Rastreio de Ocorrência de Quedas e Análise Retrospetiva numa População com Doença de Parkinson

Screening the Occurrence of Falls in a Parkinson's Disease Population and Retrospective Analysis

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Resumo

Introdução: As quedas são comuns na doença de Parkinson aumentando a incapacidade e a morbidade. A participação em programas de reabilitação e a modificação de fatores de risco podem melhorar os resultados. Pretendeu-se caraterizar uma população com doença de Parkinson, nomeadamente a autoperceção do equilíbrio e a participação em programas de reabilitação e encontrar possíveis associações com a ocorrência de quedas.

Métodos: Estudo retrospetivo е transversal, compreendendo todos os doentes com doença de Parkinson de uma Unidade de Saúde Familiar. Foram definidos dois grupos, os que caíram e os que não caíram anteriormente. Os fatores sociodemográficos, a participação em programas de reabilitação, a pontuação na escala Activities-specific Balance Confidence (ABC-16) e outros fatores de risco foram colhidos através de questionário administrado por telefone e complementado com os registos clínicos. Foi realizada uma análise comparativa entre ambos os grupos, foi calculado o valor de corte para a pontuação da escala ABC-16 e foi realizada uma regressão logística para determinação do efeito das variáveis na probabilidade de ocorrência de quedas.

Resultados: Trinta e quatro doentes foram elegíveis após aplicação dos critérios de exclusão, dos quais 29,4% eram fisicamente ativos. No ano precedente, 41,2% realizaram programa de reabilitação e 18 reportaram pelo menos um episódio de queda. O modelo de regressão logística explicou 70% da variância das quedas reportadas (p <0,005, sensibilidade 87%; especificidade 94%): a pontuação baixa na escala ABC-16 (OR: 0.94), a não participação em programas de reabilitação (OR: 15,3) e o género feminino (OR: 11,4) aumentaram a probabilidade de episódios de queda durante o ano precedente. Foi determinado o valor de corte de 63 para a pontuação da escala ABC-16.

Conclusão: A aplicação remota de um questionário incluindo a escala ABC-16 pode representar uma ferramenta de rastreio para avaliar o risco de queda na doença de Parkinson. O género feminino e a não participação em programas de reabilitação esteve associada a história de quedas. Estes achados enfatizam a necessidade de implementação de programas de prevenção de quedas nesses doentes.

Palavras-chave: Doença de Parkinson/complicações; Doença de Parkinson/reabilitação; Equilíbrio Postural; Quedas Acidentais/prevenção e controlo.

Abstract

Introduction: Falls are common in Parkinson's disease increasing disability and morbidity. Rehabilitation programs and modification of risk factors can improve outcomes. We aimed to characterize a Parkinson's disease population, its self-perceived balance and participation in rehabilitation programs and to find possible associations with the occurrence of falls.

Methods: Cross-sectional and retrospective study, comprising all Parkinson's disease patients of a family health unit. Two groups, fallers and non-fallers, were defined. Sociodemographic factors, participation on RP, Activities-specific Balance Confidence (ABC-16) scale score and other risk factors were recorded through questionnaire

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administration by telephone and complemented with clinical records. A comparative analysis was made between both groups, a cutoff value for ABC-16 scale score was determined and a logistic regression was performed to ascertain variables effect on the likelihood of falls occurrence.

Results: Thirty-four participants were eligible after exclusion criteria, of which 29.4% were physically active. In the last year, 41.2% were on a rehabilitation program and 18 reported at least one fall. Logistic regression model explained 70% of the variance in reported falls (p < 0.005, sensibility 87%; specificity 94%): low ABC-16 score (OR: 0.94), non-participation in rehabilitation program (OR: 15.3) and female gender (OR: 11.4) had increased likelihood of falling episodes in the last year. A cutoff value of 63 for ABC-16 score was determined.

Conclusion: The remote application of a questionnaire including ABC-16 scale may represent a screening tool to assess fall risk in Parkinson's disease. Female gender and non-participation on rehabilitation programs were associated with history of falling. These findings emphasize the need of fall prevention programs implementation.

Keywords: Accidental Falls/prevention & control; Parkinson Disease/complications; Parkinson Disease/ rehabilitation; Postural Balance.

Introduction

Parkinson's disease (PD) is the second most common neurodegenerative disease in the world¹ and its prevalence in Portugal is estimated to be 1.29/1000 inhabitants.² PD is a progressive disease affecting multiple neural systems, mainly basal ganglia, resulting from an interaction process between genetic and environmental risk factors.³ It is known by typical motor manifestations, particularly bradykinesia, rigidity, resting tremor, gait changes and postural instability.⁴ Parkinsonian gait is frequent and responsible for significant disability burden. It is characterized by short stride length, slow cadence, increased duration of double limb support phase, reduced upper limb swing and festination.⁵ Turns are slow and executed through several small steps and a freezing phenomenon may be present. Postural instability is manifested by flexed posture, impaired trunk rotation, abnormal anticipatory postural adjustments and weak reactive postural responses.6,7

Gait pattern changes and postural instability stand for high prevalence of falls in these patients.⁸

Falls are common in PD (40%-70%) and represent a major concern secondary to adverse outcomes.^{8,9} Physical damage (e.g. fractures, around 35%) and negative

psychological impact (e.g. fear of falling – FoF) lead to mobility limitation, impairment of activities of daily living (ADL), physical deconditioning, higher institutionalization risk and increased mortality.^{10,11}

Non-modifiable risk factors for fall in PD include the occurrence of falls in the previous year,¹² disease severity, longer disease duration, high levodopa dose and use of neuroleptics.13-15 Modifiable risk factors for fall in PD comprise low steadiness threshold, muscular weakness at the knee and tibiotarsal joints, impaired anticipatory postural adjustments, weak reactive postural responses, gait abnormalities, freezing, FoF and dual-task defective performance.^{6,11,16-19} Additionally, there are general risk factors for fall which can be divided in intrinsic and extrinsic. Intrinsic include older age, ADL dependence level, visual impairment, hearing loss, musculoskeletal alterations, rheumatic diseases, psychopathology, cognitive impairment, balance disorders, cardiovascular disease, diabetes mellitus, urinary incontinence, previous stroke and drugs. Extrinsic include footwear type, in-home obstacles, loose carpets, paving material, stair use, living alone, among others.²⁰

In line with above mentioned problems, healthcare overuse, increasing financial expenses and expected rise in PD prevalence along the next decades, it is plausible to develop preventive strategies focused on functional disability related to PD.²¹ Approaching methods of neuromotor rehabilitation in PD aim to improve muscular strength, aerobic capacity, balance, gait and functional mobility.²² Exercise techniques showed a significative reduction in fall rate (approximately 60%), either short or long-term.²³ Multimodal interventions have long-term favorable effects on motor signs, ADL and PD severity. Gait or balance training revealed positive outcomes regarding performance, gait capability and reduction of falls, that persist 3 to 12 months after intervention. Training programs focused on progressive endurance and aerobic capacity have great benefit on muscular strength, balance, functional mobility and quality of life over 12 months.²⁴

There are several measurement instruments to evaluate PD patients, based on scales and tests designed to assess disease severity, aerobic capacity, gait pattern, functional mobility, balance, fall risk and FoF. Considering the last three, the Activities-specific Balance Confidence-16 (ABC-16) scale is a measure of balance self-efficacy that evaluates balance while performing sixteen specific ADL, in a wide spectrum of difficulty, and can be self-ministered or applied through telephone or in-person interview.²⁵ A Portuguese version was conceived and validated with good intra and interobserver reliability and internal consistency assessing balance self-confidence in several ADL.²⁶ In a subsequent study a correlation was found between its score and risk of falling.²⁷

The authors main objective is to study the impact of rehabilitation programs (RP) addressing motor and balance impairments, physical activity (PA) practice and self-perceived balance (measured through ABC-16 score) on the risk of falling in patients with PD in a Primary Health Care (PHC) setting. As secondary objectives, it is intended to perform a descriptive and comparative analysis of patients' characteristics and known risk factors for fall, namely ADL dependence level (using Barthel scale), comorbidities, drugs, footwear type and spatial home conditions.

Methods

This is an observational, cross-sectional, retrospective and analytic study, performed between January and April, 2018. The study was approved by local institutional review board and ethics committee. In order to avoid potential adverse impact on representativeness and lower statistical significance, we decided to study every patient with diagnosis of PD. Population data was collected by census of patients listed as having PD in an urban family health unit at January 31, 2018. A nominal list of patients with PD was extracted via electronic clinical process, identified by code N87 of International Classification of Primary Care, second edition.

Exclusion criteria were bedridden patients, under palliative care, institutionalized, with parkinsonic syndrome not PD, bilateral deafness, speech disability, dementia and absence of valid phone contact.

Formal oral and written consent was requested to family physicians. Patients were contacted by phone directly by the researchers, who explained study objectives and ensured right of refusal, anonymization, confidentiality and data usage only for statistical purposes. Upon acceptance and given oral consent, the patient was enrolled and answered a questionnaire previously subjected to pilot testing, comprising six sections: sociodemographic characterization, anthropometrics and personal habits, autonomy, medical history, participation in RP, and extrinsic factors. Every participant was encoded with a sequential number, recorded in an encrypted database protected by password. Two scales were applied: ABC-16 and Barthel. ABC-16 scale comprises 16 questions on balance selfconfidence during 16 ADL, measured from 0 to 100% in multiples of 10, scoring a total minimum of 0 and maximum of 1600 which is subsequently divided by 16 to obtain an average score. ABC-16 scores of <50, 50-80, >80 indicated low, moderate and high level of balance confidence, respectively, in older adults. The Portuguese version of the ABC-16 scale was used in this study.²⁶

PA was considered according to World Health Organization's standards²⁸ (³150 minutes of moderate-intensity aerobic PA

throughout the week or ³75 minutes of vigorous-intensity aerobic PA throughout the week or an equivalent combination of both).²⁸

RP consisted of conventional physical therapy sessions encompassing gait, balance, cueing and strength training performed in clinic rehabilitation services after referral by family medicine physicians.

Our population was split in two groups according to the occurrence or nonoccurrence of fall episodes in the previous year. Comparative analysis between the two groups was performed in relation to gender, age, body mass index, PA, participation in RP, ABC-16 score, Barthel index score, home conditions, alcohol and tobacco use, date of PD diagnosis, current anti-parkinsonian drugs and other drug classes, comorbidities, home conditions, most commonly used footwear and use of mobility aids. Mann-Whitney U-test was used to compare differences in continuous variables. Chi-square tests were used to compare nominal variables between the two groups.

The receiver operating characteristic (ROC) curve for ABC-16 score was generated and the best cut-off value was determined. A logistic regression using stepwise forward selection (likelihood ratio) was also performed to ascertain the effect of some of the studied variables on falls occurrence in the previous year.

Results

A total of 61 patients were listed as having PD. After application of exclusion criteria 34 patients were eligible to participate. The summarized demographic and clinical data are presented in Table 1. Based on reported falls in the previous year, 16 individuals reported no falls (non-fallers) and the other 18 individuals were classified as fallers in which 10 reported two or more falls. Seventeen were independent, 9 mildly dependent and 8 moderately dependent in ADL. Fourteen enrolled a RP in the previous year comprising a median of 85 rehabilitation sessions and only 5 were physically active. Eleven individuals were using mobility aids.

Fallers group accounted 77.8% women compared to 25.0% in non-fallers group (p = 0.002). Participation on RP was greater for non-fallers group with 11 patients performing a median of 36 rehabilitation sessions compared to only 3 patients that participated in RP in fallers group (p = 0.002).

Median ABC-16 score in fallers was 37.5 and in non-fallers was 70.0. The four activities with the lowest reported confidence were "standing on chair to reach something" (item 6), "walk in crowded mall/bumped" (item 13), "step onto or off an escalator while holding onto parcels" (item 15) and "walk outside on icy sidewalks" (item 16).

Table 1 - Characterization of our studied population.

	M (minmax.) / M (IR) / N (%)				
Parameter	ΔII	Non-Fallers	Fallers	р	
		(n=16)	(n=18)		
Reported falls – M (minmax.)	1.00 (0-12)	0	2 (1-12)	-	
Age – years, M (IR)	77.5 (19)	75.0 (18)	80.0 (16)	0.422	
Gender – female, N (%)	18 (52.9%)	4 (25.0%)	14 (77.8%)	0.002	
Body Mass Index - kg/m2, M (IR)	28.69 (7.0)	28.36 (6.0)	29.48 (10.0)	0.384	
Years since PD diagnosis – M (IR)	4 (5)	4 (4)	3 (6)	0.878	
Comorbidities – N (%)					
Arterial hypertension	29 (85.3%)	14 (87.5%)	15 (83.3%)	0.732	
Diabetes	8 (23.5%)	3 (18.8%)	5 (27.8%)	0.536	
Dyslipidemia	23 (67.6%)	11 (68.8%)	12 (66.7%)	0.897	
Obesity	15 (44.1%)	6 (37.5%)	9 (50.0%)	0.464	
Cardiac conduction disorder	4 (11.7%)	2 (12.5%)	2 (11.1%)	1.000	
Hearing loss	6 (17.6%)	2 (12.5%)	4 (22.2%)	0.660	
Vertigo	4 (11.8%)	2 (12.5%)	2 (11.1%)	1.000	
Reduced visual acuity	10 (29.4%)	5 (31.3%)	5 (27.8%)	1.000	
Osteoarticular disorder	21 (61.8%)	9 (56.3%)	12 (66.7%)	0.533	
Depressive disorder	12 (35.2%)	4 (25.0%)	8 (44.4%)	0.236	
History of stroke	4 (11.8%)	2 (12.5%)	2 (12.5%)	1.000	
Alcohol consumption - N (%)	9 (26.5%)	5 (31.3%)	4 (22.2%)	0.703	
Tobacco consumption – N (%)	3 (8.8%)	1 (6.2%)	2 (5.5%)	1.000	
Anti-Parkinsonian drugs - mg/day, M (IR)				-	
Levodopa	300.0 (325.0)	300.0 (250.0)	300.0 (450.0)	0.606	
Carbidopa	81.2 (81.3)	100.0 (75.0)	75.0 (112.5)	0.683	
Other drugs – N (%)					
Psychotropic medication	25 (73.5%)	11 (68.8%)	14 (77.8%)	0.703	
Antihypertensive drugs	31 (91.2%)	14 (87.5%)	17 (94.4%)	0.591	
NSAID	3 (8.8%)	0 (0%)	3 (16.7%)	0.230	
Narcotic pain medication	6 (17.6%)	3 (18.8%)	3 (16.7%)	1.000	
Statins	14 (41.2%)	6 (37.5%)	8 (44.4%)	0.728	
Anticholinergic drugs	2 (5.9%)	1 (6.3%)	1 (5.6%)	1.000	
Participation on Rehabilitation Program – N (%)	14 (41.2%)	11 (68.7%)	3 (16.7%)	0.002	
Rehabilitation Sessions - M (minmax.)	0 (0-220)	36 (0-220)	0 (0-20)	0.002	
Physical activity according to WHO standards – N (%)	10 (29.4%)	7 (43.8%)	3 (16.7%)	0.084	
Home conditions – N (%)				1	
- Staircase	23 (67.6%)	10 (62.5%)	13 (72.2%)	0.545	
- Handrail	18 (52.9%)	9 (56.3%)	9 (50.0%)	0.716	
- Elevator	4 (11.7%)	3 (18.8%)	1 (5.6%)	0.323	
- Rugs	18 (52.9%)	8 (50.0%)	10 (55.6%)	0.746	
- Tile pavement	16 (47.1%)	7 (43.8%)	9 (50.0%)	0.716	
- Carpet pavement	5 (14.7%)	2 (12.5%)	3 (16.7%)	1.000	
- Wooden pavement	17 (50.0%)	9 (56.3%)	8 (44.4%)	0.732	
- Bathroom handrail	5 (14.7%)	4 (25.0%)	1 (5.6%)	0.164	

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Most commonly used footwear - N (%)				
- Low or no heel	21 (61.8%)	8 (50.0%)	13 (72.3)	0.183
- Slippers	13 (38.2%)	8 (50.0%)	5 (27.9)	
Mobility aids - N (%)	11 (32.35)	5 (31.25)	6 (33.35)	0.897
Barthel index score (out of 100) – M (IR)	92.5 (45.0)	100.0 (45.0)	70.0 (45.0)	0.266
ABC-16 score (%) – M (IR)	55.6 (45.0)	70.0 (20.0)	37.5 (40.6)	0.001
Item 1	75 (50)	90 (30)	60 (38)	0.064
Item 2	50 (53)	70 (38)	45 (50)	0.015
Item 3	50 (45)	70 (80)	40 (33)	0.002
Item 4	55 (45)	85 (43)	50 (23)	0.005
Item 5	40 (53)	70 (45)	35 (35)	0.008
Item 6	30 (60)	50 (38)	5 (40)	0.01
Item 7	70 (55)	85 (38)	50 (45)	0.05
Item 8	80 (45)	90 (35)	60 (43)	0.009
Item 9	60 (50)	90 (30)	50 (50)	0.003
Item 10	60 (53)	80 (43)	40 (45)	0.004
Item 11	50 (45)	70 (38)	30 (43)	0.001
Item 12	55 (60)	75 (28)	25 (33)	0.002
Item 13	35 (50)	55 (28)	10 (20)	0.002
Item 14	40 (53)	70 (48)	25 (40)	0.001
Item 15	25 (60)	55 (55)	15 (33)	0.002
Item 16	20 (49)	50 (48)	10 (30)	0.005

N (%) – number of cases and respective proportion, M – median, min. – minimum, max. - maximum, IR – interquartile range, ABC – activities-specific balance confidence, NSAID – nonsteroidal ant-inflammatory drugs, PD – Parkinson's disease, SD – standard deviation, WHO – World Health Organization.

We did not find statistically significant differences between fallers and non-fallers for other known risk factors such as age, disease duration, ADL dependence level (Barthel index score), visual impairment, hearing loss, balance disorders, cardiovascular disease, diabetes, depressive disorder, drugs, footwear type and home conditions.

Using the ROC curve for ABC-16 score (Fig. 1) a cutoff value of 63 can distinguish fallers from non-fallers with a sensibility of 89% and a specificity of 69%. The area under the ROC curve was 0.816 (95% CI 0.67-0.97), providing an excellent level of discrimination.

The stepwise forward selection for logistic regression resulted in a model, presented in Table 2, that included ABC-16 score, gender and participation on RP. This model was statistically significant ($\boxtimes 2=25.233$, p < 0.0005). The model explained 70% of the variance in the reported falls and correctly classified 91% of cases (sensitivity 87%, specificity 94%). Gender (OR: 11.40), ABC-16 score (OR: 0.94) and participation on RP (OR: 15.29) were all statistically significant.



Figure 1 - Receiver operating characteristic (ROC) curves for determining the optimal cutoff ABC-16 score. The area under the ROC curve 0.816 (95% CI 0.67-0.97).

	в	SE	Wald	df	n	Odds Ratio	95% C.I. for Odds Ratio	
		0.2.	Wald		P		Lower	Upper
ABC-16 score	- 0.07	0.03	4.97	1.00	0.03	0.94	0.88	0.99
Gender	2.43	1.22	3.99	1.00	0.05	11.40	1.05	123.96
Non-Participation on rehabilitation programs	2.73	1.19	5.29	1.00	0.02	15.29	1.50	155.97
Constant	0.71	1.47	0.23	1.00	0.63	2.04		

Table 2 - Logistic regression parameters that predicts likelihood of falls occurrence in the previous 1 year based on gender,ABC-16 score and participation on rehabilitation programs.

Note: Gender is for females compared to males.

ABC-16 - activities-specific balance confidence; CI - confidence interval; SE - standard error.

Discussion

We found that lower balance confidence was associated with an increased likelihood for the occurrence of falls in the previous year particularly those with an ABC-16 score <63. ABC-16 score combined with gender and participation in RP showed greater accuracy for prediction of fall occurrence. Non-participants in RP and females had 15 times and 11 times higher odds, respectively, of reporting at least one fall in the previous year compared to the opposite group.

Female gender is considered a risk factor for falls in elderly.^{20,29-34} With age executive functions decline³⁵ and gait variability³⁶ is more pronounced in women than in men. In PD there are more prevalent symptoms in women compared to men which can increase the risk of falling, mostly a reduction in visuospatial cognition, postural instability, dyskinesias and PD-associated depression.³⁷ Considering the higher rates for fall-related injuries, principally fractures, among women,³⁰ a fall prevention strategy should be prioritized for women with PD.

ABC-16 score as a measure of perceived balance ability in PD is related to falls occurrence. Median ABC-16 score for fallers was 55.6 and a cutoff value of 63 was determined. Cole MH *et al* and Mak MK *et al* established that ABC-16 score in PD was a significant predictor of future recurrent falls.^{38,39} One study demonstrated that ABC-16 score <69 at baseline was a strong predictor of future recurrent falls in people with PD.¹¹ Foongsathaporn *et al* found a negative correlation between the number of falls in the previous month and a mean ABC-16 score.⁴⁰

Higher levels of falls self-efficacy (measured with ABC scale) are related to lower levels of fear of falling and the former mediates the effects of the latter on functional outcomes.⁴¹ Higher levels of FoF is associated with greater knee muscle weakness, increased gait instability and postural difficulty.⁴²

FoF should be addressed to avoid negative consequences of activity restriction and reduced quality of life and effort should be made to increase balance confidence.⁴³ Specific activities with the lowest scores were the same described by Foongsathaporn *et al* which are predominantly related to switching of movements in vertical orientation.⁴⁰ Perception of verticality is affected in PD patients and along with disturbed processing of graviceptive pathways, postural instability occurs.⁴⁴ Therefore, those activities should be cautiously performed and under supervision if possible.

Falls and FoF are associated with less PA.⁴⁵ Only 29.4% were physically active according to WHO recommendations. Non-fallers group accounted more physically active individuals than fallers group, however with no statistically significant difference probably due to the small population size.

Non-participation in RP which included conventional physiotherapy was predictor of falls occurrence. Conventional physiotherapy comprises gait and balance training, cueing, strength training and other falls prevention strategies which improves gait speed, step length, walking and turning, balance and motor disabilities. All these interventions are effective in enhancing balance confidence and reducing the risk of falls in older people^{42,46-48} and certainly explain our results. Another advantage settles on full supervised environment that is particularly important to reduce falls in patients with high severity disease.⁴⁹

Group or home-based fall prevention exercise programs also proved to reduce fall events, particularly those covering muscle strengthening and balance training.⁵⁰ Such programs can be managed in PHC setting and may be cost-effective.⁵¹ Fall prevention strategies should feature physical activity and address multiple risk factors such as home conditions, footwear modifications, drug therapy optimization and cognitive behavioral education. A strength of authors' approach was to minimally influence data collection through standardized interview by the same investigator. It was also valuable the articulation between primary and secondary healthcare, optimizing PD management and increasing awareness to higher risk patients that may benefit the most.

Our study had some limitations. We recognize possible selection bias related to coding bias, where some patients could not have been classified as having PD and where not included in the study. Consequently, population's reduced size may limit our findings, reducing statistical significance of several variables. During data collection, we perceived a low health literacy of participants, which may lead to misunderstanding of questions and inherent difficulty on ABC-16 scale application. Also, a recall bias on selfreporting of events and falls could adversely impact our conclusions. As we complemented data with clinical records, there is a possible registration bias of comorbidities and clinical aspects related to PD assessment and control. We could not compare the RP in clusters due to high heterogeneity, encompassing a wide range of specific exercises and techniques. The retrospective component of our work could not properly assess the impact of the studied variables on future balance and occurrence of falls, however fall history is a significant factor in predicting future recurrent falls.^{12,15,50,52} Finally, precaution is required when extrapolating to populations from other regions as community and health resources may be different and accessibility to optimized management can be limited, compromising better outcomes.

Conclusion

In conclusion, this study showed that the remote application of a questionnaire with ABC-16 scale, a self-perceived balance confidence scale, can serve as a screening tool to determine fall risk in PD. Female gender and nonparticipation on RP addressing impairments in PD were associated with history of falling in the previous year. These findings reinforce the need to increase the accessibility of fall prevention programs in PHC setting. Such programs should include proper addressment of postural, gait stability and balance confidence as well as implementation of multifactorial intervention strategies.

Conflitos de Interesse: Os autores declaram a inexistência de conflitos de interesse na realização do presente trabalho. Fontes de Financiamento: Não existiram fontes externas de financiamento para a realização deste artigo. Confidencialidade dos Dados: Os autores declaram ter seguido os protocolos da sua instituição acerca da publicação dos dados de doentes. Proteção de Pessoas e Animais: Os autores declaram que os procedimentos seguidos estavam de acordo com os regulamentos estabelecidos pelos responsáveis da Comissão de Investigação Clínica e Ética e de acordo com a Declaração de Helsínquia da Associação Médica Mundial. Proveniência e revisão por pares: Não comissionado; revisão externa por pares.

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