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SECTIONS

ARTICLES

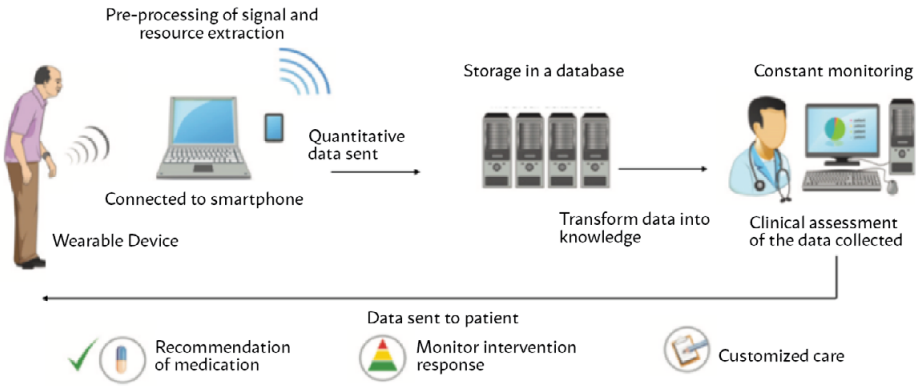

FIGURE ILLUSTRATING HOW WEARABLE DEVICES ARE USED FOR THE REMOTE MONITORING OF CLINICAL MANIFESTATIONS IN PATIENTS WITH PARKINSON'S DISEASE.

RAMB REVISTA DA ASSOCIAÇÃO MÉDICA BRASILEIRA
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SECTIONS

ARTICLES

REVIEW ARTICLES

EDITORIAL

Right ventricular function in dilated cardiomyopathies with chagasic and idiopathic etiologies

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Chagas' disease has marked epidemiological importance, even with the significant reduction of its transmission, due to the contingent of infected individuals with potential for severe forms of development[1]. Chronic chagasic cardiopathy is the most serious manifestation of the disease, constituting an important cause of heart failure in Brasil[2]. Approximately 30 to 40% of infected individuals will present some degree of cardiac involvement during their life[3]. Chagasic cardiomyopathy (MCh) presents a variable clinical course, with a worse prognosis in comparison to other myocardiopathies.

The involvement of the right ventricle represents a peculiar characteristic of Chagas' disease, especially when described in the early stages of the disease[4]. However, few studies have evaluated the functional and anatomical conditions of the right ventricle in MCh, compared to idiopathic dilated cardiomyopathy (MDI).

Right ventricular function is determined by the intrinsic contractility of this chamber and ventricular preload and afterload conditions. In MCh, VD dysfunction can be attributed to the inflammatory process itself, secondary to the infection by the parasite, causing depression of its contractility, but without clinical manifestations. Some abnormalities are not detectable through conventional echocardiographic techniques, requiring more accurate techniques to analyze their contractility. With the elevation of pressure in the pulmonary artery, secondary to left ventricular dysfunction, there is an increase in the post-load, favoring dysfunction with clinical evidence of systemic congestion[5].

The prognostic value of impaired right ventricular function was also verified in ischemic and non-ischemic heart failure[6]. Right ventricular dysfunction was associated with mortality[6]. Lewis et al. 1993, after studying 67 patients with MDI, found that the right ventricle area was the only significant predictor of death. In addition, a study of a subgroup of 205 more stable patients with moderate heart failure showed that the prognostic value was independent of right ventricular function[7].

Regardless of the cause of myocardiopathy, LV function contributes to VD performance through septal contractility. The interventricular septum represents an integral component of the VD architecture and mechanics. Under physiological conditions, septal contraction constitutes 1/3 of the VD contraction, evidencing the systolic interaction between the ventricles[8]. Ghio et al. 2001, studying 377 patients with heart failure and significant left ventricular dys-

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function, found no association between mean pulmonary artery pressure and right ventricular ejection fraction[9]. The ejection fraction of the right ventricle constituted an independent prognostic predictor of mortality or urgent transplantation.

VD dysfunction may be related to the worse prognosis of MCh, when compared to other cardiomyopathies. Patients with cardiomyopathy of different etiologies and similar degrees of left ventricular impairment may present different patterns of clinical evolution. The VD function would be implicated in this heterogeneity of presentation and prognosis[9].

Thus, in this edition, we used original studies to analyze right ventricular function in the different cardiomyopathies using new echocardiographic techniques derived from tissue Doppler, and to compare the parameters of VD function among patients with MCh and MDI so that we can extrapolate for clinical studies.

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Urinary lithiasis: evaluation of the use of laser vs. Pneumatic ureteral lithotripsy

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The Guidelines Project, an initiative of the Brazilian Medical Association, aims to combine information from the medical field in order to standardize producers to assist the reasoning and decision-making of doctors.
The information provided through this project must be assessed and criticized by the physician responsible for the conduct that will be adopted, depending on the conditions and the clinical status of each patient.

Urinary lithiasis is a frequent pathology, and procedure indication is based on the confirmation of the stone, its size, location, and density. The goal of this evaluation is to define the role of the use of laser power in comparison to the conventional method(s) for treating patients with an indication of fragmentation of urinary calculi through ureterolithotripsy. It was conducted from a systematic review of the literature and performed without period restriction, in the MEDLINE database, retrieving 86 papers, of which 9 (Nine) were selected to respond to clinical doubt. The details about the methodology and the results are set out in Appendix I.

INTRODUCTION

Urinary lithiasis is a frequent pathology, which makes it noteworthy among pathologies of the urinary tract. Its diagnosis and treatment have changed with the incorporation of new technologies to extract stones via the urinary route. These changes have had a great impact on the cost of treatment, and the procedures need to be evaluated regarding their effectiveness and risks.

Procedure indication is based on the confirmation of the stone through exams that indicate precisely its size, location, and density, essential information to determine the type of technology to be used: the type of lithotritor [extracorporeal (EC) or intracorporeal (IC)] and the type of energy (ballistic/pneumatic (EC); ultrasound (US); Electro-hydraulic (EH) or laser (L).

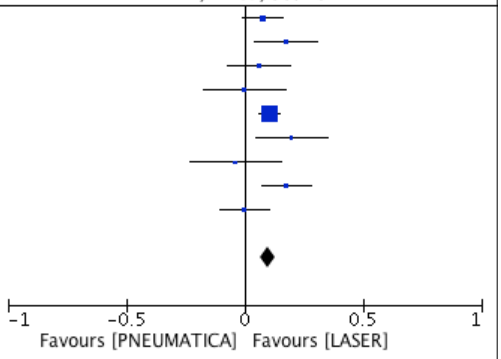
The goal of this evaluation is to define the role of the use of laser power in comparison to the conventional method(s) for treating patients with an indication of fragmentation of urinary calculi through ureterolithotripsy.

RESULTS OF THE COMPARATIVE ANALYSIS OF THE OUTCOMES

1.. THERAPEUTIC SUCCESS

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Difference M-H, Fixed, 95% CI
Bagbanci S 2017	116	130	106	130	14.3%	0.08 [-0.01, 0.16]
Binbay M 2011	39	40	32	40	4.4%	0.17 [0.04, 0.31]
Cimino S 2014	52	60	46	57	6.4%	0.06 [-0.07, 0.19]
Kassem A 2012	32	40	32	40	4.4%	0.00 [-0.18, 0.18]
Li L 2015	450	493	395	489	53.9%	0.11 [0.06, 0.15]
Maghsoudi R 2008	37	39	30	40	4.3%	0.20 [0.05, 0.35]
Manohar T 2008	21	25	22	25	2.7%	-0.04 [-0.23, 0.15]
Razzaghi MR 2013	56	56	46	56	6.1%	0.18 [0.08, 0.28]
Salvadó JA 2012	22	23	44	46	3.4%	0.00 [-0.10, 0.10]
Total (95% CI)		**906**		**923**	**100.0%**	**0.10 [0.07, 0.13]**
Total events	825		753			

Heterogeneity: Chi² = 12.70, df = 8 (P = 0.12); I² = 37%
Test for overall effect: Z = 6.13 (P < 0.00001)

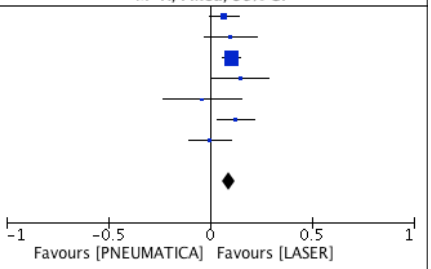


Regarding the outcome of therapeutic success, we included nine studies[1-9] for analysis, totaling 1,829 patients (906 laser and 923 pneumatic). The analysis revealed a higher rate of therapeutic success with patients undergoing laser treatment: an increase of 10% (NNT: 10), ranging from 7% to 13%. Heterogeneity of <50%.

2. STONE FREE RATE INDEX

Study or Subgroup	LITOTRIPSIA A LASER Events	LITOTRIPSIA A LASER Total	LITOTRIPSIA PNEUMATICA Events	LITOTRIPSIA PNEUMATICA Total	Weight	Risk Difference M-H, Fixed, 95% CI
Bagbanci S 2017	121	130	112	130	16.0%	0.07 [-0.00, 0.14]
Kassem A 2012	38	40	34	40	4.9%	0.10 [-0.03, 0.23]
Li L 2015	450	493	395	489	60.5%	0.11 [0.06, 0.15]
Maghsoudi R 2008	37	39	32	40	4.9%	0.15 [0.01, 0.29]
Manohar T 2008	21	25	22	25	3.1%	-0.04 [-0.23, 0.15]
Razzaghi MR 2013	56	56	49	56	6.9%	0.13 [0.03, 0.22]
Salvadó JA 2012	22	23	44	46	3.8%	0.00 [-0.10, 0.10]
Total (95% CI)		**806**		**826**	**100.0%**	**0.09 [0.06, 0.13]**
Total events	745		688			

Heterogeneity: Chi² = 6.84, df = 6 (P = 0.34); I² = 12%
Test for overall effect: Z = 5.86 (P < 0.00001)

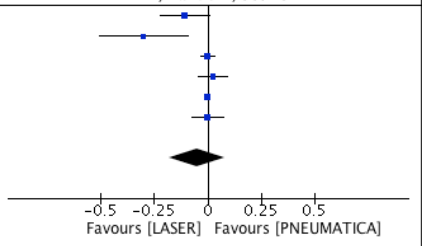


Regarding the outcome of stone free rate, we included seven studies[1,4-9] for analysis, totaling 1,632 patients (806 laser and 826 pneumatic). The analysis revealed a higher rate of stone free rate with patients undergoing laser treatment: an increase of 9% (NNT: 11), ranging from 6% to 13%. Heterogeneity of <50%.

3. NEED FOR URETERAL STENT

Study or Subgroup	LITOTRIPSIA A LASER Events	LITOTRIPSIA A LASER Total	LITOTRIPSIA PNEUMATICA Events	LITOTRIPSIA PNEUMATICA Total	Weight	Risk Difference M-H, Random, 95% CI
Bagbanci S 2017	79	130	93	130	16.1%	-0.11 [-0.22, 0.01]
Binbay M 2011	13	40	25	40	12.4%	-0.30 [-0.51, -0.09]
Cimino S 2014	60	60	57	57	18.2%	0.00 [-0.03, 0.03]
Kassem A 2012	1	40	0	40	17.5%	0.03 [-0.04, 0.09]
Li L 2015	493	493	489	489	18.4%	0.00 [-0.00, 0.00]
Manohar T 2008	25	25	25	25	17.3%	0.00 [-0.07, 0.07]
Total (95% CI)		**788**		**781**	**100.0%**	**-0.05 [-0.18, 0.08]**
Total events	671		689			

Heterogeneity: Tau² = 0.02; Chi² = 261.24, df = 5 (P < 0.00001); I² = 98%
Test for overall effect: Z = 0.76 (P = 0.45)

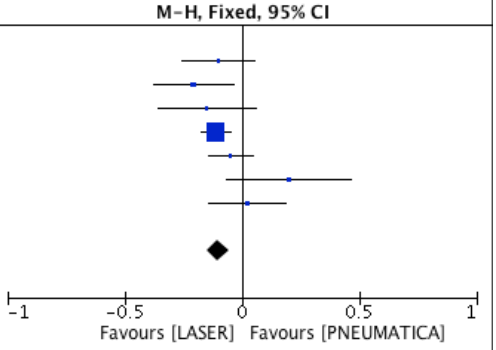


Regarding the outcome of need for ureteral stent, we included six studies[1-5,7] for analysis, totaling 1,569 patients (788 laser and 781 pneumatic). The analysis showed no difference regarding the risk of ureteral stent between the two modalities of treatment — heterogeneity of≥ 50%.

4. COMPLICATIONS

Study or Subgroup	LASER Events	LASER Total	PNEUMATICA Events	PNEUMATICA Total	Weight	Risk Difference M-H, Fixed, 95% CI
Bagbanci S 2017	15	30	19	130	0.0%	5.84 [2.46, 13.88]
Binbay M 2011	4	40	8	40	5.5%	-0.10 [-0.25, 0.05]
Cimino S 2014	16	60	27	57	8.1%	-0.21 [-0.38, -0.04]
Kassem A 2012	12	40	18	40	5.5%	-0.15 [-0.36, 0.06]
Li L 2015	232	493	285	489	67.8%	-0.11 [-0.17, -0.05]
Maghsoudi R 2008	1	39	3	40	5.5%	-0.05 [-0.14, 0.05]
Manohar T 2008	17	25	12	25	3.5%	0.20 [-0.07, 0.47]
Salvadó JA 2012	3	23	5	46	4.2%	0.02 [-0.14, 0.19]
Total (95% CI)		**720**		**737**	**100.0%**	**-0.10 [-0.15, -0.05]**
Total events	285		358			

Heterogeneity: $Chi^2 = 9.94$, df = 6 (P = 0.13); $I^2 = 40\%$
Test for overall effect: Z = 4.12 (P < 0.0001)

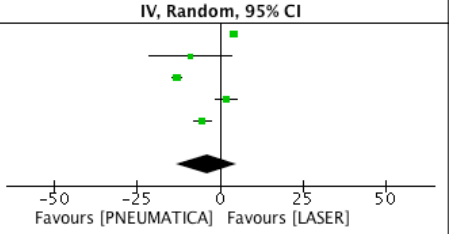


Regarding the outcome of complications, we included eight studies[1-7,9] for analysis, totaling 1,457 patients (720 laser and 737 pneumatic). The analysis revealed a lower rate of complication risk with patients undergoing laser treatment: an increase of 10% (NNT: 10), ranging from 5% to 15%. Heterogeneity of <50%.

5. PROCEDURE TIME

Study or Subgroup	LASER Mean	LASER SD	LASER Total	PNEUMATICA Mean	PNEUMATICA SD	PNEUMATICA Total	Weight	Mean Difference IV, Random, 95% CI
Bagbanci S 2017	16.48	4.74	130	12.24	3.95	130	21.4%	4.24 [3.18, 5.30]
Kassem A 2012	44.5	28.2	40	53.5	29.2	40	15.3%	-9.00 [-21.58, 3.58]
Li L 2015	28	9.2	493	41	12.4	489	21.4%	-13.00 [-14.37, -11.63]
Manohar T 2008	9.82	7.58	25	7.86	3.25	25	20.9%	1.96 [-1.27, 5.19]
Salvadó JA 2012	21.78	2.8	16	27.14	4.7	14	21.0%	-5.36 [-8.18, -2.54]
Total (95% CI)			**704**			**698**	**100.0%**	**-3.97 [-13.18, 5.25]**

Heterogeneity: $Tau^2 = 102.99$; $Chi^2 = 393.85$, df = 4 (P < 0.00001); $I^2 = 99\%$
Test for overall effect: Z = 0.84 (P = 0.40)



Regarding the outcome of procedure time, we included five studies [1,4,5,7,9] for analysis, totaling 1,402 patients (704 laser and 698 pneumatic). The analysis showed no difference regarding the procedure time between the two modalities of treatment — heterogeneity of≥ 50%.

In the analysis of the outcomes of therapeutic success, stone free rate, and complications there was no bias of inconsistency (heterogeneity <50%). However, in the analysis of the outcomes of need for ureteral stent and procedure time, the heterogeneity was ≥50%.

SUMMARY OF EVIDENCE - WEAK

In patients with urinary lithiasis and stones <20 mm affecting the ureter.

There is no difference in the procedure time and the need for ureteral stent between the two types of treatment (laser and pneumatic ureterolithotripsy).

The laser treatment offers increased rates of therapeutic success and stone free rate outcomes and reduces the risk of complications when compared with pneumatic ureterolithotripsy.

APPENDIX I

Clinical question

In the treatment of urinary lithiasis by ureterolithotripsy, is the use of a laser energy source superior to the conventional one (pneumatic)?

Structured clinical question

P	Patients with urinary lithiasis
I	Laser ureterolithotripsy
C	Conventional ureterolithotripsy
O	Therapeutic success, stone free rate index, ureteral stent, complications, procedure time

Eligibility criteria

PICO

Study design: Systematic Reviews (SR) and Randomized Clinical Trials (RCT)

Period: no limit for RCTs; two years for SR

Languages: English, Portuguese, and Spanish

Full texts available

Search for papers

Database

The scientific databases consulted were Medline (via PubMed), Embase, and manual search.

Search strategy

(Urolithiasis OR Nephrolithiasis OR Ureterolithiasis OR Ureteral Calculi OR Urinary Calculi OR Kidney Calculi OR Ureteral Calculi OR Urinary Bladder Calculi) AND laser AND Random*

Manual search - Reference of references, reviews, and guidelines.

Critical evaluation

Relevance - clinical importance

This guideline was prepared by means of a clinically relevant question in order to gather information in medicine to standardize approaches and assist in decision-making.

Reliability - Internal validity

The selection of the studies and the evaluation of the titles and abstracts obtained from the search strategy in the databases consulted were independently and blindly conducted in total accordance with the inclusion and exclusion criteria. Finally, studies with potential relevance were separated. When the title and the summary were not enlightening, we sought for the full article. Only studies with texts available in its entirety were considered for critical evaluation.

Results application - External validity

The level of scientific evidence was classified by type of study, according to Oxford[10] (Table 1).

TABLE 1. GRADES FOR RECOMMENDATION AND LEVELS OF EVIDENCE

A: Experimental or observational studies of higher consistency.
B: Experimental or observational studies of lower consistency.
C: Uncontrolled case/study reports.
D: Opinion deprived of critical evaluation, based on consensus, physiological studies, or animal models.

The selected evidence was defined as a randomized controlled clinical trial (RCT) and submitted to an appropriate critical evaluation checklist (Table 2).

The critical evaluation of RCTs allows to classify them according to the Jadad score[11], considering Jadad trials < three (3) as inconsistent (grade B) and those with score ≥ three (3), consistent (grade A), and according to the Grade[13] score (strong or moderate evidence).

When the evidence selected was defined as a comparative study (observational cohorts, or non-randomized clinical trial), it was subjected to an adequate critical assessment checklist (Table 3), allowing for the classification of the study, according to the NEWCASTLE OTTAWA SCALE [12], which considered consistent cohort studies with scores ≥ 6, and inconsistent <6.

TABLE 2. PROCESS FOR CRITICAL EVALUATION OF RANDOMIZED CONTROLLED TRIALS

Study data Reference, study design, Jadad, level of evidence	Sample size calculation Estimated differences, power, significance level, total number of patients
Patient selection Inclusion and exclusion criteria	Patients Recruited, randomized, prognostic differences
Randomization Description and blinded allocation	Patient follow-up Time, losses, migration
Treatment protocol Intervention, control, and blinding	Analysis Intention to treat, analyzed intervention and control
Outcomes considered Primary, secondary, measurement instrument for the outcome of interest	Results Benefits or harmful effects in absolute data, benefits or harmful effects on average

TABLE 3. PROCESS FOR CRITICAL EVALUATION OF COHORT STUDIES

Representativeness of the exposed and selection of the non-exposed (Max. 2 points)	Exposure definition (Max. 1 point)	Demonstration that the outcome of interest was not present at the beginning of the study (Max. 1 point)	Comparability on the basis of the design or the analysis (Max. 2 points)	Outcome assessment (Max. 1 point)	Adequate follow-up time (Max. 2 points)	Scores and level of evidence

Method of extraction and result analysis

For results with available evidence, the population, intervention, outcomes, presence or absence of benefits and/or harmful effects, and controversy will be specifically defined whenever possible.

The results will be presented, preferably in absolute data, absolute risk, number needed to treat (NNT) or number needed to harm (NNH) and, eventually, in mean and standard deviation values (Table 4).

TABLE 4. SPREADSHEET USED FOR DESCRIBING AND PRESENTING THE RESULTS OF EACH STUDY

Evidence included
Study design
Selected population
Follow-up time
Outcomes considered
Expression of results: percentage, risk, odds, hazard ratio, mean

RESULTS

1. FLOWCHART OF STUDIES RETRIEVED AND SELECTED (PRISMA 2009)

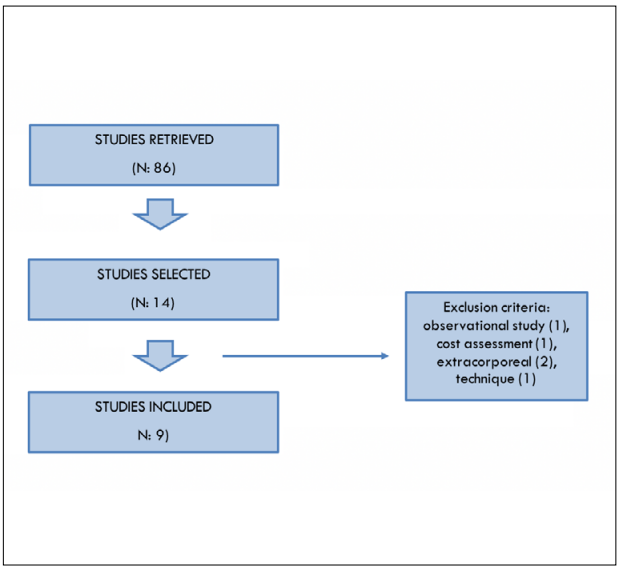
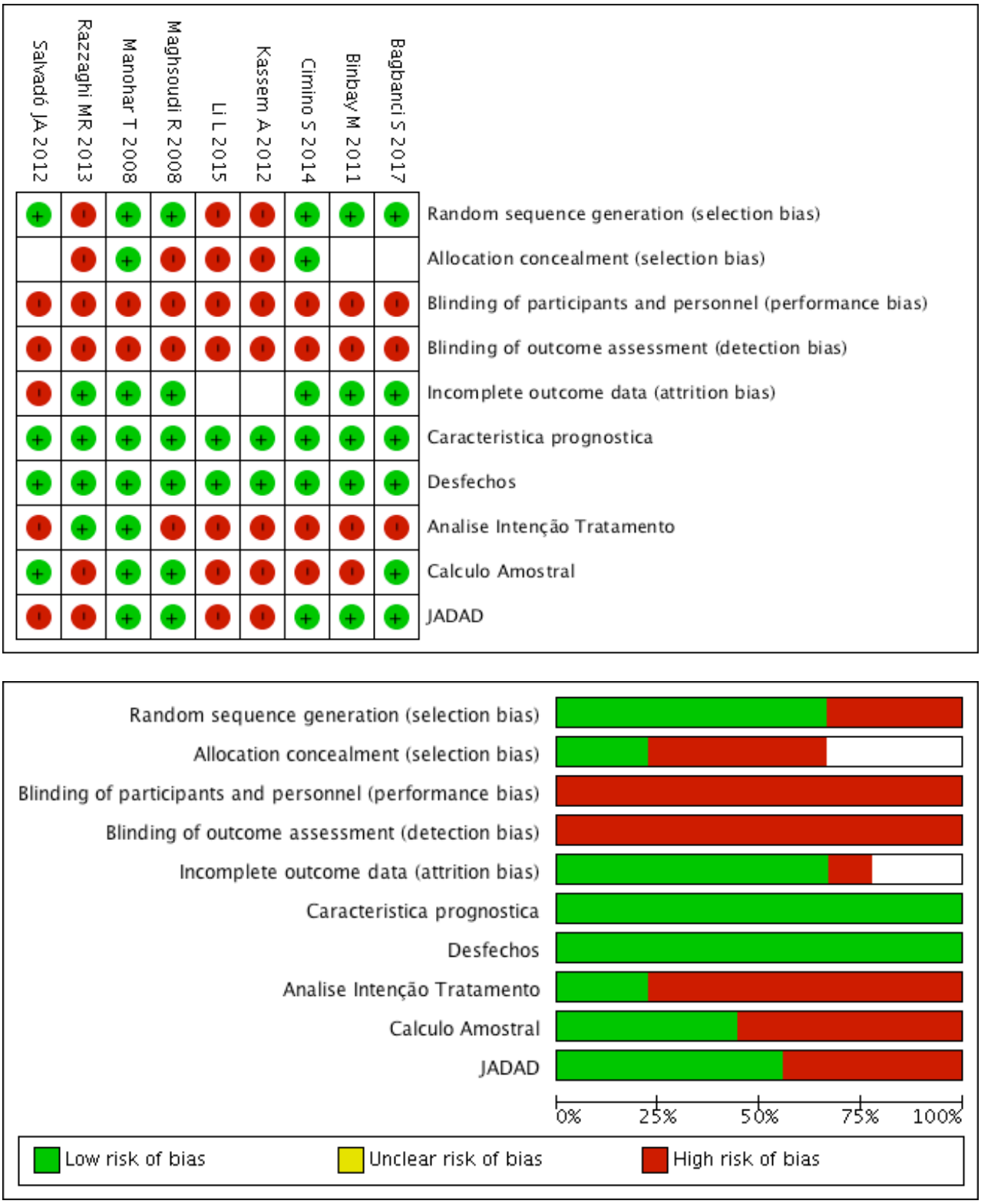


TABLE 5. CHARACTERISTICS OF STUDIES INCLUDED

Study	Population	Intervention	Comparison	Outcomes	Time of follow-up
Bagbanci S 2017[1]	Superior ureteral stone (260)	Laser (130) 1.0–2.0 J 5–10 Hz	Pneumatic (130)	Success, procedure time, ureteral stent, complication	1 year
Binbay M 2011[2]	Urethral stone <2 cm (80)	Laser (40) 1.5–2.0 J 5-12 Hz	Pneumatic (40)	Success, surgery time, ureteral stent, complication	15-16 months
Cimino S 2014[3]	Single ureteral stone (117)	Laser (60) 0.5-1.0 J 5–10 Hz	Pneumatic (57)	Success, surgery time, complication	3 months
Kassem A 2012[4]	Urethral stone <2 cm (80)	Laser (40) 0.6-1.2 J 5-15 Hz	Pneumatic (40)	Complications, success	1 month
Li L 2015[5]	Urethral stone <1.5 cm (982)	Laser (493) 0.8-1.0 J 10-15 Hz	Pneumatic (489)	Complications, success, procedure time	1 year
Maghsoudi R 2008[6]	Urethral stone <1.5 cm (79)	Laser (39) 0.5-1.0 J 5–10 Hz	Pneumatic (40)	Success, complication	1 year
Manohar T 2008[7]	Stone <20 mm (50)	Laser (25) < 1.2 J < 15 Hz	Pneumatic (25)	Procedure time, success	3 months
Razzaghi MR 2013[8]	Superior ureteral stone (1-2 cm)(112)	Laser (56) 5–10 Hz	Pneumatic (56)	Complications, surgical time, success	3 months
Salvadó JA 2012[9]	Distal urethral stone (89)	Laser (23) 0.8-1.5 J 12-20 Hz	Pneumatic (23)	Procedure time, complication, ureteral stent, success	3 months

FIGURE 1. RISK OF BIAS OF THE STUDIES INCLUDED



None of the studies is blinded, 30% did not properly randomize, 50% did not have blindfolded allocation, did not calculate the sample, and Jadad was inconsistent (<3), in 80% the analysis was not by intention to treat, and 10% had ≥20% losses, thus, by these criteria, with high overall risk of bias.

Application of evidence - Recommendation

The recommendations will be elaborated by the authors of the review, with the initial characteristic of synthesis of evidence, being subject to validation by all authors who participated in creating the Guideline.

The overall summary will be drafted considering the evidence described; its strength will be estimated (Oxford[10]/Grade[14]) as 1b and 1c (grade A) or strong, and as 2a, 2b, and 2c (grade B) or moderate weak, or very weak.

Conflict of interest

There is no conflict of interest related to this review that can be declared by any of the authors.

Final declaration

The Guidelines Project, an initiative of the Brazilian Medical Association in partnership with the Specialty Societies, aims to reconcile medical information in order to standardize approaches that can aid the physician's reasoning and decision-making process.

The information contained in this project must be submitted to the evaluation and criticism of the physician responsible for the conduct to be followed, given the reality and clinical condition of each patient.

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Urinary lithiasis: diagnostic investigation

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Question: What evaluation is needed for better diagnosis and planning of patients with complex renal lithiasis who must be submitted to surgical treatment, such as percutaneous kidney lithotripsy?

Answer: For the best therapeutic planning, patients who are candidates to percutaneous kidney lithotripsy must be submitted to computed tomography for detailing of the anatomical structures, the collecting system, and the stone, in order to plan the puncture pathway. The use of intravenous contrast-enhanced computed tomography should be considered in complex anatomical situations, such as malformations or previous kidney surgery, in which it is desirable to know the anatomy of the renal collecting system. Alternatively, excretory urography can be used to evaluate the anatomy of the renal collecting system, but it does not replace the computed tomography since it does not allow the visualization of neighboring organs and their relationships with the kidney.

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The effects of physical activity during childhood, adolescence, and adulthood on cardiovascular risk factors among adults

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SUMMARY

OBJECTIVES: *To analyze the association between physical activity during life and cardiovascular risk factors among adults.*

DESIGN: *The sample was composed of 101 adults (59 men) between 30 and 50 years old, who were recruited from different gyms and from a University in Brasil. Participants were divided according to their engagement in sports in early life (self-reported) and current physical activity (pedometer) (sports participation during childhood/adolescence and currently active [n=26], sports participation during childhood/adolescence and currently inactive [n=26], and control [n=49]). Cardiovascular risk factors were measured, such as body fat (through DXA), HDL-C, triglycerides, HOMA index, systolic blood pressure, diastolic blood pressure, and C-reactive protein. We adopted the covariates of chronological age, sex, alcohol consumption, tobacco, and body mass index. General estimating equations were used, with p<0.05. Results: After the adjustments of the final model, individuals engaged in sports during childhood and adolescence and inactive during adulthood presented lower body fat, when compared to participants persistently inactive (p<0.001). Participants persistently active presented lower body fat (p<0.001) and lower c-reactive protein (p=0.010) when compared to the control group.*

CONCLUSION: *Early sports participation was associated with reduced body fat, and being physically active throughout life was associated with reduced body fat and C-reactive protein.*

KEYWORDS: *Motor activity. Sports. Chronic disease. Exercise.*

INTRODUCTION

Physical activity is recognized as a protective factor for several diseases during adulthood[1-3]. Physical activity during childhood and adolescence can also affect cardiovascular diseases, through indirect pathways, as the maintenance of physical activity practice, or protecting against morbidities developed during childhood and adolescence, and prolonged to adulthood[4-5]. However, recent evidence

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highlights a possible direct association between physical activity during early ages and cardiovascular diseases during adulthood, particularly through epigenetics[5-6].

Similarly, in addition to the association between early physical activity and prospective cardiovascular outcomes through direct pathways[2,7], the literature has shown that the benefits can be greater among individuals who remain active throughout life[8]. However, this issue is not clear among adults.

In this sense, our aim was to analyze the association between physical activity during childhood, adolescence, and adulthood, and cardiovascular risk factors among adults.

METHODS

Sample

The present study has been carried out in Presidente Prudente, a middle-sized city located in the western region of Sao Paulo State, Brasil. The sample comprised 122 adults (69 men and 53 women), aged between 30 and 50 years old who were recruited in fitness clubs (spread out in different regions of the city) and in the campus of the Sao Paulo State University (fitness clubs, n = 100; university staff, n = 22). The sample size calculation was based on an equation for correlation, which indicated the need to evaluate at least 114 subjects to detect correlation coefficients of r = 0.26, with a power of 80% and a statistical significance of 5%.

To participate in the study, the individuals fulfilled all inclusion criteria previously established: (i) Sports participation in early life (both childhood and adolescence) or absence of sports participation in early life (control group); (ii) aged between 30 and 50 years old; (iii) no previous history of stroke or infarction; (iv) no amputation or visual impairment due to diabetes mellitus. Due to missing data, 15 (five men) individuals were excluded from the sample; moreover, six individuals were excluded because they did not practice physical activity during childhood and adolescence and became physically active during adulthood. All participants agreed to participate and signed a consent form. The study protocol was previously approved by the Research Ethics Committee of the University. More detailed procedures were previously published[9]. Thus, the final sample included 101 subjects (59 men and 42 women).

Early sports participation and current physical activity

Early sports participation, which comprised the period of childhood and adolescence, was assessed by two questions: 1) "Outside of school, did you engage in any organized/supervised sports for at least one year between agews seven and ten?"; 2) "Outside of school, did you engage in any organized/supervised sports for at least one year between the ages of 11 and 17?". Early sports participation was adopted as one of the inclusion criteria of the study; therefore, only participants who responded "yes" or "no" to both questions were included in the study.

Current physical activity (Current-PA) was monitored using a pedometer (Digi- Walker Yamax, SW200) for seven consecutive days. At the end of each day, the participant recorded the number of steps accumulated, and, in the following morning, the device was reset to start a new count. The mean number of steps of the week was used in the analyses.

Body fat

Body fat was estimated through the use of a Dual Energy X-ray Absorptiometry device (DXA) (Lunar Model – DPX-NT General Electric [GE]®). Body fat was expressed in percentage (%BF) using a GE Medical Systems Lunar software, version 4.7.

Cardiovascular risk factors

The measurement of systolic (SBP) and diastolic blood pressure (DBP) were performed according to the Brazilian guidelines of hypertension[10]. The participants were evaluated three times with an interval of one minute between each measurement. The final value of blood pressure was the average of the last two measurements.

To measurement of metabolic variables and inflammatory marker (high sensitive C-reactive protein [hsCRP]), collection of blood samples and biochemical analyses were performed in a private laboratory that met the criteria of standardization and quality control adopted by the Brazilian Health Ministry. Blood samples were collected after a fasting period of 12 hours. To calculate the HOMA-IR (Homeostatic Model Assessment-Insulin resistance), we used the dosage of fasting blood glucose (mmol/L) and insulin (IU/mL) applying the formula: HOMA-IR = (Fasting glucose * insulin) ÷ 22.5 [11]. To measure the fasting glucose, total cholesterol (TC), triglycerides (TG), and high-density

lipoprotein cholesterol (HDL-C), an enzymatic colorimetric kit processed in an Autohumalyzer A5 unit was used.

Covariates

Current smoking (yes or no) and alcohol consumption (weekly consumption) were accessed through a face-to-face interview. To estimate body mass index, we measured height using a stadiometer (Standard, Sanny®, Brasil), with a precision of 0.1cm and body mass was measured using a digital scale (PL 200, Filizola, Brasil), with a precision of 0.1kg.

Statistical analyses

Descriptive statistics was composed of mean and standard deviation. The Mann-Whitney test was used to compare groups, while general estimating equations (GEE) were used to compare individuals with early sports participation and physically active, early sports participation and physically inactive, and no sports participation and physically inactive, adjusted by covariates. Statistical significance (p-value) was set at 0.05, and the statistical software STATA (version 15.1) was used in all analyses.

RESULTS

The final sample included 101 adults (59 men) between 30 and 50 years old; the characteristics of the sample are presented in Table 1. In general, men presented higher systolic blood pressure ($p<0.001$), diastolic blood pressure ($p<0.001$), and triglycerides ($p=0.001$), and lower HDL-C ($p<0.05$). On the other hand, women presented more body fat ($p<0.001$).

General estimating equation models of the association between cardiovascular risk variables and physical activity maintenance patterns are presented in Table 2. Model 1 is adjusted by chronological age and sex. Both the group of physical activity only during childhood and adolescence and the group of physical activity during childhood/adolescence and adulthood presented lower body fat (%), Triglycerides, HOMA, and C-reactive protein as well as greater HDL-C ($p<0.001$) compared to the control group.

After the first set of analyses, models were also adjusted by other covariates (tobacco smoking, alcohol consumption, and BMI) (model 2). The variables that remained significant were body fat, triglycerides, and HOMA. The C-reactive protein was significantly lower only for the group of individuals physically active during childhood, adolescence, and adulthood. After this, significant values from model 2 were included as covariates in model 3 (body fat, triglycerides, HOMA, and C-reactive protein) in addition to the other covariates. The group of physical activity during childhood and adolescence but not during adulthood, and the group of physical activity during childhood, adolescence, and adulthood presented lower body fat (Wald=54.91; $p<0.001$). On the other hand, only the group of physical activity during childhood, adolescence, and adulthood remained with lower C-reactive protein (Wald=9.16; $p=0.010$).

DISCUSSION

Our main findings were that after the adjustment for all covariates, individuals who were physically active during childhood and adolescence, but were not physically active during adulthood, presented lower body fat when compared to the control group, while the group engaged in sports during childhood and adolescence, and still physically active during adulthood, presented lower body fat and C-reactive protein when compared to the control group.

This finding is consistent with the classic hypothesis that physical activity during childhood and adolescence can affect later body composition through modifications in body fat induced during the early ages and prolonged to adulthood[4,5,12]. Also, concerning the direct association of early sports participation with reduced body fat, physical exercise can promote DNA methylation in some genes associated with body adiposity[13], having a direct association in this path.

On the other hand, only the group with physical activity during childhood, adolescence, and adulthood presented lower C-reactive protein. This finding can be explained because C-reactive protein is more dependent on the current levels of physical activity[14], especially because C-reactive protein is an indicator of the actual inflammation process. In this sense, the role of previous physical activity should pass through the maintenance of physical activity from childhood to adulthood[2]. Another potential mechanism of this association should be body-fat maintenance throughout life, which is an important factor related to C-reactive protein[15], and, in our study, presented association

TABLE 1. CHARACTERISTICS OF THE SAMPLE (N=101).

Variables	Men (n=59)	Women (n=42)	p
Chronological age (years)	39.3 ± 5.8	40.2 ± 6.8	**0.513**
BMI (kg/m^2)	27.2 ± 3.8	25.3 ± 5.0	**0.004**
Body fat (%)	27.3 ± 8.2	37.3 ± 10.9	**<0.001**
Systolic blood pressure (mmHg)	117.3 ± 9.8	104.5 ± 11.9	**<0.001**
Diastolic blood pressure (mmHg)	81.4 ± 5.5	74.8 ± 7.6	**<0.001**
HOMA (score)	1.63 ± 1.36	1.27 ± 0.91	**0.148**
HDL-C (mg/dL)	47.1 ± 9.9	58.9 ± 12.1	**<0.001**
Tryglicerids (mg/dL)	142.0 ± 100.0	87.7 ± 43.7	**0.001**
C-reactive protein (mg/dL)	2.90 ± 3.40	3.69 ± 4.55	**0.959**
Mean number of steps (n)	8,314 ± 3,494	8,324 ± 3,399	**0.995**
Current physically active (%)	25.4%	27.9%	**0.931**
Early sports practice (%)	54.2%	46.5%	**0.512**
Tobacco smoking (%)	6.8%	0%	**0.085**
Alcohol drinking (≥2x week) (%)	20.3%	11.9%	**0.264**

Values are presented in means and standard deviations BMI, body mass index.

TABLE 2. GENERAL ESTIMATING EQUATIONS OF THE ASSOCIATION BETWEEN PHYSICAL ACTIVITY PATTERNS AND CARDIOVASCULAR RISK FACTORS (N=101).

	Physical activity patterns				
	Control (n=49)	Early practice / inactive (n=26)	Early practice / active (n=26)		
	Mean (95%CI)	Mean (95%CI)	Mean (95%CI)	Wald	p
Model 1					
Body fat (%)	37.8 (36.3 to 39.5)	26.0 (23.5 to 28.7)[a]	23.6 (21.0 to 26.6)[a]	90.21	<0.001
HDL-C (mg/dL)	47.6 (45.3 to 50.1)	55.3 (51.1 to 59.8)[a]	55.7 (51.8 to 60.0)[a]	16.77	<0.001
Triglycerides (mg/dL)	144.3 (125.3 to 166.3)	84.0 (71.8 to 98.3)[a]	90.9 (70.1 to 117.8)[a]	27.76	<0.001
HOMA (score)	2.06 (1.71 to 2.47)	0.95 (0.78 to 1.15)[a]	0.87 (0.74 to 1.02)[a]	54.01	<0.001
Systolic blood pressure (mmHg)	113.8 (110.8 to 116.9)	110.3 (106.5 to 114.2)	109.5 (106.0 to 113.0)	4.09	0.130
Diastolic blood pressure (mmHg)	79.8 (77.8 to 81.8)	78.1 (76.3 to 79.9)	76.7 (74.4 to 79.1)	4.10	0.129
C-reactive protein (mg/dL)	4.76 (3.69 to 6.13)	2.20 (1.22 to 3.98)[a]	1.30 (0.85 to 1.98)[a]	29.11	<0.001
Model 2					
Body fat (%)	35.0 (33.7 to 36.4)	27.48 (25.5 to 29.7)[a]	24.72 (22.7 to 26.9)[a]	66.65	<0.001
HDL-C (mg/dL)	49.1 (46.6 to 51.8)	53.5 (49.6 to 57.8)	53.8 (50.3 to 57.7)	4.89	0.087
Triglycerides (mg/dL)	132.3 (118.4 to 147.8)	89.63 (75.8 to 105.9)[a]	96.03 (73.7 to 125.1)[a]	15.64	<0.001
HOMA (score)	1.67 (1.44 to 1.93)	1.07 (0.90 to 1.27)[a]	1.01 (0.85 to 1.21)[a]	17.66	<0.001
Systolic blood pressure (mmHg)	110.7 (108.1 to 113.3)	113.0 (108.8 to 117.3)	112.14 (109.1 to 115.3)	0.85	0.654
Diastolic blood pressure (mmHg)	78.8 (76.9 to 81.1)	78.98 (76.9 to 81.1)	77.48 (75.3 to 79.8)	1.16	0.560
C-reactive protein (mg/dL)	4.08 (3.18 to 5.22)	2.41 (1.35 to 4.31)	1.44 (0.95 to 2.18)[a]	17.51	<0.001
Model 3					
Body fat (%)	34.8 (33.3 to 36.3)	27.5 (25.6 to 29.5)[a]	24.9 (22.9 to 27.1)[a]	54.91	<0.001
HDL-C (mg/dL)	-	-	-	-	-
Triglycerides (mg/dL)	126.7 (107.7 to 149.1)	92.1 (77.6 to 109.3)	98.4 (72.5 to 133.5)	5.47	0.065
HOMA (score)	1.43 (1.24 to 1.66)	1.18 (1.02 to 1.37)	1.14 (0.97 to 1.34)	4.11	0.128
Systolic blood pressure (mmHg)	-	-	-	-	-
Diastolic blood pressure (mmHg)	-	-	-	-	-
C-reactive protein (mg/dL)	4.12 (2.83 to 5.99)	2.13 (1.47 to 3.09)	1.33 (0.77 to 2.29)[a]	9.16	0.010

Notes. Model 1: Adjusted for sex and chronological age. Model 2: Model 1 + tobacco smoking, alcohol consumption, and body mass index. Model 3: Model 2 + Body fat, triglycerides, HOMA, and C-reactive protein. a = p<0.05 vs. control. CI = confidence interval. Significant differences in bold

with both groups (physical activity in early life but not currently, and physical activity throughout life).

Regarding the strength of our study, the adjustment of the analysis by several potential confounders, as well as the approach of adopting physical activity maintenance patterns, are the most important factors. On the other hand, our findings should be inferred with caution due to some limitations, such as reduced sample size, which did not allow us to stratify the results by sex, retrospective design, which can reduce causal inference due to super estimation of previous sports engagement, as well as the lack of socioeconomic indicator. It was not possible to include a fourth group (physical activity during adulthood, but no sports participation in childhood and adolescence) because of the low prevalence in our sample (5.6%). Moreover, we did not present an indicator of physical fitness, which could be a potential mediator. On the other hand, we presented good measures of body fat[16], direct physical activity through pedometer, and metabolic variables.

CONCLUSION

Thus, early engagement in sports (during childhood and/or adolescence, but not adulthood) was associated with reduced body fat, and physical activity during childhood, adolescence, and adulthood were associated with lower body fat and C-reactive protein, independent of potential confounders. Therefore, intervention strategies aiming to promote physical activity should be conducted even among children, aiming to impact cardiovascular health in adulthood.

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Conflict of interest

The authors report no conflicts of interest

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RESUMO

OBJETIVO: *Analisar a associação entre atividade física durante a vida e fatores de risco cardiovasculares entre adultos.*

DESIGN: *A amostra foi composta por 101 adultos (59 homens) entre 30 e 50 anos, os quais foram recrutados em diferentes academias de ginástica e uma universidade brasileira. Os participantes foram divididos de acordo com o engajamento prévio (autorrelatado) e atual de atividade física (mensurada por pedômetro) (participação esportiva durante a infância/adolescência e prática atual [n=26], participação esportiva durante a infância/adolescência e ausência de prática atual [n=26] e controle [n=49]). Como fatores de risco cardiovasculares foram mensurados gordura corporal (por meio de DXA), HDL, triglicérides, índice Homa, pressão arterial sistólica e diastólica, além da proteína c-reativa. Foram adotadas como covariáveis: idade cronológica, sexo, consumo de álcool e índice de massa corporal. Equações gerais de estimativa foram utilizadas adotando p<0,05.*

RESULTADOS: *Após os ajustes no modelo final, indivíduos engajados em esporte durante a infância e adolescência e inativos durante a idade adulta apresentaram menor gordura corporal quando comparados com participantes persistentemente inativos (p<0,001). Participantes persistentemente ativos apresentaram menor gordura corporal (p<0,001) e proteína c-reativa (p=0,010) quando comparados ao grupo controle.*

CONCLUSÃO: *Prática esportiva prévia (durante infância e adolescência) foi associada com redução da gordura corporal e ser fisicamente ativo ao longo da vida foi associado à redução da gordura corporal e proteína c-reativa.*

PALAVRAS-CHAVE: *Atividade motora. Esportes. Doença crônica. Exercício.*

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ORIGINAL ARTICLE

Bronchodilator test in extreme old age: Adverse effects of short-acting beta-2 adrenergic agonists with clinical repercussion and bronchodilator response

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SUMMARY

OBJECTIVE: *To evaluate chronological age as a limiting factor to perform the bronchodilator test, determine significant adverse effects of short-acting beta 2 agonists with clinical repercussions, and assess bronchodilator response in extreme-old-age patients who undergo the spirometry test.*

METHODS: *This is a cross-sectional and retrospective study. The sample was extracted from the database (spirometer and respiratory questionnaire) of a pulmonary function service. Patients over 90 years old were included in the research, and we evaluated their bronchodilator response and its significant adverse effects that may have clinical repercussions related to the bronchodilator.*

RESULTS: *A sample of 25 patients aged 92.12 ± 2.22 years (95% CI, 91.20 - 93.04), with a minimum age of 90 years and a maximum of 97 years and a predominance of females with 72% (18/25). The bronchodilator test was performed in 84% (21/25) of the patients. The bronchodilator response was evaluated in 19 of the 21 patients (90.47%) who underwent the bronchodilator test. Two tests did not meet the criteria of acceptability and reproducibility. No clinical adverse effects were observed with the bronchodilator medication (salbutamol) during or after the exam.*

CONCLUSIONS: *Chronological age is not a limiting factor for the bronchodilator test, short-acting beta-2 agonists did not present adverse effects with significant clinical repercussion and were useful in the diagnosis and therapeutic guidance of extreme-old-age patients.*

KEYWORDS: *Bronchodilator agents; aged; aging; respiratory function tests; Spirometry; longevity.*

INTRODUCTION

The geriatric population has been increasing in Brasil and worldwide as a result of the decline in fertility and the significant increase in life expectancy[1-3]. It is estimated that, by 2050, the "fourth age" population (≥85 years) will have more than tripled worldwide[1,2] and, in Brasil, the extremely elderly population (≥90 years) will go from 394,000 in 2010 to around 3.5 million by 2050[3].

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The prevalence of respiratory diseases and symptoms, such as cough and dyspnea, increases in the elderly population, so diagnostic investigation is required for the appropriate medical decision-making[4,5].

Spirometry is the pulmonary function test most available and used in clinical practice to screen for respiratory diseases, and the bronchodilator test should be an integral part of the spirometry to aid in the diagnosis, treatment, and therapy follow-up of different respiratory pathologies[6-9].

The chronological age is questioned as a limiting factor to properly perform spirometry[10], and there is some insecurity from the lay population and even from health professionals regarding the use of short-acting beta-2 agonists on elderly people and/or with heart disease[11,12], even in a single dose for an additional examination.

The goal of this study was to assess if the chronological age is a limiting factor for performing the bronchodilator test, determine the adverse effects with significant clinical significance of short-acting beta-2 agonists, and evaluate the bronchodilator response of spirometry in the fourth age.

METHODS

This is a retrospective study conducted at the University of Tiradentes (Unit), in the city of Aracaju (SE).

The sample was extracted from the database (spirometer and respiratory questionnaire) of a private laboratory of pulmonary function, from January 2012 to April 2017.

The research was approved by the Research Ethics Committee of Unit (CAAE: 67734717.2.0000.5371). There were no conflicts of interest.

The standardized respiratory questionnaire used in the spirometry assessed the anthropometric and demographic factors, respiratory symptoms, smoking, comorbidities, lung diseases and previous hear diseases, professional history, previous surgery and intubation, medications in use, clinical indication, and identification of the physician who requested the exam.

The study included patients ≥87 years of chronological age and excluded those ≤86 years.

In the first stage of the research, to assess the adverse effects of the inhaled bronchodilator, we considered only the first spirometry of each patient.

In the second stage, we evaluated the bronchodilator response of the patients who underwent the bronchodilator test. Based on the diagnosis of the request for the spirometry test by the assistant physician and on the respiratory questionnaire, for purposes of statistical evaluation of the bronchodilator response, the patients were divided into two groups: obstructive respiratory disease and non-obstructive. Then, in order to assess the influence of chronological age on the bronchodilator response and significant adverse effects, patients were divided into two groups, one from 87 to 89 years old, and another ≥90 years. Exams that did not meet the criteria for acceptability and reproducibility were excluded[6].

Spirometry tests were performed in the same room, using the same spirometer with a pneumotachograph coupled to a computer (model Microlab-3500; Micro Medical Ltd., Kent, England), where the tests were saved, which allowed to retrieve individual exams stored by means of menu selection. Each exam was evaluated regarding flow-volume and volume-time curves, and the conventional spirometric variables, such as forced vital capacity (FVC), forced expiratory volume during the first second (FEV1), FEV1/FVC ratio, peak expiratory flow (PEF), and middle expiratory flows[13].

The technical rules for examinations, criteria for acceptability, reproducibility, and interpretation of the spirometry test were determined according to the guidelines of the Brazilian Society of Pulmonology and Phthisiology[6], and interpreted by the same pulmonologist, associated to the SBPT, and certified on spirometry.

The spirometry results were classified based on the lower limit of normality for the FEV1, FVC, and FEV1/FVC ratio. The bronchodilator test was considered with a significant variation when there were elevations of the FEV1 and/or FVC ≥200 ml and 12%, and variations in volume, flow, or both, in relation to its initial value[14].

Soon after the completion of the initial spirometry, the bronchodilator test was performed by inhaling 100 mcg sprays of salbutamol from a inhaler coupled with a spacer, repeated sequentially after an interval of 15 to 30 seconds, between maneuvers, four times, totaling 400 mcg salbutamol. Then, the patient remained at rest for 15 to 20 minutes to repeat the spirometry after the use of the bronchodilator. The following were observed and considered adverse reactions with significant clinical repercus-

sion from the use of salbutamol: induction of heart arrhythmia, coronary failure, heart failure, hypertensive crisis, cardiac arrest, and respiratory failure. The adverse effects were observed immediately after inhaling the bronchodilator drug during the waiting period to repeat the exam and after the exam was completed, when the patients were cleared to go home. Minor adverse effects, without clinical repercussions or increased risk to patients that justified a contraindication to the bronchodilator test, such tremors, reflex tachycardia, palpitations, flushing, and headache, were not taken into account.

The statistical analysis was performed using the Statistical Package for Social Sciences, version 21.0 (SPSS Inc., Chicago, IL, USA). Continuous variables were described as mean and standard deviation, and categorical variables were summarized by means of simple and relative frequencies. The chi-square test was used to assess the differences in bronchodilator response between the groups of patients. The significance level adopted was $p<0.05$.

TABLE 1. DEMOGRAPHIC, ANTHROPOMETRIC, SMOKING ACTIVITY, AND COMORBIDITIES CHARACTERISTICS OF ELDERLY INDIVIDUALS ≥87 YEARS

Variables	≥ 87 years	CI 95%
Female, n (%)[1]	44 (58.7%)	
Age[2], years	89.34 ± 0.29 year	88.74 - 89.94
Height, meters [2]	1.52 ± 0.01	1.50 - 1.55
BMI[2]	27.02 ± 0.58	25.86 - 28.18
Weight, Kg[2]	63.30 ± 1.52	60.26 - 66.35
Nonsmokers1	46 (61.3%)	
Former smokers[1]	26 (34.7%)	
Smokers1	3 (4%)	
Comorbidities, n (%)1		
Asthma	20 (26.7%)	
COPD	22 (29.3%)	
Allergic rhinitis	23 (30.7%)	
SAH	33 (44%)	
Dyslipidemia	17 (22.7%)	
OSA	16 (21.3%)	
Diabetes mellitus	14 (18.7%)	
Cerebrovascular	6 (8%)	
Cognitive deficit	7 (9.3%)	
GERD	5 (6.7%)	
Prostatic Hyperplasia	4 (5.33%)	
Arrhythmias	4 (5.33%)	
Other comorbidities	16 (21.33%)	

1. Values as n (%). 2 Values as mean ± SD. CI 95%: Confidence interval; BMI Body Mass Index, SAH: Systemic arterial hypertension; OSA: Obstructive sleep apnea. Other comorbidities (depression, anxiety, coronary failure, previous breast neoplasia, interstitial lung disease, pulmonary nodule, osteoarthritis, chronic cough, hypothyroidism, auditory deficit). Some patients had one or more comorbidities. Main Author: Saulo Maia d'Avila Melo

RESULTS

Among the 4,126 spirometric tests performed during the period evaluated, 77 (1.86%) were of elderly individuals ≥87 years. Two patients were excluded from this study for having repeated the exam. In total, we selected for this study 75 patients with a mean age of 89.34 ± 0.29 years (CI 95% 88.74-89.94), minimum age of 87 years, and a maximum of 97 years, predominantly females (58.7%, 44/75). There were 61.3% (46/75) non-smokers, 34.7% (26/75) former smokers, and 4% (3/75) active smokers. Table 1 shows the demographic, anthropometric, smoking activity, and comorbidities of the general sample.

The bronchodilator test was performed in 86.6% (65/75) of the patients; 13.3% (10/75) did not undergo the bronchodilator test. One patient (1/75; 1.33%) refused to use the bronchodilator medication, and, in nine tests (9/75; 12%), the assistant physician, when requesting the examination, excluded the bronchodilator test (Figure 1).

The assessment of significant response to the bronchodilator was performed in 63 of the 65 (96.92%) patients who underwent the bronchodilator test; two examinations were excluded because they did not meet the criteria for acceptability and reproducibility and were, therefore, considered inconclusive tests (D Quality), making it impossible to interpret the bronchodilator test.

Among the 63 patients analyzed, 20.63% (13/63) had a significant response to the bronchodilator; two patients (2/63; 3.17%) responded to flow, three to volume (4/63; 6.34%), and seven to flow and volume (7/63; 11.11%). The bronchodilator response was not significant in 79.63% (50/63) of the patients who underwent the bronchodilator test.

After assessing the bronchodilator response per group, a positive response was found in both groups (obstructive: 9/34; 26.47%; non-obstructive: 4/29; 13.79%), with no significant difference between the groups ($p<0.11$).

The chronological age did not influence the positive bronchodilator response in the groups per age group (87 to 89 years old: 10/44; 22.72%; and ≥90 years: 3/19; 15.78%; $p<0.23$). No adverse effects were observed with a significant clinical repercussion of the bronchodilator medication during or after the test completion in all patients from both groups, so they were all discharged from the pulmonary function service a few minutes after the spirometry was completed.

DISCUSSION

Even with healthy aging, there is a reduction of the physiological capacity of all organs, in particular of the respiratory system. Elderly patients have an increased risk for respiratory diseases, since the frequent exposure to environmental toxins over a lifetime, particularly to tobacco smoke, environmental pollution, occupational dust, and respiratory infections, predispose to a higher risk of acute or chronic lung disease[5].

Inhaled bronchodilator therapy is the basis for the treatment of obstructive respiratory diseases[8,9]. Spirometry with a bronchodilator test is commonly performed as a fundamental part of the evaluation of pulmonary function and has a preponderant role in the diagnosis, assessment of severity, and estimation of therapeutic response of respiratory diseases[6-9,14-16].

There is currently a limited number of studies on spirometry in elderly patients and no discussion regarding the use of bronchodilators in the fourth age[6,7].

In a recent publication that included more than 97,000 spirometric tests from five continents, in 33 countries, only 0.8% of individuals were more than 80 years old (chronological age), and of these, only 26 were ≥90 years[7].

We evidence here, in a pioneering way, the importance and the security of bronchodilators in the fourth age, with no adverse effects with significant clinical repercussions. A significant response to salbutamol was observed in 20.63% (13/63) of the patients in both groups (obstructive and non-obstructive), which demonstrates that there are no contraindications, so the repetition of the spirometry after bronchodilation should be routine, with safety, since it useful as a diagnostic aid and in therapeutic orientation, contributing to the clinical decision-making process in this elderly population.

In real life, the cardiovascular side effects of bronchodilators are one of the major concerns, and there is controversy regarding the relative systemic safety of the chronic use of fenoterol and salbutamol[17-20]. However, the safety of these medications in obstructive lung disease patients in acute crisis (asthma and COPD) is demonstrated in previous research[8,9,11,12].

The cardiovascular and systemic safety of high doses of inhaled fenoterol and salbutamol has been demonstrated in asthmatic patients in severe acute crisis[18]. In COPD exacerbations, the use of short-acting beta-2 agonists, through inhaling did not increase the risk of fatal or nonfatal myocardial infarction[11,19].

Spirometry is an outpatient elective examination in which bronchodilators are used in a single dose or in low doses when compared to those used during crises of acute or chronic lung disease patients. Our patients were not in an acute crisis; therefore, they had a lower probability of triggering cardiovascular complications.

Bronchodilators are safe drugs when used in the recommended doses[8,9,11,12,20]. In spirometry, it is recommended using a short-acting beta-2 (salbutamol) or a short-acting anticholinergic (ipratropium bromide), preferably in spray, because of its availability, ease of use, and cost[6,14-16]: the dose of spray salbutamol, 400 mcg (4 jets of 100 mcg), preferably with a spacer, with a repetition of the examination after 15 minutes, and a

TABLE 2. CONTRAINDICATIONS OF SPIROMETRY AND BRONCHODILATOR TEST [15]

Absolute	Relative
Hemodynamic instability.	Age under 5 to 6 years.
Pulmonary embolism. Acute retinal detachment.	Confused patient or with dementia; uncooperative.
Recent pneumothorax (≤2 weeks).	Recent abdominal or thoracic surgery.
Active respiratory infection: viral, tuberculosis, others.	Acute diarrhea or vomiting, nauseated state.
Acute hemoptysis.	Hypertensive crisis.
Recent myocardial infarction. Thoracic aortic aneurysm >6 cm.	Oral and maxillofacial disorders that prevent oral coupling to the device.
Unstable angina. Unstable arrhythmia.	Chest or abdominal pain that prevents ventilatory maneuvers.
Intracranial hypertension.	Recent brain, eye, or otorhinolaryngologic surgery.

Relative contraindications for the bronchodilator test [15] Known or likely adverse reactions to the intended bronchodilator. Known heart arrhythmia. Patient's fear regarding the use of bronchodilators.
If there is a contraindication to spirometry, the bronchodilator test should not be performed. The relative contraindications for the bronchodilator test should be assessed individually with changes of the type of bronchodilator and analyzed on a case by case basis, by evaluating the risk-benefit ratio. Table adapted[15] .

TABLE 3. GENERAL CONTRAINDICATIONS TO THE USE OF SELECTIVE SHORT-ACTING BETA-2 ADRENERGIC AGONIST AND IPRATROPIUM BROMIDE [21, 22]

Beta-2 adrenergic agonists
Hyperthyroidism. / Subvalvular aortic stenosis. / Hypertrophic obstructive heart disease. / Tachyarrhythmias. / Sensitivity to sympathomimetic drugs. / Hypersensitivity to any component of the formulation.

Ipratropium Bromide
Hypersensitivity to any component of the formulation. / Hypersensitivity to atropine or its derivatives. / Use with caution in narrow-angle glaucoma, bladder obstruction, prostate hyperplasia, and myasthenia gravis.

Table adapted(21, 22).

dose of ipratropium bromide, of 160 mcg (8 jets x 20 mcg), with a repetition of the examination after 30 to 45 minutes[9,14-16]. Ipratropium bromide presents a lower incidence of adverse effects, especially cardiovascular ones, in comparison to beta-2 agonists[21].

With there is a contraindication to spirometry, the bronchodilator test, consequently, should not be performed (Table 2).

Research regarding contraindications specific to the bronchodilator test during spirometry is limited[6,14-16]. We did not find in the literature any absolute contraindication for the bronchodilator test, and important adverse effects (severe cardiac arrhythmia, hypertensive crisis, coronary failure, heart failure, or respiratory failure) triggered by the bronchodilator test.

The contraindications, in general, to bronchodilators used in the bronchodilator test (short-acting beta-2 agonists and ipratropium bromide) are shown in Table 3.

Reports of smaller risks without clinical repercussions, including tremors of the extremities, reflex tachycardia, excitation, flushing, palpitations, headache, and dizziness do not justify a contraindication to the bronchodilator test, since these cause only concern to patients (often due to lack of prior guidance) and health professionals who are not used to the medication. However, spirometry requests that specify the non-use of the bronchodilator test are justified, particularly in elderly patients or with heart disease.

Therefore, when there is no contraindication to spirometry, the bronchodilator test should be performed respecting its contraindications, which should be analyzed on a case by case basis by evaluating the risk-benefit ratio (Tables 2 and 3).

The use of a specific questionnaire to assess adverse effects without significant clinical repercussions, the potassium dose, and the lack of cardiovascular monitoring during and after the completion of the bronchodilator test were limitations of our study because of its retrospective design.

CONCLUSION

Our study demonstrated that chronological age is not a limiting factor for bronchodilator tests, that short-acting selective adrenergic beta-2 agonists presented no adverse effects with significant clinical consequences, and that they were useful to assist in the diagnosis and therapeutic orientation of patients in the fourth age.

Contribution of the authors

SMAM - Concept, creation, and formatting of the research, literature review, submission to the Research Ethics Committee, database review, discussion of the results and statistics, discussion with the literature, and drafting of the article.

LAO; RAR; JLFW - Literature review, drafting, and review of the database, discussion of the results and statistics, discussion with the literature, and drafting of the article.

RESUMO

OBJETIVOS: *Avaliar se idade cronológica é um fator limitante para realizar prova broncodilatadora, determinar efeitos adversos significativos com repercussão clínica dos beta-2 agonistas de curta ação e avaliar a resposta broncodilatadora na espirometria, na velhice extrema.*

MÉTODOS: *Estudo transversal, retrospectivo. Amostra extraída do banco de dados (espirômetro e questionário respiratório) de um serviço de função pulmonar. Incluídos na pesquisa pacientes com ≥90 anos, sendo avaliados a resposta broncodilatadora e efeitos adversos significativos com repercussão clínica ao broncodilatador.*

RESULTADOS: *Amostra de 25 pacientes com idade de 92,12 ± 2,22 anos (IC 95%; 91,20 – 93,04), idade mínima de 90 anos e máxima de 97 anos, predominando o sexo feminino, com 72% (18/25). A prova broncodilatadora foi realizada em 84% (21/25) dos pacientes. A avaliação da resposta ao broncodilatador foi feita em 19 dos 21 pacientes (90,47%) que realizaram a prova broncodilatadora, uma vez que dois desses exames não preencheram os critérios de aceitabilidade e reprodutibilidade. A resposta broncodilatadora foi significativa em 10,52% (2/19) dos pacientes, ambos portadores de pneumopatia obstrutiva. Não foram observados efeitos adversos com repercussão clínica da medicação broncodilatadora (salbutamol) durante ou após sua realização.*

CONCLUSÕES: *A idade cronológica não é um fator limitante para a realização da prova broncodilatadora, os beta-2 agonistas de curta ação não apresentaram efeitos adversos com repercussão clínica significativa e foram bastante úteis para auxiliar no diagnóstico e orientação terapêutica na velhice extrema.*

PALAVRAS-CHAVE: *Broncodilatadores. Idoso. Envelhecimento. Testes de função respiratória. Espirometria. Longevidade.*

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ORIGINAL ARTICLE

Electronic prescription: frequency and severity of medication errors

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SUMMARY

OBJECTIVE: *To assess the frequency and severity of prescriptions errors with potentially dangerous drugs (heparin and potassium chloride for injection concentrate) before and after the introduction of a computerized provider order entry (CPOE) system.*

METHODS: *This is a retrospective study that compared errors in manual/pre-typed prescriptions in 2007 (Stage 1) with CPOE prescriptions in 2014 (Stage 2) (Total = 1,028 prescriptions), in two high-complexity hospitals of Belo Horizonte, Brasil.*

RESULTS: *An increase of 25% in the frequency of errors in Hospital 1 was observed after the intervention (p<0.001). In contrast, a decreased error frequency of 85% was observed in Hospital 2 (p<0.001). Regarding potassium chloride, the error rate remained unchanged in Hospital 1 (p>0.05). In Hospital 2, a significant decrease was recorded in Stage 2 (p<0.001). A reduced error severity with heparin (p<0.001) was noted, while potassium chloride-related prescription severity remain unchanged (p> 0.05).*

CONCLUSIONS: *The frequency and severity of medication errors after the introduction of CPOE was affected differently in the two hospitals, which shows a need for thorough observation when the prescription system is modified. Control of new potential errors introduced and their causes for the adoption of measures to prevent these events must be in place during and after the implementation of this technology.*

KEYWORDS: *Patient safety. Electronic prescribing. Medication errors. Drug prescriptions.*

INTRODUCTION

A prescription error is a type of error related to writing the prescription itself or an error in the therapeutic decision process. Like any medication error, it has the potential to lead to inappropriate medication use and harm to the patient. Among main prescription errors are illegible writing, use of confusing abbreviations, omission of pharmaceutical form, concentration, administration route, interval, infusion rate, error in drug unit and others[1].

In 2011, it was shown that one out of every 854 deaths of hospitalized patients is due to medication errors, which translates into 7,000 deaths per year, and that 72% of errors are related to prescription. This is underestimated data, given the difficulties of

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reporting adverse events. In addition, this elevated number evidences the vulnerability of the prescription process[2].

The computerized prescription process is a complex system that provides the opportunity for standardized and improved communication among health teams. Studies have shown the advantages of electronic prescription systems, such as improving document readability and reducing prescription errors and adverse events, with a positive impact on prescription quality and morbimortality rates[3-5]. Corroborating with this data, in the U.S., estimated annual savings of US$ 81 billion were achieved in 2005, based on the implementation of the electronic prescribing system (EPS), as well as benefits to patient health and safety, strengthening prevention and improving treatment of chronic diseases[6].

However, despite data addressing the advantages and benefits of EPS use, a systematic review that evaluated the influence of electronic systems on prescription errors has shown that published studies confirm the reduced frequency of medication errors with the implantation of systems, but the question remains as to whether the severity of adverse events caused by prescription errors is reduced[7].

Therefore, this study aimed to evaluate the prescribing profile of selected potentially dangerous drugs (PDD) (unfractionated heparin and potassium chloride for injection concentrate) as to the frequency and severity of prescriptions errors before and after implementation of an EPS in two large hospitals of Belo Horizonte, Mina Gerais.

METHODS

This is an experimental two-stage retrospective study performed in two public teaching hospitals located in the city of Belo Horizonte, Minas Gerais (Hospital 1 and Hospital 2). Both hospitals are large and with closed medical staff and with a total capacity of 956 beds.

Sample

In Stage 1, manual and pre-typed prescriptions elaborated on 30 consecutive days (from November 17 to December 16, 2007) were analyzed. In Stage 2, electronic prescriptions elaborated on 30 consecutive days (from 01 to 30 September 2014) were also analyzed after the implementation of an EPS without clinical support (which would be a computer-based program that analyze data within EPS to provide prompts and reminders to assist health care providers in implementing evidence-based clinical guidelines at the point of care). The implementation of the EPS occurred simultaneously in 2009 in both hospitals and an extensive training for doctors, pharmacists and nurses was provided by the hospital during that year to guarantee a successful process.

In both stages, we evaluated prescriptions containing at least one of the following PDDs that are associated with a high frequency of errors and significant severity: (1) 10% potassium chloride (KCl), injectable solution, 10 mL vial; (2) unfractionated heparin (UFH), injectable solution, 0.25 mL ampoule with 5,000 IU; or (3) UFH, injectable solution, 5 mL vial with 5,000 units per mL . Prescriptions with one of the PDDs selected but whose dispensation was not effected by the pharmacy for any reason were rejected, as well as prescriptions of outpatients (serviced only in emergency and outpatient services).

A random number table was used to establish the sample of prescriptions to be analyzed. Three hundred forty-nine Stage 1 prescriptions were compared with 679 Stage 2 prescriptions. The sample for Stage 2 was calculated by accepting an error α=5% (0.05), error β=0.20 (20%) and a power of 0.80 (80%), and with the possibility of detecting a difference of at least 7.5% among the samples compared.

Study Variables and Data Collection

Prescriptions were categorized as “pre-typed”, “mixed” or “handwritten” (types available in Stage 1) or “electronic” (available in Stage 2).

Prescription errors were identified in the sample of prescriptions evaluated in both stages as to their frequency, type and severity. Dean, Barber and Schachter (2000) criteria were used to identify and classify prescribing errors as to type, which include[8]:

- A) errors in the decision process: erroneous prescriptions of the pharmaceutical form, concentration, administration route, interval, dose and infusion rate;
- B) errors in the writing of the prescription: (partial or total) illegibility and errors of omission of prescription components. Patient’s name, date and information on the body of the prescription – pharmaceutical form, concentration, administration route, interval and PDD name were considered prescription components.

The PDD dose was classified as a "wrong dose" (when the prescribed dose was 20% higher or lower than recommended) or as "overdose" (when the prescribed dose was higher than the maximum established by the product's manufacturer or those defined in the literature)[9-11].

The criteria for judgment of the concentration, administration route, interval and infusion rate were the same as for the pharmaceutical form. The readability of PDDs' names was evaluated and each word was examined separately, trying to avoid interpretation or deduction, according to established standard.

Pharmaceutical form, concentration, administration route, interval and infusion rate were classified as: "wrong" (when the prescription was confronted with references on pharmacology, with the product leaflet and the dictionary of medicinal products, and was incorrect); "Incomplete" (where the pharmaceutical form has not been fully described in the prescription); "Dubious/unclear" (where it was not possible to clearly distinguish the prescribed pharmaceutical form); and "missing" (when the pharmaceutical form was not recorded in the prescription)[9-11].

PDDs names' readability was also evaluated according to the readability standard and classified as "good readability", "difficult to read" or "illegible". Thus, each word was examined separately, avoiding interpretation or deduction, as per established standard. The Kappa index was used to determine reliability of the readability assessment. Readability was verified by the supervising pharmacist of each hospital and by one more pharmacist independently.

Error severity analysis was based on index 1 to 6 proposed by the National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP)[12] modified by Forrey et al.[13]: (1) no error; (2) an error that would not reach the patient; (3) an error without harm but that could reach the patient and requires monitoring to avoid harm; (4) an error that could lead to temporary harm; (5) an error that could lead to permanent harm; (6) an error that could lead to death.

The prescription error (at least one error or some type of prescription error) was defined as a dependent variable. We considered hospitals (1 or 2) or study stage (1 or 2) as independent variables.

Data review

A univariate analysis was performed to evaluate differences between the two hospitals and between the two stages. We used the chi-square test for this study, or the Fisher-Freeman-Halton test for frequencies lower than five. The Kruskal-Wallis test was used for the comparison between hospitals and stages. All the results were significant for a probability of significance of less than 5% ($p<0.05$). Statistical Package for Social Sciences (SPSS) software version 17.0 was used for all analyses.

Ethical Aspects

The proposed research was registered in the National Health System and National Commission of Ethics in Research (SISNEP/CONEP) under Nº 0028.1.191.000-05 and was approved by the Research Ethics Commissions / Committees of the two hospitals participating in the project.

RESULTS

Errors Involving Unfractionated Heparin

During Stage 2 at Hospital 1, there was a statistically significant increase in the frequency of prescriptions with at least one error and in the number of pharmaceutical form errors, and the first variable was directly affected by the increase of the second one. On the other hand, a reduced number of errors involving the concentration and dose of UFH was detected. In Hospital 2, there was a statistically significant reduction in the frequency of all variables, except errors associated with the administration route (Table 1).

Errors Involving Potassium Chloride

Regarding potassium chloride (Table 2), we observed a statistical relevance for the variables: some error, pharmaceutical form and drug administration route. In Hospital 1, the frequency of errors remained unchanged ($p>0.001$) regardless of stages for the variables some error and pharmaceutical form, and there was an increase of 46.5% ($p<0.001$) in the error frequency of the drug administration route. In Hospital 2, there was a statistically significant reduction of errors for the three variables in Stage 2.

Error Severity Assessment

By analyzing the most frequent types of prescriptions of UFH errors (errors associated with the pharmaceutical form and concentration), a significant reduction of its severity rate was observed after the implementation of the EPS. Regarding errors observed in the prescription of KCl, no statistically significant changes were identified in its severity profile (Table 3).

TABLE 1. COMPARATIVE ANALYSIS BETWEEN HOSPITALS AND STAGES REGARDING TYPES OF ERRORS OBSERVED IN THE PRESCRIPTIONS OF UNFRACTIONATED HEPARIN

Type of Error	Stage	Error Frequency Number of prescriptions with errors/ Total number of prescriptions (%)		p-value
		Hospital 1	Hospital 2	
Prescription with at least one error	1	156/203 (76.8)	141/146 (96.6)	<0.001
	2	352/352 (100)	6/327 (1.8)	<0.001
	p-value	<0.001	<0.001	
Pharmaceutical form	1	148/203 (72.9)	129/146 (88.4)	<0.001
	2	352/352 (100)	6/327 (1.8)	<0.001
	p-value	<0.001	<0.001	
Concentration	1	91/203 (44.8)	107/146 (73.3)	<0.001
	2	90/352 (25.6)	6/327 (1.8)	<0.001
	p-value	<0.001	<0.001	
Administration route	1	0/203 (0.0)	2/146 (1.4)	0.174
	2	3/352 (0.9)	3/327 (0.9)	1.000
	p-value	0.303	0.646	
Administration interval	1	0/203 (0.0)	4/146 (2.7)	0.003
	2	0/352 (0.0)	0/327 (0.0)	-
	p-value	-	0.009	
Dose	1	59/203 (29.1)	59/146 (40.4)	0.027
	2	0/352 (0.0)	0/327 (0.0)	-
	p-value	<0.001	<0.001	

TABLE 2. COMPARATIVE ANALYSIS BETWEEN HOSPITALS AND STAGES REGARDING TYPES OF ERRORS OBSERVED IN THE PRESCRIPTIONS OF POTASSIUM CHLORIDE FOR INJECTION CONCENTRATE

Type of Error	Stage	Error Frequency Number of prescriptions with errors/ Total number of prescriptions (%)		p-value
		Hospital 1	Hospital 2	
Prescription with at least one error	1	65/65 (100)	45/45 (100)	-
	2	91/91 (100)	18/85 (21.2)	<0.001
	p-value	-	<0.001	
Pharmaceutical form	1	65/65 (100)	42/45 (93.3)	0.066
	2	91/91 (100)	1/85 (1.8)	<0.001
	p-value	-	<0.001	
Concentration	1	4/65 (6.2)	6/45 (13.3)	0.312
	2	0/91 (0.0)	0/85 (0.0)	-
	p-value	0.029	0.001	
Administration route	1	35/65 (53.8)	41/45 (91.1)	<0.001
	2	91/91 (100)	1/85 (1.2)	<0.001
	p-value	<0.001	<0.001	
Administration interval	1	0/65 (0.0)	2/45 (4.4)	0.165
	2	0/91 (0.0)	3/85 (3.5)	0.111
	p-value	-	1.000	
Dose	1	21/65 (32.3)	9/45 (20.0)	0.154
	2	0/91 (0.0)	0/85 (0.0)	-
	p-value	<0.001	<0.001	

DISCUSSION

Prescription errors are cited as one of the most common types of errors. While this is an alarming fact, international and national studies indicate that these are the most likely to be adapted to increase the safety of hospitalized patients[14].

Such errors were very much the case in Stage 1 prescriptions in both hospitals because non-standard manual prescriptions were used. Despite the high initial frequency of errors in both hospitals, the introduction of EPS brought divergent results for the two analyzed institutions, since there was an increased frequency of errors in Hospital 1 and reduced frequency in Hospital 2.

In Hospital 2, most of Stage 1 prescriptions contained considerable writing errors (e.g. data omission, illegibility and use of dangerous abbreviations) that were easily corrected after implementation of an EPS with appropriate parameterization containing drug name, pharmaceutical form, presentation, posology and administration route. Thus, the EPS contributed directly to reduced frequency of errors involving UFH and KCl.

The increased overall error frequency in Hospital 1 and in the errors involving the pharmaceutical form of UFH and KCl and in the administration route errors for KCl can be explained by the implementation of a system with inadequate parameterization of the prescription that did not take into account issues that are important to prescription safety, such as permission to use dangerous abbreviations, lack of automatic filling of standardized items (e.g. pharmaceutical form), permission of incorrect dosage and administration route prescriptions.

In the specific case of KCl in Hospital 1, the missing drug form in the EPS caused systematically repeated errors every time the drug was prescribed. Therefore, 100% of the prescriptions had some error. In the prescription of UFH in both hospitals, the most frequent types of initial errors were of pharmaceutical form that were associated with the availability of two presentations of this medicine in both institutions. On the one hand, the adequate parameterization of UFH presentations in the EPS of Hospital 2 allowed a reduced frequency of errors in the mentioned variables. In Hospital 1, whose EPS allowed each prescriber to parameterize his prescription individually, incorrect pharmaceutical form errors increased.

In spite of EPS's advantages over manual prescription, this study corroborates with the international literature that shows the EPS' potential to increase the number of errors and adverse events during the first years after its implantation, since its creation can evidence failures that are detected and corrected only after a given period[6,15,16]. In this perspective, patient safety experts health professionals must be directly involved in the development and adequacy of the EPS with a view to designing systems that are safer and more efficient[15].

Analysis of error severity showed a statistically significant reduction in the frequency of severe errors (category 4) with UFH ($p<0.001$), which was mainly due to the fact that prescriptions were more complete and organized in Stage 2, reducing errors associated with the pharmaceutical form of this medicinal product. This fact contradicts what has been detected in other international studies[16] and is extremely relevant, since this type of error has the potential of a

TABLE 3. COMPARATIVE ANALYSIS BETWEEN HOSPITALS AND BETWEEN STAGES REGARDING THE SEVERITY OF ERRORS OBSERVED IN THE PRESCRIPTIONS OF UNFRACTIONATED HEPARIN AND POTASSIUM CHLORIDE FOR INJECTION CONCENTRATE BY STUDY STAGE

	Type of Error	Stage	Severity Number of prescriptions with errors (%)			p-value
			1	2	4	
Heparin	Pharmaceutical form	1	1(0.7)	122(83.0)	24(16.3)	<0.001
		2	0(0.0)	351(100)	0(0.0)	
	Concentration	1	1(1.1)	65(72.2)	24(26.7)	<0.001
		2	1(1.1)	89(98.9)	0(0.0)	
Potassium Chloride	Pharmaceutical form	1	1(1.6)	62(96.8)	1(1.6)	0.169
		2	0(0.0)	91(100)	0(0.0)	
	Administration route	1	2(6.7)	27(90.0)	1(3.3)	0.222
		2	3(3.3)	88(96.7)	0(0.0)	

wrong choice among UFH presentations available at the institution. Thus, since the injectable solution of the ampoule is four times more concentrated than the vial solution and considering the high frequency of prescription of this drug in the hospital environment, the wrong choice between the two presentations due to drug prescription failure can lead to defining errors in health and adverse events, such as thromboembolic or hemorrhagic events that may contribute to the worsening of the general state of the patient and even his death[17].

In the KCl prescriptions, no statistically significant differences were detected in the severity of errors with the advent of EPS. However, it should be noted that, in manual prescriptions, many errors were gross with prominence for the readability of prescriptions, subject to different interpretations and, therefore, errors were potentially more serious. On the other hand, regarding typed prescriptions, errors were serial, systematic and repetitive due to failures in the system itself, leading to an increased number of errors. In addition, data such as patient information and readability of prescriber's signature were found in almost 100% of electronic prescriptions. This result evidences that, although electronic prescription minimizes interpretation errors caused by illegible or similar spelling of the nomenclature of pharmacological compounds, care should be taken to avoid technical errors[6,18].

Some studies have already shown that EPS promote benefits in patient health and safety. The importance of reducing the frequency of prescription errors is also related to lower unnecessary expenses due to correction and prevention of incidents and adverse events that can, for example, prolong hospital stay and require additional examinations. We emphasize that an unreadable prescription usually requires contacting the prescriber for content elucidation and can extend the length of the medication process. These are direct and indirect costs that are borne by the institution and increase the total costs of health care[17,19,20].

CONCLUSIONS

The implementation of EPS has improved the prescription process when one considers the organization and readability of prescriptions as contributing factors in reducing error frequency. The full parameterization of prescriptions was instrumental to the achievement of these results, since, there was a statistically significant decline in the overall frequency and specific types of errors in the hospital where drug description in the computerized system was complete.

The severity of medication errors after the introduction of EPS was affected differently in both hospitals, evidencing the need for careful observation when the prescription system is created and implemented. Therefore, it should be noted that control must be exerted over potential new errors introduced and their causes for the adoption of measures for their prevention during and after the implementation of this technology.

RESUMO

OBJETIVO: *Avaliar a frequência e a gravidade de erros em prescrições envolvendo medicamentos potencialmente perigosos (heparina e cloreto de potássio concentrado injetável) antes e após a introdução de um sistema de prescrição eletrônica.*

MÉTODOS: *Trata-se de estudo retrospectivo que comparou erros em prescrições manuais e pré-digitadas de 2007 (Fase 1) com prescrições eletrônicas de 2014 (Fase 2) (total = 1.028 prescrições), em dois hospitais de alta complexidade de Belo Horizonte.*

RESULTADOS: *Foi observado no hospital 1 aumento de 25% dos erros depois da intervenção (p<0,001), e no hospital 2 foi verificada redução de 85% (p<0,001). Para o cloreto de potássio, a frequência de erros permaneceu a mesma no hospital 1 (p>0,05), independentemente da fase e, no hospital 2, ocorreu redução significativa na fase 2 (p<0,001). Foi identificada redução da gravidade dos erros com a heparina (p<0,001), mas não houve alteração na gravidade dos erros com cloreto de potássio (p>0,05).*

CONCLUSÕES: *A frequência e a gravidade dos erros de medicação após a introdução de prescrição eletrônica foram impactadas de forma diferente nos dois hospitais, demonstrando necessidade de observação criteriosa quando o sistema de prescrição é modificado. Durante e após a implantação dessa tecnologia, deve existir controle dos novos erros potenciais introduzidos e suas causas para a adoção de medidas de prevenção desses eventos.*

PALAVRAS-CHAVE: *Segurança do paciente. Prescrição eletrônica. Erros de medicação. Prescrições de medicamentos.*

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ORIGINAL ARTICLE

Burnout syndrome should not be underestimated

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SUMMARY

OBJECTIVES: *Burnout syndrome can be seen among health professionals at every stage of their careers. The incidence of burnout syndrome among health care professionals has increased in recent years and varies between countries and depending on different areas of specialization and work units. It is known that burnout syndrome significantly affects the work and social life of individuals. We aimed to investigate the effect of burnout syndrome on trauma and infection.*

METHODS: *The study was conducted in the Alanya Alaaddin Keykubat University, Faculty of Medicine, Training and Research Hospital. All health professionals working at the hospital were included in the study. The Maslach Burnout Inventory was applied to the participants, who were asked about infective disease and trauma history over the past year.*

RESULTS: *The total burnout rate was 77.8% among participants. We found that the rate of trauma and infective disease history was significantly high in employees who had burnout syndrome ($p<0.05$).*

CONCLUSION: *Burnout syndrome is a common and important problem among health professionals that also has adverse effects on people's daily life, especially increasing the incidence of infection and trauma.*

KEYWORDS: *Burnout, Professional. Occupational Diseases. Occupational Health. Wounds and Injuries. Infection.*

INTRODUCTION

Burnout syndrome (BOS) was first described by Freudenberger in 1974 and is defined as the response to long-term stress due to the unfavorable working conditions of the workplace[1]. Burnout was defined by Maslach as a symptom of physical and psychological dimensions, including negative attitudes towards work, life, and other people, which are the result of exhaustion, fatigue, despair, and hopelessness in individuals[2]. Burnout syndrome can affect employees in all sectors[1,3].

BOS can be seen among health professionals at every stage of their careers[4]. The incidence of BOS among health care professionals varies among countries, ranging from 25% to 75%, depending on different areas of specialization and work units. Studies conducted on nurses and assistant health personnel have provided BOS rates of approximately 30-50%. The frequency of BOS among doctors varies depending on the branches and the work units[5].

Although there are different models developed for BOS, the most commonly used model is the one developed by Maslach[2,6]. In it, burnout is generally described as insensitivity towards other persons, feeling of emotional exhaustion, and a decrease in personal competence and in the sense of achievement in the

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professionals who work closely with people. According to this model, there are three different subdimensions of burnout: emotional exhaustion, depersonalization, and a reduced sense of achievement[4]. The Maslach Burnout Inventory (MBI) is accepted as the gold standard in determining the severity and risk of burnout[4].

METHODS

The study was conducted between February 2018 and March 2018 in Alanya Alaaddin Keykubat University, Faculty of Medicine, Training and Research Hospital. All of the health professionals working at the hospital were included in the study. In the questionnaire, participants were asked about their sociodemographic characteristics, such as age, gender, and marital status, as well as the units in which they worked, their working patterns (night, daytime, shifts), and total working time. The MBI[2] was applied to the participants, and all participants completed the adapted MBI translated into Turkish in 1992[7]. In addition, participants were asked about the frequency of infection (upper respiratory tract infection, soft tissue infection, otitis, urinary tract infection, among others) that had been treated in outpatient settings in the past year, and their incidence (1-3, 4-6, 7-10 and >10). Infection incidence of 4-6 and above was considered significant. Participants were also questioned about severe infections (i.e., pneumonia, pyelonephritis, bronchitis, cholecystitis) requiring hospitalization within the last year and all types of trauma, including small domestic traumas such as falls, minor traffic accidents, and home accidents in the past year. At least one or more severe infections and exposures to trauma were considered significant. Employees who were diagnosed with any psychiatric disease or treatment were excluded from the study.

Maslach Burnout Inventory and Assessment

Participants in the study were given the MBI, which has been widely used for BOS and described by Maslach and Jackson in 1981[2]. This scale, consisting of 22 items, assesses burnout in three subdimensions: emotional exhaustion (EE), depersonalization (DP), and personal accomplishment (PA).

The EE subscale has eight questions about fatigue, frustration, and reduced emotional energy. Items 1, 2, 3, 6, 8, 13, 16, and 20 are intended to measure this dimension. The DP subscale describes how an individual behaves in an emotionally deprived way towards those for whom he/she provides care and service. There are six questions (items 5, 10, 11, 15, 21, and 22) on the subscale of DP. The PA subscale describes the situation in which a person feels himself or herself to be sufficient and successful. This scale consists of 8 questions and includes items 4, 7, 9, 12, 14, 17, 18, and 19.

Scoring the Maslach Burnout Inventory

Subscale scores were obtained with the MBI, which consists of three subscales: EE, DP, and PA. EE and DP subscales were scored from 1 to 5 for each item (1 point: never, 5 points: always). In our study, as in many studies on this subject, scores for each question were added up; the higher the EE and DP subscales scores and the lower the PA subscale scores, the more severe is the burnout syndrome[11]. In this study, taking into account the maximum score that could be obtained from the scale, participants were assigned to three groups: low, medium, and high burnout. The minimum points were subtracted from the maximum points that could be scored on the subscales, and the cut-off points were calculated by dividing this by three. For the EE subscale, scores of 30 and above were accepted as burnout; scores between 19-29 were accepted as moderate; and scores of 8-18 were accepted as low. In the DP subscale, scores of 23 and above were accepted as burnout; scores between 15-22 were accepted as moderate; and scores of 6-14 were accepted as low. In the PA subscale, scores between 8 and 18 were accepted as burnout; scores between 19 and 29 were accepted as moderate burnout; and scores 30 and above were accepted as low burnout[12].

Statistical Analysis

Mean, standard deviation, median lowest, highest, frequency, and ratio values were used in the descriptive statistics of the data. The distribution of the variables was measured by the Kolmogorov-Smirnov test. The Kruskal-Wallis and Mann-Whitney tests were used in the analysis of independent quantitative data. The Chi-square test was used for analyzing independent qualitative data, and Fisher's test was used when Chi-square test conditions were not met. The Spearman correlation analysis was used for correlation analysis. SPSS 22.0 program was used in the analyses.

RESULTS

A total of 258 respondents were included in the study; 26 were excluded due to missing sociodemographic information or incomplete answers, and the

calculation was made from the data obtained from a total of 232 participants. The mean age of the participants was 38 years (mean±SD=37.4±7.8). The sex distribution was 68.5% female (n=159) and 31.5% male (n=73). The results of the sociodemographic and hospital work characteristics of the participants are presented in Table 1.

The mean levels of decrease in personal achievement were found to be high in 97.8% (n=227) and moderate in 2.2% (n=5) of participants; mean levels of EE were high in 15.1% (n=35) and moderate in 40.5% (n=94). The mean levels of DP were high in 73.7% (n=171) and moderate in 20.7% (n=48) of participants. The total burnout rate was 77.8% in our study; there was no significant (p>0.05) correlation between age, the total duration of work, and the duration of work at the current site with EE, DP, and reduced PA.

EE, DP, and reduced PA test scores were not significantly different in men and women (p> 0.05). The incidence of hospitalization due to infective disease in the last year did not differ significantly in women and men (p>0.05). However, the incidence of infectious disease was significantly higher among women in the last year than among men (p<0.05).

EE, DP, and reduced PA scores did not significantly differ between single and married women (p>0.05). The incidence of infectious disease and hospitalization for infectious disease in the last year did not differ significantly between single and married participants (p>0.05). However, the rate of trauma history in the last year was significantly higher (p<0.05) in single women than in married women.

EE, DP, and reduced PA scores were not significantly different in the non-NICU and NICU services (p>0.05). The rates of hospitalization due to infectious disease and trauma in the last year did not show any significant difference (p>0.05). However, the incidence of infectious disease in the last year was significantly higher in the ICU workers than in the non-ICU employees (p<0.05).

According to working patterns' DP score, rates of hospitalization due to infectious disease and trauma in the last year did not show any significant difference (p>0.05). EE and reduced PA scores were higher in the night shift and night on-call working group than in the daytime-only group. (p<0.05) However, EE and reduced PA scores did not differ significantly between the night shift and night on-call working group (p>0.05).

The EE and DP scores were significantly higher in the group who experienced trauma in last year compared to those who did not (p<0.05). There was no significant difference in the reduced PA score between the groups with and without trauma in the last year (p>0.05). The EE and DP scores were significantly higher in the group with a history of infectious disease in the last year than in the group without it (p<0.05). The reduced PA score did not differ significantly between the groups with and without a history of infectious disease in the last year (p>0.05).

The EE and DP scores were significantly higher in the group with a history of hospitalization due to infectious disease in the last year than in the group without it (p<0.05). The reduced PA score was not significant between the groups with and without a history of hospitalization due to infectious disease in the last year (p>0.05).

TABLE 1. DISTRIBUTION OF PARTICIPANTS ACCORDING TO THEIR SOCIODEMOGRAPHIC CHARACTERISTICS AND WORKING PATTERNS

		Minimum-Maximum	Median	Mean±s.d. /n-%
Age		20 - 66	38	37,4 ± 7,8
Gender	Female Male			159 - 68,5% 73 - 31,5%
Marital Status	Single Married			73 - 31,5% 159 - 68,5%
Duration of employment	Total Current site	1.0 - 37.0 0.1 – 20.0	14.0 4.0	14,7 ± 7,6 5,2 ± 4,0
Working pattern	Only night			115 - 49.6% 57 - %24.6 60 - %25.9
Department	ICU Non ICU			152 - %65.5 80 - %34,5

DISCUSSION

The incidence of BOS in health professionals varies among countries. In a study including 665 general surgeons in the United States in 2014, the frequency of decrease in PA was 16%, EE was 57%, and DP was 50%; burnout syndrome was found to be higher in women than in men (73% in women, 65% in men), and no significant relationship was found between marital status and burnout[13]. In a study conducted on 328 GIS surgeons in France in 2013, reduced PA was found in 47% (severe) and 38.7% (moderate) of the cases, while EE was present in 24.7% (severe) and 39.8% (moderate); DP was seen in 44.6% (severe) and 35.5% (moderate). In that study, the incidence of burnout was higher in women (42.5%); however, there was no significant

difference in terms of work pattern (night shift or weekly) and marital status[14]. In a study conducted among 370 health professionals in Turkey in 2017, the burnout rate was found to be 61.2%, and no sex or marital status differences were found. However, it was reported that burnout was associated with the profession, duration of employment in the hospital, and educational level[15]. The rate of reduced PA was 21%, EE was 14%, and DP was 4% in a study conducted among 171 hemodialysis nurses in Turkey in 2016[16]. In our study, the rate of severely reduced PA was 97.8%, and the moderate reduction was 2.2%; severe EE was 15.1%, and moderate EE was 40.5%; severe DP was 73.7%, and moderate DP was 20.7% in 232 health professionals. The remarkable point in the results of our study is that the reduced PA and DP, components of the burnout syndrome, were higher compared to other studies.

The relationship between age and gender and burnout syndrome is controversial[13]. Although many studies have indicated that there is no significant relationship between burnout levels and gender and marital status, the results obtained in these studies are disputed[17]. Examination of 15 studies on burnout reported that there is no relationship between burnout and gender[18]. However, many studies have reported that the frequency of DP is higher in males than in females[18,19]. There are also studies that reported higher BOS rates for women[13,14]. In our study, no statistically significant difference was found between age, gender, and marital status in terms of EE, DP, and reduced PA ($p>0.05$).

The relationship between the risk of developing BOS and the work pattern has been reported in many studies.[20] It has been emphasized that reducing work time would lead to increased quality of life and, consequently, decreased incidence of BOS[21]. Personnel in emergency and intensive care units are reported to have higher BOS rates than other health professionals. It has been reported that intensive care personnel has higher rates of BOS due to working conditions and high-stress exposure[22]. Emergency room workers are reported to have higher rates of BOS due to various reasons, including stressful working conditions, encountering a wide range of patients and illnesses, and 12 or 24 hours of continuous work because of the shift system[23]. In our study, EE, DP, and reduced PA incidence scores were not significantly different between ICU and non-ICU workers ($p>0.05$). EE and reduced PA scores frequency were higher in those who worked night shifts and daytime and night-time on-call group than in the daytime only group ($p<0.05$).

It has been reported that BOS and related findings affect the individual's personal experience and individual success; furthermore, factors such as stress in private life and family life play a role in the development of BOS[24]. BOS not only reduces health professionals' success in their work-life but also increases their risks. In a study conducted in the United States, doctors diagnosed with BOS were found to have a higher prevalence of antibiotic prescriptions for acute upper-respiratory-tract infections[25]. In a study conducted in 2015, 333 nurses were surveyed on the relationship between BOS and self-protection against infections and contagious diseases during frequent procedures such as injections. Although there are limited numbers of studies on the subject, it has been reported that as the BOS rate increased, the self-protection index of the employees diminished[26]. Accordingly, in our study, a total of 9 employees were admitted to the hospital due to infectious disease in the last year with different diagnoses (four pneumonia, two bronchitis, one cholecystitis, one gastroenteritis, and one cryptic tonsillitis). In addition, a total of 43 workers had a history of trauma in the last year (16 falls, 12 small house accidents, eight traffic accidents, four bone fractures, two burns, and one soft tissue trauma due to sprain). As a result of the statistical analysis, among the employees who had a history of 4 or more infectious diseases in the last year and those who had required hospitalization due to infectious diseases in the last year, the EE and DP scores were significantly higher than in the group without a history of infectious disease and hospitalization in the last year ($p<0.05$). Likewise, EE and DP scores were significantly higher in the employees with a history of trauma in the last year than in employees who had no trauma history in the last year ($p<0.05$). To our knowledge, there is no other study about the relationship between trauma and infection with BOS in the English literature.

CONCLUSIONS

Burnout syndrome is a common and important problem among health professionals that also has adverse effects on people's daily life, especially increasing the incidence of infection and trauma. BOS can leads to serious health problems, as shown in our study. This situation also reflects on the health workers' interaction with patients and causes inefficiency in the work place. There is still no systematic approach

to prevent and treat BOS. More studies should be done to determine the factors leading to BOS, to get an early diagnosis, treatment, and systematic approaches.

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Conflict of Interest

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RESUMO

OBJETIVOS: *A Síndrome de Burnout pode ser vista entre os profissionais de saúde em todas as etapas de suas carreiras. A incidência de Síndrome de Burnout entre os profissionais de saúde aumentou nos últimos anos e varia de país para país, dependendo das diferentes áreas de especialização e unidades de trabalho. Sabe-se que a Síndrome de Burnout afeta significativamente o trabalho e a vida social dos indivíduos. Nosso objetivo foi investigar o efeito da Síndrome de Burnout no trauma e na infecção.*

MÉTODOS: *O estudo foi conduzido na Universidade de Alanya Alaaddin Keykubat, Faculdade de Medicina, Hospital de Treinamento e Pesquisa. Todos os profissionais de saúde que trabalham no hospital foram incluídos no estudo. O Maslach Burnout Inventory foi aplicado aos participantes e a história de doença infecciosa e trauma no último ano foi solicitada.*

RESULTADOS: *A taxa total de Burnout foi de 77,8% dos participantes. Descobriu-se que a taxa de trauma e história de doença infecciosa foi significativamente alta em funcionários que tinham Síndrome de Burnout (p<0,05).*

CONCLUSÃO: *A Síndrome de Burnout é um problema comum e importante entre os profissionais de saúde, e essa condição também teve efeitos adversos na vida diária das pessoas, especialmente aumentando a incidência de infecção e trauma.*

PALAVRAS-CHAVE: *Esgotamento profissional. Doenças profissionais. Saúde do trabalhador. Ferimentos e lesões. Infecção.*

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COMMENTARY

Comment: "Burnout syndrome should not be underestimated"

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The national and international literature show that health professionals have high prevalence rates of Burnout Syndrome, a phenomenon that affects mainly those who are in frequent contact with service end users. This fact can be confirmed by the results of the article "Burnout syndrome should not be underestimated", which found a prevalence of 77.8% of Burnout Syndrome in health professionals working in a hospital in Turkey.

Previous studies in the literature also emphasize the seriousness of the consequences of the syndrome on the physical and emotional health of professionals, among which we must highlight depression, psychosomatic complaints, drug use, intention to abandon work, absenteeism, high turnover of staff, and errors in professional practice. In this sense, the article brings an important contribution to the scientific community by noting that Burnout Syndrome is also associated with an increased incidence of infection and trauma, such as falls and accidents. These results make it an original study that enriches and deepens the assessment of the consequences of Burnout in health professionals.

The title of the article summarizes the main conclusions by the authors, who, from the results obtained, reaffirm the seriousness of the consequences of Burnout Syndrome and alert to the urgent need to deepen the studies related to the prevention of its symptoms.

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ORIGINAL ARTICLE

Burnout Syndrome in medical internship students and its prevention with Balint Group

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SUMMARY

BACKGROUND: *We intend to estimate the Burnout Syndrome prevalence and its associated factors among medical internship students at a public university in northeastern Brasil, besides investigating the Balint Group (BG) contribution in its prevention.*

METHODS: *We conducted a cross-sectional study in February/2018 with Medical Internship Students at the University researched. We applied a structured questionnaire developed by the authors about socio-demographic data, educational process with BG participation, and current psycho-emotional experiences, in addition to the Maslach Burnout Inventory – Student Survey (MBI-SS), for Burnout Syndrome screening. We performed descriptive data analysis, logistic regression, and cluster analysis.*

RESULTS: *A total of 184 students (98%) participated in the study, with a mean age of 25.9±3.9 years, of which 54.9% were men. The prevalence of Burnout Syndrome was 10.3% based on the three-dimensional criterion and 35.9% on two-dimensional criterion (Exhaustion and Cynicism); it was higher in those who thought about quitting the program (OR=2.14), were dissatisfied with the teaching strategies (OR=2.67) and their performance (OR=2.64) and made use of licit drugs (OR=2.37). The variables associated with Burnout Syndrome allowed individuals to be discriminated, classifying them into three subgroups. Burnout Syndrome prevalence decreased, and vulnerability factors were attenuated when there was a higher frequency of students participating in BG.*

CONCLUSIONS: *The prevalence of two-dimensional Burnout Syndrome was high, with factors associated with the educational process. Participation in BG was associated with a lower Burnout rate prevalence. Longitudinal studies should be conducted.*

KEYWORDS: *Students, Medical. Burnout, Psychological. Mental health. Education, Medical.*

INTRODUCTION

Medical training is quite complex, because important stressors, such as daily dealing with pain and death, associated with factors related to the personality of students, can contribute to mental health aggravations that are not always investigated during the program, such as Burnout Syndrome. This psychic manifestation of occupational stress is defined as a response, even though inadequate, to chronic stressors of the work/study environment[1].

Burnout may be described in students based on

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its three dimensions: emotional exhaustion (feelings of exhaustion caused by educational demands), cynicism (feelings of negativism, cynicism, and distant attitude in relation to study), low professional efficacy (feeling of incompetence as a student)[2].

Balint Group (BG) is a method used to deepen the understanding of the doctor-patient relationship and improve communication skills of professionals and students in the health care area, with a patient-centered approach. This tool can also contribute to the increase of satisfaction at work/study because the participants use frustrating experiences to reflect and, concomitantly, seek to develop alternatives to stressful situations, which could reduce the levels of Burnout Syndrome[3].

In medical programs with a traditional teaching method, it is during the internship that students experience more intensely the medical practice, making it a crucial period for the construction of their professional identity[4]. However, depressive symptoms were identified in this population[5], in addition to negative attitudes toward death and conflicting attitudes in relation to mental disorders[4].

Thus, research that favors the early detection of Burnout Syndrome among medical interns and seeks means of intervention and prevention, aiming at returning a well-prepared physician, including mentally, to the community is very relevant.

This study aims to estimate the prevalence of Burnout Syndrome and its associated factors among medical interns of a public university in the Northeast of Brasil, in addition to investigating the contribution of BG in its prevention.

METHODS

Study site

The medical program of the Federal University of Sergipe (UFS), on the Aracaju Campus, adopts a traditional model of teaching, with a duration of six years: the first two are the Basic Cycle of Health Sciences, the following two a Pre-Clinical Cycle, and the last two a Clinical Cycle, also called Internship. To promote the well-being of students and improve the doctor-patient relationship, the BG started being applied once again at the institution in June 2017 for interns in the Mental Health module, after some years of interruption due to a leave of absence of its moderator to pursue masters and doctoral degrees.

Study population

A study carried out with all the medical interns of the medical school searched. At the time of collection, there were 186 students enrolled, but two refused to participate.

Study design

A cross-sectional study from February 2018.

Data collection

The data were collected before theoretical internship classes since that was the time when there was a greater number of interns present. The students signed the Informed Consent Form, which was placed in a separate non-identified envelope, and completed the questionnaires with their identities preserved.

Instruments

We used two self-administered questionnaires.

The first was a structured questionnaire designed by the authors and tested in a previous study with a similar population from the same institution, comprising 26 pre-coded close-ended questions addressing sociodemographic characteristics, educational process, and current psychological/emotional experiences.

The second was the Maslach Burnout Inventory - Student Survey (MBI-SS), adapted and validated for the screening of Burnout Syndrome in students[2], whose Portuguese version also showed adequate reliability and validity[6]. The questionnaire assesses three dimensions of Burnout Syndrome by means of 15 items: five for emotional exhaustion, four for cynicism, and six for professional efficacy. Each item is quantified based on frequency by adopting a Likert scale ranging from 0 (never) to 6 (every day). The diagnostic criterion is a score above 14 in exhaustion, above 6 in cynicism, and below 23 in efficacy. Low-risk scores correspond to the sum below 10 in exhaustion, below 2 in cynicism, and above 27 in efficacy[7]. Another method of evaluation is two-dimensional, which uses only the Exhaustion and Cynicism dimensions[8].

In relation to the BG applied in the institution, each class has about ten students and meets once a week during ten consecutive weeks, the duration of the Mental Health module, and is mediated by a psychiatrist/psychotherapist trained as moderator of Balint groups.

Data Analysis

After entering the data collected into a statistics software, the population profile was characterized with descriptive statistics. Then, in order to identify the factors associated with Burnout Syndrome, a bivariate analysis was initially performed by calculating the gross OR. Then, the significant variables ($p<0.25$) were included in the logistic regression model. The final model contained only the independent variables that remained associated with the outcome after adjustment ($p < 0.05$), according to the likelihood ratio test.

Subsequently, we excluded questionnaires that were not fully answered and ran a multivariate analysis of groupings to evaluate the variables with greater capacity to discriminate between individuals, enabling them to classify them into three subgroups. We used F-statistic to determine the variables' discrimination capacity.

Ethical considerations

The study was approved by the Human Research Ethics Committee of the institution researched under CAAE 38995814.1.0000.5546 and conducted in accordance with ethical policies.

RESULTS

A total of 184 interns (98%) participated in the study, with an average age of 25.9+3.9 years, with a minimum of 21 and maximum of 46, 54.9% of which were males, 82.6% single, 74.5% living with relatives, 84.2% did not work in addition to studying, 70.1% with family income <10 minimum wages, and 37% had doctors in the family. More than half comes from the state capital, 13% from the interior of the state, 30.4% from other states.

As for the psychological/emotional factors, 16.8% make use of a psychiatric medication prescribed by a doctor, and the same number of students have a prior mental disorder diagnosed by a psychiatrist. In addition, 45.7% make use of legal psychoactive substances, 21.7% use illicit drugs, 61.4% practice physical activity, and 72.7% have experienced severe illness themselves or in a family member.

In relation to the educational process, 73.2% reported dissatisfaction with the teaching-learning strategies, and 85.3% claimed they do not receive emotional support as part of the program. Regarding academic performance, 75.4% of the students considered it satisfactory, while 14.7% said they had failed a discipline during the program. Although 98.4% expressed satisfaction with the choice of a medical career, 34.2% had thought of abandoning the program, and 36.4% said that the program was below their expectations.

Only 40.8% of interns believe that the BG contributes to medical training, and 39.1% do not believe it; however, only 28.8% declared to participate or have participated in it.

The prevalence of Burnout Syndrome was 10.3% base on the three-dimensional criterion and 35.9% based on the two-dimensional. After evaluating each dimension, we found a high level of emotional exhaustion in 53.3% and high cynicism in 52.2%. However, low professional efficacy corresponded to 19% (Table 1).

In the logistic regression, we used the two-dimensional criterion of Burnout Syndrome due to the adequate number of subjects. The variables that showed a strong association with the syndrome are presented in Table 2. The presence of Burnout Syndrome was 2.67 times higher in those who were dissatisfied with the teaching strategies and 2.64 times higher in those dissatisfied with their academic performance. The desire to abandon the program (OR=2.14) and the use of licit drugs (OR=2.37) also showed a significant correlation with two-dimensional Burnout Syndrome.

It was not possible to verify the correlation between lack of emotional support and presence of

TABLE 1. PREVALENCE OF BURNOUT SYNDROME AND LEVELS OF EACH DIMENSION* AMONG MEDICAL INTERNS OF UFS. ARACAJU - SE, BRASIL, 2018

	n=184	%
Burnout Syndrome three-dimensional	19	10.3
Burnout Syndrome two-dimensional (Exhaustion and Cynicism)	66	35.9
Emotional Exhaustion		
Low (<10)	33	17.9
Moderate (10-14)	43	23.4
High (>14)	98	53.3
Cynicism		
Low (<2)	25	13.6
Moderate (2-6)	58	31.5
High (>6)	96	52.2
Professional Efficacy		
High (>27)	98	53.3
Moderate (23-27)	42	22.8
Low (<23)	35	19.0

*The scores of the levels of each dimension were based in Maroco & Tecedeiro (2009).

TABLE 2. RESULTS OF THE LOGISTIC REGRESSION ANALYSIS FOR VARIABLES ASSOCIATED WITH BURNOUT SYNDROME AMONG MEDICAL INTERNS OF UFS. ARACAJU - SE, BRASIL, 2018.

Variables	Gross OR	OR CI 95%	Adjusted OR	OR CI 95%	p
Thought of abandoning the program					
No	1				
Yes	3.26	1.72-6.18	2.14	1.06-4.31	0.033
Perception of academic performance					
Satisfactory	1				
Unsatisfactory	3.95	1.95-7.98	2.64	1.23-5.67	0.013
Satisfaction with teaching strategies					
Yes	1				
No	3.29	1.48-7.32	2.67	1.14-6.23	0.023
Use of a licit psychoactive substance					
No	1				
Yes	2.59	1.39-4.80	2.37	1.21-4.63	0.012

TABLE 3. RESULTS OF THE GROUPING ANALYSIS: SOCIODEMOGRAPHIC CHARACTERISTICS AND FREQUENCY OF VARIABLES ASSOCIATED WITH BURNOUT SYNDROME AMONG MEDICAL INTERNS OF UFS. ARACAJU - SE, BRASIL, 2018.

Variables	G1 (%) n=72	G2 (%) n=27	G3 (%) n=27	p
Mean Age (years)	25.8±2.8	25.7±2.4	25.3±3.6	
Gender				
Female	36.1	63.0	59.3	0.02
Male	63.9	37.0	40.7	
Participated in the Balint Group	40.3	55.6	18.5	0.019
Believe the Balint group contributes to medical training	50.9	56.5	25	0.08
Have two-dimensional Burnout Syndrome	25	40.7	55.6	0.014
Have three-dimensional Burnout Syndrome	5.6	7.4	22.6	0.039
Consider their academic performance to be satisfactory	97.2	96.3	0	0.0001
Declare to be satisfied with educational strategies	38.9	33.3	0	0.001
Thought of abandoning the program	0	100	59.3	0.0001
Use licit drugs	34.7	55.6	44.4	0.16

G1 – Group 1; G2 – Group 2; G3 – Group 3.

Burnout Syndrome, due to the insufficient number of subjects, but only 1.5% (1) of students with Burnout Syndrome reported having such support, in contrast with 22% of those without the Syndrome.

In the analysis of groups, after excluding questionnaires that were not completely answered, there were 126 remaining students (67.7%) with an average age of 25.7+3.1 years, with a minimum of 21 and maximum of 38, 53.2% of which were males, 82.5% were single, 54% from the capital, 67.5% with family income <10 minimum wages, 73.8% living with relatives, and 85.7% did not work in addition to studying. The variables associated with Burnout Syndrome allowed discriminating three groups (Table 3).

Group 1 presented the lowest prevalence of Burnout Syndrome and lower frequency of use of licit drugs and of desire to abandon the program; it also had a higher frequency of satisfaction with the academic performance and teaching strategies. Their frequency was higher in BG participation and in the belief that it contributes to medical training.

Group 3 presented the highest prevalence of Burnout Syndrome and lower frequency of BG participation and of the belief in its contribution to the program. Nobody showed satisfaction with the educational strategies, and all were dissatisfied with their academic performance. The use of licit drugs and the desire to abandon the program had high rates.

Group 2 presented the highest rate of students who use licit drugs, and all of them thought about quitting the program. However, the prevalence of Burnout Syndrome was intermediate, there was a high rate of good academic performance, and intermediate frequency in satisfaction with the teaching strategies. We noted the highest frequency of BG participation, as well as of the belief in its contribution.

DISCUSSION

The prevalence of Burnout Syndrome was 10.3% based on the three-dimensional criterion, the same value found by Oliva-Costa et al.[1] In 2009, but lower

than the national estimate (13.1%)[9]. In other Brazilian medical schools, the rates were even higher among their answered 1st to 4th-year students, a total of 19.6% in a public university in Bahia and 26.4%[10] in a private one from São Paulo[11]. Based on the two-dimensional criterion, the prevalence was 35.9%, consistent with the literature, which describes values of 37.4%[1] to 44.9%[11].

After evaluating each dimension, we noticed high rates of emotional exhaustion and cynicism, but lower rates in reduced professional efficacy. The same was described by other authors[1,10], suggesting that a high level of professional efficacy can compensate for the stress of academic life in medical students.

Most factors found to be associated with Burnout Syndrome refer to the educational process, as described in other studies[1,12] whereas the association between Burnout Syndrome and the use of licit drugs was reported in medical residents, with the increased use of alcohol associated with high levels of Burnout Syndrome, depression and perceived stress[13].

We found no significant association between Burnout Syndrome and the sociodemographic data, like another study that found no difference between genders when it came to Burnout Syndrome[14]. However, some researchers have found an association of gender with two of the Burnout Syndrome dimensions[15].

In our study, we were unable to verify the correlation between lack of emotional support and the presence of Burnout Syndrome due to the insufficient number of subjects, but one study revealed social support as an important moderator of educational stressors[12].

Based on the cluster analysis, the data shows that when there is a higher frequency of BG participation, there is a lower prevalence of Burnout Syndrome. Furthermore, non-participation was associated with lower academic performance and greater dissatisfaction with teaching strategies, variables that are significantly associated with Burnout Syndrome, whereas a higher frequency of participation is associated with the improvement of these factors.

We also noted that even when other variables that are significantly associated with Burnout Syndrome (thinking of abandoning the medical program and use of licit drugs) are present with a high frequency, the Burnout Syndrome prevalence is moderate when there is greater BG participation. This suggests that the BG interferes directly in the educational factors associated with Burnout Syndrome and mitigate vulnerability factors; therefore, it could be a resource for protection against the syndrome.

The association between BG participation and lower levels of Burnout Syndrome has already been demonstrated in doctors[3], but we did not find other studies that addressed this topic in students before our study. The studies found are on the increase of empathy and of the understanding of the doctor-patient relationship in this population[16-18]. Now, our results are added to these, showing the beneficial effect of BG in medical schools.

The limitations of this study refer to its cross-sectional design and that it analyzes exposure and effect at the same time, so it is not possible to assign causation to the associations found. However, we were able to identify potential associations that can contribute to the planning of preventive measures relating to the psychological symptoms reported.

CONCLUSIONS

The prevalence of Burnout Syndrome was high based on the two-dimensional criterion and factors related to the educational process. BG participation was associated with a lower prevalence of Burnout Syndrome and the mitigation of vulnerability factors. However, further studies in populations with similar profiles, including longitudinal studies, may strengthen our findings.

Our research contributes to raising awareness among the academic community about their important role in the promotion and maintenance of physical/mental health and in the prevention of Burnout Syndrome, as well as in relation to the use of Balint groups as a possible protective factor against injuries to the mental health of medical students, so it can be replicated among other classes of this medical school and others with similar profiles.

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Author contributions

Dâmaris Calcides, Rayssa de Nóbrega Didou – Responsible for data collection, analysis, and interpretation, as well as drafting, reviewing, and giving final approval of the text.

Enaldo Melo - Responsible for the study design, analysis, and interpretation of data, as well as review and approval of the final text.

Edméa Oliva-Costa - Responsible for the conception and design of the study, as well as for the analysis and interpretation of data, review, and approval of the final text.

RESUMO

OBJETIVO: *Estimar a prevalência de Síndrome de Burnout (SB) e fatores associados entre os internos de medicina de uma universidade pública no Nordeste do Brasil, além de investigar a contribuição do Grupo Balint (GB) na sua prevenção.*

MÉTODOS: *Estudo transversal em fevereiro/2018 com os internos de medicina da universidade pesquisada. Aplicou-se um questionário estruturado elaborado pelos autores sobre características sociodemográficas, processo educacional com participação do GB e vivências psicoemocionais atuais, além do Maslach Burnout Inventory – Student Survey (MBI-SS) para triagem de SB. Realizaram-se análise descritiva, regressão logística e análise de agrupamentos.*

RESULTADOS: *Participaram 184 estudantes (98%), com idade média de 25,9±3,9 anos, sendo 54,9% do sexo masculino. A prevalência de SB foi 10,3% pelo critério tridimensional e 35,9% pelo bidimensional (Exaustão e Descrença), sendo maior naqueles que pensaram em abandonar o curso (OR=2,14), estavam insatisfeitos com as estratégias de ensino (OR=2,67) e com seu desempenho acadêmico (OR=2,64) e faziam uso de drogas lícitas (OR=2,37). As variáveis associadas à SB permitiram discriminar os indivíduos classificando-os em três subgrupos. A prevalência de SB diminuiu e fatores de vulnerabilidade foram atenuados quando houve maior frequência de estudantes participantes do GB.*

CONCLUSÕES: *A prevalência de SB pelo critério bidimensional foi alta, com fatores associados ao processo educacional. A participação no GB foi associada à menor prevalência de SB. Estudos longitudinais devem ser realizados.*

PALAVRAS-CHAVE: *Estudantes de medicina. Esgotamento psicológico. Saúde mental. Educação médica.*

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ORIGINAL ARTICLE

Cardiac and extra-cardiac pathologies in patients with acute arterial occlusion

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SUMMARY

OBJECTIVE: *We aimed to investigate cardiac and extra-cardiac pathologies in patients who were operated for acute arterial occlusion.*

METHODS: *Between March 2010 and March 2018, a total of 120 patients who underwent surgical treatment for acute arterial occlusion were included in this retrospective study.*

RESULTS: *84 (70%) and 27 (22. 5%) of the patients had cardiac and extra-cardiac pathologies, respectively. In 9 (7. 5%) of the cases, no reason for arterial occlusion could be found. Pure atrial fibrillation was found in 39 (32. 5%) patients. Atrial fibrillation and cardiac valvular pathologies were detected in 45 patients (37. 5%). Among those with a cardiac valvular pathology, 9 patients (7. 5%) had pure mitral stenosis, 21 patients (17. 5%) had moderate to advanced mitral stenosis with tricuspid regurgitation, 9 patients (7. 5%) had 2^0-3^0 mitral regurgitation with 3^0 tricuspid regurgitation, 3 patients (2. 5%) had moderate mitral stenosis, 3^0-4^0 tricuspid regurgitation and 2^0-3^0 aortic stenosis, and 3 patients (2. 5%) had 3^0 mitral regurgitation, 1^0- 2^0 tricuspid regurgitation, calcific moderate aortic stenosis, and coronary artery disease. Among those 27 patients with an extra-cardiac pathology, 21 patients (22. 5%) had peripheral artery disease, 3 patients (2.5%) had an abdominal aortic aneurysm, and 3 patients (2. 5%) had Behçet's Disease.*

CONCLUSION: *Cardiac and extra-cardiac pathologies should be kept in mind in patients with acute arterial occlusion. Thus, detected pathologies could be treated, and the development of additional peripheral emboli could be prevented.*

KEYWORDS: *Arterial Occlusive Diseases. Embolectomy. Thromboembolism.*

INTRODUCTION

Acute arterial occlusion can occur in any peripheral artery of the extremities and can lead to limb ischemia. Also, prolonged ischemia cause increased morbidity and mortality in patients with acute arterial occlusion[1]. It was known that acute arterial occlusion is generally the result of thrombus. The term 'embolus' originates from the Greek word 'embolos', which means stopper or plug[2]. In patients with acute peripheral arterial obstruction, early embolectomy operation is recommended without preoperative invasive examination to prevent distal thrombus migration and recurrent thrombus formation[3]. It was known that acute arterial occlusion could be of cardiac or extra-cardiac (atheroembolic or thrombotic) origin. We aimed to investigate cardiac and extra-cardiac pathologies in patients who were operated for acute arterial occlusion.

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METHODS

Between March 2010 and March 2018, A total of 120 patients (63 females [52. 5%], 57 males [47. 5%], aged 24-79 years, mean age of 45 ± 8.5 years] who underwent surgical treatment for acute arterial occlusion were included. Records of these patients were analyzed. Informed consents of the patients were obtained before the operation. Approval of the local ethics committee was obtained. The main complaints were coldness and pain in their toes, feet, fingers, and arms. The diagnosis was made through physical examination, Doppler ultrasonography (USG), and infrequently through peripheral computed tomography (CT) angiography. The time between the onset of pain at the affected extremity and admission at the hospital was between 2 hours to 5 days [mean duration 19±6 hours]. Unilateral and bilateral femoral embolectomies were performed to the femoral artery in 87 (72. 5%) and 24 (20%) of the patients, respectively. Also, unilateral brachial artery embolectomy was performed in 9 (7. 5%) patients. Echocardiography and electrocardiography that had been performed for cardiac pathologies and cardiac rhythm problems in all patients were evaluated. Additional investigation modalities were performed in patients who were suspected of having different pathologies.

RESULTS

A total of 84 (70%) and 27 (22. 5%) patients had cardiac and extra-cardiac pathologies, respectively. In 9 (7. 5%) of the cases, no reason for arterial occlusion could be found, as shown in Figure 1. Pure atrial fibrillation was found in 39 (32. 5%) patients as a cardiac pathology. Atrial fibrillation and cardiac valvular pathologies were detected in 45 patients (37. 5%). Among those with a cardiac valvular pathology, 9 patients (7. 5%) had pure mitral stenosis, 21 (17. 5%) had moderate to advanced mitral stenosis with tricuspid regurgitation, 9 (7. 5%) had 2°-3° mitral regurgitation with 3° tricuspid regurgitation, 3 (2. 5%) had moderate mitral stenosis, 3°-4° tricuspid regurgitation and 2°-3° aortic stenosis, and 3 patients (2. 5%) had 3° mitral regurgitation, 1°- 2° tricuspid regurgitation, calcific moderate aortic stenosis and coronary artery disease (Table 1). Among those 27 patients with an extra-cardiac pathology; 21 (22. 5%) had peripheral artery disease (atherosclerosis), 3 (2. 5%) had abdominal aortic aneurysm, and 3 (2. 5%) had Behçet's Disease.

A total of thirty- five patients (32. 1%) had additional surgical operations, of which 8 (6. 6%), 9 (7. 5%), 12 (10%) and 6 (5%) had re-embolectomy, peripheral arterial bypass operation, fasciotomy, and amputation, respectively. Re-embolectomy operation was successful in 2 patients, but ischemia was not recovered in 6 of the patients who had had drop-feet, ischemic, and infected wounds when they arrived at the hospital. In these patients, fasciotomy was performed for compartment syndrome caused by ischemia-reperfusion damage after the re-embolectomy operation, and after that, amputation was performed (below-knee amputations). On the other hand, extremities in other 6 (5%) patients with fasciotomy operation were saved with medical treatment, and fasciotomies were closed later.

FIGURE 1. ETIOLOGIES DETECTED IN PATIENT

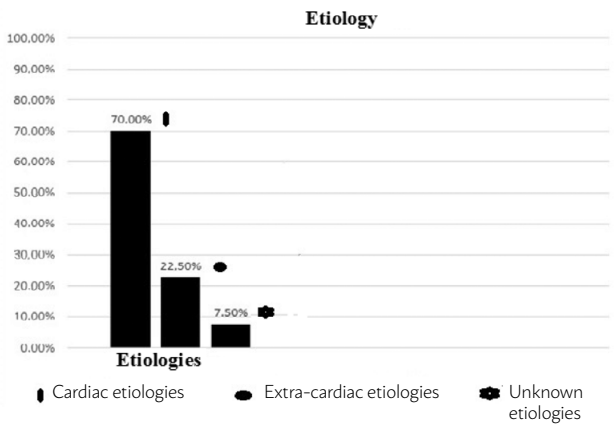

TABLE 1. DISTRIBUTION OF EMBOLIES ACCORDING TO ETIOLOGY

Etiology	number (n)	percentage (%)
Cardiac causes	84	70
Pure atrial fibrillation	39	32. 5
Atrial fibrillation + pure mitral stenosis	9	7. 5
Atrial fibrillation + multiple valvular pathologies	33	27. 5
Atrial fibrillation + multiple valvular pathologies + coronary artery disease	3	2. 5
Extra-cardiac pathology	27	22. 5
Peripheral artery disease	21	17. 5
Abdominal aortic aneurysm	3	2.5
Behçet's disease	3	2. 5
Unknown etiology	9	7. 5

TABLE 2. COMPLICATIONS OF PERIPHERAL ARTERIAL EMBOLECTOMY OPERATION

Complication	number (n)	percentage (%)
Wound Infection	3	2.5
Compartment syndrome	12	10
Amputation	6	5
Hematoma/ecchymosis	9	7.5
Bleeding	3	2.5
Cerebral embolism	3	2.5

Peripheral CT angiography was performed in patients who had ongoing extremity ischemia after embolectomy operation, and patients indicated for peripheral artery bypass operation were detected. After that, femoropopliteal artery by-pass with 6 mm polytetrafluoroethylene (PTFE) synthetic graft and cross-femoral artery by-pass with 7 mm PTFE synthetic graft were performed in 6 (5%) and 3 (2. 5%) patients, respectively. After these operations, patients' extremities were recovered, and there was no need for any additional attempts.

Wound infection, hematoma, bleeding from the incision, amputation, compartment syndrome and cerebral embolism developed in 3 (2. 5%), 9 (7. 5%), 3 (2. 5%), 6 (5%), 12 (10%), and 3 (2. 5%) patients, respectively, in the early postoperative period. These complications are presented in Table 2.

All patients received 175 IU/kg/day low-molecular-weight heparin for three days in the early postoperative period. Warfarin was started later in patients with atrial fibrillation, whereas antiplatelet therapy with N-acetyl salicylic acid 300 mg/day and/or clopidogrel 75 mg/day were given to other patients. Warfarin doses were adjusted for an international normalized ratio (INR) of 2 - 3. Following coumadinization, the low-molecular-weight heparin treatment was discontinued. During the follow-up period, the patients' vital signs were stable, so they were discharged. The patients were called at the outpatient clinic one week after discharge. Peripheral artery bypass grafts and extremity artery lumens at the thrombectomy sites were patent, and their treatment was continued. There was no in-hospital mortality.

DISCUSSION

Prevalence of acute arterial occlusion is between 7- 37.5% among all vascular diseases[3]. In previous years, arterial embolism was most commonly seen between the ages of 40 and 50[4]. Currently, the average patient age has shifted to the 70s, as the etiologic factor, atherosclerotic heart disease and its complications are frequently found to be responsible for it[4]. Embolism was first described by Virchow in 1854[1]. The thrombotic material in acute arterial occlusion due to arterial embolism detaches from a distant site and occludes a normal blood vessel. Embolectomy operation has been performed for a long time, and the first successful embolectomy operation was performed by Labey in 1911[4]. The balloon catheter was developed by Fogarty in 1963[5]. Then it started to be used in embolectomy operations of patients with arterial thromboembolism. In physical examination, the 6 Ps that are diagnostically important are pain, paleness, paresthesia, pulselessness, paralysis, prostration (shock), and poikilothermia[1]. The differential diagnosis is very important in acute arterial occlusion. Advanced diagnostic methods such as Doppler USG, intravascular USG, and magnetic resonance (MR) can be used[3]. On the other hand, Bahçıvan et al.[6] have reported reaching a diagnosis with clinical findings and hand Doppler USG in most patients in their study, without using any radiological examinations with an intention not to cause an increase in the duration of acute ischemia. We accurately diagnosed our patients by using hand Doppler USG, Doppler USG, peripheral CT angiography after a physical examination, especially pulse examination.

In cases with acute arterial occlusion, an increase in the duration from the onset of complaints to admission to the hospital has a negative effect on the success of arterial embolectomy operation. It was known that this duration should not exceed 6-8 hours. Likewise, Mutirangura et al.[7] have reported that the 24- hour duration of arterial embolism may be a crucial factor influencing the outcome in the management of this disease. Moreover, Pung and Mohamed[8] have detected that the cause for poor results were related to the delay in definitive treatment and the poor general state of the patients. In our patients, the time between the onset of pain in the extremity and admission to the hospital was between 2 hours and 5 days [mean duration 19 ± 6 hours], and patients underwent emergency embolectomy after the diagnosis without any delay. However, this time in patients who underwent fasciotomy was between 48 – 120 hours (mean duration 72 ± 12 hours).

Cardiac origin is detected in most of the cases of

peripheral arterial embolism[9,10], which is the most frequent cause of acute arterial occlusion. Ege et al.[1] have reported this rate as 80-90% in their study, and have remarked that arterial embolus was observed secondary to heart diseases such as rheumatic valvular heart disease, atrial fibrillation, and myocardial infarction. Other cardiac causes include post-valve replacement, cardiac/aortic tumor, and paradoxical embolism[10]. However, atrial fibrillation accounts for most of the sources of the cardiac embolism in patients with peripheral arterial embolism[10]. On the other hand, Keçeligil et al.[4] have found a cardiac origin and an extra-cardiac origin in 62. 56% and 30. 72% of the cases, respectively, and could not find any origin in 6.7% of the patients. However, in the same study, the embolic origin was expressed as cardiac in 78% of cases with acute peripheral arterial occlusion, in all series[4]. Also, Yetkin et al.[2] have reported that for the 51 patients who underwent urgent unilateral femoral embolectomy, it was determined that 28 (55%) had serious cardiac pathologies. Among these 28 patients, 14 (50%) underwent the required open-heart surgery interventions after the completion of further examinations. In our study, cardiac pathology was detected in 70% of the patients compatible with the medical literature, and extra-cardiac pathologies were detected in 22.5% of the cases, and 7.5% had unknown etiology. However, over time, rheumatic heart disease-induced cardiac embolism is decreasing, but the incidence of acute arterial occlusion due to acute thrombosis that develops based on atherosclerotic vascular disease is increasing[11].

Acute arterial thrombosis is an important cause of extremity loss, and embolectomy intervention does not provide sufficient circulation in some patients. For example, in this study, 8 (6. 6%) and 9 (7. 5%) of patients have had re-embolectomy operation and peripheral arterial bypass operation, respectively due to ongoing ischemia and previous peripheral artery disease. Peripheral arterial bypass operation was performed after the effective visualization of vascular structure was shown by CT angiography.

The presentation of arterial emboli depends on the arterial bed that is affected. The two most common sites for embolic events are brain and lower extremities. On the other hand, less frequent sites are upper extremities[12], mesenteric vessels, and the renal arteries[12]. Erkut et al.[13] have reported timely arterial embolectomy under local anesthesia to be the most effective method of treatment in acute arterial occlusion. Also, Erentuğ et al.[3] have mentioned that standard treatment of acute peripheral arterial occlusion consists of heparinization and embolectomy, but thrombolytic therapy [such as urokinase, streptokinase, recombinant tissue plasminogen activator (r-tPA)] in recent years is preferred, especially in patients with acute occlusion that develops on a chronic atherosclerotic basis. However, Vinayagam et al.[14] have reported that peripheral thrombolysis is associated with a 10% risk of hemorrhage, which may require blood transfusion, operation, or cause death from bleeding. Also, intracranial hemorrhage (0 to 2. 5%), compartment syndrome (1 to 10%), and distal embolization (1 to 5%) could be seen as other complications of catheter-directed thrombolysis for acute arterial occlusion[15]. Moreover, Ouriel[16] have emphasized in his article that thrombolysis has been associated with hemorrhagic complications, a slow rate of thrombus dissolution, and a higher risk of rethrombosis. Whereas, in this study, heparin was administered, and emergency arterial embolectomy operation was performed as soon as possible in all patients with acute arterial occlusion after the diagnosis.

Various postoperative complications, such as wound infection, hematoma, bleeding from the incision, amputation, cerebral embolism, and compartment syndrome, could also be seen in the early postoperative period. Compartment syndrome is a clinical condition that is characterized by a functional loss of muscle and nerve tissues and develops as a result of ischemia, which can occur due to increased perfusion pressure within closed muscle fascia of the extremities[17]. Tissue reperfusion after ischemia can cause reperfusion syndrome[17]. Fasciotomy might be needed for decreasing the pressure on all tissues under the skin. Thus, adequate perfusion could be provided. Erentuğ et al.[3] have reported the rate of fasciotomy in their study as 4.7% [3]. Burma et al.[18] have suggested that patients should be followed up after embolectomy operation and fasciotomy should be performed before the irreversible ischemia-reperfusion phase. As well, Tawes et al.[19], reported that their 20-year experience with lower extremity thromboembolism in 739 patients was associated with a mortality rate of 12%, a wound complication rate of 19%, and a morbidity (amputation) rate of 5%. Also, Dag et al.[20] had focused on risk factors for amputation in 822 cases with acute arterial emboli in their study and reported that an interval of more than 6 hours between the onset of complaints and operation

and re-embolectomies increase the risks of amputation. Kempe et al.[21] reported that the 90-day major amputation rate was 15%, and the 30-day mortality rate was 18%. Also, they reported in that study, the 5-year estimated limb salvage was 80%, and survival was 41%[21]. In this study, fasciotomy was performed in 12 (10%) patients with acute lower extremity compartment syndrome in the early postoperative period. Then, below-knee amputation was performed in 6 (5%) of them despite medical treatment.

It was known that arterial thromboembolism could be caused by various diseases. Investigation of all patients for additional pathologies was performed after the surgery. Definitive diagnosis was made, and then additional treatment was applied for etiology. For example, abdominal aortic aneurysm and Behçet's disease that were of extra-cardiac pathology were detected in a total of 6 (5%) patients as a result of the investigation. During the treatment and follow up, cardiac and extra-cardiac pathologies that were detected were also treated. We could not find any etiology in 9 (7. 5%) patients.

This study has some limitations. First, it is a retrospective study, and it lacked mid-term and long term control findings of patients. Second, we had a small sample size. Third, the patients were discharged, and the treatments for additional cardiac and extra-cardiac pathologies were performed later. Therefore, detailed information about these treatments was not mentioned in this study.

CONCLUSION

In conclusion, cardiac and extra-cardiac pathologies should be kept in mind in patients with arterial thromboembolism, and a detailed cardiovascular examination is of utmost importance for the differential diagnosis and treatment plan. Thus, other serious pathologies detected could be treated as soon as possible, and the development of additional peripheral emboli could be prevented. Also, the arrangement for appropriate treatments may prolong the life span of these patients.

Declaration of conflict of interest

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Author's contribution

MK – Conceptualization, Data curation, Validation, Investigation, Methodology, Project administration, Writing-original draft

UH - Formal analysis, Software, Supervision, Writing-review & editing

MT - Data curation

ZY – ResourcesOD - Funding acquisition, Visualization

RESUMO

OBJETIVO: *O objetivo do estudo é investigar patologias cardíacas e extracardíacas em pacientes operados por oclusão arterial aguda.*

MÉTODOS: *Entre março de 2010 e março de 2018, um total de 120 pacientes submetidos a tratamento cirúrgico para oclusão arterial aguda foram incluídos neste estudo retrospectivo.*

RESULTADOS: *Dos pacientes incluídos, 84 (70%) e 27 (22.5%) apresentavam, respectivamente, patologias cardíacas e extracardíacas. Em 9 (7.5%) dos casos, nenhuma cause para a oclusão arterial foi encontrada. Fibrilação atrial isolada foi encontrada em 39 (32.5%) pacientes. Fibrilação atrial e valvopatias cardíacas foram detectadas em 45 pacientes (37.5%). Entre aqueles com valvopatias cardíacas, 9 (7.5%) tinham estenose mitral isolada, 21 (17. 5%) tinham estenose mitral moderada a avançada com regurgitação tricúspide, 9 (7. 5%) tinham 2º-3º de regurgitação mitral com 3o regurgitação tricúspide, 3 (2. 5%) tinham estenose mitral moderada, 3º-4º regurgitação tricúspide e 2º-3º estenose aórtica, e 3 (2.5%) tinham 3o mitral, 1º- 2º regurgitação tricúspide moderada, estenose aórtica moderada calcificada e doença coronariana. Entre os 27 pacientes com patologia extracardíaca, 21 (22.5%) tinham doença arterial periférica, 3 (2,5%) tinham aneurisma da aorta abdominal, e 3 (2.5%) tinham Doença de Behçet.*

CONCLUSÃO: *Patologias cardíacas e extracardíacas devem ser consideradas em pacientes com oclusão arterial aguda. Assim, patologias detectadas podem ser tratadas e o desenvolvimento de trombos periféricos adicionais pode ser evitado.*

PALAVRAS CHAVE: *Arteriopatias Oclusivas. Embolectomia. Tromboembolia.*

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ORIGINAL ARTICLE

Seasonal variation of clinical characteristics and prognostic of adult patients admitted to an intensive care unit

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SUMMARY

OBJECTIVE: *To evaluate seasonal variations of clinical characteristics, therapeutic resource use, and outcomes of critically ill patients admitted to an intensive care unit.*

METHODS: *A retrospective cohort study conducted from January 2011 to December 2016 in adult patients admitted to the intensive care unit (ICU) of a University Hospital. Data were collected on the type of admission, APACHE II, SOFA, and TISS 28 scores at ICU admission. Length of hospital stay and vital status at hospital discharge were recorded. A significance level of 5% was adopted.*

RESULTS: *During the study period, 3.711 patients were analyzed. Patients had a median age of 60.0 years (interquartile range = 45.0 – 73.0), and 59% were men. The independent risk factors associated with increased hospital mortality rate were age, chronic disease, seasonality, diagnostic category, need for mechanical ventilation and vasoactive drugs, presence of acute kidney injury, and sepsis at admission.*

CONCLUSIONS: *It was possible to observe variations of the clinical characteristics and prognosis of patients; summer months presented a higher proportion of clinical and emergency surgery patients, with higher mortality rates. Sepsis at ICU admission did not show seasonal behavior. A seasonal pattern was found for mortality rate.*

KEYWORDS: *Critical care. Clinical evolution. Severity of illness index. Seasons.*

INTRODUCTION

The concept of grouping patients by severity criteria to improve care and achieve better prognoses is well established in the literature[1]. Intensive care units (ICU) were created to provide specific care to critical patients and rely on a multidisciplinary, specialized, and skilled team and special equipment and technologies[2].

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There is evidence demonstrating the growing need for more intensive care beds in relation to the number of hospital beds. In the United States, over a period of five years, there was an increase two-times greater of the number of ICU beds in comparison to the number of hospital beds, with a consequent increased cost of the care of critical patients[3].

In this moment of a growing need for specialized intensive care beds and limited healthcare resources, it is necessary to improve the decision-making process to screen and prioritize the admission of patients into intensive therapy[4]. Early admission of critical patients to an ICU bed is beneficial and capable of reducing mortality; therefore, the knowledge of the clinical profile and the use of therapeutic interventions, as well as their seasonal variations, can help understand and plan the allocation of specialized ICU beds[5,6].

The objective of this study is to describe seasonal variations of clinical standards, use of resources and outcomes of hospitalized adult patients admitted to the ICU.

METHODS

The present study was submitted to and approved by the local Research Ethics Committee, and the need to obtain free informed consent forms was waived by decision 1.557.487; CAAE: 56182816.4.0000.5231, report date: May 23, 2016.

A retrospective cohort study carried out from January 2011 to December 2016 in the intensive care unit (ICU) for adult patients of the University Hospital of the State University of Londrina. The adult ICU of the Hospital has 20 beds and is a general ICU for clinical and surgical patients. Within the same institution, there is another ICU specialized in the treatment of severely burned patients, but those beds were not included in this analysis.

We used a convenience sampling of all adult patients admitted to the ICU consecutively during the study period. We included patients with ICU stay time greater than or equal to 24 hours. We excluded patients younger than 18 years old and with ICU readmissions during the period of hospitalization.

The data collected for all ICU admissions were: age, sex, date of admission into hospital and the ICU, type of admission, area of origin, diagnosis for ICU admission, presence of chronic disease. Upon ICU admission, we recorded diagnoses of sepsis and acute renal injury, need for mechanical ventilation, and use of vasoactive drugs. Acute kidney injury was defined as an increase by 50% of the basal value of serum creatinine[7], and sepsis was defined as a potentially fatal organic dysfunction caused by an infection[8]. The Acute Physiology and Chronic Health Evaluation (APACHE II), Sequential Organ Failure Assessment (SOFA), and Therapeutic Intervention Scoring System (TISS 28) scores were calculated [9]. Other variables collected were the ICU and hospital stay times. The year was divided into four seasons - summer, fall, winter, and spring, according to the national calendar.

Data collection was performed prospectively and daily by a trained health care professional, so as not to allow losses. The data collection is part of the clinical management of the unit that generates quality indicators. The present study was considered retrospective because it is a retrospective analysis of prospectively collected data. The sources used for data collection were the medical records of the patient and the hospital electronic database. All data used for score calculations were collected as raw data, using the extremes of abnormality during the first 24 hours of ICU stay. The scores were calculated according to the definitions of the respective systems[10,11,12]. Patients were followed-up until the outcome at hospital discharge.

STATISTICAL ANALYSIS

Continuous variables were expressed as mean and standard deviation (SD) when there was a normal distribution, and as median and interquartile range (IQR) If the distribution was not normal. The categorical variables were expressed as proportions. Descriptive statistics were used to present all relevant variables. The data were presented in graphs and tables. The Kruskal-Wallis test was used for comparison of continuous variables. Categorical variables were compared using the chi-square test of Cochran-Armitage for identifying trends. The variables to predict in-hospital mortality outcomes were presented as unadjusted odds ratios, obtained by logistic regression in enter mode. The stepwise method was used to adjust other predictors of in-hospital mortality in the multivariate analysis, in which variables whose p-value was greater than 0.1 were removed from the model or maintained if $p < 0.05$. Patients in the "elective surgery" and "win-

ter" groups were considered as the reference categories for logistic regression.

To analyze the effect of seasonality in the main results of the present study, we run a temporal series analysis. In order to do that, we initially studied three monthly time series: total frequency of patients admitted to the ICU (TF), frequency of patients admitted due to sepsis (SF), and frequency of ICU patients who died (DF). With six years of observations, each series includes 72 observations. For better data interpretation, we use frequency rates in relation to the total frequency of patients admitted to the ICU in each month. Thus, the studied series are monthly admission rates due to sepsis (SR=SF/TF) and monthly death rate (DR=DF/TF). Then, to transform the series into stationary, we performed a Box-Cox[13,14] transformation to stabilize the variance. The correlograms present the autocorrelation functions in the time domain, while the periodogram presents the characteristics of the series in the frequency domain. The latter is an important tool to identify periodicities in the data. Based on their estimated frequencies, it is possible to check seasonality and cycles in the series. A Fisher test[15] was carried out to verify if the seasonal factors were significant.

The level of significance adopted was 5%, and the analyses performed used the MedCalc software for Windows, version 18.5 (MedCalc Software, Ostend, Belgium), and the R Project software, 2018 (Austria, Vienna).

RESULTS

The collection and analysis of data from adult patients admitted to the university hospital ICU from 2011 to 2016 resulted in a total number of 4,004 patients, of which 82 were excluded due to age under 18 years old and 211 due to readmission, leaving 3,711 patients to be analyzed in this study (Figure 1). The annual bed-occupation rates of the unit in the study period ranged from 90.5% to 96.6%. The median age of patients was 60.0 years (IQR= 45.0 - 73.0), and 65.8% were in the range of 31 to 70 years old. In relation to sex, 2,191 (59.0%) were men. The median ICU-stay time was 4.0 days (IQR= 1.0 - 11.0), and 58.1% remained for up to 5 days in the ICU. The hospitalization time presented a median of 16.0 days (IQR = 9.0 - 30.0), and 66.2% remained in the hospital for more than 21 days (Table 1).

As to the diagnoses for ICU admission, the most frequent were sepsis, in 955 patients (25.7%), postoperative of the neurological system in 336 (9.1%), of

FIGURE 1. FLOWCHART OF PATIENTS ADMITTED TO THE INTENSIVE CARE UNIT - ADULTS OF THE UNIVERSITY HOSPITAL, FROM 2011 TO 2016

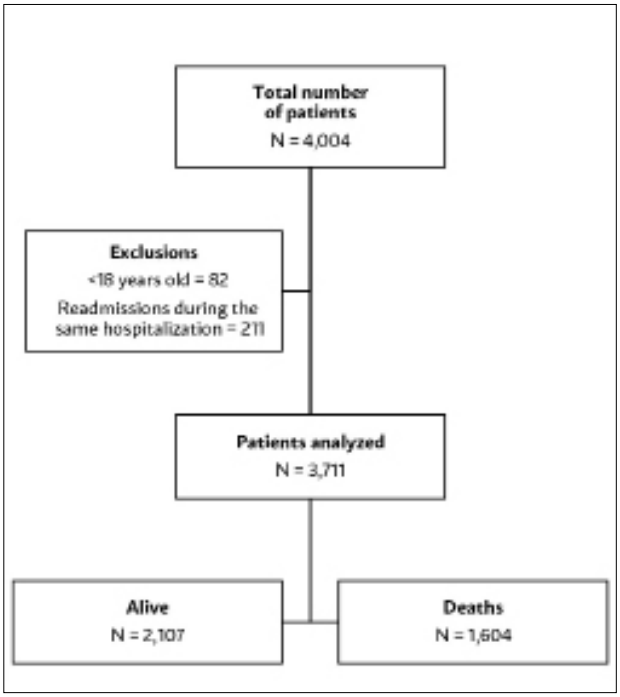


TABLE 1. GENERAL CHARACTERISTICS OF PATIENTS ADMITTED TO THE INTENSIVE CARE UNIT - ADULTS OF THE UNIVERSITY HOSPITAL, FROM 2011 TO 2016

General Characteristics	Total (n=3,711)
Age*	60.0 (45.0- 73.0)
Male†	2191 (59.0)
Days of ICU Stay*	4.0 (1.0- 10.75)
Days of Hospital Stay*	16.0 (9.0- 30.0)
Apache II*	19.0 (13.0-27.0)
Sofa at admission*	6.0 (3.0-11.0)
Tiss-28 at admission*	26.0 (20.0- 31.0)
Mechanical ventilation†	1,954 (52.7)
SRI at admission†	1,004 (27.1)
Diagnostic category at admission†	
Clinical	1,248 (33.6)
Elective Surgery	1,438 (38.7)
Emergency Surgery	1,025 (27.6)
Chronic Disease†	414 (11.2)
Sepsis at Admission†	955 (25.7)
ICU Mortality†	1,196 (32.2)
In-Hospital Mortality†	1,604 (43.2)

Legend: *= median (interquartile range 25%-75%); †= number (percentage); ‡= average (standard deviation)

FIGURE 2. MONTHLY VARIATION OF THE SEPSIS AND DEATH RATES IN THE INTENSIVE CARE UNIT - ADULTS OF THE UNIVERSITY HOSPITAL, FROM 2011 TO 2016

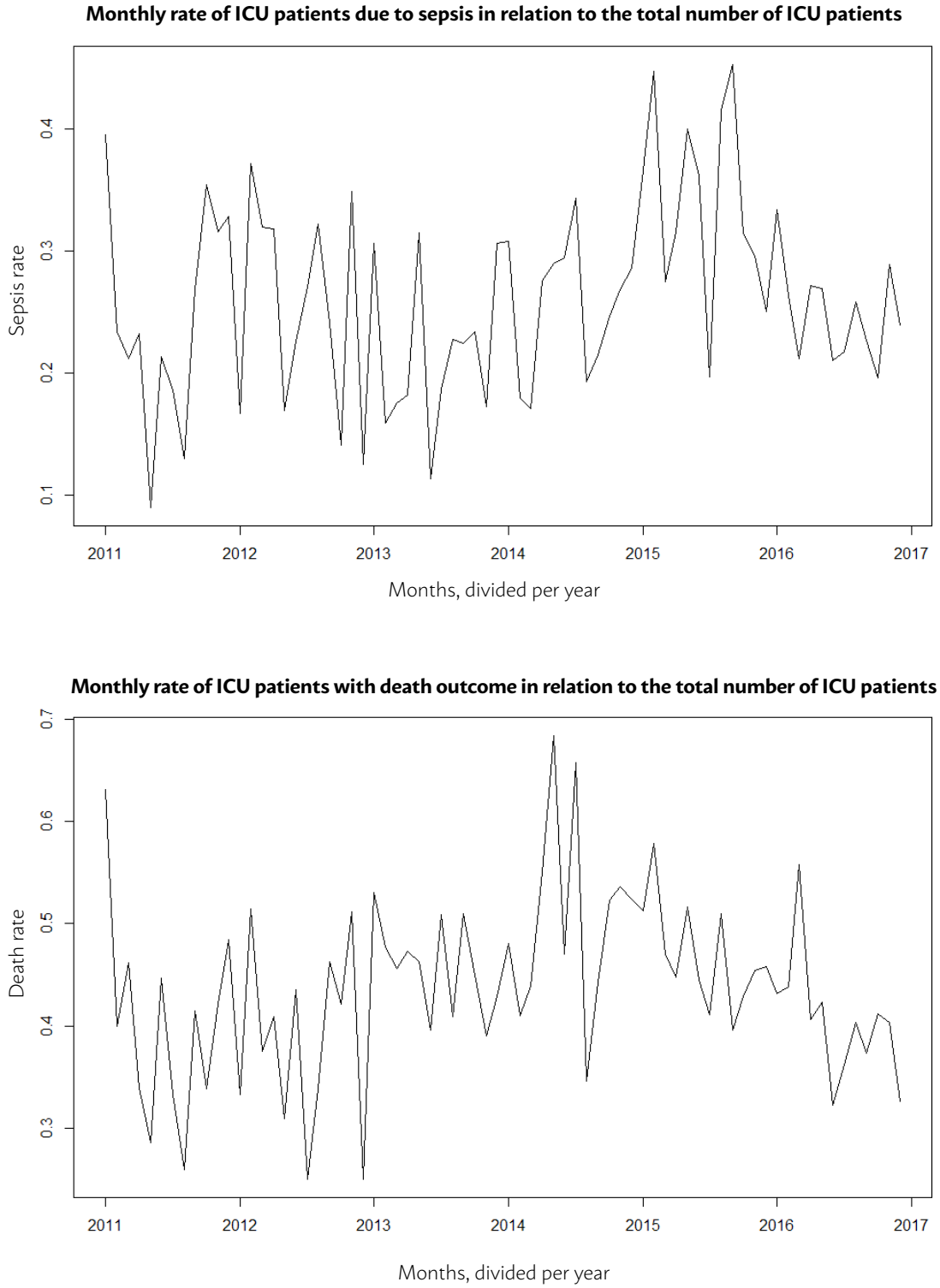
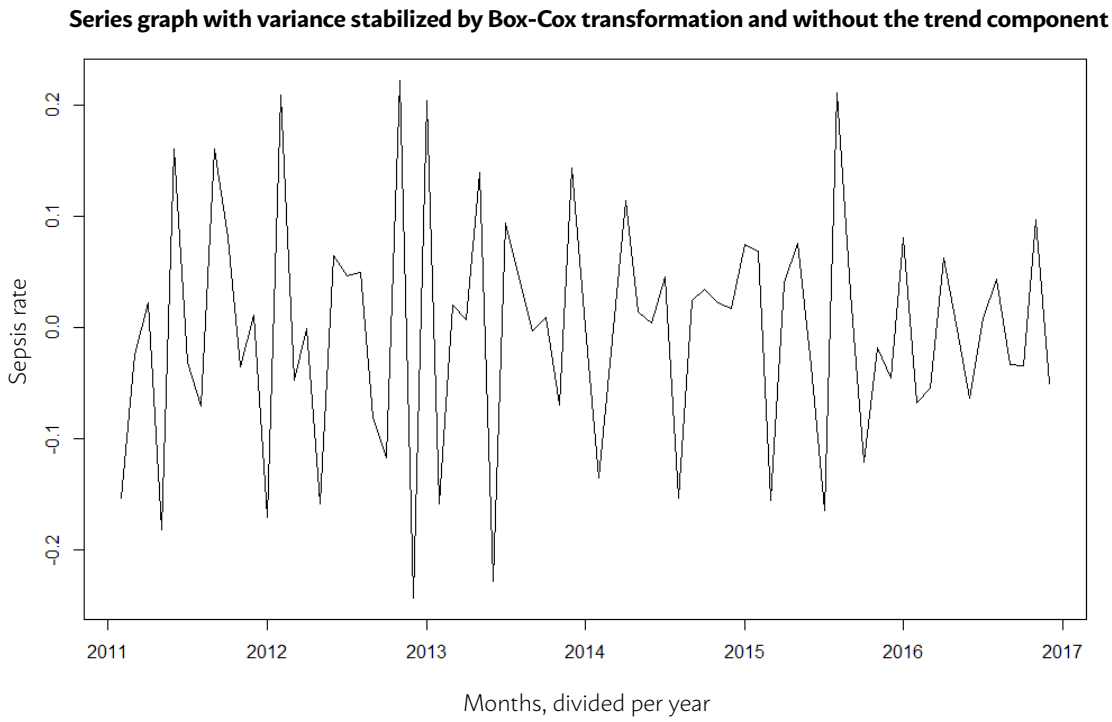


FIGURE 3. GRAPH OF THE TEMPORAL SERIES OF THE SEPSIS RATE AND SEPSIS PERIODOGRAM FOR THE INTENSIVE THERAPY UNIT - ADULTS OF THE UNIVERSITY HOSPITAL, FROM 2011 TO 2016



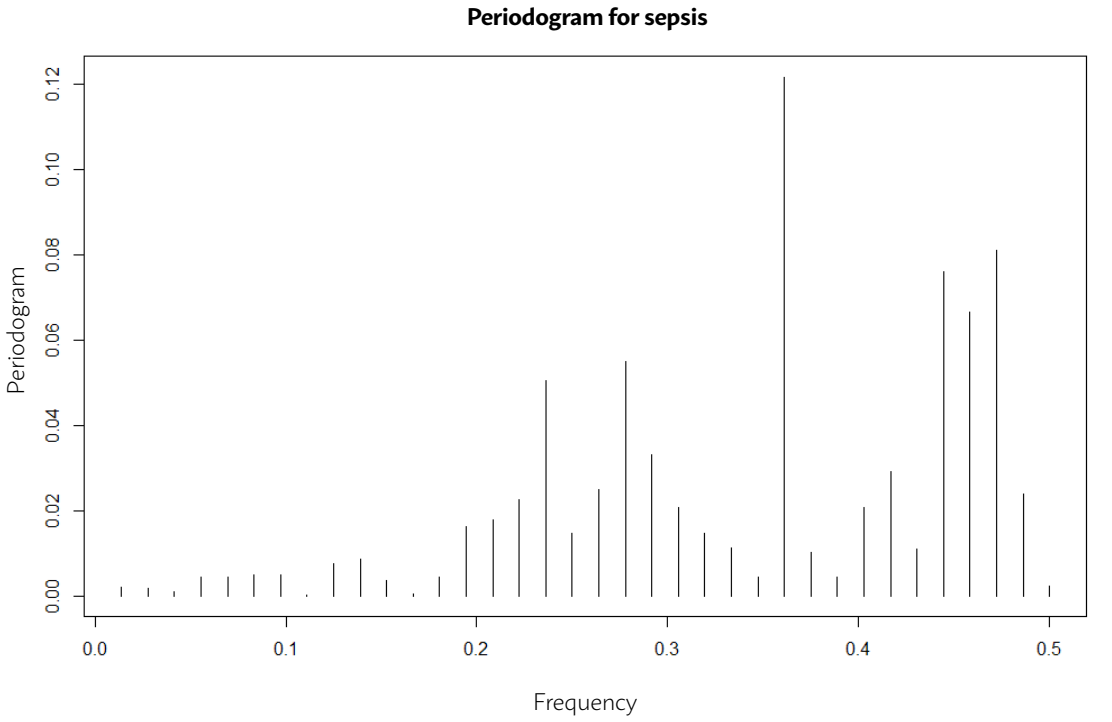
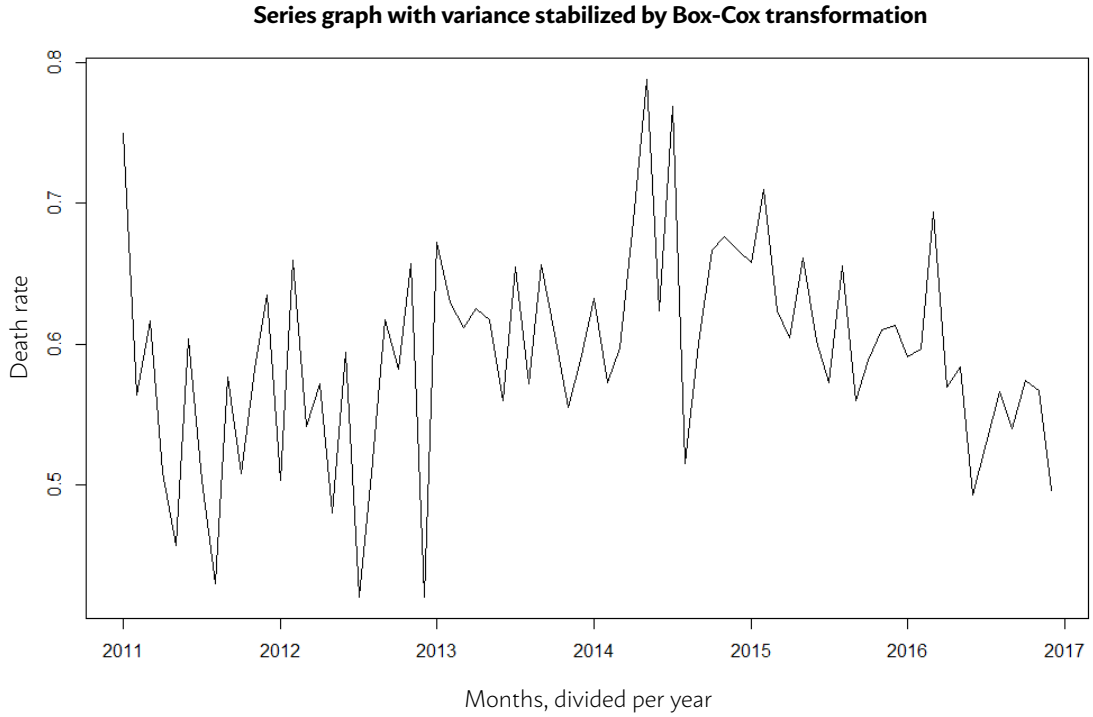


FIGURE 4. GRAPH OF THE TEMPORAL SERIES OF MORTALITY RATE AND DEATH PERIODOGRAM FOR THE INTENSIVE CARE UNIT - ADULTS OF THE UNIVERSITY HOSPITAL, FROM 2011 TO 2016



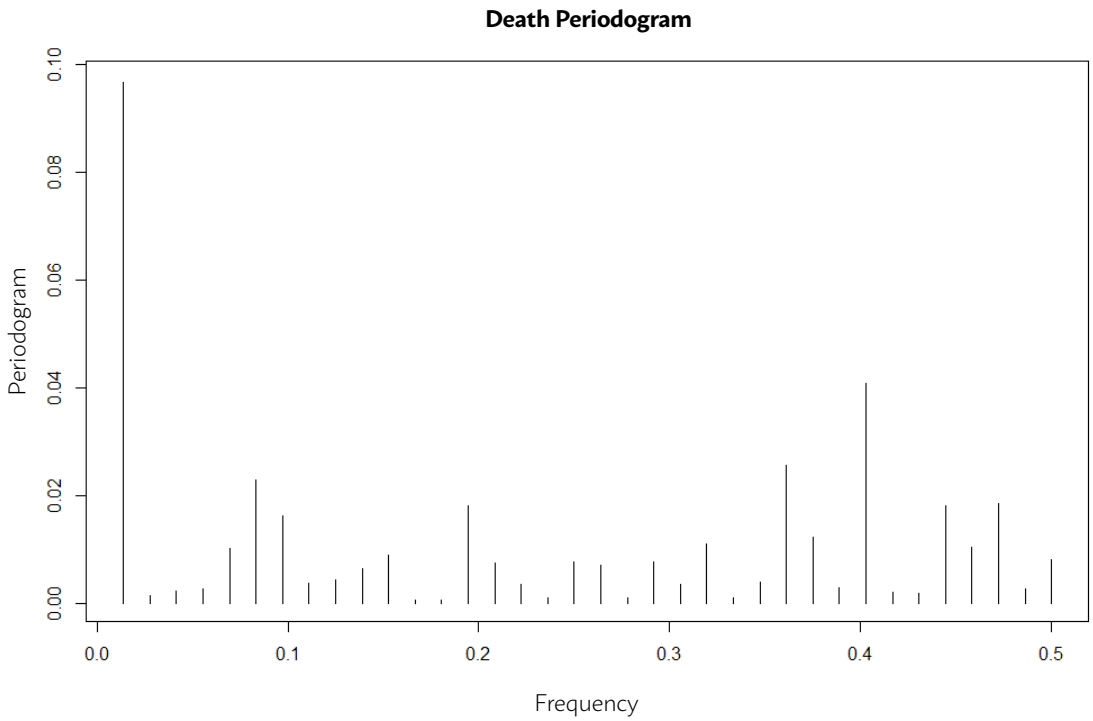


TABLE 2. CHARACTERISTICS OF PATIENTS ADMITTED TO THE INTENSIVE CARE UNIT - ADULTS OF THE UNIVERSITY HOSPITAL, FROM 2011 TO 2016

	Summer (n=840)	Autumn (n=970)	Winter (n=1007)	Spring (n=894)	p
Age (years): median (IQR)*	60 (45-73.5)	59 (45.5-73.5)	60 (45-72)	61 (46-73.5)	0.525
Male: N (%) †	472 (56.2)	577 (59.5)	610 (60.6)	532 (59.5)	0.265
Diagnostic Category †					<0.001
Clinical: N (%)	320 (38.1)	294 (30.3)	302 (30.0)	338 (37.8)	
Elective Surgery: N (%)	296 (35.2)	402 (41.4)	407 (40.4)	349 (39.0)	
Emergency Surgery: N (%)	224 (26.7)	274 (28.2)	298 (29.6)	207 (23.1)	
Apache II: Median (IQR) *	19 (13-28.5)	19 (12.5-27)	18 (12.5-26)	19 (13-28.5)	0.250
Sofa: Median (IQR) *	6 (3-11.5)	6 (3.5-11)	6 (3.5-10.5)	6 (3.5-11)	0.111
Tiss-28a: Median (IQR) *	26 (20-31)	25 (20.5-31)	26 (20.5-31)	26 (20.5-31.5)	0.652
Chronic Disease: N (%) †	92 (10.9)	100 (10.3)	102 (10.2)	120 (13.4)	0.350
Sepsis at ICU admission: N (%)†	232 (27.6)	238 (24.5)	254 (25.2)	231 (25.8)	0.487
Mechanical ventilation: N (%)†	449 (53.4)	505 (52.0)	529 (52.5)	471 (52.7)	0.948
SRI at admission: N (%)†	222 (26.4)	253 (26.1)	263 (26.1)	266 (29.7)	0.223
Days in ICU: Median (IQR) *	4 (1-12)	4 (1.5-11)	4 (1.5-11.5)	4 (1-9)	0.053
Days in hospital: Median (IQR) *	16 (10-31.5)	17 (9-30)	16 (8.5-29.5)	16 (8-28)	0.131
ICU Mortality: N (%)	306 (36.4)	294 (30.3)	303 (30.1)	293 (32.7)	0.013
In-Hospital Mortality: N (%)	398 (47.4)	415 (42.8)	398 (39.5)	393 (43.9)	0.008

Legend: IQR = Interquartile range; Apache = Acute Physiology and Chronic Health Evaluation; Sofa = Sequential Organ Failure Assessment at admission; TISS-28a =Therapeutic Intervention Scoring System at admission; ICU = Intensive Care Unit; SRI = Severe renal injury; *= Kruskal-Wallis Test; †= Chi-square test for trends.

TABLE 3. BIVARIATE AND MULTIVARIATE ANALYSIS OF RISK FACTORS FOR IN-HOSPITAL DEATH OF PATIENTS ADMITTED TO THE INTENSIVE CARE UNIT – ADULTS OF THE UNIVERSITY HOSPITAL, FROM 2011 TO 2016

	Unadjusted odds ratio	CI 95%	p	Adjusted odds ratio	CI 95%	p
Age	1.01	1.01 – 1.02	<0.001	1.03	1.02 – 1.04	<0.001
Male	0.87	0.76 – 1.00	0.050			
Diagnostic category						
Elective surgery (reference)						
Emergency surgery	5.23	4.33 – 6.31	<0.001	2.54	2.00 – 3.23	<0.001
Clinical	11.95	9.92 – 14.38	<0.001	3.78	2.92 – 4.89	<0.001
Seasonal						
Winter (reference)						
Spring	1.20	0.99 – 1.44	0.050			
Summer	1.37	1.14 – 1.65	<0.001	1.31	1.07 – 1.61	0.008
Autumn	1.14	0.95 – 1.36	0.141			
Apache II	1.20	1.18 – 1.21	<0.001			
Sofa at admission	1.40	1.37 – 1.43	<0.001			
Tiss 28 at admission	1.16	1.15 – 1.18	<0.001			
Chronic disease	1.31	1.14 – 1.50	<0.001	1.22	1.01 – 1.48	0.034
Sepsis at admission	6.68	5.64 – 7.90	<0.001	1.45	1.15 – 1.83	0.001
Use of mechanical ventilation	10.72	9.15 – 12.56	<0.001	4.06	3.25 – 5.08	<0.001
Use of vasoactive drugs	7.12	6.14 – 8.26	<0.001	2.74	2.26 – 3.32	<0.001
SRI at admission	6.40	5.43 – 7.54	<0.001	2.36	1.93 – 2.98	<0.001

Legend: Apache = Acute Physiology and Chronic Health Evaluation; Sofa = Sequential Organ Failure Assessment; Tiss 28 = Therapeutic Intervention Scoring System; SRI= Severe real injury; CI = 95% Confidence interval.

the cardiovascular system in 298 (8.0%), respiratory system in 247 (6.7%), and clinical post-cardiac arrest in 135 cases (3.6%).

We recorded prior diagnoses of chronic diseases in 11.2% of the patients, and the most frequent were: immunodeficiency (4.4%), heart failure (2.1%), chronic obstructive pulmonary disease (1.8%), chronic renal insufficiency (1.5%), and liver cirrhosis (1.4%). The average APACHE II score was 20.3 (SD = 19), Sofa average was 6.9 (SD = 4.8), and Tiss 28 median was 25.8 (IQR = 20.0 - 31.0). Mortality at ICU discharge was 32.2%, and at hospital discharge, 43.2% (Table 1).

After analyzing the variation of illness severity upon ICU admission over the seasons, we found that, although no variation in the severity of patients by age means, presence of chronic disease, or prognostic scores was found, a higher proportion of "Clinical" ($p<0.001$) and Sepsis diagnosis was identified during the summer months ($p=0.048$). These differences in the clinical profile of the patients admitted during the summer resulted in higher hospital mortality rates, compared to the other seasons of the year ($p=0.007$) (Table 2).

After studying the risk factors for death at hospital discharge by using the multivariate logistic regression model, seasonality was an independent factor associated with increased in-hospital mortality rates. Furthermore, in the summer, there was an increase of 31% in the death odds compared to winter months (reference season used in the model). In addition to seasonality, age, diagnostic category, the need for invasive mechanical ventilation, use of vasoactive drugs, presence of chronic disease, diagnosis of acute kidney injury, and sepsis on ICU admission were found to be independent risk factors for death at hospital discharge (Table 3).

To analyze the effect of seasonality in the mortality pattern and its association with the sepsis diagnosis, the temporal series were transformed into a stationary series. Thus, we performed a Box-Cox transformation to stabilize the variance. According to the Wald-Wolfowitz test, it was necessary to subtract the series to remove the trend component. Figure 3 shows the temporal series of monthly sepsis rates. The correlograms with the autocorrelation function in the time domain show that the sepsis rate series does not peak at the beginning and end of each year, during the summer. It is possible to see around three or four peaks of sepsis per year. After analyzing the periodogram for the sepsis rate, we found that the spectral element of order 26 is the one with the highest value. Considering there are 71 observations (we lost one observation after subtraction to remove the trend), this harmony corresponds to a frequency of 71/26 = 3 months, approximately. Therefore, there is evidence of seasonal behavior of Period 3, i.e., there are peaks of ICU admission due to sepsis every three months, which corroborates what was shown in the series graph.

Similarly, we used the Box-Cox transformation to stabilize the variance of the death rate series. Based on the runs test, the series did not present any trend. Therefore, it was not necessary to do any subtractions in the death rate series. Figure 4 shows the death rate series graph with the Box-Cox transformation and the periodogram. The highest value in the Periodogram is the first spectral element. A Fisher test was performed to check if the seasonality of Period 3 for sepsis and of Period 1 for deaths are significant. According to the test, at a 5% level of significance, the seasonality for sepsis was not significant, while it was for deaths.

DISCUSSION

This study presents a detailed description of the clinical characteristics and prognostic indexes of patients admitted to the ICU over a period of six years. It is an intensive care unit with a high occupation rate during the entire study period and a high rate of refusal of admission due to lack of beds. In this context, we found observed an increase of clinical admissions during the summer months, as well as a higher frequency of sepsis diagnosis and the need for invasive mechanical ventilation. Seasonality, age, diagnostic category, the need for invasive mechanical ventilation, use of vasoactive drugs, presence of chronic disease, diagnosis of acute kidney injury, and sepsis on ICU admission were independent risk factors for in-hospital death.

Sepsis is more common in patients with advanced age and chronic disease[16]. It is considered a clinical diagnosis at ICU admission and, by definition, is a condition that presents organic dysfunctions — such as acute kidney injury —, which often require support therapy, such as invasive mechanical ventilation and vasoactive drugs[8]. Due to the association of these variables with the diagnosis of sepsis, we proposed a time-series analysis to confirm the suspected association between seasonal variation, sepsis diagnosis,

and mortality rate. We confirmed the seasonal pattern of deaths, but not of sepsis diagnosis at the ICU admission.

This variation in the performance of the unit studied is probably due to multiple factors. A recent study of the national registry database for adult patients described a tendency of increased admissions of clinical patients and emergency surgeries over the years and a proportional reduction of elective surgeries[17]. In the institution studied, there is a constant demand for ICU beds that is inhibited. Thus, clinical patients are often treated outside the ICU with the aid of a team specialized in the care of severe patients. During the summer, which coincides with the end of year recesses and holidays, there is a reduction of elective surgeries and increased availability of beds for urgent clinical and surgical patients.

Sepsis was the main clinical diagnosis for patient admission to the ICU. This finding is similar to other data in the literature that demonstrates the impact of sepsis on the occupation rate of intensive care beds[18]. These patients present organic dysfunction at admission with a possibility of worsening during the first hours of care, even after intensive treatment is started, which reflects their severity[19]. A meta-analysis from 1979 to 2015 that evaluated 27 major studies compared the results from the variation of sepsis incidence and found an increase from 288 to 437 cases/100,000 inhabitants/year, and from 148 to 270 cases/100,000 inhabitants/year of cases of severe sepsis, with high rates of in-hospital mortality. In low- and middle-income countries, it is possible that the number of sepsis cases reaches 31.5 million, with 5.3 million deaths/year[20].

In-hospital mortality rates may be considered high in the present study. It is demonstrated in the literature that high-income countries have lower mortality rates[16,21] when compared to middle- and low-income countries[22,23]. These differences are due to several factors, among which the structural organization of intensive care units and the ease of access associated with increased availability of intensive care beds in countries with lower mortality rates.

Another Brazilian study, called Orchestra, included 59,693 patients from 78 ICUs and described the association between organizational aspects and mortality rates. The units with a higher level of organization, professionals specialized in intensive care, and use of protocols had the lowest mortality rates[24]. Our study demonstrates that the planning of human resources, equipment, and training should take into account the seasonal changes in the clinical profile of patients admitted. Characteristically, clinical and post-emergency-surgery patients have a higher risk of death; thus, they require more complex treatments and may have longer hospital stays[25].

The strength of the present study lies in the large number of observations and its long period, allowing detailed descriptions and analysis of annual variations of the outcomes observed. The limitations of the study are due to its single-center design, which limits the extrapolation of results to the populations of institutions with similar characteristics. The study's retrospective nature can also be considered a limitation, but since this is a retrospective analysis of data that were prospectively collected, there were no losses due to incomplete data. To better understand the analysis results of the temporal series, it would be interesting to have a study with a larger number of observations. Although the study involved a long period, the number of observations may not have been sufficient to have the volume of information required to understand the seasonality regarding mortality rates.

CONCLUSION

In intensive care units with a high occupation rate, it was possible to find a seasonal variation of the clinical profile and prognosis of patients admitted. The summer months had a higher proportion of clinical and emergency-surgery patients, with higher rates of mortality. The suspicion that the sepsis diagnosis at ICU admission had a seasonal 12-month behavior was not confirmed by the time series analysis. We found a seasonal pattern for the mortality rate.

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RESUMO

OBJETIVO: *Analisar variações sazonais dos padrões clínicos, uso de recursos terapêuticos e resultados da internação de pacientes adultos admitidos na unidade de terapia intensiva.*

MÉTODOS: *Estudo de coorte retrospectivo realizado de janeiro de 2011 a dezembro de 2016 em pacientes adultos na unidade de terapia intensiva (UTI) de Hospital Universitário. Foram coletados dados do tipo de admissão, escores Apache II, Sofa e Tiss 28 da admissão na UTI. O tempo de permanência e o desfecho na saída hospitalar foram registrados. O nível de significância adotado foi de 5%.*

RESULTADOS: *Foram analisados 3.711 pacientes no período do estudo. Os pacientes apresentaram mediana de idade de 60,0 anos (intervalo interqualítico = 45,0 – 73,0), sendo 59% homens. Os fatores independentes associados ao aumento de taxa de mortalidade hospitalar foram idade, doença crônica, sazonalidade, categoria diagnóstica, necessidade de ventilação mecânica e uso de drogas vasoativas, diagnóstico de injúria renal aguda e sepse na admissão. Pela análise de série temporal, a sazonalidade para sepse não foi significativa, enquanto a sazonalidade para óbitos foi significativa.*

CONCLUSÕES: *Foi possível observar variação do perfil clínico e de prognóstico dos pacientes admitidos, sendo que os meses de verão apresentam maior proporção de pacientes clínicos e cirúrgicos de urgência, com maiores taxas de mortalidade. Sepse na admissão da UTI não apresentou comportamento sazonal. Foi encontrado padrão sazonal para a taxa de mortalidade.*

PALAVRAS-CHAVE: *Terapia intensiva. Evolução clínica. Índice de gravidade de doença. Sazonalidade.*

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ORIGINAL ARTICLE

Predictive value of ATRIA risk score for contrast-induced nephropathy after percutaneous coronary intervention for ST-segment elevation myocardial infarction

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SUMMARY

BACKGROUND: *The AnTicoagulation and Risk factors In Atrial fibrillation (ATRIA) risk score used to detect the thromboembolic and hemorrhagic risk in atrial fibrillation patients has been shown recently to predict poor clinical outcomes in patients with acute myocardial infarction (ACS), regardless of having atrial fibrillation (AF). We aimed to analyze the relationship between different risk scores and contrast-induced nephropathy (CIN) development in patients with ACS who underwent urgent percutaneous coronary intervention (PCI) and compare the predictive ability of the ATRIA risk score with the MEHRAN risk score.*

METHODS: *We analyzed 429 patients having St-segment Elevation Myocardial Infarction (STEMI) who underwent urgent PCI between January 2016 and February 2017. Patients were divided into two groups: those with and those without CIN and both groups were compared according to clinical, laboratory, and demographic features, including the CHA2DS2-VASc and ATRIA risk score. Predictors of CIN were determined by multivariate regression analysis. Receiver operating characteristics (ROC) curve analysis was used to analyze the prognostic value of CHA2DS2-VASc and ATRIA risk score for CIN, following STEMI.*

RESULTS: *Multivariate regression analysis showed that Athe TRIA risk score, Opaque/Creatinine Clearance ratio, and low left ventricular ejection fraction was an independent predictor of CIN. The C-statistics for the ATRIA risk score and CHA2DS2-VASC risk score were 0.66 and 0.64 (p<0.001, and p<0.001), respectively. A pair-wise comparison of ROC curves showed that both scores were not inferior to the MEHRAN score in predicting CIN.*

CONCLUSION: *The ATRIA and CHA2DS2-VASC scoring systems were useful for detecting CIN following STEMI.*

KEYWORDS: *ATRIA risk score, St-segment Elevation Myocardial Infarction, Contrast induced nephropathy*

RUNNING HEAD: *The relationship between ATRIA risk score and contrast induced nephropathy*

INTRODUCTION

Quick restoration of coronary blood flow in an occluded coronary artery is the fundamental aim of early ST-elevation myocardial infarction (STEMI) therapy. Primary percutaneous coronary intervention (p-PCI) is the preferred reperfusion strategy for acute STEMI patients within the first few hours after the onset of symptoms.[1] However, life-threatening complications such as contrast-induced nephropathy (CIN) can be seen after p-PCI. A strong correlation between CIN and high mortality and morbidity in patients with STEMI has been shown. Additionally, these patients tend to have a long duration of hospitalization.[2,3] It was shown that different clinical and laboratory variables such as contrast media volume,

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presence of diabetes mellitus, chronic congestive heart failure, anemia and decreased renal perfusion were associated with CIN development.[4] Patients at high risk of CIN should be administered with early prophylactic measures such as hydration to prevent CIN. Additionally, high-risk patients should be followed up for creatinine progression after the procedure.[2] Therefore, scoring systems should be developed to predict the development of CIN.

The CHA2DS2-VASc and Anticoagulation and Risk Factors in Atrial Fibrillation (ATRIA) risk scores are cheap and easy scoring systems used to predict the risk of thromboembolism in non-valvular atrial fibrillation (AF) patients.[5,6] Additionally, these scoring systems have been shown to accurately predict worse clinical outcomes in patients with acute coronary syndrome regardless of having AF. [7,8] Moreover, we showed that the CHA2DS2-VASC score has predicted AF following STEMI and associated with epicardial fat tissue. [9,10] The components of these scoring systems, such as advanced age, presence of hypertension, presence of diabetes mellitus, low ejection fraction, and female gender have been associated with poor outcomes, including recurrent ischemic events.[7,11]

In this study, we aimed to investigate the predictive value of different thromboembolic risk scores in atrial fibrillation for the development of CIN.

METHODS

Study population

This was a prospective single-center study. The overall study population included 459 patients undergoing primary percutaneous coronary intervention diagnosis of ST-elevation myocardial infarction. The exclusion criteria included hyperthyroidism (5 patients), age <18 years, end-stage renal failure (10 patients), patients treated with emergent coronary artery bypass graft surgery (10 patients), sepsis (5 patients), exposed to contrast injection within 7 days before primary percutaneous coronary intervention (30 patients), known malignancy, severe hepatic dysfunction, and inflammatory disease. Patients who presented with cardiogenic shock or died during the first 72 hours of their hospital stay, or during revascularization, were also excluded from the study. Therefore, the final study cohort consisted of 399 patients with STEMI. The study protocol was reviewed and approved by the Local Ethics Committee of the Süleyman Demirel University Medical School (Approval number: 72867572.050.01.04-299118) in accordance with the Declaration of Helsinki.

Diagnosis of contrast-induced nephropathy

CIN was defined as the impairment of renal function and measured as either a 25% increase in serum creatinine from the baseline or a 0.5 mg/dL increase in the absolute value when there was no alternative etiology within 72 hours of the first procedure[4]. Creatinine Clearance was calculated using the Cockcroft-Gault Equation.[12]

Diagnosis of thromboembolic risk

The CHA_2DS_2-VASc risk score is calculated by assigning a score of 1 point for each of the following conditions: congestive heart failure (ejection fraction< 40%), hypertension, age between 65 and 74 years, diabetes mellitus, vascular disease (myocardial infarction or peripheral arterial disease), and female gender; a score of 2 points for the following conditions: history of stroke or transient ischemic attack (TIA) and age > 75 years. The score is then used to predict the risk of thromboembolism in non-valvular AF patients. [5]

The ATRIA score was developed from the ATRIA study cohort and calculated using the following: anemia (hemoglobin <13 g/dL in men and <12 g/dL in women) (3 points), severe renal disease (estimated glomerular filtration rate <30 mL/min/1.73 m^2) (3 points), age ≥75 years (2 points), prior bleeding, and hypertension. An ATRIA score of 0 to 3 is defined as "low risk," a score of 4 is defined as "intermediate risk," and a score ≥5 is defined as "high risk".[6]

Diagnosis of STEMI

Diagnoses were recorded by the participating physicians based on clinical, electrocardiographic and biochemical (elevated troponin levels) criteria. The type of myocardial infarction (ST-elevation vs. non-ST-elevation) and unstable angina were homogeneously defined based on current guidelines. All patients were treated according to the currently available guidelines. Primary percutaneous coronary intervention (PCI) was performed in all patients. [13]

Blood sampling

Blood samples were drawn from the antecubital vein by careful venipuncture using a 21 G sterile syringe without stasis between 08.00–10.00 AM after

a fasting period of 12 h. Glucose, creatinine, and lipid profiles were determined by standard methods. Hemogram parameters were measured in a blood sample collected in dipotassium EDTA tubes (Vacuette). An automatic blood counter (Beckman-Coulter Co, Miami, FL, USA) was used for whole blood counts.

STATISTICAL ANALYSIS

SPSS version 16.0 software package was used for statistical analyses in this study. Categorical variables were expressed as frequency (%) and compared using the $\chi 2$ test. Kolmogorov-Smirnov test was used to test the distribution of numeric variables; those with normal distribution were expressed as mean ± standard deviation and compared with Student's t-test. Data without normal distribution were expressed as median (Inter-quartile range (IQR) of 25%-75% percentiles) and compared with the Mann-Whitney U test. In all statistical analyses, a p-value <0.05 was considered statistically significant. The correlations between the CHA2DS2-VASc and ATRIA risk scores, CIN and other clinical, laboratory, and echocardiographic parameters were measured by Pearson or Spearman correlation analysis when appropriate. Univariate analysis and backward conditional binary logistic regression were performed to estimate the odds ratio (OR) and 95% confidence interval (95% CI) for the prediction of CIN. Receiver operating characteristics (ROC) curve analysis was used to analyze the prognostic value of the CHA2DS2-VASc and ATRIA risk scores for CIN, following STEMI. C-Statistic (area under the curve) was presented as a unified estimate of sensitivity and specificity according to the cutoff value that was obtained by the ROC curve analysis. The optimal cutoff value was defined as the value yielding the maximal Youden index, or the best-combined sensitivity and specificity.[14] All ROC comparisons were performed using the DeLong test. [15] C-Statistic (area under the curve) was presented as a unified estimate of sensitivity and specificity.

RESULTS

A total of 399 patients (mean age: 63±11 years; range, 28–91 years) were included in this study. During the follow-up period, 88 patients (22 %) developed CIN. The demographic and clinical characteristics of the patients with and without CIN are listed in Table 1. The patients with CIN were significantly older and more often female when compared to the patients without CIN (p< 0.001 and p= 0.015, respectively). Diabetes mellitus, hypertension, obesity, and hyperlipidemia rates were similar between patients with and without CIN (for all parameters p> 0.05). There were no statistically significant differences between patients with and without CIN with regards to cholesterol parameters (for all parameters p> 0.05). Left ventricle ejection fraction was significantly lower in patients with CIN than in patients without CIN (p= 0.016). Initial creatinine levels were similar between patients with and without CIN, but the 72-hour creatinine levels were higher in patients with CIN than in patients without CIN (p< 0.001)

The incidence of previous use of renin-angiotensin system (RAS) blockers was lower in patients with CIN than in patients without CIN (p= 0.055). There were no statistically significant differences between patients with and without CIN with regards to the use of beta-blockers, acetylsalicylic acid, clopidogrel, or statins. Among in-hospital treatments, the use of RAS blockers was lower in patients with CIN (p= 0.003), but other medications were similar among patients with and without CIN (p> 0.05). Patients with CIN had a longer period of stay at the Coronary Care Unit and a longer follow-up duration than patients without CIN (2.2± 0.7 versus 2.0± 0.4; p= 0.02 and 6.0 ± 2.2 versus 5.1 ± 1.7; p < 0.001, respectively).

The mean CHA2DS2-VASc, ATRIA, and MEHRAN scores were significantly higher in patients with CIN than in patients without CIN (2.6 ± 1.4 versus 1.9 ±1.4, p< 0.001; 4.3 ±2.7 versus 3.1 ± 2.7, p< 0.001; 5.3± 2.7 versus 4.3 ± 2.7, p< 0.001; respectively).

Prediction of Contrast-induced nephropathy

Univariate analyses showed that high CHA2DS2-VASc and ATRIA risk scores, low left ventricle ejection fraction, advanced age, opaque amount, opaque amount/Creatinine Clearance ratio, and female gender were significantly associated with a higher risk of development of CIN (Table 2). On the other hand, pre and in-hospital use of RAS blockers were inversely associated with the risk of incident CIN (Table 2).

A multivariate binary logistic regression analysis was carried out, including all characteristics that were associated with the development of CIN in the univariate analysis. This analysis showed that the opaque amount/Creatinine Clearance ratio (OR: 1.22; 95 % CI: 1.00-1.50, p= 0.04), ATRIA score (OR: 1.12; 95 % CI: 1.00-1.25, p= 0.04) and left ventricle ejection

TABLE 1. DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF PATIENTS WITH AND WITHOUT CONTRAST-INDUCED NEPHROPATHY

	Contrast-Induced Nephropathy		
	No (n=311)	Yes (n=88)	P-value
Female gender n, (%)	59 (19.9)	28 (31.8)	0.015
Diabetes Mellitus n, (%)	71 (23.9)	27 (30.7)	0.127
Hypertension n, (%)	142 (47.8)	48 (54.5)	0.161
Hyperlipidemia n, (%)	57 (19.2)	19 (21.6)	0.360
Age (years)	61.4 ± 13	67.9 ±9	< 0.001
Previous treatment			
RAS blockers n, (%)	45 (15.2)	7 (8.0)	0.055
B Blockers n, (%)	47 (15.8)	10 (11.4)	0.127
Statins n, (%)	31 (10.4)	10 (11.4)	0.469
In hospital Treatment			
RAS blockers n, (%)	248 (83.5)	61 (69.3)	0.003
B Blockers n, (%)	275 (92.6)	86 (97.7)	0.07
Statins n, (%)	292 (98.3)	87 (98.9)	0.585
Left ventricle ejection fraction (%)	45.8 ± 9.5	42.5 ± 10	0.016
CHA2DS2-VASc Risk score	1.9 ±1.4	2.6 ± 1.4	< 0.001
ATRIA Risk Score	3.1 ± 2.7	4.3 ± 2.7	< 0.001
Opaque amount (cc)	124 ± 38	169 ± 44	< 0.001
Opaque/CrCl ratio	1.9 ± 1.3	2.8 ± 1.4	< 0.001
Mehran Risk Score	4.3 ± 3.7	5.3 ± 2.7	< 0.001
Initial creatinine (mg/dl)	1.1 ± 0.3	1.0 ± 0.2	0.168
72th hour creatinine (mg/dl)	1.1 ± 0.3	1.5 ± 0.5	< 0.001
Duration of CCU stay (day)	2.0 ± 0.4	2.2 ± 0.7	0.02
Total Hospitalization stay (day)	5.1 ± 1.7	6.0 ± 2.2	< 0.001

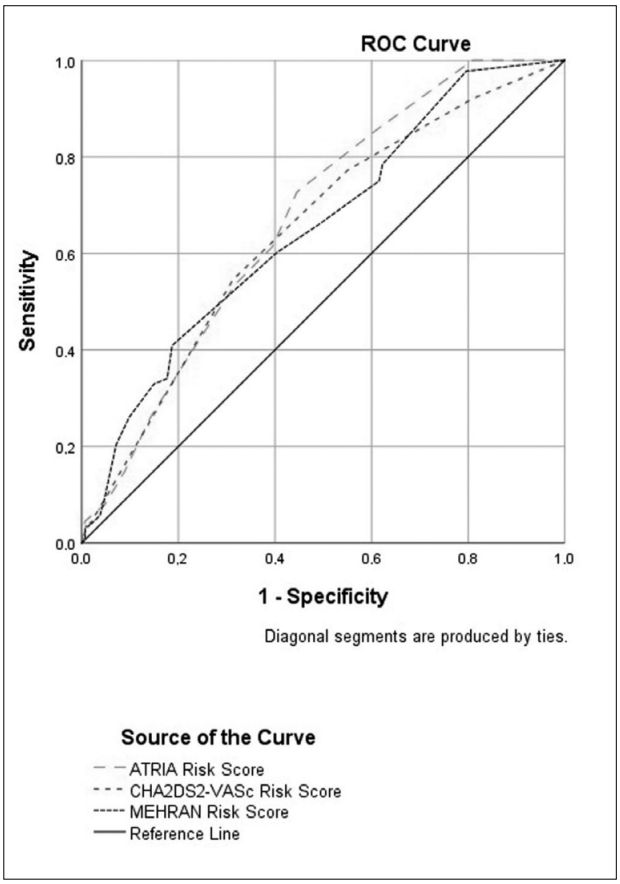
Data presented as mean ± standart deviation or number (%) of patients. Abbreviations: RAS = renin-angiotensin system; CHA2DS2-VASc= congestive heart failure, hypertension, age ≥ 75 years, diabetes mellitus, previous stroke, vascular disease, age 65 to 74 years, female gender; ATRIA - Anticoagulation and Risk Factors in Atrial Fibrillation Risk Score; CrCl: Creatinine Clearance, CCU: Coronary care unit

TABLE 2. UNIVARIATE AND MULTIVARIATE REGRESSION ANALYSIS OF PREDICTORS OF CONTRAST-INDUCED NEPHROPATHY IN THE STUDY POPULATION.

	Unadjusted Odds Ratio	Confidence interval	P-value	Adjusted Odds Ratio	Confidence interval	P-value
Female gender	1.88	1.1-3.2	0.02			
Left ventricle ejection fraction	0.96	0.94-0.99	0.007	0.97	0.95-1.00	0.09
Previous ACEi using	2.0	0.89-4.76	0.08			
In-hospital ACEi using	2.2	1.29-3.87	0.004			
CHA2DS2-VASc Risk score	1.3	1.17-1.63	< 0.001			
High CHA2DS2-VASc group	2.7	1.57-4.70	< 0.001			
ATRIA Risk Score	1.16	1.07-1.27	< 0.001	1.12	1.00- 1.25	0.04
Opaque amount	1.024	1.01-1.03	< 0.001			
Opaque/CrCl ratio	1.44	1.22-1.70	< 0.001	1.22	1.00-1.50	0.04
Mehran Risk Score	1.13	1.06-1.20	< 0.001			

fraction (OR: 0.97; 95 % CI: 0.95-1.00, p= 0.09) remained as independent factors for CIN development (Table 3). the ROC curve analysis showed that both ATRIA (C-statistic: 0.66; 95% CI: 0.61-0.71, p< 0.001) and CHA2DS2-VASc scores (C-statistic: 0.64; 95% CI: 0.59-0.76, p< 0.001) were significant predictors of CIN following STEMI (Figure 1) We calculated that a cut-off point of 2 for ATRIA and CHA2DS2-VASc scores could estimate the presence of CIN with a sensitivity of 72% and 55% and a specificity of 54% and 68%, respectively. Additionally, the ROC curve analysis showed that the opaque amount/Creatinine

FIGURE 1. ROC CURVE WITH CALCULATED AREA UNDER THE CURVE AND OPTIMAL CUT-OFF POINT FOR THE CHA2DS2-VASC SCORE AND ATRIA SCORE TO IDENTIFY THE PRESENCE OF CIN.



Clearance ratio (C-statistic: 0.70; 95% CI: 0.66-0.75, p<0.001) was a significant predictor of CIN following STEMI. We performed a pair-wise comparison of ROC curves, and recorded that the predictive value of the ATRIA risk score with regard to CIN development was similar to that of the MEHRAN risk, CHA2DS2-VASc, and ATRIA risk scores (by DeLong method, AUC ATRIA vs. AUC MEHRAN z test= 0.712, p= 0.476; AUC ATRIA vs. AUC CHA2DS2-VASc z test= 0.813, p= 0.07; AUC MEHRAN vs. AUC CHA2DS2-VASc z test= 0.238, p= 0.812)

DISCUSSION

The current study showed that higher CHA2DS2-VASc and ATRIA scores were independently associated with the development of CIN in STEMI patients treated with p-PCI; consequently, both scores could be helpful and appropriate scoring systems for predicting CIN after STEMI treated with p-PCI. Additionally, the opaque amount/Creatinine Clearance ratio is a powerful predictor of CIN development.

CIN is a serious complication of p-PCI after STEMI and is associated with worse clinical outcomes, such as prolonged length of hospital stays, rising costs, and increased short- and long-term morbidity and mortality.[2,3] It is important to anticipate which patients may develop CIN. There are several risk scores that have been established to predict CIN development.[4,16,17] The MEHRAN score, created for predicting CIN,[4] includes physical examination, laboratory tests, and various demographic and angiographic parameters. Additionally, Gurm et al.[16] defined a new model for predicting CIN after PCI. However, similar to the MEHRAN score, this score is complex and time-consuming as it also requires clinical and laboratory variables that may not be available to the clinician immediately. Therefore, these scoring systems are confusing and impractical due to their plurality and lack of ease of use. Conversely, the CHA2DS2-VASc and ATRIA scores are simple and easy scoring systems and may be used for predicting CIN in patients with STEMI before the procedure.

Although the underlying mechanisms of CIN are not entirely understood [18,19], previous studies have shown that renal vasoconstriction, endothelial dysfunction, and endothelial damage contribute to the process of CIN development by renal tubular injury and medullary hypoxia.[20] Diabetes mellitus, hypertension, advanced age, congestive heart failure, volume depletion, myocardial infarction, renal dysfunction are the most important risk factors for CIN development. [4,21-23] The risk factors of CIN are similar to the components of the CHA2DS2-VASc and ATRIA risk scores.[4] Furthermore, these scores can be used to predict the risk of CIN. Kurtul et al [8] showed that the CHA2DS2-VASc score can be used as a simple and useful tool for predicting CIN in patients with acute coronary syndrome (ACS). The data of the current study corroborate the results of Kurtul et al. Additionally, we showed that the ATRIA score can also be used to predict CIN following STEMI. Moreover, not only was the ATRIA score more powerful than the CHA2DS2-VASc score in predicting CIN, it was found to be non-inferior to the MEHRAN score in predicting CIN.

In the present study, female gender, low ejection fraction, opaque amount, opaque/eGFR ratio were risk factors for the development of CIN. Previous studies have also shown similar results. [8,24,25] Contrast volume and basal renal insufficiency are important risk factors for CIN;[19] accordingly, the

opaque/eGFR ratio is a good indicator for CIN.[25] Our study also indicated that opaque/eGFR ratio was a powerful predictor of CIN development.

Patients at high risk of CIN should be managed with early additional measures to prevent CIN. Although there are different established scoring systems to predict CIN risk, most of these include clinical, biological, and variables that can only be obtained after invasive interventions not available pre-procedure. However, the ATRIA and CHA2DS2-VASc scoring systems can be evaluated at the first contact with a physician. Additionally, measures such as hydration may be administrated to high-risk patients, who also should be followed up for creatinine progression after the procedure.

Importantly, this study has some limitations. First, it had a relatively small sample size and engaged in a single-center experience. Second, we have only estimated our model performance in a derivation cohort, while data for a confirmation cohort are lacking. Third, we did not follow up with major adverse cardiovascular events data. Our results should, therefore, be verified by future multi-center prospective longitudinal studies with larger sample sizes. The limitations of this study should be considered while interpreting these results.

CONCLUSION

We have shown in the current study that the ATRIA and CHA2DS2-VASc scoring systems were useful for detecting CIN following STEMI. Additionally, when the ATRIA risk score was compared with previously well-validated scores, it was found to be similar in power for predicting the development of CIN. Patients at high risk, according to the ATRIA and CHA2DS2-VASc scoring systems, should be followed up for creatinine progression after the procedure and administrated intravenous hydration before the procedure.

RESUMO

OBJETIVO: *O escore Anticoagulação e Fatores de Risco na Fibrilação Atrial (Atria), usado na detecção do risco tromboembólico e hemorrágico de pacientes com fibrilação atrial (FA), recentemente demonstrou predizer resultados clínicos ruins em pacientes com infarto agudo do miocárdio (SCA), independentemente de ter FA. Nosso objetivo foi analisar a relação entre os diferentes escores de risco e o desenvolvimento de nefropatia induzida por contraste (NIC) em pacientes com SCA submetidos à intervenção coronária percutânea (ICP) urgente e comparar a capacidade preditiva do escore de risco Atria com o escore de risco Mehran.*

MÉTODOS: *Foram analisados 429 pacientes com infarto agudo do miocárdio com elevação do segmento ST (IAM-ST) submetidos à ICP de urgência entre janeiro de 2016 e fevereiro de 2017. Os pacientes foram divididos em dois grupos: aqueles com e sem NIC, e ambos os grupos foram comparados de acordo com as características clínicas, laboratoriais e demográficas, incluindo os escores de risco CHA2DS2-VASc e Atria. Preditores de NIC foram determinados por análise de regressão multivariada. A análise da curva características de operação do receptor (ROC) foi utilizada para analisar o valor prognóstico dos escores de risco CHA2DS2-VASc e Atria para NIC, após IAM-ST.*

RESULTADOS: *A análise de regressão multivariada mostrou que o escore de risco Atria, a relação opaca/crCl e a baixa fração de ejeção do ventrículo esquerdo foram preditores independentes de NIC. A estatística-C para o escore de risco Atria e o escore de risco CHA2DS2-VASC foi de 0,66 e 0,64 (p<0,001 e p<0,001), respectivamente. Uma comparação de pares de curvas características de operação do receptor mostrou que ambos os escores foram não inferiores ao escore Mehran na previsão de NIC.*

CONCLUSÃO: *Os sistemas de pontuação Atria e CHA2DS2-VASC foram sistemas úteis para a detecção de NIC após IAM-ST.*

PALAVRAS-CHAVE: *Escore de risco Atria. Infarto do miocárdio com elevação do segmento ST. Nefropatia induzida por contraste.*

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ORIGINAL ARTICLE

Chagas disease is associated with a poor outcome at 1-year follow-up after cardiac resynchronization therapy

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SUMMARY

BACKGROUND: *Cardiac resynchronization therapy (CRT) is a therapeutic modality for patients with heart failure (HF). The effectiveness of this treatment for event reduction is based on clinical trials where the population of patients with Chagas' disease (DC) is underrepresented.*

OBJECTIVE: *To evaluate the prognosis after CRT of a population in which CD is an endemic cause of HF.*

METHODS: *A retrospective cohort conducted between January 2015 and December 2016 that included patients with HF and left ventricular ejection fraction (LVEF) of less than 35% and undergoing CRT. Clinical and demographic data were collected to search for predictors for the combined outcome of death or hospitalization for HF at one year after CRT implantation.*

RESULTS: *Fifty-four patients were evaluated, and 13 (24.1%) presented CD as the etiology of HF. The mean LVEF was 26.2± 6.1%, and 36 (66.7%) patients presented functional class III or IV HF. After the mean follow-up of 15 (±6,9) months, 17 (32.1%) patients presented the combined outcome. In the univariate analysis, CD was associated with the combined event when compared to other etiologies of HF, 8 (47%) vs. 9 (13,5%), RR: 3,91 CI: 1,46–10,45, p=0,007, as well as lower values of LVEF. In the multivariate analysis, CD and LVEF remained independent risk factors for the combined outcome.*

CONCLUSION: *In a population of HF patients undergoing CRT, CD was independently associated with mortality and hospitalization for HF.*

KEYWORDS: *Heart Failure. Chagas Disease. Cardiac Resynchronization Therapy.*

INTRODUCTION

Heart failure (HF) is the common final stage of most diseases that affect the heart and one of the most important current clinical challenges in health[1]. Currently, there is a prevalence of 23 million people worldwide, and almost 300,000 deaths are attributed to HF every year[2,3]. Data from Datasus have demonstrated that, in 2012 alone, there were 26,694 deaths due to HF in Brasil. In association with that, 50% of all hospitalized patients with that diagnosis are readmitted within 90 days after hospital discharge, and the readmission becomes one of the major risk factors for death in this syndrome[4].

Patients with advanced HF may have left ventricular systolic dysfunction and cardiac dyssynchrony[5].

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Cardiac resynchronization therapy (CRT), by means of multisite pacing, can restore cardiac synchrony, reducing the hospitalization rate of these patients[2]. Thus, TRC can be used as an adjuvant therapy to pharmacological treatment, reducing the morbidity and mortality of patients with advanced HF[6].

Chagas disease (CD) produces progressive myocardial damage and later results in Chronic Chagas Cardiomyopathy and is the third cause of HF in Brasil and the number one non-ischemic cause in Latin America[7]. Knowing that some of the main mechanisms of death in CD are the progression to advanced HF and left ventricular systolic dysfunction, the CRT is an attractive option, in addition to clinical therapy, to improve the prognosis of these patients[8,9]. Due to the high prevalence of CD in Latin America and its emergence in non-endemic areas, such as the United States, due to the process of globalization and migratory flows, more studies are needed directly relating TRC with Chagas disease[6,10].

Currently, there are studies that address CRT in patients with heart failure, especially those affected by ischemic etiology. However, when we look at CRT in patients with HF due to Chagas disease in previous works, such as guidelines and large *trials*, there are no clear results or, often, the etiology is not contemplated in the study population. Thus, the present study aims to evaluate the prognosis of the TRC in a population in which Chagas disease is considered endemic.

METHODS

Population

This is a retrospective cohort study whose recruitment was conducted between January 2015 and December 2016. We consecutively included outpatients who underwent CRT, monitored by the heart failure unit of the Ana Nery Hospital of the Federal University of Bahia. All patients were over 18 years old, had symptoms of advanced heart failure, with left ventricular ejection fraction (LVEF) ≤35%, with QRS complex duration >150 ms.

Chagas disease was confirmed by specific serological tests. We excluded from the study patients with prior use or indication for combined therapy with implantable cardioverter-defibrillator (ICD), patients who still had no investigation of the etiology of the heart disease, with chronic inflammatory systemic diseases, malignant neoplasm under treatment, who refused to undergo the procedure, or who declined to give informed consent.

Follow-up and Outcomes

The patients were followed-up on an outpatient basis at the institution after hospital discharge. Those who did not return after one year of the TRC implantation were contacted by phone. As an outcome measure, we used the combined event of hospitalization due to decompensated heart failure and death from all causes. If patients presented more than one event, we considered only the first.

Ethics Committee

The Research Ethics Committee of the Ana Nery Hospital - Salvador (BA) approved the study, and all procedures were performed per the Declaration of Helsinki.

Statistical analysis

The Kolmogorov-Smirnov test was used to verify the normal distribution of continuous variables. Variables with normal distribution were described by means and standard deviations and compared by Student's t-test. Categorical variables were compared using the chi-square test. The Log-Rank test was used to compare the time distribution for the primary outcome. A p-value < 0.05 was considered statistically significant. We used the Cox model for multivariate analysis, including variables likely to be associated with the outcome. We used the stepwise variable entry method, with an entry criterion of a p-value = 0.15 and as the exclusion criterion a p-value = 0.25. The Statistical Package for Social Sciences (SPSS) software version 20.0 was used to analyze all data.

RESULTS

During the recruitment period, 61 patients were evaluated for CRT implantation. Of these, four were excluded for having an indication for ICD implantation and three for not yet present investigation of the HF etiology. A total of 54 patients were included in the final study population. CD was the most frequent etiology of HF, along with ischemic and idiopathic etiologies, 13 (24.1%) each.

The Chagas and non-Chagas groups were balanced for the variables: male sex 4 (30.7%) *vs.* 27 (65.9%),

age 64.7 years (±9.3) *vs* 61.6 years (±13.0), LVEF 27% (±5.3) *vs* 26.1% (±6.4), FC III-IV, 10 (76.9%) *vs.* 26 (63.4%), respectively. Demographic data are described in Table I.

After a mean follow-up of 15 (±6.9) months, 17 (31.4%) patients presented the combined outcome of death or hospitalization due to HF, 8 of which (47%) had CD (Table II). In the univariate analysis, CD was associated with the combined outcome when compared to other HF etiologies: 8 (47%) *vs.* 9 (13.5%), RR: 3.91 CI; 1.46-10.45, p= 0.007. The ejection fraction of the left ventricle was also inversely associated with the combined outcome, RR: 0.90 CI; 0.83-0.98, p= 0.014 (Table III).

After multivariate analysis, including the variables for Chagas disease and LVEF, both remained

TABLE 1. DEMOGRAPHIC CHARACTERISTICS

		Chagas	Non-Chagas	P*
	n = 54	n = 13	n = 41	
Age, (Mean + SD)	62.3 (+12.2)	64.7 (+9.3)	61.6 (+13.0)	0.169
Male, n (%)	31 (57.4%)	4 (30.7%)	27 (65.9%)	0.051
FC III or IV, n (%)	36 (66.7%)	10 (76.9%)	26 (63.4%)	0.468
LVEF (Mean + SD)	26.2 (+6.1)	27.0 (+5.3)	26.1 (+6.4)	0.179
Diabetes, n (%)	14 (25.9%)	2 (15.3%)	12 (29.2%)	0.475
Atrial fibrillation, n (%)	4 (7.4%)	0 (0%)	4 (9.7%)	0.562
Prior pacemaker, n (%)	9 (16.7%)	4 (30.8%)	5 (12.2%)	0.195
HF etiology				
Ischemic, n (%)			13 (24.1%)	
Idiopathic, n (%)			13 (24.1%)	
Hypertensive, n (%)			9 (16.7%)	
Valvular, n (%)			4 (7.4%)	
ARB or ACE inhibitors	31 (57.4%)	8 (61.5%)	23 (56.1%)	1.0
Beta-blocker	28 (51.9%)	6 (46.2%)	22 (53.7%)	0.75
Spironolactone	32 (59.3%)	8 (61.5%)	24 (58.5%)	1.0

FC = New York Heart Association functional class ; LVEF = Left ventricle ejection fraction; CRI = Chronic renal insufficiency; HF = Heart failure; ACE = Angiotensin-converting enzyme; ARB = Angiotensin receptor blockers

* Comparison between Chagas and Non-Chagas.

TABLE II. DESCRIPTION OF THE OUTCOMES

	n = 54	CHAGAS n = 13	NON-CHAGAS n = 41	P
Combined outcome, n (%)	17 (31.4%)	8 (61.5%)	9 (21.9%)	0.007
Death, n (%)	5 (9.2%)	3 (23.0%)	2 (4%)	0.620
Hospitalization due to HF, n (%)	12 (22.2%)	5 (38.5%)	7 (17.0%)	0.620

HF = Heart failure.

TABLE III. UNIVARIATE AND MULTIVARIATE ANALYSIS OF PREDICTORS FOR THE COMBINED OUTCOME

	Univariate Analysis		Multivariate Analysis	
	RR (95% CI)	P	RR (95% CI)	P
Age, (years)	0.99 (0.96 – 1.03)	0.68	-	-
Male	1.38 (0.49 – 3.87)	0.53	-	-
FC III or IV	1.36 (0.38 – 4.81)	0.64	-	-
LVEF (%)	0.90 (0.82 – 0.98)	0.01	0.88 (0.81 – 0.97)	<0.01
CRI	1.08 (0.14 – 8.59)	0.94	-	-
Atrial fibrillation	1.86 (0.23 – 15.34)	0.56	-	-
Chagas disease	3.91 (1.46 – 10.45)	<0.01	4.40 (1.48 – 13.12)	<0.01
Diabetes	1.30 (0.36 – 4.63)	0.68	-	-

FC = New York Heart Association functional class ; LVEF = Left ventricle ejection fraction; CRI = Chronic renal insufficiency.

independent risk factors for the combined outcome: Chagas disease, RR 4.40 CI 1.48 to 13.12, P=0.008, LVEF, RR 0.88 CI 0.81 to 0.97, P=0.008.

DISCUSSION

The study sample had 24.1% of patients with HF secondary to CD, a relatively good representation of the condition. Upon comparing the Chagas disease group with other etiologies, we found a similarity in the predominance of FC III-IV, as well as in the average age and LVEF. After a mean follow-up of 15 months (±6.9), 17 (31.4%) patients presented the combined outcome of death or hospitalization due to heart failure, 8 of which (47%) had CD. In the univariate analysis, CD and lower values of LVEF were associated with the combined outcome of death or hospitalization due to heart failure. After the multivariate analysis of predictors, CD and LVEF remained independent risk factors for the combined outcome.

The study showed a high rate of cardiovascular events when compared with the average follow-up time. In studies such as those by Cleland et al.[8] and Moss et al.[6], the follow-up time required for the prevalence of cardiovascular events *versus* the follow-up period to be similar to that of the present study was 2.5 and 4.5 years, respectively.

There are risk factors in the study sample that may justify the high rate of cardiovascular events in short follow-up time. The low socioeconomic and educational level of this population favors poor medication adherence, with greater difficulty of establishing optimized clinical treatment, thus increasing the incidence of negative outcomes[1]. In our sample, the rate of non-use of beta-blockers, spironolactone, ARB or ACE inhibitors was little more than half in both groups, i.e., Chagas and non-Chagas' Disease. In addition, the population is severe, with a predominance of FC III-IV and ≤35% LVEF; previous studies have found that the survival rate of these patients is only 16% at 36 months[2].

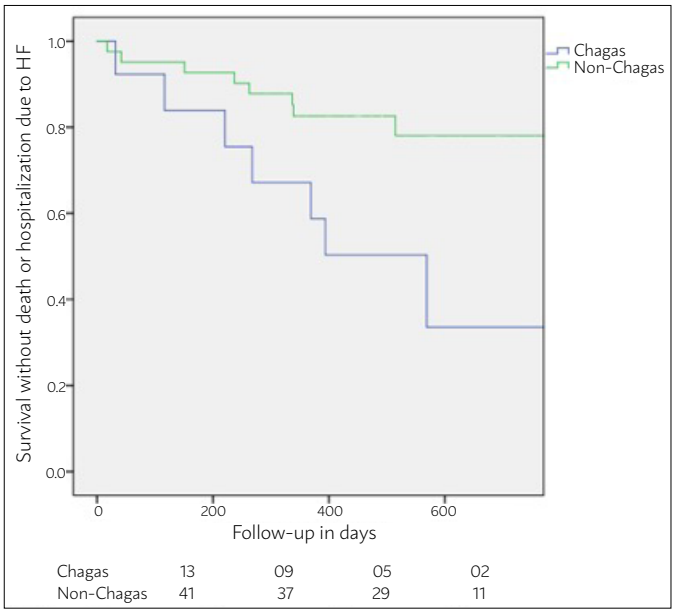
According to the Brazilian Guideline of Implantable Electronic Cardiac Devices[11], class I recommendations for implantation of a cardiac resynchronizer are: patients with LVEF <35%, sinus rhythm, HF with FC III-IV, despite optimal drug treatment and with QRS >150 ms or 120-150 ms and proof of dyssynchrony by imaging method. The studies that have led to this consensus, such as the Miracle[12] and the Companion[13], had as a sample HF patients with functional class III or IV, QRS >120 ms, and ischemic heart disease as the main etiology of the heart failure. In both studies, CD was under-represented or not mentioned as a possible etiology of HF. Unlike in our study, in which, despite having a similar population regarding the FC and QRS value criteria, Chagas disease was well represented and considered as an independent predictor of death or hospitalization due to heart failure after CRT.

Mortality due to CD is intimately linked to the degree of myocardial involvement in the course of the disease[2]. Pathological studies on Chagas disease have found sites of prominent myocardial fibrosis. After imaging studies by magnetic resonance, they found that the areas most affected by the fibrosis are the apex of the left ventricle and post-lateral sites[14,15]. Bleeker et al.[16] showed that patients with scar tissue in the post-lateral wall do not respond to CRT, even in the presence of dyssynchrony in the left ventricle.

Sudden cardiac death is the main cause of death in the CD and is considered one of the most common phenomena of this pathology, with a prevalence of 55-65%. Thus, ICD implantation associated with optimal drug treatment is a strategy for the primary and secondary prevention of sudden cardiac death in this disease[14,17]. Sales et al.[18] demonstrated the null effect of resynchronization therapy on the incidence of sudden death.

The present study presents some limitations due

FIGURE 1



to its unicentric retrospective cohort design, in which the variables were collected by means of electronic records, subjecting the work the biases inherent to this design. Thus, it was not possible to evaluate the degree of cardiac dyssynchrony by ECHO before the CRT, not even measures related to the systolic and diastolic diameter of the left ventricle and LVEF after the resynchronization therapy. Incomplete ECG data did not allow us to analyze the prevalence of right branch block in patients with Chagas disease, because, when present, it decreases the success rate of CRT. The absence of data relating to the magnetic resonance imaging prevented the analysis of the extent and location of myocardial fibrosis in patients submitted to this procedure, which may have interfered with the effectiveness of the therapy.

After analysis and discussion of the results found in this article, we confirmed the need for more prospective studies that address the combined outcome of death or hospitalization due to HF in patients with CD undergoing CRT. These studies will be important to identify risk predictors for this outcome and, consequently, therapeutic measures that involve such factors to enable a better prognosis for HF patients of Chagas etiology.

CONCLUSION

In a population of HF patients who underwent CRT, among which the Chagas etiology is frequent, Chagas cardiomyopathy was associated with a worse prognosis in the short-term follow-up.

RESUMO

INTRODUÇÃO: *A terapia de ressincronização cardíaca (TRC) é uma modalidade terapêutica para pacientes com insuficiência cardíaca (IC). A eficácia desse tratamento para redução de eventos baseia-se em ensaios clínicos em que a população de pacientes com doença de Chagas (DC) é sub-representada.*

OBJETIVO: *Avaliar o prognóstico após TRC em uma população em que a DC é uma causa frequente de IC.*

MÉTODOS: *Coorte retrospectiva realizada entre janeiro de 2015 e dezembro de 2016, sendo incluídos pacientes portadores de IC com fração de ejeção do ventrículo esquerdo (Feve) menor que 35% e submetidos à TRC. Os dados clínicos e demográficos foram coletados para pesquisa de preditores para o desfecho combinado de morte ou internação por IC após implante da TRC.*

RESULTADOS: *Foram avaliados 54 pacientes, dos quais 13 (24,1%) apresentavam a DC como etiologia da IC. A Feve média foi de 26,2% (±6,1) e 36 (66,7%) pacientes apresentavam classe funcional de IC III ou IV. Após o seguimento médio de 15 meses, 17 (32,1%) pacientes apresentaram o desfecho combinado. Na análise univariada, a DC esteve associada ao evento combinado quando comparada a outras etiologias de IC, 8 (47%) **vs** 9 (13,5%), RR: 3,91 IC: 1,46–10,45, p=0,007, assim como valores mais baixos da Feve. Na análise multivariada, a DC e a Feve permaneceram como fatores de risco independentes para o desfecho combinado.*

CONCLUSÃO: *Em uma população de pacientes com IC submetidos à TRC, a doença de Chagas esteve independentemente associada à mortalidade e internação por insuficiência cardíaca no seguimento de 15 meses.*

PALAVRAS-CHAVE: *Insuficiência cardíaca. Doença de Chagas. Terapia de ressincronização cardíaca.*

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ORIGINAL ARTICLE

Prevalence of falls in elderly people: a population based study

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SUMMARY

INTRODUCTION: *The occurrence of falls is related to a complex interaction of risk factors, aggravated by aging. This research aimed to investigate the occurrence of falls in the elderly, as well as to identify the risk factors for this event.*

METHODS: *A cross-sectional, population-based study conducted in a municipality in the extreme south of Brasil. Probabilistic sampling was used, the sample unit being the census tracts. Data were collected through home interviews. The research was approved by the research ethics committee.*

RESULTS AND DISCUSSION: *This study was performed using a sample of 211 elderly individuals. The prevalence of falls was 28.9% (95% CI 22.8 to 35.0). (P = 0.01), living alone (p = 0.04), self-perception of regular or poor health (p = 0.03), and obesity (p= 0.01).*

CONCLUSIONS: *We found that approximately one in three elderly individuals fell in the last year.*

KEYWORDS: *Aged. Accidental falls. Public health. Epidemiology. Risk factors.*

INTRODUCTION

A fall episode is defined as an unintentional change of body position resulting in contact with the ground or another lower level that is not the consequence of an intrinsic event or great danger[1]. The Ministry of Health considers falls among elderly individuals an important public health problem, given its high incidence and its possible consequences to health, such as injury, disability, institutionalization, and death[2]. Fall episodes involving the elderly are more frequent than health and social issues and can have consequences on the family environment, on the economic aspect, as well as on the physical and mental health of individuals[3].

In Brasil, data from the Brazilian Institute of Geography and Statistics (IBGE)[4] show that the population with age equal to or greater than 60 years is around 25,964,619 inhabitants. The total number of hospitalizations due to falls among elderly Brazilians, in hospital units of the Unified Health System (SUS), between 2005 and 2010, was 399,681, with a cost reported by the Hospital Admission Authorization (AIH), a mandatory document that enables all hospital admissions in the SUS, of R$ 464,874,275.91 in the same period[5].

A Brazilian study, whose data collection was carried out between 1996 and 2012, pointed out that 66,876 deaths were recorded due to falls and 941,923

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hospitalizations resulting from it in elderly individuals aged 60 years or more[6]. The aging process increases risk factors and comorbidities, especially of chronic-degenerative diseases[7]. As a consequence, for a significant portion of individuals, these pathologies will bring some degree of disability, with decreased physical capacity and restrictions to autonomy and independence[2,8].

Falls are related to a complex interaction of risk factors that are aggravated with aging[9]. The main risk factors can be classified as a) biological agents, such as age, gender, and race, associated to changes due to aging; b) behavioral, related to human actions, emotions or daily choices that are potentially modifiable; c) environment, which includes the interaction of physical conditions of individuals and the environment that surrounds them; d) socioeconomic factors, such as inequality of work/income, education, housing without conditions of sanitation, limited access to health care and social assistance in priority areas and lack of resources in the community[8,9].

Despite the importance of the issue, in view of its frequency, deleterious effects on health, and its cost to the public health system, there is still a lack of population-based studies in the country on this topic. Therefore, the objective of this study was to analyze the occurrence of falls and identify groups at risk among elderly patients of a municipality in the extreme south of Brasil.

METHODS

This is a population-based cross-sectional study that is part of a larger project called "*Saúde da população riograndina*". This project was developed in 2016 with the objective of evaluating health aspects of the adult population (≥ 18 years) living in the city of Rio Grande, in the state of Rio Grande do Sul, Brasil.

The inclusion criteria were: age greater than or equal to 65 years and residing in the urban area of the municipality of Rio Grande. Individuals institutionalized in nursing homes, hospitals, and prisons and those with physical and/or intellectual disabilities that prevented them from answering the questionnaire were excluded. The research project was submitted to and approved by the Health Research Ethics Committee (Cepas) of the Federal University of Rio Grande (FURG), under process number 20/2016. Further methodological details about the study can be found in another publication[10].

The sampling process occurred in two stages; the first stage was the selection of census sectors, and the second, the selection of households. A total of 72 census sectors were systematically selected out of the 293 of the urban area of the municipality. To select the census sectors, a list was drawn up of all households in descending order according to the monthly income of the head of the family. Soon after, 711 households were selected in proportion to the size of the sector. Out of these households, 676 were sampled (95% of the total), and in 164 of them, there was at least one elderly individual (aged 65 years or more), which corresponded to 24% of the households sampled in this research. Since in some households there were more than one elderly individuals, the study sample comprised 211 individuals. The sample studied (N=211) had a power of 80% to detect prevalence ratios equal to or greater than 2.0, with a frequency of exposed ranging from 20% to 80%.

The dependent variable in this study was the occurrence of a fall in the past 12 months, with the following question, "Since <MONTH> of last year, have you suffered a fall at home or on the street?". The independent variables analyzed were: age (65 to 69/70 to 79/80 or more); gender (male/female); skin color (white/other); marital status (married/single, separated or widowed); reside alone (no/yes); years of formal education (0 to 8/greater than or equal to 9); index of goods into terciles (poorest/intermediary/richest); physical activity during leisure time (no/yes); self-perception of health (excellent, very good, good/regular, bad); stress into terciles (lowest/intermediary/Highest); arterial hypertension (yes/no); arthritis or rheumatism (no/yes); chronic back pain (no/yes), and obesity (no/yes).

The instrument was a questionnaire standardized for the study. The index of goods variable was created from 11 items on household characteristics and presence of domestic goods by means of principal component analysis, in which the first component that explained more than 30% of the variability of all the others was extracted. Physical activity during leisure time was measured by the long version of the International Physical Activity Questionnaire (IPAQ), validated for use in Brasil[11]. Stress was measured by the Scale of Perceived Stress[12]. Data on hypertension and arthritis or rheumatism were collected from the self-reported medical diagnosis. Chronic back pain was considered as a complaint of pain for more than three consecutive months.

Obesity was defined as a body mass index (BMI) ≥ 30 kg/m², from self-reported weight and height.

The data were collected from April to July 2016 by interviewers trained for this purpose, by means of face to face home interviews. The data was input to EpiData 3.1 software, and the analysis was performed in the Stata statistical package, version 11.2. Univariate analysis was made by means of absolute and relative frequencies. The bivariate and multivariate analyses were carried out through Poisson regression, taking into account the effect of the sampling design. The prevalence ratios (PR) with 95% confidence intervals (95% CI) were presented. For the multivariate analysis, we built a five-level model of analysis, namely: gender, skin color, marital status, and living alone (first level); formal education, and index of goods (second level); physical activity, self-perception of health, and stress (third level); hypertension, arthritis or rheumatism, chronic back pain, and obesity (fourth level). The level of statistical significance was 5% for two-tailed tests.

RESULTS

This study was conducted using a sample of 211 elderly individuals. The occurrence of falls was 28.9% (95% CI 22.8 to 35.0). The effect of the sample design found was 0.96 (intraclass correlation coefficient = 0.014). The average age of the sample was 73 years (SD=6.6), ranging from 65 to 96 years of age.

Table 1 shows the descriptive data of the sample studied in this research. It included mostly women (62.1%), of white skin color (85.3%), married (51.2%), with up to eight years of formal education (66.7%), who did not practice physical activity (70.3%) and who had hypertension (57.8%). As for the other comorbidities, a fifth (20.1%) were obese, approximately 30% had arthritis or rheumatism, and approximately one fourth (25.6%) reported chronic back pain. The self-perception of health was assessed as regular or bad by half of the sample (49.3%).

The occurrence of falls over the past year was 28.9% (95% CI 22.8 to 35.0). The occurrence varied from 9.1% in elderly individuals who perceived their health as excellent, very good or good, to 42.5% in those with obesity, and 43.2% in those who lived alone. For the other groups, the occurrence of falls ranged between 20% and 40%, except for the male gender, which was 17.5% (Table 2).

Table 2 also presents the gross and adjusted associations between the occurrence of falls in accordance with the characteristics investigated. We found, in the gross analysis, that the occurrence of falls was more frequent among females (p=0.01), those who live alone

TABLE 1. DESCRIPTION OF THE CHARACTERISTICS FROM THE ELDERLY SAMPLE OF RIO GRANDE, RS, 2016 (N=211).

Variable	N	%
Age range (years)		
65 to 69	77	36.5
70 to 79	99	46.9
≥80	35	16.6
Gender		
Male	80	37.9
Female	131	62.1
Skin color		
White	180	85.3
Others	31	14.7
Marital status		
Married	108	51.2
Single, separated, widowed	103	48.8
Lives alone		
No	167	79.1
Yes	44	20.9
Formal education (years)		
0 to 8	140	66.7
≥9	70	33.3
Index of property (tertiles)		
1 (lower)	85	40.3
2 (intermediate)	52	24.6
3 (higher)	74	35.1
Physical activity during leisure		
No	147	70.3
Yes	62	29.7
Self-perception of health		
Excellent/very good/good	107	50.7
Regular/bad	104	49.3
Stress (tertiles)		
1 (lower)	87	41.8
2 (intermediate)	72	34.6
3 (higher)	49	23.6
Hypertension		
No	89	42.2
Yes	122	57.8
Arthritis or rheumatism		
No	149	70.6
Yes	62	29.4
Chronic back pain		
No	157	74.4
Yes	54	25.6
Obesity		
No	157	79.7
Yes	40	20.3
Total	211	100.0

TABLE 2. DISTRIBUTION OF FALLS ACCORDING TO THE CHARACTERISTICS OF THE ELDERLY IN RIO GRANDE, RS, 2016 (N=211).

Variable	% falls	Unadjusted analysis		Adjusted analysis	
		PR(95%CI)	P-value	PR(95%CI)	P-value
Age range (years)			0.38		0.33
65 to 69	23.4	1.00		1.00	
70 to 79	33.3	1.43 (0.86; 2.36)		1.45 (0.89; 2.36)	
≥80	28.6	1.22 (0.65; 2.35)		1.20 (0.64; 2.24)	
Gender			0.01		0.01
Male	17.5	1.00		1.00	
Female	35.9	2.05 (1.19; 3.55)		1.98 (1.16; 3.37)	
Skin color			0.36		0.16
White	27.8	1.00		1.00	
Others	35.5	1.28 (0.75; 2.18)		1.41 (0.87; 2.30)	
Marital status			0.19		0.44
Married	25.0	1.00		1.00	
Single, separated, widowed	33.0	1.32 (0.87; 2.01)		0.81 (0.46; 1.40)	
Lives alone			0.02		0.04
No	25.2	1.00		1.00	
Yes	43.2	1.72 (1.11; 2.66)		1.60 (1.03; 2.49)	
Formal education (years)			0.28		0.57
0 to 8	31.4	1.29 (0.81; 2.08)		1.14 (0.72; 1.82)	
≥12	24.3	1.00		1.00	
Index of property (tertiles)			0.04		0.17
1 (lower)	38.8	1.69 (1.02; 2.80)		1.52 (0.87; 2.66)	
2 (intermediate)	21.2	0.92 (0.47; 1.79)		0.91 (0.47; 1.75)	
3 (higher)	23.0	1.00		1.00	
Physical activity during leisure			0.20		0.26
No	31.3	1.39 (0.84; 2.29)		1.32 (0.81; 2.13)	
Yes	22.6	1.00		1.00	
Self-perception of health			0.01		0.03
Excellent/very good/good	9.1	1.00		1.00	
Regular/bad	39.4	2.11 (1.26; 3.53)		1.78 (1.06; 3.00)	
Stress (tertiles)			0.14*		0.85*
1 (lower)	24.1	1.00		1.00	
2 (intermediate)	29.2	1.21 (0.68; 2.14)		1.04 (0.62; 1.76)	
3 (higher)	36.7	1.52 (0.88; 2.64)		1.05 (0.59; 1.87)	
Hypertension			0.05		0.58
No	21.4	1.00		1.00	
Yes	34.4	1.61 (1.00; 2.60)		1.18 (0.66; 2.11)	
Arthritis or rheumatism			0.54		0.62
No	27.5	1.00		1.00	
Yes	32.3	1.17 (0.70; 1.97)		0.85 (0.45; 1.61)	
Chronic back pain			0.38		0.36
No	27.4	1.00		1.00	
Yes	33.3	1.22 (0.78; 1.90)		0.82 (0.52; 1.27)	
Obesity			0.01		0.01
No	24.2	1.00		1.00	
Yes	42.5	1.76 (1.15; 2.68)		1.70 (1.16; 2.51)	

PR: Prevalence Ratio; 95% CI: confidence interval of 95%. *P-value of the test for linear trend

(p=0.02), the poorest (p=0.04), those with a perception of poor or regular health (p=0.01), hypertensive patients (p=0.05), and obese (p=0.01). After adjustment for confounding factors, only females (p=0.01), living alone (p=0.04), regular or poor self-perception of health (p=0.03), and obesity (p=0.01) remained statistically significant associations (Figure 1). The other variables were not significantly associated with the outcome.

DISCUSSION

The aim of this study was to investigate the association between falls of elderly individuals and demographic, socioeconomic, behavioral, and health characteristics. We found that almost one in every three elderly individuals experienced falls over the past year. The most affected groups were women, individuals who live alone, with a worse perception of health, and obese.

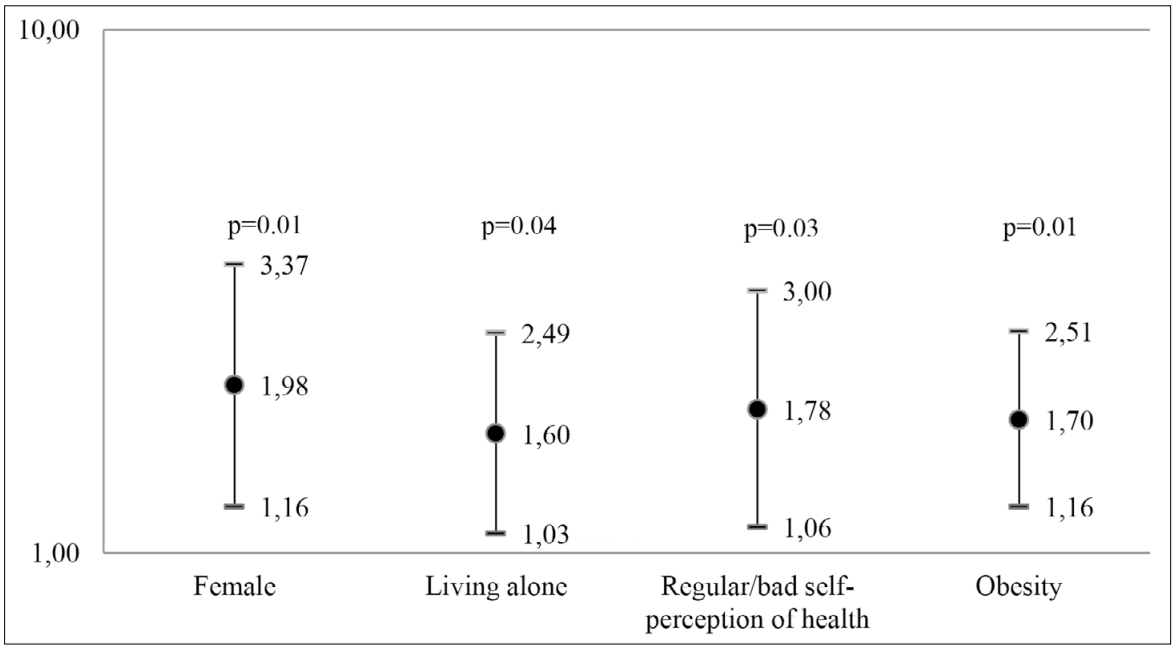
The frequency of falls found in this study (28.9%) resembled a few national and international studies. A study conducted in several municipalities of Brasil[13], with a sample of 6,624 individuals, reported an occurrence of 27.6% (95% CI: 26.5-28.7). A survey with 683 elderly individuals in Montes Claros, MG, pointed to an occurrence of 28.3% in the last 12 months[14]. At an international level, individuals older than 65 years in the United States of America had 28.7% of occurrence of falls in 2014[15]. In the English Longitudinal Study of Aging, the weighted occurrence for the past two years was 28.4%[16].

The greater occurrence of falls among females is consistent in the literature. Both Brazilian[3,13,17] and foreign studies[16.18] presented this finding. The causes cited to justify the greater occurrence of falls among elderly women are increased bone fragility in relation to men, higher occurrence of some chronic diseases, greater exposure to domestic activities, and physical-functional decline[15,19,20].

Elderly people who lived alone had a higher risk of falls. The hypothesis presented in some studies point is that elderly individuals are more exposed to a greater number of activities (at home and in other places)[20], and that this age group presents a greater likelihood of disability relating to basic and instrumental activities[21] and, therefore, greater vulnerability in tasks that would produce a greater number of situations that present a risk for falls[22].

An association was found between the perception of regular or poor health and the likelihood of falls. The self-perception of health is considered an important indicator of health, widely used in health research and surveys, both due to its easy applicability and its low cost compared to other more complex methods. It is also a predictor of morbidity and mortality: people with restrictions and limitations develop dissatisfaction, which is reflected in this criteria[14,23,24]. However,

FIGURE 1. PREVALENCE RATIO OF FALL-RELATED FACTORS THAT WERE STATISTICALLY SIGNIFICANT IN THE ADJUSTED ANALYSIS. RIO GRANDE, RS, 2016 (N=211).



a worsened perception of health can be the result of episodes of falls, so it can suffer the influence of reverse causality bias.

As to the association with obesity, in line with other studies[13,25], it is justified by the postural imbalance as a result of excess weight and fat accumulation in the abdominal region. Furthermore, obese individuals have a lower amplitude of movement and greater torque in the ankle joint to maintain the balance[13,25]. This finding shows the importance of interventions aiming at weight maintenance or reduction among the elderly since this is a modifiable risk factor[13,25]. It stands out, however, that some studies found no association between BMI and falls[9,26].

The results of this study demonstrated a lack of association between the presence of arthritis or rheumatism and chronic back pain with fall events in the population assessed. The literature indicates that musculoskeletal disorders, which result in joint stiffness and pain and chronic inflammatory processes, are linked to instability in walking and balance[20,27-29]. Still, the increase in chronic diseases and the occurrence of severe pain are concomitant to the loss of functional capacity, an increase of immobility and physical dependence are associated with a greater likelihood of falls in men and women[16]. However, it is worth noting that elderly individuals with physical limitations (such as arthritis, or rheumatism, or back pain) are less exposed to risk situations due to their conditions.

It is important to point out some limitations of this study. This research is part of a larger project, which was not intended only for this research object, nor only to elderly subjects. As a result, the sample size was not very large, which may have affected the accuracy of the study. However, it is worth noting that all associations with PR greater or equal to 1.60 were detected as statistically significant. Perhaps there was not enough power to detect the association with individuals of lower socioeconomic level (PR=1.52; p=0.17). It should also be noted that we did not investigate the characteristics of the fall episode, such as, if it was the first time it happened, where it happened, possible sequelae, such as fracture or hospitalization, and use of medications. Thus, we can only make inferences on the frequency of falls and their associated factors.

Due to the increase in the elderly population in our country, and acknowledging that several changes are needed in the care and follow-up of this population, identifying risk factors and factors associated with falls is of paramount importance to reduce morbidity and mortality. This study is representative of the local population and can be extrapolated to other groups of elderly individuals, so these data can be used as a tool for health managers and professionals to plan for public policies that allow for the organization of the health services care offered to the elderly population. We recommend that other studies include the rural population of the municipality and survey the health care costs from elderly people who suffer falls. Finally, interventional studies that evaluate strategies for preventing this situation are compelling and scarce.

CONCLUSION

We found an occurrence of 28.9% of falls among elderly individuals with a mean age of 73 years. The significant risk factors were female (p=0.01), living alone (p=0.04), regular or poor self-perception of health (p=0.03), and obesity (p=0.01).

Conflict of interest

The authors declare there are no conflicts of interest.

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Approval by the research ethics committee

Health Research Ethics Committee (Cepas) of the Federal University of Rio Grande (FURG), under process number 20/2016.

Contribution of the authors

LMSA conceived the study, collected the data, and wrote the article. RDM and SCD analyzed the data, critically reviewed the article, and oversaw the work. All authors approved the final version of the manuscript.

RESUMO

INTRODUÇÃO: *A ocorrência de quedas está relacionada a uma interação complexa de fatores de risco, agravados com o envelhecimento. Esta pesquisa teve como objetivo investigar a ocorrência de quedas em idosos, bem como identificar os fatores de risco a esse evento.*

METODOLOGIA: *Estudo transversal, de base populacional, conduzido em município do extremo sul do Brasil. Utilizou-se amostragem probabilística, sendo a unidade amostral os setores censitários. A coleta de dados ocorreu por meio de entrevistas domiciliares. A pesquisa foi aprovada por comitê de ética.*

RESULTADOS E DISCUSSÃO: *Este estudo foi realizado utilizando amostra de 211 idosos. A ocorrência de quedas foi de 28,9% (IC95% 22,8 a 35,0). Mantiveram associação estatística, após ajuste para fatores de confusão, apenas sexo feminino (p=0,01), morar sozinho (p=0,04), autopercepção da saúde regular ou ruim (p=0,03) e obesidade (p=0,01).*

CONCLUSÕES: *Verificou-se que aproximadamente um em cada três idosos sofreu queda no último ano.*

PALAVRAS-CHAVE: *Idoso. Acidentes por quedas. Saúde pública. Epidemiologia. Fatores de risco.*

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COMMENTARY

Comment: "Prevalence of falls in elderly people: a population based study"

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In the article "Prevalence of Falls in Elderly People: A Population Based Study"[1], the authors discuss a matter of high importance for the population because falls cause high morbidity and mortality in this age group and still considerably encumber health services and its employees. Based on a population-based cross-sectional study of appropriate methodological rigor, it sought to identify significant risk factors, so that it is possible to act in prevention, and found 28.9% (95% CI 22.8 to 35.0) falls in a sample of 211 elderly people in the municipality of Rio Grande in the past year. After adjustment for confounding factors, only the variables of females (p=0.01), living alone (p=0.04), regular or poor self-perception of health (p=0.03), and obesity (p=0.01) remained statistically significant associations[1].

In contrast, a similar study previously conducted in Porto Alegre evaluated 267 elderly individuals and found the following risk factors as predisposing to falls: higher age range; poor self-perception of the vision and poor self-perception of health and sight; elderly individuals who reside at home, and monthly income equal to or less than one minimum wage[2]. Another descriptive study, conducted in Brasilia, included 83 elderly women and found no statistically significant relationship between age, sociodemographic factors, dizziness, psychotropic medication, poor perception of health and sight, and presence of depression with the phenomenon of falling. However, these were related to the condition of body balance, assessed by the Functional Range Test and the Tinetti Balance and Gait Score, suggesting that these tests may be used to evaluate and identify improvements in body balance after training[3].

Given the seriousness of the topic "falls among the elderly", we highlight the importance of studies of this nature to direct more attention to the health of the elderly and better define education programs.

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Therapy for patients with burns - an integrating review

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SUMMARY

OBJECTIVE: *to identify, through an integrative review, national studies published over the last ten years highlighting products and therapies used in burns.*

METHODS: *integrative research with studies published in the last ten years. Including clinical studies describing the use of the already established or innovative therapies in burns and the results obtained, published in national journals in the last ten years. Excluding articles published before 2007 and those that did not present results regarding the use of products in burns.*

RESULTS: *ten articles that met the inclusion criteria were selected. Collagenase, 1% silver sulfadiazine, and porous cellulose membrane were some of the therapies cited.*

CONCLUSION: *the casuistry was low; however, the good results obtained with porous cellulose membrane and silver nanocrystalline dressing are highlighted, since they were used in a larger number of patients in the studies evaluated.*

KEYWORDS: *Burns. Burn units. Wound Healing. Debridement. Bandages.*

INTRODUCTION

Burns are secondary injuries from accidents involving thermal, chemical, or electrical energy capable of producing excessive heat, damaging the skin and/or other tissues, leading to cell death. They are classified according to the depth of the site affected, as first, second, or third grade. First degree burns (Figure 1A) affect the epidermis and do not form blisters; they cause pain, hyperemia, and edema. Second-degree burns (Figure 1B) affect the epidermis and the dermis, forming blisters; they can be superficial, with the basis of the blister pink, wet and painful, or deep, with the basis of the blister white, dry and less painful[1]. Third-degree burns (Figure 1C) affect even deeper structures; there is no pain due to the destruction of the nerve endings; there is no capillary return, and blood vessels are compromised due to coagulation; there is no spontaneous regeneration, grafting is indicated and, when there is healing, there is retraction of edges[2-4].

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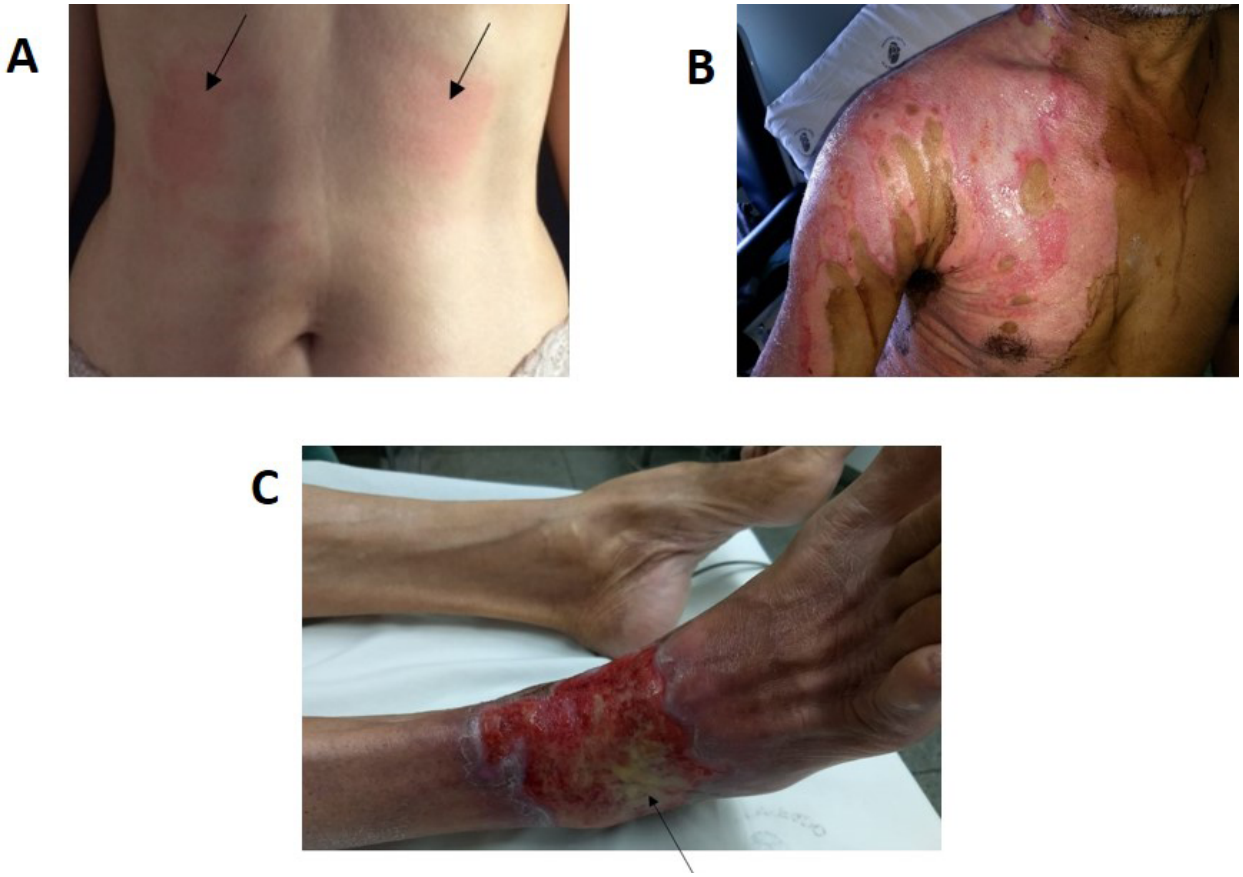
FIGURE 1. ILLUSTRATIVE IMAGES OF DIFFERENT DEGREES OF BURNS. A: FIRST-DEGREE BURN; B: SECOND-DEGREE BURNS; C: THIRD-DEGREE BURNS; SOURCE: PRIVATE FILE.



The therapy of burned patients has always been a global challenge, both due to the complexity of lesions and to the need for intensive and multidisciplinary care involving several health professionals, such as clinicians, intensivists, psychologists, nutritionists, physical therapists, and nurses with expertise in this area[5]. A complex wound raises the rates of morbidity and mortality, increases the overall costs of treatment (inputs and human resources), and leads to longer hospital stays[6]. The systemic treatment of burn patients focuses on reducing edema, maintaining hemodynamics and renal function, preventing or combating infections, preserving the viable tissues, protecting the microcirculation, strengthening innate defenses, and providing essential substrates to support viable tissues and recovery[7].

The topical therapy appropriate to an injury due to burns considers the use of products that control bacterial growth, remove the devitalized tissue, and promote healing[8]. Several studies mention the products used in the treatment of burns. One of them mentions that the first option of health institutions for the treatment of burns from the second degree is silver sulfadiazine 1%[9], a topical antimicrobial drug of the sulfanilamide class found in the presentation of a white, odorless, and soluble cream[10]. Another report mentions silver sulfadiazine at 1%, cream or solution, and its combination with cerium nitrate, besides other preparations with silver[11]. Hyperbaric oxygen therapy for burns was also highlighted in a study[7], as well as the use of hyaluronic acid (HA)[12]. HA is involved in several cellular functions, including cell proliferation, cell locomotion, and interactions with leukocytes. It is used clinically to treat articular disease and in ophthalmic surgical devices; some studies suggest benefits from using it in wound healing[13].

Another paper highlighted silver sulfadiazine in the first 48-72 hours, topical chemical debridement until the necrotic tissue is removed, a topical product with a growth factor, surgery for removal of devitalized tissue, and bandage embedded in saline solution[8]. Other authors have cited as topical agents, mostly antimicrobials, the associations between neomycin sulfate and bacitracin; between clostebol acetate and 5 mg of neomycin sulfate and silver sulfadiazine 1%[14].

Other researchers have pointed out that in cases in which the burned surface area (BSA) is extensive, because of the greater complexity of therapy, other substances and techniques that stimulate and encourage healing must be used, such as heparin, papain, lidocaine, surgical treatment of autologous graft of the skin and/or debridement[15].

In folk medicine, plants are used for the treatment of burns: *Aloe barbadensis Mill* (aloe vera), and *Symphytum officinale* (comfrey), which have healing action and are used generally *in natura*, as a poultice or decoction[16]. Aloe vera and comfrey are funded by the Ministry of Health for availability in the public health network and are part of the Brazilian Pharmacopoeia Phytotherapics List[17,18].

Other authors mention the use of Silver Sulfadiazine 1%, calcium alginate, hydrocolloid, petrolatum, and hydrogel, depending on the condition of the wound, with there is necrosis, exudate and/or bleeding[14].

Due to the several options available on the market, more studies are necessary to define those that allow lower repair time, less retraction, lower probability of infection, and better pain control. Choosing an appropriate therapy for burns and hypoalgesia or analgesia is the goal of professionals who treat patients with this type of injury. Therefore, it is important to have scientific evidence to base adequate clinical behavior.

OBJECTIVE

To identify, by means of an integrative review, national studies published over the past ten years that highlight products and therapies used in burns.

METHODS

To build this integrative review, six distinct stages were followed[19]:

1 - Research question: What therapies that have been cited in the literature for the treatment of lesions secondary to burns, in the last ten years?

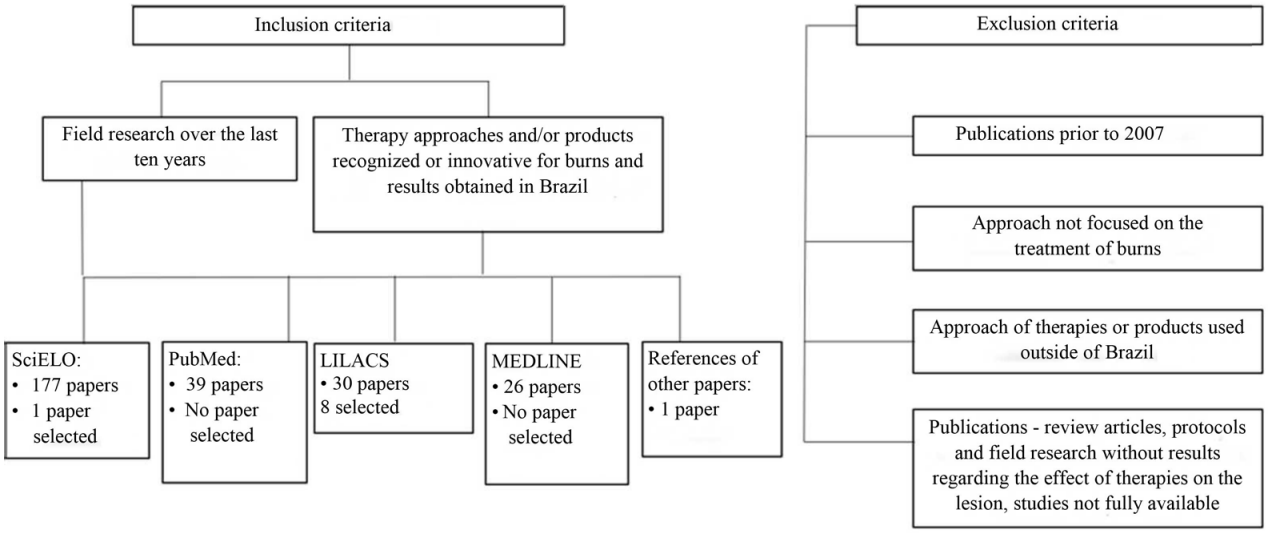
2 - Inclusion criteria: We used all field studies that described the use of established or innovative therapies for burns and the results obtained and published in online Brazilian journals over the past ten years (2007 to 2017). Exclusion criteria: We excluded articles published before 2007, those who do not focus on the treatment of lesions secondary to burns, that did not present results regarding the use of products on burns, and those that described therapies used outside of Brasil.

3 - Categorization of studies: Extraction of information, database formation. The keywords were selected in accordance with the Health Sciences Descriptors (DeCs): burns, burns Units, healing, debridement, dressings. The relationship established between these words obeyed the following criteria: the search should relate three of them and, in the event of a negative result, relate two of them. The databases consulted were: SciELO, Lilacs, Medline-Bireme, and PubMed. The abstracts were read, and those relevant to the topic were selected for later in-depth reading.

The search in SciELO retrieved 177 papers; of these, one was selected. The search in PubMed retrieved 39 papers, but none met the inclusion criteria. In Lilacs, the search retrieved 30 papers, and eight were selected. The papers that were not selected approached burns related to the quality of life, team, and work in Burns Units, development of products for skin lesions, analgesia, epidemiological aspects, and animal studies, and many were not used because they were published before 2007. Some papers were not selected because their full text was not available. The search on Medline-Bireme, linking the keywords, resulted in 26 papers, but none was used because they were about animal studies, or studies were before 2007, or studies that addressed matters not relevant to the subject, or studies without permission for full access. One paper was included from the references for another study. Thus, in total, ten papers were selected.

Four field studies were also discarded because, although they described the use of products in burn patients, they did not describe how these products influenced the repair of tissues. One mentioned the use of silver sulfadiazine 1% and papain[20]; another approached, in a case report, a patient with burns in several regions of the body and treatment with collagenase, silver sulfadiazine, among others, as needed: exudate, slough, bleeding[21]; another that described the use of products such as silver sulfadiazine, adaptic and carboxymethylcellulose in burned patients,[5] and a final one that designed a guideline which included silver sulfadiazine at 1%, silver sulfadiazine at 1% with cerium nitrate at 2.2% and essential fatty acid[22]. A study published in a na-

FIGURE 2 . FLOWCHART OF THE RESULTS OF THE STUDY SELECTION PROCEDURE ROSADÉLIA MALHEIROS CARBONI



tional magazine reports the use of dermal regeneration matrix in burns and described the result, but it was developed in Lisbon, Portugal; therefore, it was not used in this study[23]. Below, a flowchart describes the results of the study selection procedure (Figure 2).

RESULTS

Based on the results obtained, we designed a figure compiling all the information from the selected studies, such as the author, title of the study, objective, type of research, the therapy used, and results. The research was conducted from April to June 2017.

FIGURE 3. INFORMATION FROM THE ARTICLES INCLUDED IN THE INTEGRATIVE REVIEW. ROSADÉLIA MALHEIROS CARBONI

Authors	Title	Objective	Type of study	Therapy used	Results
Gonçalves et al.[24], 2016	Comparação dos efeitos do ácido hialurônico 0,2% e ácidos graxos essenciais em paciente com queimadura por fertilizante: relato de caso.	Compare the effects of hyaluronic acid 0.2% and essential fatty acids in a patient with burns caused by fertilizer: case report.	A case report of a patient with superficial second-degree burns and small areas of deep second degree on both hands caused by the use of fertilizer, without signs of infection or other complications.	Hyaluronic acid (Hyaluderm® - TRB Pharma) Essential fatty acids (Skinbasis®)	The hyaluronic acid 0.2% cream was well tolerated by the patient, without any incident of local or systemic adverse events identified during the study, with better performance, in relation to healing, than the essential fatty acid (EFA) in the case reported.
Moser et al.[25], 2014	Uso de curativos impregnados com prata no tratamento de crianças queimadas internadas no Hospital Infantil Joana de Gusmão.	Analyze the results of the use of silver dressings in the treatment of partial burns.	A cross-sectional epidemiological study.	Silver sulfadiazine 1% Nanocrystalline Silver	Patients who used the silver nanocrystalline dressing and dressings associated with a non-traumatic interface of the wound made of absorbent foam presented a lower reepithelialization time those who used the silver sulfadiazine dressing.
Teles et al.[26], 2012	Tratamento de queimadura de segundo grau em face e pescoço com heparina tópica: estudo comparativo, prospectivo e randomizado.	Assess the epithelization time, pain, and infection rate, comparing the use of topical heparin to the use of collagenase (control group) in the treatment of superficial face and neck second-degree burns.	A prospective study of patients with superficial second degree burns on their faces and necks from less than 24 hours.	Topical heparin Collagenase	The results of this study showed that the collagenase group presented a shorter healing time than the heparin group ($p<0.05$).

Authors	Title	Objective	Type of study	Therapy used	Results
Proto e Gozzano[27], 201[2]	Curativo de espuma e silicone suave: uma alternativa para o tratamento de queimadura em mãos.	Demonstrate the use of soft foam and silicone dressings as an alternative in the treatment of hand burns.	A case report of a patient with a second degree burn in their left hand by direct contact with bike fumes.	Soft foam and silicone dressing	The dressing of soft silicone foam and is a good treatment option for burns in joint areas, such as the hand, avoiding long immobilizations, retractions, and sequelae
Vieira et al.[28], 2017	Porous cellulose membrane in the treatment of burns.	Review the concepts of porous cellulose membrane (PCM) dressing, its use indications, and demonstrate the clinical results obtained.	A prospective study in patients with second degree burns, superficial and deep, with an average of 12% of body surface area burned.	Porous cellulose membrane dressing	Superficial second-degree burns epithelialized satisfactorily in seven days, without the need to change the membrane. No complications were observed, such as wound infection, delayed healing, or early detachment of the dressing.
Silva et al.[29], 2017	Efeitos do tratamento tópico com ácido hialurônico 0,2% em queimadura de segundo grau: um relato de experiência.	Test the daily and prolonged topical use of hyaluronic acid 0.2% in the healing of burns in elderly patients, observing the following parameters: healing time, presence or absence of hypertrophic scars, and the final aesthetic effect resulting from the treatment.	Case reports of a patient with a superficial second-degree burn and small areas of deep second-degree burns.	Hyaluronic acid 0.2%(Hyaludermin® - TRB Pharma)	The data allow us to conclude that the topical application of HA 0.2% in burns of an elderly patient helped to accelerate healing, improved treatment evolution, and aesthetic results.
Buelvas e Ohana[30], 2016	Uso de Omiderm® em queimadura grave: relato de caso.	Report the case of a child with severe burns attended at the Burn Treatment Center of the Municipal Hospital Pedro II in Rio de Janeiro, RJ, in which treatment with Omiderm® was used.	A case report of a patient with 1 year and 5 months of age; 31% of burned surface area (BSA) by the Lund and Browder rule. Most burns were of deep second degree, with small areas of superficial second degree.	Omiderm®, Semi-biological skin substitute, transparent, adherent, and semipermeable	After 11 days of treatment with balneotherapy (cleaning of wounds with running water and 2% chlorhexidine antiseptic, debridement of necrotic tissue and occlusive dressing) and Omiderm®, the child progressed with clean and dry wounds, without signs of inflammation, with burns fully satisfactory epithelialization of burns.
Calegari e Queiroz Venancio[31], 2012	O princípio da similitude no tratamento de queimaduras.	Report the evolution of the healing process in order to disclose this practice, which is one of the axes of the National Policy on Complementary and Integrative Therapies (PNPIC) in the SUS, as a possible and necessary part of Family Health strategies.	Case reports Patient 1, 7 years old, with first and second-degree burns on the face, ear lobe, shoulder, chest, armpits, and the proximal region of the arm on the right side. Patient 2, 42 years old, with first and second degree burns on the anterior region of the right leg.	A solution of 2 liters of warm water and 200 ml of alcohol applied on the burn with local compress	In patient 1, on the 13th day of treatment, complete restoration and healing with good aspect were noticed, with only a small area of keloid only in the proximal region of the right arm. In patient 2, on the 16th day of the homeopathic dressing, fully favorable evolution was observed, considering the time elapsed after the injury and the fact that the lower limbs had varicose veins, an important factor due to their size; there was also centripetal healing.
Costa Filho et al.[32], 2012	Tratamento ambulatorial de queimaduras com prata nanocristalina em malha flexível: uma alternativa terapêutica.	To evaluate treatment efficacy and duration on patients in outpatient treatment with nanocrystalline silver in flexible mesh in the Burn Treatment Unit of the Regional Hospital of Sorocaba.	Case reports of patients with second degree burns affecting between 1% and 2% of the body surface, according to the table of Lund and Browder.	Acticoat® Flex - Smith and Nephew (flexible polyester mesh, with nanocrystalline silver, with broad-spectrum antimicrobial action)	The average time of treatment was 13 days. The flexible polyester mesh proved to be effective in the healing of burns and good alternative therapy.
Rocha et al.[33], 2012	Avaliação comparativa do uso de hidroalginato com prata e o curativo convencional em queimaduras de segundo grau.	Compare the conventional treatment of second-degree burns, superficial (four-layer dressing) and deep (four-layer dressing + 1% silver sulfadiazine), and the use of silver hydro-alginate regarding the following criteria: pain, burn evolution, and practicality of use.	A prospective study with patients with superficial or mixed (deeper superficial) second degree burns with burned surface area (BSA) of up to 3%, on upper limbs, lower limbs, and thorax.	Dressing 1: four layers, made of rayon gauze, burn gauze (cheese type), absorbent cotton and tape Dressing 2: four layers, namely, silver sulfadiazine at 1%, rayon gauze, burn gauze (cheese type), absorbent cotton, and tape. Dressing 3: 51% calcium alginate (guluronic acid), 9% carboxymethyl cellulose, 32% nylon, and 8% elemental silver.	The use of the conventional four-layer dressing had worse evolution of the areas of the mixed second degree, possibly due to the difficulty of changing the dressing without removing, at least partially, of the rayon gauze. The use of the silver hydro-alginate dressing had superior restoration results when compared to the conventional dressing in mixed second-degree burns.

DISCUSSION

Of the studies mentioned, one of them stressed that hyaluronic acid had better results than the essential fatty acid, but this was observed in a single patient[22]. Another more recent study, from 2017, also highlighted the use of hyaluronic acid, but it was a single case report[29].

Essential fatty acid (EFA) has been used in clinical practice as a preventive and for wound treatment for many years, and some brands on the market are considered correlated[34]. Linoleic acid and linolenic acid are the most important fatty acids for treating wounds, and EFA-based products may contain one or both and have, in addition, vitamins A and E and soy lecithin[35].

A systematic review highlighted that the topical action of the combination of hyaluronic acid and silver sulfadiazine showed significantly favorable response in the mean time for healing of partial and deep-partial thickness burns[12].

A study that analyzed 132 medical records of children aged zero to 14 years old, affected by burns, found that the results from nanocrystalline silver dressings and those associated with the non-traumatic interface of the wound and of absorbent foam were better than the silver sulfadiazine[25]. Metallic silver in the form of nanoparticles is a potent antimicrobial agent[36], with a more powerful fast bactericidal capacity greater than sulfadiazine and silver nitrate-based dressings[37].

In another study, conducted with 20 patients, researchers reported that in those who used collagenase (10 patients), the healing time was shorter than in those who used topical heparin (ten patients)[26]; sodium heparin, which is known for its anticoagulant action [38]. Researchers have pointed out that the effect of parenteral sodium heparin has been studied on thermal injuries in animals and in humans, with favorable effects[26].

Other researchers, in a case study, revealed that the soft silicone and foam dressing is a good option for treating burns in joint areas, such as the hand, avoiding long immobilizations, retractions, and sequelae[27]. In research on 29 patients, it was reported that second degree burns epithelialized using the porous cellulose membrane, without the need of changing dressings. The authors emphasized that the membrane provides ease of application, excellent adhesion to tissues, reduction of pain, adequate visualization of the lesion, spontaneous drainage, reduction or absence of dressing changes, and increased intervals of medical supervision[28].

These studies cited used several topical therapies, and the results consist of a number of 184 patients, i.e., the sample was low.

In relation to hyaluronic acid, there were two cases presented, and a soft silicone and foam dressing was used in one case. Even though the authors highlighted good results, this is insufficient to assert that they are beneficial for burns[27,29].

In relation to silver sulfadiazine 1%, in the 132 patients studied, this type of therapy had lower results than nanocrystalline silver dressings and those associated with the non-traumatic interface of the wound and of absorbent foam[25]. In another study with 20 patients, sulfadiazine was also compared with silver hydro-alginate, which had the best results in the healing[33]. Nanocrystalline silver was also used in a study with eight patients and proved effective in the healing of burns[32]. One study presented the use of a compress soaked in a solution of 2 liters of warm water at a temperature between 38 and 40 °C and 200 ml of alcohol on the burn; however, only two cases were reported[31]. Researchers used Omiderm®, a biosynthetic dressing that is a semibiological substitute of the skin in a study with patients and reported favorable results in the healing of burns. The product is transparent, adherent, and semipermeable therefore has the property to protect and maintain the moisture in the wound[30].

CONCLUSION

We highlight, in this study, the good results obtained with porous cellulose membrane and nanocrystalline silver dressings in virtue of having been used in a larger number of patients in the 10 studies evaluated.

Many Brazilians suffer burns; however, in the literature, there are few articles that present the topical therapy used and its results. This study presented only 10 papers that met the inclusion criteria. Considering what was found in the literature, it is necessary to disseminate other studies showing the effectiveness of topical therapies, since burned patients are extremely vulnerable, suffer from hyperalgesia and have the injuries heal, often, after a long time, with retractions and impaired self-esteem.

There are more modern burn dressings, such as the Mepitel®(Mölnlycke), which has a double layer

of silicone, with perforated aspect; Biatain Silicone® (Coloplast), an absorbent foam dressing with soft silicone; Mepilex ®Ag (Mölnlycke), a foam dressing with antimicrobial, with a bioburden-reducing action; Urgotul® (Urgo Medical), with a layer of flexible contact with the TLC healing matrix (made of flexible polyester mesh impregnated with a layer of carboxymethylcellulose and lipophilic particles dispersed); the negative pressure therapy (NPT), which provides uniform subatmospheric pressure to the wound, whose mechanism of action involves biological and physical effects[39], among others, but no published studies were found on these dressings for the treatment of burns.

RESUMO

OBJETIVO: *Identificar, por meio de revisão integrativa, estudos nacionais publicados nos últimos dez anos que destaquem produtos e terapêuticas utilizados nas queimaduras.*

MÉTODOS: *Pesquisa integrativa com estudos publicados nos últimos dez anos. Incluídos os estudos clínicos que descreveram a utilização de terapias já consagradas ou inovadoras em queimaduras e os resultados obtidos e publicados em periódicos nacionais nos últimos dez anos. Excluídos os artigos publicados antes de 2007 e os que não apresentaram resultados quanto ao uso de produtos nas queimaduras.*

RESULTADOS: *Selecionados dez artigos que atenderam aos critérios de inclusão, sendo colagenase, sulfadiazina de prata 1% e membrana celulósica porosa algumas das terapias descritas.*

CONCLUSÕES: *A casuística foi baixa, porém, ressaltam-se os bons resultados obtidos com a membrana celulósica porosa e o curativo com prata nanocristalina, em virtude de terem sido utilizados em um maior número de pacientes nos estudos avaliados.*

DESCRITORES: *Queimaduras. Unidades de queimados. Cicatrização. Desbridamento. Bandagens.*

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REVIEW ARTICLE

Parkinson's disease and wearable devices, new perspectives for a public health issue: an integrative literature review

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SUMMARY

Parkinson's disease is the second most common neurodegenerative disease, with an estimated prevalence of 41/100,000 individuals affected aged between 40 and 49 years old and 1,900/100,000 aged 80 and over. Based on the essentiality of ascertaining which wearable devices have clinical literary evidence and with the purpose of analyzing the information revealed by such technologies, we conducted this scientific article of integrative review. It is an integrative review, whose main objective is to carry out a summary of the state of the art of wearable devices used in patients with Parkinson's disease. After the review, we retrieved 8 papers. Of the selected articles, only 3 were not systematic reviews; one was a series of cases and two prospective longitudinal studies. These technologies have a very rich field of application; however, research is still necessary to make such evaluations reliable and crucial to the well-being of these patients.

KEYWORDS: *Parkinson's Disease. Wearable Electronic Devices. Technology. Review. Public Health.*

INTRODUCTION

Parkinson's disease (PD) is a progressive neurodegenerative disease and characterized mainly by three typical motor symptoms: bradykinesia, muscle rigidity, and resting tremors[1]. PD is the second most common neurodegenerative disease, with an estimated prevalence of 41 cases for every 100,000 individuals aged between 40 and 49 years and 1,900 cases for every 100,000 individuals aged 80 years or more. According to these calculations, respecting the differences of the populations studied, the diagnostic criteria and methods used, by 2030, there will be about 9 million people with PD[2].

Given this scenario, the therapeutic management of patients has been one of the main challenges, mainly due to the lack of instruments to properly measure the therapeutic response to the treatment instituted and the motor signs displayed by the patient in their daily lives[3].

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In this context, the implementation of smart technologies for PD applications has increased in recent years. In particular, wearable sensors, which are a fundamental aid for early diagnosis, differential diagnosis, and in the objective quantification of symptoms in outpatients[4]. The use of wearable technologies to measure daily data is an important tool that is currently viable to obtain frequent parameters for patient assessment, mainly because they demonstrate the reality of the individual's behavior outside of the clinical environment, which differs from the examination normally done in clinics.

Thus, there is an increasing demand for new and better technologies that are useful and clinically validated for the treatment or monitoring of diseases, PD included, even more so due its complexity and heterogeneity, which implies the need of clinical assessment and appropriate management, with constant analysis of symptoms, fluctuations, and observation of worsening of symptoms and progression of the disease[3,5-9]. Currently, PD diagnosis is based on the assessment of motor and non-motor symptoms, as well as a neurological assessment. However, the diagnostic methods and approaches for monitoring disease progression disease remain below the ideal for the management of PD[10], with failures or gaps that can and should be improved. For example, although highly relevant for PD, the use of clinical scales such as the *Unified Parkinson's DiseaseRating*(UPDRS), is restrictive, since it depends on the *patient's status* at the moment of the evaluation (there may be, for example, an assessment bias in patients who have the ON/OFF phenomenon on motor symptoms), it is limited by subjectivity and the clinical experience of the professional assessing the patient. Wearable devices, therefore, overcame many of these limitations by objectively quantifying results that are clinically relevant so that the test variations are reduced by their use[9,11,12]. The measurement of motor symptoms by wearable devices is, in general, accurate and comparable to more established methods, with some of its aspects already tested and validated. The criteria evaluated refers to most of the motor symptoms (tremors, bradykinesia, dyskinesia) and have presented mostly moderate to high equivalence to standard clinical scales (for example, UPDRS, Modified Bradykinesia Rating Scale, among others)[13].

Continuous long-term monitoring, therefore, has much more to offer in comparison to in-person clinical evaluations that may not reveal the true extent of symptoms[14,15]. Currently, such monitoring can be done from devices that utilize accelerometers, gyroscopes, magnetometers, and electromyography sensors, with possible uses such as the clinical observation of falls, tremors, bradykinesia, gait disorders, and mobility fluctuations[15]. The most appropriate way to measure the motor performance of patients seems to be the use of wearable devices based on inertial sensors, which can acquire data with a high sampling rate[13,16-18]. This has been developed for the assessment of several motor symptoms using a single or multiple systems.[19,21,14,22-24]

The main purpose of domestic monitoring is to provide optimal management of PD. Therefore, wearable devices with inertial sensors may represent an optimal solution for healthcare applications both in the clinical and domestic environment[12]. Under this perspective, the importance of wearable devices in the diagnosis[25] and management of PD is clear[9] since they can provide the physician with an understanding of the patient's scenario even in a simple evaluation[9].

METHODS

This is an integrative review; according to Whitemore and Knalf[26], the "term integrative originated from the integration of opinions, concepts, or ideas from research used in the method," which "highlights the potential to build science." Furthermore, an integrative review is a subtype of a systematic literature review, which can be subdivided into meta-analysis, systematic review, qualitative review, or integrative review.

Thus, in line with what is presented by Botelho et al.[27] and Redeker[28], this integrative review has the main objective of summarizing the state of the art of wearable devices used in PD patients. In addition, we also analyzed in which types of symptoms (motor or not) such technologies are used and if the data presented demonstrated superior monitoring by wearable devices in comparison with outpatient follow-up, or if these are complementary approaches.

The review consisted in searching the IEEEXplore, Lilacs, PubMed, SciELO, Arxiv, and ScienceDirectdatabases by using the following groups of descriptors (in accordance with the MeSH terms, DeCS, and Bireme): ("Monitoring, Ambulatory" OR "Wearable Electronic Devices" OR "Biosensing Techniques") AND "Parkinson Disease" AND "Motor Symptoms" AND ("Dis-

TABLE 1. DESCRIPTORS USED ACCORDING TO THE PICO METHOD FOR SYSTEMATIC REVIEWS.

Problem	Parkinson Disease AND Parkinson Disease AND Motor Symptoms
Intervention	Wearable Electronic Device OR Monitoring, Ambulatory or Biosensing Techniques
Comparison	-
Outcome	Disease Progression AND/OR Treatment Outcome

ease Progression" OR "Treatment Outcome"). These were reviewed following the PICO method for systematic reviews (Table 1).

The inclusion criteria were: original articles, of meta-analysis, systematic, or integrative review, published between 2011 and 2018, peer-reviewed, in English, with data related to the use of wearable devices in the therapeutic management of symptoms of PD patients. The exclusion criteria were papers on subjects unrelated to the research topic, gray bibliography, duplicate references, articles on books, written in languages other than English. Also, references that did not include any type of wearable sensor (device). On that basis, we initially retrieved 24 papers (Graph 1), of which, after reading of the titles and abstracts and applying the inclusion and exclusion criteria, seven remained for evaluation in their entirety. After that, we excluded one paper, which was a systematic review of all types of technologies in the bradykinesia evaluation of Parkinson's patients. However, it did not specifically evaluate the wearable devices. In addition, the references of the articles retrieved were evaluated manually in order to select other studies that had not been included during the database search. We added one more paper, a systematic review (Table 2), with a total of eight papers included in this review.

RESULTS

After the review, we found eight articles, which are listed in Table 2 with some of the conclusions by the authors of this paper after analyzing the data presented. Considering the data presented in Table 2, we noted a scarcity of articles whose objective is to demonstrate the longitudinal follow-up of PD patients through the use of wearable devices.

Out of the eight articles selected, only three were not systematic reviews; one was case series and two prospective longitudinal studies. Patel et al.[29] demonstrated in their study that by using a device called Mercurylive they could remotely assess two aspects of the UPDRS scale (Unified Parkinson's Disease Rating Scale), which is used mainly in the clinical environment, with the presence of the patient, to check, in particular, motor symptoms. The aspects evaluated in this study, as well as by the other two (Tzallas et al.[24]; Pastorino et al.[21]) are related to bradykinesia or daily motor fluctuations (ON/OFF phenomenon) (Figure 1). Considering that, in order to estimate the UPDRS scale, Patel et al.[29] showed that a longitudinal follow-up with evaluations in three days had an error of 0.4 points in relation to the clinical evaluation performed by a trained professional.

Tzallas et al.[24] used the Perform system (a prospective longitudinal study), which comprises three subsystems: a wearable device, a local-based unit, and a unit located at the hospital. With that, they

GRAPH 1. LIST OF THE NUMBER OF PAPERS FOUND IN THE RESPECTIVE DATABASES, WITH THE DESCRIPTORS USED.

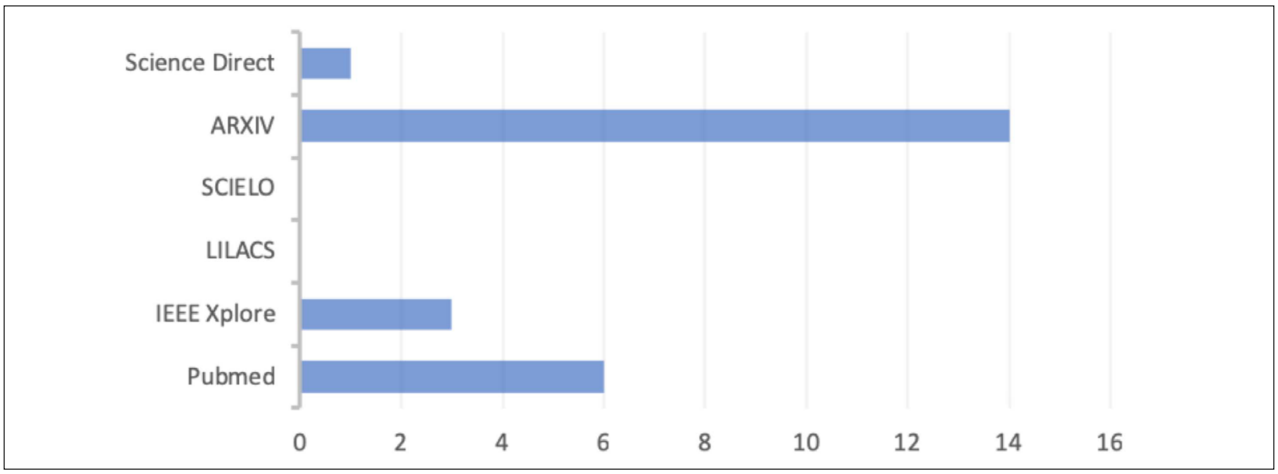


TABLE 2. LIST OF THE PAPERS SELECTED, THEIR GOALS, AND CONCLUSIONS.

AUTHORS/ YEAR	TITLE OF ARTICLE	TYPE OF STUDY	STUDY OBJECT	STUDY SUMMARY
Patel et al.[29], 2011	"Longitudinal Monitoring of Patients with Parkinson's Disease via wearable sensor technology in the home setting"	Prospective longitudinal study	Estimate the UPDRS score, by means of wearable devices (Mercurylive, developed by the authors), which will evaluate two aspects: stomping heel first on the floor repeatedly and alternating pronation and supination of both hands.	The authors concluded that it is possible to evaluate the UPDRS score in its integrity using wearable devices with an acceptable range of error. However, it is still a challenge to develop this type of technology that can be applied in the home of patients; it would be necessary to have techniques to deal with the uncontrolled environment of patients' homes.
Son et al.[30], 2018	"Mobility monitoring using smart technologies for Parkinson's disease in free-living environment"	Systematic review	Gather and review studies that tested the feasibility of technology (wearable devices) for non-ambulatory continuous monitoring of PD patients.	There are several wearable devices (WD) with different goals, such as to evaluate motor symptoms and their fluctuations or provide instant feedback (both positive and negative) to the patient about their posture. However, despite this myriad of WDs and the problems associated with its adoption and acceptance, they proved to be effective as an adjuvant factor to the therapeutic process of PD patients.
Pastorino et al.[21], 2013	"Preliminar results os ON/OFF detection using an integrated system for Parkinson's disease monitoring"	Case series	Assess the motor fluctuations throughout the day of PD patients (ON/OFF effects) by means of wearable devices. Such assessments are carried out in patients' homes (uncontrolled environment) and later compared with data collected from diaries kept by patients based on motor symptoms throughout the day.	It is concluded that wearable devices are a great tool to assess PD patients (particularly motor symptoms and their daily fluctuations) remotely so that the doctor can adjust doses or change medications. In addition, it is associated with a low cost for patients with chronic diseases. However, there is a need for greater accuracy of wearable devices so that they can be used indiscriminately.
Tzallas et al.[24], 2014	"PERFORM: a system for monitoring, assessment and management of patients with Parkinson's disease"	Prospective longitudinal study	Describe the technological system for remote management and monitoring of PD patients regarding their: characteristics; features compared to other systems; assessment of motor symptoms in PD patients; analyses and aid in the management of the disease.	The management and treatment of PD are difficult challenges since the treatment is different and individualized, and management requires the active participation of the patient for an assessment of the daily routine and feedback. It shows the types of analysis of the signs and symptoms by the system, in addition to pointing out that, with the Perform system, the health professional can have a remote, precise and efficient assessment of the state of the patient by means of gyroscopes and accelerometers, and the continuous analysis of motor symptoms, both quantitatively and qualitatively outside the hospital environment, especially regarding clinical information on medication response.
Ossig et al.[31], 2016	"Wearable sensor-based objective assessment of motor symptoms in Parkinson's disease"	Systematic review	Evaluate relevant data obtained by wearable devices based on sensors for assessing motor symptoms in PD patients. The research focused on systems based on accelerometers and/or gyroscopes.	It is concluded that although it has been shown that some devices or technologies are useful to distinguish between patients with or without PD and provide access to quantified methods of continuous monitoring, the feasibility of data obtained from devices based on wearable sensors remains unclear as a defining tool for trials and to improve routine clinical care of PD patients.
Del Din et al.[9], 2016	"Free-living monitoring of Parkinson's disease: lessons from the field"	Systematic review	Generally analyze the current state of the use of wearable devices by patients outside the clinical environment and describe the benefits and disadvantages, future developments, evidence and usefulness, and main challenges of passive patient evaluation devices regarding PD, in the precise detection and measurement of clinical data.	The advantages of the use of wearable devices in PD have reached a stage in which they surpass evaluations that require attention and concentration, in addition to scales (although important) that are subjective and dependent on the patient. Therefore, devices can quantify relevant clinical results and response to treatment, thus reducing variations in assessments and improving patient engagement in the treatment. In general, technologies are a necessity and promising, but further studies and development are still needed, along with a multidisciplinary approach of sectors, so that they can be finally adopted clinically and broadly.
Godinho et al.[32], 2016	"A systematic review of the characteristics and validity of monitoring Technologies to assess Parkinson's disease"	Systematic review	Perform a systematic review to list, compare, and classify technological devices (wearable, not wearable, and hybrids) used to evaluate the motor symptoms of PD patients.	It is concluded that there is a rise in the development of technologies to evaluate PD patients (with clinical evaluations or not and related to motor symptoms or not). However, attention must be paid to the clinical-measurement properties of these devices.

found an accuracy of more than 80% to identify daily motor fluctuations (ON/OFF phenomenon), with an accuracy of 87.5% to identify resting tremors, 74.5% for bradykinesia, 79% for changes in gait, and 85.4% of accuracy for patients in the ON stage. The most significant error was of 0.79 in the identification of changes in gait.

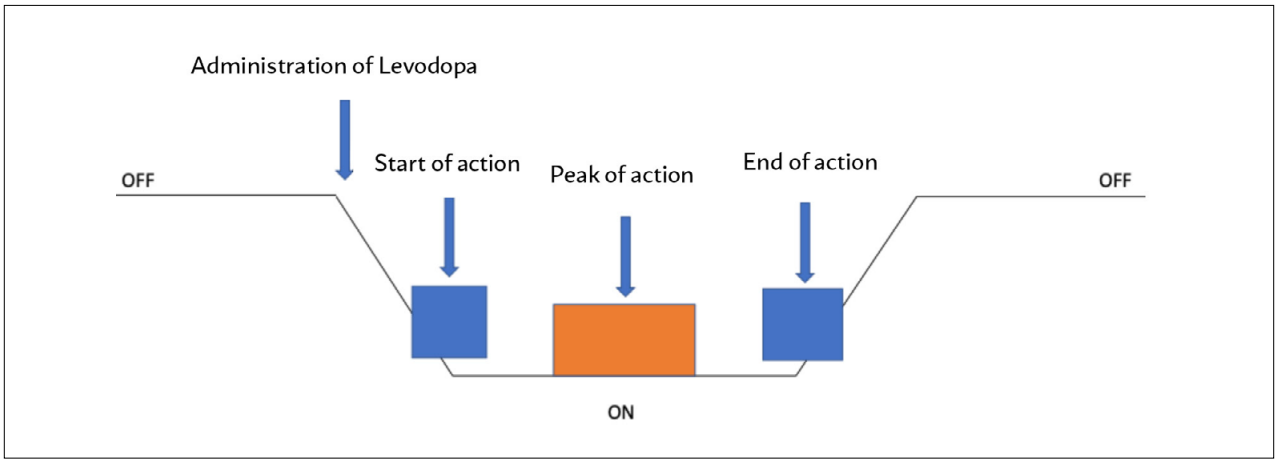
Pastorino et al.[21], in a case series, assessed, for two consecutive days, the ON/OFF phenomenon by comparing the evaluation of wearable device with a self-assessment by the patient performed every 30 minutes, with three possible answers: OFF, ON with dyskinesia, and ON without with dyskinesia. We obtained an accuracy of 93.7% using the wearable device to identify motor fluctuations, compared with the self-assessment. They was also evaluated the comfort of using the technology, and 16% did not consider the device comfortable.

The other studies selected (Son et al.[30]; Ossig et al.[31]; Del Din et al.[9]; Godinho et al.[32]) are systematic reviews that compiled studies, still incipient, about the use of wearable devices in PD patients.

DISCUSSION

Wearable devices mark the beginning of a new era in medical assistance, taking medicine to unimaginable new places and providing more precise and efficient diagnostics and treatments[33]. In addition, the space occupied by this type of technology in modern medicine is evident. PD is a nosological entity that can be remotely evaluated by means of wearable devices[9,21,24,29-32,34], which can be defined as technologies that can be, literally, worn by the patient without interfering in activities of daily life or the progression of the disease. That is, they can be watches or sensors that send data to centrals (which may be located in the assistant physician clinic), for future evaluation of the evolution of the clinical condition[35-40] (Figure 2). There are several devices, still under development, which evaluate different aspects of PD patients to assess the progression of symptoms, motor or not, or even to estimate some clinical scales, such as the *Unified Parkinson's Disease Rating Scale* (UPDRS)[21,30,34]. The Perform study aimed to describe the technological system for remote management and monitoring of PD patients regarding their: characteristics; features compared to other systems; assessment of motor symptoms in PD patients; analyses, and aid in the management of the disease.[24]. It is of great value for clinicians who follow-up these patients if these wearable devices can assist in monitoring patients, either in the initial approach, in diagnosis, prognosis, or even during treatment. In addition, it is important to check if there is a relevance of these evaluations by means of technologies comparing them to the evaluation performed by physicians. Hasan et al.[34] conducted a study to estimate the UPDRS scale through evaluations conducted by patients and devices, which were then compared against each other and subsequently compared with clinical evaluations carried out by neurologists. However, they concluded that the use of such technologies was not superior to clinical assessments, despite having minimal errors in estimating the scale value[34]. It is worth noting that the diagnosis of PD is eminently clinical[41]. Moreover, in most cases, the monitor-

FIGURE 1. DAILY MOTOR FLUCTUATIONS IN PATIENTS WITH PARKINSON'S DISEASE (ON/OFF PHENOMENON).



ing and treatment are also performed at outpatient clinics, except for patients who require deep brain stimulation[42]. Thus, it becomes clear that the use of technologies must demonstrate superior data to those already well known from clinical assessments, using once again the UPDRS scale as an example, which is summarized in clinical parameters by which the physician evaluates the progression of the disease and, most importantly, the motor symptoms, as well as the ON/OFF phenomenon, very common in patients with PD[21].

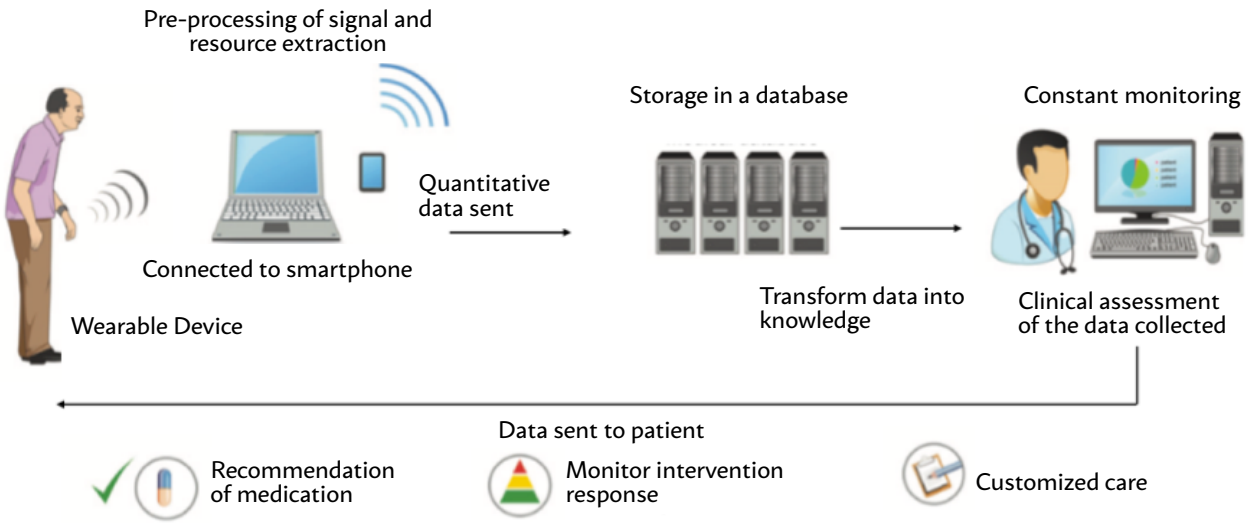
Studies have been developing wearable devices to evaluate and monitor patients with Parkinson's disease[9,21,24,29-32,34]. However, after analyzing the scope of each of them, it is noted that most focus on the assessment of motor symptoms, which are already very well known. In addition, not all motor symptoms are assessed, most devices assess, basically, bradykinesia and, consequently, the development or not of the ON/OFF phenomenon. In addition, those that aim to estimate some clinical scale do so by means of a few aspects, in comparison with the various tests performed in outpatient evaluations. It is undeniable that with the knowledge of artificial intelligence and technology in medicine, some medical approaches have become obsolete. In the case of patients with Parkinson's Disease, wearable devices are able to carry out a full evaluation of the patient at times when it is not possible for a physician to do the same. Consequently, they can detect oscillations in symptoms that do not occur during an outpatient evaluation performed by neurologists or other trained professionals[34].

However, studies that assess the use of wearable devices are still few and bring previous results and a small sample of patients, so they are not representative of the entire population of PD patients. In addition, these technologies were not superior to clinical assessments, even though they cannot identify symptoms fluctuations throughout the day. Thus, further studies are necessary to assess other aspects of PD, such as non-motor symptoms that predict the prognosis of patients. Attention should also be paid to the wearability of these devices, i.e., their comfort, and the cost they will generate for health systems or individuals with the disease. Therefore, it is evident the need for controlled and prospective that confirm their effectiveness, since there are still some points to be improved, such as the duration of batteries, diagnosis differentiation between other motor disorders, and predictive values for PD or other conditions in pre-motor stage or very early diagnosis, which are still considered "enigmatic"[16,21].

Considering the above, in agreement with Rocha et al.[43], wearable technologies used in PD must include the following features of any wearable device: monitoring, data transmission, analysis, diagnosis, and therapy, being able to minimize public health problems related to these patients.

The present study has some limitations; the technologies presented herein are restricted to those mentioned by scientific papers published

FIGURE 2. FIGURE ILLUSTRATING HOW WEARABLE DEVICES ARE USED FOR THE REMOTE MONITORING OF CLINICAL MANIFESTATIONS IN PATIENTS WITH PARKINSON'S DISEASE.



in indexed journals. However, there may be other technologies that are in use and feature more reliable parameters than those clinically assessed. In addition, other factors should be taken into account, such as the populations in which technology was applied, the stage of the disease, as well as adherence to the pharmacological treatment established by the physician. These parameters are of paramount importance in patient assessment and in the results obtained with such technologies. We should also remember that some technologies may be in development, considering the results presented by these studies in order to improve the assessment and monitoring of patients with Parkinson's Disease.

CONCLUSION

The use of wearable devices is becoming very important for the development of medical care. Several companies are investing in technologies that are able to check motor fluctuations, such as in PD, or even identify the heart rate and possible acute arrhythmias. Thus, such technologies become allies of doctors, aiding in the diagnosis of certain diseases or in the monitoring to evaluate how the patient adapts to the therapy established.

PD is characterized as a public health issue, especially among the elderly population, and can benefit from these wearable devices, whether it is to evaluate daily fluctuations of motor symptoms, such as the ON/OFF phenomenon, or to predict the results of clinical scales, such as the UPDRS.

However, there are still several barriers to overcome because the results presented are still scarce and do not demonstrate superiority to the evaluations performed on an outpatient basis by the physician. In addition, it is of utmost importance that the various aspects that make up the clinical condition of patients are assessed, such as the motor symptoms (already evaluated, but not in its entirety) and the non-motor as well, which have not been evaluated by any wearable device. In short, these technologies can have very broad applications, yet more research is still needed for these assessments to be reliable and crucial to the well-being of patients.

RESUMO

A doença de Parkinson figura como a segunda doença neurodegenerativa mais comum. Sua prevalência é estimada de 41 por 100.000 pessoas entre 40 e 49 anos a 1.900 por 100.000 pessoas com 80 anos ou mais. Baseando-se na essencialidade de averiguar os dispositivos vestíveis que possuem evidências clínicas literárias e com o objetivo de analisar as informações reveladas por tais tecnologias, temos a construção deste artigo científico de revisão integrativa. Trata-se de uma revisão integrativa que tem como principal objetivo realizar um sumário do estado da arte de dispositivos vestíveis utilizados em pacientes com doença de Parkinson. Após realizada a revisão, obtiveram-se oito artigos. Pode-se observar que dos artigos selecionados, apenas três não eram revisões sistemáticas, sendo um deles uma série de casos e outros dois, estudos longitudinais prospectivos. A utilização dessas tecnologias possui um campo muito rico para atuar, contudo ainda são necessárias pesquisas para que tais avaliações sejam fidedignas e cruciais para o bem-estar desses pacientes.

PALAVRAS-CHAVE: *Doença de Parkinson. Dispositivos eletrônicos vestíveis. Tecnologia. Revisão. Saúde pública.*

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