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Beneficial Effects of Alternative Exercise in Patients with Diabetes Type II

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1. Introduction

First of all, let's define the meaning of alternative exercise which means exercise activities aside from the ones that generally perform: running, walking, swimming, or biking [1]. This chapter provides reasons for encouraging alternative exercise to patients with diabetes type II. Moreover it provides knowledge of general modes of alternative exercise and their effects in diabetes and non-diabetes individuals. The exercise modes which are too difficult, aggressive, sports or normally performed such as swimming, cycling or running are not included. The clinical instruction such as indication or contraindication of the exercise is not described because it has already been mentioned elsewhere in this book. Moreover, other recommendation for these patients is well suggested in a previous study [2]. Finally, it described scientific knowledge of an alternative exercise i.e. Arm swing exercise (ASE) on improving glycaemic control and antioxidant activity in patients with diabetes type II. Further studies investigating the effects of ASE on other systems in patients with Diabetes Type II are needed.

2. Reasons for encouraging alternative exercise to patients with diabetes type II

Although moderate exercise (mostly are western style e.g. swimming, running or aerobic dance) at least 30 minutes of moderate-intensity exercise at least three days per week was recommended to prevent cardiovascular disease in diabetes patients [3], it is difficult to encourage them to these modes of exercise regularly. Alternative exercise is defined as various exercise modes performed alternatively e.g. Yoga, Martial Arts, TaeKwonDo and many others. Factors affecting the boring in exercise are intensity, equipment, complicated mode and

duration. This alternative exercise should reduce boring and encourage people to do exercise regularly.

3. General modes of alternative exercise

This topic described many modes of alternative exercise which some of them are scientific proved in patients with diabetes type II but some are not proved.

3.1. Yoga

The word yoga means "union" in Sanskrit, the ancient Indian language [6].



Figure 1. A posture of Warrior which is one of yoga positions [4]

Yoga is an old, traditional, Indian psychological, physical and spiritual exercise regimen that already has been known for its beneficial effects both the symptom and complication of patients with diabetes type 2 including;

- Decreasing reaction time [7]
- Improving lipid profile [7]
- Improving oxidative stress [8, 9],
- Can be incorporated along with the conventional medical therapy for improving cognitive brain functions in diabetes [8] and improve nerve function in mild to moderate Type 2 diabetes with sub-clinical neuropathy [10]
- Reducing Body mass index (BMI) and improving well-being [11]
- Reducing anxiety [8]
- Improving blood pressure, insulin, triglycerides and exercise self-efficacy indicated by small to large effect sizes. [12]

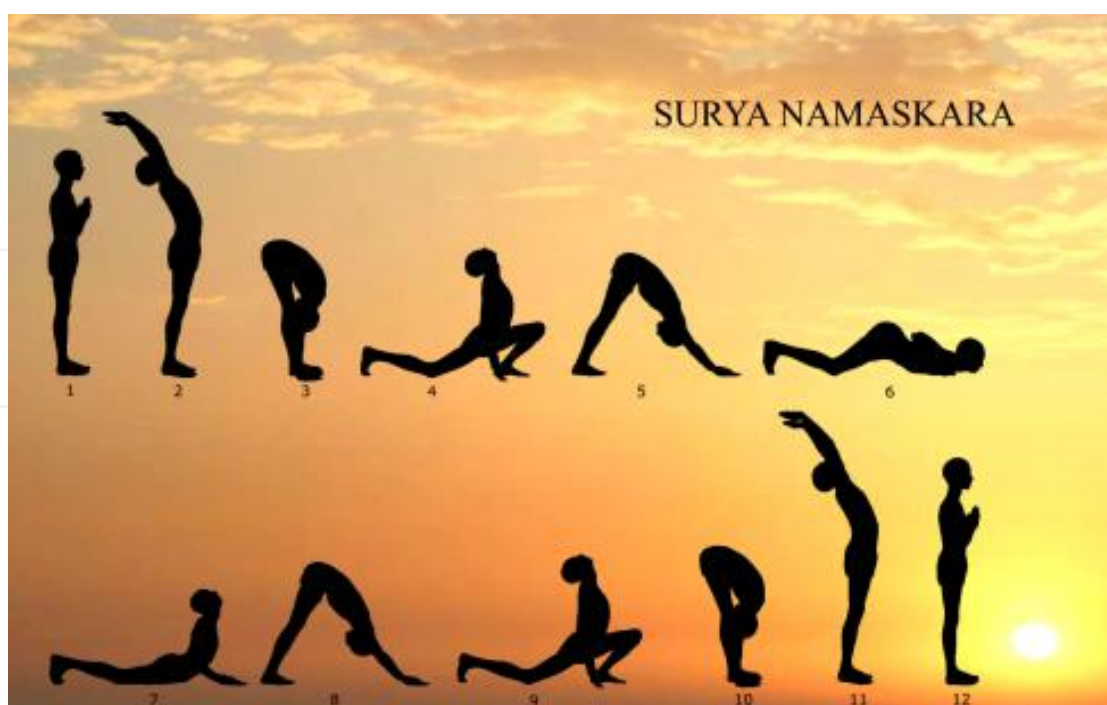


Figure 2. Postures of Surya Namaskara [5]

- Yoga-nidra with drug regimen had better control in their fluctuating blood glucose and symptoms associated with diabetes, compared to those were on oral hypoglycaemics alone. [13]
- Yoga asanas and pranayama improve glycaemic control and pulmonary functions [10].

Moreover, yoga practice was shown to improve pre-existing complication for those diabetic patients. Importantly, Yoga have a role even in prevention of diabetes. Yoga helps improving mind, body and spirit, leading to well-being and increased lovingly [15]. This may be due to mechanisms of reduction in stress and increase relaxations or noninvasive nature.

3.2. Bikram yoga

Bikram yoga is a system of yoga that Bikram Choudhury synthesized from traditional hatha yoga techniques [17] and popularized beginning in the early 1970s [18, 19]. Bikram Yoga sessions run for exactly 90 minutes and consist of a set series of 26 postures including 2 breathing exercises [20]. Bikram Yoga is ideally practiced in a room heated to 105°F ($\approx 40.6^{\circ}\text{C}$) with a humidity of 40%,.

Bikram is a newer form of the practice that benefits blood circulation, improves cardiovascular conditioning and improves detoxification by increasing perspiration.

3.3. Koga

Koga combines the stretching and strengthening of Yoga with the cardiovascular workout of Kickboxing. Like yoga, Koga connects body with mind, and maintaining balance throughout.



Figure 3. A posture of Bikram yoga [16]

Practicing Koga can help improve flexibility, increase muscle toning, relieve stress, increase lung capacity and decrease overall body fat.

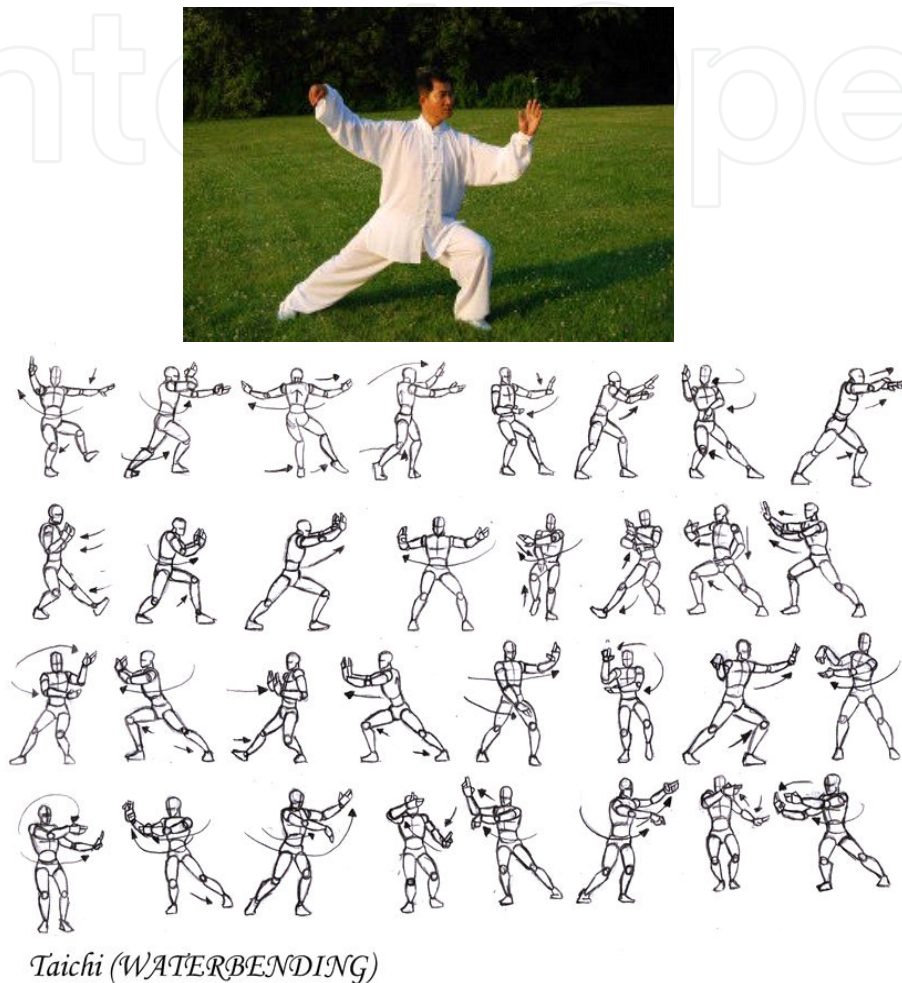


Figure 4. A posture of Koga [21]

3.4. Tai Chi

The Chinese characters for Tai Chi Chuan can be translated as the 'Supreme Ultimate Force' which is often associated with the Chinese concept of yin-yang, the notion that one can see a dynamic duality in all things. Tai Chi, can be thought of as a moving form of yoga and meditation combined. Many of these movements are originally derived from the martial arts although the way they are performed in Tai Chi is slowly, softly and gracefully with smooth

and even transitions between them. Tai Chi is also situated in a wider philosophical context of Taoism. This is a reflective, mystical Chinese tradition first associated with the scholar and mystic Lao Tsu, an older contemporary of Confucius. He taught in the province of Honan in the 6th century B.C. and authored the seminal work of Taoism, the Tao Te Ching.



02

Figure 5. Postures and movements of Tai chi [22]

Tai chi was shown to have many beneficial effects as the following;

- Improved indicators of health related quality of life (HR-QOL) including physical functioning, role physical, bodily pain and vitality in people with elevated blood glucose or diabetes who were not on diabetes medication [23]
- Improvements in fasting blood glucose and peripheral nerve conduction velocities [24].
- Improvements in physical and social functioning [25]
- Improvements in many parameters, such as BMI, lipid profile, C-reactive protein, and malondialdehyde [26]

- Preventing and improving psychological health and was associated with general health benefits for older people [27]
- Tai chi for those with type 2 diabetes could be an alternative exercise intervention to increase glucose control, diabetic self-care activities, and quality of life [28].

However, few studies did not support these beneficial effects of Tai chi [29]. Most of the studies are based on within group changes rather than attention control group comparisons [27].

3.5. Thai yoga (TY)

TY is a traditional form of exercise which appears to be a very light- to light-intensity exercise and have a low-impact alternative to jogging and walking for elderly individuals and requires no special equipment. TY may also have benefits in terms of stress management stemming from the meditation, relaxation and message aspects of the system. If individuals perform TY for longer duration especially standing position, they may gain benefits including reduction in cardiovascular mortality, reduction of symptoms, improvement in exercise tolerance and function capacity, and improvement in psychological well-being and quality of life [32].

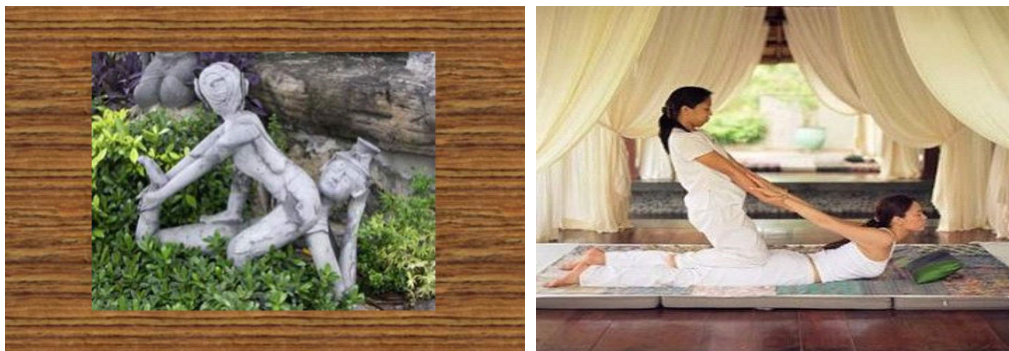


Figure 6. Postures of Thai yoga [30] [31]

3.6. Thai wand exercise

General health perceptions subscale of health related quality of life, functional capacity, body flexibility and obesity can be improved by Thai Wand Exercise training in older individuals [33]. This may partly reduce some cardiovascular disease risk factors. An advantage of this form of exercise is that this is a convenient, low impact on the joints and effective at home fitness program, with the only equipment need, a four feet long stick. But the major attraction is that it is also suited for the elderly who are not allegeable for the common training procedures.

3.7. Martial arts

Most people who are concerned with fitness often overlooked the martial arts. Besides learning to fight, it provides a true total body workout with improving core, upper and lower body strength. The core muscle generated the power in kicking and punching techniques. Impor-

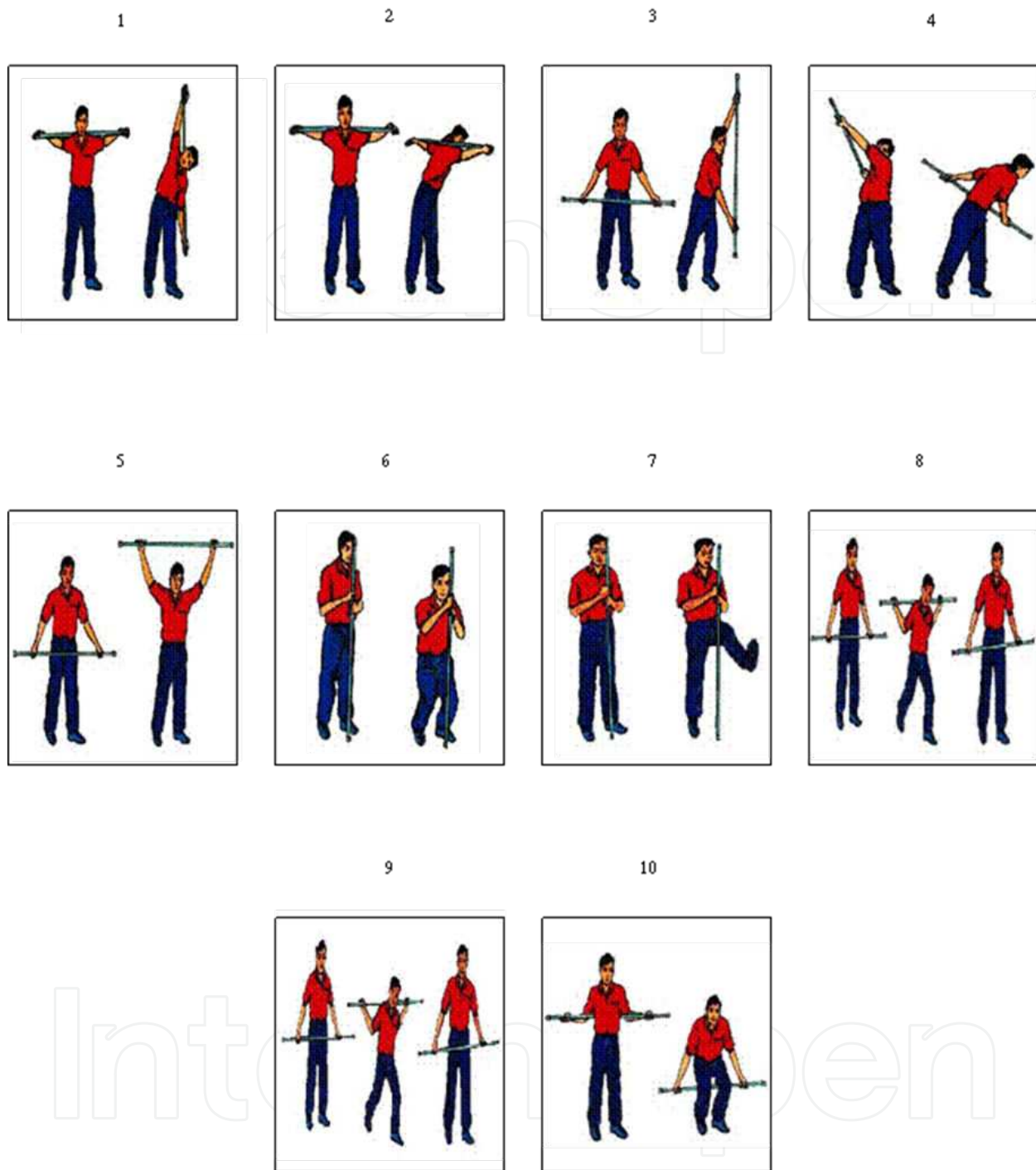


Figure 7. Postures and movements of Thai wand exercise

tantly, its training provides other benefits that are simply not found in an exercise class. First, it can help protecting someone from danger. It can also improve confidence and self-discipline which may change someone's life. Finally, it creates the friendships during training.

Example; Boxing-chaiya, Muay Thai, Chinese martial art, Judo, TaeKwonDo



Figure 8. A posture of Boxing-chaiya [34]



Figure 9. A posture of Muay Thai [35]



Figure 10. A posture of Chinese martial art [36]



Figure 11. A posture of Judo [37]

3.8. Dancing

Dancing burns 2015 kilojoules an hour. It was shown to reduce risks for heart disease and diabetes in elementary school children [41]. Dancing 2 times per week for 12 weeks can reduce systolic BP and body fat in diabetes [42].



Figure 12. A posture of Taekwondo [38]



Figure 13. A posture of dancing [39]



Figure 14. Postures of dancing [40]

3.9. Walking

Walking is recommended for preventing or treating diabetes patients [43]. However, walking with others can actually help patients stick with their health and fitness goals [44].



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Figure 15. Detail of various postures and movements during walking

3.9.1. Brisk walking

The prescription of brisk walking represents an equally effective intervention to modulate glycaemic control and cardiovascular risk profile in type 2 diabetes patients when compared with more individualised medical fitness programmes. The Centers for Disease Control and Prevention (CDC) defined that brisk walking is at a pace of three miles per hour or more (but not race walking) or roughly 20 minutes per mile. This equates to about five kilometers per hour or 12 minutes per kilometer [45]. The exercise intensity of Brisk walking is moderate which heart rate is about 50-70% maximum heart rate or shouldn't be able to sing.

3.10. Go Ape

An exciting range of forest-based high-wire activities, comprise challenging courses that involve climbing, zip wires, balance beams and a whole range of fun-filled activities [47].



Figure 16. Different activities of Go Ape [46]

This activity lasts for 2 to 3 hours which some stamina to complete the course is needed. Upper body and legs will get benefit from this activity. Arm and leg flexibility will be maintained stretching and reaching for hand-holds along the course. Coordination will be definitely improved because of continually coordinating hands and feet as traverse the various obstacles.

3.11. Dinghy sailing

Dinghy sailing is the activity of sailing small boats by using five essential controls: [47]

- The sails



Figure 17. Movement of the crew during Dinghy sailing [48]

- The foils (i.e. the daggerboard or centreboard and rudder and sometimes lifting foils as found on the Moth).
- The trim (forward/rear angle of the boat in the water)
- Side to side balance of the dinghy by movement of the crew, particularly in windy weather ("move fast or swim").
- The choice of route (in terms of existing and anticipated wind shifts, possible obstacles, other water traffic, currents, tides etc.).

Dinghy sailing increases stamina because of the vigorous sailing especially shifting position to balance the boat. Rigging and de-rigging to hauling on the sheets increase upper body strength. Additionally, if there is a less stable boat situation abdominal and back muscles will be stimulated. Good flexibility is very necessary for dinghy sailing. Having a good range of movement and being able to stretch during balancing against the wind is vital. Successful small boat sailing requires because of frequently hauling on the sheets, tacking, shifting position and balancing all at the same time. This will certainly improve coordination.

3.12. Horse riding

Training of horse riding can increase insulin sensitivity in patients with diabetes type 2 [51, 52].

Generally, horse riding increases stamina according to maintaining an upright posture while continually controlling a moving horse at speed. It also strengthens core muscles in order to control horse's movements while maintaining an upright posture. However, there are few flexibility benefits from horse riding, but a good measure of all-round mobility to successfully riding is still needed. Coordination is important for marrying up small body movements with control of the reins — plus hand-to-eye coordination will be required during negotiating trails and obstacles [47].



Figure 18. Upright postures during Horse riding [49] [50]

3.13. Fishing

During fishing, endurance is important for spending the best part of a day standing in a river, walking up and down a beach or fighting with a really big specimen for a few hours. Leg strength is increased from continually working a fly at full stretch. Casting a line is a skill that needs excellent arm and shoulder flexibility so upper body flexibility in particular will be improved by fishing. Casting the line and controlling the rod when reeling fish in requires good hand-to-eye coordination.



Figure 19. Standing posture during Fishing [53]

3.14. Lunge walking

The following is the movement of Lunge walking [54]:

- Stand upright, feet together, holding two light (5-8 pound) dumbbells at your sides (palms facing in).
- Take a controlled step forward with your left leg.
- Lower hips toward the floor and bend both knees (almost at 90 degree angles). The back knee should come close but never touch the ground. Your front knee should be directly over the ankle and the back knee should be pointing down toward the floor.

- Push off the weight with your right foot and bring it forward to starting position (#1). This completes one rep.
- Next step forward and repeat with the right leg.
- Do 2 sets of 15 reps.



Figure 20. Series of movements of Lunge walking [54]

3.15. Make the most of the outdoors

Activities outdoors such as park benches, the kerb, and stairs for simple exercises are health benefit according to exposure to sun shine.

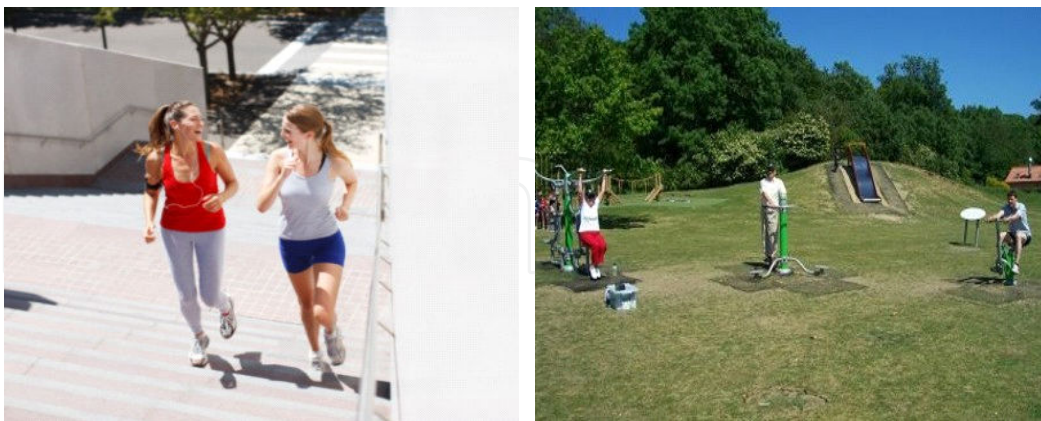


Figure 21. Activities outdoors such as park benches, and stairs [55] [56]

3.16. Surf

Feel the sun on your face and the thrill of catching waves along beautiful coastlines.



Figure 22. A posture under the wave during surfing [57]

3.17. Cardio tennis

Cardio Tennis is a new kind of group exercise that combines endurance with tennis skills. It includes thinking how to hit a backhand, followed by footwork exercises on a rope ladder and running drills. Then it’s back to the volley line and hitting balls again. It was started in the US by the Tennis Industry Association as a way to get more people into tennis, but the programme has since rolled out to 1500 work-out sites in 25 countries.



Figure 23. Activities of Cardio Tennis [58]

Each class includes 5-10 minutes warm-up segment including stretching and footwork drills and 50-55 minutes cardio segment including fun drills [58].

It provides:

- Much more fun than working out on a machine
- It's a fun group activity for advanced beginner and above players
- Elevate your heart rate into your aerobic training zone
- The focus is on getting a great workout while having fun!

3.18. Housework

Housework is so useful because it both increases energy expenditure, cardiovascular response and tidy a house. But if someone have balance problems, they must be careful going down-stairs. It's very easy to fall, especially when carrying a vacuum cleaner. Whenever you see a set of stairs, use them. If there's time (and you're really enthusiastic), go back down and climb them again. If flexibility and balance aren't an issue, take two steps at a time.



Figure 24. A posture of Housework [59]



Figure 25. Activities of Housework [60] [61]

3.19. Alexander technique

Invented by an Australian in the 1890s, this technique helps to restore the body's capacity for ease by releasing tension, particularly in the head and neck. It aims to allow the body to reach its full potential.

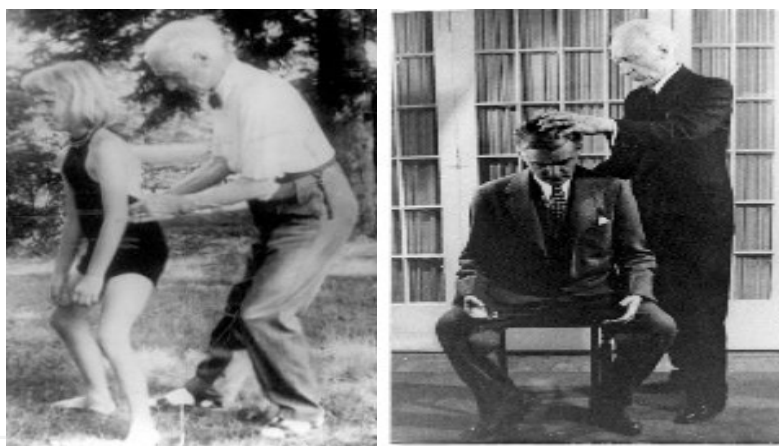


Figure 26. Alexander Technique [62]

"The Alexander Technique is a way of learning to move mindfully through life. The Alexander process shines a light on inefficient habits of movement and patterns of accumulated tension, which interferes with our innate ability to move easily and according to how we are designed. It's a simple yet powerful approach that offers the opportunity to take charge of one's own learning and healing process, because it's not a series of passive treatments but an active exploration that changes the way one thinks and responds in activity. It produces a skill set that can be applied in every situation. Lessons leave one feeling lighter, freer, and more grounded." [62]

The Alexander technique has been shown to be helpful for back pain and Parkinson's [63].

3.20. Feeldenkrais method

Developed in the 1940s, Moshé Feldenkrais (1904–1984) is a practical discipline to help develop awareness of body movement [65]. Feldenkrais aims to reduce pain or limitations in movement, to improve physical function, and to promote general wellbeing by increasing students' awareness of themselves and by expanding students' movement repertoire [66].



Figure 27. A posture of Feeldenkrais method [64]

3.21. Pilates

Invented in the early 20th century by Joseph Pilates, Pilates combines East and West, gymnastic and yogic principles, mind and body [70]. Pilates is a body conditioning routine that may help build flexibility, muscle strength, and endurance in the legs, abdominals, arms, hips, and back. It puts emphasis on spinal and pelvic alignment, breathing, and developing a strong core or center, and improving coordination and balance. Pilates' system allows for different exercises to be modified in range of difficulty from beginning to advance. Intensity can be increased over time as the body conditions and adapts to the exercises [71].

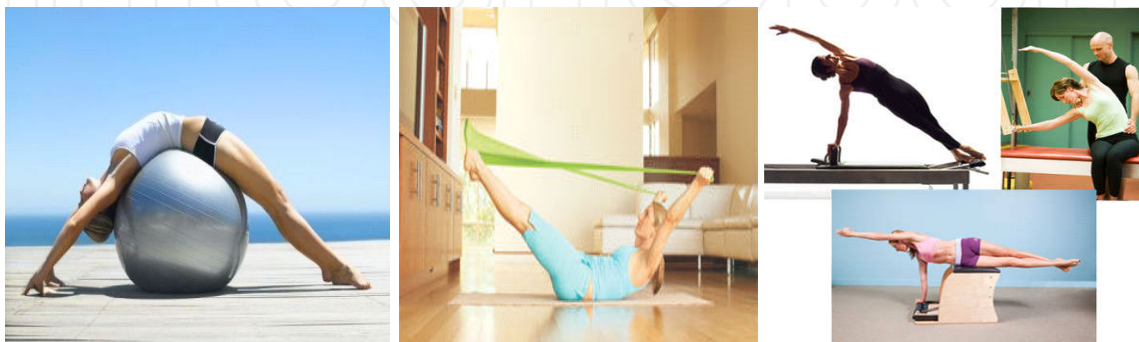


Figure 28. Postures of Pilates [67] [67] [68]



Figure 29. A posture of Pilates [69]

4. Beneficial effects of arm swing exercise on glycaemic control and oxidative stress in patients with diabetes type II [72]

4.1. Introduction

Although moderate exercise (mostly are western style e.g. swimming, running or aerobic dance) at least 30 minutes for five days per week was recommended to prevent cardiovascular disease in diabetes patients [2], it is difficult to encourage them to exercise regularly. Many Asian styles of exercise such as arm swing exercise seem to be more appropriate because of its simple, low impact to joint and easily accessible exercise.

Arm Swing Exercise (ASE) is a traditional Chinese exercise [73] which is convenient for diabetes patients to perform. It is believed to improve cardiovascular systems. However there were no scientific data concerning the beneficial effect and mechanism of this exercise on the glycaemic control. Therefore, this study aimed to investigate effects of the ASE training on blood glucose (glycated haemoglobin; HbA_{1c}), oxidant (determined by malondialdehyde; MDA) and antioxidant (determined by glutathione; GSH) in subjects with type 2 diabetes.

4.2. Experimental design and protocol

All subjects performed 2 study periods consecutively; i) maintaining daily life without regular exercise for 8 weeks (week 1-8) ii) performing 30-min ASE per day, 3 days per week for 8 weeks (week 9-16). Fasting blood glucose, HbA_{1c}, insulin, lipid profiles, C reactive protein (CRP), MDA and reduced GSH concentrations were analyzed using blood samples collected from the antecubital vein. Anthropometry and body composition were also measured before and after of each study period. HbA_{1c} was used to determine glycaemic control because it is more stable throughout 2-3 months and related to the complications.

Insulin sensitivity was determined using Homeostatic Model Assessment – Insulin Resistance (HOMA-IR) [74]. Pharmacology, dietary and exercise treatment, were not modified during the

study period. During the exercise period, patients performed the ASE program as prescribed. They were requested to record the 24-hour dietary composition and energy expenditure for 2 weekdays and 1 weekend day before the start and the last week of each period.

4.3. Arm Swing Exercise (ASE)

ASE is a traditional Chinese exercise which has been practiced for 50 years (Figure 1) and claimed for treatment of cancer and alimentary disorders by increasing blood flow [73]. The number of swing was 200 or 300 repetitions in the beginning and gradually increased to 1000-2000 repetitions or up to half an hour depending on the strength of the patients. The intensity of ASE is mild because it was around 23 percentage of maximal oxygen consumption and 45 percentage of maximal heart rate.



Figure 30. Postures and movements of body during the ASE

During ASE period participants learned to perform the ASE correctly on the first day of the experiment. For the next 8 weeks they performed the training at home via a video tape recording one session per day (30 minutes), 3 days/week. Each participant was telephoned every week to check their compliance to the program and to emphasize them to maintain their usual daily physical activity apart from the ASE program.

4.4. Statistical analysis

All dependent variables were analyzed using a two-way ANOVA with repeated measures (within subject factors were exercise and time) by Sigma Stat version 2 program. The Bonferoni method was used to adjust the multiple comparisons. A probability of $p < 0.05$ was taken to indicate significance. Results are presented as means SE.

4.5. Results

Nine male and 33 female patients with type 2 diabetes mellitus completed the study. Before the experiment, they had high cardiovascular risks such as hyperglycaemia, overweight or obesity (based on criteria of World Health Organization Western Pasific region), high fasting blood glucose, haemoglobin A1c (HbA_{1c}), high sensitive C reactive protein (hsCRP), MDA and low reduced glutathione (GSH) concentrations. There were no differences in body mass, body

mass index, fat mass, fat free mass, waist circumference, hip circumference, waist to hip circumference ratio, and physiological characteristics between the two periods. Mean daily dietary intakes were similar in both periods ($1,468.6 \pm 58.6$ kJ and $1,462.2 \pm 56.0$ kJ; control and exercise periods, respectively). Mean energy expenditure in the exercise period was significantly higher than that in the control period ($1,593.4 \pm 54.6$ and $1,472.7 \pm 47.6$ kJ, respectively; $p < 0.05$).

4.6. Clinical chemistry

HbA_{1c} concentration was 0.2% lower after ASE training for 8 weeks compared with the control period ($p < 0.05$, Table 1). However, there was no significant difference in fasting blood glucose between periods. There were no effect of ASE training on insulin sensitivity, hsCRP concentration and lipid profiles between periods

4.7. Oxidative stress

ASE training significantly reduced plasma MDA concentration ($p < 0.05$) and increased antioxidant blood GSH concentration ($p < 0.05$). No correlation between oxidative stress and HbA_{1c} at any periods was found.

4.8. Discussion

The results showed that the ASE training improves glycaemic control and oxidative stress in patients with type 2 diabetes. Thus, this simple and accessible exercise may have a potential effect on the prevention of complications of diabetes mellitus.

Previous studies also found the decreased HbA_{1c} after the arm exercise training [75-77]. Jeng et al (2002) have reported that arm exercise training for 10-40 min could induce a significant decrease in the HbA_{1c} concentration in patients with type 2 DM. Data from the United Kingdom Prospective Diabetes Study Group (UKPDS) have suggested that a 1% rise in HbA_{1c} concentration represents a 37% increased risk for microvascular complications (95% CI 33 to 41, $P < 0.0001$) [78]. Based on this information, a 0.2% decrease in HbA_{1c} after the ASE training detected in this study may reduce 7.4% of risk for microvascular complications.

Possible mechanisms that could explain for the benefit effect of the ASE training on improving glycaemic control include the reduced HbA_{1c} and the effect of exercise per se on improving the oxidative stress. The reduced HbA_{1c} may decrease many adverse effects of hyperglycaemia such as hyperglycaemia-induced glucose autooxidation, non-enzymatic glycation of proteins, and reactive oxygen species generation, in leading to the progression of diabetic vascular complications. These processes were shown to increase oxidant stress and decrease antioxidant agent [79-81]. The imbalance of oxidative stress with greater oxidant stress contributed to the cellular destruction and therefore vascular complications [82]. The decreased MDA found in this study indicated a reduction in lipid peroxidation, a process of oxidative stress, which then reflects an attenuation of the cellular damage in the patients. The increased level of non-enzymatic antioxidant GSH after the ASE training observed in the present study also supports the preventive effect of exercise on vascular complication. As found in the present study, the

improved glycaemic control positively indicate a preventive action of ASE training in the vascular complications in type 2 diabetic patients via the improved oxidative stress [82].

The second mechanism is due to the effect of exercise per se on improving the oxidative stress. This is supported by the absence of relationship between HbA_{1c} and MDA and GSH at any periods in this study. Importantly, this may remind that only improvement of HbA_{1c} from medication or diet control may not be enough to prevent the complication. Previous studies in both animal and human also supports that low-intensity exercise could itself improve oxidative stress [83-86]. Moien-Afshari et al have confirmed that the low-intensity exercise could enhance antioxidant agent giving rise to less endothelial dysfunction independently on the improvement of hyperglycaemia.

The present study showed that ASE has no adverse effects such as exercise-related injury or hypoglycaemia. This was shown by the similar level of CRP in both periods. Therefore ASE is appropriate and safe for the patient with diabetes. The other strength of the present study is a study design which each subject performed both control and exercise periods. This eliminates the effect of inter-individual variation.

4.9. Conclusion

In conclusion, the present study showed that the ASE training, a low-intensity exercise contribute to protective effects on vascular complication which is a major problem of type 2 diabetic patients. This may attribute to an improved oxidative stress according to either improved glycaemic control or exercise per se. The major attraction is that it is suited for not only diabetic patients but also other people who are not allegeable for the common training procedures such as elderly adults and patients with lower limb disorders.

5. Beneficial mechanisms of exercise on type 2 diabetic patients

There are many possible mechanisms explaining the beneficial effects of exercise training on type 2 diabetic patients (T2D).

These are described based on their roles.

6. Improve glucose control

6.1. Insulin-independent mechanism

1. Exercise leads to an insulin independent increase in glucose transport, mediated in part by AMP activated protein kinase. Changes in protein expression may be related to increased signal transduction through the mitogen-activated protein kinase (MAPK) signaling cascades, a pathway known to regulate transcriptional activity [87].

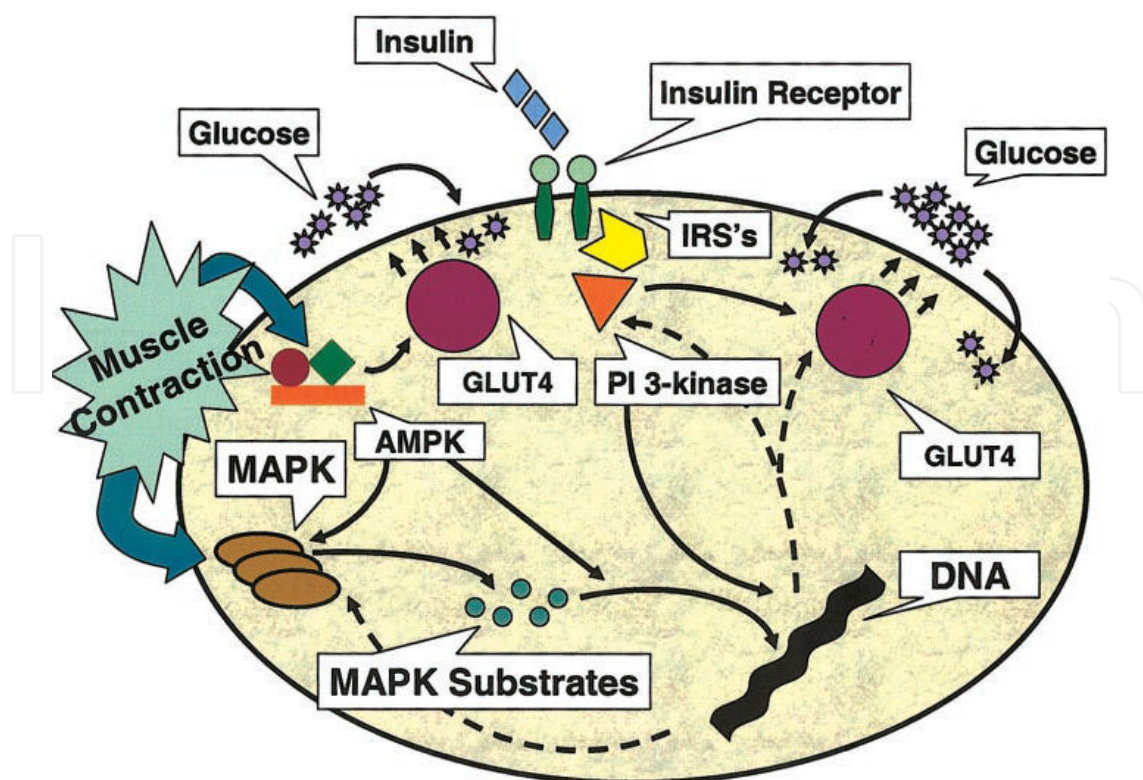


Figure 31. Exercise training-induced changes in insulin signaling via insulin-independent pathway in skeletal muscle [87].

2. Exercise increased skeletal muscle c-Jun N-terminal kinase (JNK) activity throughout the experiment, whereas insulin did not significantly increase JNK activity. The p38 activity was slightly stimulated by exercise and not by insulin [88]. However, the other previous study noted that exercise training improves basal glucose metabolism without a change in the stress kinases, JNK, the nuclear factor B (NF-B) pathway and Hsp72. Moreover, nuclear regulation of NF-B activity in diabetic muscle could be regulated independently of the cytosolic pathway [89].
3. The sodium-dependent glucose co-transporter system (hSGLT3), an insulin-independent glucose transporter, is activated by exercise and it may play a significant role in improving glycemic control [90].
4. Exercise training increases insulin-stimulated glucose disposal primarily by increasing GLUT4 protein expression without enhancing insulin-stimulated PI 3-kinase signaling, and that once the glucose enters the myocyte, increased glycogen synthase activity preferentially shunts it into glycogen synthesis [91].

6.2. Insulin dependent mechanism

The beneficial effect of exercise training on the control of glucose via insulin signaling has been reviewed by many previous studies [92-94]. In addition, many studies investigated the effects of exercise

1. More recent observations indicate that interactions exist at the distal signaling level of AS160 and atypical protein kinase C (aPKC) [95].
2. Acute exercise reverses TRB3 expression and insulin signaling restoration in muscle. Thus, these results provide new insights into the mechanism by which physical activity ameliorates whole body insulin sensitivity in type 2 diabetes [96]. TRB3 is an inducible gene whose expression is regulated by stress response and insulin and associated with insulin resistance and metabolic syndrome.
3. Exercise training increases skeletal muscle Nicotinamide phosphoribosyltransferase (NAMPT) which is known as pre-B-cell colony-enhancing factor 1 (PBEF1) or visfatin, is an enzyme belonging to the family of glycosyltransferases, to be specific, the pentosyltransferases. NAMPT was reported to be an activate insulin receptor and has insulin-mimetic effects, lowering blood glucose and improving insulin sensitivity [97].
4. Blood glucose concentration can be improved by exercise training-induced increases in muscle glycogen content. This could be regulated by multiple mechanisms, including enhanced insulin sensitivity, glycogen synthase expression, allosteric activation of glycogen synthase, and PP1 activity [98]. The increased muscle glycogen also plays important role in muscle strength [99]. This can improve glucose uptake and then glucose control.
5. Exercise overrules free fatty acid-mediated inhibition of pyruvate dehydrogenase (i.e., carbohydrate oxidation). This may improve carbohydrate oxidation although high fat was ingested [100]. The improved carbohydrate oxidation then enhances insulin sensitivity resulting in improved glucose control.
6. The metabolic outcomes were divided into six domains: glycogen, glucose facilitated transporter 4 (GLUT4) and insulin signaling, enzymes, markers of inflammation, lipids metabolism and so on. Beneficial adaptations to exercise were seen primarily in muscle fiber area and capillary density, glycogen, glycogen synthase and GLUT4 protein expressions [101]. This adaptation then play important role on improved glycaemic control.
7. Exercise training results in a persistent increase in insulin sensitivity in skeletal muscle from obese and insulin-resistant individuals [102]. Chronic exercise upregulated phosphorylation and expression of AMPK upstream kinase, LKB1. Particularly exercise reversed the changes in protein kinase C (PKC) ζ/λ phosphorylation, and PKC ζ phosphorylation and expression. In addition, exercise also increased protein kinase B (PKB)/Akt1, Akt2 and GLUT4 expression, but AS160 protein expression was unchanged. Chronic exercise increased Akt (Thr (308)) and (Ser(473)) and AS160 phosphorylation. Finally, exercise increased peroxisome proliferator-activated receptor- γ coactivator 1 (PGC1) mRNA expression in the soleus of diabetic rats. These results indicate that both chronic and acute exercise influence the phosphorylation and expression of components of the AMPK and downstream to PIK3 (aPKC, Akt), and improve GLUT4 [103].
8. Exercise training reversed abnormality in subjects with type 2 diabetes i.e. increase in both IkappaB alpha and IkappaB beta protein, IkappaB alpha and IkappaB beta protein,

decrease in tumor necrosis factor alpha muscle content and an increase in insulin-stimulated glucose disposal [104].

9. Training significantly improved glucose tolerance in obese humans [105]. This may be benefit in control blood glucose concentration leading to prevention for patients diabetes type II.
10. Both moderate- and vigorous-intensity exercise training improved beta-cell function to the extent that the disposition index (DI) accurately reflects beta-cell function. Although through distinct mechanisms [106] were modeled from an intravenous glucose tolerance test. $[DI = S(i) \times AIRg]$ (insulin sensitivity ($S(i)$), acute insulin response to glucose ($AIRg$))
11. In diabetic rats, exendin-4 and exercise stimulate insulin receptor substrate (IRS)-2 expression [107, 108] through the activation of cAMP responding element binding protein in the islets [109]. This enhanced their insulin/insulin like growth factor-1 signaling. The potentiation of the signaling increased the expression of pancreas duodenum homeobox-1, involved in beta-cell proliferation. In conclusion, exendin-4 and exercise equivalently improved glucose homeostasis due to the induction of IRS-2 in the islets of diabetic rats through a cAMP dependent common pathway.
12. Exercise training substantially reduces the exposure of islets to exogenous lipid, thereby providing a potential mechanism by which exercise can prevent islet beta-cell failure leading to diabetes type 2 [110].
13. Exercise may have beneficial effects via monocyte since monocyte peroxisome proliferator activated receptors gamma ($PPAR\gamma$) activation has been linked to beneficial antidiabetic effects. This is supported by the association between exercise-induced upregulation of monocytic $PPAR\gamma$ -controlled genes and reverse cholesterol transport and anti-inflammatory effects. Thus, exercise-induced monocyte $PPAR\gamma$ activation may contribute to rationale for prescribing exercise to type 2 diabetes patients [111].
14. High-intensity progressive resistance training, in combination with moderate weight loss, effectively improved glycemic control in older patients with type 2 diabetes. This may result from increased muscle mass leading to increased glucose uptake [112].

6.3. Weight reduction

Swim training can effectively prevent body weight gain, adiposity and lipid disorders caused by leptin receptor deficiency, in part through activation of UCPs in adipose tissue and skeletal muscle [113]. The training also increased carnitine palmitoyl transferase (CPT I) activity and became less sensitive to inhibition by malonyl-CoA, reduced both total ceramide content. In addition, it improved capacity for mitochondrial FA uptake and oxidation leads not only to a reduction in muscle lipid content but also to change in the saturation status of lipids [114]. These may contribute to alleviating weight reduction for patients with diabetes type 2.

6.4. Normalization of blood lipid profiles

Decreases in total cholesterol, increases in HDL, oxidized LDL (oxLDL), leukocyte mRNA expression for PPARgamma which was reinforced by increased PPARgamma DNA-binding activity and gene expression were observed for the oxLDL scavenger receptor CD36 LXRalpha. Two LXRalpha-regulated genes involved in RCT, namely, ATP-binding cassette transporters A1 and GI (ABCA1 and ABCG1, respectively), were significantly up-regulated post-exercise [115].

6.5. Improved nitric oxide-mediated skeletal muscle blood flow

1. Exercise training improves endothelium-dependent vasodilator function, not only as a localised phenomenon in the contracting muscle group, but also as a systemic response when a relatively large mass of muscle is activated regularly during an exercise training program. Shear stress-mediated improvement in endothelial function provides one plausible explanation for the cardioprotective benefits of exercise training [116].
2. In addition to being a possible modulator of blood flow, nitric oxide (NO) from skeletal muscle regulates muscle contraction and metabolism. Recently, human data indicate that NO plays a role in muscle glucose uptake during exercise independently of blood flow. Exercise training in healthy individuals increased NO bioavailability through a variety of mechanisms including increased NOS enzyme expression and activity. This contributed to increased exercise capacity and cardiovascular protection. Exercise training with high cardiovascular risk can increase NO bioavailability and may represent an important mechanism by which exercise training takes benefit in the prevention [117].

6.6. Improvement of nervous system function

Progressive exercise training significantly decreases diabetes-associated neuropathic pain, including thermal hyperalgesia and mechanical allodynia. In rats, this protective effect is related to the increase of Hsp72, but not TNF- α and IL-6, expression in the spinal cord and peripheral nerves of STZ-induced diabetes. [118]

6.7. Improved oxidative stress

Acute exercise was reported to elevate Ox LDL, SOD and GSH-Px levels which are associated with in type 2 diabetic patients [119]. Exercise training including low-intensity exercise can increase antioxidant and decrease oxidant [72]

6.8. Prevention of microangiopathy

Mitochondrial oxidative capacity appears to be involved in the overall mechanism by which exercise prevents microangiopathy in rats with type 2 diabetes. Luminal capillary diameter of the diabetic group was significantly lower than that of the control group, succinic dehydrogenase (SDH) activity was significantly higher in the diabetic with exercise group than in the control and diabetic groups [120].

6.9. Improve metabolic control

Exercise training results in an increase in the oxidative capacity of skeletal muscle by up-regulating lipid oxidation and the expression of proteins involved in mitochondrial biogenesis. This decreased liver triacylglycerol content [121].

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