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Adverse Effects of Sedentary Lifestyles: Inflammation, and High-Glucose Induced Oxidative Stress

—A Double Blind Randomized Clinical Trial on Diabetic and Prediabetic Patients

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Abstract

Sedentary lifestyles promote adipose tissue accumulation that generates systemic inflammation and oxidative damage. Physical activity induces cardiovascular fitness, increases muscle mass, and healthy blood glucose regulation, while reducing visceral fat, triglycerides and low-density lipoproteins. It is theoretically possible to develop a long-term multi-exercise regimen for health management and enhancement. Pragmatically, time and career restraints, individual choices, genetic factors, or demoralization due to the draconian commitment involved in weight loss, have rendered over a billion of individuals obese, or overweight, burdened by excess lipids, insulin resistance, elevated glucose levels, and inflammation, that foster a number of medical conditions including diabetes. Strenuous overtraining has ensued adverse effects, including an upsurge of proinflammatory cytokines, and hyperglycemia. We implemented an one-month long innovative method with 20 diabetic and prediabetic patients. Results demonstrated a statistically significant reduction of both fasting and PP blood glucose. Fasting and PP insulin reached optimal levels. There was a substantial decline in dyslipidemia, reflecting a reverse relationship of elevated HDL versus triglycerides descending towards the normal range. The notable visceral fat reduction was validated by sonography reports that indicated no evidence of fatty liver in seven patients previously diagnosed with hepatic steatosis. These findings have important implications in improving the health status of obese diabetic and prediabetic individuals, by helping them jumpstart an active lifestyle, or by serving as an exercise alternative to reduce lipids, blood glucose levels and insulin resistance.

Keywords

Inflammation, Oxidative Stress, Visceral Adiposity, Lipoproteins, Triglycerides, Blood Glucose, Insulin, Hepatic Steatosis, Dyslipidemia, Analgesia, Diabetes, Prediabetes, Weight Loss, Exercise

1. Introduction

Regular exercise increases cardiovascular health, and leads to optimal blood glucose regulation while positively impacting on lipids, high-density lipoprotein (HDL) and low-density lipoprotein (LDL) [1]. Resistance training lowers LDL and optimally elevates HDL, a multi-protein particle that modulates vascular health by removing excess cholesterol from peripheral tissues and reverse-transporting them to the liver [2] [3]. Prolonged exercise decreases triglycerides in both endurance athletes and untrained men [4]. Lack of physical activity due to work load and time restraints and the popularity of cheap, energy-dense food has resulted in a global alarming increase of obese, and overweight individuals to over 1.7 billion [5]. Excess body weight, combined with a sedentary lifestyle, promotes insulin resistance, and increases blood glucose which induces tissue injury due to DNA disintegration; additionally, it causes abnormal increases in caspase-3, the executioner of apoptosis, in charge of eliminating DNA fragments, and decomposed cytoskeletal proteins [6] [7]. Diabetic nephropathy and non-alcoholic fatty liver are some examples of the adverse consequences of degraded systemic controls regulating blood glucose [8]. The liver is crucial for glucose metabolism which, in turn, is necessary for the synthesis of adenosine triphosphate (ATP), the primary source of biological energy. High concentrations of glucose are a biological trigger for liver damage, due to an overstimulation of metabolic oxidation that transforms molecules into unpaired-electron ions, termed free radicals [9]. Even mild increases in glucose provoke an overproduction of reactive oxygen species (ROS), inevitably causing oxidative stress, partial depletion of ATP, and neuronal apoptosis [10]. Oxidative stress emanates from an imbalance between the generation of excess free radicals, and the electron-donation process by anti-oxidants that replenish and rebalance the ROS unpaired electrons [11]. ROS are released by phagocyte cells to eliminate invading pathogens or harmful bacteria; therefore, in moderation, they serve as an immune system defence [12].

Oxidative stress, as measured by urinary 8-epi-prostaglandin F2 alpha (8-epiPGF2a) concentration, is specifically implicated in visceral fat accumulation [13]. Systemic inflammation is the result of visceral adipose tissue secreting inflammatory adipokines, such as interleukin-6 (IL-6), into the portal veins of the blood circulatory system. This was demonstrated by research looking at inflammatory markers such as C-reactive protein (CRP), and interleukin-6 (IL-6) that were 50% greater in the portal vein blood samples, rather than the radial artery blood samples of 25 obese patients [14]. Intraabdominal adiposity is also

characterized by a reduced production of adiponectin, a hormone involved in regulating glucose fatty acids breakdown. Adiponectin has anti-diabetic, anti-inflammatory and anti-oncogenic properties, and it is inversely correlated with visceral fat [15]. Accumulated adiposity is accompanied by elevated apolipoprotein B (apoB), the primary component of low-density lipoproteins (VLDL, IDL, LDL), and dyslipidemia, defined as a combination of high triglycerides/low HDL [16]. It is also associated with an over-secretion of tumor necrosis factor-alpha (TNF-α) that induces insulin resistance [17]. In conclusion, visceral adipose tissue as evidenced by imaging techniques is associated with hyperinsulinemia, glucose intolerance, hypertriglyceridemia, dyslipidemia, inhibited HDL, oxidative stress and inflammation marked by increases in IL-6, CRP and TNF-α.

Obesity or being overweight combined with insulin resistance promotes the pathogenesis of type 2 diabetes and hypertension, the major predisposing factors of cardiovascular disease (CVD) that kills about 18 million individuals yearly [18]. Diabetes and CVD have been connected to a higher mortality rate from infectious diseases. According to a recent report a high prevalence of COVID 19 patients are classified as overweight [19].

Obesity is defined as the excess accumulation of adipose tissue predisposing the body to unmanageable oxidative stress and inflammation. The elevated production of free radicals during hyperglycemia disrupts both insulin signaling, and insulin secretion by pancreatic B cells, escalating and promoting diabetes [20]. Diabetes is a group of metabolic diseases defined by slow healing, B-cell insufficiency, insulin resistance, and chronic high blood glucose that eventually damages vital organs including the eyes, kidneys, heart, and the nervous system. Type 1 diabetes is characterized by a compromised autoimmune process as a result of a selective loss of B cells of the pancreas, leading to inadequate insulin secretion, and deficient insulin-tissue protein communications. In type 2 diabetes B cells are available but dysfunctional, exhibiting secretory and signaling defects, which are exacerbated by obesity and insulin resistance [21]. This deficiency is accompanied by an excess of pancreatic A-cells that appear to contribute to the hyperglycemia of this condition [22].

There is evidence that hyperglycemia elevates oxidative stress, while significantly compromising systemic antioxidant defences. In vitro, the mitochondria of obese type 2 diabetics produce significantly more ROS, with a notable decrease of the antioxidant enzymes glutathione (GSH) peroxidase, and superoxide dismutase [23]. Moreover, diabetics' erythrocytes present reduced levels of GSH, juxtaposed by high levels of glutathione disulfide (GSSG), which is the oxidized form of GSH [24]. Diabetics manifest abnormal glucose levels despite fasting glucose treatments, due to a combination of glucose toxicity and lipotoxicity, resulting by the metabolic oxidation of elevated lipid levels in the blood. According to this view, both hyperglycemia and hyperlipidimia eventuate a dysfunctional B-cell activity [25]. Both obesity and type 2 diabetes are associated with an increase in inflammatory markers including TNF-α and IL-6 that pre-

sumably inhibit insulin signalling, leading to a dysfunctional glucose insulin regulatory system [26]. Triglycerides, one of the common denominators underlying both conditions, is implicated in low-grade inflammation, and is one of the best predictors of atherosclerosis [27] [28]. Excess lipids in the blood accumulate in the liver, often causing lipotoxicity and insulin resistance [29]. Non-alcoholic (NA) steatosis or fatty liver, one of the consequences of visceral adiposity, is the result of an imbalance between intrahepatic triglycerides' production and export. It often progresses to steatohepatitis, fibrosis, and cirrhosis. Overall, lipotoxicity, inflammation, and visceral fat are associated with excess triglycerides that represent the core components of arterial plaques [30]. On the other hand, high-density lipoprotein (HDL) has been correlated with cardiovascular health. At optimum levels HDL is anti-inflammatory, and inhibits oxidized phospholipids, and low-density lipoproteins [31]. However in systemic inflammatory states like atherosclerosis, HDL loses its protective properties and becomes pro-inflammatory [32]. This apparent contradiction is the outcome of systemic balance, where in moderation, all biological mechanisms are purposeful and necessary. Optimal levels of triglycerides serve as an energy source. In excess, however, triglycerides pose a significant health risk.

Obesity and diabetic or prediabetic conditions characterized by visceral fat accumulation, are very difficult to treat due to multiple complications including inflammation, insulin resistance, and high-blood glucose which provokes oxidative stress. Laser and radiofrequency studies are sparse, and suffer from methodological issues, or lack of clarity on their measuring variables. Sixteen minutes of Low-level laser therapy (LLLT), combined with one hour of aerobic and resistance training, reported visceral fat reduction as measured by a conductance scale. However it is unclear if the results were due to the LLLT or the exercise [33]. A follow up study by the same investigators demonstrated no visceral fat differences between the experimental and control groups [34]. A radiofrequency study, published in Cairo University Bulletin, showed an overall fat loss in the experimental group; however, there was no clear indication of visceral adipose tissue decrease [35]. In conclusion, most laser and radiofrequency studies report results on overall fat reduction, without specifically addressing visceral adiposity.

Randomized placebo-controlled data demonstrated some modest reduction of visceral adipose tissue, and fatty liver improvement following eight weeks of aerobic exercise [34]. Resistance training resulted in significantly lower levels of the low-density lipoprotein (LDL), and an improvement in muscular strength, but no differences in BMI, in obese postmenopausal women who usually manifest a greater prevalence of visceral fat [36] [37]. Exercise was effective in both reducing visceral fat, and inflammation, as measured by the inflammatory marker CRP; however, there were no visible results in terms of BMI decrease or physical fitness [38]. Although short-term exercise appears to be moderately effective in reducing visceral fat, long-term physical activity seems necessary to sustain, and further reduce visceral adipose tissue. Intense interval running is ef-

ficient in improving cardiorespiratory fitness and glucose tolerance; but it has no effect on total bone mass or muscle mass, unlike strength training interventions. Prolonged training is necessary to treat hyperlipidemia and obesity [39]. Low-volume intense exercise reduced hyperglycemia in type 2 diabetic patients [40]; yet, a single session of this type of physical activity demonstrated a non-significant reduction of blood glucose ($p = 0.16$) [41]. Overall, exercise is beneficial in enhancing and safeguarding health; however it requires a substantial investment in time and effort, as well as a prolonged commitment to constantly performing a combination of different types of physical activity that include both aerobics and strength/resistance gymnastics. Juxtaposed to these well documented advantages, there is evidence that overtraining results in the release of excess muscle-derived IL-6 into the bloodstream, resulting in increased inflammation [42]. Maximal dynamic exercise increases blood glucose levels leading to hyperglycemia in both healthy adults and non-insulin-dependent diabetics (NIDD). In this clinical trial, NIDD manifested a significantly greater 60-min post-exercise hyperglycemia and hyperinsulinemia [43]. This negative exercise effect appears to be due to the disproportionate increase of seven- to eightfold glucose production (GP), as a result of intensified catecholamine signaling, while glucose utilization (GU) is only three- to fourfold. The inordinate GP > Gu relationship is exacerbated during the exhaustion stage, aggravating high blood glucose and triggering a significant rise in insulin to regulate glucose levels. Obviously, such response would be unavailable in type 1 diabetes sustaining their hyperglicemia, hence adversely affecting their condition [44] [45]. Despite the adverse effects of overtraining, regular exercise performed in moderation is widely recommended. Resistance exercise decreases triglycerides, LDL, and enhances HDL and optimal blood glucose regulation. Aerobics reduce visceral fat and inflammation and improve fatty liver. Intense interval running improves cardiovascular fitness, and strength training increases bone and muscle mass. Performing all these different modes of exercise in moderation can perhaps avoid the unwanted effects of strain that disturbs the balance between GP and GU. This is feasible with an active lifestyle centred around physical activity. On the other hand, an obese individual may perceive intense workouts as a quixotic endeavour, involving insurmountable amounts of energy, discipline, determination, and persistence. Pragmatically, investing the time and energy required to reshape the body requires a measure of financial security, time off from work and family, and a long-term significant commitment in gymnastics that may often be undesirable, unattainable, or permanently postponed by a large number of overweight/obese individuals. Two recent studies mention a new method of simulated strenuous activity without the effort and fatigue involved in overtraining. This investigator reports a significant reduction in visceral adipose tissue, VLDL, and triglycerides, and an elevation in the Free T3 metabolic hormone, accompanied by an increase in skeletal muscle mass. Subjects reported experiencing a large variety of 8-secs long, vigorous contractions, some of them resembling resistance and

strength exercises, others subjectively perceived as body twists, or fast-paced aerobics [46] [47].

In the current study we examined triglycerides and HDL levels in 20 diabetic and prediabetic subjects. Fasting and postgrandular (PP) blood glucose levels were measured in the twelve diabetic subjects and fasting and PP insulin was measured in the eight prediabetic subjects. Seven out of the twenty subjects with evidence of fatty liver also provided their before and after sonography reports.

2. Methodology

We adopted a London University invention, completed in 2008 by G. Pollock, an electronics engineer, on the basis of his combined research with D. Gilbert, a molecular biology London University professor. The technology boards were patented in the early 80s when the empirical studies started, however no papers were ever published on the proprietary formula that synthesizes, and regulates the complex waveforms which generate the sensation of a multi-exercise regimen, experienced as fast paced or slow/resistance physical training. The device has two waveform control knobs with twelve options each, corresponding to a total of 24 square complex waveforms, each synthesized by a variety of 4000 sine waveforms; each having a specific resultant frequency that ranges from 55 Hz to 888 Hz. This 16-channels technology is hand-made analogue to offer a series of voltage driven, unlimited resolution waveform composites that produce 1000 full body musculature contractions per hour, each sustained for 8 seconds, with 2-secs rest time. It has a maximum voltage of 15V at 500 Ω, 25 V at 2000 Ω, and 50 V at 10 KΩ. Any current generated by the voltage, based on Ohm's law, is minuscule and cannot be measured. The leakage is 0.007 μa (μa = 10^{-6} A). The technology is classified as IEC class I according to IEC60601-1 standard, and it is used with 3-pin din and 4-pin din IEC 60601-1 compliant cables. It has a CE marketing directive of Class I, with electromagnetic compatibility regulations applied standards EN 50081-1, and EN 50082-1. It complies with the EEC UK directive of electrical equipment safety applied standard EN 60601-1. The technology has had no known side effects, in the past 20 years that it has been used in clinical practice by over 5430 physicians, and aesthetic practitioners. The only contraindication, according to the FDA, is having an implanted device like a pacemaker. The main caution is pregnancy. Adverse reactions are limited to temporary skin redness from the gel pads, that occurs sporadically and usually dissipates within an hour. Earlier versions of this technology based on the same electronic design have FDA clearance numbers K132158 and K132179.

Measuring instruments included: 1) a blood test that measured triglycerides, HDL, fasting and PP glucose and insulin levels; 2) a conductance scale that calculated BMI, weight, overall fat, visceral fat, and skeletal muscle mass (SMM); 3) tape measurements of the upper and lower abdomen, and the umbilicus; 4) Seven subjects reported the results of their sonography tests. 5) A structured interview intended to assess back pain.

Procedure

Twenty obese and overweight adults, 15 - 82 years, with an average BMI of 35.41, eleven females and nine males, with either a diabetic or prediabetic condition, participated and completed the study, after they signed a consent form. Fifteen of the subjects were of Indian descent and five of them were Caucasian. Selection was made by randomly selecting medical history files from two different clinics and making sure that the participants fulfilled both the inclusion and exclusion criteria: Inclusion: 1) Overweight or obese; 2) BMI < 45; 3) Age above 12 years old; 4) Controlled hypothyroidism; 5) Controlled hypertension; 6) At least three months after a surgery procedure; 7) At least three months after childbirth; 8) Diabetes; 9) Prediabetes.

Exclusion: 1) Pregnancy; 2) An implanted device like a cardiac pacemaker; 3) Severe hypothyroidism or other advanced endocrine condition; 4) Severe hypertension; 5) Hepatic cirrhosis; 6) Renal failure; 7) Surgery or childbirth less than three months prior to treatment; 8) Cancer; 9) Hernia; 10) Other severe medical or mental condition. Inclusion and exclusion criteria were once again verified by a certified physician in each of the two clinics, conducting a comprehensive clinical evaluation who made sure that all selected participants had been cleared by their private physicians to undertake the treatment. In addition to the diabetic status, two of the subjects were diagnosed with hypothyroidism, two with hypertension and one with both hyperthyroidism and hypertension. Seven subjects had fatty liver and ten subjects suffered from chronic back pain.

A physician was available in each clinic, during the entire duration of this trial to ensure the comfort and safety of the participants. All subjects underwent the treatment with no adverse reactions or side effects. There was no subject attrition.

Every precaution was taken to protect the subjects' privacy and the confidentiality of their personal information. Subjects were informed that they had the right to discontinue treatment at any time. Subjects were not in a dependent relationship with the technology operators, the lab and measurement technicians, or the author. The subjects were given some general diet instructions like increasing their vegetables, lean protein, and fruit intake, while reducing sugar and oily foods. About 70% of the subjects reported complying with the diet instructions, however, there was no structured measure of calculating daily caloric intake or the veracity of their statements. Seven out of 20 subjects were on several medications for their medical conditions. All seven subjects were instructed to continue taking their meds and to comply with all the recommendations of their treating physicians.

Two independent labs, one from each of the two participating clinics, were assigned to take blood samples before and after the completion of twelve one-hour treatments that took place three times a week, for four weeks. Subjects were asked to fast for twelve hours before going to the lab for their blood tests. The conductance scale and tape measurements were performed in a separate room by an independent technician with no personal interest in the direction of the

results. Only one of the clinics offered measurements on skeletal muscle mass. Seven of the subjects offered their sonogram results before and after the twelve treatments, but without releasing the full sonography reports. Two subjects were diagnosed with grade-2 fatty liver, and five were diagnosed with grade-1 fatty liver.

Following blood tests and measurements, each subject went to a private treatment room, and lay on a massage table, where the gel pads and cables from the 16 channels of the device were attached onto his/her body by the technology operator. The cables from ten of the channels were attached onto the gel pads of the umbilicus, upper and lower abdomen, and the cables from the six remaining channels were attached onto the gel pads placed along the lymphatic system pathways of the legs and arms, to enhance lymphatic drainage during treatment. The technology operator was instructed to constantly check if the subject was comfortable during the entire procedure.

All subjects gave a detailed report of their subjective experience during and after the treatments, when their overall health status was reassessed. The ten subjects that had reported chronic back pain, were given an additional structured interview to specifically assess the level of analgesia after the 12 treatments.

The procedure was in accordance with the ethical standards and principles for medical research involving human subjects.

3. Results

Statistical analysis was based on a repeated measures design where subjects' results after the twelve treatments were compared to their baseline. Table 1 displays the subjects' medical status and their before and after results on overall fat, visceral adipose tissue and skeletal muscle mass (SMM). The SMM data was limited because it was only provided by the clinic that supplied the 5 subjects. The average overall fat loss was 16.99%. The average overall visceral fat loss was 21%. Visceral fat decrease appeared to decline with age as shown in Figure 1. Overall fat reduction also appeared to decline with age, but results were not linear with that variable. Table 2 depicts the subjects' BMI and the weight loss in kilograms (kg), pre and post the twelve treatments.

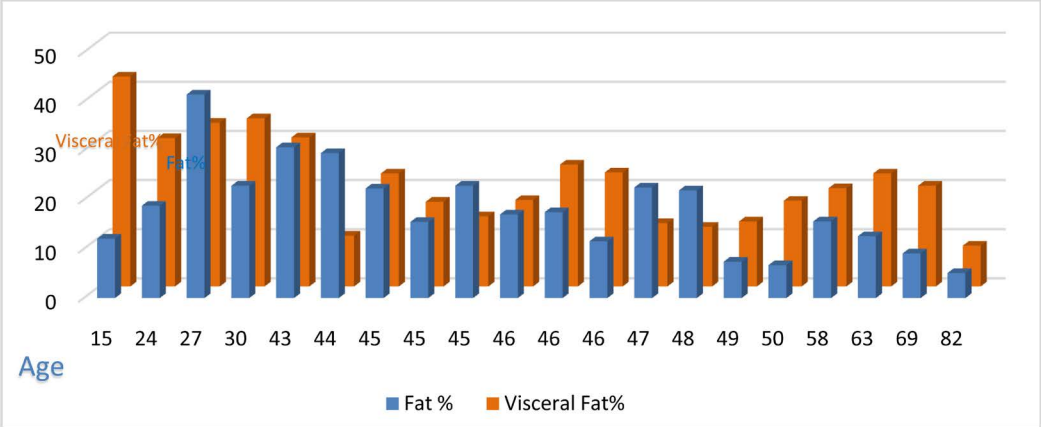
Results were analysed with the t test for dependent means (Table 6). Results for overall fat loss were statistically significant at $p < 0.00001$; with a mean of −7.25, a square deviation of 245.69, a T value of $t = -9.01646$. Results for visceral fat reduction were also highly statistically significant at $p < 0.00001$; with a mean of −4.88, a square deviation of 94.11, a T value of $t = -9.805937$. The results of skeletal muscle mass (SMM) increase were statistically significant at $p < 0.001$; with a mean of +5.18, a square deviation of 7.63, a T value of $t = +8.387633$ and a p value of $p < 0.00055$. The data on SMM included only five subjects, therefore these results should be interpreted with caution.

Table 3 displays the subjects' fasting and postglandial (PP) blood glucose, and fasting and PP insulin levels. The decrease of both fasting and PP blood glucose

Table 1. Pre and post treatment results on overall fat, visceral fat, and skeletal muscle mass (SMM).

SS	Gender	Age	Health Status	Overall Fat Pre	Overall Fat Post	Fat % Lost	Visceral Fat Pre	Visceral Fat Post	Visceral Fat % Lost	SMM Pre	SMM Post	SMM % Increase
1	Female	45 y	Diabetes; Fatty liver Grade-2; on Meds	42.1	32.7	22.32%	25.6	19.7	23%			
2	Male	69 y	Diabetes; Hypothyroidism; On Meds	35.2	32	9.1%	22	20.5	6.8%			
3	Male	46 y	Diabetes; Hypertension; On Meds	39.8	35.2	11.55%	27	23.2	14%			
4	Female	50 y	Diabetes; Hypothyroidism; On Meds	44.8	41.8	6.7%	27.5	22.7	17.45%			
5	Female	49 y	Diabetes; Hypertension; Hyperthyroidism; On Meds	47.2	43.7	7.41%	31	26.9	13.22%			
6	Female	46 y	Diabetes Fatty Liver Grade-1	44.6	36.8	17.48%	35	24.8	29.14%	22.1	26.4	19.45%
7	Female	48 y	Diabetes Fatty Liver Grade-2	42.9	33.5	21.91%	33	29	12.12%	23.8	29.7	24.8%
8	Male	44 y	Diabetes Fatty Liver Grade-1	34.9	24.6	29.51%	29	26	10.34%	34.5	41.3	19.7%
9	Female	43 y	Prediabetes	36.5	25.8	30.68%	21.6	15	30.33%			
10	Female	27 y	Prediabetes	43.2	35.3	18.28%	19.5	13	33.33%			
11	Female	63y	Prediabetes	46	37.4	12.60%	21	16.5	23%			
12	Female	24 y	Prediabetes Hypothyroidism	43.6	35.4	18.80%	20.5	14.3	30.2%			
13	Female	30 y	Prediabetes	34.1	26.3	22.87%	19	12.5	34.21%			
14	Female	45 y	Diabetes; Fatty Liver Grade-1	34	28.7	15.5%	29	24	17.24%	20.7	26.3	27%
15	Female	47 y	Diabetes Fatty Liver Grade-1	36	27.9	22.5%	31	27	12.9%	23.5	26.8	14%
16	Male	45 y	Diabetes IHD; On Meds	35	27	22.86%	21	18	14.28%			
17	Male	82 y	Diabetes Hypertension; On Meds	39.5	37.5	5.1%	30	27.5	8.3%			
18	Male	15 y	Prediabetes Fatty Liver Grade-1	36.4	32	12.1%	22	12.6	42.72%			
19	Male	58 y	Prediabetes	37.1	31.3	15.6%	16	12.8	20%			
20	Male	46 y	Prediabetes	41.1	34.1	17%	16.5	13.6	17.6%			
MEAN OVERALL FAT DECREASE %						16.99%	MEAN VISCERAL FAT DECREASE %		21%	MEAN SMM % INCREASE		20.99%

Table 2 The visceral fat decrease appeared to be quite significant when compared to the overall body fat percentage decrease, possibly suggesting that there was a true visceral adiposity reduction that was consistently attained by all subjects.



Visceral and overall fat were plotted on the Y-axis with age being plotted on the X-axis. Visceral fat percentage lost (red bars) appeared to be more consistently affected by age.

Figure 1. Fat % Loss and Visceral Fat % Loss Plotted against Age.

Table 2. Pre and Post BMI and Weight in Kg.

SS	Gender	Age	Health Status	BMI Pre	BMI Post	BMI % Decrease	Weight (kg) Before	Weight (kg) After	Total kg lost
1	Female	45 y	Diabetes	37.9	34.4	9.2%	92.2	83.7	8.5
2	Male	69 y	Diabetes	30.1	28.5	5.3%	77.5	73.3	4.2
3	Male	46 y	Diabetes	36.8	35.3	4.3%	104	99.8	4.2
4	Female	50 y	Diabetes	39.6	38	4%	89.6	86	3.6
5	Female	49 y	Diabetes	43.1	40.5	6%	120	113	7
6	Female	46 y	Diabetes	39.2	36.2	3%	129	115	14
7	Female	48 y	Diabetes	41.2	38.5	6.6%	123	118	5
8	Male	44 y	Diabetes	42.6	38.2	10.3%	130	119	11
9	Female	43 y	Prediabetes	31.2	27.7	11.2%	75.8	67.2	8.6
10	Female	27 y	Prediabetes	37.4	35.4	4.2%	87.5	82.8	5
11	Female	63 y	Prediabetes	34.3	30.7	10.5%	87.8	78.7	4.7
12	Female	24 y	Prediabetes	38.3	33.9	11.5%	95.5	84.6	10.9
13	Female	30 y	Prediabetes	34.0	32.0	5.9%	113.8	107	6.8
14	Female	45 y	Diabetes	32.0	30.1	5.9%	72	61	11
15	Female	47 y	Diabetes	29.1	25.1	13.7%	69	63	6
16	Male	45 y	Diabetes	34.2	29.4	14%	83	78	5
17	Male	82 y	Diabetes	34.8	34.5	0.9%	90.2	89.4	0.8
18	Male	15 y	Prediabetes	32.8	31.8	3%	86	83.5	2.5
19	Male	58 y	Prediabetes	29.7	28.9	2.3%	90	87.7	3
20	Male	46 y	Prediabetes	33.2	30.6	7.8%	79.5	73.2	6.35
		Mean BMI % Decrease		6.98%		Average Weight Loss in Kgs		6.4	

Table 2 There was some reduction in BMI perhaps signifying the necessity for more treatments before achieving a greater difference. The aged diabetic subject seemed to demonstrate the least BMI decrease. There was some weight loss in kgs that may have been affected by exchanging overall fat to build skeletal muscle.

Table 3. Pre and Post Treatment Results on Blood Glucose (Fasting and PP), and Insulin (Fasting and PP). (F: Female; M: Male, D: Diabetes; PD/Prediab.: Prediabetic status Bord: Borderline).

Fasting Blood Glucose: Normal < 100 mg/dL; Prediabetes = 100 - 125 mg/dL; Diabetes >126 mg/dL
Blood Glucose Postglandial (PP): Normal < 140 mg/dL; Prediabetes = 140 - 199 mg/dL; Diabetes > 199 mg/dL
Insulin Fasting: Normal < 25 mIU/ml
Insulin Postglandial (PP): Normal < 75

Gender /Age	Blood Glucose Fasting mg./dL Pre	Blood Glucose Fasting mg/dL Post	Blood Glucose Normal < 100 mg/dL	Blood Glucose PP mg/dL Pre	Blood Glucose PP mg/dL Post	Blood Glucose PP Normal < 140 mg/dL	Insulin Fasting mIU/ml Pre	Insulin Fasting mIU/ml Post	Insulin Fasting Normal < 25 mIU/ml	Insulin PP mIU/ml Pre	Insulin PP mIU/ml Post	Insulin PP Normal <75 mIU/ml
1 F - 45 y; D	178	104	Bord Normal	260	185	PD						
2 M - 69 y; D	209	108	Bord. Prediab	230	125	Normal						
3 M - 46 y; D	131.7	99.15	Normal	290	183.2	PD						
4 F - 50 y; D	177	106	Bord. Prediab	221	176	PD						
5 F - 49 y; D	103	100	Bord Normal	186	139	Normal						
6 F - 46 y; D	192	102	BN	248	175	PD						
7 F - 48 y; D	189	115	Prediab	224	163	PD						
8 M - 44 y; D	178	109	Prediab	196	162	PD						
9 F - 43 y; PD							72	15.7	Normal	174.3	73.9	Normal
10 - 27 y; PD							25.8	8.7	Normal	136	14	Normal
11 F - 63 y; PD							105	12.27	Normal	150	16.2	Normal
12 F - 24 y; PD							34	21	Normal	139.9	21.8	Normal
13 M - 30 y; PD							27.4	18.5	Normal	241	24.6	Normal
14 F - 45 y; D	186	117	Prediab	197	123	Normal						
15 F - 47 y; D	169	102	Bord Normal	243	178	PD						
16 M - 45 y; D	135	92	Normal	178	156	PD						
17 M - 82 y; D	136	87	Normal	191	142	Bord Normal						
18 M - 15 y; PD							29	10.9	Normal	136.6	14.8	Normal
19 M - 58 y; PD							50.4	24	Normal	246	68.4	Normal
20 M - 46 y; PD							25.56	12.4	Normal	68.8	23.5	Normal

Table 3 Both fasting and PP blood glucose that were previously abnormally elevated, dived towards the upper end of the normal range, suggesting a significant improvement in blood glucose regulation following the 12 treatments. 25% of diabetes subjects' blood glucose dropped down to the normal range; while the blood glucose of 75% of them descended to the prediabetic range. Both insulin fasting and PP of prediabetic subjects that was previously well above the normal range was significantly reduced to be within the confines of the normal range after the 12 treatments.

levels were analysed with the one-way ANOVA for repeated measures. Results were highly statistically significant with a standard deviation of 49.3311, an F value of $F = 54.31322$, and a p-value of $p < 0.00001$. The reduction of both fasting and PP insulin were also highly statistically significant with a standard deviation of 67.1899, an F value of $F = 35.88055$, and a p-value of $p < 0.00001$.

Table 4 depicts the measurement results on the upper and lower abdomen

Table 4. Measurements of upper abdomen, umbilicus, lower abdomen and weight pre and post treatment.

SS	Gender	Age	Health Status	Upper Abdomen (cm) Before	Upper Abdomen (cm) After	Total cm lost	Umbilicus (cm) Before	Umbilicus (cm) After	Total cm lost	Lower abdomen Before	Lower abdomen After	Total cm lost
1	Female	45 y	Diabetes	108	98	10	111	100	11	115	100	15
2	Male	69 y	Diabetes	100	94	6	105	98	7	107	100	7
3	Male	46 y	Diabetes	130	120	10	134	124	10	130	120	10
4	Female	50 y	Diabetes	109	100	9	118	111	7	128	120	8
5	Female	49 y	Diabetes	125	112	13	137	123	14	145	129	16
6	Female	46 y	Diabetes	134	122	12	138	118	20	152	127	25
7	Female	48 y	Diabetes	137	128	9	136	128	8	138	129	9
8	Male	44 y	Diabetes	126	120	6	128	121	7	131	124	7
9	Female	43 y	Prediabetes	97	82	15	100	88	12	105	94	11
10	Female	27 y	Prediabetes	96	87	9	103	91	12	114	101	13
11	Female	63 y	Prediabetes	118	108	10	122	110	12	125	114	11
12	Female	24 y	Prediabetes	108	90	18	119.5	101	18.5	126	107	19
13	Female	30 y	Prediabetes	112	109	3	125	113	12	128	112	16
14	Female	45 y	Diabetes	76	65	11	69	65	4	78	66	12
15	Female	47 y	Diabetes	81	74	7	69	58	11	77	63	14
16	Male	45 y	Diabetes	95	88	7	98	90	8	100	92	8
17	Male	82 y	Diabetes	118	106	12	119	113	6	117	114	3
18	Male	15 y	Prediabetes	114	109	5	117	113	4	116	112	4
19	Male	58 y	Prediabetes	118	105	13	120	106	14	120	104	16
20	Male	46 y	Prediabetes	104	96	8	107	98	9	104	98	6
				Upper Abdomen Average cm loss		9.65	Umbilicus Average cm loss		10.2	Lower Abdomen cm loss		11.5

Table 4 The average cm loss from the upper abdomen was 9.65 cm; the umbilicus 10.2 cm; and the lower abdomen 11.5 cm. These abdominal measurements were consistent with the reduced visceral adiposity observed on **Table 1**.

and the umbilicus in centimetres (cm), before and after the 12 treatments. Subjects lost an average of 9.65 cm off the upper abdomen, 10.2 cm off the umbilicus, and 11.5 cm off the lower abdomen. The cm loss around the lower abdomen that usually accumulates visceral adipose tissue appears consistent with the visceral fat reduction results. The cm loss was disproportionally higher than the kgs lost (**Table 2**), suggesting that overall fat was perhaps replaced by skeletal muscle mass; a hypothesis supported by the results of the significantly increased skeletal muscle mass (SMM) on **Table 1**. The results of the upper and lower abdomen reduction in cm were analysed by the one-way ANOVA for repeated measures, and were highly statistically significant with a standard deviation of 18.43043, an F value of $F = 43.37643$, and a p-value of $p < 0.00001$. The results of the umbilicus reduction in cm and weight loss in kgs were also analysed by the one-way ANOVA for repeated measures, and were highly statistically significant with a

standard deviation of 22.4058, an F value of F = 108.22199, and a p-value of p < 0.00001.

Table 5 displays the subjects' triglycerides and HDL levels, the 7 subjects' results with Grade-1 and Grade-2 fatty liver, and the ten subjects reports on back pain. After the 12 treatments there was no evidence of hepatic steatosis in all seven subjects' sonography reports (100%). All ten subjects who experienced back pain prior to treatment, reported pain analgesia after the 12 treatments (100%).

Triglycerides and HDL from Table 5 were also analysed with the one-way ANOVA for repeated measures unveiling very significant results at p > 0.01;

Table 5. Triglycerides, High-Density Protein (HDL), Presence of Fatty Liver and Back Pain Pre and Post Treatment. (F: Female; M: Male; Bord.: Borderline).

Triglycerides Normal Range: >150 mg/dL;
High-Density Lipoprotein (HDL) Normal Range: Men > 60 mg/dL; Women > 60 mg/dL
High-Density Lipoprotein (HDL) At Risk: Men: <40 mg/dL; Women < 50 mg/dL

Gender	Age	Health Status	Fatty Liver	Fatty Liver	Back Pain Pre	Back Pain Post	Triglycerides mg/dL Pre	Triglycerides mg/dL Post	Triglycerides mg/dL decrease	HDL mg/dL Pre	HDL mg/dL Post	(HDL) mg/d Increase
1 F	45	Diabetes	Grade-2	Nil	Yes	No	203	158	Bord Normal	32	39	Improved at risk
2 M	69	Diabetes			Yes	No	215	128	Normal	35	47	Bord. Not at risk
3 M	46	Diabetes					230	153	Bord Normal	28	37	Improved at risk
4 F	50	Diabetes			Yes	No	86.7	84.3	Normal	49.6	53	Not at risk
5 F	49	Diabetes			Yes	No	103	88	Normal	34.5	38	Improved at risk
6 F	46	Diabetes	Grade-1	Nil	Yes	No	287	176	Improved (abnormal)	32	39	Improved at risk
7 F	48	Diabetes	Grade-2	Nil	Yes	No	266	147	Normal	29	41	Bord. Not at risk
8 M	44	Diabetes	Grade-1	Nil	Yes	No	283	189	Improved (abnormal)	30	35	Improved at risk
9F	43	Prediabetes			Yes	No	294	197	Improved (abnormal)	36	42	Bord. Not at risk
10 F	27	Prediabetes					192	126	Normal	36	48	Bord. Not at risk
11 F	63	Prediabetes					155	117	Normal	45	47	Bord. Not at risk
12 F	24	Prediabetes					88	86	Normal	45	52	Not at risk
13 M	30	Prediabetes					156	124	Normal	37	46	Not at risk
14 F	45	Diabetes	Grade-1	Nil	Yes	No	225	179	I Improved (abnormal)	33	40	Improved at risk
15 F	47	Diabetes	Grade-1	Nil	Yes	No	237	188	Improved (abnormal)	31	41	Improved at risk
16 M	45	Diabetes					112	105	Normal	41	45	Not at risk
17 M	82	Diabetes					97	94	Normal	26	38	Not at risk
18 M	15	Prediabetes	Grade-1	Nil			187	132	Normal	36	42	Not at risk
19 M	58	Prediabetes					141	136	Normal	43.1	46.8	Not at risk
20 M	46	Prediabetes					262	158	BN	52.3	56	Not at risk

Table 5 Triglycerides' levels dropped down to the normal range for 60% of the subjects with another 15% of the subjects being within a borderline normal range after the 12 treatments. 25% of the subjects improved significantly dropping down to the borderline abnormal range. The HDL levels of 35% of the subjects climbed up at the not-at-risk range. 40% of them entered the borderline-not-at-risk range, and 35% improved significantly but remained within the at-risk range.

with a standard deviation of 76.197, an F value of F = 88.81568 and a p-value of $p < 0.00001$.

All variables were analysed with t-tests for dependent means. The significance table of the variables are given in Table 6.

Figure 2 displays the before and after photos of three of the subjects who gave consent for the pictures to be released. All subjects reported a subjective experience

Table 6. T-test statistical significance.

	MEAN	SQUARE DEVIATION	T-VALUE	P-VALUE	Significance level
Overal Fat Loss	−7.25	245.69	T = −9.01646	P < 0.00001	P < 0.00001
Visceral Fat Loss	−4.88	94.11	T = −9.805937	P < 0.00001	P < 0.00001
SMM increase	5.18	7.63	T = 8.387633	P < 0.00055	P < 0.001
BMI decrease	−2.59	31.58	T = −8.98461	P < 0.00001	P < 0.00001
Fasting Blood Glucose	−61.88	7675.12	T = −8.115002	P < 0.00001	P < 0.00001
Blood Glucose PP	−63.07	7353.39	T = −8.459736	P < 0.00001	P < 0.00001
Insulin Fasting	−30.71	5961.47	T = −2.976561	P < 0.01031	P < 0.01
Insulin PP	−129.43	18065.62	T = −7.20586	P < 0.00009	P < 0.0001
Upper Abdomen reduction in cm	−9.65	244.55	T = −12.029159	P < 0.00001	P < 0.00001
Umbilicus reduction in cm	−10.32	344.14	T = −10.849653	P < 0.00001	P < 0.00001
Lower Abdomen reduction in cm	−11.5	553	T = −9.532945	P < 0.00001	P < 0.00001
Weight loss in kgs	−6.58	224.56	T = −8.551201	P < 0.00001	P < 0.00001
Triglycerides decrease	−52.72	30161.79	T = −5.917505	P < 0.00001	P < 0.00001
HDL increase	7.06	203.91	T = 9.644717	P < 0.00001	P < 0.00001

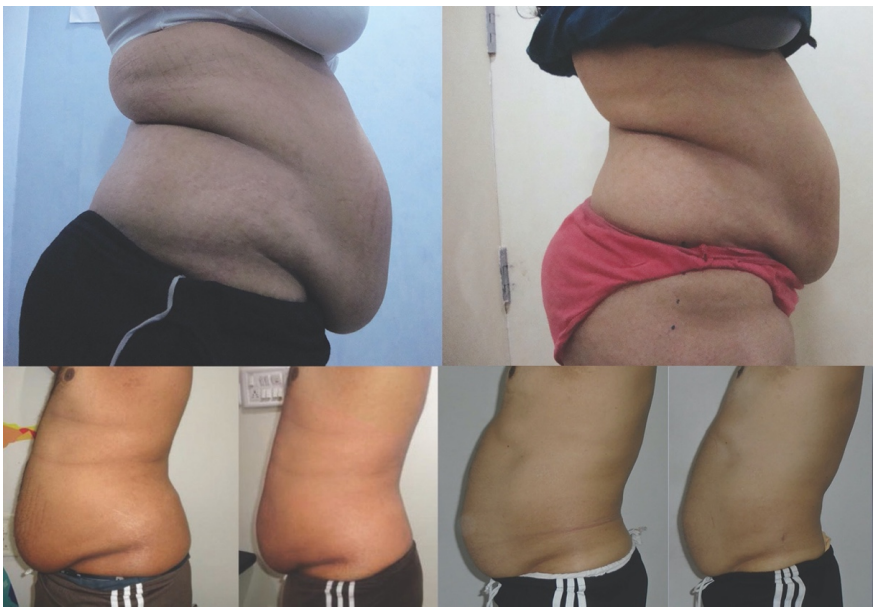


Figure 2. Before (left) and after (right) of three subjects who consented to release their photos.

of what felt like strenuous exercise, which however, was comfortable and effortless.

4. Discussion

Results demonstrated a significant improvement in blood glucose regulation and insulin resistance, along with reduced dyslipidemia, reflecting an optimal reverse relationship of elevated HDL versus triglycerides descending towards the normal range. The substantial reduction of visceral fat was supported by the cm loss around the umbilicus and lower abdomen which represent the body areas where visceral adiposity accumulates; it was also confirmed by the sonography reports of seven subjects diagnosed with hepatic steatosis who presented evidence of no fatty liver after the twelve treatments. It is unclear if more subjects that participated in the study suffered from non-alcoholic steatosis, since none of the remaining thirteen subjects were tested with imaging techniques. Ten of the subjects reported a significant pain analgesia after the twelve treatments, most likely due to improved posture after the weight loss. However, there was no follow up to assess for back pain reoccurrence. Weight loss was statistically significant but relatively modest (6.4 kgs), possibly signifying an exchange of fat for SMM. However, this premise cannot be supported by the SMM data that was derived by the small sample of only five subjects. Therefore, more research is required to substantiate this hypothesis. BMI decrease was also statistically significant, but appeared to signify the need for more treatments, especially when offering this method to aged diabetics. Overall, results were encouraging, in terms of using this method as an alternative to exercise, offering an improved health status and weight loss within one month for obese and overweight diabetic and prediabetic individuals. The subjects received some basic diet recommendations, however, neither of the clinics monitored daily food intake.

Our findings have significant implications for optimal health that can be enhanced and safeguarded by incorporating this method as part of an exercise regimen to reduce lipids, blood glucose levels and insulin resistance. Sustained physical training necessary to reduce visceral adiposity, along with its inherent inflammation and oxidative damage, is often experienced as cumbersome, exhausting, and demanding a lengthy commitment of several months to produce a visible body change. Obese diabetics and prediabetics usually resist exercise due to difficulty moving, embarrassment triggered by body image issues, fatiguing, and prolonged effort with no fast results that is often demoralizing. Adopting this method can bring the light at the end of the tunnel, and jumpstart an active lifestyle that will eventually improve their health.

There were several improvements that could be applied to the present study that were not currently feasible, due to our limited research budget, and the lack of financial assistance from an outside source: imaging techniques for all subjects; a direct investigation of inflammatory, and oxidative damage markers such as CRP, IL-6, TNF-a and 8-epi-PGF2a; a more extensive lipoprotein profile that

includes LDL and VLDL; an extensive protein analysis, examining adiponectin, leptin and ghrelin that regulate appetite to avoid a weight gain rebound. This clinical trial included both diabetics and prediabetics; therefore, the blood glucose results were based on twelve subjects and the insulin levels were derived from eight subjects, rendering both samples rather small. Additional research with more subjects, and more testing measures and variables should be conducted in order to replicate, and validate these findings.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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