Effects of Yoga Exercises on Diabetic Mellitus as Validated by Magnetic Resonance Imaging

Abstract

Context and Aims: Effects of practicing yoga in diabetic mellitus (DM) patients have been identified to improve in control of blood glucose levels. The purpose of this work is to evaluate changes in blood flow of calf muscles after specific yoga postures for patients with DM using magnetic resonance imaging (MRI) techniques. Time of flight (TOF) magnetic resonance angiography maximum intensity projection (MIP), T_1 maps, T_2 maps, and diffusion-weighted Imaging are performed on volunteers and DM patients both pre- and post-exercise. **Materials and Methods:** TOF MIP, T_1 maps with variable flip angles, and T2-weighted spin-echo imaging were performed on four volunteers (aged 30 ± 5) and DM patients (aged 32–68) preexercise, on a 1.5 T Siemens scanner. The total acquisition time was 6 min 20 s. Each volunteer and DM patient were then requested to perform yoga postures Supta Padangusthasana, Utkatasana, and Calf raise for 6 min 30 s at maximum effort, outside the scanner, and subsequently rescanned. To calculate significant signal increase, region of interests was drawn on TOF MIP coronal images in arteries of calf muscles. Student t-tests were performed to determine statistical significance. **Results:** Among volunteers, a significant signal increase in arteries of calf muscles was noticed, signal intensity graphs were plotted. In DM patients, signal increase in TOF MIP, T2-weighted images were seen in specific arteries (posterior, anterior tibial, and posterior tibial) of calf muscles postexercise. **Discussion and Conclusions:** The study indicates that yoga has a positive short-term effect on multiple DM-related foot complications. This study depicts that MRI provides potential insight into the benefits of yoga for DM patients through deriving biomarkers for preventive medicine relevant to yoga interception.

Keywords: Calf Muscles, diabetic mellitus, diffusion-weighted imaging, magnetic resonance angiography, yoga

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Introduction

Diabetic mellitus (DM), widely termed as diabetes, is a diverse group of diseases distinguished by high blood glucose levels over an elongated period. The human body breaks down the consumption of sugar and carbohydrates into glucose. Glucose fuels the cells of the human body. A hormone termed insulin is responsible for carrying glucose into the bloodstreams. DM occurs in cases of the pancreas not producing enough insulin or due to cells of the body not responding to the insulin produced. Symptoms include weight loss, polyuria (frequent urination), (polydipsia) increased thirst, and (polyphagia) increased hunger.[1] Higher blood glucose levels damage blood vessels of the organs, especially the eyes, heart, nervous system, and kidneys. DM is classified into Type 1 diabetes, Type 2 diabetes, and gestational diabetes. Type 1 diabetes is due to the autoimmune destruction of the beta-cells in the pancreas. People diagnosed with Type 1 diabetes require regular insulin dosages to sustain life. Type 2 diabetes also termed as adult-onset diabetes or noninsulin-dependent diabetes accounts for approximately 90–95% of those with DM.[2] In people with Type 2 diabetes, cells are partially or completely incapable to respond to the insulin produced. The possibility of developing Type 2 DM increases with age, obesity, and lack of physical activity. Gestational DM occurs in cases of pregnancy and may increase or disappear after delivery. Management includes changes in the diet, regular blood glucose monitoring, and insulin injection in some cases.

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As of 2015, 415 million people have been estimated to be diagnosed with diabetes worldwide, with Type 2 DM comprising about 90% of the cases, representing 8.3% of the adult population, with equal rates in both women and men. According to the World Health Organization (WHO) Statistics in India, 31,705,000 million people were diagnosed with DM in the year 2000.[3] By the year 2030, it is also predicted to rise to 79,441,000 million in India by the WHO. The existence of DM is globally predicted to double from 171 million in the year 2000 to 366 million in the year 2030, with a maximum increase in India.

Complications of the foot due to diabetic mellitus

DM leads to severe complications in the foot such as diabetic peripheral neuropathy, peripheral artery disease, intermittent claudication, and advanced peripheral arterial disease (ischemic rest pain). DM results in narrow and hardening of the blood vessels in the foot and leg. Poor blood circulation forges the foot to be least resistant to fight infections. Nerve damage in arms or legs termed as diabetic peripheral neuropathy (DPN) results from long-term hyperglycemia (increased blood glucose levels), decreasing blood flow to the foot in Type 2 diabetes.[4] Nerve damage decreases the capability to feel pain, heat, and cold, resulting in loss of feeling in cases of injury. Peripheral artery disease occurs due to clogging of the plague (fatty substance) in the arteries of the extremities of the body such as legs and foot.[5] The buildup of plaque calls the arteries in becoming narrow and hard, obstructing blood flow, resulting in atherosclerosis. People with DM feel pain in the calves during running or brisk walk, and the condition is termed as intermittent claudication. Advanced peripheral artery disease outcomes in insufficient blood flow to the tissues, severe pain in the legs, and shrinking of calf muscles. High blood pressure, excess cholesterol levels, smoking, and obesity due to lack of exercise accelerate the effects of DM.

Yoga exercises for diabetic mellitus of the foot

Effects of practicing yoga exercises in DM patients have been identified to improve in control of blood glucose levels.[6] Regular practice of yoga exercises is effectual measures in the prevention of Type 2 diabetes, where the causes are attributed to lifestyle and stress.[7] Due to muscular exercise involved, regular yoga practice helps in reduced high glucose levels in the blood, maintaining nominal blood pressure levels, reduces the symptoms, and decreases the rate of progression of diabetes, as well as lessening the severity of further complications. Studies have emphasized the regular practice of yoga postures as a positive impact in lines with pancreatic secretion through alternate abdominal contractions and relaxation during yoga exercises. Yoga exercises alleviate calf pain by improving blood flow and muscle suppleness. Yoga exercises related to the calf muscles aid in stretching of the soleus (inner calf muscle) and the gastrocnemius (outer thigh muscles).

Some of the yoga exercises related to the DM of the foot are Supta Padangushtasana (Reclining Big Toe), Uttanasana (Standing forward Bend), Utkatasana (chair pose), Garudasana (Eagle Pose), and calf raises.[8,9] These asanas stretch tones and strengthen the calf muscles, thereby easing the blood circulation as depicted in Figure 1.

Materials and Methods

Experimental setup and participant population

The experiments were carried out on a Siemens 1.5T Magnetom Avanto magnetic resonance imaging (MRI) scanner with a body coil for a duration of 6 months. The participants were requested to lie down in a prone position on the magnetic resonance (MR) scanner table. Two studies were performed, among which one is a study of fat distribution preexercise, and the other is to observe blood flow changes postexercise when compared to preexercise. Fiducial marker for correlation between pre- and post-exercise scan images, Vitamin E capsules visible through MR images were tapped onto the participants' imaging section. The study was performed with an informed consent obtained from the participants as per the guidelines of an ongoing ethical review board approved the study. The study was conducted on a total of nine participants (seven volunteers [aged 25 ± 5] and two patients with DM [aged 35 ± 5]).

Magnetic resonance image acquisitions

T1 maps axial slices with variable flip angles were obtained preexercise with the parameters (Slice thickness = 5 mm, TR/TE = 20/4.4500 ms, averages = 1, flip angles = 9°, 47°, field of view = 128 mm, and pixel bandwidth = 130 Hz/pixel). Pre- and post-exercise imaging was performed with the following parameters: T2 maps axial slices (slice thickness = 5 mm, TR/TE = 2600/22 ms, averages = 1, flip angle = 180°, Field Of View = 128 mm, and pixel bandwidth = 130 Hz/pixel), time of flight (TOF) angiography maximum intensity projection (MIP) coronal slices (TR/TE = 36/8.7000 ms, flip angle = 10°), diffusion-weighted axial images using a Stejskal–tanner diffusion sensitizing gradients and a single-shot echo-planar imaging (b-values 0,500 s/mm^2, averages = 6, slice thickness = 5 mm, TR/TE = 4000/84 ms, Pixel
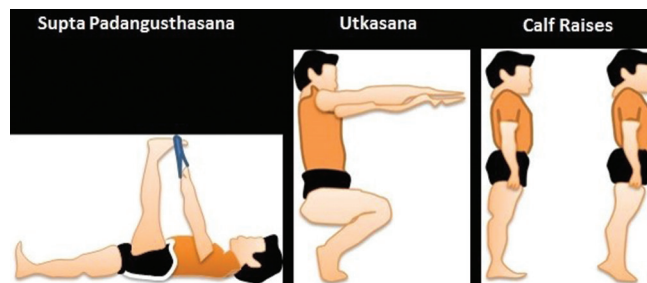

Figure 1: Illustration of the yoga postures that stimulate the blood flow in the calf muscles

bandwidth = 1345 Hz/pixel, matrix size = 128 × 128). Total acquisition time was 13 min (6 min 30 s for each protocol). Each image obtained was further processed and normalized to its maximum intensity. T_1 and T_2 maps were acquired in axial slices. T1-weighted imaging is performed in typically axial, to assess for fat saturation which appears bright on these images. Through the selection of an axial slice, we are creating images perpendicular to the Z direction. For most applications, the flow direction is along the body, so axial slices were obtained.

Yoga protocols

Each participant was requested to perform yoga postures (outside the scanner) at maximum effort and subsequently rescanned (postexercise scan). The protocol involved Supta Padangusthasana, Utkatasana, and Calf Raises. In Supta Padangusthasana, participants were requested to lie on their back with legs stretched, inhale, bend the right knee upward toward the chest, wrap a belt/strap around the sole, and hold the ends of the belt with hands by straightening their leg perpendicular to the floor. Participants stayed in this pose for 1 min 30 s, breathing evenly. The above protocol was repeated by switching on to the left knee. The total exercise duration was 3 min. In Utkatasana, participants were asked to stand erect with both the legs a foot apart, stretch hands to the front with palms facing downward, and bend the knees by gently pushing the pelvis downward (as if sitting in an imaginary chair) and look frontward. The total exercise duration was 1 min 30 s. In calf raises, participants were asked to stand erect and raise heels a few inches above standing on tiptoes. The position was repeated in intervals, by holding it for a few seconds and lowering the heels, thereby feeling a stretch in the calves. The total exercise duration was 2 min.

Statistical analysis

GraphPad software 2365 Northside Dr. Suite 560 San Deigo, CA 92108, the software was used for statistical analysis of data. Region of interests was drawn three times on the N1 and N2 area, and the respective total number of pixels in the area was obtained. To illustrate fat distribution in calf muscles, the number of pixels in the area of N1 was subtracted from the number of pixels in the area of N2, i.e., N3 = N2–N1 percentage of fat voxels were calculated using the formula (N3/N1) ×100. TOF MR angiography (MRA) MIP images region of interests was drawn six times on popliteal artery, peroneal artery, anterior tibial artery, posterior tibial artery to gather signal intensities both pre- and post-exercise. The mean ± standard deviation was calculated from obtained signal intensities. The same was depicted using a grouped column graph plotting mean ± standard deviation on it to compare significant signal intensity differences between pre- and post-exercise. Diffusion-weighted images apparent diffusion coefficient maps were generated through fitting diffusion into a mono-exponential model

as in equation (1). S0 and S are signal intensities without and with diffusion, b is the attenuation factor, and D is the diffusion coefficient. MATLAB's curve fitting tool was used to generate the curve using nonlinear least squares (NLS) based on the trust-region algorithm, data to fit in was specified through a matrix of x rows and y columns, in which the signal intensity S is fit against each b-value ranging from 0 to 500 s/mm².

$$S=S_0e^{-bD} \qquad (1)$$

Results

Fat distribution

Normal calf muscles are used as a standpoint in delineating signal intensities from musculoskeletal pathologic findings. Normal calf muscles substantiate slightly higher signal intensity when compared to water on T1-weighted MR images.[10] Below the Figure (2a,b) illustrates a T1 map axial slice data of volunteer and patient preexercise. The table in Figure 2c depicts fat distribution in calf muscles (40.94% ± 2.01% in left calf muscles and 48.59% ± 1.51% in right calf muscles). Below the Figure 2c illustrates a T1 map axial slice data of DM patient preexercise. The table in Figure 2d depicts fat distribution in calf muscles (53.11% ± 0.77% in left calf muscles and 52.60% ± 1.96% in right calf muscles).

In T2-weighted MR images, the water signal depicts higher signal intensity than fat. Volunteer's calf muscle evident slightly lesser signal intensities in comparison with water on T2-weighted MR images. Below the Figure S1 shows a T_2 map axial slice of calf muscle labeled with its arteries and veins for reference. Figure 3a shows a representative volunteer data depicting the T_2 map axial slice. An increase in signal intensity is observed in the Fibula and Plantaris region of the calf muscle postexercise when compared to preexercise depicting its response level to exercise. Figure 3b shows a representative DM patient data depicting the T_2 map axial slice. An increase in signal intensity is observed in the soleus region of the calf muscle postexercise when compared to preexercise depicting its response to exercise.

Time of flight magnetic resonance angiography maximum intensity projection

It can be noticed from Figure 4a TOF MIP that there is a statistically significant signal increase in anterior tibial, peroneal, and posterior tibial arteries of calf muscles postexercise among volunteers. Labeling of the arteries of calf muscles is shown for reference. Figure 4b shows the TOF signal intensity plot of arteries in calf muscles pre- and post-exercise for volunteers. Dotted lines indicate the arteries of the right leg.(*) indicate a statistical signal difference ($P < 0.05$) between pre- and post-exercise for the corresponding arteries. In DM patients, signal increase in TOF MIP can be seen in specific popliteal,
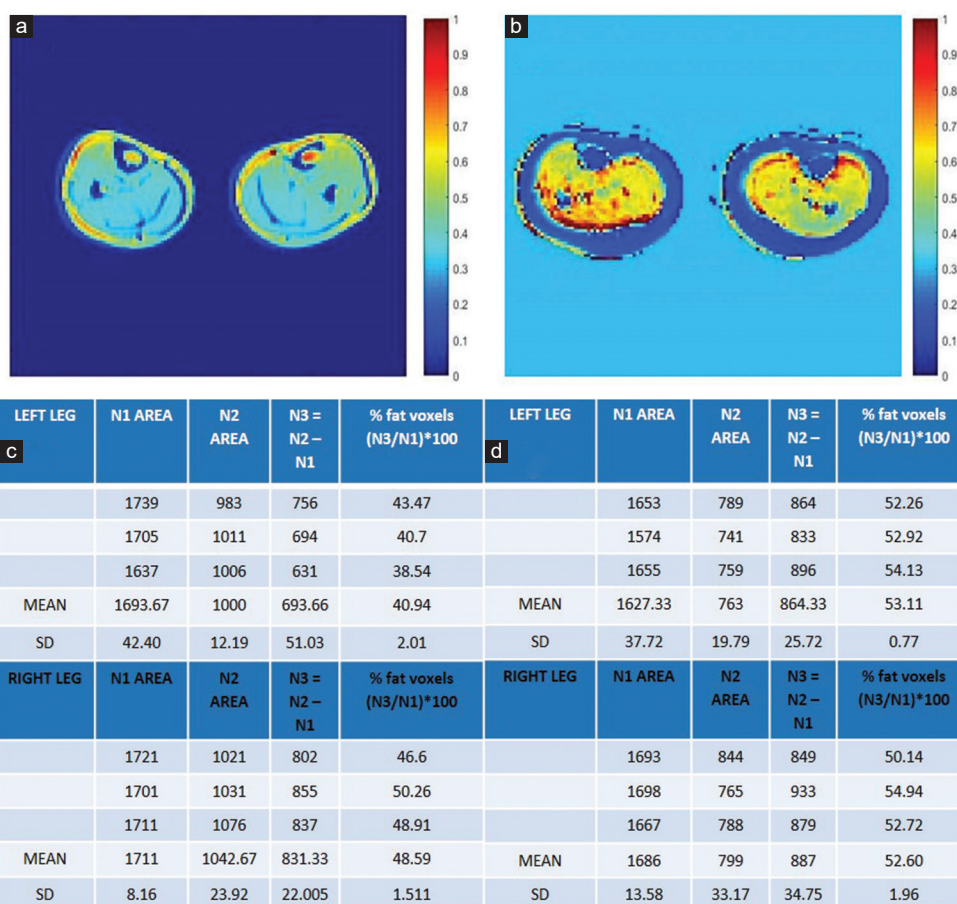
Figure 2: (a) Representative T1 map axial slice data of a volunteer preexercise, (b) representative T1 map axial slice of a diabetic mellitus patient preexercise, (c) percentage of fat voxels depicting T1 fat distribution in calf muscles of a volunteer, (d) percentage of fat voxels depicting T1 fat distribution in calf muscles of diabetic mellitus patients
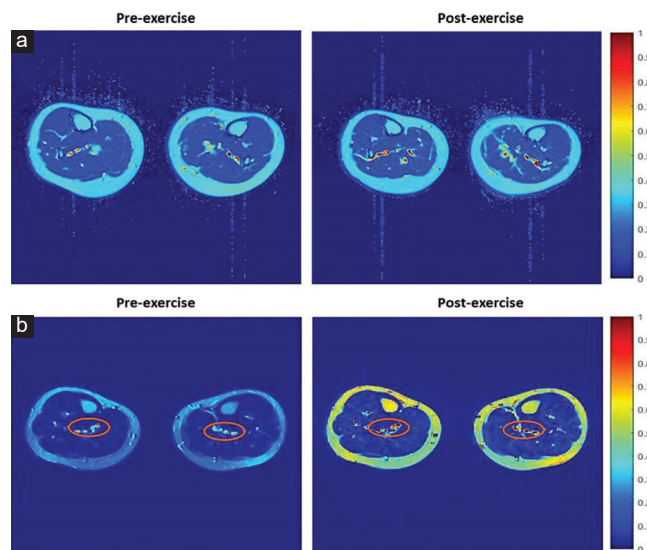
LEFT LEG	N1 AREA	N2 AREA	N3 = N2 − N1	% fat voxels (N3/N1)*100	LEFT LEG	N1 AREA	N2 AREA	N3 = N2 − N1	% fat voxels (N3/N1)*100
	1739	983	756	43.47		1653	789	864	52.26
	1705	1011	694	40.7		1574	741	833	52.92
	1637	1006	631	38.54		1655	759	896	54.13
MEAN	1693.67	1000	693.66	40.94	MEAN	1627.33	763	864.33	53.11
SD	42.40	12.19	51.03	2.01	SD	37.72	19.79	25.72	0.77
RIGHT LEG	N1 AREA	N2 AREA	N3 = N2 − N1	% fat voxels (N3/N1)*100	RIGHT LEG	N1 AREA	N2 AREA	N3 = N2 − N1	% fat voxels (N3/N1)*100
	1721	1021	802	46.6		1693	844	849	50.14
	1701	1031	855	50.26		1698	765	933	54.94
	1711	1076	837	48.91		1667	788	879	52.72
MEAN	1711	1042.67	831.33	48.59	MEAN	1686	799	887	52.60
SD	8.16	23.92	22.005	1.511	SD	13.58	33.17	34.75	1.96

Figure 3: (a) Representative volunteer data depicting T2 map axial slice, pre- and post-exercise, (b) representative diabetic mellitus patient data depicting T2 map axial slice, pre- and post-exercise showing signal intensity increase in soleus

anterior tibial, posterior tibial arteries of calf muscles postexercise as evident in Figures 4c. Their corresponding

signal intensity graphs Figure 4d are depicted. Figure 4e depicts a statistical comparison of signal intensity increase/decrease in specific arteries of TOF MIP MRA images between DM patients and volunteers. Figure S2 depicts a statistical analysis of the same employing an interleaved column graph in terms of mean and standard deviation. The mean and standard deviation of the signal intensities are determined. It is to observe that signal intensity in DM patients postexercise is significantly higher in the popliteal artery, posterior tibial artery, and anterior tibial artery in comparison with volunteer data. In DM patients, the signal intensity has not been observed on the peroneal artery for both pre- and post-exercise and hence not been plotted.

Diffusion-weighted imaging

Apparent diffusion coefficient (ADC) maps generated from diffusion-weighted images by fitting diffusion in the mono-exponential model for both volunteers and DM patients are illustrated and described in the proceeding sections. As per the literature survey, the range of ADC values across the arteries of the calf muscles is from 0 to 1.7 ± 0.25 ($\times 10^{-3}$ mm^2/s).[11] Figure 5a shows representative volunteer data depicting ADC maps for both pre- and

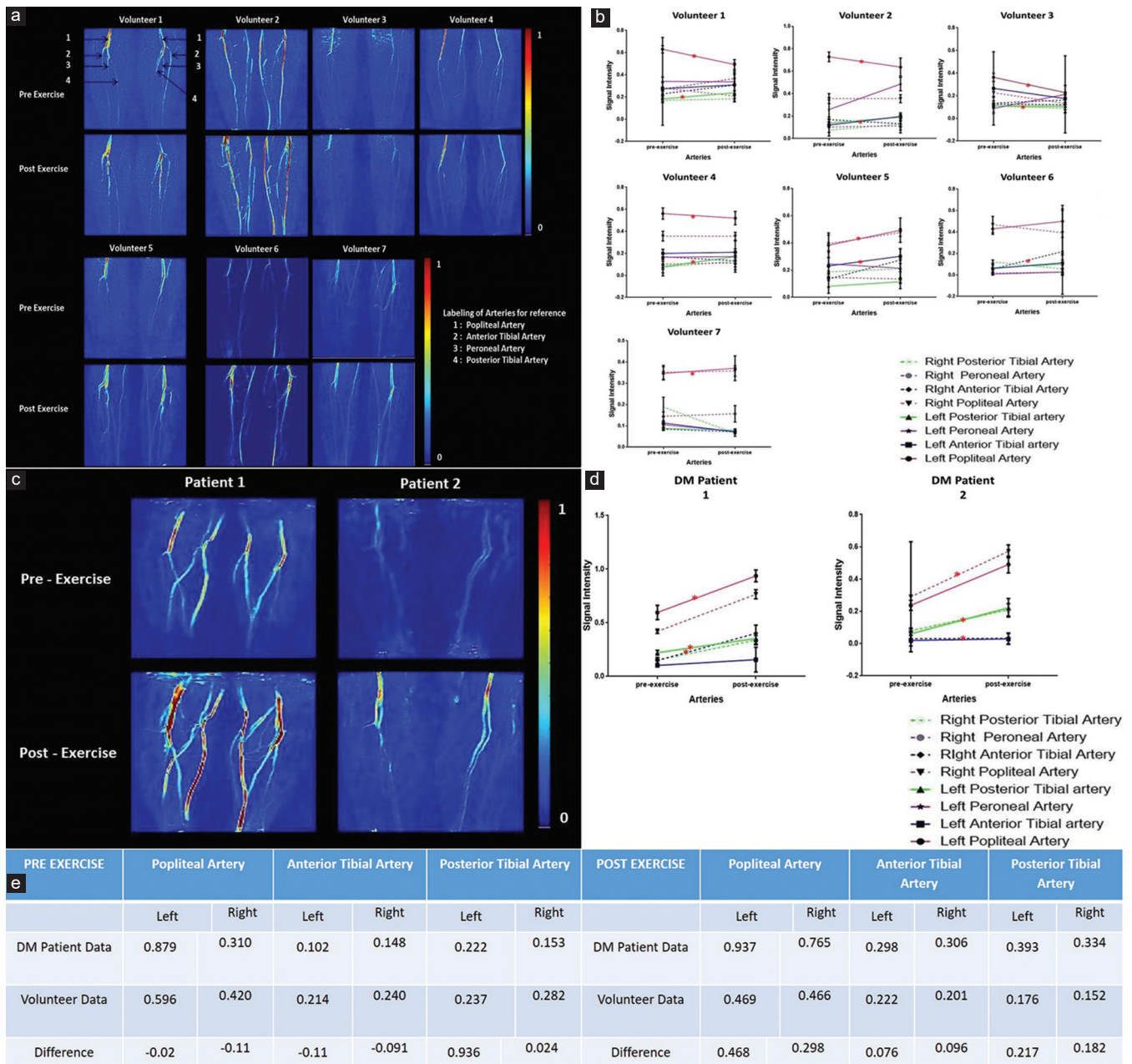| PRE EXERCISE	Popliteal Artery		Anterior Tibial Artery		Posterior Tibial Artery		POST EXERCISE	Popliteal Artery		Anterior Tibial Artery		Posterior Tibial Artery	
	Left	Right	Left	Right	Left	Right		Left	Right	Left	Right	Left	Right
DM Patient Data	0.879	0.310	0.102	0.148	0.222	0.153	DM Patient Data	0.937	0.765	0.298	0.306	0.393	0.334
Volunteer Data	0.596	0.420	0.214	0.240	0.237	0.282	Volunteer Data	0.469	0.466	0.222	0.201	0.176	0.152
Difference	-0.02	-0.11	-0.11	-0.091	0.936	0.024	Difference	0.468	0.298	0.076	0.096	0.217	0.182

Figure 4: (a) Data of volunteers depicting time of flight magnetic resonance angiography maximum intensity projection slices at rest and after yoga exercise showing a selective increase in signal intensity, (b) signal intensities across various arteries, their average and standard deviations of volunteers, (c) data of diabetic mellitus patients depicting time of flight magnetic resonance angiography maximum intensity projection coronal slice, pre- and post-exercise, (d) signal intensities across various arteries, their average, and standard deviations of diabetic mellitus patients. Dotted lines indicate the arteries of the right leg. (e) Statistical analysis of signal intensities of images between volunteers and diabetic mellitus patients

post-exercise. The table in Figure 5b depicts a statistical comparison of ADC values ($\times 10^{-3}$ mm^2/s) increase/decrease in specific arteries of the calf muscles. As per the statistical analysis, a significant increase in ADC values is observed in tibia, gastrocnemius (medial head), soleus regions of the calf muscles postexercise when compared to preexercise. Figure 5c shows representative DM patient data depicting ADC maps for both pre- and post-exercise. The table in Figure 5d depicts a statistical comparison of ADC values ($\times 10^{-3}$ mm^2/s) increase/decrease in specific arteries of the calf muscles. As per the statistical analysis, a significant

increase in ADC values is observed in the left tibia, left gastrocnemius (medial head), left soleus regions of the calf muscles postexercise when compared to preexercise. A decrease in ADC values postexercise is observed in the right tibia, right gastrocnemius (medial head), and right soleus regions of the calf muscles when compared to preexercise.

Discussion

This study demonstrates a signal increase in anterior, peroneal, and posterior arteries for volunteers and an

Volunteer data (c)

PRE EXERCISE	Tibia		Gastrocnemius (Medial Head)		Soleus		POST EXERCISE	Tibia		Gastrocnemius (Medial Head)		Soleus	
	Left	Right	Left	Right	Left	Right		Left	Right	Left	Right	Left	Right
	1.12	1.47	1.39	1.22	0.75	1.07		1.49	0.94	1.59	1.29	1.45	1.57
	1.02	1.36	1.29	1.16	0.82	0.19		1.31	0.89	1.38	1.46	1.42	1.54
	1.04	1.51	1.41	1.20	1.18	1.46		1.03	1.10	1.45	1.49	1.38	1.46
Mean	1.06	1.44	1.36	1.19	0.91	0.90	Mean	1.27	0.97	1.47	1.41	1.41	1.52
SD	0.043	0.063	0.052	0.024	0.188	0.53	SD	0.18	0.08	0.08	0.08	0.02	0.04

Patient data (d)

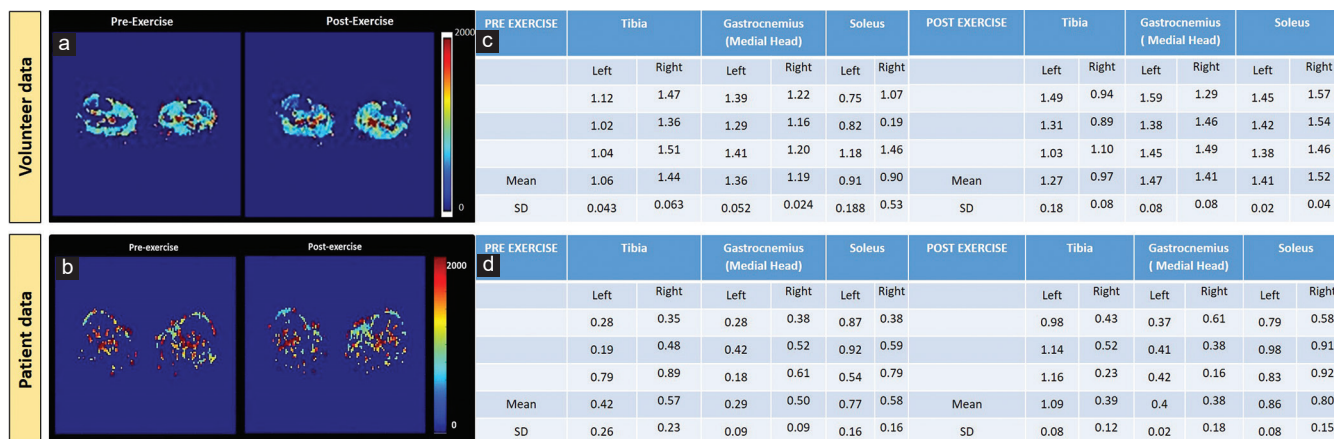| PRE EXERCISE	Tibia		Gastrocnemius (Medial Head)		Soleus		POST EXERCISE	Tibia		Gastrocnemius (Medial Head)		Soleus	
	Left	Right	Left	Right	Left	Right		Left	Right	Left	Right	Left	Right
	0.28	0.35	0.28	0.38	0.87	0.38		0.98	0.43	0.37	0.61	0.79	0.58
	0.19	0.48	0.42	0.52	0.92	0.59		1.14	0.52	0.41	0.38	0.98	0.91
	0.79	0.89	0.18	0.61	0.54	0.79		1.16	0.23	0.42	0.16	0.83	0.92
Mean	0.42	0.57	0.29	0.50	0.77	0.58	Mean	1.09	0.39	0.4	0.38	0.86	0.80
SD	0.26	0.23	0.09	0.09	0.16	0.16	SD	0.08	0.12	0.02	0.18	0.08	0.15

Figure 5: (a) Representative data depicting MATLAB generated apparent diffusion coefficient map for slice 1 of DW axial images pre- and post-exercise, (b) statistical analysis of increase/decrease in apparent diffusion coefficient values ($\times 10^{-3}$ mm2/s) in both pre- and post-exercise conditions, (c) representative data depicting, MATLAB generated apparent diffusion coefficient map for slice 1 of DW axial images Pre- and Post-exercise, (d) statistical analysis of increase/decrease in apparent diffusion coefficient values ($\times 10^{-3}$ mm2/s) in both pre-and post-exercise conditions

increase in popliteal, anterior, and posterior arteries for DM patients in calf muscles postexercise. No significant signal increase was found in popliteal arteries among volunteers. This in turn can be attributed to deoxygenation of muscles during yoga postures and delayed re-oxygenation after yoga postures.[12] The volunteers and DM patients had no experience of yoga in the past. The study bespeaks that performing yoga postures has a positive interim effect on foot complications concerning DM.

The current work integrates yoga and variations in calf muscles for both DM patients/volunteers validated by MRI. In contrast, previous work carried out included impact of yoga on blood glucose level.[11] Prediction of diabetes from the perspective of public health[13] and MR utilized as a tool for osteomyelitis in diabetic foot infections.[14] The work does not focus on regular practice yoga. That might have given more insights on the anatomy considered with respect to regular yoga practice. The quantification of fat distribution and predictive models in the calf muscle is not focused in the current work.

Future work includes perfusion imaging and MRI monitoring of patients performing yoga on a periodical basis for validation of benefits that can be accrued through interceptive medicine. This is expected to aid in the development of predictor models based on yoga for diabetes with a focus on understanding the fat distribution and blood flow in calves.[15] The data presented here forms part of an ongoing study. In the present work, data for volunteers and DM patients are low in number. The data are expected to provide further insight over the next 6 months through an increased sample size for this ongoing study. It can be inferred through this study that MRI provides potential insight into the benefits of yoga for DM patients through deriving biomarkers for preventive medicine relevant to yoga interception.

Conclusions

The study demonstrates increase in blood flow at anterior, peroneal, and posterior arteries for volunteers and an increase in popliteal, anterior, and posterior arteries for DM patients. Regular practice of yoga postures might regulate the blood flow in the calf muscles.

Ethical clearance

The work was carried out with the approval of the Institutional Ethical Review Board. Assessment procedure was explained and consent was obtained from participants.

Financial support and sponsorship

Conflicts of interest

There are no conflicts of interest.

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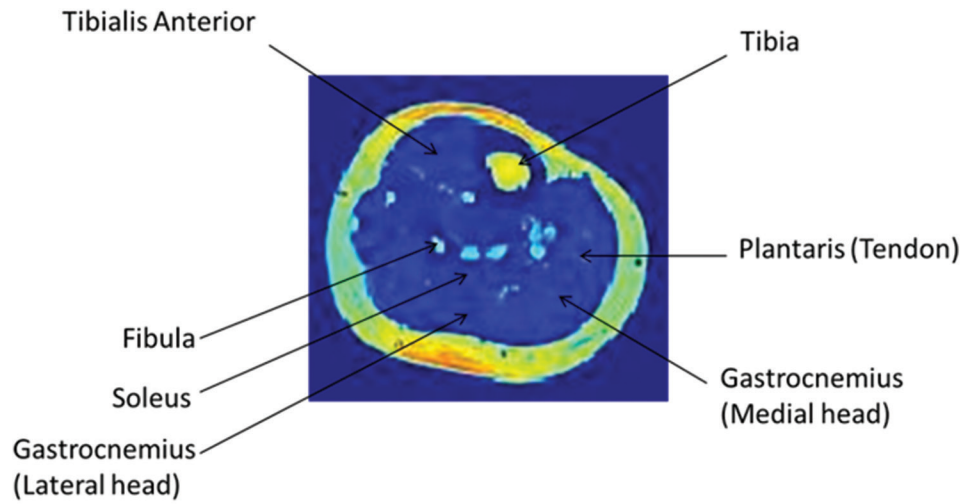
Figure S1: A T$_2$ map axial slice of a calf muscle postexercise
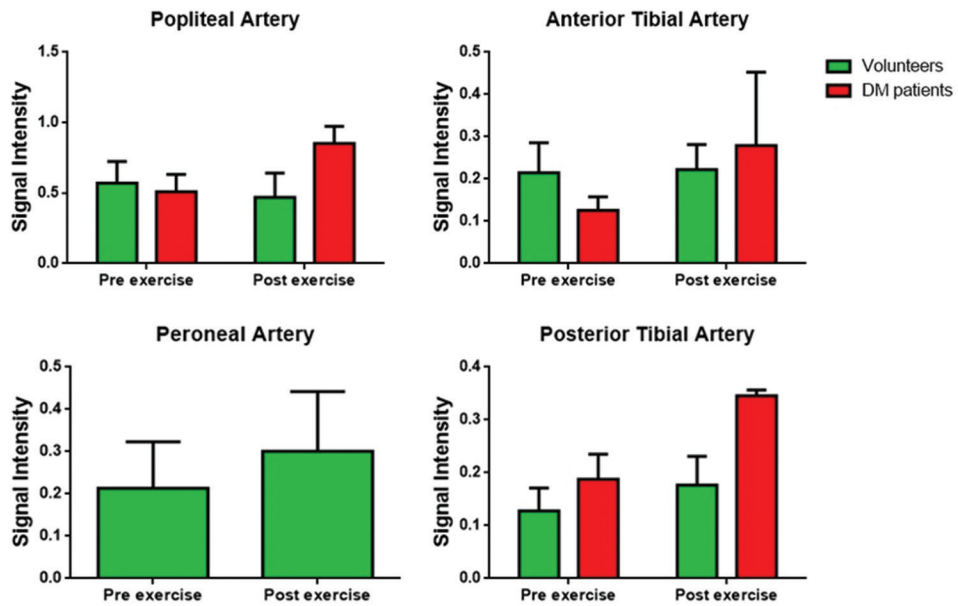

Figure S2: Time of flight, magnetic resonance angiography, maximum intensity projection, signal intensities across various arteries of calf muscles, their average and standard deviations of all volunteers. In diabetic mellitus patients, signal intensity has not been observed on peroneal artery for both pre- and post-exercise and hence not been plotted