Dong and Sun, J Gerontol Geriatr Res 2016, 5:1
DOI: 10.4172/2167-7182.1000275

Journal of Gerontology & Geriatric Research

Research Article Open Access

Inflammatory Markers and Disability in Chinese Older Adults

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Abstract

Background: There is growing evidence that higher levels of inflammatory markers are associated with physical decline in older persons, possibly through the catabolic effects of inflammatory markers on muscle. The aim of this study was to investigate the association between serum levels of inflammatory markers and disability and physical performance in older persons.

Methods: We conducted analyses of 70 adults aged 61 and older, examined serum levels of IL-6, IL-10, TNF-α , MIP-1α , MIP-1β , MCP-1 , and MCP-3 from 59 patients with disability and 11 normal controls. We further categorized the 59 patients with disability into either mild (n=34), moderate (n=15) or severe disability (n=10) using the Disability Level Assessment of the Elderly. The levels of the inflammatory markers were compared amongst these groups as well as with the control. We also evaluated the relationship of several inflammatory markers and physical performance in elderly people with disability. The levels of inflammatory markers were measured by the Luminex Technology.

Results: The levels of IL-6 , IL-10 , TNF-α , MIP-1α , MIP-1β , and MCP-3 in patients with disability were significantly higher than those in the control group; higher levels of the IL-6 and MCP-3 were associated with disability($P<0.01$ and $P<0.05$, respectively).The levels of IL-6, IL-10, MCP-3, MIP-1β, and TNF-α were highest in the severe disability group. Patients in the moderate disability group had higher levels of these markers compared to the mild disability group. The level of IL-6, MCP-1, MCP-3, MIP-1β, and TNF-α were positively correlated with the level of disability ($p<0.05$).

The level of IL-6, IL-10, MCP-1, MCP-3, MIP-1β, TNF-α were significantly correlated with physical performance ($r=-0.444$, $r=-0.444$, $r=-0.394$, $r=0.413$, $r=-0.417$, $r=-0.417$, respectively).

Conclusions: Inflammation, measured as elevated levels of IL-6, IL-10, TNF-α, MIP-1α, MIP-1β, and MCP-3, is significantly associated with disability in older persons and the levels of IL-6, MCP-3 are positively correlated with an increasing level ofof disability. Also, high levels of IL-10, MIP-1β, MCP-1, MCP-3, and TNF-α are associated with poor physical performance. The assessment of inflammatory markers may represent a useful screening test may be used as potential predictors of poor physical performance and disability.

Keywords: Disability; Physical performance; Inflammation; Interleukin-6; Interleukin-10; Tumor necrosis factor-alpha; Macrophage inflammatory protein-1 alpha; Macrophage inflammatory protein-1 beta; Monocyte chemoattractant protein-1; Monocyte chemoattractant protein-3

Introduction

Increasing evidence indicate that aging is associated with a mild pro-inflammatory state that directly influences pathophysiologic processes and contributes to disability [1]. Disability is defined as difficulty or dependency in carrying out activities essential to independent living. These activities include essential roles, tasks needed for self-care, living independently in a home, and desired activities important to one's quality of life [2]. As the population ages, the functional capacity in performing basic activities of daily living (ADL) and instrumental activities of daily living (IADL) are becoming increasingly limited. For the diagnosis of disability as a medical condition, self-reported questionnaires or performance-based tests are used [3]. Disability incorporates the levels of ADL as well as IADL. ADLs are basic self-care activities such as washing one's face and hands, washing and drying oneself, dressing and undressing, eating and drinking, getting into and out of bed, moving about indoors, and going to the toilet. IADLs include shopping, preparing meals, travelling independently, doing light household tasks, and managing money. A recent American study reported that the probability of a non-disabled 65-year-old male surviving to age 80 while also being non-disabled prior to death was 26%. For a 65-year-old woman, the probability of surviving to age 85 and being non-disabled prior to death was 18% [4]. The number of individuals aged 80 years or older is growing worldwide and this growth has been accompanied by a concurrent increase in physical disability. Identifying useful bio-markers to assess physical performance could be of great value in the elderly.

According to the figure of "The Sixth National Census of Chinese Population," our country has 5.22 million elder people, whose overall disability rate is 2.95%, with 2.52% of males and 3.35% of females. The figure predicts that the total number of disabled elderly individuals is 5 220 883. The greatest percentage is in the Si Chuan Province (433 474). Moreover, it is worth noting that China's population of people aged 60 and above is 177 648 705, 13.26% of the total population. The number of individuals aged 65 years or older is 118 831 709, accounting for 8.87% of the total population. The population in China has been trending towards an older population. The number of individuals 80 years or older comprises 11.82% of the total number of elderly population [5].

Decline in physical functioning leading to disability creates a considerable burden for many older people and their families. It is imperative to identify risk factors for disability to prevent or reduce the occurrence of disability. There is great variability in functional decline

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Received November 06, 2015; **Accepted** January 23, 2016; **Published** January 27, 2016

Citation: Dong B, Sun B (2016) Inflammatory Markers and Disability in Chinese Older Adults. J Gerontol Geriatr Res 5: 275. doi:10.4172/2167-7182.1000275

in old age and the process may originate from comorbid diseases, physiologic changes with aging, genetic predisposition, life style behaviors, and social and economic factors. However, the mechanism of physical disability is not fully understood. Current research suggests that aging is associated with a mild pro-inflammatory state that may directly contribute to disability. Aging is accompanied by increased circulating levels of pro-inflammatory cytokines and the presence of other factors, including increased fat mass, sub-clinical infection, and chronic diseases. They may contribute to the low-grade inflammation status. If the inflammatory state could be precisely measured, it may have important clinical significance [6,7].

Aging is characterized by a chronic low-grade systemic inflammatory status that is involved in the pathogenesis of several age-related disorders and enhances mortality risk. Inflammation is known to be important in aging and is sometimes suggested as a principal aging mechanism. We often refer to this phenomenon as "inflamm-aging", and this new term indicates that aging is accompanied by an age-dependent, up-regulation of the inflammatory response. Numerous studies have shown that the levels of cytokines increase with age even in otherwise healthy individuals in the absence of acute infection. This is in contrast to younger individuals where the levels of cytokines are tightly regulated at very low levels. Cytokine levels seen in older adults range from low levels to modest elevations, but are much lower than the levels seen with acute infection.

The exact mechanisms for the increase of inflammatory markers with age and disability have not been fully understood; however, research suggests involvement of low-grade and sub-clinical inflammation. Inflammation may either be a common underlying cause or it may represent a final common pathway.

In the process of aging, the role of a low-grade inflammation state is as follows

1. Inflammatory cytokines have a direct effect on muscle catabolism. This provides additional rationale for inflammation as a common mechanism for functional decline and disability [8]; for example, in humans, there is a positive correlation between whole-body protein breakdown and TNF-α production [9]. IL-6 causes loss of muscle fibers, muscle wasting, and decreases the rate of protein synthesis, thus reducing the total skeletal muscle amino acid concentration and leading to sarcopenia and disability [10]. With increasing age, muscle strength may eventually decline to a level where weakness starts to restrict the ability to carry out everyday tasks. Muscle strength is significantly associated with functionality. One study showed that middle-aged men with higher hand-grip strength were protected from old age disability regardless of the diseases that may have developed over a 25-year follow-up [11]. Higher levels of serum pro-inflammatory markers have been found to have a strong correlation with lower muscle strength and muscle mass [12].

2. A number of other chronic diseases are associated with chronic low-grade inflammation in older populations. In vitro evidence shows that chronic inflammation disrupts bone homeostasis, increasing the possibility of the development of osteoporosis [13]. Cauley et al. reported that high levels of serum inflammatory markers predict a higher incidence of fractures during a 5.8-year follow-up period in the Health ABC cohort. This association was found to be particularly strong in subjects with higher levels of two or three markers [14]. Fractures will bring inconvenience to the elderly and will exacerbate the inflammatory state.

3. Inflammatory bio-markers may also have an effect on physical function by promoting age-related changes in body composition with, primarily, more central abdominal or visceral fat deposits and muscle loss. A higher relative amount of adipose tissue acts as an active endocrine organ that is capable of secreting a number of cytokines and adipokines, including tumor necrosis (TNF-α) and interleukin 6(IL-6) [15]. The increased amount of intra-abdominal fat with aging, especially in women, is connected with low-grade inflammation and insulin resistance in obese subjects [10,16]. TNF-α as well as IL-6 also affect the coagulation system and the metabolism of lipids, causing a pro-coagulant state and dyslipidemia [17]. As mentioned above, increasing fat mass contributes to increasing production of inflammatory cytokines, which in turn contributes to muscle catabolism and loss of muscle mass [18-20].

Inflammation is a necessary response of the immune system to different stimuli such as infection and injury, resulting in the elevated production of cyokines. However, when inflammation is chronic, it appears to have detrimental effects. Different pro-inflammatory factors play different roles in the immune system

1. Tumor necrosis factor-alpha (TNF-α) is a first-line factor in promoting and developing the inflammation pathway.

2. IL-10 has an important regulatory effect on immunological and inflammatory responses because of its capacity to inhibit the production of pro-inflammatory cytokines by monocytes.

3. IL-6 is one cytokine that has been shown to be multi-functional in nature but whose main role appears to be the induction of the acute inflammatory response and B-lymphocyte proliferation and differentiation. In the absence of an inflammatory condition, expression of IL-6 appears to be tightly regulated, with very little IL-6 detectable in plasma. However, a number of studies have now demonstrated that with increasing age, IL-6 increases to measurable levels even in the absence of significant disease. This has led to the suggestion that IL-6 is "a cytokine for gerontologists". Previous studies have shown that high IL-6 levels are significantly associated with poor physical performance, muscle strength, and disability in older individuals. Several studies have shown cross-sectional and prospective associations of high IL-6 levels with functional disability [21].

Monocyte chemoattractant protein-1(MCP-1) is an important inflammatory factor secreted by macrophages, endothelial cells, mononuclear cells, myocardial cells and smooth muscle cells

1. It can induce telomerase via macrophage colony stimulating factors causing mononuclear cells to produce osteoclasts, thus promoting further bone absorption and inflammatory response.

2. It is abundantly expressed in atherosclerotic plaques and macrophages of atherosclerotic tissue. Lipid oxidation results in the formation of foam cells, a key component in the formation of atherosclerosis, coronary heart disease, myocardial autoimmune injury and inflammation. Foam cells have a positive association with the degree of myocardial inflammation.

3. MCP-1 influences the function of adipocytes. It is a recruitment factor for macrophages and may be a crucial link amongst chemokines between adipose tissue inflammation and insulin resistance. Inflammatory proteins, such as TNF, IL-6 and monocyte chemoattractant protein 1 (MCP-1) are secreted from adipose tissue and influence the metabolism, insulin signaling, and endocrine activities of fat cells. It has recently been shown that adipocytes secret a

factor (s) that up-regulates adhesion molecules on endothelial cells and increases the chemotaxis of monocytes W [22].

4. MCP-1 increases the number of mononuclear cells, basophils, and T cells for inflammation. It also induces mononuclear cells and endothelial cells to express adhesion molecules to release cell factors such as interleukin (IL-6).

5. Macrophage Inflammatory Protein (MIP)-1 (α and β) affect neutrophil function and causes local inflammation and fever. It is mainly divided into two categories:

6. MIP-1α is a member of the C-C family of Chemokine's. Under the action of different stimulation factors, it can be converted into a variety of cells, for example: mononuclear macrophages, endothelial cells, fibroblasts, neutrophils, etc. It can induce chemo taxis and activate mononuclear macrophages and T lymphocytes to enhance the surface expression of integrin, thus strengthening adhesion to endothelial cells. MIP-1α can also induce natural killer cells (NK cells) involved in the inflammatory response and produce TNF-α and IL-6 [23].

7. MIP-1β can be characterized by the ability to chemoattract human monocytes to sites of tissue injury and infection. It plays an important role in the pathogenesis of various disease states and therefore the inhibition of MCP-1 is discussed as a potential therapeutic target [24].

If inflammation is indeed part of the pathway to physical decline and disability, it will be interesting to expand research to these inflammatory markers in orders to better understand mechanisms that underlie age-related performance.

The aim of our study was to evaluate the potential association between inflammation and disability and physical performance. In our study, we explored the relationship between levels of several inflammatory markers (such as IL-6, IL-10, TNF-α, MIP-1α, MIP-1β, MCP-1, MCP-2) with three different levels of disability (mild group, moderate group, severe group) and physical performance (assessed through measures of lower extremity performance) [25].

Methods

A total of 59 cases of disability were selected from Oct 2010 to Aug 2012, which was conducted in 2 cities (Chengdu and Suining) in Sichuan province in China. These cases included 14 males and 45 females between the ages of 61-91 with an average age of 75.64 ± 8.64. Exclusion criteria included individuals younger than 60 years and those who were bed bound due to illness. There were 34 cases of mild disability, 15 cases of moderate disability, and 10 cases of severe disability. An additional 11 healthy individuals were selected for the control group, including 8 males and 3 females between the ages of 60-76 with an average age of 66.18 +/- 4.35. There was no significant difference in gender and age between the experimental group and the control group.

Physical Performance Tests

An assessment of disability level is listed in Table 1. To assign a disability level score, 30 questions were graded on a seven point scale, with seven indicating normal function and 1 indicating full dependence on others. The sum of the scores indicate the level of disability with 210 being healthy, 179-209 indicating mild disability, 140-178 indicating moderate disability, and 81-139 indicating severe disability.

Performance of the lower extremities was assessed using three tests of walking speed, ability to stand from a chair, and maintaining balance in progressively more challenging positions. Walking speed was defined as the best performance (time in seconds) out of five 4-meter walks at a usual pace along a corridor. For the chair-stand test, the participant was asked to ris6chair, maintaining balance in progressively more challenging positions, and having a walking speed of more than 30s. A summary of physical performance score ranging from 0 to 3 was calculated by adding these three re-scaled scores.

ITEM	7 point	6 point	5 point	4 point	3 point	2 point	1 point[a]
Eating and drinking							
Washing face and hands							
Going to the toilet							
Washing and drying oneself							
Dressing and undressing outerwear							
Dressing and undressing trousers,							
Move bowels							
The frequency of fecal incontinence							
Pee							
The frequency of urinary incontinence							
Moving beside the chair and bed							
Going into and out of the toilet							
Going into and out of the bathroom							
Moving about indoors with or without wheelchair							
Up and down the stairs							
Using transportation							
Shopping							
Doing housework							
Managing money							
Prescribed medication							
The capability to solve problems							
Memory							
Directional force							
Attention							
Emotional state							
Social skills							
Understanding ability							
Presentation skills							
Reasonable use of leisure time							
Safely to be alone in the community, hospitals, family							

NOTE: [a]The rating is divided into seven levels. 7 point–Fully care; 6 point–Need auxiliary equipment; 5 point–Need tips or help from others; 4 point–Need little help (25%) from others; 3 point–Need some help (50%) from others; 2 point–Need more help (75%) from others; 1 point–Fully rely on others.

Table 1: The assessment of disability level of the elderly.

Inflammation markers

The venipuncture was done in the morning after a 12-hour fast and

after the patient had been sedentary in a sitting or supine position for at least 15 minutes. The sampled blood was transferred as to make sure it flowed down the side of the collecting tube as never directly ejected into the center of the tube in order to minimize the mechanical disruption or turbulence that could result in hemolysis. The serum samples were then frozen and stored at -80°C until the Luminex Technology tests were performed. The serum samples did not undergo any freezing and defrosting. IL-6, IL-10, TNF-α, MIP-1α, MIP-1β, MCP-1, and MCP-3 were quantified with immuno-assay kits (Human Cytokine/Chemokine Panel I; Chengdu Bio-atom Biotechnology Co, Ltd.) The sensitivity of detectable concentration of IL-6 was 0.4 pg/ml, 0.1pg/ml for IL-10, 0.6 pg/ml for MCP-1, 1.1 pg/ml for MIP-1α, 4.7 pg/ml for MIP-1β, and 0.4 pg/ml for TNF-α.

Mean ± SE or % (N=70)		
Control group Experimental group		
	N=11	N=59
Sociodemographic characteristics		
Age(y)	66.18 ± 1.31	75.64 ± 1.12
Gender(female)	27.2	76.2
Mini-Mental State Examination	26.36 ± 1.13	18.22 ± 1.18
Education(y) 8 ± 1.3	5.5 ± 0.8	
Smoking		
Never	45.5	86.4
Former	18.20	1.70
Current 36.40	11.90	
BMI(kg/m^2)		
<20	0	18.60
20-24.9	81.80	59.30
25-30	18.20	13.60
>30	0	3.40
Missing	0	5.10
Comorbid condition		
Hypertension	9.10	61.00
Angina/myocardial infraction	0	10.20
Stroke	0	15.30
Cancer	0	3.40
Diabetes	0	11.90
COPD	0	22.00
Congestive heart failure	0	11.90
Biological markers		
Creatinine(mg/dl)	94.35 ± 4.19	92.69 ± 2.97
Total cholesterol(mg/dl)	5.33 ± 0.47	5.46 ± 0.16
HDL cholesterol(mg/dl)	1.47 ± 0.13	1.51 ± 0.06
Inflammatory markers		
IL-6	0.54 ± 0.05	15.19 ± 4.35
IL-10	1.01 ± 0.20	1.98 ± 0.38
MCP-1	478.71 ± 142.52	338.83 ± 43.45
MCP-3	4.55 ± 2.89	20.98 ± 5.54
MIP-1α	51.07 ± 18.67	231.41 ± 90.11
MIP-1β	47.42 ± 11.49	103.66 ± 27.70
TNF-α	19.65 ± 7.54	33.50 ± 7.01
Physical performance tests		
Summary performance score(0-3)	2.82 ± 0.18	1.78 ± 0.14
Walking test	0.91 ± 0.09	0.46 ± 0.07
Chair-stand test	0.91 ± 0.09	0.81 ± 0.05
Balance test	1.00 ± 0.00	0.51 ± 0.07
NOTE: SE: standard error; BMI: body mass index; COPD: chronic obstructive pulmonary disease; HDL: high-density lipoprotein; IL: interleukin; TNF-α: tumor necrosis factor –alpha.		

Table 2: Main Characteristics of the Sample Population

Inflammatory Markers	Experimental group	Controlgroup value	t value	p
	(pg/ml)	(pg/ml)		
IL-6	15.19 ± 33.43	0.54 ± 0.18 0.0013	3.366	0.0013
IL-10	1.97 ± 2.89	1.01 ± 0.65 0.277	-1.095	0.27
MCP-1	338.83 ± 333.76	478.71 ± 472.67	0.939	0.366
MCP-3	20.98 ± 42.56	4.54 ± 9.25	-2.650	0.010
MIP-1α	231.41 ± 692.13	51.07 ± 61.92	-0.858	0.394
MIP-1β	103.66 ± 212.80	47.42 ± 38.12	-0.869	0.388
TNF-α	33.50 ± 53.85	19.65 ± 24.99	-1.346	0.188

Table 3: The levels of inflammatory makers between experimental group and control group.

Inflammation Markers Group (pg/ml)	Mild Disability Group	Moderate Disability	Severe Disability Group
IL-6	1.63 ± 3.01	6.45 ± 6.12[a]	74.44 ± 48.87 [bc]
IL-10	0.97 ± 0.45	2.80 ± 2.73	4.18 ± 5.60
MCP-1	179.38 ± 304.40	603.65 ± 239.41[b]	483.76 ± 229.57[b]
MCP-3	30.19 ± 49.87	3.57 ± 3.19[a]	15.82 ± 41.03
MIP-1α	52.87 ± 121.76	475.25 ± 1262.40	472.67 ± 519.21
MIP-1β	36.26 ± 42.30	187.62 ± 377.23	206.90 ± 152.22[a]
TNF-α	10.12 ± 25.63	46.63 ± 56.05[a]	83.55 ± 80.17 [b]
Notes: [a]control with mild group p value<0.05, [b]control with mild group p value<0.01, [c]control with moderate group p value<0.01.			

Table 4: The level of inflammatory markers between mild disability group, moderate disability group, and severe disability group.

Statistical analyses

All data were analyzed by SPSS 21. The differences in IL-6, IL-10, MIP-1α, MIP-1β, MCP-1, MCP-3 and TNF-α between experimental group and control group were analyzed by t test; the differences between the mild group, the moderate group, and the severe group were analyzed by analysis of variance. Spearman's correlation tests were used to evaluate correlations of inflammatory markers with physical performance.

Results

The main characteristics of the participants considered in the present study are shown in Table 2.

The levels of inflammatory makers (IL-6, IL-10, MCP-1, MCP-3, MIP-1α, MIP-1β, TNF-α) between experimental group and control group are shown in Table 3. The mean age of the sample population was 74.16 ± 8.80 years and 68.8% were female.

Results from Table 3 demonstrate that IL-6 is highly associated with disability in the elderly . The high levels of IL-6 plays an important role in the prediction of disability. In order to further understand the function of pro-inflammatory chemokines, we divided disability into the three groups according to Table 1 with the results listed in the Table 4.

Table 4 shows that high levels of IL-6 has a significant association with disability; the level of IL-6 in the severe disability group is the highest of three groups and the level of IL-6 in the moderate disability group higher than the mild disability group. At the same time, MCP-1 and TNF-α also demonstrate an association with different levels of disability. For all inflammatory markers in the elderly, the moderate and severe disability groups have higher levels than the mild disability group.

Spearman's correlations between inflammation markers and

physical performance are shown in Table 5. IL-6, IL-10, MCP-1, MCP-3, MIP-1β, and TNF-α were highly corrected with the summary physical performance score(r=-0.444, r=-0.444, r=-0.394, r=0.413, r=-0.417, and r=-0.417 respectively) and with each single test.

Discussion

The present study evaluated the relationship between inflammation and the different levels of disability and physical performance. Several previous studies have suggested an effect of inflammation on disability [26-28]. Our findings show that high IL-6, TNF-α, MCP-1, MCP-3 levels are significantly and independently associated with poorer physical performance in the elderly. The pro-inflammatory cytokine IL-6 is the most robustly associated marker with functional status in the elderly, which is consistent with many studies identifying IL-6 as the gerontologist's cytokine [29].

There is less information about how MCP-1 (α,β), MIP-1, and MIP-3 influences disability and physical performance in the elderly. There is a study that introduces the idea that MCP-1 may influence the function of adipocytes and activate chemokine's thus representing a crucial link between adipose tissue inflammation and insulin resistance. Obesity is associated with an increased expression of MCP-1 in adipose tissue, thereby increasing metabolism and leading to lower muscle mass and strength [30]. MIP-1, MIP-3, MCP-1α, and MCP-1β all participate in the immune-mediated inflammation process and play an important role in the migration of leukocytes under both normal ailing conditions. They can induce directed migration of lymphocytes and monocytes. They may also play a key role in the development of many autoimmune diseases [31-34].

The results of our study indicate that IL-10, MCP-1, MCP-3, MIP-1 (α,β) and TNF-α do not have an association with different levels of disability. However, IL-10, MCP-1, MCP-3, MIP-1β, and TNF-α is highly associated with poor physical performance.IL-10 has an important function of inhibiting the production of pro-inflammatory cytokines by monocytes. TNF-α is a first-line factor in promoting and developing the inflammation pathway. Their unique functions can explain their role at the beginning of inflammation. But when the infection persists, inflammatory factors play a role of chemotaxis recruiting T lymphocytes, NK cells, and monocytes to the inflammatory peripheral region thus leading to the decrease of inflammatory factors in peripheral blood.

Our study has several limitations. The cross-sectional design does not allow us to evaluate the cause-effect association between inflammation and physical decline or disability. Further investigation aimed at assessing the predictive value of inflammatory maker level on physical decline and disability is needed. Another limitation is the small sample size. This will increase the risk of statistically false negative results (type II errors), whereas false positive results (type I errors) are less likely. Previous research from aging population studies reported that many pro-inflammation cytokines were associated with disability. However, our study is the first to show the relationship between the pro-inflammatory cytokines and the different levels of disability. It shows that expression of pro-inflammatory cytokines in the disabled elderly patients are higher than those of healthy elderly patients; the mildly disabled elderly group had slightly higher levels of pro-inflammatory cytokines than the healthy elderly group and the moderate to sever groups had higher levels than the mild group. However, despite these limitations we provide adequate data that demonstrates the strong association between inflammatory immune responses can also promote chronic diseases of aging. High levels of inflammation have been strongly implicated in the pathophysiology of arterial degeneration and immunosenescence, as well as in a wide variety of chronic diseases including diabetes, metabolic syndrome, congestive heart failure, and Alzheimer's disease. These links between inflammation and major health problems support the hypothesis that inflammation is a common mechanism of many degenerative conditions linked to aging [35-39]. Accordingly, chronic low-grade inflammatory activity has an important role in the process of chronic disease, disability and aging. This association between inflammatory cytokines and disability suggest that biological markers may be useful in identifying elderly patients most at risk for disability. Ultimately, this may provide utility by guiding specific therapeutic and preventative practices targeted to these patients.

Summary performance	scoretest	Walking test	Chair standing	Standing balance test
IL-6	-0.444[b]	-0.333[b]	-0.285[a]	-0.382[b]
IL-10	-0.444[b]	-0.297[a]	-0.325[a]	-0.386[b]
MCP-1	-0.394[b]	-0.303[a]	-0.327[a]	-0.230
MCP-3	0.413[b]	0.227	0.314[a] 0.360[b]	
MIP-1α	-0.256	-0.276[a]	-0.086	-0.175
MIP-1β	-0.417[b]	-0.290[a]	-0.279[a]	-0.374[b]
TNF-α	-0.417[b]	-0.347[b]	-0.299[a]	-0.317[a]
NOTES: [a] P value <0.05 [b] P value <0.01				

Table 5: Spearman's correlations between inflammation markers and physical performance measures.

This study was supported by The ministry of health for public welfare fund (NO.201302008) and The Center of Coordination and Innovation for Aging Care and Health Promotion of Sichuan. The sponsor has no role in the design, methods, data collection, analysis and preparation of the paper. The authors declare no conflicts of interest.

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