Prevalence of metabolic syndrome and cardiovascular changes in patients with chronic plaque psoriasis and their correlation with disease severity: A hospital-based cross-sectional study

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ABSTRACT

Background: Previous epidemiological studies suggest an association between psoriasis and metabolic syndrome and risk of subclinical atherosclerosis. However, there is a paucity of data in the Indian population on these associations. Objectives: To evaluate the prevalence of metabolic syndrome and subclinical atherosclerosis in patients with chronic plaque psoriasis compared to healthy controls and to correlate the prevalence of metabolic syndrome with severity of psoriasis. Methods: A hospital-based cross-sectional study was performed on 140 patients with chronic plaque psoriasis and 140 controls. Psoriasis was categorized as mild, moderate and severe based on psoriasis area and severity index (<10, 10–14 and ≥ 15, respectively) and as disease of short (<1 year), intermediate (1–3 years) and long duration (>3 years). In all patients and controls, body mass index was calculated, blood pressure and waist circumference were measured and fasting blood sugar and lipid profiles were estimated. Metabolic syndrome was diagnosed by the presence of 3 or more of the modified National Cholesterol Education Program’s Adult Treatment Panel III criteria. A subset of 30 psoriatic patients and 30 healthy controls were selected by the systematic sampling method for cardiac evaluation including electrocardiography, echocardiography and carotid intima-media thickness measurement. Results: The prevalence of metabolic syndrome was significantly more in psoriatic patients than in controls (39.3% vs. 17.1%, odds ratio = 3.13). Psoiatric patients also had a significantly higher prevalence of hypertension, abdominal obesity and diabetes. There was a significant trend to increase in prevalence of metabolic syndrome, hypertension and type 2 diabetes with increased severity and longer duration of the psoriasis. Patients with psoriasis had significantly higher carotid intima-media thickness (mean 0.61 mm ± 0.01 mm vs. 0.37 mm ± 0.01 mm) than controls. Limitation: This was a hospital-based cross-sectional study with a relatively small sample size. A prospective study with a larger sample would have validated the results further. Conclusion: There is a significantly higher prevalence of metabolic syndrome in psoriasis patients as compared to controls; the prevalence of metabolic syndrome and its components increases with severity and duration of psoriasis. There is a higher prevalence of subclinical atherosclerosis in patients with psoriasis thus increasing the risk of cardiovascular disease. We suggest that patients with moderate to severe psoriasis be screened routinely for metabolic syndrome and cardiovascular disease and encouraged to correct modifiable cardiovascular risk factors.

Key words: Metabolic syndrome, psoriasis and comorbidities, subclinical atherosclerosis

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**INTRODUCTION**

Psoriasis is a chronic, systemic, inflammatory disease with several clinical variants, the most common being chronic plaque psoriasis. It affects 1–3% of the population worldwide.[](1) Despite the fact that psoriasis carries minimal risk of mortality, it is associated with significant morbidity which may have a significant impact on quality of life of patients even if a relatively limited body surface area is involved.[](2) Globally, psoriasis has been reported to be associated with metabolic syndrome including obesity, dyslipidemia, diabetes, hypertension and more recently, atherosclerosis.[](3-6) However, most of these associations are based on computerized medical databases. Despite evidence suggesting that Indians are genetically and environmentally more susceptible to develop metabolic syndrome, there is a paucity of data on the association between psoriasis and metabolic syndrome from the Indian subcontinent.[](7-12) Our objective was to evaluate the prevalence of metabolic syndrome in patients of chronic plaque psoriasis compared to healthy controls and to correlate the prevalence of metabolic syndrome with severity and duration of psoriasis. We also evaluated the prevalence of cardiac changes and subclinical atherosclerosis in cases and controls selected from the original cohort.

**METHODS**

This cross-sectional study was conducted at All India Institute of Medical Sciences, New Delhi between January 2011 and October 2012, after receiving ethical clearance from the Institute’s ethical board.

Sample size was calculated using the following data: from the available information, it was expected that 30% of patients with psoriasis would have metabolic syndrome.[](7,10) The required sample size for an error margin of 8% and confidence level of 95% was 140. Consecutive patients with chronic plaque psoriasis attending the dermatology outpatient department were recruited after obtaining written informed consent. We included patients who were 18 years or older and excluded patients who had taken systemic therapy for psoriasis including acitretin, cyclosporine, methotrexate, phototherapy or biologics in the 2 months before their enrollment. After taking informed consent, healthy controls of similar age and sex were chosen from the general population including colleagues, hospital staff and relatives or attendants of dermatology inpatients. From this original cohort, 30 patients and 30 controls were selected by the systemic sampling method to study the prevalence of cardiac changes and subclinical atherosclerosis.

The study groups were evaluated by a dermatologist who recorded their demographic, biometric and the other relevant data, including age, sex, weight, height, body mass index, waist circumference, blood pressure, smoking and alcohol consumption habits, duration of disease, type and severity of psoriasis, presence and distribution of psoriatic arthropathy and concomitant medications. Smokers and alcohol drinkers were classified into current and ex-smokers or alcohol drinkers. Current smokers were defined as persons smoking tobacco at the time of study and those who stopped smoking less than 6 months ago. Ex-smokers were those who had stopped smoking more than 6 months before enrollment in the study. Non-smokers were persons who had never smoked a tobacco product. Similarly, current alcohol drinkers were defined as those who continued to have alcoholic beverages at the time of study and those who had stopped alcohol intake for less than 6 months. Ex-drinkers were defined as those who had not consumed alcohol for more than 6 months before enrollment. Non-drinkers were persons who had never consumed alcoholic drinks.

Psoriasis was classified as of short (<1 year), intermediate (1–3 years) or long (>3 years) duration. Patients were classified as having mild, moderate or severe psoriasis based on the psoriasis area and severity index (PASI) score (<10, 10-14 and >14 respectively). Body mass index was calculated as the ratio of weight in kg to the square of height in m². Waist circumference was measured by locating the uppermost part of the hip bone and placing a measuring tape around the abdomen snugly but without causing compression of the skin, ensuring that the tape was horizontal. Blood pressure was recorded as an average of two measurements, taken 5 min apart after subjects had been at rest for at least 10 min. A venous blood sample was taken in all patients and controls, after overnight fasting (at least 8 h) to estimate the fasting blood sugar (enzymatic method) and fasting lipid profile (enzymatic method).

The diagnosis of metabolic syndrome was made based on the presence of ≥3 criteria of the modified National Cholesterol Education Program’s Adult Treatment Panel III:[](13) waist circumference >102 cm in men or
>88 cm in women, hypertriglyceridemia ≥150 mg/dL, high-density lipoprotein cholesterol <40 mg/dL in men or <50 mg/dL in women, blood pressure ≥130/85 mmHg and fasting plasma glucose ≥100 mg/dL.

Thirty patients and 30 controls were then selected for evaluating the prevalence of subatherosclerosis and cardiac changes. Cardiac changes were studied with electrocardiography and echocardiography by a cardiologist. Carotid intima-media thickness (CIMT) of both common carotid arteries was measured by a cardiovascular radiologist using a high-resolution B-mode ultrasound (ATL 3500) with the 5–10 MHz linear array broadband transducer positioned in the common carotid artery, 1 cm distal to the carotid bifurcation in the posterior wall. Scanning involved examination of the common carotid artery both in longitudinal and transverse planes [Figure 1].

**Statistical analysis**

Data analysis was done using Stata software version 11.1 (StataCorp. 2009, College Station, TX: StataCorp LP). Quantitative characteristics such as age, waist circumference, systolic and diastolic blood pressures, high-density lipoprotein and triglyceride levels were compared between patients and controls using a two-sample t-test. Wilcoxon rank-sum (Mann–Whitney) test was also used for non-normally distributed values such as carotid intima-media thickness. Qualitative variables such as sex, duration and severity classifications of disease, smoking and alcohol use were compared between patients and controls using Chi-square test. The prevalence of metabolic syndrome and its components in patients with chronic plaque psoriasis of different severities and durations was compared using a trend Chi-square test. The prevalence of metabolic syndrome among patients was calculated as a proportion along with a 95% confidence interval. Odds ratios with 95% confidence intervals were calculated for different exposures using logistic regression analysis. Multiple logistic regression was employed to adjust for possible confounders. The correlation of different study parameters with severity of psoriasis was assessed by one-way ANOVA followed by Bonferroni correction for multiple comparisons. Odds ratio was also calculated along with 95% confidence intervals after categorizing study variables. A $P < 0.05$ was considered to be statistically significant.

**RESULTS**

Demographic characteristics of the study population and disease characteristics are reported in Table 1. Cases and controls were residents of various states of Northern India. The duration of psoriasis in our patients ranged from 3 months to 35 years while the psoriasis area and severity index (PASI) score of the 140 patients with psoriasis ranged from 2 to 30.

Based on modified National Cholesterol Education Program’s Adult Treatment Panel III criteria, metabolic syndrome was diagnosed in 55 (39.3%) patients with chronic plaque psoriasis and 24 (17.1%) healthy controls. This difference was statistically highly significant ($P < 0.001$) with an odds ratio of 3.13 with 95% confidence interval 1.80–5.45 ($P = 0.01$). This association persisted even after adjusting for differences in age, gender, body mass index, smoking and alcohol use with the adjusted odds ratio being 2.50 with 95% confidence interval 1.34–4.67 ($P < 0.01$) [Table 2a]. Adoption of the South Asia Modified cutoffs for abdominal obesity (≥90 cm for males and ≥80 cm for females) did not change the results overall ($P < 0.001$). The prevalence of metabolic syndrome in cases was then 59/140 (42.1%) and 30/140 (21.4%) in controls with an odds ratio of 2.67 (1.58–4.51) and adjusted odds ratio of 2.10 (1.15–3.82).

On studying the components of the metabolic syndrome, the following were found to be more common in psoriasis patients than in controls: central obesity in 26.4% versus 11.4% (odds ratio = 2.8, confidence interval 1.46–5.29), hypertension in 50.0% versus 29.3% (odds ratio = 2.4, confidence interval 1.47–3.95) and type 2 diabetes mellitus in 42.1% versus 21.4% (odds ratio = 2.5, confidence interval 1.48–4.26) [Table 2a].
Correlation of prevalence of metabolic syndrome and its components with severity and duration of chronic plaque psoriasis

There was a linear trend of increase in the prevalence of metabolic syndrome with increasing severity of psoriasis in patients compared to controls ($P < 0.001$) and it remained statistically significant with odds ratio for metabolic syndrome being $3.2$ (95% confidence interval, $1.41–7.45; P < 0.005$) among patients with moderately severe psoriasis and $7.1$ (95% confidence interval, $2.26–21.85; P < 0.001$) among patients with severe psoriasis vis-a-vis patients with mild psoriasis [Table 2b]. Patients with psoriasis of long duration had a higher prevalence of metabolic syndrome ($52, 55.9\%$) when compared to those with disease of short and intermediate duration [$11 (17.7\%)$ and $3 (36.7\%)$ respectively] There was also a statistically significant linear trend of increase in the prevalence of metabolic syndrome with increase in the duration of having had chronic plaque psoriasis ($P = 0.04$). As regards the association of components of metabolic syndrome with severity of psoriasis, patients with severe chronic plaque psoriasis had significantly higher prevalences of hypertension and diabetes than those with mild psoriasis [Table 2b and Figure 2]. We did not observe a significant difference in the prevalence of dyslipidemia between psoriasis patients and healthy controls.

Cardiovascular changes, subclinical atherosclerosis and chronic plaque psoriasis

Ten ($33.3\%)$ of 30 patients with chronic plaque psoriasis had abnormal findings on electrocardiography versus two ($6.7\%)$ of 30 controls, and the difference was statistically significant ($P = 0.01$, Chi-square test).
The most common electrocardiographic abnormality was ST/T wave changes, present in 5 (16.6%) patients. On echocardiography, 7 (23.3%) of 30 patients with chronic plaque psoriasis had abnormal findings in contrast to 2 (6.7%) of 30 controls, but this difference was not statistically significant ($P = 0.07$, Chi-square test). The most common change on echocardiography was a low ejection fraction. One patient had both global ventricular hypertrophy and a low ejection fraction (50–55%). Going further, we compared cardiologic abnormalities among smokers and non-smokers in the patient group. Electrocardiographic abnormalities were noted in 45% of chronic plaque psoriasis patients who smoked as against 25% of non-smoker

### Table 2a: Prevalence of metabolic syndrome and its components in 140 patients with chronic plaque psoriasis and 140 controls based on NCEP ATP III criteria

| Study parameter | Psoriasis n (%) | Control n (%) | $P^*$ | OR (95% CI) |
|-----------------|----------------|---------------|-------|-------------|
| WC (>102 cm (male), >88 cm (female)) | 37 (26.4) | 16 (11.4) | <0.001 | 2.78 (1.46-5.29) |
| Hypertension (>130/85 mmHg) | 70 (50.0) | 41 (29.3) | <0.001 | 2.41 (1.47-3.95) |
| Triglyceride (>150 mg/dL) | 40 (28.6) | 37 (26.4) | 0.68 | 1.11 (0.66-1.88) |
| HDL (<40 mg/dL (male), <50 mg/dL (female)) | 76 (54.3) | 75 (53.6) | 0.90 | 1.03 (0.64-1.65) |
| Type 2 diabetes mellitus (FBS>100 mg/dL) | 59 (42.1) | 30 (21.4) | <0.001 | 2.53 (1.48-4.26) |
| MS* | 55 (39.3) | 24 (17.1) | <0.001 | 3.12 (1.80-5.45) |
| MS$ | 59 (42.1) | 30 (21.4) | <0.001 | 2.67 (1.58-4.51) |

*P value using Chi-square test, *Using National Cholesterol Education Program’s Adult Treatment Panel III criteria, $Using South Asian-modified National Cholesterol Education Program’s Adult Treatment Panel III criteria. WC: Waist circumference, FBS: Fasting blood sugar, HDL: High-density lipoprotein, CI: Confidence interval, OR: Odds ratio

### Table 2b: Association of metabolic syndrome with severity of chronic plaque psoriasis

| Characteristics | Mild psoriasis (n=89) | Moderate psoriasis (n=33) | Severe psoriasis (n=18) | $P$ |
|-----------------|-----------------------|---------------------------|-------------------------|-----|
| Waist circumference (cm) | | | | |
| Mean±SD | 88.4±12.23 | 88.8±8.28 | 94.7±11.12 | 0.10 |
| Obesity (%) | 22 (24.7) | 8 (24.2) | 7 (38.9) | 0.44 |
| OR (95% CI) | 1.0 | 0.97 (0.38-2.47) | 1.94 (0.67-5.61) |
| Blood pressure (mmHg) | | | | |
| Systolic (mean±SD) | 127.4±15.31 | 132.4±12.87 | 133.9±10.72 | 0.08 |
| Diastolic (mean±SD) | 81.4±9.71 | 84.2±7.62 | 87.2±9.9* | 0.05 |
| Hypertension (%) | 37 (41.6) | 20 (60.6) | 13 (72.2) | 0.02 |
| OR (95% CI) | 1.0 | 2.16 (0.96-4.89) | 3.65 (1.20-11.13) |
| Triglyceride (mg/dL) | | | | |
| Mean±SD | 125.2±66.50 | 138.2±76.85 | 140.1±74.13 | 0.54 |
| High triglyceride (%) | 22 (24.7) | 12 (36.4) | 6 (33.3) | 0.40 |
| OR (95% CI) | 1.0 | 1.74 (0.74-4.10) | 1.52 (0.51-4.54) |
| HDL (mg/dL) | | | | |
| Mean±SD | 42.3±7.75 | 45.1±7.04 | 40.2±6.69 | 0.52 |
| Low HDL (%) | 48 (53.9) | 17 (51.5) | 11 (61.1) | 0.80 |
| OR (95% CI) | 1.0 | 0.91 (0.41-2.02) | 1.34 (0.48-3.78) |
| FBS (mg/dL) | | | | |
| Mean±SD | 96.2±15.56 | 100.2±16.21 | 106.9±21.31* | 0.04 |
| Diabetes (%) | 31 (34.8) | 17 (51.5) | 11 (61.1) | 0.06 |
| OR (95% CI) | 1.0 | 1.99 (0.88-4.47) | 2.9 (1.04-8.34) |
| Components of metabolic syndrome | | | | |
| 0 | 12 (13.5) | 5 (15.2) | 2 (11.1) | |
| 1 | 28 (31.5) | 7 (21.2) | 2 (11.1) | |
| 2 | 25 (28.1) | 3 (9.1) | 1 (5.6) | |
| ≥3 | 24 (26.9) | 18 (54.5) | 13 (72.2) | <0.01 |
| MS | 24 (27.0) | 18 (54.6) | 13 (72.2) | <0.001 |
| OR (95% CI) | 1.0 | 3.2 (1.42-7.45) | 7.0 (2.27-21.86) |

*Significantly different from mild psoriasis. CI: Confidence interval, OR: Odds ratio, SD: Standard deviation, HDL: High-density lipoprotein, FBS: Fasting blood sugar
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patients. Similarly, only 15% of non-smokers showed echocardiographic abnormalities compared to 36% of smokers amongst the patients of chronic plaque psoriasis.

Carotid intima-media thickness of the right common carotid artery in patients with chronic plaque psoriasis ranged from 0.4 to 1.2 mm with a mean of 0.7 mm ± 0.01 mm and median of 0.6 mm while in controls, it ranged from 0.3 to 0.6 mm with a mean of 0.4 mm ± 0.01 mm and median of 0.4 mm. Similarly, in the patients with chronic plaque psoriasis, the carotid intima-media thickness of the left common carotid artery ranged from 0.3 to 1.0 mm with a mean of 0.6 mm ± 0.01 mm and median of 0.6 mm while in controls, it ranged from 0.2 to 0.5 mm with a mean of 0.3 mm ± 0.01 mm and median of 0.3 mm. On applying the Student’s t-test, carotid intima-media thickness of both the right and left common carotid arteries was found to be significantly higher in patients than in controls (P < 0.001) [Table 3 and Figure 3]. One patient with psoriasis aged only 34 years had evidence of a soft plaque in the left common carotid artery near the carotid bulb causing a 30% stenosis [Figure 4]. The same patient had sinus tachycardia on electrocardiography while the echocardiogram was normal. The duration of disease in this patient was 8 years and the psoriasis area and severity index (PASI) score was 18.

DISCUSSION

We found a linear increase in the occurrence of metabolic syndrome as the severity and duration of psoriasis increased. Though Gisondi et al. in a study of patients with psoriasis of longer than 6 months’ duration observed an increased occurrence of metabolic syndrome in psoriasis patients, they did not find any correlation of metabolic syndrome with the severity of psoriasis.[14] In a study from Germany, Sommer et al. noted that hospitalized treatment-resistant patients with chronic plaque psoriasis were significantly more likely (odds ratio: 5.92) to have metabolic syndrome as compared to controls and this correlation was stronger for patients with greater body surface area involvement.[15] They did not observe any difference in the prevalence of metabolic syndrome amongst patients who had had their psoriasis for less than or more than 15 years. However, 15 years may have been too long a cut-off period as it probably takes the inflammatory triggers of psoriasis much less time to initiate metabolic syndrome. Langan et al. also observed an increasing trend of the presence of metabolic syndrome with increasing severity of psoriasis.[16] However, in this study based on retrieval of computerized medical records, only psoriasis patients aged 45–65 years were included.

There is a paucity of studies from India on the prevalence of metabolic syndrome in psoriasis patients. Nisa and Qazi reported an increased prevalence of metabolic syndrome in patients with psoriasis (28%) as

Figure 2: Correlation of prevalence of metabolic syndrome (MS), hypertension and type 2 diabetes mellitus in 140 patients with chronic plaque psoriasis of different severities (PASI: Psoriasis area and severity index)

Figure 3: Mean intima-media thickness of the right and left common carotid artery in 30 patients with chronic plaque psoriasis and 30 controls (CIMT: Carotid intima-media thickness, CCA: Common carotid artery)

Table 3: Thickness (mm) of common carotid arteries in 30 patients with chronic plaque psoriasis and 30 controls

| Vessel   | Psoriasis | Controls | P     |
|----------|-----------|----------|-------|
| Left CCA | 0.57±0.01 | 0.33±0.01| <0.001|
| Right CCA| 0.66±0.01 | 0.42±0.01| <0.001|
| Both CCA | 0.61±0.01 | 0.37±0.01| <0.001|

CCA: Common carotid artery
compared to controls (6%) with an odds ratio of 6.09. The high odds ratio in their study may be attributable to the high psoriasis area and severity index (PASI) scores (mean, 15.2 ± 13.9 and median, 13.05) of their patients, comparable to the scores of the patients with severe psoriasis in the present study (odds ratio of 7.2 for developing metabolic syndrome). However, Pereira et al. in a study on 77 patients with chronic plaque psoriasis from Mumbai, India and Lakshmi et al. in a study of 40 patients with chronic plaque psoriasis from South India were not able to demonstrate any significant association between metabolic syndrome and psoriasis in comparison to controls. More recently, Madanagobalane and Anandan with the use of the South Asian-modified National Cholesterol Education Program’s Adult Treatment Panel III criteria observed that metabolic syndrome was significantly more common in psoriasis patients (44.1%) than in controls (30%) but did not note any correlation with severity. Sharma et al. had also shown increased risk of metabolic syndrome in patients with psoriasis, especially in those with long-standing psoriasis and active joint disease.

There is substantial data to suggest that prevalence of various components of metabolic syndrome is higher in patients with psoriasis. From India, while Madanagobalane and Anandan, reported a higher prevalence of obesity in psoriasis patients than in controls, Nisa and Qazi did not observe any such difference in the occurrence of central obesity. The latter study needs to be interpreted keeping in mind the National Family Health Survey 2007 report in which a relatively lower prevalence of obesity was reported in the general population in Jammu and Kashmir (8.7%) compared to other North Indian states. We observed a linear relationship between the severity of psoriasis and prevalence of hypertension and diabetes. Though several studies from the West have shown an association between hypertension and psoriasis, Indian studies have been equivocal. However, the studies by Pereira et al., Madanagobalane and Anandan, Nigam and Dayal and Sundharam et al. corroborate our observations on the association of psoriasis and diabetes. Langan et al. noted a similar relationship of severity of psoriasis to the presence of obesity, hypertension and elevated fasting blood sugar. However, they categorized the severity of disease based on the percentage of body surface area involvement which may be a poor marker of the severity of inflammation. Of all the components of metabolic syndrome, inconsistencies across various studies are maximal with respect to dyslipidemia, with some studies indicating an association of dyslipidemia with psoriasis and others noting an association with respect to levels of some components of serum lipids. However, several workers were not able to corroborate these findings.

In keeping with our findings, a study from Israel also observed higher electrocardiographic abnormalities in patients with psoriatic arthritis when compared to controls. Nearly more than a fifth had abnormal echocardiogram findings in comparison to 6.7% of controls (P = 0.07). Similar findings have been reported by Biyik et al. in a study of 216 Turkish patients with psoriasis. These are the only available reports on electrocardiographic and echocardiographic abnormalities in psoriasis patients. In these societies, smoking is known to be nonexistent/very low, whereas our patient series showed a 37% prevalence.
of smoking. Our results indicate that smoking could be an additional contributor for electrocardiographic and echocardiogram abnormalities in chronic plaque psoriasis. However, this needs to be confirmed in other Indian settings with large sample sizes and long follow-up.

Our findings are also consistent with previous studies of Gonzalez-Juanatey et al., Yiu et al. and Mongy et al. all of whom had also observed carotid plaques in their patients with psoriasis.[6,27,28] Karoli et al. in a study of 100 patients from India had shown that in patients with psoriasis, carotid intima-media thickness was associated with increased severity and duration of psoriasis.[10] There was no significant correlation in electrocardiography, echocardiogram and carotid intima-media thickness findings in the present as well as previous studies.[6,28]

A limitation of our study, since it was cross-sectional, was that it does not take into account the directionality of the association to be set. The hypothesis that metabolic syndrome can occur more frequently in psoriasis needs to be validated in large prospective studies.

CONCLUSION

We found a higher prevalence of metabolic syndrome and its individual components in patients with psoriasis; these could play a role in accelerating the development of atherosclerosis. Though the association was seen at all severities of psoriasis, it increased as severity increased.

We also observed a significant increase in carotid artery intima-media thickness in psoriasis patients. There is a paucity of data on cardiovascular changes and prevalence of subclinical atherosclerosis in patients with psoriasis in comparison to controls in the Indian population but our study suggests a need to evaluate these aspects further with larger, prospective studies.

We suggest that patients with moderate to severe psoriasis and those with psoriasis for longer than 3 years be screened routinely for metabolic syndrome and cardiovascular disease and also be encouraged to correct their modifiable cardiovascular risk factors aggressively.

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Conflicts of interest

There are no conflicts of interest.

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