The American Journal of Chinese Medicine, Vol. 40, No. 6, 1143–1156 © 2012 World Scientific Publishing Company Institute for Advanced Research in Asian Science and Medicine DOI: 10.1142/S0192415X1250084X

The Effect of Qigong Exercise on Immunity and Infections: A Systematic Review of Controlled Trials

Chong-Wen Wang,* Siu-Man Ng,* Rainbow T.H. Ho,* Eric T.C. Ziea,[‡] Vivian C.W. Wong[†] and Cecilia L.W. Chan*

*Centre on Behavioral Health [†]School of Chinese Medicine, LKS Faculty of Medicine The University of Hong Kong, HKSAR, China [‡]Department of Chinese Medicine Hospital Authority, HKSAR, China

Abstract: The objective of this review was to summarize and critically evaluate the clinical evidence of the effect of qigong exercise on immunity and its efficacy in the prevention or treatment of infectious diseases. Thirteen databases were searched from their respective inceptions through January 2011, and all controlled clinical trials of qigong exercise on immunity and infections were included. Quality and validity of the included studies were evaluated using standard scales. Seven studies including two randomized controlled trials (RCTs), two controlled clinical trials (CCTs) and three retrospective observational studies (ROSs) met the inclusion criteria. One study focused on functional measures of immunity (antigen-induced immunity) and six studies on enumerative parameters of immunity. No study on clinical symptoms relevant to infectious diseases could be identified. Overall, the included studies suggested favorable effects of qigong exercise on immunity, but the quality of research for most of the studies examined in this review was poor. Further rigorously designed studies are required, which should adhere to accepted standards of methodology for clinical trials.

Keywords: Qigong; CAM; Infection; Immunity; Review.

Introduction

Qigong, a form of ancient martial arts and a complementary and alternative modality of traditional Chinese medicine, is a combination of physical movements, meditative practice

Correspondence to: Dr. Cecilia L.W. Chan, Centre on Behavioral Health, The University of Hong Kong, 5 Sassoon Road, Pokfulam, Hong Kong. Tel: (+852) 2831-5172, Fax: (+852) 2816-6710, E-mail: cecichan@hku.hk

and controlled breathing. The gentle movements integrating body with mind are designed to cultivate spirit and achieve a harmonious flow of vital energy (qi) in the body so as to improve physical fitness and overall well-being. With regular practice and rehearsal of the structured movements as well as the attunement of mind and breath, practitioners can experience greater stress management and emotional control. Long term practice of qigong exercise may help to prevent illness or heal the body from diseases. Although the underlying mechanism for its health benefits is not yet well understood, there are increased reports of its effects on health (Ng and Tsang, 2009; Vincent *et al.*, 2010; Wright *et al.*, 2011). Basically, there are two categories of qigong: internal qigong and external qigong. Internal qigong or qigong exercise is self-directed and involves the use of movements, meditation and control of breathing pattern, whereas external qigong or emitted qi, is usually performed by a trained practitioner using their hands to direct qi energy onto the patient for treatment. Their underlying mechanisms that provide potential benefits are different.

It is hypothesized that qigong exercise as a form of mind-body intervention may improve immune functions (Goldrosen and Straus, 2004). Many studies have documented the effects of qigong exercise on immunological parameters, but few systematic reviews have examined the scientific evidence of the effects of qigong exercise on immunity. It is well known that infections such as influenza and herpes zoster are associated with the human body's immunity, and that individuals who have a substantial decline in immune function are at increased risk for a number of infectious diseases. Epidemiological studies have suggested that moderate exercise training is associated with reduction in incidence of upper respiratory tract infection (URTI), whereas high intensity of exercise may increase the risk for URTI (Sim *et al.*, 2009). However, few reviews have examined the effectiveness of qigong exercise as a therapeutic intervention on prevention and treatment of infectious diseases. Thus, this review aims to summarize and critically assess the evidence of the effects of qigong exercise on immunity and infections.

Methods

1144

Data Sources and Search Strategies

The following electronic databases were searched from their respective inceptions through January 2011: PubMed/MEDLINE, Cochrane Central Register of Controlled Trials, Cumulative Index to Nursing and Allied Health Literature, Excerpta Medica Database, Allied and Complementary Medicine, Qigong and Energy Medicine Database, China Journals Full-text Database-Medicine/Hygiene Series, China Proceedings of Conference Full-text Database, Chinese Master Theses Full-text Database, Chinese Doctoral Dissertations Full-text Database, Electronic Theses and Dissertation System (Taiwan), Taiwan Electronic Periodical Services, and Index to Taiwanese Periodical Literature System. The search terms used for this systemic review included: qigong, qi-gong, qi gong, chi chung, chi gong, qi chung, qi-training, nei gong, neigong, influenza, infection, inflammatory, immune, immunity, immunological, lymphocyte, and antibody. Both

traditional and simplified Chinese translations of these terms were used in Chinese databases. Reference lists of all included studies, relevant reviews, and other archives of the located publications were hand-searched for further relevant articles.

Selection of Studies

All prospective controlled clinical trials were included if they examined the effects of qigong exercise on the improvement of immune function or the incidence and severity of infectious diseases. Given the limited number of prospective clinical trials in the field, retrospective controlled observational studies were also included to provide alternative evidence. Uncontrolled observational studies and studies measuring acute effects of short term qigong exercise were excluded due to their susceptibility to bias and lack of significant evidence. Studies with qigong as a component of an intervention package involving other forms of exercise were excluded for the difficulty to explain the results of the studies. Case reports and qualitative studies were excluded for lack of significant evidence. Studies in cancer patients were also excluded due to the different mechanisms and different indicators of immunity for cancer diseases. For all included studies, the primary data from the original sources were reviewed and analyzed.

To evaluate the effects of gigong exercise on immunity and its effectiveness in the treatment of infectious diseases, outcome measures such as biomarkers of immunity and physical symptoms relevant to infections were considered. Generally, assessment of an individual's immune status can be completed using either enumerative or functional measures (Miller and Cohen, 2001). Functional measures assess how well a specific immune system process is performed. One of the most commonly used functional measures in clinical practice is the assessment of people's immune responses to antigens to which they are highly sensitive. This technique involves placing a small piece of antigen directly underneath the skin, a process that causes a local inflammatory response that consists of induration (a swollen round bump) and erythema (redness around the bump), and measuring the magnitude of this response immediately or 24–48 hours later depending on the antigen that is used. Enumerative measures involve counting different immune system components (or parameters), including white blood cell populations (leukocytes, monocytes, lymphocytes, natural killer cells), antibody populations in the blood (serum immunoglobulins A, G, and M; complements 3 and 4) and in saliva (secretory immunoglobulin A), and antibodies to specific pathogens. The current review will focus on the number and percentage of white blood cells, mainly T-lymphocytes, and levels of serum immunoglobulins and complements in peripheral blood, since they are commonly used parameters in clinical practice and in the field of exercise research. Psychosocial outcomes such as quality of life were not considered since it is difficult to attribute the effects of such outcomes to the change on immunity.

Data Extraction and Quality Assessment

For each included study, data were extracted by one main researcher and then verified by another researcher. Any discrepancies were resolved by discussion. The strength of the C.-W. WANG et al.

evidence was evaluated for all included studies using the criteria for levels of evidence recommended by the Oxford Centre for Evidence-based Medicine (2009). These criteria grade the methodological rigor of studies from level 1 or grade A (systematic review of RCTs, 1a; individual RCT with narrow confidence interval, 1b) to level 5 or grade D (expert opinion). The quality and validity of the included RCTs were also evaluated using the Jadad Scale (Jadad *et al.*, 1996), a standard in systematic reviews of RCTs, which is based on three criteria: description of randomization and allocation concealment, double-blinding, and withdrawals or dropouts (the score ranges from 0 to 5). Given that it was difficult to blind the patients to qigong invention, we only evaluated assessor blinding. The risk of bias in the included studies was assessed using the framework for methodological quality recommended by Jüni *et al.* (2001). According to this framework, biases fall into four categories: selection bias (biased allocation to comparison groups), performance bias (unequal provision of care apart from intervention under evaluation), detection bias (biased assessment of outcomes), and attrition bias (biased occurrence of loss to follow-up).

Results

Our searches identified 276 potentially relevant articles, of which 226 articles were excluded because they were related to external qigong, not related to qigong, not a clinical trial, not related to immunity or infection, and *in vivo* or *in vitro* studies. Full reports of 50 studies were acquired and 43 were further excluded due to that they were: (1) uncontrolled observational studies, (2) studies not focusing on qigong, (3) studies on acute effects of qigong, (4) studies with outcome measures not related to identified components of immune system, (5) studies with unparallel control, (6) case reports, (7) qualitative studies, and (8) studies among cancer patients (Fig. 1).

Seven studies including two RCTs (Manzaneque *et al.*, 2004; Yu and Wang, 2007), two CCTs (Yan, 1989; Yao, 1989) and three ROSs (Ryu *et al.*, 1995a, 1995b; Lee *et al.*, 2006) met the inclusion criteria. Subjects in these studies included young college students (Yan, 1989; Manzaneque *et al.*, 2004), adults aged 20 to 50 (Ryu *et al.*, 1995a, 1995b; Lee *et al.*, 2006), and patients with aplastic anemia (AA) (Yao, 1989). One study focused solely on males (Ryu *et al.*, 1995a). Sample sizes ranged from 25 to 137. In total, this review covered 462 subjects including 299 in the intervention groups and 163 in the control groups. Characteristics of the included studies are presented in Table 1.

Durations of qigong intervention ranged from 1 to 6 months for prospective trials including RCTs and CCTs (Yan, 1989; Yao, 1989; Manzaneque *et al.*, 2004; Yu and Wang, 2007), and from one to longer than 25 months for ROSs (Ryu *et al.*, 1995a, 1995b; Lee *et al.*, 2006). Five studies were conducted with a two-armed parallel group design, one study with a 3-armed parallel group design (Lee *et al.*, 2006), and one study with a five-armed parallel group design (Ryu *et al.*, 1995a). The intervention groups were generally compared with a wait-list control group (Ryu *et al.*, 1995a, 1995b; Lee *et al.*, 2006) or a control group with usual activities (Manzaneque *et al.*, 2004; Yu and Wang, 2007) or usual medical care (Yao, 1989), except for one study (Yan, 1989) in which qigong exercise was compared with taiji exercise.

1146

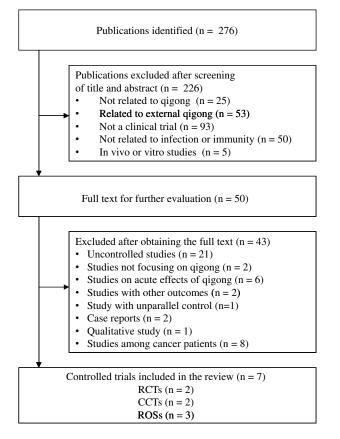


Figure 1. Selection process for included studies.

One study focused on functional measures of immunity (antigen-induced immunity) (Ryu *et al.*, 1995a), and six studies on enumerative parameters of immunity (Yan, 1989; Yao, 1989; Ryu *et al.*, 1995b; Manzaneque *et al.*, 2004; Lee *et al.*, 2006; Yu and Wang, 2007). No study focused on clinical symptoms relevant to infections. The most often emerged outcome measure among the included studies was T-lymphocytes (Yao, 1989; Ryu *et al.*, 1995a; Manzaneque *et al.*, 2004; Yu and Wang, 2007), followed by immunoglobulins and complements (Yan, 1989; Manzaneque *et al.*, 2004).

These studies were conducted in Korea (Ryu *et al.*, 1995a, 1995b; Lee *et al.*, 2006), mainland China (Yan, 1989; Yao, 1989; Yu and Wang, 2007), and Spain (Manzaneque *et al.*, 2004). Of them, four were published in English (Ryu *et al.*, 1995a, 1995b; Manzaneque *et al.*, 2004; Lee *et al.*, 2006), two were published in Chinese (Yao, 1989; Yu and Wang, 2007), and the last one was a conference proceeding (Yan, 1989). Overall, the quality of research was poor for most of the included studies. Levels of evidence for all included studies were ranked as "B" or "C". No study could be ranked as "A". Jadad scores for the two included RCTs were 2.

	Table 1.	. Summary	of Controlled Clinical Trial.	s of the Effects of	Qigong Exercise	on both Functional and E	1. Summary of Controlled Clinical Trials of the Effects of Qigong Exercise on both Functional and Enumerative Measures of Immunity	nity	
Studies/Design	Subjects	u	Intervention (Frequency)	Control	Follow Up	Outcomes	Results		Level of Evidence
Manzaneque <i>et al.</i> , 2004 RCT	University Students (18–21 yr)	QG:16 CG:13	Ba Duan Jin (eight pieces of brocade) (30 min, 20 sessions)	Routine activities	1 month	 Leukocytes (count) Monocytes (count) Lymphocytes (count) Lymphocytes (%) Lymphocytes (%) LgA TgG 8. tgA 9. C3 10. C4 	QG/CG: 1. $p = 0.03$ in favor of CG 2. $p = 0.02$ in favor of CG 3. n.s. 5. n.s. 6. n.s. 7. n.s. 8. n.s. 8. n.s. 9. $p = 0.004$ in favor of CG 10. n.s.		B (2b)
Yu and Wang, 2007 RCT	Middle-aged and older adults $(M:61.6 \pm 3.8 \text{ yrs})$ (F: 58.5 \pm 4.1 yrs)	QG:50 CG:50	Wuqinxi (a mimic-animal exercise) (45 min, 4 times per week)	Routine activities	6 months	CD4+/CD8+	QG (pre-/post-): M: $p < 0.05$ F: $p < 0.01$	CG (pre-/post-): M: n.s. F: n.s.	B (2b)
Yan, 1989 CCT	College students (n.r.)	QG:30 CG:40	Group qigong exercise (n.r.)	Taijiquan exercise	1 month	 IgA lgG lgM LgM	QG (pre-/post-): 1. n.s. 2. n.s. 3. n.s. 5. $p < 0.05$ 5. $p < 0.01$	CG (pre-/post-): 1. $p < 0.01$ 2. $p < 0.01$ 3. $p < 0.01$ 4. $p < 0.01$ 5. $p < 0.01$	C(4)
Yao, 1989 CCT	Patients with AA (QG: 20-42 yrs) (CG: 14-69 yrs)	QG:10 CG:13	Self-controlling qigong exercise plus usual medical care (1 hour per day)	Usual medical care	1 month	1. Тs 2. Th 3. Th/Ts	QG/CG: 1. n.s. 2. $p < 0.02$ 3. $p < 0.02$		B (3b)
Lee et al., 2006 ROS	Qigong trainees (20-40 yrs)	QG1: 52 QG2: 63 CG: 22	QG1: Qigong training for 1–12 months QG2: Qigong training for >12 months (n.t.)	Healthy volunteers	Retrospective	 CD4+/CD8+ Memory CD4+/naïve CD4+ 	QGI/CG: 1. <i>p</i> < 0.001 2. n.s.	QG2/CG: 1. $p < 0.001$ 2. $p < 0.001$	B (3b)

C.-W. WANG et al.

Byu. et al., 1955Qegong traineesCG: 13Chun Do Sun BupqioonHealthyRetrospectiveCDH+/CDB+GG1/CG: n.s.ROS(M: 20-50 yrs)QG1:12U-4 monthsQG1:02UUnueersQG2:02UQG3:05P<005QG3:17QC3:17QC3:20 goog exercise for QG3:17QC3:20 goog exercise for 13-24 monthsS-12 monthsQG3:07 c; $p < 0.05$ QG3:05P<005QG3:17QC3:02 goog exercise for 13-24 monthsQG3:02 goog exercise for 13-24 monthsS-12 monthsQG4:02 p < 0.05QG4/CG: $p < 0.05$ QG3:02 goog exercise for 13-24 monthsS-24 monthsQG4:02 goog exercise for 13-24 monthsRetrospectiveSin tests for DCH withThe maximal antigen responseRyu. et al. 1995Qigong traineesQC:16Qigong training for months (n.r.)NolumeersSin tests for DCH withThe maximal antigen responseRyu. et al. 1995Qigong traineesQC:16Qigong training for months (n.r.)NolumeersSin tests for DCH withThe response antigen responseRyu. et al. 1995Qigong traineesQC:16Qigong training for months (n.r.)NolumeersSin tests for DCH withThe response antigen responseRyu. et al. 1995Qigong traineesQC:16Qigong traineis for months (n.r.)NolumeersQC4CC: 4 mid8 hrRyu. et al. 1995Qigong traineesQC:16Qigong traineis for months (n.r.)NolumeersQC4CC: 4 mid8 hrRyu. et al. 1995Qigong traineesQC:16Qigong trainegongQC3CC: 4 mid8 hrQ	Studies/Design	Subjects	u	Intervention (Frequency)	Control	Follow Up	Outcomes	Results	Level of Evidence
Qigong trainees QG:16 Chun Do Sun Bup qigong Healthy Retrospective Skin tests for DCH with (20-45 yrs) CG:12 Qigong training for volunteers ubiquitous seven more than 12 more than 12 antigens	Ryu. <i>et al.</i> , 1995a ROS	Qigong trainees (M: 20-50 yrs)		Chun Do Sun Bupqigong QGI: Qigong exercise for 1-4 months QG2: Qigong exercise for 5-12 months QG3: Qigong exercise for 13-24 months QG4: Qigong exercise for 2-25 months (n r)	Healthy volunteers	Retrospective	CD4+/CD8+	QG1/CG: n.s. QG2/CG: $p < 0.05$ QG3/CG: $p < 0.05$ QG4/CG: $p < 0.05$	B (3b)
3.79 mm (p < 0.05)	Ryu, <i>et al.</i> 1995b ROS	Qigong trainces (20-45 yrs)	QG:16 CG:12	Chun Do Sun Bup qigong Qigong training for more than 12 months (n.r.)	Healthy volunteers	Retrospective	Skin tests for DCH with ubiquitous seven antigens	The maximal antigen response time: $QG/CG: 24$ hr/48 hr QG/CG: 24 hr/48 hr (p < 0.01) The response antigen number: QG/CG: 6 antigen 44 antigens $(p < 0.01)$ Induration diameter after 24hr: QG/CG: 5.14 mm/ 3.79 mm $(p < 0.05)$	B (3b)

Table 1. (Continued)

Randomized Controlled Trials

Manzaneque *et al.* (2004) conducted a RCT to assess immunological parameters following a qigong training program in Spain. Twenty-nine students aged 18–21 years were randomly allocated to an experimental group (n = 16) and a control group (n = 13). The experimental subjects received qigong training half an hour daily for one month, whereas the control subjects were asked to follow their usual life-styles. Blood samples from all participants were taken pre- and post-intervention. Results revealed statistically significant differences in the change of some parameters between the two groups, but with the experimental group showing lower numbers of total leukocytes (p = 0.03) and eosinophils (p = 0.04), lower number (p = 0.02) and percentage (p = 0.05) of monocytes, as well as lower level of complement 3 concentration (p = 0.004). No significant differences were observed in the levels of IgA, IgM, IgG, and complement 4 between the two groups.

In another RCT, Yu and Wang (2007) examined the effect of qigong exercises on T lymphocytes among a group of middle-aged and old healthy adults. One hundred of the participants were randomly allocated either to the qigong intervention group (n = 50) or the control group with routine activities (n = 50). Participants in the intervention group underwent qigong exercise 45 minutes a day, four times per week for six months. Compared with baseline values, the number of CD8⁺ decreased significantly (p < 0.05 for men and p < 0.01 for women) and the ratio of CD4⁺/CD8⁺ increased significantly (p < 0.05 for men and p < 0.01 for women) in the qigong group, but no significant changes were observed in the control group.

Non-Randomized Controlled Clinical Trials

Yan (1989) compared the effects of qigong and taiji exercises on parameters of humoral immunity over one month in a non-randomized controlled trial. Seventy college students were assigned either into a qigong group (n = 30) or a taiji group (n = 40). Frequency of exercise in both groups was not reported. Outcome measures included serum immune globulins (IgG, IgA, IgM), complement 3 (C3), and saliva lyssozyme. Compared with baseline values, only the levels of serum C3 and saliva lysozyme in the qigong group were significantly increased post-intervention (p < 0.05 and p < 0.01 respectively), while all outcome measures in the taiji group were significantly increased (p < 0.01 for all outcomes).

(Yao, 1989) conducted a study to observe the change of T lymphocytes in patients with aplastic anemia treated with qigong. Twenty patients were non-randomly divided either into an intervention group (n = 10) or a waiting-list control group (n = 10). Participants in the intervention group received qigong training one hour daily for one month. It was observed that the number of helper T cells (Th) and the ratio of Th/Ts (Ts: suppressor T cells) were significantly elevated post-intervention in the intervention group, compared to the control group (p < 0.05, p < 0.05 respectively).

1150

Retrospective Observational Studies

Lee *et al.* (2006) conducted a study to examine the effect of qigong training on the concentrations of peripheral T lymphocytes. Two groups of qigong practitioners having received qigong training for 1–12 months (n = 52) and for >12 months (n = 63) respectively were compared with a normal healthy control group (n = 22). Significant differences in the ratio of CD4⁺/CD8⁺ (p < 0.001) and the ratio of memory CD4⁺/ naïve CD4⁺ (p < 0.001) were observed between the two groups in favor of qigong trainees.

Ryu *et al.* (1995a) assessed the effect of qigong training on the proportions of peripheral T lymphocytes. In order to avoid any modulation of immune functions by steroid hormones during the menstrual cycle, only males (aged 20 to 50 years) were recruited into the study. Blood sampling was done between 6:00 p.m. and 9:00 p.m. to avoid diurnal change in the proportion and the number of T lymphocytes. Sixty-three participants were divided into four groups according to the duration of qigong training: Group I received qigong training for 1–4 months (n = 12), Group II for 5–12 months (n = 21), Group III for 13–24 months (n = 17), and Group IV for more than 25 months (n = 12). A group of healthy volunteers who had not received any qigong training was taken as a control group (n = 13). The results showed that the ratio of CD4⁺/CD8⁺ increased as much as 50% in the groups having received qigong training for more than five months (Groups II, III, and IV), compared to the control group (p < 0.05).

Ryu *et al.* (1995b) examined the difference in cellular immunity between a qigong trainee group (n = 16) and a normal healthy group (n = 12). Cellular immunity was measured with skin tests for delayed cutaneous hypersensitivity (DCH) for seven ubiquitous antigens including tetanus antigen, diphtheria antigen, streptococcus antigen, tuberculin antigen, candida antigen, trichophyton antigen, and proteus antigen. All of the 16 qigong trainees had received programmed qigong training for more than 12 months. The results indicated that the maximal antigen response time was faster and the response antigen number was higher in the qigong trainee group compared to controls (p < 0.01 and p < 0.01 respectively); the average induration diameter 24 hours after is larger in the qigong trainees than healthy subjects (p < 0.05).

Discussion

This systematic review aimed to examine the empirical evidence available from controlled clinical trials of the effect of qigong exercise on immunity and infections. Unfortunately, no controlled clinical trials of qigong exercise on infectious diseases could be identified. Instead, numerous studies in the field have documented the effects of qigong exercise on enumerative or functional parameters of immune system, but our review reveals that the number of rigorous clinical trials of qigong exercise on the improvement of immunity is still limited.

Overall, the available evidence has demonstrated favorable effects of qigong exercise on the increase of effective components of immune system, mainly T lymphocytes, and the improvement of immune function, but the findings are inconsistent. Specifically, one ROS (Ryu et al., 1995b) on antigen-induced virus-specific cell-mediated immunity and antibody response in human body's immune system suggested that gigong exercise could augment immune response to virus and influenza vaccine. One RCT (Yu and Wang, 2007), one CCT (Yao, 1989), and two ROSs (Ryu et al., 1995a; Lee et al., 2006) suggested that the number of lymphocytes, mainly $CD4^+$, and the ratio of $CD4^+/CD8^+$ were significantly higher in those who underwent gigong regularly compared to individuals in control groups. However, another RCT in Spain (Manzaneque et al., 2004) suggested that no significant changes were observed in any of the lymphocyte measures after one month of gigong practice, and that the experimental group had lower values than the control group in the total number of leukocytes, eosinophils, and monocytes. Two studies on immunoglobulins (Yan, 1989; Manzaneque et al., 2004) suggested that no significant changes were observed in any components of the serum immunoglobulins in the qigong group. With regard to complements in peripheral blood, one CCT (Yan, 1989) suggested a significant change of C3 in favor of qigong trainees, whereas a RCT (Manzaneque et al., 2004) demonstrated that the gigong group had a lower value of C3 than the control group with routine activities.

The risk of bias was assessed based on the description of randomization, allocation concealment, blinding, and withdrawals (Jadad et al., 1996; Jüni et al., 2001). A high risk of bias might exist in the included studies, which might have led to false-positive results. Of the seven included studies, only two were RCTs (Manzaneque et al., 2004; Yu and Wang, 2007); none of which had described the method of randomization and allocation concealment or made an attempt blinding assessors or investigators, which might have introduced selection bias and detection bias. Although details of drop-outs and withdrawals were described in the two RCTs (Manzaneque et al., 2004; Yu and Wang, 2007), none of these studies adopted intention-to-treat analysis, which might have led to the exclusion of some particular patients and introduced attrition biases. The included two CCTs (Yan, 1989; Yao, 1989) and three ROSs (Ryu et al., 1995a, 1995b; Lee et al., 2006) were subject to a high risk of selection bias. Moreover, the three ROSs did not adjust the values of baseline measures. Three studies (Yao, 1989; Ryu et al., 1995a; Manzaneque et al., 2004) had a small sample size with the number of participants less than 30 and therefore their results were prone to type II error. Furthermore, there was a great variability of the dosage and quality of qigong exercise across the included studies, which might have introduced a risk of performance bias.

Compared to the limited number of controlled trials in the field, around twenty uncontrolled observational studies have been published reporting a favorable effect of qigong exercise on the improvement of immunity (Yue *et al.*, 1989; Zhang *et al.*, 1989; Yu *et al.*, 1993; Higuchi *et al.*, 1997, 2000; Xu *et al.*, 1997; Jang, 1989; Wang, 1998; Yang, 1998; Bultorov *et al.*, 2001; Jones, 2001; Higuchi *et al.*, 2002; Lee *et al.*, 2006, 2003a; 2003b, 2004a, 2004b, 2009, 2005; Lee and Ryu, 2004; Kimura *et al.*, 2005; Wu and Yu, 2006; Bayat-Movahed *et al.*, 2008). Unfortunately, such data are highly susceptible to bias and hence provide little scientific evidence of the specific effects of qigong exercise on the improvement of immune function.

A combination of qigong with other forms of exercise may often be used in day-to-day life. We found one CCT with two publications (Yang *et al.*, 2007, 2008), which examined

whether five months of moderate qigong and taiji (tai chi) exercise could improve the immune response to influenza vaccine in older adults. Participants in the intervention group participated in three one-hour classes of qigong and taiji exercise per week for 20 weeks, whereas participants in the control group were asked to continue their routine activities. Each class consisted of equal parts of qigong and taiji form practice. All participants received the influenza vaccine during the first week of the intervention. The study suggested favorable effects of qigong and taiji exercise. Given that qigong and taiji are close relatives sharing theoretical roots, common operational components, and similar links to health and wellness within the paradigm of traditional Chinese medicine (Jahnke *et al.*, 2010), the results may provide alternative evidence, but should be further confirmed by RCTs.

Assuming that qigong exercise is potentially beneficial for immunity, the underlying mechanism may be of interest. One possible mechanism is that qigong as a form of low-to-moderate impact exercise may modulate immune response by promoting release of neuroendocrinological factors such as catecholamines (adrenaline, noradrenaline), growth hormone, β -endorphins, corticotrophin, and cortisol through the sympathetic–adrenal medullary (SAM) axis (Hoffman-Goetz and Pedersen, 1994). An additional possibility is that qigong as a modality of mind-body intervention may lead to improvement of psychological stress and thus induce alterations in immune function through the hypothalamic–pituitary–adrenal (HPA) axis (Goldrosen and Straus, 2004; Kohut *et al.*, 2005). It is also speculated that qigong as a form of exercise may increase the level of "immuno-surveillance", an ability of the host to respond to an infectious challenge (Bishop, 2006; Nieman, 2000). Qiqong may also increase the level of immunoglobulin-A, which is an important defense mechanism against pathogens trying to enter through the oral mucosa (Bishop, 2006). However further evidence is required to support the speculations.

It should be noted that most of the included studies are conducted among healthy adults and the clinical implications of the changes in these parameters in healthy people are unclear. It has been argued that changes in cell number may just reflect changes in the dynamics of lymphocyte migration and recirculation, or shifts in plasma volume, rather than absolute changes in total cell numbers (Burns, 2006). It would be inappropriate to conclude that qigong exercise related changes in any specific immune parameter signal a state of "immune enhancement" or resistance to infectious diseases (Miller and Cohen, 2001). Practically, it is difficult to identify or recruit patients with impaired immune function. For patients with infectious diseases, apart from those affected by human immunodeficiency virus (HIV), their immune responses may be defensively or conditionally strengthened. Therefore, future studies to examine the incidence or the severity of infectious diseases among individuals practicing qigong exercise may provide alternative evidence.

In line with other reviews on qigong (Chen and Yeung, 2002; Lee *et al.*, 2009), this review reveals some methodological flaws in the included studies, such as the varied dosage and quality of qigong exercise, heterogeneous comparison groups and outcome measures. Future studies of qigong exercise on immunity should adhere to accepted standards of RCT methodology. Following the principles of allocation concealment, assessor blinding, and intention-to-treat analysis are important for reducing bias.

1154 C.-W. WANG *et al.*

Several limitations may exist in this review. Similar to any systematic review, one of the limitations is the potential incompleteness of the evidence reviewed. We aimed to identify all controlled trials in the field. A large number of databases were queried with relevant terms in title, abstract, and keywords. We are confident that all relevant data have been located; however, a degree of uncertainty remains. Another limitation may be related to selective publishing and reporting in the literature, which is also a major cause of bias. In addition, we were unable to perform meta-analyses due to heterogeneity of study designs and outcome measures in the included studies. Despite these limitations, this review was the first to summarize the evidence of the effectiveness of qigong exercise on immunity and infections.

Conclusions

To summarize, rigorous studies of qigong exercise on immunity and infections are scarce. The available evidence appears to suggest that qigong exercise may improve both cellmediated immunity and antibody response in immune system, but it is still unclear whether or not the improvement of immune function is sufficient to provide definitive protection from infectious diseases. Further well-designed RCTs are required to test the effectiveness and efficacy of qigong exercise on the improvement of immunity and the prevention or treatment of infectious diseases.

Acknowledgments

This review was supported by the Hospital Authority of Hong Kong (HA105/48 PT5). The funding sources had no further role in the design; in collection, analysis and interpretation of data; in the writing of the report; and in the decision to submit the paper for publication.

References

- Bayat-Movahed, S., Y. Shayesteh, H. Mehrizi, S. Rezayi, K. Bamdad, B. Golestan and M. Mohamadi. Effects of qigong exercises on 3 different parameters of human saliva. *Chin. J. Integr. Med.* 14: 262–266, 2008.
- Bishop, N.C. Exercise and infection risk. In: M. Gleeson (ed.), *Immune Function in Sport and Exercise*. British Association of Sport and Exercise Sciences, Churchill Livingstone Elsevier, Edinburgh, 2006.
- Bultorov, I., A. Vlas and V. Vlas. Clinical benefits for chronic bronchitis by Qigong-therapy. *The First World Symposium on Self-Healing and Consciousness Power*, 2001.
- Burns, V.E. Psychological stress and immune function. In: M. Gleeson (ed.), *Immune Function in Sport and Exercise*. British Association of Sport and Exercise Sciences, Churchill Livingstone Elsevier, Edinburgh, 2006.
- Chen, K. and R. Yeung. Exploratory studies of qigong therapy for cancer in China. *Integr. Cancer Ther.* 1: 345–370, 2002.
- Goldrosen, M.H. and S.E. Straus. Complementary and alternative medicine: assessing the evidence for immunological benefits. *Nat. Rev. Immunol.* 4: 912–921, 2004.

- Higuchi, Y., Y. Kotani, H. Hibuchi and Y. Minegishi. Endocrine and immune changes during Guolin New Qigong. J. Int. Soc. Life Info. Sci. 15: 320–325, 1997.
- Higuchi, Y., Y. Kotani, H. Higuchi and Y. Minegishi. Immune changes during cosmic orbit meditation of qigong. J. Int. Soc. Life Info. Sci. 18: 352–354, 2000.
- Higuchi, Y., Y. Kotani, Y. Hayashi and S. Momose. Immune response during Zhang method qigong. *J. Int. Soc. Life Info. Sci.* 20: 449–452, 2002.
- Hoffman-Goetz, L. and B.K. Pedersen. Exercise and the immune system: a model of the stress response? *Immunol. Today* 15: 382–387, 1994.
- Jadad, A.R., R.A. Moore, D. Carroll, C. Jenkinson, D.J. Reynolds, D.J. Gavaghan and H.J. McQuay. Assessing the quality of reports of randomized clinical trials: is blinding necessary? *Control Clin. Trials* 17: 1–12, 1996.
- Jahnke, R., L. Larkey, C. Rogers, J. Etnier and F. Lin. A comprehensive review of health benefits of qigong and TaiChi. Am. J. Health Promot. 24: e1–e25, 2010.
- Jang, J. A brief view of Kong Jin qigong's influence on immunological function. In: *The 2nd International Conference on Qigong*, 1989.
- Jones, B.M. Changes in cytokine production in healthy subjects practicing Guolin Qigong: a pilot study. *BMC Complement. Altern. Med.* 1: 8, 2001.
- Jüni, P., D.G. Altman and M. Egger. Systematic reviews in health care: assessing the quality of controlled clinical trials. *BMJ* 323: 42–46, 2001.
- Kimura, H., F. Nagao, Y. Tanaka, S. Sakai, S.T. Ohnishi and K. Okumura. Beneficial effects of the Nishino breathing method on immune activity and stress level. J. Altern. Complement. Med. 11: 285–291, 2005.
- Kohut, M.L., W. Lee, A. Martin, B. Arnston, D.W. Russell, P. Ekkekakis, K.J. Yoon, A. Bishop and J.E. Cunnick. The exercise-induced enhancement of influenza immunity is mediated in part by improvements in psychosocial factors in older adults. *Brain Behav. Immun.* 19: 357–366, 2005.
- Lee, M.S. and H. Ryu. Qi-training enhances neutrophil function by increasing growth hormone levels in elderly men. *Int. J. Neurosci.* 114: 1313–1322, 2004.
- Lee, M.S., C.W. Kang and H. Ryu. Effect of qi training on neutrophil function in young and elderly males. J. Altern. Complement. Med. 10: 681–683, 2004.
- Lee, M.S., C.W. Kang, H. Ryu and S.R. Moon. Endocrine and immune effects of qi-training. *Int. J. Neurosci.* 114: 529–537, 2004.
- Lee, M.S., M.H. Pittler and E. Ernst. Internal qigong for pain conditions: a systematic review. *J. Pain* 10: 1121–1127, 2009.
- Lee, M.S., M.K. Kim and H. Ryu. Qi-training (qigong) enhanced immune functions: what is the underlying mechanism? *Int. J. Neurosci.* 115: 1099–1104, 2005.
- Lee, M.S., M.K. Kim, H. Ryu, B.C. Shin and Y.S. Kim. Qi-training and immunological parameters: a cross-sectional study. *Int. J. Neurosci.* 116: 921–926, 2006.
- Lee, M.S., S.M. Jeong, Y.K. Kim, K.W. Park, M.S. Lee, H. Ryu and S.R. Moon. Qi-training enhances respiratory burst function and adhesive capacity of neutrophils in young adults: a preliminary study. Am. J. Chin. Med. 31: 141–148, 2003a.
- Lee, M.S., S.S. Hong, H.J. Lim and H.J. Kim. Retrospective survey on therapeutic efficacy of qigong in Korea. Am. J. Chin. Med. 31: 809–815, 2003b.
- Manzaneque, J.M., F.M. Vera, E.F. Maldonado, G. Carranque, V.M. Cubero, M. Morell and M.J. Blanca. Assessment of immunological parameters following a qigong training program. *Med. Sci. Monit.* 10: CR264–270, 2004.
- Miller, G.E. and S. Cohen. Psychological interventions and the immune system: a meta-analytic review and critique. *Health Psychol.* 20: 47–63, 2001.
- Ng, B.H. and H.W. Tsang. Psychophysiological outcomes of health qigong for chronic conditions: a systematic review. *Psychophysiology* 46: 257–269, 2009.

- Nieman, D.C. Is infection risk linked to exercise workload? *Med. Sci. Sports Exerc.* 32(suppl): S406–S411, 2000.
- Oxford Centre for Evidence-based Medicine. Levels of Evidence (March 2009). Available at: http:// www.cebm.net/index.aspx?o=1025. Accessed 10 November 2010.
- Ryu, H., C.D. Jun, B.S. Lee, B.M. Choi, H.M. Kim and H.T. Chung. Effect of qigong training on proportions of T lymphocyte subsets in human peripheral blood. Am. J. Chin. Med. 23: 27–36, 1995a.
- Ryu, H., H.Y. Mo, G.D. Mo, B.M. Choi, C.D. Jun, C.M. Seo, H.M. Kim and H.T. Chung. Delayed cutaneous hypersensitivity reactions in qigong (chun do sun bup) trainees by multitest cell mediated immunity. *Am. J. Chin. Med.* 23: 139–144, 1995b.
- Sim, Y.J., S. Yu, K.J. Yoon, C.M. Loiacono and M.L. Kohut. Chronic exercise reduces illness severity, decreases viral load, and results in greater anti-inflammatory effects than acute exercise during influenza infection. J. Infect. Dis. 200: 1434–1442, 2009.
- Vincent, A., J. Hill, K.M. Kruk, S.S. Cha and B.A. Bauer. External qigong for chronic pain. Am. J. Chin. Med. 38: 695–703, 2010.
- Wang, Z.Y. The impact of qigong exercise on respiratory and immune function of human being. *Chinese Qigong* 6: 8, 1998.
- Wright, P.A., K.E. Innes, J. Alton, V.E. Bovbjerg and J.E. Owens. A pilot study of qigong practice and upper respiratory illness in elite swimmers. Am. J. Chin. Med. 39: 461–475, 2011.
- Wu, J.M. and D.H. Yu. Effects of "Wuqinxi" exercise on the subgroups of T-cells in peripheral blood of middle-aged and old people. J. Beijing Sport Univ. 29: 1074–1075, 1078, 2006.
- Xu, Z.L., L. Xu, S.M. Tao, L. Chen, J.X. Xie and M. Tang. Effects of qigong exercise on the subgroups of T-cells in peripheral blood of the patients with chronic diseases. J. Conval. Rehabil. 12: 53–54, 1997.
- Yan, H. Research on the relationship between immunity of human body and physical training, taijiquan and qigong. In: *The 2nd International Conference on Qigong*, 1989.
- Yang, F. Analysis of 270 cases of hepatitis B with hepatitis B powder in combination with qigong. In: *The 4th World/Conference for Academic Exchange of Medical Qigong*, p. 142, 1998.
- Yang, Y., J. Verkuilen, K.S. Rosengren, R.A. Mariani, M. Reed, S.A. Grubisich and J.A. Woods. Effects of a taiji and qigong intervention on the antibody response to influenza vaccine in older adults. *Am. J. Chin. Med.* 35: 597–607, 2007.
- Yang, Y., J. Verkuilen, K.S. Rosengren, R.A. Mariani, M. Reed, S.A. Grubisich, J.A. Woods and B. Schlagal. Effects of a traditional taiji/qigong curriculum on older adults' immune response to influenza vaccine. *Med. Sport. Sci.* 52: 64–76, 2008.
- Yao, B.S. A preliminary study on the changes of T-cell subsets in patients with aplastic anemia treated with qigong. *Zhong Xi Yi Jie He Za Zhi* 9: 341–342, 324, 1989.
- Yu, D.H. and J.H. Wang. The impact of 6 months "Wuqinxi" qigong practice on T lymphocyte subsets in human peripheral blood. *Chin. J. Sports Med.* 26: 206–207, 2007.
- Yu, Y. R. Zhang, X. Huang, Y. Guo and W. Cao. Effect of self-controlling qigong therapy on the immune function of cancer patients. In: *The 2nd World Conference for Academic Exchange of Medical Qigong*, 1993.
- Yue, Q., S. Zhao, W. Ma, G. Wu, Z. Li, S. Hong, C. Tao and D. Su. Study of effect on normal human peripheral blood lymphocyte by Shaolin Nia Jin Ye Zhi Zhan Qigong. In: *The 2nd International Conference on Qigong*, 1989.
- Zhang, Y., S. Luo and Y. Wu. Preliminary observation on influence of spontaneous Wuqinxi qigong on human immune function. In: *The 2nd International Conference on Qigong*, 1989.

Copyright of American Journal of Chinese Medicine is the property of World Scientific Publishing Company and its content may not be copied or emailed to multiple sites or posted to a listserv without the copyright holder's express written permission. However, users may print, download, or email articles for individual use.