

## Original Articles

# Insulin sensitivity and cardiac autonomic function in young male practitioners of yoga

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### ABSTRACT

**Background.** While yoga is thought to reduce the risk of chronic non-communicable diseases such as diabetes, there are no studies on insulin sensitivity in long term practitioners of yoga. We assessed insulin sensitivity and cardiac autonomic function in long term practitioners of yoga.

**Methods.** Fifteen healthy, young, male practitioners of yoga were compared with 15 young, healthy males who did not practice yoga matched for body-mass index. Fasting insulin sensitivity was measured in the fasting state by the hyperinsulinaemic-euglycaemic clamp.

**Results.** There were no significant differences between the groups in their anthropometry or body composition. However, the fasting plasma insulin was significantly lower in the yoga group. The yoga group was also more insulin sensitive (yoga 7.82 [2.29] v. control 4.86 [1.97] (mg/[kg.min])/( $\mu$ U/ml),  $p < 0.001$ ). While the body weight and waist circumference were negatively correlated with glucose disposal rate in the controls, there were no similar correlations in the yoga group. The yoga group had significantly higher low-frequency power and lower normalized high-frequency power.

**Conclusion.** Long term yoga practice (for 1 year or more) is associated with increased insulin sensitivity and attenuates the negative relationship between body weight or waist circumference and insulin sensitivity.

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### INTRODUCTION

Obesity, type 2 diabetes and cardiovascular disease are major public health problems globally<sup>1-3</sup> in which insulin resistance (IR) has a central role. Prospective studies have shown that IR is an important predictor of whether or not an individual will develop diabetes later.<sup>2,3</sup> There is an interest in the potential role that non-

pharmacological interventions may play to prevent the onset of IR at an early age.

Exercise and daily physical activity is generally accepted as a part of the non-pharmacological approach to IR. For example, dynamic strength training improves insulin sensitivity (IS) in men with IR, independent of weight loss.<sup>4</sup> Low intensity and low volume exercise training has been found to be effective in reducing IR in healthy elderly subjects, due mainly to exercise-induced improvement in fitness levels.<sup>5</sup> The effect of exercise is also graded, in that an exercise prescription of 170 minutes/week improved IS in sedentary, overweight or obese subjects more substantially than a programme of 115 minutes of exercise/week, regardless of the intensity of exercise.<sup>6</sup>

In India, yoga is widely claimed to be effective in the prevention, management and cure of many diseases. Yoga modules have, for instance, been found to be effective in the management of hypertension, diabetes and IR.<sup>7-11</sup> These may be related to reductions in stress and arousal, since the basal metabolic rate (BMR) has been found to be reduced in practitioners of yoga,<sup>12</sup> as have diurnal metabolic rates;<sup>13</sup> the reduced metabolic rate of transcendental meditation (TM) has been called 'alert rest'.<sup>14</sup> The reduction in arousal has been attributed to a diminished cardiac sympathetic tone and enhanced vagal activity.<sup>15,16</sup> Further, an increase in baroreflex sensitivity has been documented with the practice of yoga including meditation or prayers.<sup>17</sup> Plasma norepinephrine levels have been shown to be reduced in patients with cardiac failure after yoga training<sup>18</sup> and urinary catecholamines have been shown to be significantly reduced in long term practitioners of yogic *asanas*.<sup>19</sup> Finally, yoga has been found to be useful in reducing IR-related risk factors.<sup>20</sup> These studies have mainly been done on older, obese, frankly hypertensive or diabetic subjects; moreover, many studies have used surrogate measures of IR such as the homeostatic model assessment (HOMA) or fasting plasma insulin or glucose levels.

Careful studies that measure IS in young adults who routinely practice yoga are necessary because (i) type 2 diabetes mellitus in India is increasingly being reported in young adults and children,<sup>21,22</sup> and (ii) this brings a prevention-oriented, culturally acceptable, lifestyle paradigm to bear on the problem. While there are no detailed interventional studies using yoga to test the hypothesis that yoga improves IS, we undertook a pilot study to measure IS in normal young healthy volunteers who routinely practised yoga for more than 12 months in comparison with BMI-matched non-

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yoga practitioners, using the hyperinsulinaemic–euglycaemic clamp (HEC) technique.

## METHODS

### *Subjects*

The yoga group consisted of 15 male volunteers in the age range of 20–32 years, who were enrolled for various yoga courses in a residential yoga school, and had a minimum of 12 months of experience of practising yoga. The general daily practice of yoga followed was an *asana* (physical posture) for 37 minutes, *pranayama* (breathing techniques) for 18 minutes and meditation for 23 minutes; a total of about 70 minutes a day for 6 days a week. The control group consisted of 15 male volunteers; the entire group was matched for BMI, in the age range of 18–35 years, who had never practised yoga. The control group was recruited through advertisements in and around St John's Medical College campus. None of the subjects smoked or drank alcohol, and usually had less than 3–4 caffeinated beverages per day. Food intake was assessed using a food diary for 3 days, and physical activity level (PAL) was calculated using 3-day physical activity diaries with activities filled in blocks of 10 minutes. PAL was computed as the estimated total 24-hour energy expenditure from the physical activity diary divided by the estimated BMR (from standard regression equations).<sup>23</sup> Subjects on a high meat protein diet and high PAL were excluded. PAL values obtained by the diary recall method have been validated with PAL values derived using doubly labelled water method in Indians in our laboratory.<sup>24</sup> Both groups reported that their weight was stable during the past 6 months. The study protocol and potential risks involved were explained to each subject and written informed consent was obtained. All were in good health as determined by the medical history, physical examination, analysis for blood cell counts, routine blood biochemical profile and urinalysis. Subjects with a family history of diabetes, high resting blood pressure, fasting plasma blood glucose >110 mg/dl, abnormal liver function tests and on any medication were excluded from the study. The Institutional Ethical Review Board of St John's Medical College and Swami Vivekananda Yoga Anusandhana Samsthana (SVYASA) approved the research protocol.

### *Anthropometry*

The subjects reported to the laboratory in the evening before the start of the study and stayed overnight in the laboratory after being provided a standard dinner, without any caffeinated beverages. Anthropometric and skin-fold thickness measurements were done on the day of the experiment, early in the morning after an overnight fast of 10 hours. Subjects were weighed in minimal clothing to the nearest 0.1 kg and their height was measured to the nearest 0.1 cm. Their skin-folds (biceps, triceps, subscapular and supra-iliac) were measured to the nearest 0.2 mm using a skin-fold caliper (Holtain, Crymych, UK) and their body density predicted from age- and gender-specific equations; body fat proportion was calculated from body density.<sup>25–27</sup> Since most of the muscle mass is appendicular, and earlier studies have shown that the limb girth corrected for skin-fold appears to correlate best with total body skeletal mass,<sup>28</sup> whole body muscle mass was predicted from an Indian equation based on skin-fold corrected arm muscle area (CAMA).<sup>29</sup> Waist and hip circumferences were measured using a standard non-stretchable tape measure, at the narrowest point between the iliac crest and ribcage (waist) and at the level of the greater trochanter (hip).

### *Hyperinsulinaemic–euglycaemic clamp technique*

The experiment was performed after the subjects had emptied their urinary bladder. Soon after anthropometric measurements, an intravenous catheter (Jelco, 22 G, Medex Medical Ltd., Lancashire, UK) was inserted, under sterile precautions, into the antecubital vein for infusion of insulin and 25% dextrose solutions, while another catheter was inserted in an anti-flow direction into the dorsal vein of the contralateral hand for arterialized venous blood sampling (using a warm box into which the hand was placed, maintained between 60 °C and 65 °C). The latter catheter was kept patent using a slow intravenous drip of isotonic saline. The insulin infusate was prepared in 100 ml isotonic saline to which 4 ml of the subject's whole blood (previously drawn) was added, to prevent insulin adsorption onto the plastic surfaces of the syringe and tubing. Regular human insulin (Eli Lilly & Co, Gurgaon, India) was diluted with this isotonic saline to a concentration of 2083.5 µM/L (300 mU/ml). A sterile 25% dextrose solution was used to prevent hypoglycaemia during the HEC as described below. Insulin and glucose infusions began 30 minutes after cannulation, after blood samples were collected for baseline glucose and insulin measurements, and the basal heart rate and blood pressure were recorded.

The protocol for performing the clamp was as described earlier.<sup>30</sup> Briefly, a 10-minute priming insulin infusion was followed by a constant infusion at the rate of 277.80 pmol/m<sup>2</sup> surface area/minute (40 mU/m<sup>2</sup> surface area/minute) by a calibrated infusion pump (Harvard Infusion Pump, model 55-2222, Holliston, MA), for the next 110 minutes, to increase the plasma insulin concentration to about 694.5 pmol/L (100 µU/ml).<sup>30</sup> The glucose infusion, also delivered by a Harvard infusion pump, was begun at the fourth minute, and the glucose infusion rate up to the tenth minute was empirically set at 0.01 mmol/kg/minute (2 mg/kg/minute). Plasma glucose concentration was maintained at an average basal value of 5 mmol/L (90 mg/dl). Subsequent glucose infusion rates were based on arterialized venous plasma glucose values obtained every 5 minutes. These were drawn into ethylene diamine tetra acetate (EDTA) tubes (Becton Dickinson, Franklin Lakes, NJ) and the separated plasma analysed by the glucose oxidase method on a bedside glucose analyser (GM9D, Analox instruments, London, UK). The intra-assay coefficient of variation for this method (using 8 mmol/L [144.1 mg/dl] standards) was <1%, while the interassay coefficient of variation was <5%. Blood samples for insulin measurements were collected every 20 minutes in heparinized tubes (Becton Dickinson, Franklin Lakes, NJ) and centrifuged at 4 °C. The plasma was stored at –80 °C until analysis by an electrochemiluminescent method (Roche Diagnostics, Mannheim, Germany). The intra-assay coefficient of variation for this method (using tri-level lyophilized serum controls, level 1: 68.76–113.20 pmol/L [9.9–16.3 µU/ml]; level 2: 215.30–444.48 pmol/L [31–64 µU/ml]; level 3: 791.73–1173.71 pmol/L [114–169 µU/ml], Biorad, Irvine, CA) was <5% while the interassay coefficient of variation was <10%. The method and formula used for the calculation of the glucose disposal rate as the glucose infusion rate required for maintenance of the plasma glucose concentration at the nominated fasting level throughout the clamp procedure, was as previously described.<sup>30</sup> IS was calculated as the ratio of the glucose disposal rate and plasma insulin concentration for nominated periods of the clamp. Both glucose disposal rate and IS were calculated over 20–120 minutes of the clamp, as previously described.<sup>30</sup>

### Cardiac autonomic function

After a 30-minute rest period following i.v. catheterization described above, a continuous lead II ECG was obtained (Nihon Kohden RM-6000, Japan) for 10 minutes, before the start of the insulin infusion, during which the subjects were awake, lay supine and breathed normally. Subjects were asked to avoid unnecessary movements during this period. Spectral analysis of heart rate variability was performed as described earlier.<sup>31</sup> Briefly, data segments of 128-second duration were sampled at 2 Hz to create 256-point datasets. Thus, for each 10-minute recording, 6 datasets of 256 points, overlapping by 50%, were created. Linear trends were removed from each dataset to avoid its contribution to low frequency (LF) power and a Hanning window was used to attenuate spectral leakage. Spectral analysis to calculate LF and high frequency (HF) power (reflecting cardiac sympathetic and parasympathetic nerve activity, respectively) was done using a Fast Fourier Transform. In addition to the absolute power, these data were also normalized for total power minus power of the very low frequency (VLF) band (0.0–0.04 Hz).<sup>32</sup> The LF/HF ratio, which is regarded as an index of sympathovagal balance, was also computed.

### Statistical analysis

A minimum sample size of 8 subjects in each group was calculated based on the published clamp IS values,<sup>30</sup> to detect a difference of 10% in IS between groups, with a level of significance of 5% and power of 80%. We recruited 15 subjects in both the groups. Normality of data was assessed by evaluating the ratio of skewness to the standard error of skewness. Almost all the parameters were normally distributed. All data are expressed as mean and standard deviation (SD). The studied variables were IS, glucose disposal rate, metabolic clearance rate (MCR) of insulin, basal glucose and insulin, weight, BMI, percentage body fat (%BF) and waist circumference. Differences in the anthropometric, spectral and clamp variables between groups were assessed by independent sample *t* test. Pearson correlations were performed between IS, glucose disposal rate and anthropometric variables such as weight, BMI, %BF and waist circumference. Regression analyses were also performed between IS and glucose disposal rate with anthropometric variables. Differences in slopes between groups were assessed using ANCOVA. Results were considered significant if  $p < 0.05$ . All statistical analyses were performed using SPSS (v13.0, SPSS, Chicago, Ill, USA).

### RESULTS

There were no significant differences between the groups in terms of their anthropometry or PALs. However, subjects in the yoga group were slightly but significantly older by about 4 years (Table I). There were no significant differences between the groups in calculated arm muscle area or muscle mass. The yoga subjects had practised yoga for a mean of 39 (28) months (range 12–120 months).

While there was no significant difference between the groups in basal glucose levels, the yoga group's fasting plasma insulin level was lower than that of controls by about 50% (Table II). During the HEC, the glucose disposal rate and IS of the yoga group was significantly higher, as was the MCR of insulin (Table II). The difference in IS between the groups persisted after adjusting for age in an analysis of covariance model ( $p < 0.001$ ). There was a significant correlation between various anthropometric parameters and IS in the control group (weight:  $r = -0.76$ ,  $p = 0.003$ ; BMI:  $r = -0.72$ ,  $p = 0.002$ ; %BF:  $r = -0.59$ ,  $p = 0.021$ ; and waist circumference:  $r = -0.70$ ,  $p = 0.004$ , respectively) while in the yoga

group, these correlations were low and not significant (weight  $r = -0.04$ , BMI  $r = -0.40$ , %BF  $r = -0.26$  and waist circumference  $r = -0.20$ ). The slope of regression of IS on weight was close to being significantly different between the groups at  $p = 0.07$ ; and the regression of glucose disposal rate by weight was significantly different between the 2 groups ( $p = 0.03$ , Fig. 1, upper panel). The slope of waist circumference on IS between groups was not significant ( $p = 0.147$ ). However, there was a significant difference between groups in the slope of waist circumference on glucose disposal rate ( $p < 0.05$ , Fig. 1, lower panel). There were no significant differences between the slopes of BMI or %BF on IS ( $p = 0.451$ ,  $0.497$ ) or glucose disposal rate ( $p = 0.173$ ,  $0.365$ ) between the groups. Within the yoga group, there was no correlation between the duration of yoga practice and IS ( $r = -0.1$ ,  $p > 0.05$ ), although the age of the subjects and duration of yoga practice were significantly and positively correlated ( $r = 0.4$ ,  $p < 0.05$ ).

Resting heart rates were comparable between the groups. At baseline, the yoga group had a significantly higher LF power in absolute terms as well as when normalized for total power. Normalized HF power was significantly lower in the yoga group. The differences in LF and HF power between the groups translated into a higher LF/HF ratio in the yoga group compared with that in controls (Table III). Further, the significant differences in all reported parameters between the groups persisted even after adjusting for age.

### DISCUSSION

The principal finding of our study is that the practice of yoga over a period of at least 1 year is associated with greater IS in healthy young men compared with anthropometrically similar men who

TABLE I. Anthropometric parameters of the yoga and control groups

Parameter	Yoga group (n=15)	Control group (n=15)
Age (years)	26.6 (3.2)*	22.6 (3.9)
Height (m)	1.65 (0.06)	1.69 (0.05)
Weight (kg)	58.4 (7.1)	61.9 (6.3)
Body mass index (kg/m <sup>2</sup> )	21.4 (1.8)	21.7 (1.8)
Per cent body fat	15.0 (4.3)	16.4 (4.5)
Fat mass (kg)	8.9 (3.2)	10.3 (3.5)
Fat-free mass (kg)	50.0 (5.8)	51.6 (4.5)
Muscle mass (kg)	28.8 (2.8)	30.2 (2.3)
Waist-hip ratio	0.82 (0.04)	0.82 (0.03)
Physical activity level	1.50 (0.08)	1.44 (0.23)
Mid-upper arm circumference (cm)	24.5 (1.6)	25.7 (1.9)
Corrected arm muscle area (cm)	28.4 (4.7)	30.3 (4.5)
Waist circumference (cm)	71.2 (5.5)	72.9 (4.4)
Hip circumference (cm)	87.2 (4.1)	88.4 (4.0)

All values are mean (SD) \*  $p < 0.05$ , independent Student *t* test

TABLE II. Hyperinsulinaemic-euglycaemic clamp parameters in both groups

Parameter	Yoga group (n=15)	Control group (n=15)
Glucose disposal rate (mg/(kg.min))	6.0 (1.6)*	4.8 (1.6)
Insulin sensitivity (mg/(kg.min))/( $\mu$ U/ml)	7.8 (2.3) <sup>†</sup>	4.9 (1.2)
Steady state plasma insulin (pmol/L)	539.6 (65.3) <sup>†</sup>	707.7 (120.1)
Metabolic clearance rate of insulin (ml/m <sup>2</sup> .min)	559.6 (70.3) <sup>†</sup>	451.6 (84.8)
Basal glucose (mmol/L)	5.1 (0.3)	5.2 (0.5)
Basal insulin (pmol/L)	35.4 (13.1) <sup>†</sup>	73.6 (33.3)

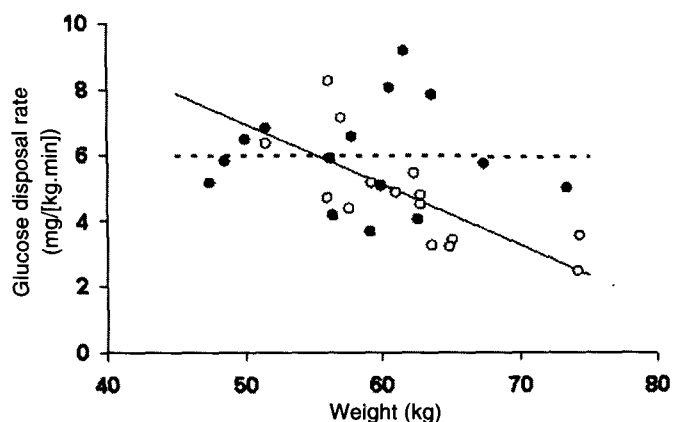
All values are mean (SD) \*  $p < 0.05$ , independent Student *t* test  
<sup>†</sup>  $p < 0.001$ , independent Student *t* test

had never practised yoga. In addition, the negative relationship between body weight, fat or waist circumference, which was evident in the control group, was attenuated in those who practised yoga. Even though the subjects were not matched for age, the IS was higher in the yoga group, who were older and would have

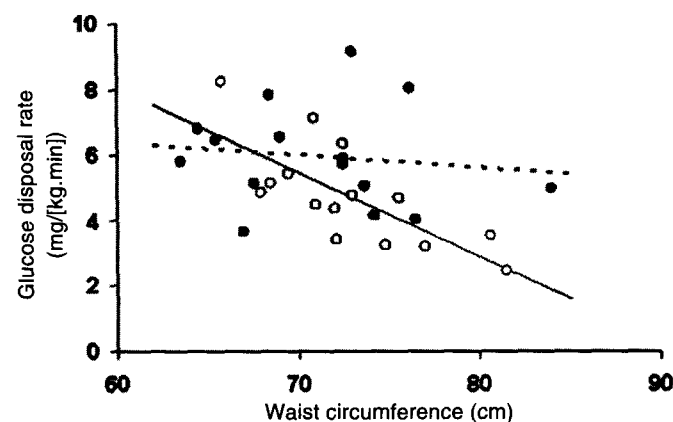
been expected to have a lower IS; further, the differences in IS between the groups persisted after the statistical analysis was adjusted for age within the model. It was noteworthy that the duration of yoga practice did not correlate with IS in the yoga group, suggesting that the beneficial effects on IS may set in relatively early, but may equally reach a ceiling effect with this type of yoga practice. On the other hand, the duration of yoga practice correlated significantly with the age of the subjects, and the latter is expected to be associated with a reduction in IS. Therefore, it might be that there are complex interactions between age, duration of yoga practice and IS. Yoga has been shown to be beneficial in people with type 2 diabetes with reported improvements in fasting and postprandial blood glucose as well as glycosylated haemoglobin levels.<sup>10,33</sup> A review of yoga and IR has indicated that yoga is associated with beneficial effects on the indices of IR.<sup>20</sup> Although our study was on healthy young volunteers without any IR-related risk factors, the results suggest that yoga increases IS even in these low risk individuals, and may be a useful lifestyle modification to prevent IR.

One possible mechanism by which yoga may have operated is by reducing stress or arousal,<sup>16,34</sup> since chronic stress is implicated in the pathogenesis of the IR syndrome.<sup>35,36</sup> There is some evidence that yoga enhances cardiac vagal activity and reduces sympathetic activity.<sup>16,20</sup> However, in this study, practitioners of yoga had higher resting sympathetic activity compared with controls, as evidenced by higher normalized LF values. This may have been related to the stress of a novel experimental setting, since in contrast to the yoga group, many of the healthy subjects in the control group had undergone other experimental procedures such as protein kinetic studies in the experimental laboratory. While autonomic nervous function is clearly related to ageing, we are not aware of studies that have indicated that a small difference in age (4 years) in young, healthy adults would result in significant changes, as observed in our study. Indeed, the scale of difference in autonomic function between the study groups was marginally larger than what was observed in previously published studies comparing young adults with older individuals (with a mean age difference of >40 years).<sup>37</sup> Ageing might be expected to decrease total power and HF power in absolute terms but both of these were in fact not different between the study groups. What is important is that enhanced sympathetic activity typically would have resulted in lower IS and it is conceivable that the differences between the groups are greater than those described in our study. However, there were no significant correlations between heart rate variability and duration of yoga practice as well as age in the pooled dataset, suggesting that the novelty of the experiment might have been the dominating factor in these considerations.

Another possible mechanism by which yoga improves IS may be related to skeletal muscle function, since a large part of the disposal of glucose in the euglycaemic resting state occurs in skeletal muscle. Since the muscle mass in both the groups was similar, it may be that muscle function rather than mass is the critical variable. Skeletal muscle function improves after yoga, since the *asanas* used involve stretching of muscles, which increases flexibility, strength and metabolic rate, which in turn could improve the muscle uptake of glucose.<sup>11</sup> Yoga has also been shown to improve muscle strength and isometric muscle endurance, although these were not recorded by us.<sup>38</sup> The stretching of muscles alternating with contraction may be an important aspect of the effect of yoga, since muscle hypertrophy due to muscle protein synthesis is known to occur with stretching in mammalian models.<sup>39</sup> The linkage between muscle stretch and glucose uptake by muscle may be linked to the expression of



- (Dashed line) Yoga group:  $r=0.00$ , Glucose disposal rate= $(-0.0003*\text{weight})+5.97$
  - (Solid line) Control group:  $r=0.74$ , Glucose disposal rate= $(-0.183*\text{weight})+16.08$
- Difference between slopes:  $p=0.03$



- (Dashed line) Yoga group:  $r=0.14$ , Glucose disposal rate= $(-0.039*\text{waist circumference})+8.703$
  - (Solid line) Control group:  $r=0.73$ , Glucose disposal rate= $(-0.257*\text{waist circumference})+23.50$
- Difference between slopes:  $p=0.049$

FIG 1. Linear regression between glucose disposal rate and weight (upper panel) and waist circumference (lower panel) in both groups

TABLE III. Resting heart rate and heart rate variability in the frequency domain in the study groups

Parameter	Yoga group (n=15)	Control group (n=15)
Resting heart rate (beats per minute)	62 (7)	65 (9)
Total power (0–0.4 Hz) $\text{ms}^2$	3406 (1703)	2711 (2251)
Normalized low frequency power	61.9 (15.2)*	45.4 (14.6)
Normalized high frequency power	43.1 (11.6)*	60.6 (13.1)
Low frequency/high frequency ratio	1.59 (0.83)*	0.83 (0.43)

All values are mean (SD) \*  $p<0.05$ , independent Student *t* test comparing groups at baseline

neuronal nitric oxide synthase (nNOS) in stretched or loaded muscle.<sup>40</sup> In turn, nitric oxide has been shown to positively modulate glucose uptake in muscle preparations, and this may be additive to insulin-stimulated glucose uptake.<sup>41</sup> The foregoing discussion does not discount the possibility that the effects in the yoga group might be related to an exercise paradigm, although significant exercise training would have raised the HF power in the yoga group, which was not observed. Even so, low intensity and low volume exercise has been shown to improve IR, measured by HOMA-IR, in elderly subjects independent of loss of body weight.<sup>5</sup> Exercise-based reduction in body weight may also result in improved functional capacity through greater mitochondrial content in skeletal muscle.<sup>42</sup>

Body weight and waist circumference are related to IS, and the practice of yoga over a period of time has been associated with a reduction in body weight and an improvement in body composition, possibly with the loss of body fat.<sup>43</sup> However, the lack of correlation between glucose disposal and body weight or waist circumference in the yoga group in our study is particularly interesting, suggesting that those who practice yoga over a long period have better glucose disposal and IS irrespective of their body weight and composition. None of the subjects in our study reported changes in body weight, nor were there any differences in body composition between the groups. The overall daily physical activity levels in the 2 groups were also comparable. Therefore, our preliminary cross-sectional study suggests that the practice of yoga improves IS independent of the usual anthropometric risk factors for type 2 diabetes. Clearly, more intervention trials are necessary to strengthen the findings. Also, the multidimensional mental and physical effects of yoga and its role in the prevention of the IR syndrome need further study.

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