more readings than the usual recommendation of having a minimum of 16 valid daytime and 8 valid nighttime readings.[17]

The ABPM values reported in our study are similar to those in a trial with 1141 healthy children and adolescents that reported that the 24-hour means stayed 4 to 8 mm Hg lower than daytime means for systolic ABPM and 6 to 9 mm Hg lower than daytime means for diastolic ABPM.[32] In our group's experience, we have seen that prepubertal children are different from teens and adults.[33] Although we did not include adolescents in our sample, our results regarding these differences (24-hour mean, systolic and diastolic ABPM) are closer to the lower reported limits. This may be reasonable, because in fact when isolated, children have lower BP than adolescents.

The most recent update from the Task Force on High Blood Pressure in Children and Adolescents provided population-based 95th percentile blood pressure values in children adjusted for age, sex, and height.[34,35] Most of the published reports accept the upper normal limit as the 95th percentile in a given population; however, diabetic nephropathy[36,37] and other renal diseases in adults[38,39] have been shown to progress more rapidly when the BP is within the upper, compared with the lower, normal range.

Although our sample was small, our incidence of high BP (above expected normal limits) was similar to that in a report of 5,120 children from different ethnic groups, with a prevalence of hypertension of 5%.[40]

Lurbe et al reported that values varied little over the range of age and height[41] because differences in growth and development vary with genetic influence as a function of sex and ethnic origin.[42,43,44] Indeed, within each race-sex group, mean levels of systolic pressure remain the same, whereas mean levels of diastolic pressure differ by 2 mm Hg.[35]

A German trial showed that 6,210 non-overweight boys and 5,989 non-overweight girls (children and adolescents) had lower clinical BP percentiles compared with the Fourth-Report percentiles.[44] They studied children aged 3 to 17 years. Fortunately, they present separate data according to age and BP percentiles for boys and girls. Therefore, after reanalyzing their data they found that children aged from 6 to 12 years old (the age range of our study) had systolic pressures of 103 ± 3.9 and diastolic pressures of 63.1 ± 1.7. Both values were significantly correlated to height ($r = 0.93$; $p < .001$). Although our results were quite similar to theirs, we did not have similar correlations; our smaller group size is a possible cause for the discrepancy.

Height was associated with arterial pressure in two trials. One showed that current height correlates to higher systolic pressure in a multivariable partial least squares regression of growth to 11-year olds in 5813 children from Hong Kong. Soergel et al studied 1141 healthy children stratified by height to establish the 50th, 90th, and 95th percentiles for 24-hour, day and night pressure means through ABPM.[32]

We found no correlation between blood pressure and weight or BMI, which confirms the results of a study including 11,478 Louisiana children and adolescents (aged 5–17 years) and from other trials involving only children.[35] According to Freedman et al,[35] despite the increases in obesity there were no increases in systolic or diastolic pressure levels. However, contradictions remain. Another study showed that BMI was associated with higher systolic BP and those children with BMI > 25 had lower nocturnal SBP dip and nighttime systolic hypertension probably due to the presence of insulin resistance.[45] We did not find a correlation between arterial pressure and BMI; however, the nighttime mean was correlated to weight probably because of the one child in our study considered to have prehypertension. Although this child was within the weight of the group, his nocturnal systolic pressure was above the

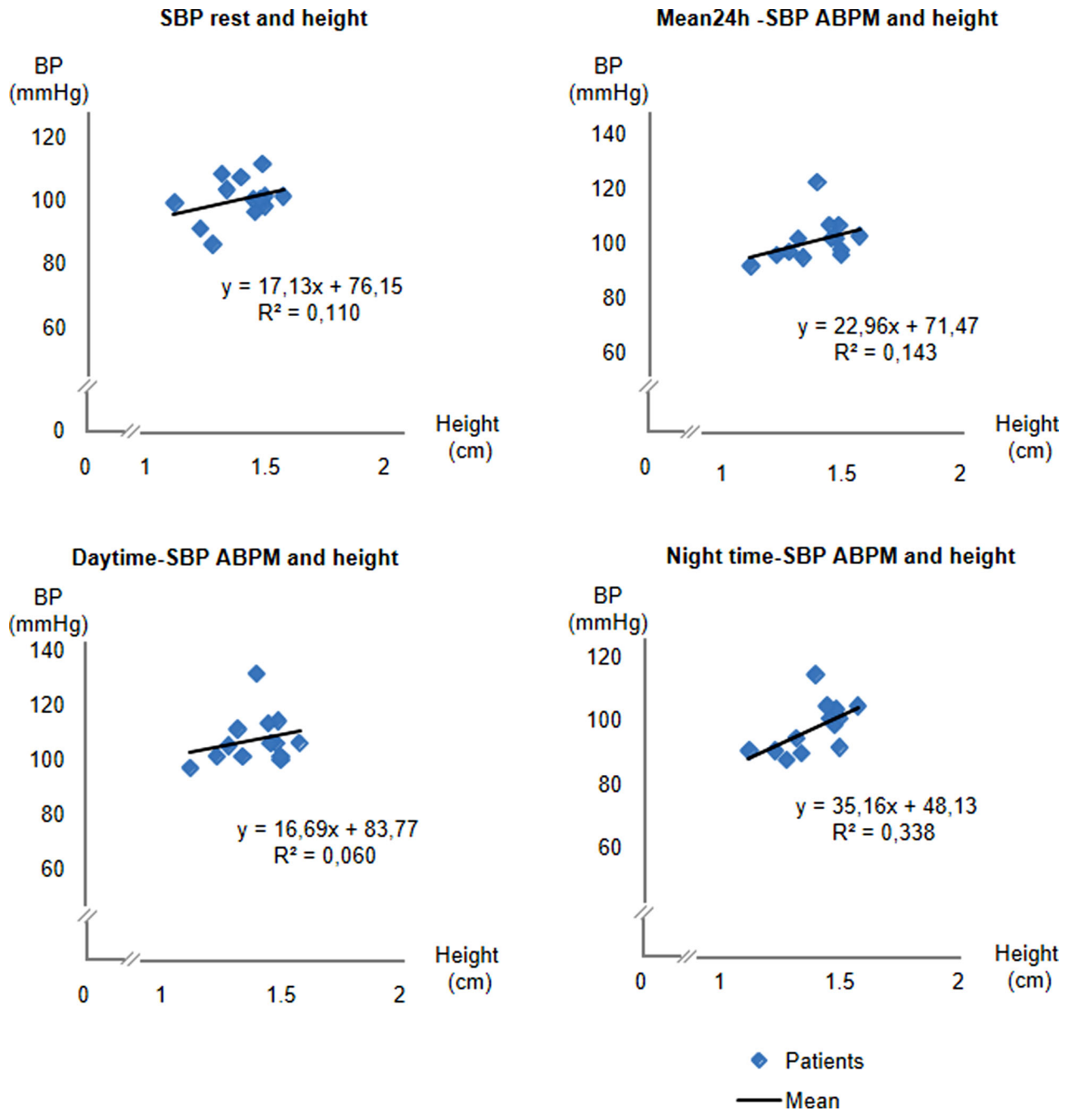

Figure 1 - Correlation of ABPM to height. ◆:Patient; Solid line: mean. BP: blood pressure. D: diastolic; S: systolic.

expected upper limits (of 114 mm Hg), which raises the mean value of the group.

Because we found no correlation with height or weight in 24-hour mean and daytime blood pressures, our results do not correlate with these last findings. This may have happened in our case because, even though our cohort was small, it did not include adolescents, but exclusively children from 6 to 12 years old. Although our children were in the linear growth phase, which usually occurs at 7 to 11 years,[44] we did not find that height had an influence on BP.

Adult patients receiving high doses of angiotensin converting enzyme (ACE) inhibitors usually have systolic pressures around 30–40 mm Hg lower than values for the healthy population. Studies with children using ACE inhibitors are recent, and this therapy is not yet well established;[47,48,49] therefore, comparisons in children may be lacking. However, our children who were receiving ACE inhibitors had similar systolic BP as that of children receiving little or no medication, but had a significant low diastolic dipping pattern. The cause of this blunted dipping phenomenon is not fully understood; however, data suggest

that non-dippers have an increase in sympathetic nervous system activity[49,50] and a decrease in parasympathetic nervous system activity throughout the night.[51]

Evidence is increasing that links this blunted nighttime dipping of arterial pressure to angiographic coronary artery stenosis in men,[52] to target organ damage[3] to left ventricular hypertrophy,[53] to extracardiac morbidity and mortality, and to worse cardiovascular outcomes,[54,55,56,57] even in subjects who are normotensive.[58] Indeed the children evaluated in this study who had received ACE inhibitors had significantly lower left ventricular ejection fraction, which has also been reported, previously, by our group to be an independent additional predictor of cardiac events (either death or transplantation).[59]

Overall, in the current sample, the systolic dipping pattern was present as expected (from 10 to 20%), because they maintained their cardiac innervation.[1,3,20,21] This finding was slightly lower than an average of 13% ± 6% for systolic and of 23% ± 9% for diastolic ABPM reported in a recent trial, perhaps because adolescents were also included in the sample. And once again, children are different from adolescents, and adolescents do not accurately reflect the scenario applicable to children.[60,61]

The use of ABPM is growing in the pediatric population; however, the procedure has several limitations.[62] Limitations to ABPM monitoring can be related to factors such as age, blood pressure values, pulse wave amplitude, time of the monitoring, all of which influence the recording quality. The younger the child, the worse is the collaboration and the lower are the valid measurement records.[41] Lower systolic values increase the potential for erroneous measurements, because the oscillation is shorter than for higher values. There is an overall increase in cost with 24-hour mean in ABPM. Short monitoring periods and high intervals for measurements may misclassify hypertension.[63] We did not observe these problems because only cooperative children were included; they all kept the device set for 24 hours; and they all had >70% of valid recordings.

Study limitation

The small sample size limited further analysis. Moreover, our results can only be applied to this specific population, which does not include post-pubertal children, nor other cardiomyopathies or other comorbidities.

Conclusion

Children with idiopathic dilated cardiomyopathy have blood pressure values and blood pressure dipping patterns in the ambulatory blood pressure monitoring similar to what normal healthy children are expected to have. However, children with low left ventricular ejection fraction have a 6% lower dipping pattern, which has a relationship to poor prognosis in adults.

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Conflict of Interest: The other authors have no conflicts of interest to disclose.

RESUMO

OBJETIVOS: O monitoramento ambulatorial da pressão arterial é recomendado para várias doenças na infância; no entanto, até o momento, não existem relatos sobre a sua utilização no acompanhamento das crianças com cardiomiopatia dilatada. Avaliamos o padrão de monitoramento ambulatorial da pressão arterial em crianças com cardiomiopatia dilatada, correlacionando estes dados com altura, peso e índice de massa corporal.

MÉTODO: crianças pré-púberes com cardiomiopatia dilatada foram avaliadas por monitorização ambulatorial da pressão arterial. Foram coletados dados de pressão arterial sistólica e diastólica. Médias para as pressões de 24 horas, pressões diurnas e noturnas, bem como padrões de redução noturna (dipping patterns) e pressões acima dos valores normais foram computados.

RESULTADOS: crianças com cardiomiopatia apresentam pressão arterial semelhante a de crianças normais. O peso corporal correlacionou significativamente com pressão sistólica noturna. Crianças com fração de ejeção ventricular esquerda < 50% têm menos de 6% descenso da pressão arterial diastólica. Essas mesmas crianças também receberam doses mais elevadas de carvedilol e captopril.

CONCLUSÕES: As crianças com cardiomiopatia dilatada idiopática têm os mesmos valores de pressão arterial e padrões de descenso da pressão arterial no monitoramento ambulatorial de pressão arterial esperados para crianças normais e saudáveis. Crianças com baixa fração de ejeção de ventrículo esquerdo têm menor padrão de descenso (dipping pattern).

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CONTRIBUTOR'S STATEMENT

Aline Cristina Tavares: study concept, design, draft of initial manuscript, data collection, initial analysis, manuscript revision and approved final manuscript.

Edimar Alcides Bocchi: reviewed and approved final manuscript.

Iram Soares Teixeira-Neto: analysis, draft of manuscript, manuscript review, final manuscript approval.

Guilherme Veiga Guimarães: coordinated and supervised data collection, critically reviewed manuscript and approved final manuscript.