

Simplified International Index of Erectile Function (IIEF-5) and Coronary Artery Disease in Hypertensive Patients

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Abstract

Background: Erectile Dysfunction (ED) is associated with increased risk of coronary artery disease (CAD).

Objective: To evaluate the association between ED, determined by the Simplified International Index of Erectile Function (IIEF-5) and CAD.

Methods: This was a cross-sectional cohort study that evaluated 263 hypertensive patients (55 [50-61] years). ED was assessed through the IIEF-5 and CAD by the history of previous myocardial revascularization and/or coronary angiography.

Results: The IIEF-5 correlated with creatinine clearance [CrCl] ($Rho = 0.23$, $p < 0.001$) and age ($Rho = -0.22$, $p < 0.001$). Forty-two patients had CAD, and IIEF-5 was able to discriminate them (area under the ROC curve = 0.63, $p = 0.006$). Patients were divided into two groups: IIEF-5 ≤ 20 ($n = 140$) and IIEF-5 > 20 ($n = 123$); those with lower IIEF-5 scores were older (57 [52-61] vs. 54 [45-60] years, $p = 0.002$), had higher prevalence of CAD (22% vs. 9%, $p = 0.004$), smoking (64% vs. 47%, $p = 0.009$) and use of calcium channel inhibitors (65% vs. 43%, $p = 0.001$), as well as lower CrCl (67.3 [30.8 to 88.6] vs. 82.6 [65.9 – 98.2] ml/min, $p < 0.001$). The IIEF-5 ≤ 20 was associated with increased risk of CAD in the logistic regression, both univariate (OR = 2.89 [95%CI: 1.39 – 6.05]), and after adjusting for age, diabetes, CrCl, smoking, mean arterial pressure and use of antihypertensive drugs (OR = 2.59 [95% CI: 1.01 – 6.61]).

Conclusion: The IIEF-5 is associated with the diagnosis of CAD and its use can add information to cardiovascular risk stratification in hypertensive patients. (Arq Bras Cardiol 2012;99(4):924-930)

Keywords: Erectile dysfunction; hypertension; coronary artery disease.

Introduction

Erectile Dysfunction (ED), the incapacity to achieve and maintain a penile erection sufficient to have satisfactory sexual intercourse¹ affects approximately 150 million men around the world² and is associated with higher prevalence of cardiovascular risk factors, such as diabetes mellitus (DM)³, Systemic Arterial Hypertension (SAH), dyslipidemia, obesity, smoking and metabolic syndrome⁴⁻⁶. In Brazil, Moreira et al.⁷, in a multicenter study involving 1286 men aged 18 years and older, described the presence of some degree of ED in 46% of the participants.

Atherosclerosis is a major cause of ED, thus individuals who develop erectile dysfunction are at increased risk for developing other manifestations of atherosclerotic disease, such as Stroke and Coronary Artery Disease (CAD)⁸⁻¹³, even after adjusting for factors traditionally related to cardiovascular disease¹⁴. Furthermore, there is evidence that the degree of ED is associated with CAD severity¹⁵.

The presence and severity of ED can be assessed using the International Index of Erectile Function (IIEF), a self-administered questionnaire consisting of 15 items, covering different areas related to sexual function (erection, orgasm, desire and satisfaction)¹⁶.

Rosen et al.¹⁷ developed a simplified version of the questionnaire, consisting of only five items (IIEF-5), which has been shown to be a practical tool for ED diagnosis and classification. Our objective was to evaluate the association between the presence of erectile dysfunction, as assessed by the IIEF-5, and the diagnosis of CAD in hypertensive patients.

Methods

Patients and methods

We performed a cross-sectional study that evaluated all men aged between 18 to 65 years, consecutively attended in the Section of Hypertension and Nephrology of Instituto Dante Pazzanese de Cardiologia (IDPC - outpatients clinic) between April 3 and May 31, 2010 and demonstrated interest in participating in the study by signing the informed consent form. The age range for inclusion is that necessary for the referral of patients to the Section of Hypertension and Nephrology IDPC outpatients clinic. The study was approved by the Ethics of Committee of IDPC.

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After detailed clinical and cardiologic assessment, patients were asked to answer the self-administered questionnaire of the International Index of Erectile Function (IIEF-5)¹⁷. The IIEF-5 questionnaire score determined the presence and severity of ED: absent (> 21), mild (17-21), mild / moderate (12-16), moderate (8-11) and severe (< 8)

All patients had weight and height measured at the time of consultation. Laboratory tests (glucose, creatinine, total cholesterol and triglycerides) performed at the Laboratory of IDPC and brought to the medical consultation, were considered in the analysis. Glomerular filtration rate was calculated by the Cockcroft-Gault equation¹⁸, adjusted for body surface area. The mean arterial pressure (MAP), calculated by the formula " $(\text{systolic blood pressure} + [2 * \text{diastolic blood pressure}]) / 3$ " was used in the analysis, as it is the best method of measuring tissue perfusion pressure. The CAD diagnosis was performed by reviewing medical records, based on the revascularization history (surgical/percutaneous) or presence of prior coronary lesion $\geq 50\%$ at the coronary angiography.

Statistical analysis

Data distribution analysis was performed using the Kolmogorov-Smirnov test. The analysis of the receiver-operating characteristic (ROC) was used to establish the value of IIEF-5 that best identified the presence of CAD. The variables were expressed as mean \pm standard deviation, median (interquartile range, IQR) or as percentage, as appropriate. As many values were not normally distributed, Spearman's rank correlation (Rho) was used to determine correlations. Groups were compared by Mann-Whitney test or Chi-square analysis, as appropriate. Crude and adjusted logistic regression analyses were performed to evaluate the association between coronary artery disease and erectile dysfunction.

Based on literature data, where the proportion of erectile dysfunction was 47% in patients with CAD and 24% in controls¹⁹, the minimum sample size required for our results to have a significance level of 5% and test power of 90 % was calculated at 178 patients (89 per group). All probabilities of significance (p values) are two-tailed and values < 0.05 were considered statistically significant. Statistical analysis was performed using SPSS 13.0 software (SPSS Inc., Chicago IL, 2004).

Results

We evaluated 263 patients with median age of 55 (50-61) years, whose demographic and clinical data are described in Table 1. One hundred and fifty-five patients (59%) had some degree of erectile dysfunction according to IIEF-5 questionnaire (Table 1 and Figure 1).

The IIEF-5 questionnaire was negatively correlated with age ($\rho = -0.22$, $p < 0.001$) and positively correlated with creatinine clearance ($\rho = 0.23$, $p < 0.001$), as shown in Table 2. Patients with a history of CAD had lower IIEF-5 (17 [8-21] vs. 21. [15-23], $p = 0.006$), Figure 2. The IIEF-5 questionnaire was able to discriminate individuals with a diagnosis of CAD (area under ROC curve = 0.63, $p = 0.006$), as shown in Figure 3, and "20" was the IIEF-5 score considered to be more appropriate for this purpose.

Table 1 - Clinical and demographic characteristics of 263 hypertensive patients included in study¹

Age (years)	55 (50 – 61)
Erectile Dysfunction [IIEF-5] (n, %)	
Absent (> 21)	108 (41%)
Mild (17 – 21)	64 (24%)
Mild-Moderate (12 – 16)	48 (19%)
Moderate (8 – 11)	16 (6%)
Severe (< 8)	27 (10%)
Diabetes mellitus (n, %)	78 (30%)
Coronary Artery Disease (n, %)	42 (16%)
Smoking (n, %)	147 (56%)
ACEI / ARB ¹ (n, %)	228 (86%)
Diuretics (n, %)	199 (76%)
Calcium Channel Blockers (n, %)	145 (55%)
Beta-blockers (n, %)	134 (51%)
BMI (Kg/m ²)	30.6 \pm 5.6
Mean Arterial Pressure (mmHg)	105 (96 – 119)
Glucose (mg/dL)	95 (86 – 112)
Creatinine Clearance (mL/min)	76.3 (46.1 – 94.7)
Total Cholesterol (mg/dL)	181 (158 – 208)
Triglycerides (mg/dL)	145 (106 – 229)

¹ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin II receptor blockers

The patients were divided into two groups according to the IIEF-5 score (≤ 20 and > 20) and their clinical and demographic characteristics are described in Table 3. In summary, patients with lower IIEF-5 were older (57 years [52-61] vs. 54 years [45-60], $p = 0.002$), had a higher prevalence of CAD (22% vs. 9%, $p = 0.004$), smoking (64% vs. 47%, $p = 0.009$) and use of calcium channel inhibitors (65% vs. 43%, $p = 0.001$), as well as a lower creatinine clearance (67.3 mL / min [30.8 to 88.6] vs. 82.6 mL / min [65.9 to 98.2], $p < 0.001$).

The logistic regression analysis (Table 4) showed that IIEF-5 score ≤ 20 was associated with the presence of CAD in both the univariate analysis (odds ratio = 2.89 [95%CI: 1.39-6.05]) and even after adjustments for potential confounders such as age, diabetes mellitus, kidney disease, smoking, mean arterial pressure, use of angiotensin-converting enzyme inhibitors / angiotensin II receptor blockers, diuretics, calcium channel blockers and beta blockers (odds ratio = 2.59 [95%CI: 1.01 – 6.61]).

Discussion

The present study showed that hypertensive patients with IIEF-5 score ≤ 20 have a 2.59-fold higher odds of presenting diagnosis of CAD, regardless of the presence of known cardiovascular risk factors (age, diabetes, kidney disease and smoking) and the use of antihypertensive drugs, known to be associated with the development of erectile dysfunction. Our results provide further evidence of the association between ED and CAD^{9,11,20-22}.

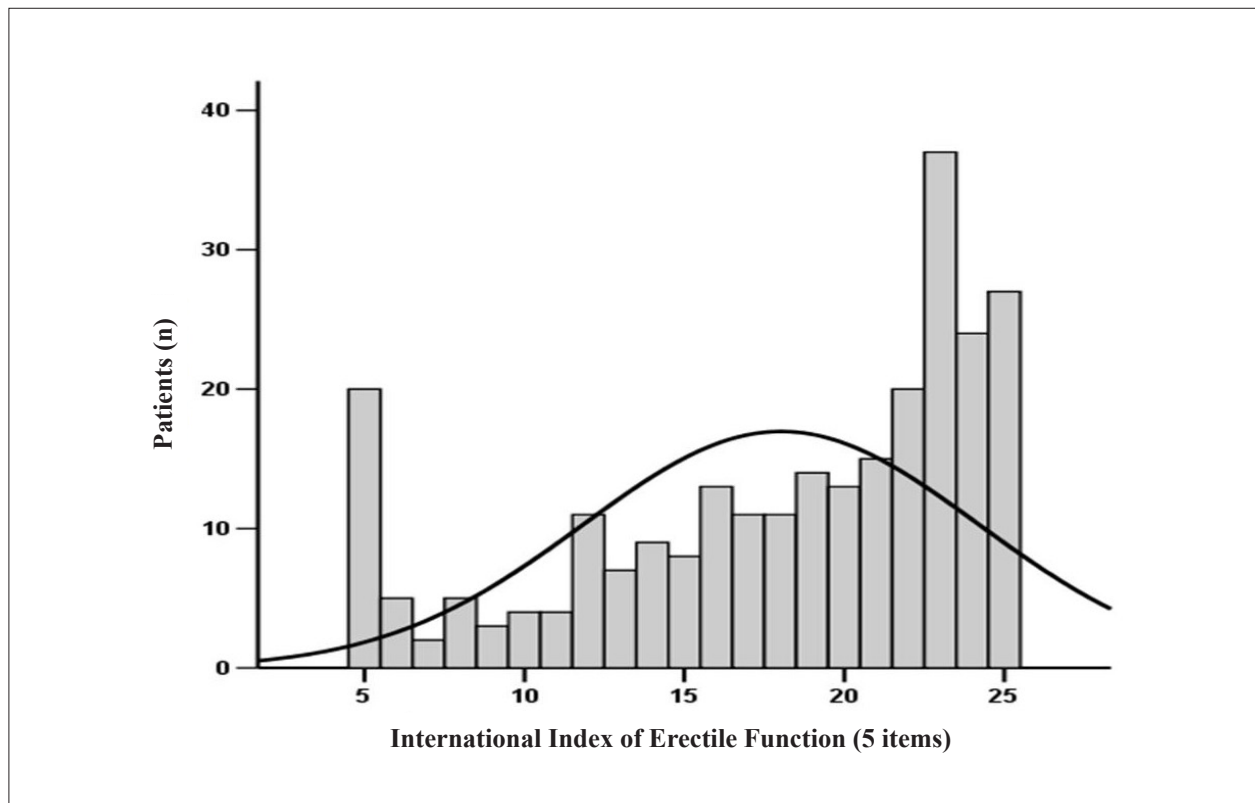


Figure 1 – Distribution of the IIEF-5 score in the 263 hypertensive patients included in the study.

Table 2 - Correlation between the international index of erectile function (5 items) and clinical and laboratory variables in 263 hypertensive patients

	Spearman's (rho)	p
Age (years)	0.22	< 0.001
BMI (Kg/m ²)	0.04	0.483
Mean Arterial Pressure (mmHg)	0.12	0.057
Glucose (mg/dL)	-0.03	0.694
Creatinine clearance (ml/min)	0.23	< 0.001
Total cholesterol (mg/dL)	-0.01	0.862
Triglycerides (mg/dL)	0.03	0.627

ED is considered a clinical manifestation of vascular functional and structural alterations, resulting from widespread cardiovascular disease, with penile circulation being affected earlier due to the smaller diameter of the penile arteries, when compared to coronary, carotid and femoral arteries¹¹. Thus, ED and CAD may be considered different manifestations of the same disease, which is highlighted by the fact that the risk factors associated with CAD are commonly found in patients with ED²³, as well as by the correlation between ED degree and CAD severity²⁴. In fact, we observed that patients with CAD, when compared to those with no history of coronary artery disease, had a significantly lower IIEF-5.

The stratification of cardiovascular risk is an essential step to establish BP goals to be achieved in hypertensive patients²⁵. Thus, given that the prevalence of ED is extremely high in patients with CAD^{19,20}, with the first being an independent risk predictor for the development of the latter, in addition to preceding it on average by three years²⁰, it would be reasonable to perform ED screening in all patients with risk factors for cardiovascular disease development. However, as this is a self-reported condition, often purposely omitted and with no specific confirmatory tests available, the investigation of erectile dysfunction by cardiologists is usually neglected.

In this set, our results, by showing the independent association between the IIEF-5 questionnaire - a simple and easy-to-use tool to diagnose the presence and severity of ED¹⁷ - and the presence of CAD, highlight their usefulness in everyday routine of medical offices, where it can be applied even in waiting rooms, both for the identification of erectile dysfunction and also for cardiovascular risk stratification.

The prevalence of erectile dysfunction in our patients (59%) was higher than that described in other studies with the Brazilian population^{7,22,27,28}, which may be attributed to the fact that our sample included only hypertensive patients^{29,30}. We also emphasize that the cutoff of 20 for the IIEF-5 adopted in our analysis includes patients with mild ED according to the original classification¹⁷, which may be related to failure in the classification or higher prevalence of psychiatric and non-organic alterations as cause of ED in patients with borderline

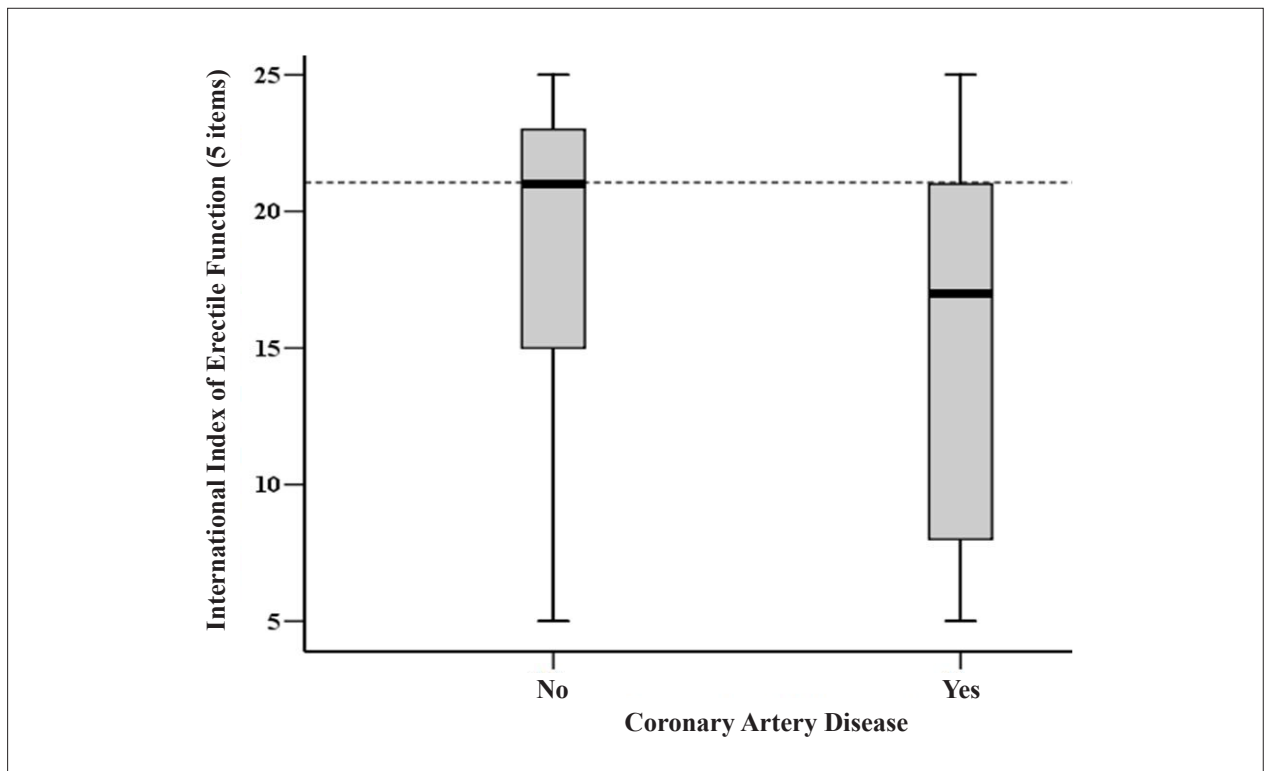


Figure 2 – IIEF-5 score in the 263 hypertensive patients enrolled in the study according to the diagnosis of coronary artery disease.

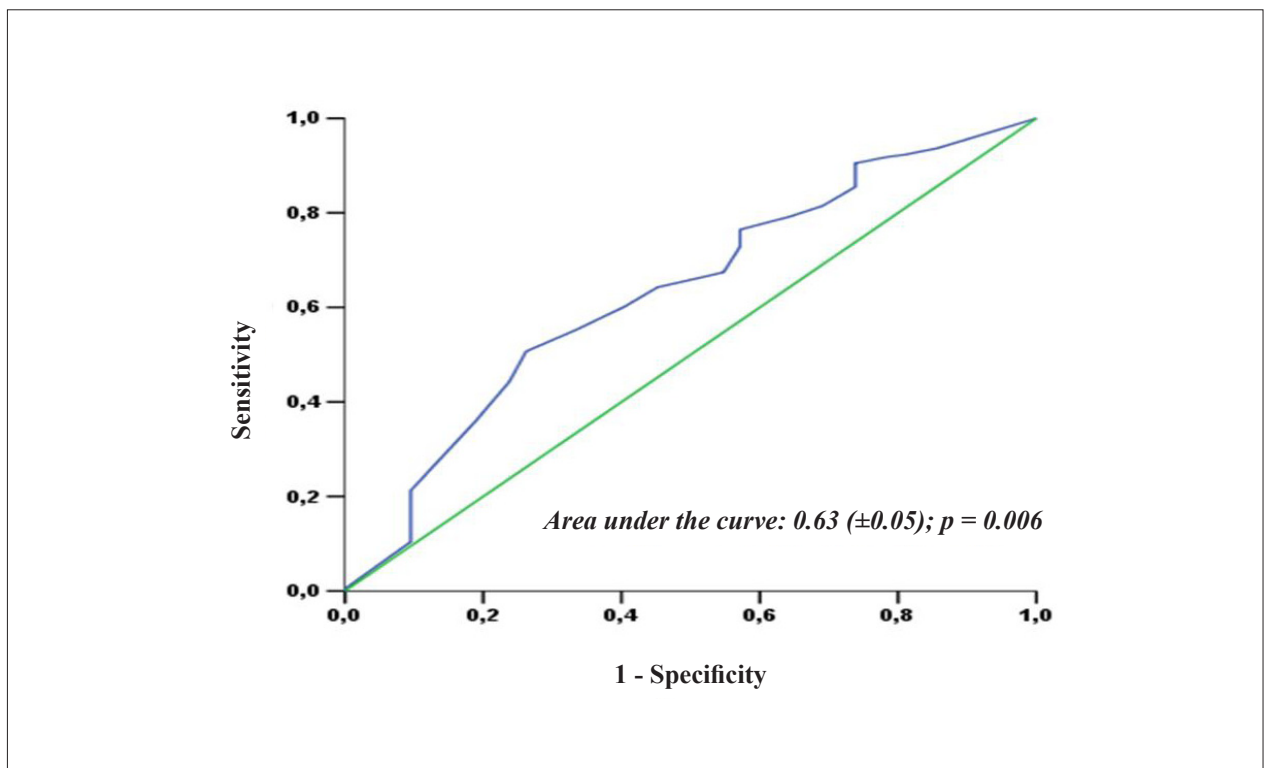


Figure 3 – Area under the ROC curve for the diagnosis of coronary artery disease according to IIEF score-5 in the 263 hypertensive patients included in the study.

Table 3 - Clinical and demographic characteristics of the 263 hypertensive patients divided according to the IIEF-5¹ score

	IIEF-5 ≤ 20 (n=140)	IIEF-5 > 20 (n=123)	P
Age (years)	57 (52 – 61)	54 (45 – 60)	0.002
Diabetes mellitus (n, %)	47 (34%)	31 (25%)	0.176
Coronary artery disease (n, %)	31 (22%)	11 (9%)	0.004
Smoking (n, %)	89 (64%)	58 (47%)	0.009
ACEI / ARB ¹ (n, %)	119 (85%)	108 (88%)	0.591
Diuretics (n, %)	109 (77.9%)	90 (73.2%)	0.391
Calcium Channel Blockers (n, %)	91 (65%)	53 (43%)	0.001
Beta-blockers (n, %)	77 (55%)	57 (47%)	0.215
BMI (Kg/m ²)	29.7 ± 5.6	30.5 ± 5.5	0.190
Mean Arterial Pressure (mmHg)	103 (93 – 117)	107 (98 – 117)	0.095
Glucose (mg/dL)	95 (85-111)	95 (87-115)	0.511
Creatinine Clearance (ml/min)	67.3 (30.8 – 88.6)	82.6 (65.9 – 98.2)	< 0.001
Total cholesterol (mg/dL)	180 (154 – 210)	181 (159 – 208)	0.686
Triglycerides (mg/dL)	144 (101 – 226)	146 (118 – 236)	0.517

¹ Data presented as mean (± standard deviation), median (percentiles 25-75) or absolute (n) and relative (%) values. ACEI: angiotensin converting enzyme inhibitor, ARB: angiotensin II receptor blockers

Table 4 – Relative risk for the diagnosis of coronary artery disease in 263 hypertensive patients according to the IIEF-5 and variables selected at the logistic regression analysis

Model ²	Variables	Odds Ratio (95% Confidence Interval)
1	International Index of Erectile Function (5 items)	2.89 (1.39 – 6.05)
2	1 + Age	2.75 (1.31 – 5.78)
3	2 + Diabetes and Creatinine Clearance	2.98 (1.28 – 6.90)
4	3 + MAP + smoking	2.93 (1.21 – 7.08)
5	4 + use of ACEI/ARB, diuretics, calcium-channel blockers and beta-blockers.	2.59 (1.01 – 6.61)

¹ Patients with IIEF-5 > 20 were chosen as reference.

² Constant < 0.001 for all models.

IIEF-5 score. Our study has limitations, including: a) its cross-sectional design, which only allows the establishment of associations, b) the small sample size; c) the lack of information regarding the antihypertensive dose used, and d) the fact that the CAD diagnosis was based only on clinical history and medical file review. However, the diagnosis of CAD is initially hypothesized based on the patient's medical history; in this sense, our study simulated the conditions experienced by clinicians in their daily routine.

Conclusion

The presence of erectile dysfunction is associated with increased risk of coronary artery disease. The use of the IIEF-5 score may add information to the cardiovascular risk stratification of patients assessed at the medical office.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

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