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Influence of Isometric Exercise Training on Quadriceps Muscle Architecture and Strength in Obese Subjects with Knee Osteoarthritis

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ABSTRACT

Obese individuals have reduced quadriceps muscle strength relative to body mass that may increase the rate of progression of knee osteoarthritis (OA). The purpose of this study was to evaluate the effects of isometric exercise training on quadriceps muscle architecture and strength in obese subjects with knee osteoarthritis. **Methods:** Forty-four obese male subjects aged 40–65 years diagnosed with knee osteoarthritis were randomly assigned into group A (n=32) and group B (n=12). Group A subjects performed a 12-week isometric exercise program. Group B subjects did not participate in any exercise program and maintained their ordinary activities for the same period. Both groups received the same conventional physical therapy program including hot packs and therapeutic ultrasonic. Muscle thickness, pennation angles and fascicle length of the vastus lateralis (VL) muscle of the affected knee were measured at rest by B-mode ultrasonography. Maximal voluntary isometric knee extension torque (MVIC) of the affected knee was measured using an isokinetic dynamometer. Knee pain and function were evaluated using visual analogue pain scale (VAS) and Western Ontario and McMaster Universities Arthritis Index (WOMAC). All variables were evaluated before and the end of the intervention period for both groups. **Results:** at the end of the program, group A subjects showed significant improvements compared with group B subjects regarding MVIC and muscle architecture parameters ($p<0.05$). Also, there was significant improvement in post-test VAS and WOMAC scores in group A subjects compared to group B subjects ($p<0.05$). **Conclusion:** A 12-week quadriceps isometric training program improves knee pain and quadriceps muscle strength and architecture in obese subjects with knee OA. These results indicate that isometric training should be regarded as a proper exercise intervention for obese patients with knee OA.

Keywords: Obesity, knee osteoarthritis, isometric exercise, muscle architecture

INTRODUCTION

Obesity is considered a major public health issue worldwide and in the Middle East with its prevalence rising rapidly in most Asian countries [1]. Obesity causes functional limitations in the skeletal muscle performance with increased likelihood of developing functional disabilities such as decreased muscle strength particularly with increasing age [2]. It has been reported that the risk of developing functional limitations increases three to four times when body mass index is more than 30 in older obese women [3].

Studies on the effect of obesity on muscle architecture and function have noted that obese people showed higher absolute maximum voluntary contraction torque and power than non-obese individuals and this was suggested to be a result of the extra mass of adiposity in obese individuals that might exert a positive training stimulus on skeletal muscle similar to that attained with resistance training [4]. Despite higher absolute maximum voluntary contraction in obese subjects relative to non-obese counterparts, they have reduced maximum muscle strength when normalized to body mass in their knee extensors compared to non-obese subjects [5]. Reduced maximum muscle strength increases joint loads [6] with consequent increase in the risk of developing joint pathologies such as knee osteoarthritis or even increasing the rate of its progression [7] which is highly prevalent in obese individuals [8].

On the other hand, osteoarthritis of the knee joint is commonly accompanied by marked weakness of the quadriceps muscles leading to dynamic knee instability and physical disability [9]. Quadriceps muscle weakness may be an identifiable risk factor for the development of knee OA and/or indicative of disease progression with strength deficits ranging from 15% to 38% in persons with knee OA [10]. As such, a vicious cycle of pain, muscle weakness, disability, and disease progression is created. Various therapeutic interventions have been implemented to interrupt this cycle. One of these interventions used to improve muscular strength is resistance training exercise which has been recommended as a non-pharmacologic therapy in the management of knee osteoarthritis [11]. Increasing muscle strength may decrease knee forces, alleviate pain, improve physical function and modify biomechanics resulting in a decreased joint loading rate or localized stress in the articular cartilage, thereby playing an important role in both initiation and progression of knee OA [12].

Resistance training could be done as isometric or dynamic exercise. Isometric exercise is a static form of exercise where muscles contract producing force without any considerable change in the muscle length and without any visible joint movement [13]. Isometric resistance training has the advantage of exerting less joint loading and stress, having lower risk-benefit ratio and requiring no or minimal equipment and can be easily and safely performed at home [14]. Hence, it has long been considered as an alternative to dynamic resistance exercise and thought to be a more effective method of muscle strengthening since the 1950's [15]. Muscle force production is strongly influenced by the muscle architecture [16] which is defined as the geometrical arrangement of muscular fibers in relation to the axis of force generation [17]. Muscle fascicle length, muscle thickness and the pennation angle, which is defined as the angle between the fascicles and the deep aponeurosis, are the most common parameters assessed to define muscle architecture. These parameters have been found to adapt to different types of resistance exercise. Adaptations in response to resistance training are increases in pennation angle and muscle size [18,19]. Also, increases in fascicle length (FL) as response to resistance training were reported by some authors [20-23].

Taking into consideration that the impact of obesity on the regulation of muscle mass and architecture is poorly understood [24] with the majority of intervention studies on muscle architecture used isotonic and isokinetic training in normal and non-obese subjects [16,25]. the purpose of this study was to evaluate the effects of isometric exercise training on quadriceps muscle architecture and strength in obese subjects with knee osteoarthritis.

MATERIALS AND METHODS

Experimental design

A randomized controlled clinical trial was conducted to evaluate the effect of a 12-week isometric quadriceps training program on quadriceps muscle architecture and strength, pain intensity and knee function in obese subjects with osteoarthritis. These variables were measured in two groups of subjects; exercise group (group A) underwent an isometric training program and control group (group B) that received no exercise training. All subjects in both groups were tested at baseline and after the 12-week intervention period. Subjects were recruited in the outpatient clinics of Prince Sattam Bin Abdulaziz University. Study procedures were carried out during the period from September 2015 to August 2016.

All subjects were informed about the study procedure and the study was carried out according to the provisions of the Declaration of Helsinki and was approved by the scientific research committee of Prince Sattam Bin Abdulaziz University.

Subjects

Sixty obese male subjects aged 40–65 years diagnosed with knee OA according to the American College of Rheumatology criteria and radiological evidence of primary osteoarthritis of grade 2 or 3 on the Kellgren Lawrence scale based on weight-bearing radiographs were enrolled, and 44 subjects completed the study. Single sex was chosen to exclude the effect of sex on the study results. In the case of bilateral knee OA, the more symptomatic knee was selected for the therapeutic intervention.

Subjects who had secondary OA, rheumatoid arthritis, deformity of the knee, and a history of knee surgery, or intraarticular injection in the past 3 months or who had performed resistance quadriceps exercise were excluded from the study. Subjects were randomly assigned to group A, composed of 32 subjects (age 54.6 ± 8.6 years) or to group B (n=12, age 53.2 ± 9.6 years).

Other than the exercise protocol for group A subjects, the same physical therapy program was applied for each subject for 12 weeks by the same physiotherapist. The physical therapy program included the use of hot packs (20 min) and therapeutic US (continuous mode, 1 MHz, 10 min). At the end of the intervention period, pain and functional assessments, US evaluations, and muscle strength measurements were repeated. To avoid the acute effects of exercise that may cause osmotic fluid shifts and may confound architectural or morphological measurements, all sonographs were taken 3-4 days post-training [26]. All subjects were asked to abstain from any other unusual physical activity during these 12 weeks [27].

Anthropometrical measurements and body composition analysis

All subjects' heights and weights were measured by a weight and height scale (Detecto, made in USA). Subjects were weighed in kilograms (kg) to the nearest 0.1 kg. Each subject's stature was measured in centimetres (cm) to the nearest 0.5 cm. BMI was calculated to select subjects with BMI higher than 30 kg/m^2. According to the formula: BMI=weight (kg)/height (m^2). Waist circumference was measured midway between the lower rib margin and the iliac crest, with a horizontal tape after gentle expiration. An average value from two measurements was considered. Body fat and fat-free mass were measured using a Hologic QDR 4500 A bone densitometer (Hologic, Bedford, MA, USA). The absorptiometry measurements were performed in the supine position as per the whole body standard protocol specified by the manufacturer.

Pain and WOMAC evaluation

A 10 cm horizontal VAS was used for pain assessment. VAS was recorded at baseline and after 12 weeks of exercise.

WOMAC is used to evaluate pain, joint stiffness, and physical function. It is a 3-dimensional, disease-specific, self-administered health status measure that is used in patients with knee OA. The WOMAC uses 17 questions concerning the degree of difficulty performing activities in daily living to assess a person's physical function. The individual scores for the 17 items were added together to obtain a summary score that could range from 0 to 68, with higher scores indicating poorer function. It also includes questions regarding pain and stiffness. The WOMAC pain subscale consists of five items and total scores range from 0 to 20, with higher scores indicating greater pain [21].

Muscle architecture

Muscle thickness, pennation angles and fascicle length of vastus lateralis muscle (VL) of the affected knee were measured *in vivo* at rest by (B-mode) with high frequency performed using a linear array transducer 10-15 MHz connected to (HI vision Avius ultrasound unit; Hitachi). Ultrasonography was performed on VL muscle as it is usually assumed that changes in VL muscle architecture are representative of the whole quadriceps muscle [25]. Subjects were laid in the supine position with fully extended legs and relaxed muscles to obtain the images. To allow fluid shift to occur, all measurements were taken after the subject was laid in the supine position for at least 20 min. Thereafter, a water-soluble gel was applied to the device transducer to aid acoustic coupling; this minimizes deformations of the muscle that can occur with excessive pressure on the underlying muscles. Sonographs were taken in the middle of the VL at 50% of the distance from the central palpable point of the greater trochanter to the lateral femoral condyle. To ensure that repeated scans were taken from the same site, scanning locations were mapped onto a malleable plastic sheet. All US scans were performed by the same investigator who was blinded to the identity of the subjects. The average of the three consecutive scans was taken and used for the subsequent analysis.

Fascicle length was defined as the length of the fascicular path between the superficial and deep aponeurosis. In most cases, the fascicles extended off the acquired image. The length of the missing portion was estimated by linear extrapolation. This was done by measuring the linear distance from the identifiable end of a fascicle to the intersection of a line drawn from the fascicle and a line drawn from the superficial aponeurosis [25]. Pennation angle was defined as the angle between the fascicular path and the deep aponeurosis of the VL muscle. A mean of three pennation angles was assessed on each ultrasound image. Muscle thickness was defined as the mean of the distances between superficial and deep aponeurosis measured at the ends of each 45 mm wide sonograph.

Muscle strength

Subjects were familiarized with the device and procedures involved through visiting the laboratory on at least one occasion before undergoing the testing procedure. Maximal isometric knee extension torque of the affected knee was measured using an isokinetic dynamometer (CSMI Humac 2009, cybex II, II+, version 129, USA) with at 70° knee flexion (full knee extension=0°) for all subjects as this angle is the optimum angle reported for maximal isometric strength of knee extensors [28]. Subjects were positioned with the hip angle at 85° (supine position= 0°). The dynamometer axis of rotation was visually aligned with the center of rotation of the knee joint and straps were applied to the waist, chest and over the other thigh to prevent any extraneous movement. The subject's arms were crossed across the chest.

Following a series of warm-up trials including 10 isokinetic contractions without resistance, subjects were instructed to perform three submaximal isometric contractions of increasing intensity (<50% of maximal capacity) at 70° knee flexion. After a 1min rest subjects were instructed to exert maximal isometric force against the dynamometer lever arm. Subjects were given verbal encouragement throughout their effort. Three successive isometric trials were performed, each contraction was held for ~2 s with a 60 s rest period between contractions. The maximal knee extension moment was recorded in each trial and the highest value was considered as maximal quadriceps strength.

Training program

Prior to training, participants were familiarized with the protocol undertaken during the test. The training protocol consisted of 3 sessions per week, separated by at least 1 day each. The subjects had to perform 3-5 sets of 5-10 repetitions of 5 s unilateral isometric knee extensions, with 30 s rest between repetitions and 1 min between sets. Sessions started in the first week with 3 sets of 5 repetitions and reached 5 sets of 10 repetitions in the 12^{th} week to minimize muscular damage resulting from the unaccustomed exercise intensities. To acclimatize to the training protocol, slightly lower loads corresponding to 50% of MVIC were used for the first week and 60% of MVIC for the second week.

To avoid muscular imbalance between right and left lower limbs due to training adaptations, training was performed on both legs using an isokinetic dynamometer (CSMI Humac 2009, cybex II, II+, version 129, USA). All the participants performed a 5 min cycling warm up at 60 W to 75 W. One minute, 10 isotonic warm-up contractions of the quadriceps through full range with no resistance and three submaximal isometric contractions of increasing intensity (<50% of maximal capacity) at 70° knee flexion before the training sets.

Statistical analysis

All statistics were calculated by using the statistical package of social sciences (SPSS) version 16. Normal data were expressed as mean ± SD. Paired t-test was applied to determine changes between pre-test and post-test within each group concerning the dependent variables. Unpaired t-test was conducted between control and exercise groups to determine changes of dependent variables and to investigate the changes in patients' characteristics between the two groups. Data were considered statistically significant if $p<0.05$.

RESULTS

Baseline characteristics of both groups are shown in Table 1. There was no significant difference between both groups in any measurement ($p>0.05$).

Table 1 Subjects' characteristics

Parameter	Group A (n=32)	Group B (n=12)
Age (years)	54.6 ± 8.6	53.2 ± 9.6
BMI (kg.m^{-2})	35 ± 4.1	34.8 ± 4.2
Waist circumference (cm)	96.6 ± 3.6	96.2 ± 2.3
FFM (kg)	49.9 ± 5.3	49.8 ± 5.5
BF (kg)	44.1 ± 7.1	42.9 ± 6.2
BF (%)	46.9 ± 3.9	46.1 ± 3.6
Duration of disease (years)	3.5 ± 4.1	3.8 ± 3.7

Values are expressed as mean ± SD Abbreviations: BMI: Body Mass Index; FFM: Fat-Free Mass; BF: Body Fat. No significant difference between both groups (p>0.05).

WOMAC and VAS scores

WOMAC and VAS scores of the subjects before and after intervention are presented in Table 2. All WOMAC items and VAS scores were significantly improved in both groups ($p<0.05$) but there was significant improvement in post-test VAS and WOMAC scores in group A subjects compared to group B subjects ($p<0.05$).

Muscle strength

Muscle strength outcomes from the isokinetic test are shown in Table 3. MVIC in group A subjects significantly improved from 148.4 ± 28.56 to 175.6 ± 20.54. No significant changes were found in group B subjects.

Muscle architecture

Data on pre- and post-training muscle architecture parameters are shown in Table 4. Fascicle length, pennation angle and muscle thickness of the VL in group A significantly increased from 8.6 ± 0.57 to 9.5 ± 0.8, 16.3 ± 1.04 to 17.6 ± 1.14 and from 2.7 ± 0.28 to 2.97 ± 0.48, respectively. No significant changes were found in group B subjects.

Table 2 Western Ontario and McMaster Universities Arthritis Index and visual analogue scale scores before and after intervention

Parameter		Group A (n=32)		Group B (n=12)	
		Pre	Post	Pre	Post
VAS		4.5 ± 1.2	2.6 ± 0.8*†	4.3 ± 1.1	3.4 ± 1.08*
WOMAC	Pain	9.03 ± 1.61	5.1 ± 1.69*†	9 ± 1.75	8.3 ± 0.49*
	Stiffness	3.3 ± 0.62	1.6 ± 0.79*†	3.1 ± 0.66	2.3 ± 0.86*
	Function	35.8 ± 4.59	19.2 ± 7.28*†	35.3 ± 5.39	24.8 ± 6.83*

Values are expressed as mean ± SD; Abbreviations: VAS: Visual Analog Scale; WOMAC: Western Ontario and McMaster Universities Arthritis Index; * p<0.05 (post-training versus baseline within group); † p<0.05 (post-training between groups).

Table 3 MVIC changes

Parameter	Group A (n=32)	Group B (n=12)
Pre-test MVIC (N.m)	148.4 ± 28.56	145.7 ± 21.5
Post-test MVIC (N.m)	175.6 ± 20.54*†	155.9 ± 12.08

Values are expressed as mean ± SD; MVIC, maximal voluntary isometric contraction; * p<0.05 (post-training versus baseline within group); † p<0.05 (post-training between groups).

Table 4 Muscle architecture before and after intervention

Parameter	Group A (n=32)		Group B (n=12)	
	Pre	Post	Pre	Post
Fascicle length (cm)	8.6 ± 0.57	9.5 ± 0.8*†	8.6 ± 0.59	8.4 ± 0.66
Pennation angle (degrees)	16.3+1.04	17.6 ± 1.14*†	16.4 ± 1.09	16.6 ± 0.89
Muscle thickness (cm)	2.7 ± 0.28	2.97 ± 0.48*†	2.7 ± 0.33	2.6 ± 0.18

Values are expressed as mean ± SD; * p<0.05 (post-training versus baseline within group); † p<0.05 (post-training between groups)

DISCUSSION

The present study sought to evaluate the *in vivo* effects of isometric exercise training on quadriceps muscle architecture and strength in obese subjects with knee osteoarthritis. It was hypothesized that isometric exercise training in obese subjects with knee osteoarthritis would lead to significant improvements in terms of muscle architecture, strength and function. The findings of the present study fully support the hypothesis as the subjects in the exercise group exhibited significant improvements in post-test MVIC, muscle architecture and knee pain and function compared to the control group. To our knowledge, this is the first study to evaluate the effects of isometric exercise on quadriceps muscle architecture and strength in obese subjects with knee osteoarthritis.

In the current study, an increase of 18% in MVIC was observed at the end of the training period in group A subjects only. Similarly, an average increase of 15.2% in maximal isometric quadriceps strength was reported in response to 8 weeks of isometric training in patients with knee osteoarthritis [29]. Moreover, several studies have demonstrated comparable changes in maximal quadriceps muscle strength following resistance training [18,22,23] The strength changes in response to isometric exercise would be explained by muscle hypertrophy that is possibly related to preferential type II muscle fiber hypertrophy [20]. Neural activation through increases in motor unit recruitment after training has also been proposed as a mechanism for improvements in muscle strength after resistance training [30] but unfortunately, we did not asses for the changes in EMG activity in response to the training program. Also, metabolic changes within the muscle and hormonal alterations appear to play a role in mediating hypertrophic signalling systems. This occurs in response to the high mechanical stress on the muscle fibers and connective tissue used in resistance training. Insulin-like growth factor, testosterone, and growth hormone are the most widely studied hormones [31].

Although obesity has been reported to have a negative effect on skeletal muscle hypertrophy on an animal model [32], our obese subjects demonstrated a significant improvement in muscle strength. It is thus suggested that the potential inhibitory effect of obesity, even with the aggravating effect of knee osteoarthritis, was too weak to counteract the positive effects of mechanical loading of isometric training on muscle strength. However, it should be noted that the baseline MVIC in our subjects was relatively lower than their non-obese counterparts in some other studies [20] which might have facilitated the effect of isometric training to cause significant improvement in MVIC within the 12-week training period. Moreover, the relatively low pretraining MVIC may denote the negative effect of carrying extra body mass on quadriceps muscle strength in patients with painful arthritic knee. It is hypothesized that obesity increases pro-inflammatory cytokines that are associated with lower muscle mass and strength, particularly in the elderly, compounded by impaired skeletal muscle regeneration capacity in obese individuals. Further, as obesity increases knee pain due to increased joint loading, the patient usually refrains from painful physical activities thus accelerating quadriceps muscle weakness [33].

Muscle strength and torque of knee extension has been reported to be related to muscle thickness [34]. Likewise, this was supported in the present study by the 10% increase in VL muscle thickness after the isometric training program. Several studies have found similar changes after isometric [20] and eccentric training programs [16,25,35]. The muscle thickness changes can be attributed to increased fascicle length, pennation angle or both as an adaptive response to resistance training [25]. The significant increase in both fascicle length and pennation angle in the current study may support this notion. Exposure of skeletal muscle to overload stimuli causes perturbations in the muscle fibers and the related extracellular matrix. This leads to adaptation of the muscle architecture (MA) in the form of increased size and amounts of the myofibrillar contractile proteins actin and myosin, and the total number and arrangement of sarcomeres [36].

On the contrary to what was expected, all baseline muscle architecture parameters were in the range of reported values in previous studies carried on healthy and non-obese subjects [20]. Actually, several factors are supposed to affect the muscle geometry in the current study. First, the mean age of exercise group subjects is 54 years which may suggest some degree of decline in the muscle architecture parameters [37]. Second, the presence of knee osteoarthritis may aggravate this decline [10]. Third, obesity is supposed to act as a chronic training stimulus leading to positive adaptations in muscle architecture [38]. The baseline muscle architecture parameters in the current study may suggest that the negative effects of aging and osteoarthritis are counterbalanced by the favourable adaptive effect of obesity on muscle architecture. Furthermore, obesity does not seem to negatively affect the intrinsic muscle contractile properties [38].

The increase in VL fascicle length following isometric training suggests the addition of sarcomeres in series. This is in line with previous reports showing that resistance is a powerful stimulant of protein synthesis with the addition of sarcomeres in series [22]. However, previous findings about fascicle length changes in response to different types of resistance training are inconsistent among studies. Several studies showed an increase in the fascicle length after resistance training [22,23,25]. For example, Reeves, et al. [22] reported that the VL muscle fascicle length during maximal contraction increased by 11% after training. Also, Seynnes, et al. [23] reported only 10 days of high-intensity resistance training increased fascicle length in VL muscle. On the other hand, no increase in fascicle length of the VL muscle was found after 8 weeks of isometric training [20]. Similarly, other studies reported no change in fascicle length after resistance exercise [39,40].

In obese subjects, fascicle length changes are not involved in the skeletal muscle adaptations to increase its force production capacity to cope with the mechanical overload. This reduces the effective contractile force exerted longitudinally onto the aponeurosis with less length range at lower shortening velocities of the muscle-tendon unit. Ultimately, this may contribute to the poor motor performance in obese subjects [24]. So, with isomeric training increasing the muscular fascicle length, it is expected that this type of resistance training may improve the muscle contraction velocity and consequently the motor performance in obese subjects.

As in the case of muscle fascicle length, conflicting data exist regarding the influence of resistance training on muscle fiber pennation angle but the majority of studies have reported increased pennation angle in response to different types of resistance training [18,20,40]. In the current study the VL pennation angle mean significantly increased from 16.3 to 17.6 (a change of 8%). In a recent study, Alegre, et al. [20] have reported a significant increase in VL pennation angles of 11.7% after 8 weeks of isometric training in healthy young men and women. Also, a 5.7% increase in pennation angle has been observed following a 12-week concentric and eccentric resistance training program. Moreover, Aagaard, et al. [18] observed increases in the VL pennation angle after 14 weeks of resistance training in normal male subjects. The responsible mechanism for the changes in pennation angles may be explained by metabolic stress resulting in addition of sarcomeres in parallel [35]. However, some studies failed to find significant changes in VL pennation angle after resistance training [41,42]. The reason for the conflicting findings with respect to muscle architectural adaptation in response to resistance training remains unclear, but it may be may be related to the measurement error of the ultrasonography/analysis technique [25] or differences in the regions where the architectural parameters were measured [40].

The results of the present study showed that post-training WOMAC and VAS scores in the exercise group significantly improved in comparison to the control group while both groups showed significant improvements in comparison to the baseline scores. As all subjects in both groups were treated with the same conventional modalities while only the exercise group undergone the isometric training program, significant improvement in post-test WOMAC and VAS scores in the exercise group in comparison to the control group may be attributed to improved quadriceps strength in response to isometric training. These results are in line with the findings of previous studies indicating that strength training reduces pain and improves physical function in people with knee OA [43-45]. It is well-known that quadriceps strengthening can reduce pain and disability in patients with knee pain and osteoarthritis [46]. One suggested mechanisms of pain relief in response to strengthening exercise may be biomechanical optimization by reducing joint loading rate, localized stress in the articular cartilage or impaired balance [12,47]. Another possible mechanism is that training may cause widespread adaptations in the central nervous system with a consequent reduction in pain sensitivity [47]. Also, improvements in psychological variables following exercise training cannot be ignored [48].

There are several limitations to this study. With respect to muscle architecture assessment, it was evaluated in VL only and it may be not representative of the whole muscle group. Also, as isometric training was done in one knee position, it is not possible to claim that the detected changes are the best could be ever got. Another limitation is that the post-test evaluation was done once at the end of the experimental period, so it was not possible to identify the time course for the changes in the study variables. Finally, data were only collected on men, and thus we cannot confirm whether similar findings would be observed in women.

CONCLUSION

In conclusion, a 12-week isometric training program improves pain and quadriceps muscle strength and architecture in obese subjects with knee OA. These results indicate that isometric training should be regarded as a proper exercise intervention for obese subjects with knee OA.

CONFLICT OF INTERESTS

Authors of this work declare that there is no conflict of interests regarding the publication of this paper.

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