Exercise epidemiology on mortality and morbidity with an emphasis on the effects of physical fitness

Nemeth, Hajnalka
Graduate School of Human-Environment Studies, Kyushu University

Kumagai, Shuzo
Institute of Health Science, Kyushu University

熊谷，秋三
九州大学健康科学センター

https://doi.org/10.15017/18337
Exercise epidemiology on mortality and morbidity with an emphasis on the effects of physical fitness

Hajnalka NÉMETH¹), Shuzo KUMAGAI²)*

Abstract
Metabolic syndrome, a cluster of metabolic and cardiovascular disorders has risen worldwide. The issue gets increasing attention because its progressive form lead to type 2 diabetes mellitus, cardiovascular diseases and premature mortality. Intervention tools are required to prevent them. Physical fitness is recognized to be a first step intervention tool. There are two purposes of this review: to give a summary of the metabolic syndrome and physical fitness; to examine two relationships, namely, the relationship between metabolic syndrome and physical fitness and the relationship between all-cause mortality and handgrip strength.

Key Words: lifestyle-related disorders, metabolic syndrome, mortality, physical fitness, muscle strength

(Journal of Health Science, Kyushu University, 32: 21-29, 2010)
Introduction

Decreased level of physical fitness has been associated with the metabolic syndrome. The syndrome leads to morbidities like type 2 diabetes mellitus (type 2 DM) and cardiovascular disease (CVD). The global number of people with diabetes is set to rise from the current estimate of 150 million to 220 million in 2010, and 300 million in 2025. Regarding the mortalities, the prevalence of global deaths in CVD is 29.2% and by 2010, CVD will be the leading cause of death in developing countries according to World Health Report 2003. Population approach and political commitment is needed to prevent these lifestyle-related diseases. The development of type 2 DM and CVDs like stroke and myocardial infarction is not settled. There are several risk factors that are linked with type 2 DM and CVDs, including hyperglycemia, insulin resistance, obesity, elevated blood pressure and dyslipidaemia. Worthy of note, all of these risk factors individually predict future type 2 DM and CVDs, when grouping them together, they convey greater risk.

Monitoring prospectively physical fitness of populations like muscle strength and cardiovascular fitness may help restraining the lifestyle-related threats. Blair et al. showed prospectively that the greatest public health benefit may arise when the most sedentary individuals become somewhat fitter. Physical fitness decreases with aging that is a physiological process. However, recently worldwide-prevalent sedentary lifestyle has been often associated with lower level of physical fitness than the assigned level. Effects of decline in physical fitness on multiple risk factors, such as biological, sociodemographic and lifestyle are of research interest. Many of the researches have been analysing the multiple risk factors simultaneously.

In this review lifestyle-related disorders and evidences for using physical fitness to predict important health outcomes are summarised.

1.1. Metabolic Syndrome as a progressive disorder

Co-occurrence of various mild metabolic and cardiovascular abnormalities is now collectively known as metabolic syndrome (MS), including essential components like glucose intolerance, insulin resistance, obesity, dyslipidaemias and hypertension. MS is a result of complex genetic and environmental interactions. Obesity and physical inactivity are the primary environmental contributors. Genetic background is found to be the major contributor in most of the studies (about 50%), and adiposity and physical inactivity share about the same importance to MS. However, measures of procoagulant and proinflammatory states (low-grade inflammation) have not been elevated to the status of diagnostic criteria of the MS, their relation with the cluster of abnormalities have been often commented. MS estimates in a population may reflect the diversity of the population and the diversity of the environment.

MS is a progressive disorder. The ultimate importance of the MS is that it helps identify individuals at high risk of both type 2 DM and CVD. Predominantly, the risk assessment of CVDs with MS diagnosis is emphasised for long-term. Furthermore, risk assessment of these life threatening diseases promotes the selection of the therapeutic method (lifestyle modification and/or pharmacological intervention). However, risk factors individually predict future type 2 DM and CVDs like stroke and myocardial infarction, grouping them together, i.e. two clustered risk factors or more (MS) convey greater risk of type 2 DM or CVD (Nippon Data 80).

The MS has become one of the major public-health challenges worldwide, both in industrialized and developing countries. Over the last century, drastic environmental changes occurred, and the trends are continuing toward a less need of human labour work and an easy access to a wide variety of foods, primarily of high-calorie content.

Despite MS definitions by several health organizations have been worked out, unified universally recognised MS definition has to be still settled. Some of the definitions, the European Group for the Study of Insulin Resistance (EGIR), American Association of Clinical Endocrinologists (AACE), (World Health Organization
(WHO)\(^7\) concentrate on either type 2 DM or CVD and the National Cholesterol Education Program-Adult Treatment Panel III (NCEP-ATP III)\(^8\) mainly focus on CVD only.

Defect in insulin action plays a fundamental role in the development of the CVD risk factors. This is the oldest syndrome concept proposed in 1988 by the WHO\(^9\). Other predominant underlying mechanism for the MS appears to be abdominal obesity (concept of International Diabetes Federation\(^10\) and the Japanese Metabolic Syndrome Criteria\(^11\)) and inflammation. Inflammatory markers have not been embedded yet among main components in either of the MS definitions. In the literature, the main controversies arise around the visible obesity markers such as overall obesity expressed by the body mass index (BMI) and upper body obesity, expressed by the waist circumference (WC) and whether the syndrome is uni- or multicausal. Recently, the American Heart Association (AHA) and National Heart, Lung and Blood Institute (NHLBI)\(^12\) jointly has proposed to lower the impaired fasting plasma glucose level from 110 mg/dL (that is included in the NCEP-ATP III criteria) to 100 mg/dL and emphasised WC to be race specific, just like being proposed in the criteria of the IDF.

Some of the most frequently used MS definitions in the literature are summarized in Table 1-4.

### Table 1

<table>
<thead>
<tr>
<th>World Health Organization (WHO): 1999</th>
</tr>
</thead>
<tbody>
<tr>
<td>IFG: FPG 110-125 mg/dL (6.1-6.9 mmol/L) or IGT (2h PG 140-199 mg/dL (7.8-11.0 mmol/L)</td>
</tr>
<tr>
<td>or Type 2 DM: FPG≥126 mg/dL (7.0 mmol/L) or 2h PG≥200 mg/dL (11.1 mmol/L), or insulin resistance</td>
</tr>
<tr>
<td>(hyperinsulinaemic, euglycemic clamp-glucose uptake in lowest 25%)</td>
</tr>
<tr>
<td>Plus 2 or more of the 4 following risk factors:</td>
</tr>
<tr>
<td>· Obesity: BMI&gt;30 kg/m(^2) or waist to hip ratio &gt;0.9 in male or &gt;0.85 in female</td>
</tr>
<tr>
<td>· Dyslipidemia: TG ≥150 mg/dL (1.7 mmol/L) or HDL-c&lt; 35 mg/dL (0.9 mmol/L) in male or &lt;39 mg/dL (1.0 mmol/L) in female</td>
</tr>
<tr>
<td>· Hypertension: BP≥140/90 mmHg</td>
</tr>
<tr>
<td>· Microalbuminuria: albumin excretion&gt;20 μg/min or albumin : creatinin ratio≥30 mg/g</td>
</tr>
</tbody>
</table>

### Table 2

<table>
<thead>
<tr>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>3 or more of the 5 following risk factors:</td>
</tr>
<tr>
<td>· Central obesity: WC&gt;102 cm in male, &gt;88 cm in female</td>
</tr>
<tr>
<td>· High TG: TG≥150 mg/dL (1.69 mmol/L)</td>
</tr>
<tr>
<td>· Low HDL-c: HDL-c&lt;40 mg/dL (1.04 mmol/L) in male, &lt;50 mg/dL (1.29 mmol/L) in female</td>
</tr>
<tr>
<td>· Hypertension: BP≥130/85 mmHg</td>
</tr>
<tr>
<td>· High FPG: FPG≥110 mg/dL (6.1 mmol/L)</td>
</tr>
</tbody>
</table>
Table 3

International Diabetes Federation (IDF): 2005

<table>
<thead>
<tr>
<th>Central obesity: ethnic specific waist circumference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plus 2 or more of the 4 following risk factors:</td>
</tr>
<tr>
<td>- High TG: TG ≥ 150 mg/dL (1.7 mmol/L), or specific treatment for this abnormality</td>
</tr>
<tr>
<td>- Low HDL-c: HDL-c &lt; 40 mg/dL (1.03 mmol/L) in male, &lt; 50 mg/dL (1.29 mmol/L) in female or specific treatment for this abnormality</td>
</tr>
<tr>
<td>- Hypertension: BP ≥ 130/85 mmHg or treatment of previously diagnosed hypertension</td>
</tr>
<tr>
<td>- High FPG: FPG ≥ 100 mg/dL (5.6 mmol/L) or previously diagnosed type 2 DM. If FPG is above the values stated above, OGTT is strongly recommended, but it is not necessary to define presence of the syndrome</td>
</tr>
</tbody>
</table>

Table 4

Japanese diagnostic criteria for metabolic syndrome 2005

<table>
<thead>
<tr>
<th>Central obesity: WC ≥ 85 cm in male, ≥ 90 cm in female (The values for both males and females correspond to visceral fat areas of ≥ 100 cm²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plus 2 or more of the following:</td>
</tr>
<tr>
<td>- High TG: TG ≥ 150 mg/dL and/or Low HDL-c: HDL-c &lt; 40 mg/dL for both males and females</td>
</tr>
<tr>
<td>- Hypertension: BP ≥ 130/85 mmHg</td>
</tr>
<tr>
<td>- High FPG: FPG ≥ 110 mg/dL (OGTT is recommended, but it is not essential for the diagnosis)</td>
</tr>
</tbody>
</table>

The point of view of the various expert groups about the cause of MS is at least partially reflected in the construction of their definitions (the manner in which the various criteria are organized and the role of excess adiposity).

However, sedentary lifestyle contributes to the syndrome, and physical fitness (and physical activity) is recognized as a first step intervention tool, physical fitness and physical activity marker have not been yet elevated to the status of official MS risk factors. Physical fitness modulates insulin action, yet it has not always been readily measured. Physical fitness that is a surrogate measure of skeletal muscle function may appropriately reflect whether a person is sufficiently insulin resistant to develop the MS, type 2 DM and CVD. Furthermore, fitness may also appropriately reflect whether a person is sufficiently viscerally obese to develop the MS, type 2 DM and CVD.

In Japan, according to the Japanese Ministry of Health, Labour and Welfare, among the 40- to 74-year olds, one of two men and one of five women were either strongly suspected to have MS or prodromal MS. In the Hisayama study, Ninomiya and colleagues showed that MS is a significant risk factor for the development of CVD in Japanese middle-aged population.

1.2. Physical fitness

Physical fitness is an ability of the body that can be associated with lifestyle-related disorders. It may even predict health-outcomes. There are various markers of physical fitness, like cardiorespiratory fitness (CRF), skeletal muscle strength and vital capacity. At least partially, all of them reflect skeletal muscle function.

1.2.1. Cardiorespiratory fitness (CRF)

The CRF has surrogate names like aerobic capacity, endurance fitness, maximal oxygen uptake (VO₂max) and peakVO₂. CRF reflects the function of the lung, cardiovascular system and skeletal muscle, thus CRF is a systemic function measure. The CRF is determined by the oxygen uptake (VO₂) (ml/kg/min) during dynamic work with a cycle ergometer or treadmill. The VO₂max is considered the international reference standard to examine the maximal endurance performance.
Depending on the used ergometer, skeletal muscles of all body (treadmill), upper limb (rowing) or lower limb (bicycle) is involved in the dynamic work. CRF is highly dependent on fibres with oxidative capacity (type 1 fibres). Endurance type of work, like, cross-country skiing, marathon running, and swimming require the highest muscle oxidative capacity. It is well known that athletes with predominately endurance-type of sport history have higher CRF compared to healthy sedentary subjects. However, CRF refers to the VO\textsubscript{2max}, it cannot be always measured. Exercise capacity may be limited in patients. Patients with certain health risk factors undergo submaximal CRF test. In that case, CRF is estimated from heart rate (70% of the individual’s maximal heart rate or above) during submaximal work by nomogram. One of the most accepted nomogram for estimation of CRF is the Åstrand and Rhyming nomogram. In the literature, some of the studies related CRF to threshold of lactate (LT), threshold of blood plasma cathecolamin concentration, threshold of ventilation (VT) or threshold of double product (DPBP). In the determination of VT and LT, some methodological problems arose in cardiac patients.

1.2.2. Muscle strength

Muscle strength indicates our “vigour” and it is a “strength fitness” indicator. Muscle strength refers to the ability of the working muscle to develop active tension that produces force. Muscle strength is a -local function-measure. Maximal muscle strength is the force produced by a single maximum voluntary muscle contraction.

Maximal isometric muscle strength (kg) can be measured on upper limb muscles by handgrip (HG). Strength of other muscle groups, such as of quadriceps muscle and hamstring muscle require isokinetic dynamometers that are less available in population researches. HG strength has significant correlations with other muscle strength measures, thus it can be considered as a good whole body muscle strength indicator.

HG strength is required in many activities of daily living and it is a preferred muscle strength test during health check-ups. Alves and Reverbel reported HG strength to be the only technique that predicted health outcome in cirrhotic outpatients. People with HG strength deficits have limitation of functional ability to perform their activities of daily living, such as decreased mobility (decreased walking speed or disability of rising from a chair), decreased self-care ability (lifting something heavy, dressing, bathing, toileting and eating).

Important factors for consideration when testing HG strength are selection of type of dynamometer, sex, height, and weight, muscle force on dominant and non-dominant sides, muscle quality, muscle mass, trial number and which HG strength result to use, encouragement, and warm-up.

1. In general, HG dynamometer is popular in epidemiologic studies because it is simple, cost-effective and easily portable. HG strength dynamometers can be hydraulic (e.g. Jamar), pneumatic (e.g. Tekdyne), mechanical (Smedley, used in used in Baltimore Longitudinal Study of Aging (BLSA) and Honolulu Heart Program/Honolulu Asia Aging Study (HHP/HAAS)) or strain-gauge types (e.g. Lafayette).

2. Sex differences in strength may emerge partially due to androgen hormones, and males have a stronger grip than females.

3. Regarding height and body weight, the larger the body size, the stronger the grip.

4. In younger men aged <60 years, rate of loss of strength is more important than actual strength levels, while in older men, aged ≥ 60 years, functional performance becomes more directly dependent on strength.

5. Difference in hand dominance (usually a 10% difference between sides), and level of subject HG effort may also exist.

6. HG strength is highly dependent on muscle fibres with glycolytic capacity.

7. HG strength is closely related to the absolute quantity of muscle mass, which is reduced with aging. This decrease in muscle mass might explain
part of the association between strength and mortality. Muscle mass can be estimated by muscle weight, creatinin excretion, or derived anthropometric measures.

8 Generally, the duration of a single HG strength trial ranges from 3–5s.

9 A decision must be made on the number of HG trials (preferably three) and whether the best (used in BLSA and HHP/HAAS), the average or the sum of the HG strength of both hands is used.

10 The examiner must decide if encouragement is provided during the HG measurement and if so, ensure that the encouragement is consistent across all testing periods.

11 Finally, warm-up trials decrease the variability of the strength measurements.

1.3. Muscle strength and its relationship with metabolic syndrome (MS)

Among the reviewed studies, all studies examining the relationship of grip strength with MS were cross-sectional studies\(^\text{30-31}\) carried out in Japanese Okayama prefecture, British regionally representative and Australian population-based samples. In the Japanese study, MS was defined by the Japanese criteria. The other two studies used both the IDF and NCEP-ATP III definitions. HG strength was measured using different grip dynamometers (Japanese study: THP-10, Sakai; British Study: Jamar; Australian study: Smedley). Used hand, trial number and grip measure varied among the studies. While the Japanese study outlined the importance of muscle strength per body weight, the British study used the force itself in the data analysis, the Australian study related the forearm force (kg) to lean arm mass (kg). All these studies demonstrated that low grip strength was accompanied by a greater likelihood of MS in men\(^\text{30,32}\) and in women\(^\text{31}\) including both younger and older subjects aged 20-79 years\(^\text{30}\) and aged 35-81 years\(^\text{32}\) or only older subjects aged 59-73 years\(^\text{31}\). In men, similar findings were observed between CRF and MS. Kumagai \textit{et al.}\(^\text{17}\) showed that high degree of CRF positively contributed to the low prevalence of MS in Japanese male patients with IGT and type 2 DM, aged 51.6±12.5 years.

HG strength has been associated with the individual features of the MS. However, because of the cross-sectional study design, the authors suggested that the potential for HG strength to be used in the clinical settings needs to be explored\(^\text{31}\).

1.4. Muscle strength and its relationship with all-cause mortality

Low grip strength was a consistent predictor of death and high grip strength was a consistent predictor of survival in studies with diverse samples of subjects. A Japanese study reported HG strength to be predictive for men but not for women\(^\text{33}\).

The time between the measurement of grip strength and the determination of outcome ranged from few years (about 5 years of follow-up\(^\text{33-39}\)) to more years (about 20 years of follow-up or more\(^\text{27, 40-45}\)). In a study of Honolulu Heart Program on ethnic Japanese men living in America suggests that midlife HG strength is important for healthy survival, without physical disability, cognitive disability and chronic disease (coronary heart disease, stroke, chronic obstructive pulmonary disease, cancer, Parkinson disease and diabetes)\(^\text{45}\). HG strength is a predictor of mortality in Caucasians\(^\text{44}\), in Japanese\(^\text{40}\) and Mexican-Americans\(^\text{34}\). In the study of Sasaki \textit{et al.}\(^\text{40}\), mortality was followed prospectively over more than 25 years, and HG strength predicted all-cause mortality in Japanese people. However, the major limitation of their study was that ischemic heart disease, stroke and diabetes were not included in the analysis and half of the subjects were exposed to A-bomb radiation. Rantanen \textit{et al.}\(^\text{44}\) found that in healthy middle-aged men, long-term mortality risk was associated with grip strength at baseline, independent of BMI. Fujita \textit{et al.}\(^\text{33}\) found, in a Japanese health promotion program, that strength independently predicts mortality for 6 years in men, but not in women. In 75 years old Finnish men and women, poor strength tested in multiple muscle groups predicted increased mortality over a follow-up of 5 years\(^\text{39}\). Metter \textit{et al.}\(^\text{27}\) found that strength predicts mortality for 40 years in men, independent of physical activity and body mass. In their study, in older men, the protective effect of muscle strength was greater than the effect of rate of change in
Exercise epidemiology on mortality and morbidity with an emphasis on the effects of physical fitness

1.5. Feature research

In our laboratory, 2 prospective studies are going on.

Title 1: Exercise epidemiology on mortality with an emphasis on the effects of handgrip (HG) strength.

In Japan, no study exists with long follow-up period in general adult population that examines the relationship between HG strength and all-cause mortality. Study that shows that HG strength predicts all-cause mortality in Japanese general adult population is needed. Target sample would include 2630 people of Hisayama town (Kyushu Island; population: 7500) who are older than 40 years. Subjects with missing data or who dropped-out or died between July 8, 1988 and December 1988 would be excluded. Baseline sample size would be approximately 2500 subjects. Baseline includes HG strength (average of maximal HG strength (kg) of both hands), biological (anthropometric, physiologic, haematological and biochemical factors), sociodemographic (education, income) and lifestyle (smoking, alcohol drinking, physical activity) data. The subjects were followed prospectively from December 1988 to November 2007 by repeated health-checks. Age- and multivariate- (BMI current smoking, current drinking, physical activity) adjusted Cox proportional hazard model (hazard ratio with 95% confidence interval) is used for the statistical analysis (SAS program). HG strength: division in quintile. Outcome: all-cause mortality.

Title 2: Exercise epidemiology on metabolic syndrome with an emphasis on the effects of handgrip (HG) strength.

No prospective study exists that examines the relationship between HG strength and the metabolic syndrome. The purpose of a new study would be to show that HG strength predicts metabolic syndrome. Target sample, follow-up period, statistics used: same would be as in the study that would investigate the relationship between all-cause mortality and HG strength. Baseline sample would include about 1000 subjects. Exclusion: same as in all-cause mortality - HG strength study and metabolic syndrome. Outcome: metabolic syndrome.

Conclusion

This review is conducted to summarize the lifestyle-related disorders and summarize the evidence for using physical fitness to predict important health outcomes.

Acknowledgements

This study is performed by scientific research grant from Ministry of Health, Labour and Welfare of Japan to Shuzo Kumagai.

Reference


