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Fitness epidemiology: Current trends and future research

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Abstract

Epidemiology in the field of sports science is relatively new compared with other areas, such as exercise physiology and biomechanics; however, it is currently one of the most popular disciplines. Physical fitness has been a traditional topic in exercise (or physical activity) epidemiology since the late 1980s. In Japan, a pioneer study investigating “fitness epidemiology”, the Tokyo Gas Study, was published in 1993. Since then, however, trends in fitness epidemiology have changed and two main trends have emerged: larger-scale studies; and subdivision of study objectives. An increasing number of large-scale cohort studies using fitness as an exposure variable have been published since the mid-2010s, confirming the findings reported by smaller-scale studies but with higher external validity and robustness. Moreover, larger-scale studies have enabled examination of the association between physical fitness and comprehensive health outcomes, including all-cause and disease-specific mortality and incidence of noncommunicable disease. However, researchers now must fill current knowledge gaps and develop more detailed study questions, which has resulted in a subdivision of study objectives. Accordingly, this short review addresses current trends in fitness epidemiology and introduces the author’s findings from a series of studies investigating the cumulative influence of physical fitness on the risk for lifestyle-related disease(s). In addition, it briefly discusses muscle-strengthening activity epidemiology, which has recently attracted attention as a new frontier beyond fitness epidemiology.

Keywords: Physical fitness, cohort study, cardiorespiratory fitness, grip strength, muscle-strengthening activity
体力の疫学

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スポーツ科学分野における疫学は、他の運動生理学やバイオメカニクス分野と比較してそれほど古くはない。しかしながら、今や疫学はスポーツ科学分野における最も盛んな分野の一つと言ってよいだろう。体力は運動（もしくは身体活動）疫学において古典的なテーマの一つであり、1980年代後半に始まる。日本における“体力疫学”的先駆的研究は1993年に報告された東京ガススタディである。それから約20年の歳月が流れ、体力疫学のトレンドもまた当時から変遷している。体力疫学の現在のトレンドは主に、研究の大規模化と研究課題の細分化の2つあるように思われる。体力を曝露要因とした大規模研究が2010年半ばから報告されるようになっており、これまで報告されていた知見が高い外的妥当性および頑健性を持って再確認されている。さらに、研究の大規模化によって健康アウトカムとの関連について網羅的な検討を行うことも可能となっている。一方、研究者は研究の空白地帯を探し出し、より詳細な研究課題を探さなければならない。これは研究課題の細分化に繋がっている。本レビューでは、体力疫学の最近のトレンドを概説し、生活習慣病の発症リスクにおける体力の累積曝露の影響について、我々の知見を研究課題の細分化の例として紹介する。さらに、近年、新たなトピックスとなっている筋トレの疫学についても簡単に紹介する。
Introduction

Epidemiology in the field of sports science is relatively new compared with other areas of research, such as exercise physiology and biomechanics. The sciences have evolved from basic to applied over time, although basic research, such as exercise physiology, has long been mainstream in the field of sports science. However, epidemiology has become one of the “hottest” disciplines in sports science, while physical fitness has been a more traditional topic in exercise (or physical activity) epidemiology since the late 1980s.

The pioneering study of “fitness epidemiology” in Japan was the Tokyo Gas Study (TGS), published in 1993, which investigated male Japanese workers residing in a metropolitan area of the country. The TGS used cardiorespiratory fitness (CRF), a primary component of physical fitness, as an exposure variable. A seminal study published by Sawada et al., which reported an inverse association between CRF and the risk for type 2 diabetes, was published in 2003. Since these pioneering studies, however, trends in fitness epidemiology have changed.

The present review addresses two current trends in fitness epidemiology: larger-scale studies and subdivision of study objectives. As an example of the latter, we introduce findings from a series of studies investigating the cumulative influence of physical fitness on the risk for diabetes, hypertension, and dyslipidemia. In addition, we briefly discuss muscle-strengthening activity epidemiology, which has recently attracted attention as a new frontier within exercise/physical activity epidemiology.

Current trends of fitness epidemiology

As mentioned, two main trends in fitness epidemiology have emerged. One notable
direction is that epidemiological studies are becoming larger in scale. Recently, studies including several hundred thousand to > 1 million participants have been published, and have confirmed the findings reported by smaller scale studies but with greater external validity and robustness. Moreover, larger-scale studies enable examination of the association between physical fitness and comprehensive health outcomes, including all-cause and disease-specific mortality and the incidence of noncommunicable disease. Another current trend is the subdivision of study objectives and, as the annual number of publications increase, researchers are required to develop novel research questions and provide nuanced answers.

Larger-Scale Studies

An increasing number of large-scale cohort studies using fitness as an exposure variable have been published since the mid-2010s. For example, one national cohort study targeted Swedish military conscripts, including approximately 1.5 million enlisted in 1969. CRF and muscle strength, measured at the time of admission, were used as exposure variables, and associations with various health outcomes, including type 2 diabetes, hypertension, atrial fibrillation, heart failure, cancer and cancer-associated mortality, disability, sleep apnea, psoriatic arthritis, and migraine were described. Recently, associations with the severity of coronavirus disease 2019 have also been reported. Another large-scale cohort investigation was the Prospective Urban Rural Epidemiology (PURE) study, involving approximately 140,000 participants from 17 countries with heterogeneous income and social structures. Leong et al. reported that grip strength, a marker of systemic muscle strength, was inversely associated with all-cause, cardiovascular, and non-cardiovascular mortality, myocardial infarction, and
Similarly, the association between grip strength and disease-specific incidence and mortality, including cardiovascular disease, respiratory disease, chronic obstructive pulmonary disease, and cancer, as well as all-cause mortality, was also reported in the United Kingdom Biobank cohort, which included > 500,000 British participants\(^9\). Compared with findings of the PURE study, this study had a more clinical perspective because it adopted a cut-off for sarcopenia in grip strength to stratify participants in addition to examining linear association(s) and examined the accuracy of predicting outcomes of interest.

One strength of large-scale studies is the ability to exhaustively examine associations with health outcomes, including rare outcomes, with higher external validity compared with previously published findings. Moreover, greater robustness is also a strength because larger study populations are more conducive to determining whether the association between fitness and health outcomes differ according to confounding factors by using sub-group or stratified analyses. These benefits explain why many of the previous studies described above have been published in top medical/science journals, and why large-scale studies are also becoming a trend in fitness epidemiology. However, there are few available large-scale studies involving Japanese populations; therefore, it is necessary to conduct such studies including Japanese participants in the future.

**Subdivision of Study Objectives**

The second trend in fitness epidemiology is the subdivision of objectives. Numerous findings regarding physical fitness and health outcomes have accumulated, and it is not an overstatement to state that fitness levels are associated with longevity and risk for disease(s), which is now widely accepted as “common sense”. Therefore, the salient
question, “is fitness related to health and longevity?” has, in large part, been resolved, and researchers now must seek new knowledge gaps and develop more detailed study questions. For example, are other components of physical fitness, such as balance and flexibility, associated with health outcomes? Can simple fitness tests predict the risk for a disease? How high and how long does an individual need to maintain their fitness level? Are there more effective ways to maintain and improve fitness?

The author and collaborators are currently investigating the potential cumulative influence of physical fitness on the risk for lifestyle-related disease(s) to address the question of “how high and how long does an individual need to maintain their fitness level?”.

As noted, it is generally accepted that physical fitness is associated with disease and longevity. Many would accept the concept that maintaining a high level of physical fitness is effective in preventing lifestyle-related diseases. However, is this true? To date, many previous studies examining the association between physical fitness and the risk for lifestyle-related diseases only considered the level of physical fitness at baseline, and did not report data directly indicating that maintaining a high level of physical fitness truly contributes to reducing the risk for lifestyle-related disease(s). In addition, even if physical fitness is not maintained at a high level, there is a possibility that the risk for lifestyle-related diseases may be lower when physical fitness is temporarily high. Therefore, the question then becomes whether consistently high fitness levels are necessary or whether only transiently high fitness is sufficient to reduce the risk for lifestyle-related diseases.

To answer this question, we used data from a multipoint observation of CRF before the start of follow-up, with type 2 diabetes defined as the outcome of interest\(^{20}\). This
study included 7158 nondiabetic men 20–60 years of age, enrolled in 1986. CRF was measured annually from 1979 to 1986 using a submaximal exercise test on a cycle ergometer. Using this multiple CRF, the area under the curve (AUC) was calculated with regard to ground (AUC_G) for CRF measurements in individuals to evaluate the accumulated level of CRF over time (Fig. 1). Those with higher AUC_G for CRF were able to maintain their CRF at a higher level during the period. The AUC_G for CRF was standardized by dividing the total area by the years of measurement period, because the frequency of CRF measurement during the period differed among the participants. Moreover, to quantify the degree of a transient temporal increase in CRF during the period, the peak AUC (AUC_P) was calculated using the peak CRF value alone in individuals, as follows: \( \text{AUC}_P = \text{peak CRF} \times \text{measurement period} \). Then, differences (\( \Delta \text{AUC}_P \)) between the AUC_G and AUC_P were calculated. The \( \Delta \text{AUC}_P \) is zero when all CRF values during the measurement period are equal, whereas it is increased when the peak CRF value deviates from the average of CRF values excluding the peak CRF value. Therefore, we regard this parameter to represent the presence and size of a “spike” in CRF during the measurement period, and may be regarded as an index of transiently high CRF. Based on these two area indicators, participants were divided into quartiles, and the risk for developing type 2 diabetes mellitus was compared. Results revealed that a higher AUC_G for CRF was associated with the risk for type 2 diabetes, rather than the \( \Delta \text{AUC}_P \) for CRP, and that the risk for type 2 diabetes was approximately 30% lower in the fourth quartile of AUC_G for CRF than in the first quartile (Fig. 2). [Insert Figure 1 and 2]

In the above study, a consistently higher level of CRF over time was necessary to reduce the risk for type 2 diabetes; however, the question remained, “How fit must one stay?” In clinical settings, regardless of how often health care professionals encourage
clients to maintain CRF at a high level through regular physical activity to reduce the risk for type 2 diabetes, clients will naturally ask, “How high, exactly?” We believe that the reference values of CRF recommended in the “Physical Activity Reference for Health Promotion 2013”, published by the Ministry of Health, Labor and Welfare (21), could be a reasonable target value. Therefore, we examined the association between achievement of a “fit” (≥ reference value) CRF level for several years and the subsequent risk for type 2 diabetes (22). Using the AUCG described in the above study, we evaluated whether participants achieved the reference values for CRF during the measurement period of CRF from 1979 to 1986. First, the reference area (AUCref) for each was calculated based on the guideline for fit reference values during the same period (Fig. 3). After calculating the ratio of AUC to AUCref, the result was multiplied by 100 (AUCratio). It was assumed that those with AUCratios > 100 achieved CRF levels above the reference values during the measurement period. Participants with an AUCratio ≥ 100 were assigned to the FitAUC group, whereas those with AUCratio < 100 were assigned to the UnfitAUC group. In addition to the AUCratio for CRF, the initial CRF measurement during the measurement period was also categorized into two groups, > reference values (Fitinitial); or < reference values (Unfitinitial), in accordance with the guideline. Finally, a combination analysis was performed using these categories. Results revealed that, compared with the Fitinitial × FitAUC group, the adjusted hazard ratios and 95% confidence intervals for type 2 diabetes were higher in the Fitinitial × UnfitAUC (1.41, 0.99–2.00) and the Unfitinitial × UnfitAUC group (1.40, 1.08–1.83), whereas there was no difference in the Unfitinitial × FitAUC group (1.18, 0.81–1.70) (Fig. 4). From these findings, it became clear that the reference values for CRF could be a feasible target value and that maintaining a CRF level above the reference values for several years is important for the prevention of type 2 diabetes.
The AUC has merit considering the serial changes in CRF compared with the simple mean, which reflects accumulated exposure doses of CRF. However, the calculation of AUC may be difficult in clinical settings; as such, a simpler index is needed. To address this problem, the frequency of achieving the recommended CRF level was considered and examined whether the frequency of achieving the recommended CRF level was inversely associated with the risk for hypertension, a major lifestyle-related disease. Results demonstrated a clear inverse dose-response relationship (Fig. 5). Moreover, clear risk reduction was observed in the group that achieved the recommended CRF level three times over the 6-year period compared to the group that did not. These findings indicated that achieving recommended CRF only one or two times in 6 years was insufficient, thus supporting the importance of continuously maintaining high CRF for the prevention of hypertension.

CRF is not readily assessed in clinical and preclinical settings due to the complexity of the measurements. Physical fitness has components other than CRF, such as muscle strength, power, flexibility, and balance, each of which is not necessarily independent, and the measurements for these components are simple and quick. Therefore, testing these components can be useful markers of the risk for lifestyle-related diseases. We examined the association between performance in fitness tests and the risk for type 2 diabetes among 21,802 Japanese adults (20–92 years of age) who underwent annual health examinations. Because the measurements, including fitness tests and covariates, were performed at baseline and during the follow-up period, these variables were considered as time-varying variables. Results revealed that lower relative grip strength (an index of muscle strength relative to body weight) and single-leg balance with eyes closed were
associated with a higher risk for type 2 diabetes (Fig. 6). For relative grip strength, compared with the fourth quartile group, the odds ratios and corresponding 95% confidence intervals for the other groups ranged from 1.16 (0.90–1.49) to 1.56 (1.23–1.98). For single-leg balance, the odds ratios ranged from 1.03 (0.83–1.29) to 1.49 (1.13–1.71). Moreover, when dyslipidemia was defined as an outcome, grip strength was inversely associated with the risk for dyslipidemia25). [Insert Figure 6]

We have described studies investigating the cumulative influence of physical fitness on lifestyle-related disease(s) as an example of the subdivision of study objectives, a current trend in fitness epidemiology. Although our studies partly fill knowledge gaps in the current body of literature regarding fitness epidemiology, many unresolved challenges remain. For example, which is more important, the initial level or secular change in fitness for the prevention of lifestyle-related diseases?

Beyond fitness epidemiology

As mentioned, muscle strength has been adopted as an exposure variable in epidemiological studies. However, in recent years, muscle-strengthening activities for improving strength and muscular endurance, such as resistance/strength/weight training, have been captured as a behavioral modality and are attracting attention as a new exposure variable26). To our knowledge, the first epidemiological study to investigate muscle-strengthening activities was reported by Tanasescu et al. in 2002, who examined the association with coronary heart disease27). This new frontier, also called as muscle-strengthening activity epidemiology, has been active since 2010, because muscle-strengthening activities were included in the National Physical Activity Guideline in the United States for the first time in 200828). This guideline recommends that adults perform
muscle-strengthening activities \( \geq 2 \) days per week in addition to aerobic physical activities for additional benefits. Since the 2010s, an increasing number of studies have examined the validation against “two or more days per week.” In Japan, Kuwahara et al. reported that participants who performed strength training demonstrated a lower risk for type 2 diabetes than those who did not\(^29\). However, to our knowledge, this is the only report examining the longitudinal association between muscle-strengthening activities and health outcomes in a Japanese population. Nevertheless, many studies involving Japanese populations are anticipated in the future.
Conflict of Interests

The author has no conflicts of interest directly relevant to the content of this article.

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Author Contributions

HM drafted and edited the manuscript.


8) Crump C, Stattin P, Brooks JD, Stocks T, Sundquist J, Sieh W and Sundquist K.


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Figure legends

Figure 1  
Scheme for calculating the area under the curve for cardiorespiratory fitness (CRF)\(^{20}\)

The area under the curve for CRF with respect to ground (AUC\(_G\)) was calculated based on a formula to calculate the trapezoid area. After calculating the area between measurement values, the sum was calculated. Furthermore, the area based on the highest CRF value between 1979 and 1986 (AUC\(_P\)) was calculated, and differences between AUC\(_P\) and AUC\(_G\) were defined as \(\Delta\)AUC\(_P\).

Figure 2  
Hazard ratios of the incidence of type 2 diabetes according to quartiles of indices of consistently (●) and transiently (○) high cardiorespiratory fitness\(^{20}\)

Figure 3  
Scheme for calculating an index of “fit” cardiorespiratory fitness (CRF) level\(^{22}\)

The area under the curve with regard to ground (AUC\(_G\)) for CRF was calculated based on a formula to calculate the trapezoid area. After calculating the area between measured values, the sum was calculated. Furthermore, based on the guideline for fit reference value\(^{21}\), the reference area (AUC\(_\text{ref}\)) for each individual during the same period was calculated. Next, we calculated the ratio of AUC\(_G\) to AUC\(_\text{ref}\) (AUC\(_\text{ratio}\)) and the result was multiplied by 100 for intuitive interpretation.

Figure 4  
Hazard ratios for the incidence of type 2 diabetes according to the combined categories
of cardiorespiratory fitness\textsuperscript{22})

Figure 5

Hazard ratios of the incidence of hypertension according to the frequency of achieving
the recommended fitness level\textsuperscript{23)}

Figure 6

Odds ratios of the incidence of type 2 diabetes mellitus according to quartiles of relative
grip strength (left) and single-leg balance with closed eyes (right)\textsuperscript{24)}. 
Figure 1
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Figure 2

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- $AUC_G (P$ for trend $= 0.001)$
- $\Delta AUC_P (P$ for trend $= 0.09)$

HRs (95% CI)
CRF (estimated METs)

\[ \text{AUC}_{\text{ratio}} = \frac{\text{AUC}_G}{\text{AUC}_{\text{ref}}} \]

Figure 3
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Figure 4
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Figure 5
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Figure 6
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