OPO OPHTHALMIC AND PHYSIOLOGICAL OPTICS
THE JOURNAL OF THE COLLEGE OF OPTOMETRISTS

Ophthal. Physiol. Opt. 2010 **30:** 724–730

Color-space distortions following long-term occupational exposure to mercury vapor

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Abstract

Color vision was examined in subjects with long-term occupational exposure to mercury (Hg) vapor. The color vision impairment was assessed by employing a quantitative measure of distortion of individual and group perceptual color spaces. Hg subjects (n = 18; 42.1 ± 6.5 years old; exposure time = 10.4 ± 5.0 years; time away from the exposure source = 6.8 ± 4.6 years) and controls (n = 18; 46.1 ± 8.4 years old) were examined using two arrangement tests, D-15 and D-15d, in the traditional way, and also in a triadic procedure. From each subject's 'odd-one-out' choices, matrices of inter-cap subjective dissimilarities were derived and processed by non-metric multidimensional scaling (MDS). D-15d results differed significantly between the Hg-group and the control group ($p < 0.05$), with the impairment predominantly along the tritan axis. 2D perceptual color spaces, individual and group, were reconstructed, with the dimensions interpreted as the red-green (RG) and the blue-yellow (BY) systems. When color configurations from the Hg-group were compared to those of the controls, they presented more fluctuations along both chromatic dimensions, indicating a statistically significant difference along the BY axis. In conclusion, the present findings confirm that color vision impairments persist in subjects that have received long-term occupational exposure to Hg-vapor although, at the time of testing, they were presenting mean urinary concentration within the normal range for non-exposed individuals. Considering the advantages of the triadic procedure in clinical evaluation of acquired color vision deficiencies, further studies should attempt to verify and/or improve its efficacy.

Keywords: color space, color vision, D-15d, mercury, multidimensional scaling (MDS), neurotoxicity

Introduction

Mercury vapor intoxication

Mercury (Hg) is a potent neurotoxic agent, which can cause a range of nervous system impairments both in its elemental form (e.g. Cavalleri *et al*., 1995; Feitosa-Santana *et al*., 2007, 2008; Urban *et al*., 2003; Ventura *et al*., 2004, 2005) and as organic compounds such as methylmercury (e.g. Hunter and Russell, 1954; Lebel

Received: 9 September 2009
Revised form: 6 May 2010
Accepted: 13 May 2010

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doi: 10.1111/j.1475-1313.2010.00764.x

et al., 1996, 1998; Rodrigues *et al*., 2007; Silveira *et al*., 2003). In spite of attempts to reduce releases of Hg into the environment (WHO, 1990, 1991), certain populations remain exposed to Hg due to its industrial uses (e.g. fluorescent lamp plants, thermometer manufacturing, metallic Hg recycling, and others) or to its accumulation in the environment (e.g. Amazonian populations: Pinheiro *et al*., 2007).

Exposure to Hg vapor has been shown to affect various visual functions (e.g. Barboni *et al*., 2009; da Costa *et al*., 2008; Gobba, 2000; Iregren *et al*., 2002; Lebel *et al*., 1996; Silveira *et al*., 2003). Color vision impairments due to Hg vapor exposure have been explored using color arrangement tests such as the D-15d test, indicating that error scores were significantly higher for the exposed groups and losses were predominantly along the tritan axis, showing impairment of the blue-yellow (BY) system (Cavalleri *et al*., 1995; Feitosa-Santana *et al*., 2007; Urban *et al*., 2003). However, recent findings showed that, along with the BY system, the red-green (RG) system is also affected, when color discrimination is assessed using the Cambridge Colour Test (CCT) (Canto-Pereira *et al*., 2005; Feitosa-Santana *et al*., 2008; Rodrigues *et al*., 2007; Silveira *et al*., 2003; Ventura *et al*., 2005). To explain the discrepancy, it is argued that the stimulus design of the CCT, with variation in both hue and saturation, involving a more naturalistic discrimination task and a computerized psychophysical procedure (Mollon and Reffin, 1989), allows the detection of subtle color vision impairment not captured by the arrangement tests such as the Farnsworth-Munsell 100-Hue (FM-100), the D-15, or the D-15d.

Color discrimination represented within a color space

A perceptual color space is a geometric representation of relations among colors, in which points represent color stimuli and the distance between a pair of colors reflects their perceptual difference (e.g. Helm, 1964). For individual color vision, a color space can be reconstructed from subjective estimates of color dissimilarity among test caps, by processing the matrix of all pairwise comparisons using multidimensional scaling, MDS (Kruskal and Wish, 1978). Its dimensions are interpreted as perceptual color systems, usually RG and BY.

In a subsequent step, color vision impairment can be considered as a distortion of the color space configuration of normal trichromats. The distortion is characterized by which dimensions, RG and/or BY, are compressed and by the degree of the compression of each one. This paradigm has been used to model color discrimination in various types of congenital color vision deficiencies (Bimler *et al*., 2000; Helm, 1964; Paramei *et al*., 1991; Shepard and Cooper, 1992). In a MDS study of color-deficient subjects and normal trichromats, Helm (1964) introduced a triadic procedure to elicit dissimilarities among caps from the D-15 test. The triadic procedure requires subjects to rank dissimilarities rather than assign numerical values to them, i.e. it implies an ordinal level of judgment rather than an interval level (Bimler *et al*., 2000). Recent applications of this non-traditional procedure have found it to be sensitive to quite subtle distortions of the color space, e.g. when comparing smokers and non-smokers (Bimler and Kirkland, 2004), or revealing subclinical disease manifestations by identifying color space impairment in patients with type 2 diabetes without retinopathy (Feitosa-Santana *et al*., 2006).

The present study focuses on evaluating color vision in subjects who had been occupationally exposed to Hg vapor for at least 5 years, and removed from the source of intoxication for at least 1 year. The persistence and the nature of any residual deficits were determined: whether they are diffuse or polar, i.e. affect both chromatic systems or only one of these. Along with using the D-15 and D-15d tests in the traditional procedure, color vision was assessed by using a set of the caps from both tests and employing the triadic procedure to obtain estimates of color dissimilarity. The goal of this approach was to represent acquired color vision impairment for the Hg-group as distortions of the controls' color space in both individual and group representations.

Method

Subjects

The Hg-group consisted of 18 subjects (13 males; 42.1 ± 6.5 years old) who were chronically exposed to Hg vapor working in fluorescent lamp industries (for details, see *Table 1*). These Hg-patients were referred by the Occupational Health Service of the Oscar Freire Institute of the University of Sao Paulo (Sao Paulo, Brazil). All had been previously discharged from work and placed on disability retirement due to medical diagnosis of Hg intoxication based on clinical and laboratory (HgU) examination.

Eighteen controls (10 males; 51 ± 12 years old) were tested with same procedures for comparison (for details, see *Table 2*).

All Hg-patients and controls were submitted to an ophthalmological examination following the inclusion criteria: best corrected Snellen visual acuity (VA) 20/30 or better, no ocular diseases or surgeries and a maximum of grade 1 for cortical opacity (C1), nuclear color (NC1), and nuclear opalescence (NO1) following the chart for the lens opacity classification system (LOCS III) (Chylack *et al*., 1993); and no clinical

Table 1. Characteristics of the mercury exposed subjects

ID	Sex	Age	VA OD	VA OS	Exp	Away	HgU 1	HgU 2
1	F	51	20/25	20/25	12.0	15.0	–	<1.0
2	M	43	20/30	20/25	10.0	4.0	9.0	<1.0
3	F	50	20/30	20/30	5.0	10.0	–	–
4	M	36	20/30	20/30	7.0	8.0	–	<1.0
5	M	34	20/20	20/20	9.0	3.0	73.8	3.0
6	M	36	20/15	20/15	6.0	4.0	–	<1.0
7	M	47	20/20	20/20	13.0	1.0	–	–
8	M	41	20/20	20/20	24.5	1.0	–	–
9	M	54	20/20	20/20	14.0	12.0	–	1.0
10	M	43	20/20	20/20	12.0	12.0	56.6	<1.0
11	F	36	20/20	20/20	8.5	2.0	1.2	2.8
12	M	43	20/20	20/20	12.0	6.0	66.0	<1.0
13	M	33	20/25	20/25	5.0	2.0	2.4	1.3
14	F	45	20/20	20/20	12.0	5.0	2.0	<1.0
15	M	36	20/20	20/20	18.0	3.0	20.0	1.6
16	M	37	20/20	20/20	6.0	10.0	134.7	3.3
17	F	42	20/25	20/25	7.0	13.0	50.0	4.2
18	M	51	20/25	20/25	6.0	11.0	–	–
Mean		42.1			10.4	6.8	41.6	1.7
SD		6.5			5.0	4.6	43.3	1.1
Minimum		33.0			5.0	1.0	1.2	1.0
Maximum		54.0			24.5	15.0	134.7	4.2

ID = subject identification number; VA = visual acuity; OD = right eye; OS = left eye; Exp = duration of exposure (years); Away = time away from the exposure to Hg (years); HgU 1 = urinary Hg concentration at the time of retirement or up to 1 year thereafter; HgU 2 = urinary Hg concentration at the time of color vision testing. The normal level is <5.0 $\mu g\ g^{-1}$ creatinine; the occupational Biological Exposure Index is 35.0 $\mu g\ g^{-1}$ creatinine (ACGIH, 1995).

Table 2. Characteristics of control subjects

ID	Sex	Age	HgU 2
1	M	37	–
2	M	62	<1.0
3	M	50	<1.0
4	F	59	1.7
5	M	50	–
6	F	40	<1.0
7	F	57	2.5
8	M	40	<1.0
9	M	40	<1.0
10	F	38	<1.0
11	F	58	1.7
12	M	35	1.3
13	F	48	<1.0
14	M	40	<1.0
15	M	46	<1.0
16	M	45	<1.0
17	F	38	<1.0
18	F	47	–
Mean		46.1	0.8
SD		8.4	0.6
Minimum		35.0	0
Maximum		62.0	2.5

ID = subject identification number; OD = right eye; OS = left eye; HgU 2 = urinary Hg concentration at the time of color vision testing. The normal level is <5.0 $\mu g\ g^{-1}$ creatinine.

signs of retinopathy. Clinical history was collected to verify the exclusion criteria: absence of systemic diseases that could affect the visual system; alcoholism; or smoking. The D-15 test (Farnsworth, 1943) was used to screen for congenital color vision deficiency (CCVD), and subjects diagnosed with CCVD were not included.

Informed consent was obtained from all patients and controls before the tests were performed. Testing procedures complied with the tenets of the Declaration of Helsinki and were approved by the Ethics Committees of the University of Sao Paulo.

Both eyes of Hg-patients were tested monocularly. For the controls, only one eye per subject was randomly tested.

Stimuli

The D-15 and the D-15d each consist of 16 colored caps. In the Munsell notation, the D-15 caps have Value = 5 and Chroma = 4 (Farnsworth, 1943); the D-15d caps have the same hue but are lighter, with Value = 8, and less saturated, Chroma = 2 (Lanthony, 1978).

For the triadic procedure, a composite assortment of 15 caps was created, involving caps from both D-15 and D-15d, every third D-15 cap was replaced with its counterpart from the D-15d. Including saturated as well as desaturated stimuli in this set ensures that along with large, suprathreshold differences, subjects consider smaller differences. Also, since the D-15 caps differ from the D-15d caps in Value (lightness) as well as in Chroma (saturation), the triadic composition provides subjects with the option of basing their triadic judgments on lightness, to compensate for any reduction in sensitivity to the chromatic axes (cf. Bimler and Kirkland, 2004).

Two fluorescent lamps provided illuminance of 500 lux at the testing surface (Octron FO32W; Sylvania, Munich, Germany) with Correlated Color Temperature = 6500 K and Color Rendering Index = 75.

Procedure

The D-15 and D-15d tests were applied in both the traditional way and the triadic procedure. For the triadic procedure, the 15-cap composite set was shuffled into five randomized groups of three (in each series presentation). The subject viewed each of these triads separately and chose the most dissimilar cap of each triad, the 'odd-one-out'. This procedure was repeated 14 times, eliciting 70 triad judgments. No time limit was set;

the average testing time was 60 min for each eye. The first presentation series (five groups of three caps) was performed with the D-15 caps, and the other 13 with the composite set. Both procedures were administered monocularly, in a randomly chosen order, for both eyes for the Hg-group, and for one eye for the controls.

Analysis

Errors in the D-15 and D-15d tests were quantified in terms of the Total Color Difference Score (TCDS) (Vingrys and King-Smith, 1988). The minimum TCDS value for D-15 is 116.9 (Bowman, 1982) and for D-15d is 56.4 (Geller, 2001), when all the caps are in consecutive order. In addition, the Color Confusion Index (CCI) (Bowman, 1982) was calculated which has a minimum value equal to 1.0. In both cases, higher values indicate poorer hue discrimination.

Data from the triadic procedure were analyzed with multidimensional scaling (MDS), in order to represent the caps as points in a low dimensional space (in this case, two-dimensional, 2D), so as to accommodate the subjects' 'odd-one-out' judgments. The algorithm begins with the caps embedded in a 15-dimensional (15D) abstract space, each one a single (arbitrary) distance unit away from the origin of the space, so that all interpoint distances are equal. These distances are then adjusted according to each of the 70 triadic judgments in turn, rotating locations of points so as to increase the distance between the 'odd-one-out' in each comparison and the other two caps, and to bring those other two closer to each other. Then, the 15D abstract space is reduced to a 2D space using non-metric MDS to distort them as little as possible. This involves an iterative steepest descent method (Kruskal and Wish, 1978). In the ideal situation where a subject's odd-one-out choices are 'correct' (i.e. predicted by the locations of the D-15 and D-15d caps around a hue circle), reduction from 15 to 2 dimensions will result in a MDS solution consisting of an incomplete circle of equally-spaced points. For a detailed mathematical explanation see Feitosa-Santana *et al.* (2006). Note that MDS gives only the relative position between caps (Kruskal and Wish, 1978), but no absolute orientation. Thus the caps' arrangement is mirrored and rotated so as to locate 5Y at the top, 2.5R to the left and 10G to the right. The RG is interpreted as the horizontal axis and the BY as the vertical axis.

Results

D-15

For the D-15, the mean TCDS [CCI] value for the controls was 118.2 ± 3.3 [1.01 ± 0.03]. For the Hg-group, the TCDS [CCI] means were 121.1 ± 7.5 [1.04 ± 0.06], OD; 118.9 ± 3.6 [1.02 ± 0.03], OS; 120.0 ± 4.2 [1.03 ± 0.04], mean of both eyes. For the controls as well as the Hg-group, the CCI values lie within the range for normal trichromats (Bowman, 1982; Vingrys and King-Smith, 1988) with no statistically significant difference between them (Mann-Whitney *U* Test).

D-15d

For the D-15d, the mean TCDS [CCI] value for the controls, 59.2 ± 4.4 [1.05 ± 0.08], was similar to that obtained from similarly aged controls in a previous study, 58.8 ± 3.53 [1.04 ± 0.06] (Feitosa-Santana *et al.*, 2007). Mean values of the TCDS [CCI] for the Hg-group are as follows: 71.0 ± 8.8 [1.26 ± 0.16], OD; 67 ± 10 [1.18 ± 0.18], OS; 69.1 ± 8.9 [1.22 ± 0.16], mean of both eyes. Compared to controls, the Hg-group values differed significantly: OD, $p < 0.001$; OS, $p < 0.05$; mean of both eyes, $p < 0.001$ (Mann-Whitney *U* Test).

MDS solutions

The 2D color spaces reconstructed using the MDS analysis of triadic data vary dramatically among the subjects, even in the control group. The variability, though, is far more pronounced in the Hg-group, indicating that color judgments of the Hg-patients contained more errors than those of the controls.

Repetitions of the triadic procedure revealed that the choice of the 'odd-one-out' cap changed on average 7% between tests, which should result in very similar compression indices. Thus individual color spaces were reproducible for a given subject.

Figure 1 presents mean color spaces for both groups of subjects. *Figure 1a* shows the mean 2D solution for the controls, with error bars indicating the confidence interval for the location of each cap. For the Hg-group, the mean color space for both eyes is shown (*Figure 1b*), as well as that for OD (*Figure 1c*) and OS (*Figure 1d*). *Figure 1b, 1c, and 1d* reveal that, along with greater variability, the color spaces are more compressed in the BY dimension, particularly in the left half, i.e. for reddish rather than greenish hues, indicating that the differences among these hues are less apparent for the Hg-patients.

The control group space was employed as a standard to calculate the degree of distortion in the Hg-patients' color spaces (individual or group) in terms of the sum of residual distances between locations of the counterpart caps. Residual distances were summed along the two dimensions separately, thus producing separate indices for the two perceptual systems, RG and BY, for both the Hg-group and controls. It should be noted that the sum of residual distances estimates the compression of

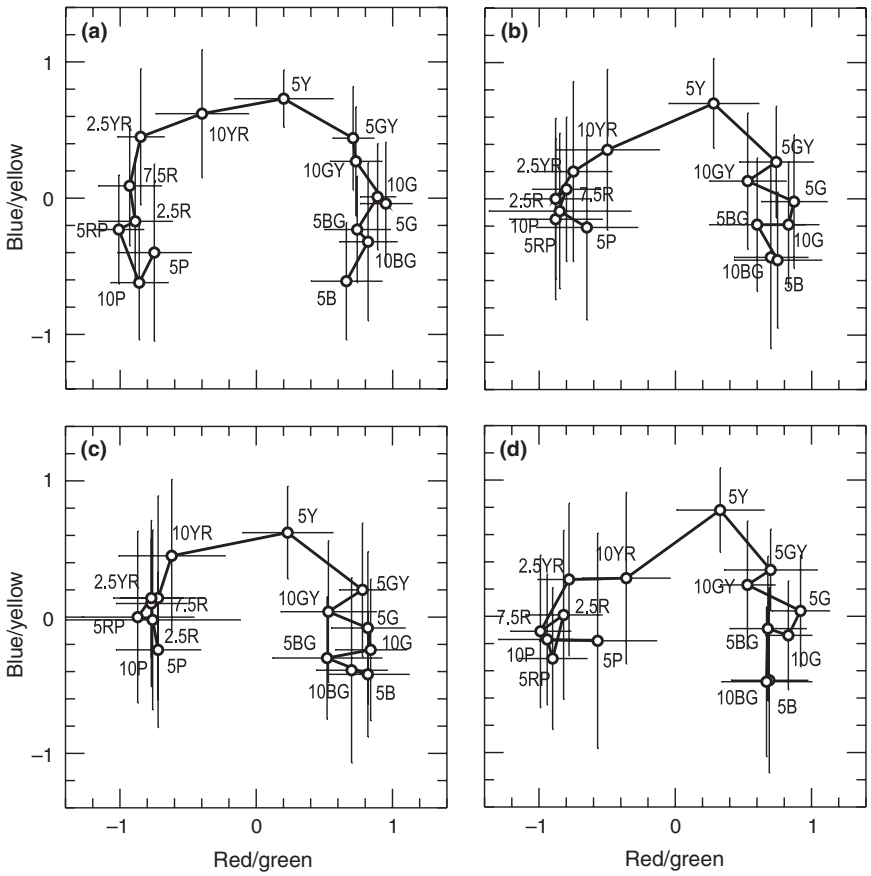

Figure 1. (a) Average color space for the control group. Color spaces for the Hg-group: (b) the mean of both eyes, (c) OD and (d) OS. Error bars centered on each point *i* indicate the variance in its coordinates x_i and y_i across individual solutions.

the subject's color space along one or the other dimension, since compression reduces the salience of consensus of color differences along that dimension and increases the chance that they will be within the limits of 'noise' in any given triad. For the Hg-patients, the residual sums were as follows: OD RG = 0.13 and OD BY = 0.24; OS RG = 0.11 and OS BY = 0.18; mean of both eyes, RG = 0.10 and BY = 0.19.

To compare residuals between the Hg-patients and controls, a multivariate analysis of variance (MANOVA) was applied. The value of Wilks' lambda statistic for the added RG and BY residuals was 0.107 ($F = 1.39$, $p > 0.10$); for RG and BY separately, Wilks' lambda was 0.502 for RG ($F = 0.97$, $p > 0.50$) and 0.333 for BY ($F = 1.72$, $p < 0.05$). Thus indicating that the Hg-subjects differed significantly from the controls with regards to compression of their color spaces along the BY dimension. The degree of compression showed no relationship with either exposure duration or urinary Hg concentration. Nor were the MDS outcomes related to age of the control or Hg-group.

Discussion

The present study shows that color spaces of subjects in the Hg-group are distorted relative to the control group, which indicates an acquired color vision deficiency due to a long-term occupational exposure to Hg vapor. The perceptual color space distortions of the Hg group are similar to the findings of Bimler and Kirkland (2004), who used the same stimulus set for the triadic procedure to compare smokers and non-smokers. In this study, MDS analysis, representing color discrimination ability as distances in color space, detected mild forms of color vision impairment associated with smoking. Compared to the study conducted to evaluate the color space distortions in patients with type 2 diabetes (Feitosa-Santana *et al.*, 2006), applying the same method as in this study, the color space distortion in the Hg-group presented here is more prominent along the BY axis, while the configuration presented by the group with type 2 diabetes is compressed along the RG and BY dimensions.

The triadic method allows color space representation and holds out the possibility of quantitatively analyzing

global losses as in the two chromatic systems separately, in which any subtle impairment is manifested by compression along the RG and/or BY dimensions. Further studies and implementations should be carried out using the triadic procedure in order to optimize the test protocol to obtain the most sensitive classification of acquired color vision deficiencies. For this purpose, it would be interesting to test different combinations in order to verify the best combination of D-15 and D-15d caps to classify color losses; to develop an index score (based on the vector analysis of the triadic procedure) to quantify the global losses as with the TCDS and CCI of D-15 and D-15d; and also to quantify the RG and BY dimensions separately.

Results from a very similar Hg-group sample reported previously (Feitosa-Santana *et al.*, 2008) (some of whom are included in the present study) showed both BY and RG losses when tested with the Cambridge Colour Test (CCT), whereas using MDS, only a BY compression was detected. Considering the similarity between the Hg-groups, it seems unlikely that the difference is due to mean age, duration of exposure to Hg, time away from the exposure source, or urinary Hg concentration. One possible explanation is that the perceptual color space obtained with the triadic procedure is based on a suprathreshold test while the CCT measures color discrimination thresholds, yielding a finer and more direct measure of the performance of the system. Another explanation is that the two tests might measure different functions, at different levels of the color vision system, and thus cannot be directly compared. A discrimination threshold may be a lower order function, compared to an ordering task. The computerized tests may have greater precision but the arrangement tests used in the triadic procedure have the advantage of portability and low cost. Further studies with the triadic procedure would be worthwhile in order to verify their precision and efficacy in clinical evaluation of color vision losses.

The long duration of testing is tiring and is a considerable negative point of the test protocol. Computerized MDS analysis of data and online results would assist in their interpretation and diagnosis. In this case, there are prospects to develop a triadic procedure as close as possible to subject's thresholds of color discrimination. However, the cost for the procedure would be as high as other computerized tests. An alternative would be streamlining the process by using a standard, optimized list of triads rather than random ones, presented in the form of printed cards, which would speed the testing and keep the cost low.

Considering the long-term of exposure to Hg in the present study, it is likely that the color vision losses reflect a *cumulative* exposure: the product of the duration and intensity of exposure. The hypothesis of a cumulative effect finds support in the fact that in all studies reporting an injurious effect of Hg on color vision, regardless of whether exposure was low- or high-level, it was extended over years: 15.6 ± 3.3 years, range 5–18 (Canto-Pereira *et al.*, 2005); 8.3 ± 5.5 years (Cavalleri *et al.*, 1995); 9.6 ± 5.9 years (Cavalleri and Gobba, 1998); about 10 ± 5 years, range 4–25 (Feitosa-Santana *et al.*, 2007, 2008); 14.7 ± 9.7 years, range 3–33 (Urban *et al.*, 2003); 9.0 ± 4.7 years, range 3–22.5 (Ventura *et al.*, 2005); 4.3 ± 2.8 years, range 1.5–9 (Barboni *et al.*, 2009).

Conclusion

The present findings confirm that color vision impairments persist in subjects who were long-term occupationally exposed to Hg vapor and, at the time of testing, were presenting mean urinary concentration within the normal range for non-exposed individuals. Further studies would be necessary to address the discrepancy between the outcomes in the present and previous study (Feitosa-Santana *et al.*, 2008); and, considering the advantages of the triadic procedure in clinical evaluation of acquired color vision deficiencies, to attempt to verify and/or improve its efficacy.

Acknowledgements

Supported by FAPESP, CNPq, CAPES/PROCAD, FINEP IBN-Net. CFS, MTSB, and NNO were FAPESP fellows; DFV, LCLS, and NNO, CNPq fellows. We thank Marcilia Medrado-Faria for permission to recruit patients and Camila Perina for help in collecting data.

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