

Retrospective Cohort Study

Rationale and design of the cardiorespiratory fitness and hospitalization events in armed forces study in Eastern Taiwan

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Abstract

AIM

To investigate the association between cardiorespiratory fitness and hospitalization events in a cohort of large voluntary arm forces in Taiwan.

METHODS

The cardiorespiratory fitness and hospitalization events in armed forces (CHIEF) is a retrospective cohort consisting of more than 4000 professional military members aged 18-50 years in Eastern Taiwan. All participants received

history taking, physical examination, chest radiography, 12-lead electrocardiography, blood tests for cell counts and fasting glucose, lipid profiles, uric acid, renal function and liver function in the Hualien Armed Forces General Hospital during 2014. In addition, participants were required to undergo two indoor resistant exercise tests including 2-min push-up and 2-min sit-up, both scored by infrared sensing, and one outdoor endurance 3000-m none weight-bearing running test, the main indicator of cardiorespiratory fitness in the Military Physical Training and Testing Center in Eastern Taiwan in 2014.

RESULTS

Hospitalization events for cardiovascular disease, acute kidney injury, rhabdomyolysis, severe infectious disease, acute psychiatric illness, diabetes, orthopedic surgery and mortality will be identified in the National Insurance Research Database for 10 years.

CONCLUSION

CHIEF will be among the largest Eastern Asian armed forces cohort, in which physical status was strictly evaluated to follow up the hospitalization events for severe illness.

Key words: Cardiorespiratory fitness; Hospitalization; Voluntary armed forces

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Core tip: Whether rigorous physical trainings including endurance and resistance exercises for professional young adults in armed forces associated with well or poor cardiovascular outcomes in their middle ages is unknown. In addition, several unhealthy factors such as cigarette smoking and depressive mood are prevalent among arm forces, which may affect the physical performance and increase the risk of hospitalization for severe illness. In this case, we will investigate the association of cardiorespiratory fitness with hospitalization events in a retrospective armed forces cohort consisting of about 4000 professional military members aged 18-50 years in Eastern Taiwan for more than 10 years.

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INTRODUCTION

Professional military members are required to take regular rigorous physical trainings including endurance and resistance exercise to maintain their outstanding fitness. Frequent exercise training and well physical fitness have

been associated with lower risk of cardiovascular disease and mortality in the general population^[1-3]. However, current evidence showed conflicting results regarding the cardiovascular outcomes in those taking repetitive strenuous exercises^[4,5]. For instance, cardiac remodeling such as left ventricular muscle hypertrophy, chamber dilatation, mitral valve regurgitation, and arrhythmia, which have been well regarded as poor prognostic predictors of acute cardiac events among patients with conventional atherosclerotic risk factors are commonly present in elite athletes^[6-8]. Whether these physiological cardiac adaptations to repetitive vigorous training on future cardiovascular disease and mortality are beneficial or hazardous to armed forces remain unknown. In addition, several unhealthy behaviors and environments such as cigarette smoking, alcohol intake, stress, insomnia, and depressive mood are prevalent among arm forces, which may affect the physical performance by reducing cardiopulmonary function and increase the risk of hospitalization for acute illness^[9,10]. However there were few studies using large military cohorts, particularly of Asian young adults, with detailed data of demographics, laboratory exams, and cardiopulmonary function evaluations at baseline, to follow up the incidence of cardiovascular disease and other severe illness events. Therefore the aim of our study is to retrospectively investigate the association between cardiorespiratory fitness and hospitalization events in a large voluntary arm forces cohort in Eastern Taiwan.

MATERIALS AND METHODS

Study population

The cardiorespiratory fitness and hospitalization events in armed forces (CHIEF) is a retrospective cohort consisting of voluntary military members aged 18-50 years in Eastern Taiwan during 2014.

Measurements of the health examinations

All participants had to undergo physical examinations, anthropometric measurements for height, weight, and waist circumference at standing position, hemodynamic status including pulse rate and blood pressures, which were automatically measured by the PARAMA TECH FT-201 blood pressure monitor over right upper arm at sitting position, after taking rest for at least 15 min, chest radiography [posteroanterior (PA) standing view], 12-lead electrocardiography which was interpreted mainly according to the computerized Minnesota Code classification system^[11], urinalysis, blood tests for cell counts and concentrations of fasting glucose, total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, triglycerides, serum uric acid, blood urea nitrogen, creatinine, estimated glomerular filtration rate (eGFR) which was defined on the basis of the Chronic Kidney Disease Epidemiology Collaboration equation^[12], aspartate transaminase (AST), alanine transaminase (ALT), and surface antigen of

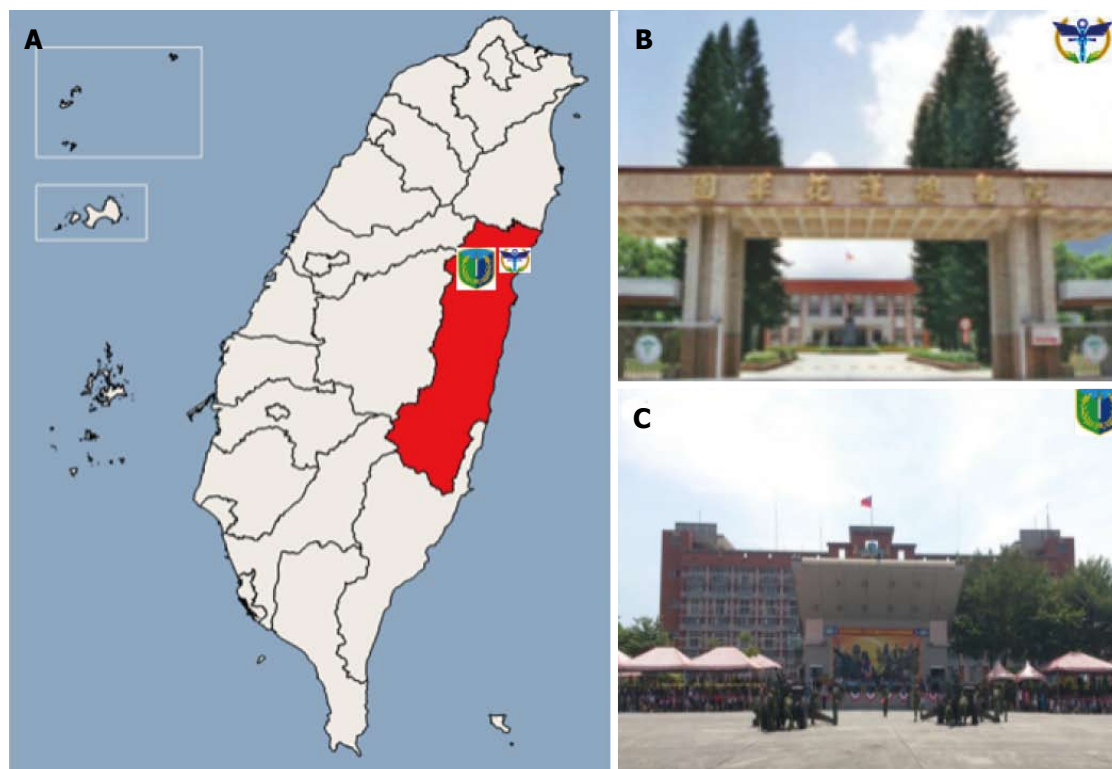


Figure 1 Geographic institutions of the cardiorespiratory fitness and hospitalization events in armed forces study performed. (A) The map of Hualien County in Taiwan is highlighted in red, and the symbols represent (B) the Hualien-Armed Forces General Hospital and (C) the Military Physical Training and Testing Center in the Army HuaDong Defense Command.

viral hepatitis B in the Hualien Armed Forces General Hospital where is the only military referral center for the professional armed forces in Hualien, Taiwan to perform the whole body health exams in 2014 (Figure 1). With regard to history taking, all participants were asked to self-report a questionnaire including demographic information, personal and third degree relatives medical history, current cigarette smoking status, current alcohol intake status, current betel chewing status, frequency of exercise persisting for at least 30 min in the past half year (never, occasionally, 0-1 time/wk, 3-5 times/wk), ever experienced any discomfort related to exercise (dizziness, chest tightness, dyspnea, or palpitation), and Brief Symptom Rating Score (BSRS-5)^[13,14] which is a 5-item Likert scale [scores of 0 (none), 1 (mild), 2 (moderate), 3 (severe), 4 (extremely severe)] for measurement of the severity of psychological distress. A higher score indicates poorer mental health^[13]. The full scale contained the following five items of psychopathology: (1) feeling tense or keyed up (anxiety); (2) feeling low in mood (depression); (3) feeling easily annoyed or irritated (hostility); (4) feeling inferior to others (interpersonal hypersensitivity: Inferiority); and (5) having trouble falling asleep (insomnia); and an additional question, "do you have any suicide ideation?" was added at the end of the questionnaire.

Measurements of the physical fitness

In addition, participants were also required to undergo 2 indoor resistant exercise tests including 2-min push-

up and 2-min sit-up and one outdoor endurance 3000-m none weight-bearing running exercise test, the main indicator of cardiorespiratory fitness in the Military Physical Training and Testing Center in Eastern Taiwan during 2014. Both 2-min push-up and 2-min sit-up contests were computerized scoring and whole courses were recorded by video. The procedure of 2-min push-up was scored only when the participants' body upward movement achieving the initial resting set height levels of shoulder and buttock simultaneously detected by infrared sensors (Figure 2A). The test would be early aborted once either elbows or knees touched down on the ground before time out. The procedure of 2-min sit-up was scored only if participants' body bended forward and elbows blew the touch sensors on both thighs (Figure 2B). With regard to 3000-m none weight-bearing running exercise test, whole course was recorded by video as well. All 3000-m none weight-bearing running tests were only allowed to be held at 16:00 pm when the risk coefficient of heat stroke, the product of outdoor temperature (°C) and relative humidity (%) × 0.1, was less than 40 or it was not raining.

Follow-up for the outcome of interests

After 2014, those retained in annual health or physical fitness exams will be followed up longitudinally. The outcome of interest will be the hospitalization events for cardiovascular disease, acute kidney injury, rhabdomyolysis, severe infectious disease, acute psychiatric illness, type 2 diabetes mellitus, orthopedic surgery,



Figure 2 Illustrations of standardized procedure for push-up and sit-up tests in the cardiorespiratory fitness and hospitalization events in armed forces study, respectively. A: A participant prepared for the push-up test surrounded by four flared sensors and a computerized monitor was ahead of him. A supervisor squatted aside by him to watch for all his procedure; B: A participant prepared for the sit-up test with two touch sensors were bound on both thighs and a computerized monitor was opposite to him. A supervisor stood aside by him to watch for all his procedure.

and mortality respectively. Hospitalization events will be identified in the National Insurance Research Database and followed up for at least 10 years. This study was approved by the Institutional Review Board of the Mennonite Christian Hospital in Hualien, Taiwan and written informed consent was obtained from all participants.

Statistical analysis

The armed forces in Eastern Taiwan who did not receive health examinations or undergo exercise tests in the index centers of Hualien during 2014 were excluded. Figure 3 shows the flow diagram to select the CHIEF study cohort. Demographic characteristics and exercise performances of men and women were reported as mean \pm SD or percent for continuous and categorical variables, respectively. The analysis will use the time for follow-up at January 1, 2014 with censoring at first occurrence of hospitalization events for specific severe illness, death, or end of follow-up (December 31, 2024). Kaplan-Meier analysis will be used to assess the sex-specific association of each exercise test performances (2-min push-up, 2-min sit-up, and 3000-m none weight-bearing running) with incident hospitalization events for specific severe illness. Cox proportional hazard regression analyses will be used to assess the sex-specific multivariable association between each exercise test performance and incident hospitalization events, adjusting for potential confounders. A 2-tailed value of P -value < 0.05 will be considered significant.

RESULTS

The historical CHIEF cohort consists of 4080 participants who received both health exams and underwent at least one exercise test during 2014. The administrative rates for 2-min sit-up, 2-min push-up, and 3000-m none weight-bearing running test were 99.5%, 98.8% and 88.6%, respectively. The descriptive statistics of baseline profiles, medical and family history, laboratory and 12-lead electrocardiographic findings, BSRS scores, and each exercise test performance of men and women

were shown in Tables 1-4 respectively. Of these participants, men accounted for about 89.9% and the mean age of men and women were about 29 and 28 years, respectively.

DISCUSSION

Previous studies have demonstrated the benefit of leisure time exercise which may reduce inflammatory response, viscosity, and the risk of cardiovascular disease in the general population^[15-18]. However, it is not clear the relationship of what kinds of exercise, how the dosing of exercise, and the performance of physical fitness in young adults with future health status in their middle age. In addition, for a population with rigorous exercise training daily for work such as athletes and professional military members, the question of exercise training and physical fitness on the health status has not been answered yet, since there were too few large cohort studies to investigate the association. Therefore the CHIEF study will be one of the largest retrospective military cohort ever in the world to retrospectively follow up the severe illness events.

In CHIEF, the anthropometric profile of men was characterized by an average overweight value defined by the body mass index criteria for Eastern Asian individuals ($> 24.0 \text{ kg/m}^2$), but within a non-obese waist circumference limit defined to be $< 85 \text{ cm}$ for Asian male populations^[19,20]. This may reflect that muscle mass may account for a higher proportion of body weight in men, which was also supported by a higher proportion of electrocardiographic left ventricular hypertrophy (17%) in men. In contrast, both levels of body mass index and waist circumference in women were within non-obese levels suggested for Asian female populations^[20]. Unlike elite athletes, many unhealthy behaviors such as cigarette smoking and alcohol consumption were prevalent in men (about 40%) and in women (10%-20%). In addition, about 40% of men reported mild to extremely severe depression or anxiety and 50% of women reported those negative psychological symptoms. Because of the

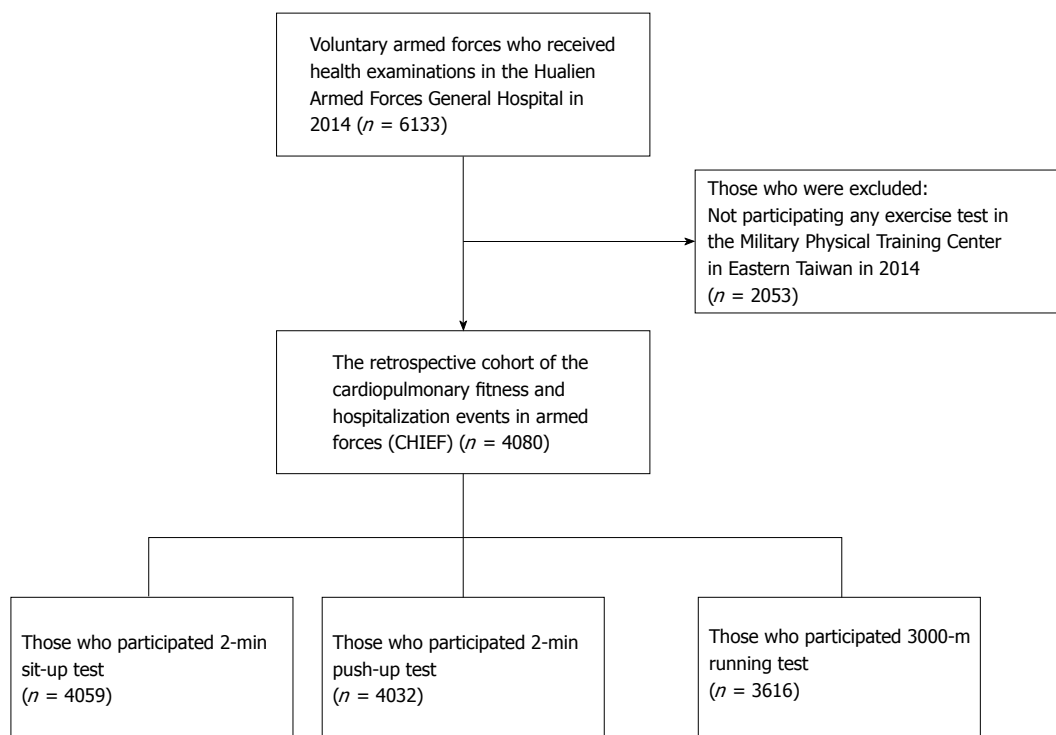


Figure 3 Flow diagram to select the eligible cardiorespiratory fitness and hospitalization events in armed forces cohort during 2014.

Table 1 Baseline demographics, hemodynamics, medical and family history, and habit of exercise of men and women in the cardiorespiratory fitness and hospitalization events in armed forces study

	Men (n = 3669)	Women (n = 411)
Age (yr)	29.3 ± 5.9	28.1 ± 6.5
Specialty (%)		
Air force	28	23.6
Army	50.5	61.6
Navy	21.5	14.8
Height (cm)	171.8 ± 5.8	160.5 ± 4.4
Weight (kg)	73.5 ± 10.2	58.1 ± 8.1
Body mass index (kg/m ²)	24.9 ± 3.1	22.5 ± 2.9
Waist circumference (cm)	83.4 ± 8.0	73.3 ± 7.4
Pulse rate (times/min)	72.2 ± 10.8	75.7 ± 10.1
Systolic blood pressure (mmHg)	118.4 ± 13.1	106.5 ± 12.4
Diastolic blood pressure (mmHg)	70.6 ± 10.1	65.2 ± 9.1
Current smoking (%)	38.1	12.2
Current alcohol intake (%)	44.7	17.1
Current betel chewing (%)	12	1.2
Medical history (%)		
Hypertension	1.5	0.2
Symptomatic arrhythmia	1.1	1.7
Chronic hepatitis B	3.4	1.7
Family history of cardiovascular disease within 3 rd relatives (%)	3.4	4.6
Frequency of exercise (%)		
Never or occasionally	19.7	30.5
1-2 times/wk	38.2	42.9
Over 3-5 times/wk	42.2	26.6
Cardiopulmonary distress symptoms related to exercise (%)	8.9	15.4

Data were presented as the mean ± SD and percentage (%).

specialty of armed forces, all these confounders should be taken into account the association between physical fitness and severe illness events.

Push-up and sit-up performance were used to assess musculoskeletal fitness. Push-up exercise is a strengthening exercise for building up strength and endurance in the muscles of the upper arm and shoulders, and sit-up exercise is performed to enhance abdominal muscular endurance. Mota *et al.*^[21] showed that low push-up and sit-up test performance is associated with increased risk for obesity and metabolic risk in adolescent girls. Furthermore, Katzmarzyk *et al.*^[22] found that sit-up but not push-up performance is predictive of mortality in the Canadian population. Performance in 3000-m (middle distance) running mainly depends on maximal aerobic power (VO₂max)^[23], which are related to several physiological parameters including maximal oxygen uptake, running economy, velocity at 4 mmol/L blood lactate concentration, and the minimal velocity at which VO₂max occurs^[24-28]. Accordingly, the performance of 3000-m none weight-bearing running test in armed forces could be regarded as a good surrogate for their cardiorespiratory fitness. As is known, adolescent cardiorespiratory fitness has been associated with adult fatness^[29]. Several previous studies in the Western countries demonstrated that superior cardiorespiratory fitness may be associated with lower risk of hospitalization events for incident hypertension, diabetes mellitus, coronary heart disease, stroke, cataract, and diverticular complications^[30-35]. Moreover, a relationship between cardiorespiratory fitness and

Table 2 Baseline laboratory and electrocardiographic findings of men and women in the cardiorespiratory fitness and hospitalization events in armed forces study

	Men (n = 3669)	Women (n = 411)
Blood routine		
Hemoglobin (g/dL)	15.2 ± 1.0	13.0 ± 1.0
Mean corpuscular volume (fl)	85.1 ± 6.3	85.2 ± 6.8
RBC count (10 ⁶ /μL)	5.3 ± 0.5	4.7 ± 0.4
WBC count (10 ³ /μL)	6.8 ± 1.7	6.6 ± 1.7
Platelet count (10 ³ /μL)	252.9 ± 50.5	274.5 ± 53.1
Blood biochemistry		
Fasting glucose (mg/dL)	93.6 ± 13.4	89.1 ± 7.5
Total cholesterol (mg/dL)	174.4 ± 34.0	167.4 ± 29.1
LDL-cholesterol (mg/dL)	106.0 ± 29.7	93.5 ± 25.3
HDL-cholesterol (mg/dL)	47.9 ± 9.8	56.9 ± 11.0
Triglycerides (mg/dL)	115.1 ± 100.3	77.7 ± 38.9
BUN (mg/dL)	12.9 ± 2.8	10.7 ± 2.4
Creatinine (mg/dL)	1.0 ± 0.1	0.7 ± 0.1
eGFR (mL/min per 1.73 m ²)	99.8 ± 14.2	109.4 ± 18.4
Uric acid (mg/dL)	6.7 ± 1.3	4.7 ± 0.9
AST (U/L)	20.7 ± 8.9	16.2 ± 5.2
ALT (U/L)	23.1 ± 17.7	12.5 ± 7.3
Urinalysis (%)		
Protein > 1+	10.3	10.5
RBC > 1+	5.3	17.4
Occult blood > 1+	3.4	17.8
WBC > 6-10	2.1	11.2
Bacteria > 1+	2.6	22.4
12-lead electrocardiography (%)		
LVH/RVH/IVCD	17.3/1.0/0.2	2.0/0.2/0
LAE/RAE	0.2/0.2	0.2/0
ICRBBB/CRBBB	3.9/0.5	0.73/0
LAFB/LPFB	0.7/0.2	0/0
1 st degree atrioventricular block	3.8	3.4
PACs/PVCs	0.4/0.6	0.2/0.2

Data were presented as the mean ± SD and percentage (%). ALT: Alanine transaminase; AST: Aspartate transaminase; BUN: Blood urea nitrogen; CHIEF: Cardiopulmonary fitness and hospitalization events in armed forces; CRBBB: Complete right bundle branch block; eGFR: Estimated glomerular filtration rate; HDL: High-density lipoprotein; ICRBBB: Incomplete complete right bundle branch block; IVCD: Intraventricular conduction delay; LAE: Left atrial enlargement; LAFB: Left anterior fascicular block; LPFB: Left posterior fascicular block; LDL: Low-density lipoprotein; LVH: Left ventricular hypertrophy; PACs: Premature atrial contractures; PVCs: Premature ventricular contractures; RAE: Right atrial enlargement; RBC: Red blood cell; RVH: Right ventricular hypertrophy; WBC: White blood cell.

all-cause and cardiovascular mortality has been well established in the general population^[1-3]. On the contrary, outstanding cardiorespiratory fitness is highly related to rigorous exercise training which may lead to hazardous cardiovascular events such as sudden death and severe cardiac arrhythmia, rhabdomyolysis, and orthopedic illness in armed forces^[36]. It is important to know how to prevent exercise related lethal complications and to obtain the best physical fitness.

The strength of the study includes that: (1) the data of the historical cohort is complete since both whole body health examinations and physical exercise tests are scheduled for all professional military members annually unless those who receive these examinations elsewhere;

Table 3 Brief symptom rating score of men and women in the cardiorespiratory fitness and hospitalization events in armed forces study

	Men (n = 3669)	Women (n = 411)
Anxiety (%)		
None (0)	69.52	59.72
Mild (1)	25.1	32.2
Moderate (2)	4.7	7.6
Severe (3)	0.4	0.2
Extremely severe (4)	0.3	0.2
Depression (%)		
None (0)	72	63.2
Mild (1)	23	28.1
Moderate (2)	4.1	7.8
Severe (3)	0.7	0.7
Extremely severe (4)	0.3	0.2
Hostility (%)		
None (0)	65.7	55.1
Mild (1)	27.3	33.9
Moderate (2)	5.8	9.8
Severe (3)	0.9	0.7
Extremely severe (4)	0.3	0.5
Insomnia (%)		
None (0)	63.5	58.8
Mild (1)	28	29.5
Moderate (2)	6.7	9.5
Severe (3)	1.4	1.2
Extremely severe (4)	0.4	1
Interpersonal hypersensitivity: Inferiority (%)		
None (0)	79.3	73.2
Mild (1)	16.5	21
Moderate (2)	4	5
Severe (3)	0.5	0.2
Extremely severe (4)	0.2	1
Suicide ideation (%)		
None (0)	96.4	95
Mild (1)	2.4	3.7
Moderate (2)	0.6	1.5
Severe (3)	0.4	0
Extremely severe (4)	0.3	0

Data were presented as percentage (%).

(2) the procedures of health examinations and physical exercise tests are standardized and performed in central labs which could avoid systemic bias completely; (3) as compared with previous studies for the association of physical fitness with severe illness, the baseline data of CHIEF includes not only demographic characteristics but also a series of laboratory and imaging findings, which could be further adjusted to prevent potential bias; and (4) both health examinations and physical exercise tests will be held annually that provide the opportunity for us to follow up the interval change of the physical fitness and investigate the association with severe illness. On the contrary, we have several limitations in the study. First, there were about one third (33.5%) of the military members in armed forces who received health examinations but did not undergo any physical exercise test in Hualien during 2014. Although the baseline characteristics of drop-out individuals were similar to

Table 4 Exercise performances of men and women in the cardiorespiratory fitness and hospitalization events in armed forces study

	Men		Women	
	<i>n</i>	Performance	<i>n</i>	Performance
2-min sit-up	3651	47.5 ± 8.2	408	37.7 ± 8.1
2-min push-up	3641	49.1 ± 11.7	391	33.9 ± 10.6
3000-m non-weight bearing running (s)	3296	859.9 ± 72.7	320	1007.1 ± 76.9

Data were presented as the mean ± SD.

those enrolled in CHIEF, we could not completely exclude the selection bias. Second, women account for only 10% of the CHIEF cohort and we may not have enough power to make a conclusion at last. Third, since CHIEF is a retrospective study, some potential confounders such as systemic inflammatory markers, cardiac biomarkers, nutritional support, diet, and the type of daily regular exercise trainings performed, which may affect the physical performance and hospitalization events for severe illness, will not be available without prospective collection.

In summary, physical fitness as an independent predictor of mortality and cardio-metabolic risk in the general population has not been confirmed in young military members of armed forces who have many traditional vascular risk factors. The CHIEF study is thus designed to be one of the largest military cohorts in the world and will retrospectively investigate the association of each physical fitness performance, the interval change of each physical fitness, and incident hospitalization events for severe illness. The result of CHIEF could be applied to the military members in armed forces to improve the physical trainings effectively and prevent the adverse effect related to heavy exercises in the future.

COMMENTS

Background

Professional military members are required to take regular rigorous physical trainings to maintain their physical fitness. However, several unhealthy factors such as cigarette smoking are prevalent among arm forces, which may affect the exercise performance and increase the risk of severe illness.

Research frontiers

Frequent exercise training and well physical fitness have been associated with lower risk of cardiovascular disease and mortality in the general population. Current evidence in the Western countries showed conflicting results for the cardiovascular outcomes in those taking repetitive strenuous exercises.

Innovations and breakthroughs

There were few studies using large military cohorts, particularly of Asian young adults, with detailed data of demographics, laboratory exams, and cardiopulmonary function evaluations at baseline, to follow up the incidence of cardiovascular disease and other severe illness events such as infectious and orthopedic disease. The cardiorespiratory fitness and hospitalization events in armed forces (CHIEF) is a retrospective cohort consisting of more than 4000 professional military members aged 18-50 years in Eastern Taiwan. CHIEF will be among the largest Eastern Asian armed forces cohort, in which physical

status was strictly evaluated to follow up the hospitalization events for specific severe illness.

Applications

The result of CHIEF could be applied to the military members in armed forces to improve the physical trainings effectively and prevent the adverse effect related to heavy exercises in the future.

Peer-review

The authors present here the protocol of a study about cardiorespiratory fitness in a military population. It is well written and seems to me it will make a fine study when finished.

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